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Romanian Journal of Military Medicine

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ORIGINAL ARTICLE

The Impact of Total Synovectomy on Blood Loss and Knee Function. A Prospective Randomized Study

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Abstract: *Synovial proliferation is a common intraoperative finding during total knee arthroplasty (TKA) and many studies have proposed synovectomy for the reduction of postoperative pain. We included 180 patients that were split into two groups, one which received a total synovectomy (TS) and the other with partial synovectomy (PS). We measured the amount of intra- and post-operative bleeding as well as perceived pain (using the Visual Analogue Scale) and knee function (using the Knee Society Knee Score) at 4 and 12 weeks. The blood loss during the surgical procedure was 367.77 ± 115.71 mL for TS, while the other group recorded 295.55 ± 106.17 mL ($p < 0.05$). Regarding postoperative bleeding, the TS group aspirated 533.77 ± 281.65 mL, which was significantly higher than the PS group (404.44 ± 211.55 mL, $p < 0.05$). No significant differences were recorded between the TS and PS groups regarding pain and knee function at 12 weeks. Total synovectomy demonstrated significantly higher blood loss and lower postoperative hemoglobin levels, even though knee function and pain level did not show improvements. We consider that the decision of performing synovectomy should rely on the clinical indication and, if conditions allow for it, a limited resection should be attempted*.

Keywords: *synovectomy; total knee arthroplasty; osteoarthritis; therapeutic method; pathophysiology; surgical technique; joint replacement*

INTRODUCTION

Osteoarthritis is common in the elderly population and is the most frequent condition affecting the synovial joints, especially the knee. Restricted range of motion, discomfort, and local pain are the main symptoms deriving from progressive cartilage deterioration of the articular surface of the knee joint [1,2]. A decisive role in cartilage degrading is played by chronic inflammation of the synovial membrane, known as synovitis [3,4]. Furthermore, residual synovial tissue can be associated with postoperative impingement and decreased range of motion [4,5].

Total knee arthroplasty (TKA) is regarded as a radical effective treatment for patients with end-stage knee osteoarthritis [6,7]. This intervention is typically reserved for individuals who experience severe, persistent pain and mobility issues that cannot be adequately addressed through more conservative interventions such as anti-inflammatory medications or physical therapy. In advanced osteoarthritis, patients experience continuous pain that is unresponsive to typical anti-inflammatory medications, and radiographic imaging shows a narrowing of the joint space and the formation of bony growths known as osteophytes [8].

During total knee arthroplasty, surgeons often identify synovial proliferation in patients with osteoarthritis or other inflammatory conditions [3,9-11]. This proliferation of the synovial membrane can contribute to inflammation and

cartilage degradation, leading to decreased joint function and increased pain. Surgical synovectomy involves excising the proliferated synovial membrane and was shown to improve joint function and reduce pain in patients with osteoarthritis [3,9,10]. However, while this procedure can be effective in reducing pain and inflammation, it also carries risks and potential complications that need to be carefully evaluated on a case-by-case basis.

Usually, the surgeon opts for the type of synovectomy depending on intraoperative assessment or personal preferences. Therefore, some surgeons perform total synovectomy as a mandatory step in the surgical technique of total knee arthroplasty, while other surgeons rather avoid performing total synovectomy because they consider it a substantial factor in postoperative bleeding [12-14]. Some researchers suggested that total synovectomy influences postoperative blood loss and operative time without being beneficial in terms of postoperative pain and knee function [12,15].

Decreasing postoperative discomfort and pain is essential to achieve a fast and efficient recovery and to improve the patient's living quality [16,17]. The primary objective of this study is to assess the influence of synovectomy performed during total knee arthroplasty for knee osteoarthritis on blood loss, postoperative pain, knee range of motion, and function.

MATERIALS AND METHODS

1. Study design

We conducted a prospective single-center randomized controlled trial between January 2022 and June 2022. A total of 180 patients were included and split into two even groups, one which received a total synovectomy (TS) and another with partial synovectomy during total knee replacement (PS). The randomization was performed by an independent doctor using sealed envelopes. The envelopes were stored in a box. The envelopes were drawn before surgery and contained instructions regarding the surgical technique.

The inclusion criteria were patients with late-stage knee arthritis. We excluded from our study patients with revisions and cases requiring a more significant constraint than a posterior stabilized TKA (constrained or hinged knee). We also excluded patients with acute coronary diseases, neurological diseases, infectious conditions, coagulation disorders, and a history of deep vein thrombosis or pulmonary embolism.

This paper was approved by the "Foisor" Orthopaedics Clinical Hospital Ethics Committee of Bucharest, Romania, approval number 6384/2021. Written informed consent was obtained from all patients included in this study. The procedures were conducted by international ethical standards and the 1964 Helsinki Declaration.

A radiological assessment was performed using plain X-rays, including an anteroposterior, lateral, and full weight-bearing lower limb, to develop proper preoperative digital planning.

2. Surgical Technique

All TKA procedures were performed according to a standard protocol by a single highly experienced orthopedic surgeon in our institution, specialized in TKA. The implant of choice was the Zimmer Biomet NexGen implant system. Preoperatively, 1 g of tranexamic acid was administered to all cases, and an additional 1 g after the procedure. All patients received spinal anesthetic with a femoral nerve block. A tourniquet was installed after three minutes of elevating the lower limb and was inflated up to 320 mm Hg before the incision and deflated after the implantation to perform hemostasis. We used a midvastus approach, an extramedullary tibial guide, an intramedullary femoral guide, and a measured resection technique. Wound closure was performed in a layered fashion and all patients received a deep drain. The drain was clamped for three hours and then released and removed 24 hours after surgery. The rehabilitation protocol was similar for both groups and began on the first day after surgery. Physical therapy was continued either at home or in a specialized clinic. All cases received Heparin for deep vein thrombosis prophylaxis for 30 days.

We recorded preoperative data, which included age, gender, knee range of motion, hemoglobin values, bleeding, and comorbidities. Knee function was measured using the Knee Society Knee Score (KSKS). The amount of bleeding was assessed by measuring the postoperative hemoglobin and bleeding during and after the surgery. Intraoperatively we measured the amount of blood aspiration by taking into account the amount of physiological serum used for lavage and the operative time. After the surgical procedure, we measured the amount of blood aspirated through the drains and hemoglobin. All complications were recorded throughout the study. For the functional evaluation, we measured flexion, extension, the Visual Analogue Scale (VAS), and KSKS score after 4 and 12 weeks. A blind independent observer evaluated all the measurements.

3. Outcome measures

The Visual Analogue Scale is a measure used to evaluate the patient's perspective of pain level. It may be dependent on the patient's mental status but is very frequently used to correlate with knee function evaluation [17,18].

The KSKS contains questions in 2 sections: knee score (pain, range of motion, stability) and function (walking distance,

ability to climb stairs, walking aids) [19]. Both measures were provided to patients for answering in the hospital and during follow-up visits.

4. Statistical analysis

All values were calculated as mean values ± standard deviation. The statistical analysis was developed using the Student t-test and Mann-Whitney U test for comparison between groups. A p-value lower than 0.05 was considered statistically significant. The data was analyzed for Windows OS using SPSS version 28.0 (SPSS Inc., Chicago, IL).

RESULTS

We recorded 180 cases split into two even groups. The patient characteristics are displayed in Table 1.

The blood loss measured during the surgical procedure was 367.77 ± 115.71 mL for the total synovectomy, while the second group recorded 295.55 ± 106.17 mL of blood loss ($p < 0.05$). Regarding postoperative bleeding, the TS group aspirated 533.77 ± 281.65 mL, which was significantly higher than the PS group, where we recorded an aspiration of 404.44 ± 211.55 mL (Table 2).

Table 1: Baseline characteristics of the study groups

	Total synovectomy	Partial synovectomy	p-value
Age (years)	70.41±7.25	70.8±7.23	0.71
Gender (M/F)	41/49	44/46	0.77
Preoperative hemoglobin (g/dL)	13.24±1.22	13.22±1.18	0.90

Table 2: Postoperative parameters of the study groups

	Total synovectomy	Partial synovectomy	p-value
Intraoperative bleeding (mL)	367.77±115.71	295.55±106.17	<0.05
Postoperative bleeding (mL)	533.77±281.65	404.44±211.55	<0.05
Postoperative hemoglobin (g/dL)	11.43±1.26	11.88±1.22	<0.05
VAS[1] score (4 weeks)	3.39±1.50	3.79±1.32	0.058
VAS score (12 weeks)	1.3±1.01	1.41±0.89	0.43
KSKS[2] score (4 weeks)	82.28±4.09	82.42±4.46	0.83
KSKS score (12 weeks)	87.9±3.7	88.33±4.11	0.47
Operating Room time (min.)	96.5±7.93	92.2±6.37	<0.05

[1] VAS=Visual Analogue Scale; [2] KSKS=Knee Society Knee Score

The mean preoperative hemoglobin was 13.24 ± 1.22 g/dL for the TS group and 13.22 ± 1.18 g/dL for the PS group ($p = 0.90$). Postoperatively, a statistically significant decrease was recorded in the two groups, the hemoglobin dropping to 11.43 ± 1.26 g/dL and 11.88 ± 1.22 g/dL, respectively, ($p < 0.05$). However, after four weeks, the VAS score was 3.39 ± 1.50 in the TS group and 3.79 ± 1.32 in the PS group, while KSKS was 82.28 ± 4.09 and 82.42 ± 4.46, respectively. Both scores' differences between groups were not significant. At the three months follow-up, both parameters showed improvements for both groups. VAS score was 1.3 ± 1.01 for the TS group, while PS patients had a score of 1.41 ± 0.89. ($p = 0.43$) KSKS score showed no statistically significant differences after three months, the results being 87.9 ± 3.7 and 88.33 ± 4.11, respectively ($p = 0.47$). However, we recorded significant differences regarding the operative room time between groups: 96.5 ± 7.93 minutes for the TS group and 92.2 ± 6.37 minutes for the PS group, respectively ($p < 0.05$).

Regarding complications, we recorded 7 cases of deep vein thrombosis in the total synovectomy group and 5 cases in the partial synovectomy group.

We recorded wound complications in three cases in the first group and two patients in the second group. Also, we noticed hemarthrosis following drain removal in 20 cases that underwent total synovectomy and 5 cases with partial synovectomy.

DISCUSSION

The synovial tissue is regarded as a critical component in the locomotor function [20,21]. The synovial tissue of the knee joint plays multiple roles, including the secretion of synovial fluid that lubricates the joint, providing nutrients to the articular cartilage, protection against infection, and removal of waste products from the joint. The aforementioned functions are responsible for the maintenance of the health and proper functioning of the knee joint. On the other hand, progressive joint degeneration, which leads to osteoarthritis, is caused by the involvement of bone, cartilage, and synovial pathological processes [21,22]. For this reason, synovectomy is performed to relieve pain or to attempt the prevention of cartilage and/or

bone destruction and to improve knee function [23,24].

During a total knee arthroplasty, total synovectomy may be performed for different reasons. One reason is to remove any inflamed or diseased synovial tissue that may be present in the joint, with the aim of improving joint function and reducing pain and inflammation. Another reason is to prevent the formation of a pseudo capsule, a thick layer of scar tissue that can form around the artificial joint and cause complications. However, total synovectomy may also have drawbacks, such as an increased risk of infection and reduced lubrication and nutrition of the articular cartilage [21,22]. The decision to perform a total synovectomy during a total knee arthroplasty should be taken individually, for each patient, by weighing the potential benefits and risks. Furthermore, proper planning of the procedure is essential to ensure shorter operating times and faster recovery; this includes digital radiological planning, choosing the ideal implant type and model, and controlling the patient risk factors [25-27].

Our study aimed to evaluate the influence of synovectomy on postoperative results and blood loss following total knee replacement. The intraoperative and postoperative blood loss was found to be significantly higher after total synovectomy compared to the partial synovectomy group. We found variable results regarding average blood loss in the literature, which ranged between 300 and 2500 mL [12,28-30]. This variability may be explained by the different surgical techniques, thromboprophylaxis treatments, or implant types that were applied. In our paper, the total synovectomy group had a blood loss from drains of 533.77 ± 281.65 mL for the total synovectomy group compared to the second group, which had 404.44 ± 211.55 mL blood loss. We consider this to be one of the main reasons behind the preference of some surgeons to avoid total synovectomy.

Our study also revealed a significantly lower postoperative hemoglobin level after synovectomy. This result was also recorded in other papers [12,21,31]. However, some studies concluded that even though the bleeding rates are higher, the blood transfusion threshold is not reached when total synovectomy is performed, therefore the two surgical techniques do not yield statistically significant differences in this regard [15,21].

Another significant result of this study was that total synovectomy demonstrated some postoperative improvements but these were not statistically significant compared to the other group and did not show any differences regarding pain relief, despite the considerable blood loss difference. It is well known that the synovium, as well as other articular structures like muscles, joint capsules, or ligaments, is well-innervated and could be a source of pain in osteoarthritis [32,33]. Even though synovectomy reduces knee pain, especially in cases with pathological synovial tissues, the VAS score in our study did not show any significant differences during the follow-ups. Also, the KSKS score showed no significant differences after 4 weeks or after 12 weeks. This result is also reported by other authors who also recorded increased concealed bleeding, higher drainage, and longer operative time in patients that underwent total synovectomy [12]. Moreover, similar studies evaluating the quality of life and complications recorded no significant improvements regarding these parameters [34].

Literature data have indicated that total synovectomy during total knee arthroplasty may be linked to an increased incidence of certain complications such as deep vein thrombosis, hemarthrosis, and wound complications [12,21,33-37]. However, it is essential to note that the available data is currently limited. Therefore, additional investigations with a larger sample size are required to establish a more robust statistical correlation on this subject. Despite this observation, it should be noted that individual patient characteristics and other factors may also contribute to the occurrence of these complications.

One major limitation of our study is that it was conducted in a single center, which may limit the generalization of our results to other study populations. Additionally, we did not evaluate hematocrit levels or blood transfusion requirements, which are important factors that could reveal further associations between total synovectomy and blood loss. Furthermore, we acknowledge that more extended follow-up periods could be beneficial in the thorough evaluation of the functional outcomes and risk of synovial recurrences associated with total synovectomy during total knee arthroplasty. Additionally, it is important to note that our study did not assess the risk of other potential complications that could arise from this procedure. Therefore, while our study provides important insights into the potential risks and benefits of total synovectomy during total knee arthroplasty, additional research with a larger sample size and more extended follow-up periods are needed to fully understand the implications of this procedure for patients undergoing knee arthroplasty.

CONCLUSIONS

Patients with total synovectomy associated with total knee arthroplasty experienced a notably more significant amount of blood loss and lower postoperative hemoglobin levels than the control group. However, no statistically significant differences were observed between the two groups in terms of knee function and pain level. Further multicenter studies with longer follow-up times are required to more comprehensively assess the potential complication rate and risk of synovial

recurrence associated with total synovectomy during total knee arthroplasty. Ultimately, more comprehensive research is required to determine the optimal approach to synovectomy and to provide the most beneficial outcomes for patients undergoing total knee arthroplasty.

Conflicts of interest and sources of funding

The authors declare no conflict of interest. This research received no external funding.

Authors' contribution

M.-A.P. and L.L.P. planned the clinical study and contributed to the concept and design of the study. M.E.G., D.C.C., and A.L. contributed to the data analysis and interpretation as well as to the translation and the critical revision of important intellectual content. C.S. and R.C. contributed to the writing of the manuscript and performed revision, language, and textual editing of the final version. All authors contributed to the original draft preparation of the manuscript. All authors have read and agreed to the published version of the manuscript.

Patient consent for publication

Informed consent was obtained from all subjects involved in the study.

Ethics approval and consent to participate

All procedures performed in this paper were by the 1964 Helsinki Declaration and its later amendments or comparable ethical standards and according to the national ethical standards. The study received approval from the "Foisor" Orthopaedics Clinical Hospital Ethics Committee of Bucharest, Romania, approval number 6384/2021 (date of approval 10th of December 2021). Informed consent was obtained from all individual participants included in the study.

References:

1. Vargas, E.S.N.C.O.; Dos Anjos, R.L.; Santana, M.M.C.; Battistella, L.R.; Marcon Alfieri, F. Discordance between radiographic findings, pain, and superficial temperature in knee osteoarthritis. Reumatologia 2020, 58, 375-380, doi:10.5114/reum.2020.102002.

2. Naoum, S. Should Hoffa's fat pad be resected during total knee arthroplasty? A review of literature. Romanian Journal of Military Medicine, 2022, 125(2): 196-201, doi: 10.55453/rjmm.2022.125.2.3.

3. Altman, R.D.; Gray, R. Diagnostic and therapeutic uses of the arthroscope in rheumatoid arthritis and osteoarthritis. The American Journal of Medicine 1983, 75, 50-55, doi:10.1016/0002-9343(83)90328-5.

4. Gonzalez, M.H.; Mekhail, A.O. The failed total knee arthroplasty: evaluation and etiology. Journal of the American Academy of Orthopaedic Surgeons 2004, 12, 436-446, doi:10.5435/00124635-200411000-00008.

5. Hunter, D.J.; Guermazi, A.; Roemer, F.; Zhang, Y.; Neogi, T. Structural correlates of pain in joints with osteoarthritis. Osteoarthritis and Cartilage 2013, 21, 1170-1178, doi:10.1016/j.joca.2013.05.017.

6. Choo, K.J.; Austin, M.; Parvizi, J. Irrigation and Debridement, Modular Exchange, and Implant Retention for Acute Periprosthetic Infection After Total Knee Arthroplasty. JBJS Essent Surg Tech 2019, 9, doi:10.2106/jbjs.St.19.00019.

7. Cristea, S.; Predescu, V.; Dragosloveanu, S.; Cuculici, S.; Marandici, N. Surgical Approaches for Total Knee Arthroplasty; 2016; 10.5772/62001pp. 25-47.

8. Fibel, K.H.; Hillstrom, H.J.; Halpern, B.C. State-of-the-Art management of knee osteoarthritis. World J Clin Cases 2015, 3, 89-101, doi:10.12998/wjcc.v3.i2.89.

9. Matsui, N.; Moriya, H.; Kitahara, H. The use of arthroscopy for follow-up in knee joint surgery. Orthopedic Clinics of North America 1979, 10, 697-708.

10. Smiley, P.; Wasilewski, S.A. Arthroscopic synovectomy. Arthroscopy 1990, 6, 18-23, doi:10.1016/0749-8063(90)90091-q.

11. Krasnokutsky, S.; Belitskaya-Lévy, I.; Bencardino, J.; Samuels, J.; Attur, M.; Regatte, R.; Rosenthal, P.; Greenberg, J.; Schweitzer, M.; Abramson, S.B., et al. Quantitative magnetic resonance imaging evidence of synovial proliferation is associated with radiographic severity of knee osteoarthritis. Arthritis and Rheumatism 2011, 63, 2983-2991, doi:10.1002/art.30471.

12. Zhaoning, X.; Xu, Y.; Shaoqi, T.; Baiqiang, H.; Kang, S. The effect of synovectomy on bleeding and clinical outcomes for total knee replacement. Bone Joint J 2013, 95-b, 1197-1200, doi:10.1302/0301-620x.95b9.31253.

13. Kim, J.L.; Park, J.H.; Han, S.B.; Cho, I.Y.; Jang, K.M. Allogeneic Blood Transfusion Is a Significant Risk Factor for Surgical-Site Infection Following Total Hip and Knee Arthroplasty: A Meta-Analysis. Journal of Arthroplasty 2017, 32, 320-325, doi:10.1016/j.arth.2016.08.026.

14. Deirmengian, C.A.; Lonner, J.H. What's new in adult reconstructive knee surgery. Journal of Bone and Joint Surgery (American Volume) 2009, 91, 3008-3018, doi:10.2106/jbjs.I.01062.

15. Ausó-Pérez, J.R.; Rodríguez-Blanes, G.M. Influence of synovectomy on blood loss and need for transfusion in standard total knee replacement. European Journal of Orthopaedic Surgery & Traumatology 2018, 28, 1151-1156, doi:10.1007/s00590-018-2160-8.

16. Kooner, S.S.; Clark, M. The Effect of Synovectomy in Total Knee Arthroplasty for Primary Osteoarthritis: A Meta-Analysis. Journal of Knee Surgery 2017, 30, 289-296, doi:10.1055/s-0036-1584560.

17. Stoica, C.I.; Nedelea, G.; Cotor, D.C.; Gherghe, M.; Georgescu, D.E.; Dragosloveanu, C.; Dragosloveanu, S. The Outcome of Total Knee Arthroplasty for Patients with Psychiatric Disorders: A Single-Center Retrospective Study. Medicina (Kaunas, Lithuania) 2022, 58, doi:10.3390/medicina58091277.

18. Spinarelli, A.; Pesce, V.; Campagna, C.; Maccagnano, G.; Moretti, B. Painful knee prosthesis: CT scan to assess patellar angle and implant malrotation. Muscles Ligaments Tendons J 2016, 6, 461-466, doi:10.11138/mltj/2016.6.4.461.

19. Goh, G.S.; Bin Abd Razak, H.R.; Tay, D.K.; Lo, N.N.; Yeo, S.J. Early post-operative Oxford knee score and knee society score predict patient satisfaction 2 years after total knee arthroplasty. Archives of Orthopaedic and Trauma Surgery 2021, 141, 129-137, doi:10.1007/s00402-020-03612-2.

20. O'Connell, J.X. Pathology of the synovium. American Journal of Clinical Pathology 2000, 114, 773-784, doi:10.1309/lww3-5xk0-fkg9-hdrk.

21. Kilicarslan, K.; Yalcin, N.; Cicek, H.; Dogramaci, Y.; Ugurlu, M.; Ozkan, H.; Yildirim, H. The effect of total synovectomy in total knee arthroplasty: a prospective randomized controlled study. Knee Surgery, Sports Traumatology, Arthroscopy 2011, 19, 932-935, doi:10.1007/s00167-010-1270-6.

22. Attur, M.; Samuels, J.; Krasnokutsky, S.; Abramson, S.B. Targeting the synovial tissue for treating osteoarthritis (OA): where is the evidence? Best Practice & Research: Clinical Rheumatology 2010, 24, 71-79, doi:10.1016/j.berh.2009.08.011.

23. Kubacki, J.; Kokosz, M.; Grygorowicz, M.; Adamczyk-Bujniewicz, H. The value of synovectomy of the knee in the treatment of rheumatoid arthritis. Ortopedia, Traumatologia, Rehabilitacja 2006, 8, 99-105.

24. Masłoń, A.; Witoński, D.; Pieszyński, I.; Grzegorzewski, A.; Synder, M. Early clinical results of open and arthroscopic synovectomy in knee inflammation. Ortopedia, Traumatologia, Rehabilitacja 2007, 9, 520-526.

25. Dragosloveanu, S.; Petre, M.-A.; Gherghe, M.E.; Nedelea, D.-G.; Scheau, C.; Cergan, R. Overall Accuracy of Radiological Digital Planning for Total Hip Arthroplasty in a Specialized Orthopaedics Hospital. Journal of clinical medicine 2023, 12, 4503, doi:10.3390/jcm12134503.

26. Dimitriu, A.L.; Ene, D.; Popescu, E.; Panaitescu, C.; Ene, R. Biotribology of the Total Hip Replacement – Review of the Current Bearing Surfaces. Romanian Journal of Military Medicine, 2023, 126(3): 306-311, https://doi.org/10.55453/rjmm.2023.126.3.10.

27. Rullán, P.J.; Zhou, G.; Emara, A.K.; Klika, A.K.; Koroukian, S.; Piuzzi, N.S. Understanding rates, risk factors, and complications associated with manipulation under anesthesia after total knee arthroplasty (TKA): An analysis of 100,613 TKAs. Knee 2022, 38, 170-177, doi:10.1016/j.knee.2022.08.009.

28. Pan, X.; Zhang, X.; Liu, Z.; Wen, H.; Mao, X. Treatment for chronic synovitis of knee: arthroscopic or open synovectomy. Rheumatology International 2012, 32, 1733-1736, doi:10.1007/s00296-011-1901-3.

29. Tanavalee, A.; Honsawek, S.; Rojpornpradit, T.; Sakdinakiattikoon, M.; Ngarmukos, S. Inflammation related to synovectomy during total knee replacement in patients with primary osteoarthritis: a prospective, randomised study. Journal of Bone and Joint Surgery (British Volume) 2011, 93, 1065-1070, doi:10.1302/0301-620x.93b8.26719.

30. Gross, J.B. Estimating allowable blood loss: corrected for dilution. Anesthesiology 1983, 58, 277-280, doi:10.1097/00000542-198303000-00016.

31. Dragosloveanu, Ş.; Dragosloveanu, C.D.M.; Stanca, H.T.; Cotor, D.C.; Dragosloveanu, C.I.; Stoica, C.I. A new perspective towards failure of gamma nail systems. Experimental and Therapeutic Medicine 2020, 20, 216, doi:10.3892/etm.2020.9346.

32. Dragosloveanu, S.; Popov, V.M.; Cotor, D.C.; Dragosloveanu, C.; Stoica, C.I. Percutaneous Chevron Osteotomy: A Prospective Randomized Controlled Trial. Medicina (Kaunas, Lithuania) 2022, 58, doi:10.3390/medicina58030359.

33. Hunter, D.J. Imaging insights on the epidemiology and pathophysiology of osteoarthritis. Rheumatic Diseases Clinics of North America 2009, 35, 447-463, doi:10.1016/j.rdc.2009.08.001.

34. Bernal-Fortich, L.D.; Aguilar, C.A.; Rivera-Villa, A.H.; Galindo-Avalos, J.; Aguilera-Martínez, P.; Torres-González, R.; Colin-Vázquez, A. A prospective randomized trial of total synovectomy versus limited synovectomy in primary total knee arthroplasty: evaluation of bleeding, postoperative pain, and quality of life with SF-12 v2. European Journal of Orthopaedic Surgery & Traumatology 2018, 28, 701-706, doi:10.1007/s00590-018-2139-5.

35. Creţu, B.; Cirstoiu, C.; Serban, B.A.; Iordache, S.-A.; Cursaru, A.; Costache, M.; Cristea, Ş. Inadequate perioperative control of modifiable risk factors in total knee arthroplasty and implications on functional results. Romanian Journal of Military Medicine, 2022, 125(1): 26-30, https://doi.org/10.55453/rjmm.2022.125.1.4.

36. Bawa, H.; Weick, J.W.; Dirschl, D.R.; Luu, H.H. Trends in Deep Vein Thrombosis Prophylaxis and Deep Vein Thrombosis Rates After Total Hip and Knee Arthroplasty. Journal of the American Academy of Orthopaedic Surgeons 2018, 26, 698-705, doi:10.5435/jaaos-d-17-00235.

37. Healy, W.L.; Della Valle, C.J.; Iorio, R.; Berend, K.R.; Cushner, F.D.; Dalury, D.F.; Lonner, J.H. Complications of total knee arthroplasty: standardized list and definitions of the Knee Society. Clinical Orthopaedics and Related Research 2013, 471, 215-220, doi:10.1007/s11999-012-2489-y

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ORIGINAL ARTICLE

Evaluation of Serum Magnesium Levels in Patients with Hypertension: A Case-control Study

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Abstract: *There are conflicting data on the effects of magnesium on hypertension in the literature. Therefore we aim this study to investigate whether there is a relationship between serum magnesium levels and hypertension in newly diagnosed. This is a case-control study. The patients were selected from the records of patients who applied to the family medicine outpatient clinic between June 2016 and May 2017. A total of 276 patients, 68 patients with newly diagnosed hypertension in the case group and 208 patients without any disease in the control group were included in the study. Binary logistic regression analysis was performed between the case and control groups. The odds ratio for magnesium was 0.1 (0.012-0.810). When the value of the magnesium variable increases by 1mg/dl, the risk of hypertension decreases by 90%. However, in the presence of magnesium as an independent variable, the predictability rate of our model was expected to increase but decreased. The odds ratio for age was 1.14 (1.092-1.186). The odds ratio for exercise was 0.18 (0.03-0.99). The odds ratio for glucose was 1.03 (1.001-1.065). In our study that magnesium deficiency causes an increased risk of hypertension, the predictability rate of our model was expected to increase instead of decrease. These findings show that a cause-effect approach or incidental association cannot explain the relationship between magnesium and hypertension*.

Keywords: *hypertension; magnesium; age; exercise; glucose*

INTRODUCTION

The prevalence of hypertension continues to increase globally [1]. The prevalence of hypertension in the adult population in the world is 31% [2]. For over forty years, the causes of most hypertensive diseases have been unknown and are defined as primary or essential hypertension. Secondary causes are accepted as 5-10% [3].

Recently, risk factors such as age, sex, race, family history, genetic composition, obesity, excessive salt intake, inactivity or lack of exercise, high-fat diet, tobacco use, and alcohol consumption have been proven to lead to the development of hypertension [4].

Magnesium (Mg) can be found in the fourth sequence in the human body and the second after potassium in the intracellular area [5]. Magnesium is an essential cation playing a crucial role in many physiological functions. It is critical in energy-requiring metabolic processes, protein synthesis, membrane integrity, nervous tissue conduction, neuro-muscular excitability, muscle contraction, and hormone secretion [6]. Given the role of magnesium in calcium and potassium transport, cell signaling, energy metabolism, genome stability, DNA repair, and replication, it should be expected that hypomagnesemia is associated with many diseases, including neurological disorders, osteoporosis, diabetes, coronary heart disease, and hypertension [7].

Magnesium levels were lower in white hypertensives than in normotensives, while no significant difference was found in black hypertensives compared to normotensives [8]. It has been shown that those with essential hypertension have a significantly higher intra-erythrocytic magnesium level than healthy individuals [9]. A systemic review and meta-analysis study suggested no relationship between serum magnesium and hypertension but that dietary magnesium supplementation reduces blood pressure [10]. Magnesium deficiency was found to be responsible for calcium and magnesium disorders in those with pregnancy-induced hypertension, and magnesium sulfate therapy was effective in

these patients [11]. In a meta-analysis of twelve studies, a reduction in diastolic blood pressure was observed, while a decrease in systolic blood pressure was not observed [12]. Again, a meta-analysis of 20 studies found a reduction in systolic blood pressure while no change in diastolic blood pressure [13]. A meta-analysis of 22 studies noted a reduction in both systolic and diastolic blood pressure [14].

The fact that there are conflicting data on the effects of magnesium on hypertension in the literature shows a need for research on this subject. For this purpose, we wanted to evaluate magnesium levels in patients with newly diagnosed hypertension. This study aims to investigate whether there is a relationship between serum magnesium levels and hypertension.

MATERIALS AND METHODS

Study Design

This study is a case-control study. The sample size was determined for logistic regression analysis, considering the number of seven independent variables, such as age, gender, body mass index (BMI), smoking, alcohol consumption, exercise status, and magnesium. For each group, using the power analysis method, the minimum sample size of at least 48 which is needed to detect a significant difference when taken into account at 0.05 type-I error (Alpha), 0.35 effect size, 0,80 power (1-beta).

Population selection

The patients included in the study were selected from those who applied to the family medicine outpatient clinic between June 2016 and May 2017 from the hospital information system and patient records. Sixty-eight people with hypertension constituted the case group. Two hundred-eight people without hypertension formed the control group. The control group was selected considering demographic characteristics such as age and gender.

Inclusion and exclusion criteria

Among the patients tested for magnesium at the time of admission, patients with hypertension newly diagnosed were included in the case group, and those with no chronic disease and no medication were included in the control group. The study did not include those with any illness and drug use before the application, those with a previous hypertension diagnosis and treatment, and those without magnesium checked at the time of application.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics (V25). A P-value below 0.05 was considered statistically significant. In the data expression, categorical data, numbers and percentages, and numerical data were expressed with averages and standard deviation. The distribution of demographic data was analyzed by frequency tests, comparison of categorical data by chi-square test, and comparison of numerical data by independent sample t-test. The stepwise enter model was used in the binary logistic regression test to evaluate the effect of magnesium on hypertension. Skewness and kurtosis analyses were used to conform the data to the normal distribution.

Ethical Considerations

Ethical approval was obtained from the İstanbul Training Research Hospital Clinical Research Ethics Committee (Decision no. 14.10.2022, 318).

RESULTS

A total of 276 people, including 68 cases and 208 control groups, were included in the study. There was no found difference between those with hypertension and those without it in terms of sex, smoking, and alcohol consumption. However, the proportion of those without exercise was found to be lower in the hypertension group (Table 1).

Table 1: Comparison of the case and control groups in terms of gender, smoking, alcohol consumption, and exercise status

Characteristics of participants		Hypertension N (%)			
		No	Yes	Total	p
Gender	Women	149 (71.6)	52 (76.5)	201 (72.8)	0.530
	Men	59 (28.4)	16 (23.5)	75 (27.2)	
Smoking	No	167 (80.3)	58 (85.3)	225 (81.5)	0.472
	Yes	41 (19.7)	10 (14.7)	51 (18.5)	
Alcohol	No	204 (98.1)	68 (100.0)	272 (98.6)	0.575
	Yes	4 (1.9)	0 (0.0)	4 (1.4)	
Exercise	No	168 (80.8)	66 (97.1)	234 (84.8)	< 0.001*
	Yes	40 (19.2)	2 (2.9)	42 (15.2)	

Chi-Square Tests: The statistically significant difference was accepted as p < 0.05

The average age and BMI were found to be higher in the group with hypertension. Additionally, glucose, total cholesterol, triglycerides, and LDL- cholesterol (LDL-C) were found to be increased in the case group. Magnesium levels were found to be higher in the control group than in the case group (Table 2).

Table 2: Comparison of case and control groups in terms of age, body mass, and biochemical parameters

	Hypertension			
	No	Yes		
	Mean ± SD		t.	p
Glucose (mg/dl)	95.25 ± 11.04	107.79 ± 15.96	-6.02	< 0.001*
Cholesterol (mg/dl)	206.55 ± 44.32	229.43 ± 35.59	-3.86	< 0.001*
Triglycerides (mg/dl)	111.96 ± 61.58	154.07 ± 60.27	-4.92	< 0.001*
HDL-C (mg/dl)	54.55 ± 12.66	52.68 ± 7.40	1.49	0.137
LDL-C (mg/dl)	129.35 ± 37.07	143.49 ± 29.66	-3.19	0.002*
Calcium (mg/dl)	9.47 ± 0.46	9.54 ± 0.43	-1.11	0.266
Magnesium (mg/dl)	1.99 ± 0.19	1.92 ± 0.15	2.82	0.005*
Sodium (mmol/L)	139.14 ± 1.99	145.24 ± 32.97	-1.52	0.133
TSH (mIU/L)	1.91 ± 1.29	1.90 ± 1.20	0.06	0.950
Vitamin B12 (ng/L)	231.69 ± 127.26	207.32 ± 90.38	1.73	0.085
Vitamin D (ng/ml)	20.08 ± 10.69	19.32 ± 9.60	0.52	0.602
Age (years)	39.69 ± 12.80	59.71 ± 11.65	-11.42	< 0.001*
BMI	25.83 ± 4.48	29.50 ± 6.25	-4.47	< 0.001*

*SD: Standard Deviation; BMI: Body Mass Index; *Independent sample t-test is significant at the 0.05 level (2-tailed)*

Binary logistic regression analysis was performed by considering the different parameters between the case and control groups. In addition to the magnesium, age, exercise, BMI, glucose, triglyceride, and LDL-C variables which were different between the case and control groups, gender and sodium variables were also included in the analysis according to the literature [4]. Total cholesterol was not included in the study because it is affected by LDL-C and triglyceride.

In the analysis in which only magnesium as an independent variable was added, the model is insignificant because the Cox-Snell R2 and Nagelkerke R2 values are smaller than the 0.2 value. However, the model is significant when other independent variables are added. Except for the step in which triglyceride was added, the model's goodness of fit is acceptable since the p-values are bigger than 0.05 in the Hosmer-Lemeshow test. Changes in -2 Log Likelihood values (Chi-square, $p < 0.05$) are significant in magnesium, age, exercise, and glucose steps.

These results show that the logistic regression analysis is generally valid (Table 3).

Table 3: Distribution of data showing the validity of the logistic regression analysis

Metod=Enter: stepwise	-2 Log Likelihood	Chi-square	P	Cox and Snell R Square	Nagelkerke R Square	Hosmer and Lemeshow Test	Predicted percentage
Beginning	308.192						75.4
+ Magnesium	299.999	8.193	0.004*	0.029	0.043	0.150	74.6
+ Age	194.958	105.041	< 0.001*	0.337	0.500	0.493	82.6
+ Exercise	186.608	8.350	0.004*	0.356	0.530	0.642	81.9
+ Gender	186.341	0.267	0.606	0.357	0.531	0.592	81.9
+ BMI	183.822	2.519	0.112	0.363	0.539	0.695	83.3
+ Glucose	179.281	4.541	0.033*	0.373	0.555	0.398	84.1
+ Triglycerides	179.265	0.015	0.901	0.373	0.555	0.044*	83.3
+ LDL-C	178.064	1.201	0.273	0.376	0.559	0.744	82.6
+ Sodium	178.059	0.005	0.944	0.376	0.559	0.746	82.6

**The statistically significant difference was accepted as $p < 0.05$*

The odds ratio for magnesium was found to be 0.1 (0.012-0.810). When the value of the magnesium variable increases by 1mg/dl, the risk of hypertension decreases by 90% (Table 4). However, in the presence of magnesium as an independent variable, the predictability rate of our model was expected to increase but decreased (Table 3). The odds ratio for age was found to be 1.14 (1.092-1.186). When the value of the age variable increases by one unit, the risk of hypertension increases by 1.14 times. The odds ratio for exercise was found to be 0.18 (0.03-0.99). When the reference group is taken as those with non-exercise, the risk of hypertension was found to be 82% less in those with exercise. The odds ratio for glucose was found to be 1.03 (1.001-1.065). When the value of the glucose variable increases by 1 mg/dl, the risk of hypertension increases by 1.03 times (Table 4).between vitamin D and total cholesterol and LDL-C in the young age group. However, serum vitamin D had no significant correlation with serum glucose, triglyceride, HDL-C, calcium, magnesium, sodium, TSH levels, and BMI scores (Table 4).

Table 4: Logistic regression analysis showing the relationship between hypertension and variables of magnesium, age, exercise, gender, BMI, glucose, triglyceride, LDL-C, and sodium

Hypertension[a]	B	SE	Wald	P	Risk (Odds) coefficient	95% C.I.for (Exp B)	
						Lower	Upper
Magnesium (mg/dl)	-2.325	1.079	4.645	0.031*	0.1	0.012	0.810
Age (years)	0.129	0.021	37.532	< 0.001*	1.14	1.092	1.186
Exercise (1: -/+)	-1.723	0.874	3.882	0.049*	0.18	0.032	0.991
Gender (1: Women/Men)	-0.628	0.456	1.898	0.168	0.53	0.219	1.304
BMI	0.031	0.040	0.621	0.431	1.03	0.955	1.115
Glucose (mg/dl)	0.032	0.016	4.140	0.042*	1.03	1.001	1.065
Triglycerides (mg/dl)	0.001	0.003	0.019	0.890	1.00	0.994	1.007
LDL-C (mg/dl)	-0.006	0.006	1.172	0.279	0.99	0.983	1.005
Sodium (mmol/L)	0.002	0.034	1.897	0.947	1.00	0.938	1.071

*[a]Dependent Variable: Hypertension; BMI: Body Mass Index; B: Estimated Coefficients; CI: Confidence Interval; SE: Standard Error; *Logistic regression analysis is significant at the p < 0.05 level (2-tailed)*

DISCUSSION

The fact that the age and BMI values, glucose, total cholesterol, triglycerides, and LDL-C levels are high in those with hypertension and the low rate of exercisers shows that the study groups are compatible with the general population.

In our study, magnesium levels were lower in those with hypertension. When the value of the magnesium variable increases by 1mg/dl, the risk of hypertension decreases by 90%. However, in the presence of magnesium as an independent variable, the predictability rate of our model for hypertensive patients decreased, while it was expected to increase [2]. In two meta-analysis studies involving seven and 11 studies, it has been suggested that magnesium supplementation provides a significant, albeit small, decrease in blood pressure [15,16]. In a meta-analysis in which thirty-four studies were evaluated, it was found that there was a decrease in both systolic and diastolic blood pressure [17]. A recent meta-analysis study claimed that oral magnesium supplementation does not affect blood pressure in normotensives and controlled hypertensives but reduces blood pressure in uncontrolled hypertensives [18]. In addition, there was no difference in magnesium levels between those with hypertensive crisis and the control group [19]. However, in light of these contradictory findings, considering that the number of participants in meta-analysis studies is high, it is a point that should not be overlooked that statistical significance will be high, even if there is no significance in reality.

In our study, it was found that when the value of the age variable increased by one unit, the risk of hypertension increased by 1.14 times. In our working model, the probability of predicting hypertensive patients in the presence of magnesium and age is relatively high. This result indicates that the age variable is an important risk factor. In the literature, age is recognized as a risk factor for hypertension [4]. Studies have been reported showing that magnesium decreases with age [20,21]. It has been suggested that this relationship may be related to decreased absorption with age and slower kidney reabsorption [22,23]. In addition, recent reports indicate that many Americans, especially older people, do not consume the recommended daily amount of magnesium [24]. In countries with high incomes, the rate of hypertension is lower than in poor countries [2]. Again, it is stated that an unhealthy diet causes hypertension [25]. All these findings and literature information suggest that the relationship between magnesium and hypertension may be an incidental association.

Our study found that the risk of hypertension decreased by 82% in those who exercised. In the literature, it is accepted that inactivity or lack of exercise is a risk factor for

hypertension [4]. It is stated that regular exercise causes a decrease in blood pressure of 5 mmHg [26]. In addition, emphasis has been placed on the curative effect of both aerobic and moderate-weight exercise on hypertension [27]. Aerobic exercise is assumed to positively affect hypertension by reducing oxidative stress [28]. A recent meta-analysis indicates that aerobic exercise is an effective adjunctive treatment method for lowering ambulatory blood pressure in hypertension patients receiving drug therapy [29].

Our study found no relationship between body mass index and hypertension. However, when the value of the glucose variable increased by one unit, the risk of hypertension increased 1.03 times, albeit very slightly. Obesity is accepted as a risk factor for hypertension in the literature [4,30]. Mechanisms of obesity causing hypertension are explained by the activation of the sympathetic nervous system activated by hormones such as leptin, insulin, melanocortin, and the activation of the renin-angiotensinogen system due to oxidative effects caused by proinflammatory cytokines released as a result of dyslipidemia [31]. Many pathophysiological mechanisms explain the relationship between diabetes and hypertension. These mechanisms are mainly hyperinsulinemia-mediated sympathetic activation, hyperglycemia-induced sodium-fluid retention, the stimulatory effect of hyperglycemia on the renin-angiotensin-aldosterone system, and increased insulin resistance as a result of oxidative stress [32,33].

An increased risk of type-2 diabetes and increased LDL-C levels were found in low magnesium [34]. It has been suggested that the positive effects of magnesium on diabetes occur by inhibiting oxidative stress [35]. It is also stated that the primary pathology in gestational hypertension in which magnesium sulfate is used in the treatment is oxidative stress [36]. The positive effects of regular and aerobic exercise on oxidative stress and its curative effects on diabetes and obesity have been emphasized [37]. Both magnesium deficiency and oxidative stress have been identified as pathogenic factors in aging and age-related diseases. Additionally, severe magnesium deficiency has been shown to increase oxidative stress in experimental animals [38]. In light of these findings, it seems complicated to define the relationship of magnesium with hypertension without fully elucidating the complex effects of oxidative stress on hypertension.

CONCLUSIONS

As a result, it was found in our study that magnesium deficiency causes an increased risk of hypertension. However, in the presence of magnesium as an independent variable, the predictability rate of our model was expected to increase but decreased. These findings show that the relationship between magnesium and hypertension cannot be explained only by a cause-effect connection or incidental association. This may explain the reason for the conflicting results in the literature. More detailed analyzes are needed in this regard.

Conflicts of interest and sources of funding

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results. This research received no external funding.

Authors' contribution

All authors made substantial contributions to the conception or design of the work or the acquisition, analysis, or interpretation of data for the work. All authors have read and agreed to the published version of the manuscript.

Patient consent for publication

Because of the retrospective study, patient consent was not obtained.

Ethics approval and consent to participate

Ethical approval was obtained from the İstanbul Training Research Hospital Clinical Research Ethics Committee (Decision no. 14.10.2022, 318).

References:

1. Forouzanfar MH, Liu P, et al. Global Burden of Hypertension and Systolic Blood Pressure of at Least 110 to 115 mm Hg, 1990-2015 [published correction appears in JAMA. 2017 Feb 14;317(6):648]. JAMA, 2017, 317(2), 165-182.

2. Mills KT, Bundy JD, et al. Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries. Circulation, 2016, 134(6), 441-450.

3. Rimoldi SF, Scherrer U, et al. Secondary arterial hypertension: when who, and how to screen? Eur Heart J, 2014, 35(19), 1245-1254.

4. Ibekwe R. Modifiable Risk factors of Hypertension and Socio-demographic Profile in Oghara, Delta State; Prevalence and Correlates. Ann Med Health Sci Res, 2015, 5(1), 71-77.

5. Fiorentini D, Cappadone C, et al. Magnesium: Biochemistry, nutrition, detection, and social impact of diseases linked to ıts deficiency. Nutrients, 2021, 13(4), 1136.

6. Laires MJ, Monteiro CP, et al. Role of cellular magnesium in health and human disease. Front Biosci, 2004, 9, 262-276.

7. Workinger JL, Doyle RP, et al. Challenges in the diagnosis of magnesium status. Nutrients, 2018, 10(9), 1202.

8. Resnick LM, Bardicef O, et al. Serum ionized magnesium: relation to blood pressure and racial factors. Am J Hypertens, 1997, 10, 1420-1424.

9. Sasaki S, Oshima T, et al. Abnormal magnesium status in patients with cardiovascular diseases. Clin Sci (Colch), 2000, 98, 175-181.

10. Han H, Fang X, et al. Dose-response relationship between dietary magnesium intake, serum magnesium concentration and risk of hypertension: a systematic review and meta-analysis of prospective cohort studies. Nutr J, 2017, 16(1), 26.

11. Huang Y, Zhang W, et al. Study of magnesium and calcium levels of plasma and within erythrocyte before and after magnesium sulfate treatment in patients with pregnancy induced hypertension. Chung Hua Fu Chan Ko Tsa Chih, 1998, 33, 325-327

12. Dickinson HO, Nicolson DJ, et al. Magnesium supplementation for the management of essential hypertension in adults. Cochrane Database Syst Rev, 2006, (3), CD004640.

13. Jee SH, Miller ER 3rd, et al. The effect of magnesium supplementation on blood pressure: a meta-analysis of randomized clinical trials. Am J Hypertens, 2002, 15(8), 691-696.

14. Kass L, Weekes J, et al. Effect of magnesium supplementation on blood pressure: a meta-analysis. Eur J Clin Nutr, 2012, 66(4), 411-418.

15. Rosanoff A, Plesset MR. Oral magnesium supplements decrease high blood pressure (SBP>155 mmHg) in hypertensive subjects on anti-hypertensive medications: a targeted meta-analysis. Magnes Res, 2013, 26(3), 93-99.

16. Dibaba DT, Xun P, et al. The effect of magnesium supplementation on blood pressure in individuals with insulin resistance, prediabetes, or noncommunicable chronic diseases: a meta-analysis of randomized controlled trials. Am J Clin Nutr, 2017, 106(3), 921-929.

17. Zhang X, Li Y, et al. Effects of magnesium supplementation on blood pressure: A meta-analysis of randomized double-blind placebo-controlled trials. Hypertension 2016, 68(2), 324-333.

18. Onor IO, Johnston EK, et al. Evaluation of serum magnesium differences in hypertensive crises and control patients: A randomly matched case-control study. J Clin Hypertens (Greenwich), 2021, 23(6), 1229-1238.

19. Rosanoff A, Costello RB, et al. Effectively prescribing oral magnesium therapy for hypertension: A categorized systematic review of 49 clinical trials. Nutrients, 2021, 13(1), 195.

20. Barbagallo M, Gupta RK, et al. Cellular ionic alterations with age: relation to hypertension and diabetes. J Am Geriatr Soc, 2000, 48(9), 1111-1116.

21. Ford ES, Mokdad AH. Dietary magnesium intake in a national sample of US adults. J Nutr, 2003, 133(9), 2879-2882.

22. Coudray C, Feillet-Coudray C, et al. The effect of aging on intestinal absorption and status of calcium, magnesium, zinc, and copper in rats: a stable isotope study. J Trace Elem Med Biol 2006, 20(2), 73-81.

23. Barbagallo M, Veronese N, et al. Magnesium in aging, health and diseases. Nutrients, 2021, 13(2), 463.

24. Cameron D, Welch AA, et al. Age and muscle function are more closely associated with intracellular magnesium, as assessed by 31P magnetic resonance spectroscopy, than with serum magnesium. Front Physiol, 2019, 10, 1454.

25. Mills KT, Stefanescu A, et al. The global epidemiology of hypertension. Nat Rev Nephrol, 2020, 16(4), 223-237.

26. Alpsoy Ş. Exercise and Hypertension. Adv Exp Med Biol, 2020, 1228, 153-167.

27. Boutcher YN, Boutcher SH. Exercise intensity and hypertension: what's new? J Hum Hypertens 2017, 31(3), 157-164.

28. Korsager Larsen M, Matchkov VV. Hypertension and physical exercise: The role of oxidative stress. Medicina (Kaunas), 2016, 52(1), 19-27.

29. Saco-Ledo G, Valenzuela PL, et al. Exercise Reduces Ambulatory Blood Pressure in Patients With Hypertension: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Am Heart Assoc, 2020, 9(24), e018487.

30. Natsis M, Antza C, et al. Hypertension in Obesity: Novel Insights. Curr Hypertens Rev, 2020, 16(1), 30-36.

31. Lim K, Jackson KL, et al. Factors Responsible for Obesity-Related Hypertension. Curr Hypertens Rep, 2017, 19(7), 53.

32. Libianto R, Batu D, et al. Pathophysiological links between diabetes and blood pressure. Can J Cardiol, 2018, 34(5), 585-594.

33. Ferrannini E, Cushman WC. Diabetes and hypertension: the bad companions. Lancet, 2012, 380(9841), 601-610.

34. Barragán R, Llopis J, et al. Influence of demographic and lifestyle variables on plasma magnesium concentrations and their associations with cardiovascular risk factors in a Mediterranean population. Nutrients, 2020, 12(4), 1018.

35. Feng J, Wang H, et al. Role of magnesium in type 2 diabetes mellitus. Biol Trace Elem Res, 2020, 196(1), 74-85.

36. Ahmad IM, Zimmerman MC, et al. Oxidative stress in early pregnancy and the risk of preeclampsia. Pregnancy Hypertens, 2019, 18, 99-102.

37. Poblete-Aro C, Russell-Guzmán J, et al. Efecto del ejercicio físico sobre marcadores de estrés oxidativo en pacientes con diabetes mellitus tipo 2 [Exercise and oxidative stress in type 2 diabetes mellitus]. Rev Med Chil, 2018, 146(3), 362-372.

38. Manuel Y, Keenoy B, et al. Magnesium status and parameters of the oxidant-antioxidant balance in patients with chronic fatigue: Effects of supplementation with magnesium. J Am Coll Nutr, 2000, 19, 374-82.

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REVIEW

Combat Stress in Military Personnel: Theory, Genesis, Prevention, and Control

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Abstract: *On February 24, 2022, the Russian-Ukrainian war began, in which hundreds of thousands of military personnel are participating. Almost all military personnel experience combat stress. In our opinion, the most fully reflecting the occurrence of stress in humans, including combat stress in military personnel, is the conservation of resource theory proposed by S. Hobfoll. According to this theory, stress occurs when: central or key resources (health, well-being, family, self-esteem, and a sense of purpose and meaning in life) are threatened with loss, are lost, or cannot be retrieved following significant effort. Combat stress in military personnel can manifest itself in the form of negative manifestations of the psychological, physical, psychophysiological, and behavioral register. The most effective system for the prevention and control of combat stress among military personnel was developed in the US Army. Such a program should contain medical and psychological work activities carried out in three stages: preparatory (before performing combat missions), the stage of direct performance of tasks in the combat zone, and the final stage (after completing tasks upon returning to permanent deployment points).*

Keywords: *stress, combat stress, military personnel, fighting, COSC*

INTRODUCTION

There are few areas of contemporary psychology that receive more attention than stress [1,2]. This literature reflects researchers' belief that stress is a major factor affecting people's lives, is intimately tied to mental health, and is very possibly linked with many problems of physical health [1]. The interest in stress has also caught the attention of the popular press, illustrating that stress is of concern to the lay public as well as the academic community [3]. However, despite the breadth of interest in the problem of stress, there is little research to substantiate the relevant theories [2]. But in psychology, as in other sciences, it is difficult to create a sincere body of knowledge without a clear theoretical foundation, because there are no definite limits to the theory that can be denied [4].

An analysis of scientific sources on the subject of combat stress has shown that a lot of applied research has been carried out to solve this rather complex problem. This is because the last fifty years have been characterized by a significant increase in local and regional armed conflicts in the world [5-7]. The localization, time, nature, goals, the pace of hostilities, and military operations varied greatly during this period. But, as a rule, the majority of military personnel in their military career took part only in a series of combat deployments [8].

However, in the 21st century, not a single country, except Ukraine, has faced the armed aggression of the Russian Federation, and a large-scale war has been going on for more than a year. Hundreds of thousands of troops from both sides are taking part in the fighting. Almost all Ukrainian servicemen experience combat stress [9-11]. These circumstances, as well

as the duration and complexity of staying in extreme (combat) conditions, put forward high demands on the mental health, army values and motivation of military personnel, as well as on their psychological qualities and the adequacy of behavior for this activity [12-18]. Despite the high motivation to conduct combat operations, the improvement of military professional training and psychological preparation, some military personnel have problems with mental health, manifested by the development of acute stress reactions, post-traumatic stress disorders (PTSD), as well as addictive and delinquent behavior, an increase in suicidal manifestations [19-25].

Similar mental, physical, and behavioral health problems have occurred in US and coalition forces during and after combat deployments in Iraq and Afghanistan [5-7,26-30]. In combatants, these disorders manifested in persistent sleep disturbances, headaches, fatigue, and other symptoms associated with the influence of various stress factors in the combat environment, as well as the occurrence of more complex and severe disorders such as PTSD, traumatic brain injury and depression [31-33].

The conducted studies revealed that the significance of the influence on the psyche of military personnel and the development of the consequences of experiencing combat stress were determined by: factors of the combat situation; individual psychological characteristics of a person; the level of professional and psychological preparation for the conduct of hostilities; the nature and level of motivation of military personnel; the influence of combat stress factors on the further life of military personnel, etc. [9,20,28,34,35].

The objective of this study

The purpose of the article was to systematize scientific research on the problem of stress, combat stress, to study the modern system of mental health care for military personnel of the leading NATO partner countries, and to determine the main directions for improving the Ukrainian system for the prevention and control of combat stress among military personnel.

BASIC STRESS THEORIES

All theories of stress, in particular, combat stress, are based mainly on medical, biological, and psychological studies that reflect the processes of a distinct reaction of the human body to stress. In general, the term “stress” was borrowed by researchers from physics: it was previously believed that people are in some sense similar to physical objects, such as metals, resisting moderate external forces, but losing their stability at some point of higher pressure [1]. Walter Cannon was probably the first researcher to apply the concept of “stress” to humans in these kinds of terms [36]. He concluded that a person can resist initial stressors of moderate strength or lower-level negative factors that cause stress. However, prolonged or more severe stressors will lead to disruption of the body’s biological systems [36].

W. Cannon’s research on stress was continued and developed by Hans Selye. He described stress as a reaction (organized defense) of the body to non-specific harmful agents and called it the “general adaptation syndrome” [37]. According to the author’s definition, the general adaptation syndrome is the body’s response to severe damage by non-specific harmful agents (for example, exposure to cold, surgical shock, excessive physical exertion, or intoxication with sublethal doses of various drugs) and it does not depend on the nature of the damaging agent [37]. Thus, the protective role of the general adaptation syndrome consisted in the formation of nonspecific resistance of the organism to pathogenic agents, regardless of their nature. The researcher believed that there is a response of the body to external factors, which go through three stages in succession: anxiety (anxious response), resistance, and exhaustion [38].

Another direction in the study of the mechanisms of development of stress has already taken into account not only responses to stressors but also directly stressful events, as well as individual differences in their assessment. Spielberger suggested that certain events are stressful if they are thought to be threats to the physical self or the phenomenological self [39]. He proved that although individuals with different personalities responded some-what uniformly to physical threats, people’s responses to ego-threats were related to personality traits. In particular, Spielberger noted that people with high trait anxiety tended to react with state elevations in anxiety to ego-threat, whereas those who were low in trait anxiety tended to be comparatively impervious to ego-threats. Thus, the researcher concluded that it is not the stimulus and not the assessment that is important, but their specific interaction. This three-step approach was a conceptual leap for stress researchers but rarely followed up in further research. Instead, many researchers have reverted to models that only assessed stress, almost completely ignoring actual environmental or personality traits; others reflected only personality characteristics, while others remained tied only to the model’s stimuli.

In modern studies of the problem of stress, the homeostatic and transactional models of stress are most often used. The homeostatic model is presented in detail by McGrath [40] but is based in large part on the work of Lazarus [41]. According to research results, McGrath proposed the definition of stress as “a significant imbalance between the needs of the environment and the ability to respond to the body” [40, p. 17].

In 1966, the concept of cognitive appraisal was proposed by Richard Lazarus [41]. According to this theory, stress is perceived as the imbalance between the demands placed on the individual and the individual's resources to cope [2]. The transactional model of stress and coping contended that a person's capacity to cope and adjust to challenges and problems is a consequence of transactions (or interactions) that occur between a person and their environment. The authors defined stress as "a particular relationship between the person and the environment that is appraised by the person as taxing or exceeding his or her resources and endangering his or her well-being" [2, p. 19].

However, according to Hobfoll, these models and their definitions have a number of shortcomings [1]. First, the author notes, these definitions state that stress is not the product of an imbalance between objective demands and the ability to respond, but is the result of the perception of these factors. Secondly, the consequences of failure should be perceived as very important for a person. Third, McGrath suggested that imbalances might manifest as underutilization rather than overload, i.e. too little need for the ability to cope with stress [1].

In our opinion, one of the leading modern paradigms of the problem of stress, which is used by both scientists and practical psychologists in their work, is the conservation of resource theory proposed by Stephen Hobfoll. According to this theory, stress arises from motivation that encourages people to both maintain their current psychological resources and seek new opportunities [1]. Its main principle is that individuals strive to obtain, retain, foster, and protect those things they centrally value. The main postulates of this theory are understanding that stress occurs when: (a) central or key resources are threatened with loss, (b) central or key resources are lost, or (c) there is a failure to gain central or key resources following significant effort [1].

Essentially, the conservation of resource theory is a motivational theory that explains much of human behavior in terms of the evolutionary need to obtain and maintain resources for survival, which is central to the genesis of human behavior [42]. Resources are defined as those objects, personal characteristics, conditions, or energies that are valued by the individual or that serve as a means for the attainment of these objects, personal characteristics, conditions, or energies. According to the authors, people must acquire and maintain both strong personal characteristics and social ties. Thus, people must use key resources not only to respond to stress but also to create a certain amount of supportive resources in case of future needs. Moreover, the acquisition and maintenance of personal, social, and material resources create in people, families, and organizations the feeling that they are able to cope with stressful situations.

According to Hobfoll, a critical tenet conservation of resource theory is that individual value is secondary to what is most valued and universal to people. Typically, these valuable resources are health, well-being, family, self-esteem, and a sense of purpose and meaning in life [42]. How these evaluations are expressed may vary across cultural backgrounds but always reflects the same basic elements. The conservation of resource theory, in general, explains the mechanisms of development and transformation of the psychological safety of personality in military personnel during activities under different conditions [43].

DEFINITION OF COMBAT STRESS

An analysis of scientific research has shown that there is no generally accepted definition of the "combat stress" construct: depending on the field of its study (medicine, biology, psychology, sociology, other social sciences), there are many definitions of this category. Specialists who study stress in military personnel during combat operations suggest using such constructs as combat mental trauma, combat stress, combat mental pathology, post-traumatic stress disorders, and others definitions.

The official website of the US Department of Defense provides the definition of combat stress, also known as battle fatigue, which is a common response to the mental and emotional strain that can result from dangerous and traumatic experiences. It is a natural reaction to the wear and tear of the body and mind after extended and demanding operations [44]. Combat stress reaction (CSR) is a term used within the military to describe acute behavioral disorganization seen by personnel as a direct result of the trauma of war. CSR is an acute reaction that includes a range of behaviors resulting from the stress of battle that decrease the combatant's fighting efficiency. The most common symptoms are fatigue, slower reaction times, indecision, disconnection from one's surroundings, and the inability to prioritize. The combat stress reaction is generally short-term. The US Army uses the term/acronym COSR (Combat Stress Reaction) in official medical reports. This term can be applied to any stress reaction in the military unit environment. Many reactions look like symptoms of mental illness (such as panic, extreme anxiety, depression, and hallucinations), but they are only transient reactions to the traumatic stress of combat and the cumulative stresses of military operations [45].

Blinov defines combat stress as a reaction of the psyche to a threat to life and health in the form of a process of experiencing mental states at the stages of adaptation using the resource potential [9].

Snedkov makes a distinction between combat stress, combat psychic trauma, and combat psychic pathology [46]. Under combat stress, the author understands "a multilevel process of adaptive activity of the human body in a combat situation, accompanied by a tension in the mechanisms of reactive self-regulation and the consolidation of specific adaptive psychophysiological changes. Combat mental trauma is a pathological condition of the central nervous system, which is formed as a result of combat stress that exceeds the adaptive potential of a particular individual and forms the 'patos' of combat mental pathology. Combat mental pathology is a syndromic and nosologically structured clinical manifestation of combat mental trauma, the occurrence of which is due to the failure of compensation and the generalization of the pathogenetic mechanism" [46, pp. 28-29].

The authors of this article define the term "combat stress" as the process of the influence of combat situation factors on a soldier, accompanied by a decrease in the level of psychological safety of personality and the appearance of non-specific preclinical psychological manifestations, which together are presented by the concept of "combat psychological trauma of personality" or reach specific nosological symptoms of mental disorders, united in the concept of "combat mental trauma". Combat stress in military personnel can manifest itself in the form of negative manifestations of the psychological, physical, psychophysiological, and behavioral register.

According to American mental health experts, combat and operational stress include all types of psychological and emotional stress that arise as a result of the dangers and requirements of performing tasks in warfare and other military operations [47]. The development of combat stress in military personnel, according to the authors, is directly influenced by: the intensity and duration of a traumatic event or situation; the level of psychological resilience and endurance of the individual; self-efficacy of a person (the ability to take certain actions to achieve a specific goal); collective effectiveness (general belief in the collective power to achieve the desired results); neurobiological factors (heredity, differences in the activity of the sympathetic nervous system, features of cortisol release in response to psychological stress, serotonin metabolism, etc.).

The effects of combat stress are mediated by a complex interaction between changing factors specific to each person and situation, as well as the dynamic interaction between them. Thus, managed moderately mild stressors can have a "hardening" or stress-modifying effect, when the body becomes less reactive to future stressors. Researchers have found that attention and arousal are essential for survival [30,48]. However, when they go beyond the maximum range, this is fraught with detrimental biological consequences: excessive and prolonged nervous excitement after an injury can increase the likelihood of developing PTSD [49].

EFFECTS OF COMBAT STRESS ON MILITARY PERSONNEL

American researchers have proposed a more detailed classification of stressors associated with external and internal factors [47]. They determined that combat-related external stressors included: self-injury; the killing of combatants; monitoring the death of people; death of colleagues; injury resulting in the loss of a limb. External stressors associated with military operations include prolonged exposure to extreme environmental conditions; reduced quality of life and communication resources for a long time; prolonged separation from important support systems (e.g., family); overseeing significant casualties across many missions (for example, overseeing the deaths of several unit comrades during combat operations). External physical stressors include exogenous (heat, cold, moisture, dust; vibration, noise, explosions); harmful odors (smoke, poison, chemical compounds); ionizing radiation; infected environment; physical work; poor visibility (bright light, darkness); difficult terrain; being at height. Physiological stressors that can cause combat stress include sleep deprivation; dehydration; malnutrition; poor hygiene; muscle and hypoxic fatigue; illness or injury; sexual frustration; the use of psychoactive substances (caffeine, alcohol, drugs); obesity; poor physical condition [47].

Mental (internal) stressors include cognitive; requirements or expectations, difficult decisions (combat rules); organizational dynamics and change; difficult choices or lack of it; work that goes beyond their own competence; preliminary failures. Emotional (internal) stressors are new to the unit; isolation, loneliness; fear and threats that cause anxiety (death, injury, failure, or loss); losses that cause grief (mourning); indignation, aggression, and frustrations, causing anger and a feeling of sadness; conflict (ambiguous) motives; inactivity that causes a feeling of sadness; religious confrontation or temptation to lose faith; interpersonal conflicts (in a unit or with comrades); family problems, nostalgia for home; victimization, sexual claims; observation of the battle, dead bodies; murder [47].

During deployment, military personnel is influenced by combat stressors (seeing dead human bodies, being attacked or ambushed, knowing someone who was injured or killed, and handling dead bodies) as well as operational stressors: long deployments, uncertain redeployment date, separation from families and lack of privacy [49,50,51]. Potentially morally compromising war circumstances, as noted by Wortmann et al., could involve prescribed roles (e.g. maiming and killing), proscribed behaviors (e.g. the use of excessive

force or cruelty), bearing witness to the aftermath of violence or terror (e.g. handling or uncovering human remains) or being a victim of others' failures to uphold a moral code [52]. As a consequence, many service members suffer moral injury, characterized by guilt, shame, anger, social withdrawal, feelings of worthlessness, self-blame, and spiritual distress [33,52].

Effects of combat stress can also cause psychological trauma in military personnel, which can manifest itself both during the performance of combat missions and in the long-term period after their completion [7,30]. However, according to Born and Zamorski, deployment-related factors and exposure to potentially traumatic deployment experiences have the strongest and most consistent association with post-deployment mental health problems [53]. They may have short-term transient signs of the pre-nosological registry or more complex and severe somatic, psychiatric disorders, which should be well documented [27].

Recovery after exposure to combat stress can be facilitated by: a person's desire to open up and social support; the feeling that the social environment will accept the person's reactions with understanding and will encourage his openness; perception of the veteran as a hero or victim, but not as a victim; a sense of connection with God, a higher power, or a philosophical teaching; trauma-focused treatment to rethink negative reactions, clear intrusive memories, and help distinguish past from present threats [47].

Post-traumatic social support and relatively rare post-traumatic negative events may also serve as protective factors that will aid recovery from trauma [54].

COMBAT AND OPERATIONAL STRESS CONTROL (COSC) PROGRAMS IN MILITARY PERSONNEL

In our opinion, programs for the prevention and control of combat stress among military personnel are more effectively implemented in the Armed Forces of the United States, Great Britain, and Israel; other countries are developing similar activities based on these programs.

Trauma Risk Management (TRiM) is a peer-support program that aims to promote help-seeking military personnel in the aftermath of traumatic events, developed by the UK Royal Navy [55]. This program reflects a peer-led, occupational mental health support process that aims to identify and assist U.K. military personnel with persistent mental ill health related to potentially traumatic events [56]. TRiM seeks to modify attitudes about PTSD, stress, and help-seeking and trains military personnel to identify at-risk individuals and refer them for early intervention.

The use of TRiM may assist in increasing the psychological resilience of military personnel through the facilitation of social support; this may have particular utility during operational deployments [57].

The Israel Defense Forces developed YaHaLOM training to teach service members how to manage ASRs in team members [58] and then adapted into ICOVER by the U.S. Army. YaHaLOM is a novel, rapid, peer-based intervention specifically designed for use amid a high-stress event.

The analysis of scientific sources made it possible to determine that the most effective system for the prevention and control of combat stress among military personnel exists in the US Army. Let's consider this system in more detail. There is a specific terminological apparatus for defining terms related to combat stress that is used by mental health professionals in the US military. They are set out in various legal documents that regulate the professional activities of these specialists: COSC programs are set out in Field Manual 4-02.51 "Combat and Operational Stress Control" and 6-22.5 "Combat and Operational Stress Control Manual for Leaders and Soldiers" [45,59].

Thus, the control of combat and operational stress in the US Army is defined as the developed programs and activities of military leaders aimed at preventing, identifying, and managing dangerous behavior and combat stress reactions that may occur in military personnel [59]. The objectives of the COSC program are optimization of task performance; maintaining combat power; preventing the harmful effects of combat stress reactions on the physical, psychological, intellectual, and social health of military personnel or minimizing these effects; prompt return of soldiers to duty [60].

Also, one of the main tasks of the COSC is to increase unit cohesion and combat capability in a highly stressful military environment and to maximize post-traumatic growth [48]. COSC includes such activities as in-depth medical examination (screening) and psychodiagnostic of recruits; long-term observation of the passage of service, especially before, during, and after combat deployment; ongoing monitoring and consultation of mental health personnel from the US home base to the combat deployment area [61].

In the past, when US military personnel participated in operations in Korea and Vietnam, the consequences of the negative impact of combat stress led to almost half of the psychogenic losses on the battlefield, depending on the complexity of the conditions [47]. Although the level of acute (combat) stress reactions remained high in the wars of the 21st century, losses were significantly reduced. This was due to the introduction of COSC programs into the functioning of military

units. According to American mental health professionals, in modern wars, military leaders can expect 95% of military personnel with ASRs should return to combat missions [47]. COSC is effective when it comes not only to military personnel but also to their training and support systems, including meaningful interpersonal relationships, families, and external resources. COSC aims to identify members of the armed forces and their families, as well as US Army civilians who may need assistance due to challenges associated with participating in combat deployments, and to ensure that they are better prepared, stable, and reliable at all stages accomplishment of combat missions. If we consider the personal level of a soldier, then the goal of COSC is to improve the readiness of each soldier and the unit as a whole to perform a combat mission. This can be achieved by: improving adaptive stress responses and preventing unproductive coping strategies; helping military personnel control combat stress responses; helping soldiers with behavioral problems [6].

Overall, the US Army's COSC is one of 10 medical systems active during pre-combat, on the battlefield, and at the end of a mission. Five professional disciplines in mental health and two additional ones are directed to the implementation of COSC. Professional disciplines include social work, clinical psychology, psychiatry, occupational therapy, and psychiatric nursing. Additional disciplines include mental health and vocational rehabilitation.

An analysis of the COSC programs of different armies of NATO partner countries in the field of international security assistance showed that they are similar in terms of organizational principles, main goals, and tasks. However, these programs differ structurally from the US Army COSC and have their own characteristics depending on the conditions of the missions in which the military personnel take part and the performance of combat missions. Such a comparison of COSC programs was made during a mission in Afghanistan among five NATO partner countries: the armed forces of Australia, Canada, the UK, the Netherlands, and the USA [8]. This allowed the authors to identify and compare organizational structures and key practices in providing mental health care and support to military personnel, identify issues, and illustrate new developments in this area.

The main comparative themes of the COSC programs were: education, prevention, early detection, intervention (care), and follow-up (support) in the field of mental health. The main method of organizing support for the mental health of servicemen was training (psycho-prophylaxis) and monitoring their mental state. The educational goal was to enhance the mental stability of individual military personnel while providing a range of mental health services. All mental health officials from these five countries have waived the need for a standard psychological debriefing after critical incidents (military deaths and large numbers of wounded). Instead, these specialists monitored the mental state of military personnel and their commanders during mandatory post-combat checkups and interviews [35].

To organize psychological support for military personnel, specialized mental health units were deployed near the line of combat, the main purpose of which was the early identification, assistance, and early return to normal activities of such military personnel in the units [62]. All countries have deployed mental health support teams made up of a variety of professionals, including psychiatrists, psychologists, social workers, nurses, and priests [63]. There was no consensus on the distribution of mental health disciplines in the war zone.

All countries, except the United States, organized psychological decompression for personnel in temporary deployment elsewhere (outside the combat zone, but in areas of temporary deployment of units) within a few days after the completion of combat deployment. Its main goal was to recognize faces with signs of combat stress reactions, to provide them with assistance, psychological support, and preparation for sending them to permanent deployment points (home). The US Army conducted intra-garrison decompression or reintegration training directly in the US [8]. But psychological decompression had a fairly comparable infrastructure in the field of psychiatric and psychological care.

Common concerns across countries included perceived stigma (unwillingness or fear of military personnel to seek help from mental health professionals), barriers to mental health care, and the need to increase awareness and acceptance of mental health issues among military personnel [64].

In addition to psychological support, modern preventive psychiatric treatment was included in all COSC programs, including a positive approach to strengthening mental stability. There has also been an emphasis on building self-regulatory skills, empowering military personnel, and several other innovations well integrated into the military context [63]. An important innovation in the operational mental health support of military personnel was the recognition of the role of social leadership and the need to increase support from colleagues.

However, not all researchers are positive about the introduction of COSC programs to prevent the development of mental disorders in military personnel that occur during and after combat deployment. Maglione et al. believe that although COSC interventions may play a valuable role in decreasing stress, decreasing absenteeism, and enabling a return to duty, a systematic review of studies that included a control/comparison group found little evidence that COSC is

effective in preventing PTSD or decreasing PTSD symptom scores in military personnel [65].

CONCLUSIONS

One of the most important directions in the development of military psychology is the study of the problem of stress. The conservation of resource theory by S. Hobfoll, in our opinion, most fully and reasonably explains the genesis of combat stress that occurs in military personnel during activities in extreme conditions. The main postulate of this theory is that stress occurs when a person's central or key resources (health, well-being, family, self-esteem, and a sense of purpose and meaning in life) are threatened with loss, lost, or there is a failure to gain key resources following significant effort. At its core, the conservation of resource theory is a motivational theory that explains much of human behavior in terms of the evolutionary need to obtain and conserve resources in order to survive.

It was revealed that during the fighting, almost all servicemen experience combat stress. Combat stress is the process of the influence of combat situation factors on a soldier, accompanied by a decrease in the level of psychological safety of personality and the appearance of non-specific preclinical psychological manifestations, which together are presented by the concept of "combat psychological trauma of personality" or reach specific nosological symptoms of mental disorders, united in the concept of "combat mental trauma".

To prevent the occurrence and development of combat stress, it is necessary to develop and implement a system for the prevention and control of combat stress in military personnel. Such a program should contain psychological work activities carried out at three stages: preparatory (before performing combat missions), the stage of direct performance of tasks in the combat zone, and the final stage (after completing tasks upon returning to permanent deployment points).

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Authors' contribution

Conceptualization and project management, I.P.; research, YaM., O.K and S.V.; methodology, V.V.; formal analysis, N.V.; software, L.B.; writing – original draft preparation, V.K. and S.M. All authors read and agreed to the published version of the manuscript.

Ethics approval and consent to participate

All procedures followed were in accordance with the ethical standards of the Helsinki Declaration of 1975, as revised in 2000.

References:

1. Hobfoll SE. Conservation of resources: A new attempt at conceptualizing stress. Am Psychol. 1989; 44(3): 513–524. Available from: https://doi.org/10.1037/0003-066X.44.3.513.

2. Lazarus RS, Folkman S. Stress appraisal and coping. Springer Pub; 1984. Available from: http://www.dawsonera.com/depp/reader/protected/external/AbstractView/S9780826141927.

3. American Psychological Association. How to cope with traumatic stress. 2019. Available from: https://www.apa.org/topics/trauma/stress.

4. Cook TD, Campbell DT. Quasi-experimentation: Design and analysis issues for field settings. Boston, MA: Houghton Mifflin; 1979. Available from: https://www.amazon.com/Quasi-Experimentation-Design-Analysis-Issues-Settings/dp/0395307902.

5. Cabrera OA, Adler AB. Psychological distress across the deployment cycle: exploratory growth mixture model. BJPsych Open. 2021; 7(3): e89. Available from: https://doi.org/10.1192/bjo.2021.50.

6. Figley CR, Nash WP, editors. Combat stress injury: Theory, research, and management. New York, NY, US: Routledge/Taylor & Francis Group; 2007. Available from: https://www.routledge.com/Combat-Stress-Injury-Theory-Research-and-Management/Nash/p/book/9781138871601.

7. Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL. Combat Duty in Iraq and Afghanistan, Mental Health Problems, and Barriers to Care. N Engl J Med. 2004; 351(1): 13–22. Available from: https://doi.org/10.1056/NEJMoa040603.

8. Vermetten E, Greenberg N, Boeschoten MA, Delahaije R, Jetly R, Castro CA, et al. Deployment-related mental health support: comparative analysis of NATO and allied ISAF partners. Eur J Psychotraumatol. 2014; 5(1): 23732. Available from: https://doi.org/10.3402/ejpt.v5.23732.

9. Blinov O. Combat stress and results of its empirical study. Psychol J. 2018; 12(2): 9–22. Available from: https://doi.org/10.31108/2018vol12iss2pp9-22.

10. Kokun O., Agayev N., Pischko I., Stasiuk V. Characteristic impacts of combat stressors on posttraumatic stress disorder in Ukrainian military personnel who participated in the armed conflict in eastern Ukraine. Int J Psychol Psychol Ther. 2020; 20(3): 315–326. Available from: https://www.ijpsy.com/volumen20/num3/554/characteristic-impacts-of-combat-stressors-EN.pdf.

11. Prykhodko I, Kolesnichenko O, Matsehora Y, Aleshchenko V, Kovalchuk O, Matsevko T, et al. Effects of posttraumatic stress and combat losses on the combatants' resilience. Cesk Psychol. 2022; 66(2): 157–169. Available from: https://doi.org/10.51561/cspsych.66.2.157.

12. Kolesnichenko O, Matsegora Y, Prykhodko I, Larionov S, Bolshakova A, Bilyk O, et al. Content, Hierarchy, Intensity of Motives and their Possibility to be Implemented in Servicemen with Various Levels of Effectiveness of Service Activity. BRAIN Broad Res Artif Intell Neurosci. 2021; 12(4): 374–410. Available from: https://doi.org/10.18662/brain/12.4/256.

13. Kolesnichenko O., Prykhodko I., Matsehora Y., Bolshakova A., Bilyk O., Storozhuk N., et al. Typology of individual values of combatants of the War in Eastern Ukraine. Rom J Mil Med. 2022; 125(1): 109–117. Available from: http://www.revistamedicinamilitara.ro/wp-content/uploads/2022/02/Typology-of-individual-values-of-combatants-of-the-War-in-Eastern-Ukraine.pdf.

14. Matsegora Y, Kolesnichenko O, Prykhodko I, Izbash S, Panok V, Marushchenko K, et al. Typology and structure of servicemen motivation. Rom J Mil Med. 2022; 125(4): 693–707. Available from: https://doi.org/10.55453/rjmm.2022.125.4.22.

15. Prykhodko I, Yurieva N, Lyman A, Bayda M, Bloshchynskyi I, Kuzina V. Psycho-Semantic Reconstruction of Psychological Risk Readiness Perceptions by the National Guard of Ukraine Servicemen. BRAIN Broad Res Artif Intell Neurosci. 2020; 11(4): 37–50. Available from: https://doi.org/10.18662/brain/11.4/140.

16. Prykhodko I, Matsegora Y, Kolesnichenko O, Pasichnik V, Kuruch O, Yurieva N, et al. Psychological Markers of Suicides in Military Service During Wartime: A Contemporary Example. Int J Psychol Psychol Ther. 2021; 21(1): 47–57. Available from: https://www.ijpsy.com/volumen21/num1/570/psychological-markers-of-suicides-in-military-EN.pdf.

17. Prykhodko I, Lyman A, Matsehora Y, Yurieva N, Balabanova L, Hunbin K, et al. The Psychological Readiness Model of Military Personnel to Take Risks during a Combat Deployment. BRAIN Broad Res Artif Intell Neurosci. 2021; 12(3): 64–78. Available from: https://doi.org/10.18662/brain/12.3/220.

18. Rybinska Y, Loshenko O, Kurapov A, Lytvyn S, Kondratieva V, Ivasiv O. Psycho-Emotional State of Ukrainian Soldiers Before Going to the Frontline. BRAIN Broad Res Artif Intell Neurosci. 2022; 13(4): 182–195. Available from: https://doi.org/10.18662/brain/13.4/382.

19. Kazmirchuk AP, Lashin OI, Druz OV, Chernenko IO. Basic predictors of post-trauma stress disorder formation among combatants. World Med Biol. 2020; 2(72): 63-67. Available from: https://doi.org/10.26724/2079-8334-2020-2-72-63-67.

20. Kokun O, Pischko I, Lozinska N. Examination of military personnel's changed psychological states during long-term deployment in a war zone. An Psicol. 2022; 38(1): 191–200. Available from: https://doi.org/10.6018/analesps.475041.

21. Kolesnichenko O., Matsegora Y., Prykhodko I., Shandruk S., Larionov S., Izbash S., et al. Typology of Personal Characteristics of Cadets Who Use Psychoactive Substances. Int J Psychol Psychol Ther. 2021; 21(3): 347–361. Available from: https://www.ijpsy.com/volumen21/num3/587/typology-of-personal-characteristics-of-EN.pdf.

22. Matsegora Y, Kolesnichenko O, Prykhodko I, Kravchenko O, Kyslyi V, Bayda M, et al. Social and psychological predictors of alcohol-related incidents involving servicemen. Rom J Mil Med. 2022; 125(4): 668–686. Available from: https://doi.org/10.55453/rjmm.2022.125.4.20.

23. Prykhodko I, Matsehora Y, Kolesnichenko O, Bolshakova A, Bilyk O, Haydabrus A V. The Main Factors and Personality Characteristics to Predict the Risk of Suicide by Military Personnel in Hostilities. BRAIN Broad Res Artif Intell Neurosci. 2020; 11(3): 72–87. Available from: https://doi.org/10.18662/brain/11.3/110.

24. Prykhodko I, Matsegora Y, Kolesnichenko O, Pasichnik V, Kuruch O, Yurieva N, et al. Psychological Markers of Suicides in Military Service During Wartime: A Contemporary Example. Int J Psychol Psychol Ther. 2021; 21(1): 47–57. Available from: https://www.ijpsy.com/volumen21/num1/570/psychological-markers-of-suicides-in-military-EN.pdf.

25. Shvets A, Sereda I, Lopin E. The medical and social importance of mental and behavior disorders among military personnel in peacetime and warfare. Rom J Mil Med. 2021; 124(4): 481–487. http://www.revistamedicinamilitara.ro/wp-content/uploads/2021/11/The-medical-and-social-importance-of-mental-and-behavior-disorders-among-military-personnel-in-peacetime-and-warfare.pdf.

26. Campbell DJ, Nobel OB-Y. Occupational Stressors in Military Service: A Review and Framework. Mil Psychol. 2009; 21(sup2): 47–67. Available from: https://doi.org/10.1080/08995600903249149.

27. de Burgh HT, White CJ, Fear NT, Iversen AC. The impact of deployment to Iraq or Afghanistan on partners and wives of military personnel. Int Rev Psychiatry. 2011; 23(2): 192–200. Available from: https://doi.org/10.3109/09540261.2011.560144.

28. Griffith J. Relationships of deployment and combat experiences to postdeployment negative health conditions among Army National Guard soldiers. Mil Psychol. 2019; 31(2): 128–137. Available from: https://doi.org/10.1080/08995605.2019.1565908.

29. Hassan AM, Jackson RJ, Lindsay DR, Rank MG. Combat Stress Control and Prevention: What Can Be Learned from an Application of Workplace Behavioral Health in a Deployed Combat Environment? J Workplace Behav Health. 2010; 25(3): 169–180. Available from: https://doi.org/10.1080/15555240.2010.496315.

30. Thomas JL, Wilk JE, Riviere LA, McGurk D, Castro CA, Hoge CW. Prevalence of Mental Health Problems and Functional Impairment Among Active Component and National Guard Soldiers 3 and 12 Months Following Combat in Iraq. Arch Gen Psychiatry. 2010; 67(6): 614–623. Available from: https://doi.org/10.1001/archgenpsychiatry.2010.54.

31. Adler AB, Gutierrez IA. Preparing Soldiers to Manage Acute Stress in Combat: Acceptability, Knowledge and Attitudes. Psychiatry. 2022; 85(1): 30–37. Available from: https://doi.org/10.1080/00332747.2021.2021598.

32. Gates MA, Holowka DW, Vasterling JJ, Keane TM, Marx BP, Rosen RC. Posttraumatic stress disorder in veterans and military personnel: Epidemiology, screening, and case recognition. Psychol Serv. 2012; 9(4): 361–382. Available from: https://doi.org/10.1037/a0027649.

33. Neria Y, Koenen KC. Do combat stress reaction and posttraumatic stress disorder relate to physical health and adverse health practices? An 18 year follow up of Israeli war veterans. Anxiety, Stress Coping. 2003; 16(2): 227–239. Available from: https://doi:10.1080/10615806.2003.10382975.

34. Campbell JS, Koffman RL. Ecological Systems of Combat and Operational Stress: Theoretical Basis for the U.S. Navy Mobile Care Team in Afghanistan. Mil Behav Heal. 2014; 2(4): 316–326. Available from: https://doi.org/10.1080/21635781.2014.963761.

35. Castro CA. The US framework for understanding, preventing, and caring for the mental health needs of service members who served in combat in Afghanistan and Iraq: a brief review of the issues and the research. Eur J Psychotraumatol. 2014; 5(1): 24713. Available from:

https://doi.org/10.3402/ejpt.v5.24713.

36. Cannon WB. The wisdom of the body. New York: Norton; 1932. Available from: https://psycnet.apa.org/record/1932-02164-000.

37. Selye H. A Syndrome produced by Diverse Nocuous Agents. Nature. 1936; 138: 32–32. Available from: https://doi.org/10.1038/138032a0.

38. Selye H. The general adaptation syndrome and the diseases of adaptation. J Allergy. 1946; 17(4): 231–247. Available from: https://doi.org/10.1016/0021-8707(46)90148-7.

39. Spielberger CD. Anxiety: Current trends in theory and research. New York: Academic Press; 1972. https://www.elsevier.com/books/anxiety/spielberger/978-0-12-657402-9.

40. McGrath JE. A conceptual formulation for research on stress. In: Social and psychological factors in stress. New York: Holt, Rinehart & Winston; 1970. p. 10–21. Available from: https://apps.dtic.mil/sti/pdfs/AD0726667.pdf.

41. Lazarus RS. Psychological stress and the coping process. Psychological stress and the coping process. New York, NY, US: McGraw-Hill; 1966. Available from: https://psycnet.apa.org/record/1966-35050-000.

42. Hobfoll SE, Halbesleben J, Neveu J-P, Westman M. Conservation of Resources in the Organizational Context: The Reality of Resources and Their Consequences. Annu Rev Organ Psychol Organ Behav. 2018; 5(1): 103–128. Available from: https://doi.org/10.1146/annurev-orgpsych-032117-104640.

43. Prykhodko I. The model of psychological safety of a soldier's personality. Curr Issues Personal Psychol. 2022; 10(2): 112–122. Available from: https://doi.org/10.5114/cipp.2021.108684.

44. An Official Defense Department. Understanding and Dealing with Combat Stress and PTSD. Military OneSource. 2022. Available from: https://www.militaryonesource.mil/military-basics/wounded-ill-injured-and-caregivers/understanding-and-dealing-with-combat-stress-and-ptsd/.

45. Headquarters Department of the Army. Combat and Operational Stress Control Manual for Leaders and Soldiers: Field Manual 6-22.5. Washington, DC; 2009. Available from: https://www.globalsecurity.org/military/library/policy/army/fm/6-22-5/fm6-22-5_2009.pdf.

46. Snedkov E V. Boevaya psykhicheskaya travma (kliniko-patohenetycheskaya dinamika, diahnostika, lechebno-reabilitatsionnye printsipy) [Combat mental trauma (clinical and pathogenetic dynamics, diagnosis, treatment and rehabilitation principles)]. St. Petersburg Military Medical Academy; 1997. https://medical-diss.com/medicina/boevaya-psihicheskaya-travma-kliniko-patogeneticheskaya-dinamika-diagnostika-lechebno-reabilitatsionnye-printsipy.

47. United States Government US Army. Combat and Operational Behavioral Health. CreateSpace Independent Publishing Platform. 2011. Available from: https://www.amazon.com/Operational-Behavioral-Textbooks-Military-Medicine/dp/0160887569.

48. Brusher EA. Combat and Operational Stress Control. Int J Emerg Ment Health. 2007; 9(2): 111–22. Available from: https://psycnet.apa.org/record/2007-12670-005.

49. Shen Y-C, Arkes J, Pilgrim J. The Effects of Deployment Intensity on Post-Traumatic Stress Disorder: 2002–2006. Mil Med. 2009; 174(3): 217–223. Available from: https://doi.org/10.7205/MILMED-D-03-4307.

50. Nassif TH, Start AR, Toblin RL, Adler AB. Self-reported mindfulness and soldier health following a combat deployment. Psychol Trauma Theory, Res Pract Policy. 2019; 11(4): 466–474. Available from: https://doi.org/10.1037/tra0000413.

51. Osório C, Jones N, Jones E, Robbins I, Wessely S, Greenberg N. Combat Experiences and their Relationship to Post-Traumatic Stress Disorder Symptom Clusters in UK Military Personnel Deployed to Afghanistan. Behav Med. 2018; 44(2): 131–140. Available from: https://doi.org/10.1080/08964289.2017.1288606.

52. Wortmann JH, Eisen E, Hundert C, Jordan AH, Smith MW, Nash WP, et al. Spiritual features of war-related moral injury: A primer for clinicians. Spiritual Clin Pract. 2017; 4(4): 249–261. Available from: https://doi.org/10.1037/scp0000140.

53. Born JA, Zamorski MA. Contribution of traumatic deployment experiences to the burden of mental health problems in Canadian Armed Forces personnel: exploration of population attributable fractions. Soc Psychiatry Psychiatr Epidemiol. 2019; 54(2): 145–156. Available from: https://doi.org/10.1007/s00127-018-1562-6.

54. Yehuda R, Vermetten E, McFarlane AC, Lehrner A. PTSD in the military: special considerations for understanding prevalence, pathophysiology and treatment following deployment. Eur J Psychotraumatol. 2014; 5(1): 25322. Available from: https://doi.org/10.3402/ejpt.v5.25322.

55. Jones N., Burdett H, Green K, Greenberg N. Trauma Risk Management (TRiM): Promoting Help Seeking for Mental Health Problems Among Combat-Exposed U.K. Military Personnel. Psychiatry. 2017; 80(3): 236–251. Available from: https://doi.org/10.1080/00332747.2017.1286894.

56. Greenberg N, Langston V, Everitt B, Iversen A, Fear NT, Jones N, et al. A cluster randomized controlled trial to determine the efficacy of Trauma Risk Management (TRiM) in a military population. J Traum Stress. 2010; 23(4): 430–436. Available from: https://doi.org/10.1002/jts.20538.

57. Frappell-Cooke W, Gulina M, Green K, Hacker Hughes J, Greenberg N. Does trauma risk management reduce psychological distress in deployed troops?. Occup Med. 2010; 60(8): 645–650. Available from: https://doi.org/10.1093/occmed/kqq149.

58. Svetlitzky V, Farchi M, Ben Yehuda A, Start AR, Levi O, Adler AB. YaHaLOM training in the military: Assessing knowledge, confidence, and stigma. Psychol Services. 2020; 17(2): 151–159. Available from: https://doi.org/10.1037/ser0000360.

59. Headquarters Department of the Army. Combat and Operational Stress Control: Field Manual 4-02.51. Washington, DC; 2006. Available from: https://irp.fas.org/doddir/army/fm4-02-51.pdf.

60. Mattila AM, Crandall BD, Goldman SB. U.S. Army combat operational stress control throughout the deployment cycle: A case study. Work. 2011; 38(1): 13–18. Available from: https://doi.org/10.3233/WOR-2011-1100.

61. Reger GM, Moore BA. Combat Operational Stress Control in Iraq: Lessons Learned During Operation Iraqi Freedom. Mil Psychol. 2006; 18(4): 297–307. Available from: https://doi.org/10.1207/

s15327876mp1804_4.

62. Melnyk YB, Prykhodko II, Stadnik A V. Medical-psychological support of specialists' professional activity in extreme conditions. Minerva Psichiatr. 2019; 60(4): 158−168. Available from: https://doi: 10.23736/S0391-1772.19.02025-9.

63. Vermetten E, Ambaum J. Exposure to combat and deployment; reviewing the military context in The Netherlands. Int Rev Psychiatry. 2019; 31(1): 49–59. Available from: https://doi.org/10.1080/09540261.2019.1602517.

64. Taal EM, Vermetten E, van Schaik DJF, Leenstra T. Do soldiers seek more mental health care after deployment? Analysis of mental health consultations in the Netherlands Armed Forces following deployment to Afghanistan. Eur J Psychotraumatol. 2014; 5(1): 23667. Available from: https://doi.org/10.3402/ejpt.v5.23667.

65. Maglione MA, Chen C, Bialas A, Motala A, Chang J, Akinniranye O, et al. Combat and Operational Stress Control Interventions and PTSD: A Systematic Review and Meta-Analysis. Mil Med. 2022; 187(7–8): e846–855. Available from: https://doi.org/10.1093/milmed/usab310.

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ORIGINAL ARTICLE

A Survey on Mental Health Status in West of Iran: A Spatial Analysis

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Abstract: *Mental disorders clearly are among the major challenges of global health causing many concerns for health systems, health experts, and health policy makers. The present study was conducted to evaluate the mental health program in comprehensive health centers and health houses under the coverage of the Ilam University of Medical Sciences in the West of Iran. The present study was conducted based on the reports obtained from the mental health program in 2019. The data were recorded into registration and evaluation forms of mental disorders with the codes 102-19-03 and 102-19-01 and then entered into the Excel software. The prevalence per 100 and 100,000 people, as well as their 95% confidence intervals, were calculated using Formula 1 ROUND (Number of cases*100000/population) and Formula 2 ROUND (Prevalence ±1.96*SQRT (Prevalence *(1-Prevalence)/population). The results showed that the prevalence of depression was 19,100 [95% CI: 18999-19201] 19100), and the prevalence of anxiety was 304,66 [95% CI: 20348-30584] per 100,000 population. The highest prevalence among mental disorders was related to depression and anxiety. Considering the high average score of mental health status in people over 65 years old, it is necessary to implement measures and interventions to improve these individuals' mental conditions and upgrade their mental health.*

Keywords: *Spatial analysis; Ilam province; Mental health; Iran*

INTRODUCTION

According to the definition provided by the World Health Organization (WHO), mental health is "a health status that turns one's potential talents into reality, enabling people to cope with routine life tensions, accomplish valuable work, and upgrade their social participation" [1]. Mental health is an important component for evaluating the health status of a population and can be evaluated using various indicators [2]. In other words, the concept of mental health falls under the general concept of health and refers to all the methods and measures used to prevent people from developing mental disorders, as well as for the treatment and rehabilitation of affected individuals. Psychologists believe that mental health can be affected by individual characteristics, mental and environmental burdens, economic, social, and familial status, failure to achieve life goals, and lack of motivation [3]. Industrialization of countries, the growth of urbanization, migration to cities, etc. are phenomena that are associated with numerous troubles, including psychological and social problems. For this reason, mental health and mental disorders are considered top priorities in today's world. The high prevalence of mental disorders and their associated morbidities render them an immediate health priority [4].

Excessive attention to physical health problems (such as infectious and contagious diseases) has caused mental health to receive less priority in many countries around the world, including its social and spiritual aspects, which have been overlooked in most cases [5]. Statistics on the global burden of mental illnesses highlight the need to pay attention to these aspects more than ever. In parallel with the estimation of the WHO, Harvard University and the World Bank declared that mental disorders were responsible for about 13% of the total

burden of diseases in 2006, which was predicted to reach 15% by 2020. The rate of morbidities caused by these disorders has been reported beyond 33% [6]. In Iran, mental health disorders account for 14.5% of the total burden of diseases, and after traffic accidents, they share the second rank with cardiovascular diseases. In women, depression claims the first place of disease burden, while in men, addiction is considered the third cause of disease burden[7]. According to studies in Iran on individuals older than 15 years old, the prevalence of mental disorders has been 25.9% in women and 14.9% in men, and it was reported that overall, 21% of people suffered from some sort of mental problems. Some studies have assessed the prevalence of mental disorders in Ilam province{8]. In a population-based study by Visani et al. [9], the prevalence of DSM-IV mental disorders in both genders was investigated in the urban areas of Ilam province. Out of 763 participants aged 15 years and older in the recent study, 25.8% showed symptoms of mental distress, and the prevalence of mental disorders was reported to be 20.9% in men and 29.8% in women. Also, the prevalence of anxiety, major depressive disorder (MDD), and obsessive-compulsive disorder was higher in women than in men (23.6% vs. 18.2%; 22.7% vs. 17.4%; 13.9% vs. 10%, respectively). In women, the prevalence of phobia was reported as 10.4%.

Studying mental health status can provide managers and decision-makers of organizations with valuable information for planning educational, therapeutic, and preventive measures to reduce the incidence of these diseases in society. Such information can be obtained by monitoring the mental health status of people in different societies [5].

Assessment and monitoring of mental disorders in the country and in Ilam province can help better understand the condition of mental health and public health in society, which is an important and influential factor affecting social productivity and wealth creation. Therefore, researchers here aimed to investigate the mental health status of the urban population of Ilam using the data recorded in the registration and assessment forms designed for mental disorders. Furthermore, we evaluated the mental health program performed in comprehensive health centers and health houses covered by the Ilam University of Medical Sciences in the West of Iran.

MATERIALS AND METHODS

The present cross-sectional study was conducted on the basis of the reports derived from the mental health program in Ilam province in 2020. According to the statistics announced in 2021, Ilam province harbors a population of over 630,000 people living in ten cities: Ilam, Ivan, Chardavl, Sirvan, Malekshahi, Mehran, Abdanan, Dehloran, Badreh, and Darrehshahr (Figure 1).

Figure 1: The geographical location of Ilam province

This study was conducted to assess the mental health program implemented in the comprehensive health centers and health houses affiliated with the Ilam University of Medical Sciences in 2019. The study was approved by the institutional ethics committee under the code IR.MEDILAM.REC.1399.266. The data were gathered by reviewing registration and evaluation forms for mental disorders with the codes 102-19-03 and 102-19-01 in all ten cities of Ilam province. Then based on the population of each city in 2021, the prevalence of mental disorders was calculated in 100 and 100,000 people.

Analytic Method

After collection, the data of each city were entered into Microsoft Excel software, and formulas 1 and 2 were used to calculate the prevalence of mental disorders (with 95% CIs) in 100 and 100,000 people.

Formula 1: ROUND (Number of cases*100000/population)

Formula 2: ROUND Prevalence ±1.96*SQRT (Prevalence *(1-Prevalence)/population)

Also, to determine the geographical distribution of mental disorders in the cities of Ilam province, the commands of spatial analysis in the STATA 11 software (Stata Corp. LLC College Station, Texas, USA) were used.

RESULTS

The results showed that in Ilam province, the prevalence of depression was 19100 (95% CI: 18999-19201), and the prevalence of anxiety was 30466 (95% CI: 20348-30584) per 100,000 people. According to the results, the highest prevalence among mental disorders was related to depression and anxiety.

The highest rate of depression belonged to Ilam (20300, 95% CI: 20137-20463) and Malekshahi (21836, 95% I: 21297-22375) cities, while the lowest rate of depression was reported in

Sirvan (16292, 95% CI: 15691-16897) and Badreh (17299, 95% CI: 16706-17892).

Also, the highest rates of anxiety were recorded in the cities of Abdanan (22298, 95% CI: 21922-22674), Ivan (22559, 95% CI: 22228-22970), and Ilam (21200, 95% CI: 210135-21365). On the other hand, the cities of Sirvan (16769, 95% CI: 16184-17404), Chardavl (16499, 95% CI: 16228-16770), and Darrehshahr (19099, 95% CI: 17790-18408) had the lowest rate of anxiety (Table 1).

Table 1: The prevalence of depression and anxiety in the population of Ilam province per 100,000 people in separate cities

Location	Population	Major Depressive Disorder Prevalence		Anxiety Disorder Prevalence	
		Number of cases	Rate per 100,000 (CI 95%)	Number of cases	Rate per 100,000 (CI 95%)
Ilam	235144	47734	21200(210135-21365)	49850	20300(20137-20463)
Abdanan	46977	9630	22298(21922-22674)	10475	20499(20134-20463)
Ivan	48833	10236	22559(22228-22970)	11036	20961(20600-21322)
Mehran	27506	5281	22402(21909-22895)	6162	19199(18734-19664)
Badreh	15614	2701	17299(16706-17892)	2701	17299(16706-17892)
Dehloran	66339	13135	18900(18602-19198)	12538	19800(19497-20103)
Darrehshahr	59551	10838	18099(17790-18408)	10778	18200(17890-18510)
Shirvan	14404	2347	16796(16184-17404)	2419	1294(15691-16897)
Chardavl	72167	12412	16499(16228-16770)	11907	17199(16924-17474)
Malekshahi	22587	4932	17196(16704-17668)	3884	21836(21297-22375)
Total	580148	110808	30466(20348-30584)	176750	19100(18999-19201)

Regarding age distribution, the results showed that the highest prevalence of depression (29%), anxiety (35.5%), and psychotic disorder (22.6%) was observed in people over 65 years of age. The psychological disorders of mania (6.3%) and obsessive-compulsive disorder (13.3%) were more commonly observed in the age group of 15-24 years compared to other age groups.

Regarding the gender distribution of mental disorders, it was noticed that depression (20.3% vs. 22.7%), mania (2.6% vs. 4.7%), anxiety (23.6% vs. 32.18%), obsessive-compulsive disorder (10% vs. 13.79%), phobia (10.4% vs. 5%), and psychotic disorder (6.17% vs. 2.4%) were more frequent in women than in men (Table 2).

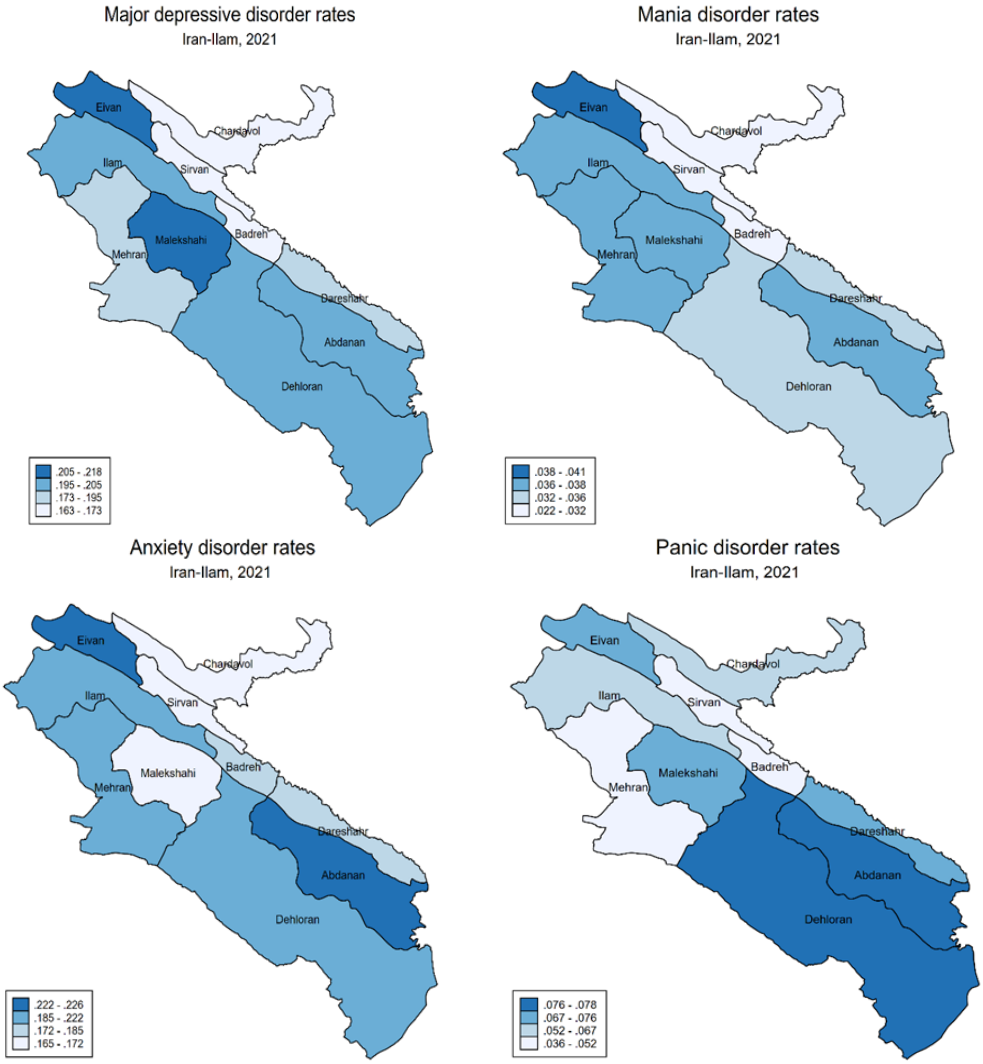
Table 2: The prevalence of mental disorders in Ilam province in various age groups and genders

Age groups/gender	Depression	Mania	Anxiety	OCD*	Phobia	Psychotic
	Prevalence (CI95%)	Prevalence (CI95%)	Prevalence (CI95%)	Prevalence (CI95%)	Prevalence (CI95%)	Prevalence (CI95%)
15-24 years	14.0 (7.08-15.1)	6.3 (5.9-7.3)	14.7 (12.1-16.8)	13.3 (9.04-15.15)	8.4 (6.9-11.1)	0.7 (0.01-5.9)
25-44 years	20.6 (18.2-22.3)	4.0 (2.6-9.1)	21.2 (16.2-18.2)	11.3 (9.13-14.2)	7.5 (6.9-11.1)	4.8 (3.6-6.3)
55-64 years	22.7 (20.2-24.3)	2.3 (1.4-2.9)	23.6 (20.3-25.2)	13.4 (8.1-16.1)	8.3 (7.9-11.3)	3.7 (1.2-5.7)
>65 years	23.6 (20.3-25.2)	0.4 (0.1-1.1)	35.5 (32.3-37.8)	9.7 (7.1-11.2)	9.7 (7.1-12.2)	22.6 (20.2-27.6)
Male	17.4 (15.1-19.6)	2.6 (1.3-8.7)	18.2 (15.2-21.1)	10.0 (8.1-12.4)	5.0 (3.7-8.2)	2.4 (1.4-4.1)

**OCD – Obsessive-compulsive disorder*

The results of the spatial analysis regarding the geographical distribution of mental disorders in Ilam province showed that depression, anxiety, and mania were more commonly observed in the northern compared to southern regions of the province, showing the highest prevalence in Ivan City. Also, panic disorder was more prevalent in southern cities of the province (Abdanan and Dehloran) than in other cities (Figure 2).

Figure 2: The results of spatial analysis. Geographical distribution of the most common mental disorders in Ilam province



DISCUSSION

The results of the present study showed that the highest prevalence of depression, anxiety, and psychotic disorders was observed in people over 65 years old. In this study, age showed a direct and significant correlation with having unsatisfactory mental health, indicating the importance of advancing age in the development of mental health problems such as depression, anxiety, and psychotic disorders. In other words, the incidence of mental health disorders increased with age, contradicting the findings of Heidari et al. [10] and Jafari et al. [11]. In recent studies, higher age was reported to be significantly associated with more favorable mental health. Other studies; however, have reported a significant relationship between mental health and advancing age, including a report by Visani et al. [12]. In another study, Noorbala et al. [13] noted that with increasing age, the likelihood of the development of mental disorders increased so the highest prevalence (49.9%) was related to people over the age of 65 years. Among the reasons for the higher prevalence of mental health disorders in older people can be retirement, menopause, loneliness-associated anxiety, and biological alterations. The results of these studies are generally consistent with our findings; nevertheless, some discrepancies can be explained by differences in the assessment tools employed and the age spectra of the studied populations.

The results of this study showed that the highest prevalence of panic disorder and obsessive-compulsive disorder was related to the age group of 15-24 years. Mental disorders in teenagers and young adults exacerbate the predicted future burden of diseases and adversely affect numerous life aspects, including educational performance, employment, income, personal relationships, and social participation, as well as workforce [14]. In a study in Brazil conducted on individuals aged 18 years and older, it was shown that younger people were more

vulnerable to mental problems [15]. In another study in Iran, Shirzadi et al. [16] declared a higher prevalence of these disorders in people aged 41 years or older compared to 18-40-year-old individuals.

Also, the results of the present study revealed a lower prevalence of depression and anxiety in women than in men. In a study, Falahzadeh and Momayezi [17], who investigated the prevalence of depression, anxiety, and stress in Yazd city of Iran, noted that depression, anxiety, and stress were more prevalent in women than in men, and this difference was statistically significant for anxiety (P=0.01) and stress (P=0.02), which was not consistent with our observation. We also noticed a higher prevalence of obsessive-compulsive disorders, phobia, and psychotic disorders in women compared to men, which was in agreement with the reports of Pendrez et al. [18], Kesler et al. [19], and Chang et al. [20]. The higher prevalence of mental disorders in women compared to men can be attributed to biological factors, gender-related differences, environmental and occupational stress, as well as limited sources of satisfaction and social participation of females.

Although in the present study, a significant portion of the urban population declared that they had unsatisfactory mental health conditions, this may not exactly match the clinical definition of adverse mental health. Therefore, the results of such subjective studies should not be regarded as a basis for judgment about the true condition of the mental health of respondents. Nevertheless, one should admit that a ratio of people, especially among women, suffer from some degree of mental health disorders. In this regard, the key measures that can be taken may be to initially achieve a correct understanding of the issue and then to implement comprehensive interventions for monitoring populations as large as possible, especially among vulnerable groups. Numerous viable strategies are available to maintain and improve public health. For example, unemployment has been pointed out as an important factor contributing to the development of mental health disorders [21]. So, an important intervention that governments can employ is to create more jobs, especially for youth, and to improve people's livelihoods as much as possible. Also, another effective measure for improving mental health is to remove the sources of distress, psychological pressure, and unnecessary tensions, which can be achieved with the help of mass media by nurturing a comfortable atmosphere. Moreover, the establishment of psychological counseling clinics can be among low-cost and beneficial measures to cover a large population, including young people, middle-aged, and elderly people, so that they can amend and improve their mental health.

CONCLUSIONS

The results of this study affirmed a relatively high prevalence of suspected mental health problems among people over 65 years of age, which is an alarming call,

requiring authorities and researchers to pay more attention to this issue and to identify and modify the factors affecting the mental health of these people. A unique observation in this study was the lower prevalence of anxiety and depression in women than in men. Also, we noticed that panic disorder and obsessive-compulsive disorder were most prevalent in the age group of 15-24 years. A reduction in the prevalence of mental disorders can enhance social liveliness. In this regard, increasing people's awareness of ways to reduce mental disorders, expanding psychological counseling centers across the city, the establishment of counseling phone lines, residing counselors and psychologists in public places such as mosques, expansion of parks and enjoyable environments, equipping parks with sports devices, and finally, encouraging people to use these services can help reduce depression and anxiety in society.

Conflicts of interest and sources of funding

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Authors' contribution

Conceptualization, E.N. and Y.V.; methodology, E.N.; formal analysis, H.S; investigation, Y.V.; data curation, F.M. and A.S; writing—original draft preparation, S.A.; and M.Kh.; writing—review and editing, S.A; F.M. and M.Kh. All authors have read and agreed to the published version of the manuscript.

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References:

1. Melnyk BM, Kelly SA, Stephens J, Dhakal K, McGovern C, Tucker S, et al. Interventions to improve mental health, well-being, physical health, and lifestyle behaviors in physicians and nurses: a systematic review. Am J Health Promot. 2020;34(8):929-41.

2. Butterworth P, Schurer S, Trinh T-A, Vera-Toscano E, Wooden M. Effect of lockdown on mental health in Australia: evidence from a natural experiment analysing a longitudinal probability sample survey. Lancet Glob Health. 2022;7(5):e427-e36.

3. Mehrabian F, Kashi S, Ganje Markieh Z. Investigating the Mental Health Status and Its Related Factors among the Students of Guilan

University of Medical Sciences. Res Med Educ. 2022;14(1):73-8.

4. Noorbala AA, Yazdi SAB, Faghihzadeh S, Kamali K, Faghihzadeh E, Hajebi A, et al. A Survey on mental health status of adult population aged 15 and above in the Province of Ma-zandaran, Iran. Arch Iran Med.. 2017;20(13):S83-S6.

5. Litz BT, Cummings MH, Grunthal B, McLean CL. A public health framework for preventing mental disorders in the context of pandemics. Cogn Behav Pract. 2021;28(4):519-31.

6. Noorbala AA, Nemani, F., Yahyavi dizaj, J., Anvari, S., & Mzhmoud Pourazari, M. Burden of Mental Disorders: A Study of the Middle East Countries for the Period 2000- 2017. J Med Counc Islam Repub. 2020;38(1):19-26

7. Rezaei N, Asadi-Lari M, Sheidaei A, Khademi S, Gohari K, Delavari F, et al. Liver cirrhosis mortality at national and provincial levels in Iran between 1990 and 2015: A meta-regression analysis. Plos one. 2019;14(1):e0198449.

8. Aryaie M, Sokout T, Moradi S, Abyad A, Asadollahi A. Frailty and Mental Health Disorders Before and During COVID-19 Occurrence in Older Population in Iran: A Longitudinal Re-peated-Measures Study. J Prim Care Community Health. 2022;13:21501319221126979.

9. Veisani Y, Delpisheh A, Mohamadian F. Prevalence and gender differences in psychiatric disorders and DSM-IV mental disorders: a population-based study. Biomed Res Ther. 2018;5(1):1975-85.

10. Heidari M, Ghodusi Borujeni M, Kabirian Abyaneh S, Rezaei P. The effect of spiritual care on perceived stress and mental health among the elderlies living in nursing home. J Relig Health.. 2019;58(4):1328-39.

11. Jafari N, Loghmani A, Montazeri A. Mental health of medical students in different levels of training. Int J Prev Med. 2012;3(Suppl1):S107.

12. Veisani Y, Delpisheh A, Mohamadian F, Valizadeh R. Trends of suicide attempts and completed suicide in Ilam province of Iran; A demographic analysis study. Bull Emerg Trauma. 2018;6(3):245.

13. Noorbala AA, Hajebi A, Faghihzadeh E, Nouri B. Mental health survey of the Iranian adult population in 2015. Arch Iran Med. 2017;20(3):128.

14. Barry MM. Addressing the determinants of positive mental health: concepts, evidence and practice. Int J Ment Health Promot. 2009;11(3):4-17.

15. Viana MC, Andrade LH. Lifetime prevalence, age and gender distribution and age-of-onset of psychiatric disorders in the São Paulo Metropolitan Area, Brazil: results from the São Paulo Megacity Mental Health Survey. Braz J Psychiatry. 2012;34:249-60.

16. Shirzadi M, Jozanifard Y, Eskandari S, Farhang S, Khazaei H. An epidemiological survey of psychiatric disorders in Iran: Kermanshah. Asian J Psychiatr . 2019;43:67-9.

17. Fallahzadeh H, Momayyezi M, Nikokaran J. Prevalence of depression, anxiety and stress in Yazd (2013). Tolooebehdasht. 2016;15(3):155-64.

18. Penders KA, Dierickx S, Steenhaut P, Dierckx E, Rossi GM. Epidemiological aspects of personality disorders in older adults. Tijdschr Gerontol Geriatr. 2020;51(2).

19. Kessler RC, Rubinow D, Holmes C, Abelson J, Zhao S. The epidemiology of DSM-III-R bipolar I disorder in a general population survey. The Science of Mental Health: Routledge; 2019. pp. 11-21.

20. Chang S, Abdin E, Shafie S, Sambasivam R, Vaingankar JA, Ma S, et al. Prevalence and correlates of generalized anxiety disorder in Singapore: Results from the second Singapore Mental Health Study. J Anxiety Disord. 2019;66:102106.

21. Mahmoud Tavousi, Ali Asghar Haeri Mehrizi, Akram Hashemi, Fatemeh Naghizadeh, Ali Montazeri. Mental health in Iran: a nationwide cross sectional study. Payesh Health Mon J. 2016;15(3):233-9.

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ORIGINAL ARTICLE

Investigating the Predictive Power of the Theory of Planned Behavior on the Behavioral Intention of Healthy Eating in Adolescents

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Abstract: *Background: Adolescence is a complex and sensitive period, and learning nutritional concepts during this period is very important. The purpose of the present study is to determine the predictive power of the theory of planned behavior on the behavioral intention of healthy eating in adolescents. Methods: 400 first-grade female students of Bandar Anzali participated in this descriptive-correlational study. Among the first secondary schools of this city, two schools were randomly selected and sampled by census method. The data collection tool was the healthy eating behavior questionnaire based on the theory of planned behavior, which included two sections of demographic information and the constructs of the theory of planned behavior, which were checked and confirmed with the content validity ratio, content validity index, and alpha coefficient. Data were analyzed using SPSS version 22 software. Results: Linear regression analysis showed that a total of 34% of the variance of healthy eating behavior intention is predicted by the constructs of perceived behavioral control and attitude. Conclusion: Considering the high predictive power of the theory of planned behavior in the field of healthy eating behavior, educational interventions based on it and centered on predictive structures are suggested.*

Keywords: *theory of planned behavior, healthy eating, adolescents*

INTRODUCTION

Non-communicable diseases (such as cardiovascular diseases, diabetes, cancer, high blood pressure, obesity, etc.) are the main cause of death worldwide [1]. Due to the increase in the death rate caused by these diseases, especially in developing countries, the World Health Organization (WHO) declared non-communicable diseases among the health priorities in developing countries two decades ago [2]. Iran, as an example of a middle-income country, accounted for 83.5% of all deaths and 78.1% of the total disease burden in 2019 due to non-communicable diseases [3-5].

The role of nutrition as the main cause of these diseases has been proven correctly [6]. In this regard, especially, the unhealthy eating behavior of teenagers is worrying [7]. Rapid growth, and changes in body composition, physiology, and endocrine system accelerate nutritional needs and increase the risk of malnutrition in this group [8]. Adolescents have more decision-making power and independence than children and are heavily influenced by friends, people around them, the environment, and various advertisements, and they turn to foods with an attractive and seductive appearance but lacking in nutritional value, many ready-made foods and snacks are among these materials [9]. Most of them do not consume enough fruits and vegetables, instead, they consume high-fat, energy-rich, and nutrient-poor foods [10].

According to the 2019 GSHS (Global School-based Student Health Survey), almost half of the countries reported that 10-30% of students aged 13-15 did not eat any fruit, a quarter reported that 10-30% of students did not eat any vegetables, and almost 70% of countries reported that at least half of their students eat junk food on a weekly basis and all countries have found that one in five students consumes carbonated drinks at least once a day [11].

Among Iranian teenagers, high consumption of junk foods and unhealthy snacks, not eating breakfast, and low consumption of fruits, vegetables, whole grains, and dairy products have been commonly reported [12] and this will cause them to develop chronic diseases in the future, especially girls who are considered as the future mothers and their eating behavior and learning nutritional concepts affect their own health and that of their children and families [13,14].

Modifying eating habits and behaviors during childhood and adolescence can prevent the occurrence of many non-communicable diseases in adulthood [15]. On the other hand, the future of any country depends on how it takes care of its children and teenagers. If action is taken to meet their health needs, the possibility that the adults of that society will have a healthy and valuable life pattern in the future will increase [16]. On the other hand, the future of any country depends on how it takes care of its children and teenagers. If action is taken to meet their health needs, the possibility that the adults of that society will have a healthy and valuable life pattern in the future will increase [17].

Studies show that the most effective educational programs are based on theory-based approaches that are rooted in behavior change patterns, and the "theory of planned behavior" is one of the well-known ones [18]. According to this theory, attitude, subjective norms, and perceived behavioral control affect the intention to perform a behavior [19]. A person's attitude is a favorable or unfavorable evaluation of behavior formed through past experiences.

Subjective norms refer to the social pressures perceived by the person who agrees or disagrees with the behavior and the media, family, and friends play a role in it. Finally, perceived behavioral control is a person's belief about how easy or difficult it is to perform a certain behavior [20]. According to the explanations provided, the present study was conducted with the aim of determining the predictive power of the theory of planned behavior on the behavioral intention of healthy eating in adolescents.

MATERIALS AND METHODS

This is a descriptive-correlational study, which was conducted in 2022. The research population was 400 first-grade high school girls in Bandar Anzali. From among the first high school girls in this city, two schools were randomly selected and sampled by census method. Inclusion criteria included: students' willingness to participate in research, lack of a special diet and not suffering from chronic diseases, and exclusion criteria were unwillingness to participate and continued cooperation by students.

The study was initiated with the permission of the ethics committee of Iran University of Medical Sciences and the necessary coordination with the education organization of Bandar Anzali city, the principals and officials of the relevant schools, and the informed consent of the students. The data collection tool was the healthy eating behavior questionnaire based on the theory of planned behavior [21].

This questionnaire includes two sections of demographic information and constructs of the theory of planned behavior. The first part of this questionnaire included 8 items related to demographic characteristics, including student age, height, weight, parent's education, parent's occupation, and household size. The second part or constructs of the theory of planned behavior consists of 32 items, and the third part, or food behavior part includes 7 items, based on the 5-point Likert scale each item, as (strongly disagree, disagree, no idea, agree, strongly agree) with a minimum and maximum score of 1 to 5. The second part of the questionnaire includes attitudes toward behavior with 12 items with an achievable score range of 12 to 60, 13 items for subjective norm with an achievable score range of 13 to 65, perceived behavioral control with 7 items with an achievable score range of 7 to 35, behavioral intention with 6 items with an achievable score range of 6 to 30. In the present study, due to the limitation of answer options for items in the questionnaire, which were 4-point Likert, the questionnaire was re-validated and reliable.

To assess the validity, content validity was used, so that the questionnaire was given to 10 health and nutrition experts, and its validity was confirmed with a content validity ratio (CVR) of 0.81 and a content validity index (CVI) of 0.8. To assess the reliability, Cronbach's alpha test method was used. For this purpose, a questionnaire was given to 20 female high school students. Cronbach's alpha coefficient was 0.85 for the attitude construct, 0.75 for the subjective norm construct, and 0.71 for the perceived behavioral control construct, 0.76 for the behavioral intention construct. Data analysis was done by SPSS software version 24.

RESULTS

In this study, the mean age of students was 14.9 ± 0.78 years. Their mean height and weight were 159.7 ±10.7 and 54.7± 1.4, respectively, and the household size was 4.1 ± 0.8. In terms of employment, the highest frequency was for fathers (45%) as self-employment and 86% of mothers were housewives. In terms of education, 42% of fathers and 45% of mothers were at the level of high school and high school diploma, each of which with the highest percentage of frequency. The mean, standard deviation, and range of obtainable scores for each construct of the theory of planned behavior in the studied students can be seen in Table 1.

Table 1: Mean, standard deviation, and range of obtainable scores for each of the constructs of the theory of planned behavior in the studied students

Variable	Mean ± SD‣	Rang of attainable score
attitude	40 ± 6.21	12-60
subjective norms	38.9 ± 6.44	13-65
perceived behavioral control	24.06 ± 6.44	7-35
behavioral intention	25.47 ± 9.21	6-30

‣*Standard Deviation*

Table 2 shows the results of Pearson correlation between the constructs of the theory of planned behavior that there is a direct and significant correlation between all constructs (attitude, subjective norm, and perceived behavioral control) with the intention of eating behavior (P<0.001). The construct of perceived behavioral control has the highest correlation with the intention of eating behavior (r=0.302).

The linear regression analysis in Table 3 showed that a total of 34% of the variance of the intention of healthy eating behavior in the studied students is predicted by the constructs of perceived behavioral control and attitude, and perceived behavioral control is the strongest construct related to the intention of eating behavior in this study.

Table 2: Correlation between the constructs of the theory of planned behavior

Variable	Attitude	Subjective norms	Perceived behavioral control	Behavioral intention
attitude	1			
subjective norms	0.191	1		
perceived behavioral control	0.276	0.145	1	
behavioral intention	0.182	0.255	0.302	1

Table 3: Predicting the behavioral intention of healthy eating based on the theory of planned behavior in the studied students

Model		B	Std. Error	Beta	sig
1	(Constant)	5.231	3.424	_	0.127
	attitude	0.157	0.070	0.113	0.024
	subjective norms	0.119	0.085	0.088	0.163
	perceived behavioral control	0.371	0.103	0.230	0.000

a. Dependent Variable: Intention of food behavior; b. R2 = 0.34

DISCUSSION

The present study was conducted with the aim of determining the predictive power of the theory of planned behavior on the behavioral intention of healthy eating in adolescents. The result of the study shows that a total of 34% of the variance of healthy eating behavior intention in the studied students is predicted by the constructs of perceived behavioral control and attitude, and perceived behavioral control is the first and strongest construct related to behavioral intention, which is consistent with studies predicting healthy eating in Danish adolescents [22] and the results of the study by Seo et al in Seoul, which implies a significant relationship between behavioral intention and perceived behavioral control construct [23]. It is also consistent with the findings by Yarmohammadi et al. [24] and Dunn et al. [25] on junk food consumption based on the theory of planned behavior. However, it is not consistent with the findings of Ickes et al. [26] on beverage consumption and the findings of Gholami et al. [27] on fruit and vegetable consumption. Perceived behavioral control may not predict behavior when a person has little information or the resources available to the person change and when new elements such as eating habits are added to the situation [28, 29].

The second construct predicting the intention of healthy eating behavior in this study is the attitude, which is consistent with the results of the study by Mousavi et al. [30] concerning beverage consumption and the study by Gronhoj et al. [22] regarding the prediction of healthy eating behavior and the study by Mamun et al. [31] on the determinants of healthy eating. Attitude shows an individual's general feeling about the desirability or undesirability of something, and sometimes people's attitude during life as well as sufficient awareness and knowledge, which is a prerequisite for attitude change, leads to the intention of performing the desired behavior in the future [27]. Therefore, the attitude that originates from feelings and internal factors can affect his eating behavior by increasing his information and experiences concerning nutrition.

In this study, the subjective norm is not a predictor of eating behavior intention, which is similar to the finding by Ismawati

et al. [32] on the application of the theory of planned behavior in the intention of healthy eating in Malaysia and the study of Brouwer et al. [33] related to healthy eating behavior prediction and finding by Dehdari et al. [34] regarding the consumption of unhealthy foods. However, it is inconsistent with the findings of Khorasani et al. [35] on unhealthy food consumption and White et al. [36] regarding intention to consume low-fat food. The reason for this inconsistency can be the difference in the gender of the participants, in the study of Dehdari et al. [34], as in the present study, the target group is girls, and in the study of Khorasani et al. [35], boys are the target group. On the other hand, diverse food cultures and customs in Iran and other countries of the world can be the reason for the discrepancy of these studies. The diversity and complexities of health behaviors in different groups and in different conditions can lead to the necessity of planning to use the appropriate theories and structures to achieve success in interventions in health education and health promotion.

CONCLUSIONS

Perceived behavioral control and attitude are among the factors predicting on the behavioral intention of healthy eating in the studied students. The research limitation in the present study was the use of self-reporting, and it is necessary to carry out educational interventions based on the "theory of planned behavior" with emphasis on the two predictive constructs mentioned.

Conflicts of interest and sources of funding

The personal interests of the authors were not related to the results of this research. The authors declare that they have no competing interests. This study did not receive any grant from funding agencies.

Authors' contribution

All authors were responsible for the study. EA, MM, and TD were accountable for the study Conceptualization and led the writing of the paper. BI conducted the Literature review and assisted in writing the paper. MM and OS performed the Statistical analysis, assisted in interpreting the data, and wrote the paper. OS, FSI, and EA assisted with the interpretation of the results and drafting of programmatic Implications. FB and MM were responsible for data collection and coordination of the study. TD co-led the conceptualization, supervised all aspects of writing the paper, and provided extensive comments on the manuscript. All the authors have read and approved the final manuscript.

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Ethics approval and consent to participate

This article is taken from the approved research project of Iran University of Medical Sciences with ethics code number: 1401.886 IR.IUMS.REC. Informed consent was obtained from all individual participants included in the study before conducting.

Consent to publish

All participants consented verbally to the publication of the interview data.

References:

1. Terzic A, Waldman S. Chronic diseases: the emerging pandemic. Clinical and translational science. 2011;4(3):225.

2. Esteghamati A, Larijani B, Aghajani MH, Ghaemi F, Kermanchi J, Shahrami A, et al. Diabetes in Iran: prospective analysis from first nationwide diabetes report of National Program for Prevention and Control of Diabetes (NPPCD-2016). Scientific reports. 2017;7(1):1-10.

3. Khosravi Shadmani F, Farzadfar F, Larijani B, Mirzaei M, Haghdoost AA. Trend and projection of mortality rate due to non-communicable diseases in Iran: A modeling study. PloS one. 2019;14(2):e0211622.

4. website GHDE. Global Burden of Disease Study 2019 (GBD 2019) results. Institute for Health Metrics and Evaluation (IHME), University of Washington …; 2019.

5. Aminorroaya A, Fattahi N, Azadnajafabad S, Mohammadi E, Jamshidi K, Rouhifard Khalilabad M, et al. Burden of non-communicable diseases in Iran: past, present, and future. Journal of Diabetes & Metabolic Disorders. 2020:1-7.

6. Organization WH. World health statistics 2015 2015 [Available from: https://apps.who.int/iris/handle/10665/170250.

7. Bauer KW, Larson NI, Nelson MC, Story M, Neumark-Sztainer D. Fast food intake among adolescents: secular and longitudinal trends from 1999 to 2004. Preventive medicine. 2009;48(3):284-7.

8. Alam N, Roy SK, Ahmed T, Ahmed AS. Nutritional status, dietary intake, and relevant knowledge of adolescent girls in rural Bangladesh. Journal of health, population, and nutrition. 2010;28(1):86.

9. Kavey R-EW, Daniels SR, Lauer RM, Atkins DL, Hayman LL, Taubert K. American Heart Association guidelines for primary prevention of atherosclerotic cardiovascular disease beginning in childhood. Circulation. 2003;107(11):1562-6.

10. Savige GS, Crawford D, Worsley A, Ball K. Food intake patterns among Australian adolescents. Asia Pacific journal of clinical nutrition. 2007;16(4):738-46.

11. Organization WH. The state of food security and nutrition in the world 2019: safeguarding against economic slowdowns and downturns: Food & Agriculture Org.; 2019.

12. Akbari F, Azadbakht L. A systematic review on diet quality among Iranian youth: focusing on reports from Tehran and Isfahan. Archives of Iranian medicine. 2014;17(8):0-.

13. Rahmati-Najarkolaei F, Tavafian SS, Fesharaki MG, Jafari MR. Factors predicting nutrition and physical activity behaviors due to cardiovascular disease in tehran university students: application of health belief model. Iranian Red Crescent Medical Journal. 2015;17(3).

14. Pirzadeh A, Hazavei MM, Entezari MH, Hasanzadeh A. The effect of educational intervention on girl's behavior regarding nutrition: Applying the beliefs, attitudes, subjective norms, and enabling factors.

Journal of education and health promotion. 2014;3.

15. Cullen KW, Baranowski T, Rittenberry L, Cosart C, Hebert D, de Moor C. Child-reported family and peer influences on fruit, juice and vegetable consumption: reliability and validity of measures. Health Education Research. 2001;16(2):187-200.

16. Stanhope M, Lancaster J. Community & public health nursing: Mosby St. Louis; 2004.

17. Sharifirad G, Entezari MH, Kamran A, Azadbakht L. The effectiveness of nutritional education on the knowledge of diabetic patients using the health belief model. Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences. 2009;14(1):1.

18. Kirby D, Obasi A, Laris B. The effectiveness of sex education and HIV education interventions in schools in developing countries. Technical Report Series-World Health Organization. 2006;938:103.

19. Ajzen I. Perceived behavioral control, self-efficacy, locus of control, and the theory of planned behavior 1. Journal of applied social psychology. 2002;32(4):665-83.

20. Ajzen I, Madden TJ. Prediction of goal-directed behavior: Attitudes, intentions, and perceived behavioral control. Journal of experimental social psychology. 1986;22(5):453-74.

21. Taghipour A, Miri MR, Sepahibaghan M, Vahedian-Shahroodi M, Lael-Monfared E, Gerayloo S. Prediction of eating behaviors among high-school students based on the constructs of theory of planned behavior. Modern Care Journal. 2016;13(4).

22. Grønhøj A, Bech-Larsen T, Chan K, Tsang L. Using theory of planned behavior to predict healthy eating among Danish adolescents. Health Education. 2013.

23. Seo H-s, Lee S-K, Nam S. Factors influencing fast food consumption behaviors of middle-school students in Seoul: an application of theory of planned behaviors. Nutrition research and practice. 2011;5(2):169-78.

24. Yarmohammadi P, Sharifirad GR, Azadbakht L, Morovati SMA, Hassanzadeh A. Predictors of fast food consumption among high school students based on the theory of planned behavior. 2011.

25. Dunn KI, Mohr P, Wilson CJ, Wittert GA. Determinants of fast-food consumption. An application of the theory of planned behaviour. Appetite. 2011;57(2):349-57.

26. Ickes MJ. Predictors of behaviors related to obesity using the theory of planned behavior in seventh and eighth grade students: University of Cincinnati; 2010.

27. Safoura G, Esfandiar M, Yasanallah P, Korosh S. Evaluating the predictors of fruit and vegetable consumption behavior in Ilam based on constructs of developed planned behavior theory. 2014.

28. Ajzen I, Driver BL. Prediction of leisure participation from behavioral, normative, and control beliefs: An application of the theory of planned behavior. Leisure sciences. 1991;13(3):185-204.

29. Ajzen I. The theory of planned behavior. Organizational behavior and human decision processes. 1991;50(2):179-211.

30. Mousavi SM, Sharafkhani N, Didarloo P, Didarloo A. Using the theory of planned behavior to explain intent to consume sugar-sweetened beverages among secondary school students. International Journal of Pediatrics. 2019;7(5):9413-22.

31. Mamun AA, Hayat N, Zainol NRB. Healthy eating determinants: A study among Malaysian young adults. Foods. 2020;9(8):974.

32. Sharkawi I, Latip, M., & Mohamed, Z. A. Applying the Theory of Planned Behavior to Healthy Eating Intention among Malaysian Adults. International Journal of Academic Research in Business and Social Sciences. 2021;11:17-26.

33. Brouwer AM, Mosack KE. Expanding the theory of planned behavior to predict healthy eating behaviors: Exploring a healthy eater identity. Nutrition & Food Science. 2015.

34. Dehdari t, Chegni m, Dehdari l. Application planned behavior in theory predicting Junk Food consumption among female students. Preventive Care In Nursing & Midwifery Journal. 2013;2(2):18-24.

35. Khorasani EC, Peyman N, Moghzi M. Application of the Theory of Planned Behavior to predict low-nutrient junk food consumption among male students. Journal of Health Sciences and Technology. 2017;1(2):75-9.

36. White KM, Terry DJ, Troup C, Rempel LA, Norman P. Predicting the consumption of foods low in saturated fats among people diagnosed with Type 2 diabetes and cardiovascular disease. The role of planning in the theory of planned behaviour. Appetite. 2010;55(2):348-54.

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ORIGINAL ARTICLE

A Conceptual Analysis of Post-psychotic Depression

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Abstract: *The conundrum of post-psychotic depression (PPD) is still present in the psychiatric literature, for more than a century since it was first described by Mayer-Gross. After a short existence in the DSM-IV and ICD-10, this nosological construct was excluded from newer versions of the mental disorders classifications. Therefore, an exploratory analysis of the PPD concept was considered useful both from clinical and theoretical perspectives. There is a high prevalence of depressive symptoms in patients with schizophrenia spectrum disorders (SSD) and, although not all of them represent cases of PPD, they are considered risk factors for suicide. The arguments and contra-arguments for/against PPD were reviewed, and the potential pharmacological interventions for this disorder were analyzed. The explored evidence indicates that PPD is worth further investigation, and in order to differentiate it from schizoaffective disorder, negative symptoms of SSD, or depressive manifestations within the acute psychotic episodes, clearly defined criteria should be found. The use of validated scales, like the Calgary Depression Scale for Schizophrenia and the InterSePT Scale for Suicidal Thinking, is recommended for the initial assessment of depression and suicidal risk in patients with SSD, but also for their monitoring during the acute and maintenance phases. Besides the administration of combined, antidepressant and antipsychotic treatment, the use of clozapine, and the recommendation to initiate treatment for SSD with atypical antipsychotics whenever possible, there is a dearth of studies exploring specific interventions for PPD. Future studies are expected to address the validity of the nosological construct of PPD and the most adequate therapeutic and prophylactic interventions in patients with SSD.*

Keywords: *post-psychotic depression, schizophrenia spectrum disorders, atypical antipsychotics, clozapine, typical anti-psychotics, antidepressants*

INTRODUCTION

Depression that may appear in the context of schizophrenia is considered a complex and heterogeneous group of disorders [1,2]. Mayer-Gross was the first author who described in 1920 the reaction to a psychotic experience that manifests itself as a clinical version of depression [3]. He considered "despair" as the main clinical characteristic of this depression that follows a full-blown psychotic episode, and considered this manifestation to be determined by the patient's increased awareness about the severity of his/her illness [3,4]. A few decades later, Semrad also explored the psychodynamic mechanisms for post-psychotic depression (PPD), emphasizing the denial, projection, and distortion of reality after the remission of acute psychotic episodes [5]. PPD was described by several authors as "retarded depression, with strong neurasthenic and schizoid components" emerging after the patient is discharged from the hospital, and often ignored by mental health specialists [6]. Depressive manifestations in patients with SSD have been conceptualized as a psychological reaction to acute psychosis, as previously mentioned, but also as a comorbidity of two distinct pathologies or a proof for the existence of a continuum between schizophrenia and mood disorders [2]. According to psychoanalysts, PPD is a reaction to psychosis, which appears after the remission of the psychotic episode, more specifically, after the Ego regained a significant proportion of its strengths [7,8].

Some authors, however, reported, based on the analysis of the temporal relationship between the onset of depressive and psychotic symptoms in 27 patients, that the first reports on mood manifestations were frequently at the same time same as the onset of psychosis [9]. Therefore, PPD is a controversial concept, as no specific pattern for its onset could be detected, leading to the assumption that depressive manifestations may be only associated with acute psychotic manifestations.

However, a series of studies focused on PPD have tried to delineate the risk factors, clinical features, and prognosis of this nosological entity, as a distinctive pathology from depressive symptoms belonging to acute schizophrenia, mood episodes within a schizoaffective disorder, or adverse events of the antipsychotics or other drugs. For example, a comparison of patients with schizophrenia presenting or not with PPD (N=30 participants in each group) showed that belonging to elementary (or nuclear) families, longer duration of psychotic phase, more frequent hospitalizations, and more sadness and anxiety-somatization during the acute phase of the disease were associated with PPD [10]. A past history of depression was also more frequently reported in the study group vs. controls [10]. Age of onset, sadness during the acute psychosis phase, premorbid adjustment, social support, and life events were significant determinants of severity for PPD, according to the multiple regression analysis [10].

A cohort study with a 10-year follow-up compared the evolution of 29 patients with schizophrenia and PPD vs. only schizophrenia [11]. Patients with PPD presented at an older age with the onset of schizophrenia and more auditory hallucinations; also, they were admitted more often, but their hospitalizations were of shorter duration [11].

A study that explored the main clinical differences between primary depression (N1= 98 patients) and PPD (N2= 71 patients) concluded that depressed mood, reduced energy, and pathological guilt were more frequently detected in patients with primary depression, while sleep disturbance and ideas of reference with a theme of guilt were more consistently associated with PPD [1].

The duration of PPD was estimated by different authors as varying between several days to several months [12], or, more specifically, between 2 and 26 weeks [8].

Depressive symptoms during a psychotic episode may be as frequent as 50%, and they may correlate with the frequency of relapses, defined by re-admission rate and total length of inpatient treatment [13]. By comparison, the prevalence of PPD reported in the literature was around 30-36% [14,15]. Higher rates of PPD were reported in patients with a first episode of psychosis (FEP), up to 50% [3,15]. Older age, a higher familial load of psychoses, a longer duration of untreated psychosis, the presence of an FEP, and a higher number of stressful life events were associated with a higher risk of PPD [14]. Depression was reported by patients with FEP as being linked to the psychotic experience and to the process of recovering from this experience [16]. Feelings of shame, doubt, and embarrassment, but also loss and social isolation, were associated with the presence of the psychotic experience [16]. Also, the onset of PPD has been correlated to the existence of positive symptoms during acute schizophrenia, especially delusions and hallucinations [17]. A study that enrolled 44 patients (aged 10-40 years) with schizophrenia, all of them during their first six months of the illness, explored the risk of developing PPD one year after discharge from the hospital [18]. Four patients were diagnosed with depression in this interval, according to a Hamilton Depression Rating Scale (HAMD) score ≥17 [18]. Only one case recovered from PPD completely during the follow-up [18]. All patients in this trial were undergoing phenothiazine treatment throughout the monitoring period [18].

In a longitudinal study, 17 patients with schizophrenia were monitored for 6 months, using the 18-item Profile for Rating Depressive and Schizophrenic Behavior (PRDSB) [19]. After recovering from acute psychosis, only 2 participants developed major depressive syndrome [19]. However, over 40% of these patients were interviewed only by telephone after their discharge, so a potential bias regarding the sensitivity of the assessment method can not be excluded [19]. Also, the ethnic homogeneity of the study group could be construed as another potential bias that limits the generalizability of the results.

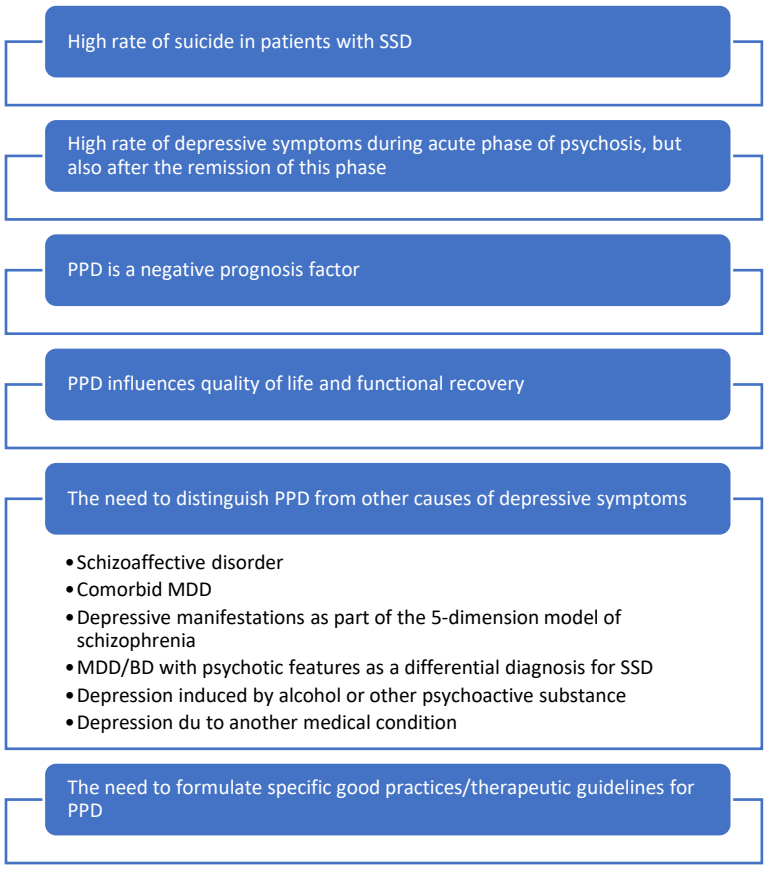
A longitudinal, observational study (N=105 patients with schizophrenia) reported during 12 months of monitoring that depression accompanied acute psychosis in 70% of cases, and remitted together with psychosis, while PPD appeared in 36% of these patients, without a concomitant increase in psychotic symptoms [20].

Focusing the analysis of the PPD concept on the most renowned classifications of mental disorders, this pathology was mentioned for the first time in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV), published in 1994 [21]. PPD, according to the cited source, involves the presence of “a Major Depressive Episode that is superimposed on and occurs only during the residual phase of schizophrenia” [21]. The definition of PPD required in the DSM-IV the presence of depressed mood, as a core symptom, and excluded the direct consequences of drug abuse, medication use, or a general medical condition [21]. However, in the fifth edition of the DSM, published in 2013, this nosological entity no longer appears [22].

The tenth edition of the International Classification of Diseases, edited by the World Health Organisation (ICD-10) in 1993, grouped PPD (named "post-schizophrenic depression") together with different types of schizophrenia, in the same chapter, coded F20 [23]. The definition of PPD was "a depressive episode, which may be prolonged, arising in the aftermath of a schizophrenic illness" [29]. It is important, according to the ICD-10, that residual schizophrenic symptoms still be present, although they cannot dominate the clinical status [23]. Newer versions of ICD-10 placed PPD in the category of "other specified depressive episodes" [24]. The latest edition of ICD (ICD-11), the first version published in 2019, did not reference PPD [25].

The convoluted trajectory of the PPD concept from its genesis to the present day is rather difficult to explain, but several important factors contributing to this conundrum represent the main objective of the current review (Figure 1).

Figure 1: Rationale for exploring post-psychotic depression



PPD= postpsychotic depression, SSD= schizophrenia spectrum disorders, MDD= major depressive disorder

The rationale for conducting this review derives from several important clinical and theoretical aspects. First, it is essential to obtain adequate control over depressive symptoms in patients with SSD, because of the high rates of suicide reported in this population [26]. PPD seems to be a factor for negative prognosis in the long-term for patients with schizophrenia, especially because of the higher risk for suicide, but also due to its significant impact on the quality of life and general well-being [17]. Second, the need to delineate clinically PPD from other causes of depression in patients with SSD, in order to find the most adequate therapeutic strategies. To support this, the data presented suggest that PPD is a distinct nosological entity from antipsychotic-induced adverse events, negative symptoms of schizophrenia, depression with psychotic symptoms, or schizoaffective disorders [14,17]. This means that good clinical practices in patients with SSD would involve differentiating between PPD and other frequently reported confounding factors.

THE MULTIFACETED CONSTRUCT OF PPD

Although the history of PPD has been over a century, there is a dearth of good-quality studies exploring this pathology's

clinical and epidemiological aspects. However, an analysis of the main dimensions of the PPD construct can be done, based on the available evidence (Table 1).

Table 1: Pros and cons in the analysis of the PPD construct

Pros	Cons
PPD was associated with any type of antipsychotic treatment, therefore it is not an adverse event to the first generation antipsychotics	PPD does not exist because it consists of adverse effects of older antipsychotics
There are longitudinal studies that confirm the persistence of depressive symptoms after the remission of acute psychosis and cases where depression followed a period of psychosis remission	The construct should not be treated as a distinct entity, it only accompanies acute schizophrenia
Negative symptoms and depression do not overlap to the point they are indistinguishable	Negative symptoms cover the presence of depression, therefore depression may be observed only after the remission of those symptoms
There are specific scales for measuring depression in patients with SSD, as well as their suicide risk	PPD can not have its own diagnosis criteria and its severity can not be determined, due to the fact that it is secondary to other symptoms

To begin with the presentation of the reasons why PPD is not yet a fully recognized diagnosis, it must be specified that PPD was correlated by different authors with the effects of first-generation antipsychotics, and they called this phenomenon "pharmacological depression" [27-29]. In a multicenter study (N=211 patients with schizophrenia), depression (quantified with HAMD) was detected in 25% of the cases, all of them treated with fluphenazine (either hydrochloride or decanoate) [30]. This study also showed that depression was associated with a more chronic psychiatric history and a higher rate of relapse [30]. Also, older drugs used to treat SSD, such as chlorpromazine or reserpine, have been associated with lethargy, psychomotor retardation, and anergy, which are acknowledged adverse events of these agents [30].

Secondly, the negative symptoms of schizophrenia may cover the depressive symptoms, making them more difficult to detect [14,17]. Anhedonia, defined as a reduced ability to experience pleasant emotions, is considered both a negative symptom in SSD, and a central manifestation in major depressive disorder (MDD) [31-34]. Therefore, it is considered "a transdiagnostic symptom", and its explained by dysfunctions of the reward and aversion pathways in the central nervous system (CNS) [31]. Furthermore, negative symptoms like alogia and avolition may prevent the detection of depressive symptoms, because they interfere with both the interview and the observation of the patients.

The third aspect refers to a contradiction: although current diagnostic classifications do not include mood symptoms in the core criteria for schizophrenia, these are frequently considered part of the clinical picture, as additional manifestations [35]. According to the five-dimension model of schizophrenia, depression is a core clinical component, together with the positive, negative, agitation-excitement, and disorganization symptoms [36]. However, as mentioned in the introductory chapter, there is no reference to PPD in the latest versions of the ICD or DSM [22,25].

The fourth facet of the PPD controversy is represented by the fact that although differentiating between schizophrenia, schizoaffective disorder, and depressive/bipolar disorder with psychotic features is quintessential, in clinical practice it is frequently difficult to make the right diagnosis. Factorial analysis using validated instruments for psychosis and mood symptoms measurement (e.g., Positive and Negative Syndrome Scale – PANSS, Young Mania Rating Scale – YMRS, Montgomery Depression Rating Scale – MADRS, and Calgary Depression Scale – CDSS) confirmed the existence of very complex structure of the clinical manifestations in patients with schizophrenia [37]. Subclinical mood symptoms have been confirmed by this type of analysis, structured within up to 15 factors – e.g., positive, negative, somatic, anxiety, neurocognitive, disorganization and manic, depressive, psychomotor agitation, hostility/violence [37]. These results support the overlapping model of phenotypes between psychotic mood disorders and SSD, and the possibility of misdiagnosing a patient with a mood disorder and associated psychotic features as having an SSD [37].

However, each of these confounding factors may be addressed. The first argument is precarious because even SSD patients treated with newer antipsychotics may develop depressive symptoms and the effect of these pharmacological agents on depressive symptoms is only small to medium [38]. According to a Cochrane review, based on five reports about

patients diagnosed with both schizophrenia and depression, there was no significant difference in efficacy (evaluated by PANSS scores) between quetiapine and haloperidol, sulpiride was significantly superior to chlorpromazine (reflected in the severity of depressive symptoms), and clozapine was superior to the association of another antipsychotic and an antidepressant (moclobemide/mianserin) [39]. A significant reduction of depressive symptoms in patients with schizophrenia was reported only if a CDSS score at baseline was ≥5, unlike the positive, negative, and general symptoms (scored with PANSS), in a naturalistic study that enrolled adult patients with ≥2 years of treatment with clozapine (N=23) or other atypical antipsychotics (N=23) [40]. At the follow-up visit, patients who received other antipsychotics led o superior results when compared to clozapine on depressive symptoms, but only when the analysis was limited to those with clinically relevant depression [40]. It can easily be deduced that the results of studies exploring the impact of antipsychotics on depressive symptoms in SSD are quite heterogenous, varying from no difference in outcomes between typicals and atypicals, to superiority of clozapine vs. other antipsychotics combined with antidepressants, and to superiority of other atypicals to clozapine, but only in certain subpopulations.

The second argument is even more difficult to support because authors exploring PPD showed that this syndrome "is usually stable phenomenologically, often lengthy, and may be resistant to all treatment modalities" [6]. Even considering the last part as an exaggeration determined by the lack of adequate therapeutic resources when that statement was formulated, there is still enough ground to back up an independent syndrome, with pharmacological and clinical peculiarities. There are authors that contradict the third argument, stating that depression is "a frequent comorbidity in the course of schizophrenia" [7], and not just a cluster of symptoms intrinsic to SSD.

The fourth argument can also be easily disqualified because there are validated instruments, currently in clinical use, that allow for the monitoring of depressive symptoms in patients with SSD. CDSS is an instrument created by Addington et al., first published in 1990, for the purpose of measuring depression in SSD, starting from selected items within HAMD and Present State Examination (PSE) [41]. This instrument was validated on 50 patients with acute psychosis, and it has 11 items, with a Cronbach's alpha of 0.84-0.89 [41,42]. The validity of CDSS in evaluating mood symptoms in patients with SSD was confirmed by subsequent studies and reviews, and this scale was significantly correlated with HAMD and MADRS [43,44]. CDSS differentiated depressive symptoms from other clinical manifestations of SSD and also had good predictive validity [44]. Another study comparing CDSS and HAMD (N=119 in-patients with acute schizophrenia) concluded that CDSS had a higher sensitivity than HAMD in assessing mild or severe depression, while the specificity was comparable high for both instruments [45].

The InterSePT Scale for Suicidal Thinking (ISST) has 12 items and was created to assess suicidal ideation in SSD patients [46]. Two validation studies (N=22 and 980 patients with SSD) confirmed that ISST is reliable and valid if used to assess ongoing suicidal ideation in patients with SSD [46]. Both ISST and CDSS can be used to provide information necessary in the case management of patients with SSD and suicidal risk [47].

Based on its properties, CDSS is considered a first-line instrument to determine the severity of depressive symptoms in patients with SSD, and a review that compared 6 different instruments targeting the same symptoms formulated this recommendation [44]. A study that explored the diagnosis of major depressive episodes in 84 patients with schizophrenia found that CDSS was superior to the Beck Depression Inventory (BDI), HAMD, and PANSS-D when evaluating the Receiver Operating Characteristics (ROC) curves [48].

However, the possibility that PPD symptoms may be, in fact, the continuation of depressive symptoms with onset in the acute psychotic phase, can not be completely excluded [7]. On the other hand, if PPD is detected after a period of psychotic symptoms remission, then it may be considered part of a new episode of schizophrenia [7].

PPD may be confounded with negative symptoms of SSD, as previously mentioned. The discussion about primary and secondary negative symptoms is a very complex topic, that clearly exceeds the objective of this paper. As a general definition, primary negative symptoms are intrinsic to schizophrenia, a specific clinical dimension, while secondary negative symptoms derive from the presence of positive symptoms, depression, antipsychotics' pharmacodynamical properties, substance use disorders (SUDs), and social withdrawal [49-51]. After the remission of psychotic symptoms, the depressive symptoms were still present, although their rate decreased from 60% during the acute psychotic episode, to 40% after 5 years follow-up [52].

In conclusion, a correct diagnosis of PPD should include a clinical and psychometric evaluation of psychotic and depressive symptoms, a thoroughly-conducted screening for comorbidities (organic, toxic, or psychiatric) [53-55], an analysis of the risk factors for the persistence of depressive symptoms [56,57], a clear collection of personal medical history (in order to establish the temporal succession of psychotic and depressive manifestations), and an accurate pharmacological anamnesis.

THERAPEUTIC INTERVENTIONS FOR PPD

Adapting the type and dosage of antipsychotic agents in patients with SSD was signaled by different authors as a method to decrease the risk of PPD [2]. Re-evaluation of the main drugs administered during the acute phase of psychosis or the prescription of adjuvant antidepressants or ECT has also been suggested as a case management strategy in PPD [2]. Psychotherapeutic, social, and institutional support are useful options for patients with PPD [2].

A review (n=20 articles) exploring the results of available pharmacological and psychosocial treatments of PPD after the first episode of psychosis did not find support for one intervention in favor of another [58]. Online psychotherapy and treatment with ω-3 polyunsaturated fatty acids (PUFA) have been associated with some favorable results [58].

Olanzapine (5-15 mg/day) was compared to risperidone (4-8 mg/day) in the treatment of PPD (according to the DSM IV criteria) in patients with schizophrenia (N=76), and a clinically significant decrease in MADRS scores (-4 points vs. baseline) was reported after 8 weeks of treatment with either antipsychotic [59]. This study used a randomized, double-blind, parallel-group design. The comparative analysis of the two interventions did not detect any significant MADRS differences at the end-point [59]. A high response rate (≥20% reduction in MADRS scores) was observed during antipsychotic treatment [59]. In order to control for possible confounders of PPD, patients with akinetic symptoms were excluded from this trial [59]. The same team reported on another randomized, placebo-controlled trial, with 24 patients diagnosed with schizophrenia or schizoaffective disorder and PPD or negative symptoms, who continued their six-month adjunctive imipramine to fluphenazine decanoate/ benztropine mesylate treatment or were tapered to placebo + fluphenazine decanoate/benztropine during one year [60]. More patients receiving a placebo relapsed into PPD, at a statistically significant level; also, patients who received placebo experienced relapses into psychoses [60]. Yet another trial conducted by the same team showed that double-blind, controlled discontinuation of imipramine after stabilization (N=14 participants with schizophrenia undergoing treatment with fluphenazine + benztropine) led to relapse into PPD in all patients with placebo vs. only two out of eight in the antidepressant-receiving group (significant difference, p=0.009) [61].

A controlled trial investigated the effects of imipramine hydrochloride for PPD for six weeks, in a double-blind manner [62]. All patients (N=33) were diagnosed with schizophrenia or schizoaffective disorder and received a stable dosage of fluphenazine decanoate and one week-trial with benztropine mesylate was initiated to rule out akinesia; all participants were either non-psychotic or only residually psychotic at baseline [62]. The PPD diagnosis was based on current major or minor depression for at least four weeks, and a HAMD score ≥12 for at least three consecutive weeks [62]. The depressive symptoms (according to HAMD and SADS, Schedule for Affective Disorders and Schizophrenia scores) were controlled better with imipramine vs. placebo and their global clinical status (according to the CGI scores) also improved more consistently in patients receiving the active drug [62]. The psychotic symptoms and tolerability profile did not change significantly between groups [62]. The use of adjunctive imipramine to fluphenazine was further explored by the same team, in a larger and more heterogenous study group [63]. The positive effects of the combined treatment were still detected in the total sample, but the significance of the results was lower [63]. These differences were explained in a post-hoc analysis by the higher level of psychotic symptoms severity, and by "more refractoriness of depression" due to failed previous trials of antidepressants [63].

In a continuation trial, four out of five patients previously stabilized on imipramine + fluphenazine decanoate + benztropine for PPD relapsed into depression six months after the tapering of the antidepressant [64]. The control group, consisting of four patients who did not discontinue imipramine, did not present depressive relapses [64]. The same research team reported on ten PPD patients with good responses to imipramine who relapsed six months after discontinuation of the antidepressant, that was added to fluphenazine decanoate and benztropine [65].

A 24-week double-blind trial compared haloperidol (mean dose 17.5 mg/day) and thiothixene (mean dose 31.8 mg/day) in 46 outpatients with schizophrenia, from their efficacy and safety properties [66]. One of the outcomes was the incidence of treatment-emergent depression, assessed by the Hamilton Depression Rating Scale (HAMD) and Zung Self-Rating Depression Scale (ZSRS) [66]. Haloperidol was superior to thiothixene on the "cognitive disturbance" HAMD factor [66]. Clinically significant symptoms were reported in five patients treated with haloperidol and three receiving thiothixene [66]. The impact on the psychotic symptoms was also more important for haloperidol, according to the Brief Psychiatric Rating Scale (BPRS) scores [66].

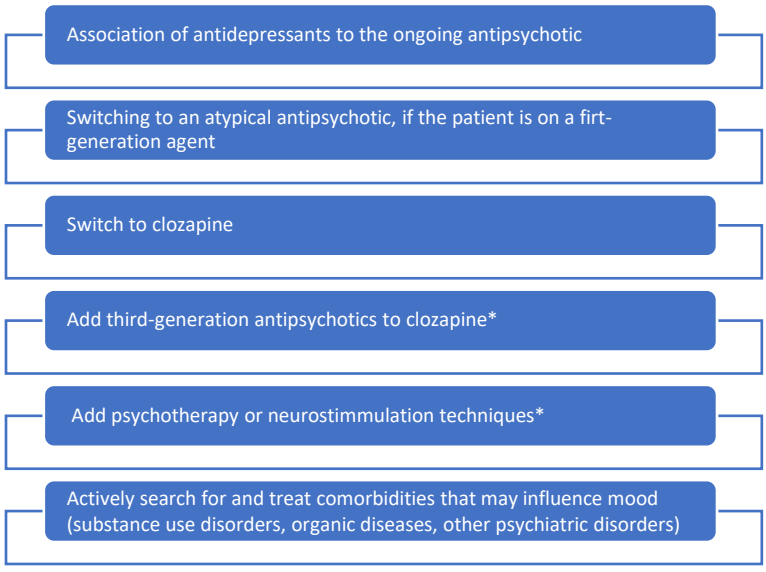
In a trial that compared the antidepressant effects of fluphenazine decanoate (mean dose 32.8 mg fortnightly) and flupenthixol decanoate (mean dose 36.9 fortnightly) administered two-weekly in a group of 48 out- and inpatients with schizophrenia during 15 weeks [67]. No significant differences could be found between groups regarding the number and severity of mood impairments and depression

[67]. Nineteen patients developed depression, and the addition of clomipramine was necessary for five participants, with a mean duration of four weeks, and an average dose of 75 mg/day [67]. The onset of depressive symptoms was reported between days 14 and 70 for outpatients and between days 7 and 77 for inpatients [67]. The onset of depression was unrelated to the antipsychotic dose [67]. The instruments used to assess depression in this trial were HAMD, von Zeersen's self-evaluation scale, and AMP-system [67].

According to a review of 7 studies focused on the use of antidepressants in patients with SSD, tricyclic antidepressants administered in combination with first-generation antipsychotics are a safe choice after the acute psychotic phase is controlled [68]. The risk of exacerbating residual psychotic symptoms is considered minimal by the authors of that review [68]. Still, these antidepressants were ineffective against anergy, considered a core symptom of PPD [68]. This is a controversial conclusion because "anergy" can be easily confounded with several negative signs of schizophrenia (such as avolition, apathy, or even anhedonia) [13,49,50,52,69,70]. The incidence of negative symptoms in patients with SSD is reported to be high, with more than 57% presenting with at least one such symptom, and 41% with at least two negative symptoms [69]. Other authors report a prevalence of negative symptoms that may reach 90% for at least one such manifestation, and up to 60% for at least one depressive symptom in FEP [70]. There is a risk of anticholinergic adverse events because of the pharmacokinetic interactions between the two classes of pharmacological agents [68].

Clozapine is considered a good therapeutic intervention in SSD associating mood disorders [71]. Risperidone was superior to haloperidol in decreasing anxiety and depression scores (at 8 mg/day and 10 mg/day, respectively), and the same atypical antipsychotic was more effective than haloperidol and levomepromazine on the Psychotic Anxiety Scale (at 8.6 mg/day, 9.2 mg/day, and 125 mg/day, respectively) [71]. Another review (n=33 studies focused on treatments for SSD with mood symptoms) concluded that combined treatments are as effective as antipsychotics used in monotherapy for acute psychotic exacerbations with depressive manifestations, although "some evidence" for superiority was detected in the case of antipsychotics [72]. For patients developing a major depressive syndrome after remission of acute psychosis, there has been found evidence to support the administration of antidepressants, as add-ons to antipsychotics [72]. The results regarding therapeutic response to antidepressants in cases of subsyndromal depression were mixed [72].

Figure 2: Potential therapeutic interventions for post-psychotic depression



**= extrapolated recommendations from studies with other populations than patients with post-psychotic depression; not yet enough evidence to support their use*

Newer antidepressants have been launched in clinical use, but their efficacy profile in patients with PPD still remains unexplored [73-77]. Also, older antidepressants may be of interest for this topic, if added to atypical antipsychotics, because, as previously reported, the rate of residual depressive symptoms in this population is quite high [52,78]. Other interventions, besides antidepressants and atypical antipsychotics, are waiting to be investigated in clinical trials for depressive symptoms or major depressive episodes associated with SSD [79-81]. Adding third-generation

antipsychotics to clozapine, in cases of ultra-resistance to treatment SSD cases, would also have to be considered a viable option for controlling depressive and negative symptoms [82,83]. Exploring organic, toxic, and psychiatric risk factors for treatment resistance is important when analyzing the most adequate treatment plan for patients with depression, PPD included [84-85].

CONCLUSIONS

The controversy surrounding the diagnosis of PPD is still under scrutiny, because (1) SSDs associate a high rate of suicide, even after the introduction of new generation antipsychotics, (2) there is a significant impact of depression on the quality of life and functional recovery in SSD patients, and (3) the case management of PPD may differ from the interventions recommended in patients with schizoaffective disorder, major depression with psychotic features, adverse events of different drugs with CNS depressogenic properties, and other conditions that may present themselves with depressive symptoms. The data about efficient interventions for PPD derives from older studies, therefore new trials exploring new generations of antidepressants are needed for this population. Based on the reviewed data, there are elements referring to risk factors, clinical characteristics, epidemiology, and even treatment for PPD, but they need to be validated by prospective, good-quality trials.

Conflicts of interest and sources of funding

None to declare.

Authors' contribution

OV conceived the idea of the review. OV, AGM, BMP, CAC, CT and CFP designed the study. OV, CFP, AGM, CAC, CFP, CT, DGV, CN and CAS screened the studies during the primary search. OV, AGM, CAC, CFP and CAS drafted the first version of the review. OV, CAC, CFP, DGV, CN and CAS revised the manuscript and elaborated the review's conclusions. All authors had full access to the data contained in this review and decided to submit the manuscript for publication.

References:

1. Rahim T, Rashid R. Comparison of depression symptoms between primary depression and secondary-to-schizophrenia depression. Int J Psychiatry Clin Pract 2017; 21(4): 314-317. doi: 10.1080/ 13651501.2017.1324036.

2. Sechter D, Vandel P. Treatment of depression secondary to psychotic disorders. Encephale 1999;25 (S.3):40-3.

3. McGlashan T, Carpenter WT Jr. An investigation of the postpsychotic depressive syndrome. Am J Psychiatry 1976 ;133 :14-19.

4. Mayer-Gross W. Uber die stellungsnahme zur abgelaufenen akuten psychose. Zeitschrift fur Gesamte Neurologie und Psychiatrie 1920 ;60 :160-212.

5. Semrad E. Long-term therapy of schizophrenia. In: Usdin G (Ed.), Psychomeuroses and Schizophrenia. Philadelphia, JB Lippincott, 1966.

6. McGlashan TH, Carpenter WT Jr. Postpsychotic depression in schizophrenia. Arch Gen Psychiatry 1976;33(2):231-9. doi: 10.1001/archpsyc.1976.01770020065011.

7. Kohler CG, Lallart EA. Postpsychotic depression in schizophrenia patients. Curr Psychiatry Rep 2002;4(4):273-8. doi: 10.1007/s11920-996-0046-7.

8. Roth S. The seemingly ubiquitous depression following acute schizophrenic episodes, a neglected area of clinical discussion. Am J Psychiatry 1970;127(1):51-8. doi: 10.1176/ajp.127.1.51.

9. Green MF, Nuechterlein KH, Ventura J, Mintz J. The temporal relationship between depressive and psychotic symptoms in recent-onset schizophrenia. Am J Psychiatr 1990;147(2):179-82. doi: 10.1176/ajp.147.2.179.

10. Chintalapudi M, Kulhara P, Avasthi A. Post-psychotic depression in schizophrenia. Eur Arch Psychiatry Clin Neurosci 1993;243(2):103-8. doi: 10.1007/BF02191572.

11. Berrios GE, Bulbena A. Post-psychotic depression: the Fulbourn cohort. Acta Psychiatr Scand 1987;76(1):89-93. doi: 10.1111/j.1600-0447.1987.tb02866.x.

12. Steinberg HR, Green R, Durrel J. Depression occurring during the course of recovery from schizophrenic symptoms. Am J Psychiatry 1967;124(5):699-702. doi: 10.1176/ajp.124.5.699.

13. Dollfus S, Langlois S, Assouly-Besse F, Petit M. Depressive symptoms and negative symptoms during schizophrenia. Encephale 1995;21 (Sp.No3):23-27.

14. Guerrero-Jiménez M, de Albornoz Calahorro CMC, Girela-Serrano B, Sánchez IB, Gutiérrez-Rojas L. Post-psychotic depression: An updated review of the term and clinical implications. Psychopathology 2022;55(2):82-92. doi: 10.1159/000520985.

15. Iqbal Z, Birchwood M, Chadwick P, Trower P. Cognitive approach to depression and suicidal thinking in psychosis. Br J Psychiatry 2000;177(6):522-8. doi:10.1192/bjp.177.6.522

16. Sandhu A, Ives J, Birchwood M, Upthegrove R. The subjective experience and phenomenology of depression following first episode psychosis: a qualitative study using photo-elicitation. J Affect Disord 2013;149(1-3):166-74. doi: 10.1016/j.jad.2013.01.018.

17. Stamouli S. Depression in schizophrenia: Relationship with other symptoms, differential diagnosis, prognosis, treatment. Psychiatriki 2010;21(2):136-47.

18. Das SLP, Kapur RL. Post-psychotic depression in schizophrenics : (A prospective study). Indian J Psychiatry 1980 ;22(3) :277-282.

19. Stern MJ, Pillsbury JA, Sonnenberg SM. Postpsychotic depression in schizophrenics. Comprehens Psychiatry 1972;13(6):591-598.doi: 10.1016/0010-440x(72)90060-0.

20. Birchwood M, Iqbal Z, Chadwick P, Trower P. Cognitive approach to depression and suicidal thinking in psychosis. 1. Ontogeny of post-psychotic depression. Br J Psychiatry 2000 ;177 :516-21. doi: 10.1192/bjp.177.6.516.

21. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, fourth edition. Washington DC, American Psychiatric Association, 1994.

22. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 5th edition. Arlington, American Psychiatric Publishing, 2013.

23. WHO. ICD-10 version 2019. Accessed at https://icd.who.int/

browse10/2019/en. Retrieved online 24 October 2022.

24. WHO. ICD-10 version 2023. Accessed at https://www.icd10data.com/ICD10CM/. Retrieved online 24 October 2022.

25. WHO. ICD-11 clinical descriptions and diagnostic guidelines for mental and behavioural disorders. Accessed at https://icd.who.int/browse11/l-m/en. Retrieved online 24 October 2022.

26. Cohen S, Leonard CV, Farberow NL, Schneidman ES. Tranquilizers and suicide in the schizophrenia patient. Arch Gen Psychiatry 1964;11:312-21. doi: 10.1001/archpsyc.1964.01720270084010.

27. Knights A, Ckasha MS, Salin MA, Hirsch SR. Depressive and extrapyramidal symptoms and clinical effects: a trial of fluphenazine versus flupenthixol in maintenance of schizophrenic outpatients. Br J Psychiatry 1979;135:515-523.

28. Mariot DH. Depression following fluphenazine treatment. BMJ 1969;3:780.

29. Carney MWP, Sheffield BF. The long term maintenance treatment of schizophrenia outpatients with depot fluphenazine. Curr Med Res Opin 1973;1:423-426.

30. Mandel MR, Severe JB, Schooler NR, Gelenberg AJ, Mieske M. Development and prediction of postpsychotic depression in neuroleptic-treated schizophrenic. Arch Gen Psychiatry 1982;39(2):197-203. doi: 10.1001/archpsyc.1982.04290020051010.

31. Horan WP, Kring AM, Blanchard JJ. Anhedonia in schizophrenia: A review of assessment strategies. Schizophr Bull 2006;32(2):259-273. doi: 10.1093/schbul/sbj009.

32. Liang S, Wu Y, Hanxiaoran L, Greenshaw AJ, Li T. Anhedonia in depression and schizophrenia: Brain reward and aversion circuits. Neuropsychiatr Dis Treat 2022;18:1385-1396. doi: 10.2147/NDT.S367839.

33. Sherdell L, Waugh CE, Gotlib H. Anticipatory pleasure predicts motivation for reward in major depression. J Abnorm Psychol 2012;121(1):51-60. doi: 10.1037/a0024945.

34. Strauss GP, Cohen AS. The schizophrenia spectrum anhedonia paradox. World Psychiatry 2018;17(2):221-222. doi: 10.1002/wps.20529.

35. Millan MJ, Fone K, Steckler T, Horan W. Negative symptoms of schizophrenia: Clinical characteristics, pathophysiological substrates, experimental models and prospects for improved treatment. Eur Neuropsychopharmacol 2014;24(5):645-92. doi: 10.1016/j.euroneuro.2014.03.008.

36. Wolthaus JE, Dingemans PM, Schene AH, Linszen DH, Knegtering H, Holthausen EA, et al. Component structure of the positive and negative syndrome scale (PANSS) in patients with recent-onset schizophrenia and spectrum disorders. Psychopharmacology (Berl). 2000;150(4):399-403. doi: 10.1007/s002130000459.

37. Fountoulakis KN, Popovic D, Mosheva M, Siamouli M, Moutou K, Gonda X. Mood symptoms in stabilized patients with schizophrenia: A bipolar type with predominant psychotic features? Psychiatr Danub 2017;29(2):148-154. doi: 10.24869/psyd.2017.148.

38. Miura I, Nosaka T, Yabe H, Hagi K. Antidepressive effect of antipsychotics in the treatment of schizophrenia: Meta-regression analysis of randomized placebo-controlled trials. Int J Neuropsychopharmacol 2021; 24(3): 200-215. doi: 10.1093/ijnp/pyaa082.

39. Furtado VA, Srihari V. Atypical antipsychotics for people with both schizophrenia and depression. Cochrane Database Syst Rev 2008;(1):CD005377. doi: 10.1002/14651858.CD005377.pub2.

40. Innamorati M, Baratta S, Di Vittorio C, Lester D, Girardi P, Pompili M, Amore M. Atypical antipsychotics in the treatment of depressive and psychotic symptoms in patients with chronic schizophrenia: A naturalistic study. Schizophr Res Treatment 2013;2013:423205. doi: 10.1155/2013/423205.

41. Addington D, Addington J, Schissel B. A depression rating scale for schizophrenics. Schizophr Res 1990;3(4):247-51. doi: 10.1016/0920-9964(90)90005-r.

42. Addington D, Addington J, Maticka-Tyndale E, Joyce J. Reliability and validity of a depression rating scale for schizophrenics. Schizophr Res 1992;6(3):201-8. doi: 10.1016/0920-9964(92)90003-n.

43. Lançon C, Auquier P, Reine G, Bernard D, Toumi M. Study of the concurrent validity of the Calgary Depression Scale for Schizophrenics (CDSS). J Affect Disord 2000;58(2):107-15. doi: 10.1016/s0165-0327(99)00075-0.

44. Lako IM, Bruggeman R, Knegtering H, Wiersma D, Schoevers RA, Slooff CJ, Taxis K. A systematic review of instruments to measure depressive symptoms in patients in patients with schizophrenia. J Affect Disord 2012;140(1):38-47. doi: 10.1016/j.jad.2011.10.014.

45. Müller MJ, Müller KM, Fellgiebel A. detection of depression in acute schizophrenia: Sensitivity and specificity of 2 standard observer rating scales. Can J Psychiatry 2006;51(6):387-392. 10.1177/070674370605100609.

46. Lindenmayer JP, Czobor P, Alphs L, Nathan AM, Anand R, Islam Z, et al. The InterSePT scale for suicidal thinking reliability and validity. Schizophr Res 2003;63(1-2):161-70. doi: 10.1016/s0920-9964(02)00335-3.

47. Ayer DW, Jayathilake K, Meltzer HY. The InterSePT suicide scale for prediction of imminent suicidal behaviors. Psychiatry Res 2008;161(1):87-96. doi: 10.1016/j.psychres.2007.07.029.

48. Kim SW, Kim SJ, Yoon BH, Kim JM, Shin IS, Hwang MY, Yoon JS. Diagnostic validity of assessment scales for depression in patients with schizophrenia. Psychiatry Res 2006;144(1):57-63. doi: 10.1016/j.psychres.2005.10.002.

49. Mosolov SN, SN, Yaltonskaya PA. Primary and secondary negative symptoms in schizophrenia. Front Psychiatry 2021;12:766692. doi: 10.3389/fpsyt.2021.766692.

50. Kirschner M, Aleman A, Kaiser S. Secondary negative symptoms-A review of mechanisms, assessment and treatment. Schizophr Res 2017 ;186 :29-38. doi: 10.1016/j.schres.2016.05.003.

51. Klaus F, Orianne D, Kaiser S. Negative symptoms in schizophrenia-overview and practical implications. Rev Med Suisse 2018;14(619):1660-1664.

52. an der Heiden W, Könnecke R, Maurer K, Ropeter D, Häfner H. Depression in the long-term course of schizophrenia. Eur Arch Psychiatry Clin Neurosci 2005;255(3):174-84. doi: 10.1007/s00406-005-0585-7.

53. Buckley PF, Miller BJ, Lehrer DS, Castle DJ. PPsychiatric comorbidities and schizophrenia. Schizophr Bull 2009;35(2):383-402. doi: 10.1093/schbul/sbn135.

54. Lu C, Jin D, Palmer N, Fox K, Kohane IS, Smoller JW, Yu KH. Large-scale real-world data analysis identifies comorbidity patterns in schizophrenia. Transl Psychiatry 2022;12:154. https://doi.org/10.1038/s41398-022-01916-y.

55. Dieset I, Andreassen OA, Haukvik UK. Somatic comorbidity in schizophrenia: Some possible biological mechanisms across the life span. Schizophr Bull 2016;42(6):1316-1319. doi: 10.1093/schbul/sbw028.

56. Vasiliu O, Vasile D, Făinărea AF, Pătrașcu MC, Morariu EA, Manolache R, et al. Analysis of risk factors for antipsychotic-resistant schizophrenia in young patients - a retrospective analysis. RJMM 2018;CXXI(1):25-29.

57. Budisteanu M, Andrei E, Lica F, Hulea DS, Velicu AC, Mihailescu I, et al. Predictive factors in early onset schizophrenia. Exp Ther Med

2020;20(6):210. doi: 10.3892/etm.2020.9340.

58. Sánchez IB, Agudo AM, Guerrero-Jiménez M, Serrano BG, Gil PA, de Albornoz Calahorro CMC, Gutiérrez-Rojas L. Treatment of post-psychotic depression in first-episode psychosis. A systematic review. Nord J Psychiatry 2022;1-9. doi: 10.1080/08039488.2022.2067225.

59. Dollfus S, Olivier V, Chabot B, Déal C, Perrin E. Olanzapine versus risperidone in the treatment of post-psychotic depression in schizophrenic patients. Schizophr Res 2005;78(2-3):157-9. doi: 10.1016/j.schres.2005.06.001.

60. Siris SG, Bermanzohn PC, Mason SE, Shuwall MA. Maintenance imipramine therapy for secondary depression in schizophrenia. A controlled trial. Arch Gen Psychiatry 1994 ;51(2) :109-15. doi: 10.1001/archpsyc.1994.03950020033003.

61. Siris SG, Mason SE, Bermanzohn PC, Alvir JM, McCorry TA. Adjunctive imipramine maintenance in post-psychotic depression/negative symptoms. Psychopharmacol Bull 1990 ;26(1) :91-4.

62. Siris SG, Morgan V, Fagerstrom R, rifkin A, Cooper TB. Adjunctive imipramine in the treatment of postpsychotic depression. A controlled trial. Arch Gen Psychiatry 1987;44(6):533-9. doi: 10.1001/archpsyc.1987.01800180043008.

63. Siris S, Pollack S, Bermanzohn P, Stronger R. Adjunctive imipramine for a broader group of post-psychotic depressions in schizophrenia. Schizophr Res 2000;44(3):187-92. doi: 10.1016/s0920-9964(99)00197-8.

64. Siris SG, Strahan A. Continuation and maintenance treatment trials of adjunctive imipramine therapy in patients with postpsychotic depression. J Clin Psychiatry 1988 ;49(11) :439-40.

65. Siris SG, Cuther J, Owen K, Mason S, Gingerich S, Lang MP. Adjunctive imipramine maintenance treatment in schizophrenic patients with remitted postpsychotic depression. Am J Psychiatry 1989;146(11):1495-7. doi: 10.1176/ajp.146.11.1495.

66. Abuzzahab FS, Zimmerman RL. Psychopharmacological correlates of post-psychotic depression: a double-blind investigation of haloperidol vs. Thiothixene in outpatient schizophrenia. J Clin Psychiatry 1982 ;43(3) :105-10.

67. Floru L, Heinrich K, Wittek F. The problem of post-psychotic schizophrenic depressions and their pharmacological induction. Long-term studies with fluspirilene and penfluridol and single-blind trial with fluphenazine-decanoate and flupenthixol-decanoate. Int Pharmacopsychiatry 1975;10(4):230-9. doi: 10.1159/000468199.

68. Plasky P. Antidepressant usage in schizophrenia. Schizophr Bull 1991;17(4):649-657. https://doi.org/10.1093/schbul/17.4.649.

69. Patel R, Jayatilleke N, Broadbent M. Negative symptoms in schizophrenia: a study in a large clinical sample of patients using a novel automated method. BMJ Open 2015;5(9):e007619. doi: 10.1136/bmjopen-2015-007619.

70. an der Heiden W, Leber A, Häfner H. Negative symptoms and their association with depressive symptoms in the long-term course of schizophrenia. Eur Arch Psychiatry Clin Neurosci 2016;266(5):387-96. doi: 10.1007/s00406-016-0697-2.

71. Azorin JM. Long-term treatment of mood disorders in schizophrenia. Acta Psychiatr Scand Suppl 1995;388:20-3. doi: 10.1111/j.1600-0447.1995.tb05940.x.

72. Levinson DF, Umapathy C, Musthaq M. Treatment of schizoaffective disorder and schizophrenia with mood symptoms. Am J Psychiatry 1999;156(8):1138-48. doi: 10.1176/ajp.156.8.1138.

73. Vasiliu O. Esketamine for treatment-resistant depression: A review of clinical evidence. Experim Ther Med 2023;25:111. https://doi.org/10.3892/etm.2023.11810.

74. Vasiliu O. Investigational drugs for the treatment of depression (Part 1): Monoaminergic, orexinergic, GABA-ergic, and anti-inflammatory agents. Front Pharmacol. 2022;13:884143. doi: 10.3389/fphar.2022.884143

75. Sakurai H, Yonezawa K, Tani H, Mimura M, Bauer M, Uchida H. Novel antidepressants in the pipeline (phase II and III): A systematic review of the US clinical trials registry. Pharmacopsychiatry 2022;55(4):193-202. doi: 10.1055/a-1714-9097.

76. Parincu Z, Iosifescu DV. Combinations of dextromethorphan for the treatment of mood disorders- a review of the evidence. Expert Rev Neurother 2023;23(3):205-212. doi: 10.1080/14737175.2023.2192402.

77. Thase ME. New medications for treatment-resistant depression: a brief review of recent developments. CNS Spectr 2017;22(S1):39-48. doi: 10.1017/S1092852917000876.

78. Emsley R, Ahokas A, Suarez A, Marinescu D, Doci I, Lehtmets A, et al. Efficacy of tianeptine 25-50 mg in elderly patients with recurrent major depressive disorder: An 8-week placebo- and escitalopram-controlled study. J Clin Psychiatry 2018;79(4):17m11741. doi: 10.4088/JCP.17m11741.

79. Vasiliu O, Vasile D, Voicu V. Efficacy and tolerability of antibiotic augmentation in schizophrenia spectrum disorders- A systematic literature review. RJMM 2020;CXXIII(1):3-20.

80. Palm U, Hasan A, Strube W, Padberg F. tDCS for the treatment of depression: a comprehensive review. Eur Arch Psychiatry Clin Neurosci 2016;266(8):681-694. doi: 10.1007/s00406-016-0674-9.

81. Padberg F, Zwanzger P, Keck ME, Kathmann N, Mikhaiel P, Ella R, et al. Repetitive transcranial magnetic stimulation (rTMS) in major depression: relation between efficacy and stimulation intensity. Neuropsychopharmacology 2002;27(4):638-45. doi: 10.1016/S0893-133X(02)00338-X.

82. Vasiliu O. Third-generation antipsychotics in patients with schizophrenia and non-responsivity or intolerance to clozapine regimen: What is the evidence? Front Psychiatry 2022;13:1069432. doi: 10.3389/fpsyt.2022.1069432.

83. Benedetti A, Di Paolo A, Lastella M, Casamassima F, Candiracci C, Litta A, et al. Augmentation of clozapine with aripiprazole in severe psychotic bipolar and schizoaffective disorders: A pilot study. Clin Pract Epidemiol Ment Health 2010;6:30-35. doi: 10.2174/1745017901006010030.

84. Molaei H, Radfar S, Radfar M, Torabi Z, Radmehr S. Prediction of anxiety, depression and social function among mothers of NICU-hospitalized infants compared to healthy infants' mothers in Baqiyatallah and Imam Hossein hospitals. RJMM 2022;CXXV(2):286-293.

85. Thase ME. Treatment-resistant depression: prevalence, risk factors, and treatment strategies. J Clin Psychiatry 2011;72(5):e18. doi: 10.4088/JCP.8133tx4c.

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ORIGINAL ARTICLE

Evaluation of Adsorption Therapy as an Extracorporeal Blood Purification Technique in Critically Ill Covid-19 Patients

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Abstract: *We aimed to evaluate the efficacy of adsorption therapy as an extracorporeal blood purification technique in critically ill patients with Coronavirus disease 2019 (COVID-19). A retrospective analysis was performed on 17 adult patients with severe COVID-19, who underwent adsorption therapy using an HA330 cartridge, at Ankara City Hospital. Each adsorption therapy was administered for three consecutive days, and each therapy session lasted three hours. Several parameters, including cytokine levels, blood count, biochemistry panel, clinical status, and mortality rate were assessed before and after each therapy session. The results obtained from this study revealed that adsorption therapy reduced IL-6 levels and improved oxygenation in the short term. However, heart rate, mean arterial pressure and SOFA score did not demonstrate significant changes. Notably, the dose of norepinephrine increased after the third session. Regrettably, only 4 out of 17 patients (23.5%) survived. Consequently, adsorption therapy appears to be effective in reducing IL-6 levels in severe COVID-19 patients. Nonetheless, further investigation is warranted to evaluate its impact on clinical outcomes.*

Keywords: *Adsorption therapy; coronavirus disease 2019; cytokine storm; extracorporeal blood purification*

INTRODUCTION

COVID-19 infects the airway epithelium, leading to widespread damage, severe inflammation, and pneumonia with a cytopathic effect. A cytokine storm, capillary leak syndrome, lung injury, and Acute Respiratory Distress Syndrome (ARDS) are all brought on by the local and circulating cytokines that are produced at this time [1-4]. In patients with severe COVID-19, several inflammatory mediators are involved, and the cytokine storm has a deleterious impact on the disease's progression [5].

Additionally, COVID-19 exhibits immunological dysfunction. Techniques for extracorporeal blood purification have previously been utilized as supportive therapy to manage immunological dysregulation in the treatment of sepsis [6]. Despite the use of a variety of treatments, critically ill COVID-19 patients have consistently significant mortality rates. As a result, the use of cytokine filters as a therapy option for these individuals is now being given further thought.

Patients with COVID-19 have considerably higher levels of proinflammatory cytokines and chemokines like tumor necrosis factor-α, interleukin 1 and 6, granulocyte-colony stimulating factor, monocyte chemoattractant protein-1, interferon gamma-induced protein-10, and macrophage inflammatory proteins 1-α [7]. In individuals with severe COVID-19, these proinflammatory cytokines and chemokines lead to a cytokine storm. The extracorporeal removal of these cytokines from COVID-19 patients' blood circulation using an adsorption therapy is hypothesized to minimize hyperinflammation and calm the cytokine storm. Extracorporeal blood purification systems do not only remove pathogenic toxins and proinflammatory mediators; they also remove regulating cytokines. As a result, their process is non-selective. These regulatory cytokines are also advantageous because they restrain the immune system from overreacting to inflammation [8]. Therefore, while the application of extracorporeal blood purification procedures may have short-term advantages, its possible adverse effects on long-term

outcomes have not yet been thoroughly assessed and understood.

An adsorption therapy, which is an extracorporeal blood purification technique can be used as a cytokine filter in severe COVID-19 patients. For this aim, an extracorporeal filter which is a cartridge with a sorbent inside is used for blood purification by combining convection and diffusion for solute removal [9]. Additionally, through ionic attraction, hydrophobic interactions, hydrogen bonds, and van der Waals interactions, the sorbent in the cartridge comes into direct contact with blood to adsorb solutes [10,11]. The sorbent in the cartridge also targets TNF, IL-1, IL-6, IL-10, IL-18, and other cytokines [11]. Thus, cytokines and solutes in the bloodstream bind to the sorbent material. Therefore, adsorption therapy can also be used for patients with autoimmune diseases, chronic uremic symptoms, intoxications, and inflammatory conditions with cytokine storms such as sepsis and pancreatitis [9,12].

For adsorption therapy in COVID-19 patients, the Jafron HA330 cartridge can be used [13]. The neutro-macroporous resin-adsorbing beads in the HA330 cartridge are constructed of the styrene-divinylbenzene copolymer. The resin beads' average diameter ranges from 0.60 to 1.18 mm and is 0.8 mm. The resin's pore sizes range from 500 D to 60 kD, whereas the HA330 cartridge removes molecular weights from 10 to 60 kDa (kiloDalton; Dalton [9,12]. Multiple pore sizes of the sorbent material allow the removal of several molecules with different molecular weights such as free hemoglobin, cytokines, complements, drugs, uremic toxins, and protein-bound or hydrophobic substances. The recommended treatment duration with an HA330 cartridge is 2-2.5 hours, while the sorbent material can be saturated if it is used for a longer period which causes a decrease in clearance efficiency [9,12].

In this study, we wanted to assess the efficacy of adsorption therapy in patients with severe COVID-19. To understand the effects of adsorption therapy using HA330 cartridges in severe COVID-19 patients in the intensive care unit (ICU), we evaluated the changes in the clinical status of patients, cytokine levels, complete blood count, and biochemistry panel before and after the administration of the therapy

MATERIALS AND METHODS

A retrospective analysis was performed on 14 male (82.3%) and 3 female (17.6%) adult severe COVID-19 patients who received adsorption therapy (HA330 cartridge, Jafron) in the ICU at Ankara City Hospital between April 2020 and October 2021 (Table 1). Before and after adsorption therapy with HA330, the patients' laboratory results and clinical outcomes were assessed. Ankara City Hospital (E2-21-983) granted permission for this study with the approval of the local ethics committee.

Table 1: Characteristics of severe COVID-19 patients treated with HA330 adsorption cartridge

Characteristics of COVID-19 patients	
Demographics	
Age (years) (median, IQR)	53.5 (45-62.5)
Gender, male (n, %) female (n, %)	14 (82.3) 3 (17.6%)
Treatment	
Methylprednisolone 40 mg (n, %)	17 (100)
IVIG (n, %)	1 (5.8)
Anakinra (n, %)	9 (52.9)
Tocilizumab (n, %)	1 (5.8)
Outcomes	
Length of ICU stay (days) (median, IQR)	22 (34)
Mechanical ventilator duration (days) (median, IQR)	20 (30)
Survived (n, %)	4 (23.5)
Died (n, %)	13 (76.5)

1 IQR: interquartile range. IVIG: intravenous immunoglobulin. ICU: intensive care unit. Anakinra: An interleukin-1 receptor antagonist. Tocilizumab: A monoclonal antibody against the IL-6 receptor. In this study, 14 male (82.3%) and 3 female (17.6%) adult patients with severe COVID-19 were treated with adsorption therapy (HA330 cartridge, Jafron©) in the ICU. The median age of the patients was 53.5 (IQR: 45-62.5). All 17 patients received a ten-day course of iv methylprednisolone 40 mg once daily. Of the patients, nine were treated with anakinra, one with tocilizumab, and one received IVIG treatment without tocilizumab or anakinra. Four patients died after the first adsorption therapy session, and another four died after the second. Nine patients completed three sessions of adsorption therapy, but five of them died due to sepsis and ARDS-related complications in the ICU. Overall, 4 out of 17 critically ill COVID-19 patients survived after adsorption therapy with an HA330 cartridge (23.5%).

Respiratory distress with peripheral capillary oxygen saturation (SpO_2) 93% in room air, dyspnea with a respiratory rate of at least 30 breaths per minute, a ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen (PaO_2/FiO_2) less than 300 mmHg, and more than 50% infiltration of the lung fields are all considered to be severe COVID-19 in adult patients [14]. Moreover, cytokine release syndrome was defined as having one or more of C-reactive protein >100 (or >50 mg/L but doubled in the past 48 hours), lymphocyte count <0.6 × 109/L, serum interleukin-6 (IL-6) level higher than 3 times of the upper normal limit, ferritin >300 ug/L with doubling within 24 hours, ferritin >600 ug/L at presentation and LDH >250 U/L, and elevated D-dimer (>1 mcg/mL) [15]. These 17 patients had confirmed COVID-19 diagnoses based on real-time reverse transcription polymerase chain reaction (RT-PCR) test results and ground glass appearance with pneumonia on thorax computed tomography before admission to the ICU. They also had previously defined severe COVID-19 disease and cytokine release syndrome features. The exclusion criteria for this study included being under the age of 18, having severe heart failure with a left ventricular ejection fraction of less than 35%, having coagulation issues, and being pregnant.

All 17 patients received methylprednisolone 40 mg iv once daily for ten days. 9 patients were treated with anakinra, whereas 1 patient was treated with tocilizumab. 1 patient received immunoglobulin (IVIG) treatment without tocilizumab or anakinra.

Adsorption therapy was initially planned for 3 hours daily with an HA330 cartridge for 3 consecutive days. However, adsorption therapy could be applied to 17 patients once, 13 patients twice, and 9 patients three times. Thus, creatinine, glomerular filtration rate, urea, albumin, alanine transaminase (ALT), aspartate transferase (AST), total bilirubin, lactate dehydrogenase (LDH), troponin, fibrinogen, D-dimer, lactate, ferritin, erythrocyte sedimentation rate, C-reactive protein (CRP), procalcitonin, interleukin-6 (IL-6), hemoglobin, neutrophil/lymphocyte ratio (NLR), number of leukocytes, neutrophils, lymphocytes, and platelets were noted before and after adsorption therapy sessions. Additionally, the patients' vital signs, requirements for vasopressor medications, partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2), and Sequential Organ Failure Assessment (SOFA) scores were recorded from their medical records before and after adsorption therapy sessions.

Statistical evaluation was performed using the Statistical Packages for the Social Sciences (v17.0, SPSS 24 Inc., Chicago, IL) software. Categorical data were presented as numbers and percentages, while quantitative data were presented as mean standard deviation or median and interquartile range (IQR), as appropriate. The differences between the two groups were evaluated with the Mann-Whitney U test and the Wilcoxon test. The statistical significance level was accepted as $p<0.05$.

RESULTS

Adsorption therapy with a Jafron HA330 cartridge was applied once to 17 patients, twice to 13 patients, and three times to 9 patients. The median age of the patients was 53.5 (IQR: 45-62.5). The median ICU length of stay was 22 (IQR:34) days. The median mechanical ventilator duration was 20 days (IQR:30). The median APACHE II score was 18 (IQR:10). The median length of stay in the ICU before the initiation of adsorption therapy was 4 days (IQR:2-6) (Table 1).

Table 2: Clinical status of patients before and after 1st, 2nd and 3rd sessions of adsorption therapy with HA330 cartridge

Clinical parameters	Before adsorption therapy (IQR)	After 1st session (IQR)	*P**	After 2nd session (IQR)	*P**	After 3rd session (IQR)	*P**
PaO_2/FiO_2 (mmHg) (n=12)	0.59 (0.46-0.92)	0.69 (0.47-0.95)	*0.12*	0.54 (0.46-0.69)	*0.44*	0.62 (0.51-0.71)	*1.0*
HR (bpm/min) (n=13)	87.0 (66.5-100.0)	80.0 (69.5-102.5)	*0.72*	77.0 (67.5-120.0)	*0.86*	90.0 (72.8-113.8)	*0.74*
MAP (mmHg) (n=14)	80.0 (73.8-102.5)	80.0 (68.8-97.5)	*0.44*	75.0 (65.0-92.5)	*0.23*	71.5 (61.2-96.0)	*0.53*
Dose of NE (μg/kg/min) (n=9)	0.12 (0.04-0.43)	0.15 (0.03-0.67)	*0.46*	0.04 (0.12-0.17)	*0.89*	0.25 (0.07-0.19)	*0.11*

*[2] Numerical data were given as a median and interquartile range (IQR). PaO_2/FiO_2: partial pressure of arterial oxygen/the fraction of inspired oxygen. HR: Heart rate. MAP: Mean arterial pressure. NE: norepinephrine. SOFA: Sequential Organ Failure Assessment. *Wilcoxon test was used.*

The first, second, and third sessions of adsorption therapy using the HA330 cartridge are shown in Table 2 along with the patients' clinical status before and after each session. For each clinical parameter, including PaO_2/FiO_2, heart rate (HR), mean arterial pressure (MAP), norepinephrine dose (NE), and Sequential Organ Failure Assessment (SOFA) score, the median and interquartile range (IQR) are shown in the table. According to these findings, the first adsorption therapy session led to a statistically significant increase in PaO_2/FiO_2 levels ($p=0.03$), whereas the second and third sessions did not. None of the three sessions of adsorption therapy resulted in statistically significant changes in heart rate, mean arterial pressure, or SOFA score.

The dose of NE showed a statistically significant increase after

the third session of adsorption therapy (p<0.11). Overall, these data imply that the use of an HA330 cartridge in adsorption therapy may improve oxygenation in patients with severe COVID-19, but larger sample sizes and additional research are required to confirm these results.

Table 3 shows the variations in cytokine levels, complete blood counts, and biochemistry panels in severely ill COVID-19 patients receiving first, second, and third adsorption therapy sessions using HA330 cartridges. A statistically significant decrease in IL-6 levels was observed after the first, second, and third adsorption therapy sessions (361, 86.5, 28, 20.3, p<0.03, p<0.03, p<0.007, respectively). There was a statistically significant increase in leukocyte count after the first adsorption therapy compared to the leukocyte count before adsorption therapy (12.2 to 14.6, p=0.02). However, the leukocyte count decreased from 14.6 to 12.9 after the 2nd session and increased to 13.5 after the 3rd therapy session, neither of which was statistically significant (p=0.42, p=0.12, respectively). When compared to the neutrophil count prior to the first adsorption therapy (10.9 to 13.6, p=0.03), there was a statistically significant rise in neutrophil count.

However, the neutrophil count climbed to 12.1 after the third therapy session but declined to 11.6 after the second (p=0.46 p=0.19). Neither change was statistically significant (Table 3).

Table 3: Statistical analysis of laboratory parameters of severe COVID-19 patients before and after first, second, and third sessions of adsorption therapy with HA330 cartridge

Laboratory parameters	Before adsorption therapy (n=17) (IQR)	After 1st session (n=17) (IQR)	*P**	After 2nd session (n=13) (IQR)	*P**	After 3rd session (n=9) (IQR)	*P**
Hemoglobin (g/dL)	11.6 (9.1-12.7)	11.0 (9.4-12.9)	0.64	11.0 (10.1-12.4)	0.48	11.0 (9.1-11.6)	0.22
Leukocyte Count x10^9/L	12.2 (9.1-14.3)	14.6 (9.7-21.0)	**0.02**	12.9 (8.8-20.2)	0.42	13.5 (8.9-14.6)	0.12
Neutrophil Count x10^9/L	10.9 (7.8-13.4)	13.6 (8.2-19.3)	**0.03**	11.6 (7.1-19.2)	0.46	12.1 (7.7-13.0)	0.19
Lymphocyte Count x10^9/L	0.64 (0.39-0.77)	0.62 (0.42-0.80)	0.96	0.55 (0.43-0.70)	0.92	0.48 (0.38-0.78)	0.82
Platelet count x10^9/L	262.0 (200.0-303.0)	274.0 (162.0-328.0)	0.47	266.0 (195.0-350.0)	0.75	213.0 (175.0-307.0)	0.60
NLR	20.2 (15.9-32.8)	28.8 (17.9-42.1)	**0.03**	24.3 (22.1-49.7)	0.20	23.4 (18.7-29.3)	0.80
Glucose mg/dL	189.5 (114.3-236.8)	211.0 (146.5-224.0)	0.51	153.0 (128.0-205.5)	0.38	151.0 (118.5-210.5)	0.53
Creatinine mg/dL	0.93 (0.56-1.93)	0.86 (0.64-2.0)	0.64	1.0 (0.73-2.40)	0.03	1.09 (0.62-1.30)	0.26
Estimated GFR ml/min/m^2	88.0 (41.0-118.0)	94.0 (43.5-112.5)	0.60	78.0 (30.0-99.5)	0.11	83.5 (59.0-108.0)	0.25
Urea mg/dL	62.0 (42.8-98.0)	65.5 (50.3-132.8)	0.06	84.5 (52.3-161.3)	0.07	73.0 (64.0-105.0)	0.24
Albumin g/L	29.0 (26.0-32.0)	28.0 (22.5-31.5)	**0.04**	30.0 (28.3-31.8)	0.20	28.0 (26.3-30.8)	0.49
ALT U/L	46.5 (27.8-126.8)	59.0 (30.0-200.0)	0.55	51.0 (30.0-225.5)	0.64	66.0 (26.0-100.5)	0.99
AST U/L	37.0 (27.3-81.0)	59.0 (32.5-228.0)	0.84	58.0 (22.5-180.5)	0.51	45.0 (21.0-63.0)	0.30
Total bilirubin mg/dL	0.9 (0.5-1.2)	0.8 (0.5-1.2)	0.84	0.6 (0.5-0.8)	0.18	0.75 (0.4-1.3)	0.21
Troponin Ng/L	49.0 (8.8-423.1)	114.4 (24.0-647.0)	0.74	186.0 (22.8-360.7)	0.07	-	-
INR	1.4 (1.2-1.7)	-	-	1.3 (1.2-1.48)	0.60	-	-
Fibrinogen g/L	6.4 (3.7-7.2)	6.5 (3.8-7.3)	0.51	5.7 (3.4-7.8)	0.65	5.0 (1.6-7.0)	0.64
D-dimer mg/L	5.8 (1.9-13.6)	4.9 (2.4-7.3)	0.35	8.6 (1.8-17.7)	0.44	7.90 (4.4-22.0)	0.98
Lactate	2.3 (1.6-3.2)	1.9 (1.3-2.9)	0.07	1.8 (1.4-2.4)	0.21	-	-
LDH U/L	600.5 (516.8-766.5)	659.0 (543.0-963.5)	0.65	671.0 (468.5-889.0)	0.97	578.5 (488.8-674.5)	0.39
Ferritin ml/ng	961.0 (393.5-1540.0)	1500.5 (880.3-5546.0)	0.06	1461.0 (1025.5-3667.0)	0.58	1236.5 (377.5-1611.5)	0.12
ESR mm/h	56.0 (21.8-108.3)	78.0 (15.0-125.0)	0.07	65.0 (22.5-103.0)	0.72	-	-
CRP mg/L	0.16 (0.13-0.218)	0.15 (0.13-0.25)	0.51	0.15 (0.09-0.17)	0.10	0.10 (0.06-0.14)	0.09
Procalcitonin µg/L	1.01 (0.17-11.3)	4.2 (0.28-11.6)	0.44	0.53 (0.22-8.84)	0.35	0.19 (0.11-0.58)	0.06
IL-6 pg/mL	361.0 (68.2-739.8)	86.5 (10.9-167.7)	**0.03**	28.0 (20.8-76.9)	**0.03**	20.3 (7.6-32.4)	**0.007**

*[3] Numerical data are given as a median and interquartile range (IQR). NLR: neutrophil-lymphocyte ratio, GFR: glomerular filtration rate, ALT: Alanine transaminase, AST: Aspartate transferase LDH: lactate dehydrogenase, INR: international normalized ratio, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, IL-6: interleukin-6. (-): data could not be retrieved. There was a statistically significant decrease in IL-6 levels after the first, second, and third adsorption therapy sessions (361, 86.5, 28, 20.3, p <0.03, p<0.03, p<0.007, respectively). *Wilcoxon test was used*

There was a statistically significant increase in the neutrophil-lymphocyte ratio (NLR) after the first adsorption therapy compared to the NLR before adsorption therapy (20.2 to 28.8, p=0.03). Although the NLR dropped from 28.8 to 24.3 after the second session and then further to 23.4 after the third (p=0.20 and p=0.80, respectively), neither of these decreases was statistically significant. When compared to the albumin level before the initial adsorption therapy, there was a statistically significant drop in albumin (29.0 to 28.0, p=0.04). However, albumin increased from 28.0 to 30.0 after the second session and reduced to 28.0 after the third (p=0.20 and p=0.49, respectively), neither of which was statistically significant.

No statistically significant changes were observed in creatinine, glomerular filtration rate, urea, alanine transaminase (ALT), aspartate transferase (AST), total bilirubin, lactate dehydrogenase (LDH), troponin, fibrinogen, D-dimer, lactate, ferritin, erythrocyte sedimentation rate, CRP, procalcitonin, hemoglobin, glucose, lymphocyte, or platelet count after the first, second, and third sessions of adsorption therapy with HA330 cartridges. Four patients died after the first, and another four patients died after the second adsorption therapy session. Nine patients completed three sessions of adsorption therapy. However, five of these nine patients died due to sepsis and ARDS-related complications in the ICU. Only 4 out of 17 critically ill COVID-19 patients survived after adsorption therapy with an HA330 cartridge (23.5%).

DISCUSSION

There are a limited number of publications in the English medical literature related to the use of extracorporeal blood purification techniques with the United States Food and Drug Administration (FDA) approved filters such as oXiris filter (Baxter, Deerfield, IL), CytoSorb filter (CytoSorbents, Monmouth Junction, NJ), Seraph 100 Microbind blood affinity filter (ExThera Medical, Martinez, CA) and the Spectra Optia Apheresis System with the Depuro D2000 Adsorption Cartridge (Terumo BCT, Lakewood, CO) for the treatment of COVID-19 patients [8]. According to Padala et al., using an oXiris filter improved clinical outcomes in two out of three patients and reduced levels of interleukin-6, erythrocyte sedimentation rate, and CRP [16]. According to Zhang et al., CRP, IL-6, IL-8, IL-10, APACHE II, and Sequential Organ Failure Assessment (SOFA) scores all significantly decreased after oXiris filter treatment, while IL-4, IL-8, and procalcitonin showed a nonstatistically significant downward trend. Unfortunately, two of five patients passed away despite treatment [2]. Ugurov et al. reported using oXiris in ten patients with COVID-19. Two of the ten patients passed away related to complications of ARDS. According to Ugurov et al., the number of white blood cells and thrombocytes increased to the normal range whereas IL-6, CRP, and fibrinogen levels decreased [17]. According to Villa et al., treatment with oXiris resulted in a significant drop in IL-6 levels as well as improvements in hemodynamic stability, multiorgan dysfunction, and oxygenation index in 37 patients [18].

Case studies of COVID-19 patients who received treatment with a CytoSorb filter were described by Rizvi et al., Melegari et al., and Berlot et al. [1, 19, 20]. All three patients survived with an improvement in CRP, IL-6, and oxygenation. Rieder et al. treated 4 patients under venovenous extracorporeal membrane oxygenation (vv-ECMO) support with cytokine adsorption with CytoSorb filter, which decreased IL-6 in COVID-19 patients [21]. According to Alharthy et al., continuous renal replacement therapy (CRRT) sessions using a CytoSorb cartridge were administered to 50 patients. Thirty-five patients who survived after CytoSorb therapy had decreased ferritin, lactate dehydrogenase, CRP, IL-6, and D-dimer levels [15].

According to Olson et al., the Seraph-100 filter was utilized in two COVID-19 patients, and as a result, post-treatment vasopressor dose, IL-6, and CRP levels decreased [22]. The use of a Seraph-100 filter on a patient with COVID-19 significantly decreased D-dimer level, according to Pape et al. [23]. Four hemodialysis patients with severe COVID-19 were treated using a Seraph-100 haemoperfusion device, according to Sandoval et al. Despite findings from other research, Sandoval et al. failed to find any appreciable drop in IL-6, D-dimer, or ferritin levels following the treatment [24]. According to Schmidt et al., 78 COVID-19 patients who received treatment with a Seraph-100 microbind affinity blood filter were evaluated. According to Schmidt et al, patients who received Seraph-100 treatment within 60 hours of ICU admission had a reduced mortality rate [25].

Reverse Takotsubo cardiomyopathy associated with COVID-19 was treated with therapeutic plasma exchange utilizing a Spectra Optia apheresis system outfitted with a Depuro D2000 adsorption cartridge, according to Faqihi et al. Following treatment, both lactate levels and left ventricular function returned to normal [26].

Koc et al. published a review of hemadsorption therapy in severe COVID-19 patients [13]. 86 patients with severe COVID-19 were included in 16 trials that were examined by Koc et al. CytoSorb®, oXiris®, Biosky filter, SeaStar® CLR filter, HA280, HA330 Jafron, and resin-directed hemadsorption cartridges were used in hemoperfusion therapy. According to Koc et al., the mortality rate, mean intubation time, and length of stay in the ICU and hospital were, respectively, 29%, 14.93 days, 17.21 days, and 31.7 days. Following hemoperfusion sessions, the

mean levels of CRP and interleukin-6 reduced (131.7 to 66.0 and 527.5 to 334.7, respectively). According to Koc et al., hemoperfusion and cytokine adsorption reduced cytokine levels, CPR, and IL-6 relative to pre-therapy, decreased mortality to 29%, and improved clinical conditions. However, these outcomes lacked statistical significance. Hemadsorption therapy was described by Koc et al. as an alternate salvage therapy for COVID-19 patients who were critically unwell. Moradi et. al reported a 73-year-old male patient was treated with hemoperfusion (HA230 cartridge, Jafron) due to a cytokine storm for 4.5 hours [27]. Moradi et al. claimed that the symptoms and need for oxygen support were alleviated during hemoperfusion treatment.

Theoretically, blocking the formation of proinflammatory cytokines can reduce hyperinflammation. The clinical outcome of severely ill COVID-19 patients can be improved by reducing hyperinflammation. Thus, anti-interleukin-6R monoclonal antibodies and corticosteroids were recommended to reduce the inflammatory response. However, IL-6 promotes neutrophil-mediated viral clearance by initiating a preliminary response against viral infections [7]. Moreover, Dienz et al. reported that IL-6 or IL-6 receptor-deficient mice could not resist Influenza A infection, which caused pulmonary damage leading to death [28]. Despite its theoretical benefit, Clark et al. reported that hemoperfusion was an experimental treatment because of its limited evidence of efficacy [29]. However, Kang et al. reported that in patients with severe COVID-19 and non-acute kidney injury, continuous renal replacement therapy using an oXiris filter might not be able to successfully reduce cytokine release syndrome [30].

Hemadsorption therapy has several additional drawbacks. Arrhythmia, coagulation issues, thrombocytopenia, and bleeding were listed as the most typical short-term hemoperfusion consequences in patients with COVID-19 by Darban et al. [31]. However, the majority of the difficulties emerged on the second and third days following hemoperfusion, not during hemoperfusion itself.

A highly biocompatible sorbent covered with a surface that inhibits platelet adherence and clotting activation is necessary for hemoperfusion. The various sorbent types utilized determine how hemoperfusion removes substances, with the effective surface area being a key factor. The sorbent material within the hemoperfusion cartridge can both absorb and lead to the loss of antibiotics and nutrients from the bloodstream [9, 10, 32].

The Jafron HA330 cartridge was the only available single-use hemoperfusion cartridge at Ankara City Hospital. Thus, we performed adsorption therapy on severe COVID-19 patients in the ICU with single-use Jafron HA330 cartridges. We used adsorption therapy as a salvage therapy when the patients did not respond to other treatment options such as antibiotics, corticosteroids, hydroxychloroquine, immunoglobulin, convalescent plasma, tocilizumab or anakinra [33].

There is still no single laboratory parameter with a cut-off value identified to initiate adsorption therapy. Moreover, the duration of therapy and the parameters to monitor the patient's response to the treatment are still under investigation [6]. Unfortunately, there is no universally accepted standardized adsorption therapy protocol. We preferentially used adsorption therapy to treat severely ill COVID-19 patients with low procalcitonin but high CRP and IL-6 levels.

Except for a decline in IL-6, we were unable to find a statistically significant link between the quantity of adsorption therapy sessions and laboratory values. The majority of the research previously cited showed that adsorption treatment reduced IL-6 levels. However, anakinra and tocilizumab might be responsible for the IL-6 decline in COVID-19 patients [34].

Moreover, our study has certain drawbacks. First of all, the sample size was quite small. Secondly, during the pandemic, we mostly served severe COVID-19 patients in our intensive care unit, which restricts the applicability of our findings to other patient populations. Finally, because a control group was not included in our investigation, additional variables, such as medication modifications and illness progression, might have an impact on the observed changes in laboratory values. Hopefully, our study contributes to the growing body of research on the use of adsorption therapy in COVID-19 patients despite these limitations.

CONCLUSION

After examining this study's data, it can be concluded that in patients with severe COVID-19, the use of an HA330 cartridge during adsorption therapy was connected to a statistically significant drop in IL-6 levels after the first, second, and third therapy sessions. Except for a rise in the leukocyte and neutrophil counts following the first session, there were no statistically significant associations between the quantity of adsorption therapy sessions and other laboratory findings.

To draw a definitive conclusion about the effect of adsorption therapy with HA330 cartridges on COVID-19 patients, further studies with larger and more diverse patient populations are needed. These studies should also consider other potential confounding factors, such as the administration of other treatments and underlying medical conditions. Nevertheless, the findings of this study point to the possibility that adsorption therapy could be a potential supplementary treatment option for individuals with severe COVID-19.

Conflicts of interest and sources of funding

The authors declare no conflict of interest. This research received no external funding.

Authors' contribution

Conceptualization, M.E.Y, N.H.S., C.M.A., S.I.; methodology, M.E.Y., S.I.; software, M.E.Y.; validation, N.H.S., C.M.A., M.E.Y., S.I.; formal analysis, M.E.Y.; investigation, M.E.Y.; resources, N.H.S., C.M.A., M.E.Y., S.I.; data curation, N.H.S, C.M.A, M.E.Y., S.I.; writing-original draft preparation, M.E.Y.; writing-review and editing, N.H.S., C.M.A., M.E.Y., S.I.; visualiza-tion, M.E.Y.; supervision, S.I.; project administration, S.I. All authors have read and agreed to the published version of the manuscript.

Ethics approval and consent to participate

The study was conducted under the Declaration of Helsinki, and local ethics committee approval for this study was obtained from Ankara City Hospital (E2-21-983).

References:

1. Rizvi S, Danic M, Silver M, LaBond V. Cytosorb filter: An adjunct for survival in the COVID-19 patient in cytokine storm? A case report. Heart Lung 2021; 50: 44-50. doi: 10.1016/j.hrtlng.2020.09.007.

2. Zhang H, Zhu G, Yan L, Lu Y, Fang Q, Shao F. The absorbing filter Oxiris in severe coronavirus disease 2019 patients: A case series. Artif Organs 2020; 44: 1296-1302. doi: 10.1111/aor.13786.

3. Stockmann H, Keller T, Büttner S, Jörres A, Kindgen-Milles D, Kunz JV, et al. CytoResc - "CytoSorb" Rescue for critically ill patients undergoing the COVID-19 Cytokine Storm: A structured summary of a study protocol for a randomized controlled trial. Trials 2020; 21: 577. doi: 10.1186/s13063-020-04501-0.

4. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: Consider cytokine storm syndromes and immunosuppression. Lancet 2020; 395: 1033-1034. doi: 10.1016/S0140-6736(20)30628-0.

5. Al Shareef K, Bakouri M. Cytokine Blood Filtration Responses in COVID-19. Blood Purif 2021; 50: 141-149. doi: 10.1159/000508278.

6. Monard C, Rimmelé T, Ronco C. Extracorporeal Blood Purification Therapies for Sepsis. Blood Purif 2019; 47 Suppl 3: 1-14. doi: 10.1159/000499520.

7. Li H, Liu L, Zhang D, Xu J, Dai H, Tang N, et al. SARS-CoV-2 and viral sepsis: Observations and hypotheses. Lancet 2020; 395: 1517-1520. doi: 10.1016/S0140-6736(20)30920-X.

8. Niazi NS, Nassar TI, Stewart IJ, Honore PM, Sharma K, Chung KK. A Review of Extracorporeal Blood Purification Techniques for the Treatment of Critically Ill Coronavirus Disease 2019 Patients. ASAIO J 2022. doi: 10.1097/MAT.0000000000001761.

9. Ankawi G, Fan W, Pomarè Montin D, Lorenzin A, Neri M, Caprara C, et al. A New Series of Sorbent Devices for Multiple Clinical Purposes: Current Evidence and Future Directions. Blood Purif 2019; 47: 94-100. doi: 10.1159/000493523.

10. Villa G, Neri M, Bellomo R, Cerda J, De Gaudio AR, De Rosa S, et al. Nomenclature for renal replacement therapy and blood purification techniques in critically ill patients: Practical applications. Crit Care 2016; 20: 283. doi: 10.1186/s13054-016-1456-5.

11. Winchester JF, Kellum JA, Ronco C, Brady JA, Quartararo PJ, Salsberg JA, et al. Sorbents in acute renal failure and the systemic inflammatory response syndrome. Blood Purif 2003; 21: 79-84. doi: 10.1159/000067860.

12. Pomarè Montin D, Ankawi G, Lorenzin A, Neri M, Caprara C, Ronco C. Biocompatibility and cytotoxic evaluation of new sorbent cartridges for blood hemoperfusion. Blood Purif 2018; 46: 187-195. doi: 10.1159/000489921.

13. Koc S, Uysal H. Literature review of hemadsorption therapy in severe COVID-19 cases: a narrative review. Clin Lab 2022; 68: 2. doi: 10.7754/Clin.Lab.2021.210839.

14. Berlin DA, Gulick RM, Martinez FJ. Severe COVID-19. N Engl J Med 2020; 383: 2451-2460. doi: 10.1056/NEJMcp2009575.

15. Alharthy A, Faqihi F, Memish ZA, Balhamar A, Nasim N, Shahzad A, et al. Continuous renal replacement therapy with the addition of CytoSorb cartridge in critically ill patients with COVID-19 plus acute kidney injury: a case-series. Artif Organs 2021; 45: E101-E112. doi: 10.1111/aor.13864.

16. Padala SA, Vakiti A, White JJ, Mulloy L, Mohammed A. First reported use of highly adsorptive hemofilter in critically ill COVID-19 patients in the USA. J Clin Med Res 2020; 12: 454-457. doi: 10.14740/jocmr4228.

17. Ugurov P, Popevski D, Gramosli T, Neziri D, Vuckova D, Gjorgon M et al. Early initiation of extracorporeal blood purification using the AN69ST (oXiris(®)) hemofilter as a treatment modality for COVID-19 patients: a single-centre case series. Braz J Cardiovasc Surg 2022; 37: 35-47. doi: 10.21470/1678-9741-2020-0403.

18. Villa G, Romagnoli S, De Rosa S, Greco M, Resta M, Pomarè Montin D et al. Blood purification therapy with a hemodiafilter featuring enhanced adsorptive properties for cytokine removal in patients presenting COVID-19: a pilot study. Crit Care 2020; 24: 605. doi: 10.1186/s13054-020-03322-6.

19. Melegari G, Bertellini E, Melegari A, Trenti T, Malaguti S, Barbieri A. Hemoadsorption cartridge and coronavirus disease 2019 infections: a case report and brief literature review. Artif Organs 2021; 45: E130-E135. doi: 10.1111/aor.13846.

20. Berlot G, Tomasini A, Roman Pognuz E, Randino A, Chiella F, La Fata C et al. The combined use of tocilizumab and hemoadsorption in a patient with SARS-COV-2-19-associated pneumonia: a case report. Nephron 2020; 144: 459-462. doi: 10.1159/000509738.

21. Rieder M, Wengenmayer T, Staudacher D, Duerschmied D, Supady A. Cytokine adsorption in patients with severe COVID-19 pneumonia requiring extracorporeal membrane oxygenation. Crit Care 2020; 24: 435. doi: 10.1186/s13054-020-03130-y.

22. Olson SW, Oliver JD, Collen J, Bunin J, Gleeson TD, Foster BE, et al. Treatment for severe coronavirus disease 2019 with the Seraph-100 Microbind affinity blood filter. Crit Care Explor 2020; 2: e0180. doi: 10.1097/CCE.0000000000000180.

23. Pape A, Kielstein JT, Krüger T, Fühner T, Brunkhorst R. Treatment of a critically ill COVID-19 patient with the Seraph 100 Microbind affinity filter. TH Open 2021; 5: e134-e138. doi: 10.1055/s-0041-1727121.

24. Sandoval D, Rama I, Quero M, Hueso M, Gómez F, Cruzado JM. Treatment for severe COVID-19 with a biomimetic sorbent haemoperfusion device in patients on haemodialysis. Clin Kidney J 2021; 14: 1475-1477. doi: 10.1093/ckj/sfab010.

25. Schmidt JJ, Borchina DN, Van't Klooster M, Bulhan-Soki K, Okioma R, Herbst L et al. Interim analysis of the COSA (COVID-19 patients treated with the Seraph® 100 Microbind® Affinity filter) registry. Nephrol Dial Transplant 2022; 37: 673-680. doi: 10.1093/ndt/gfab347.

26. Faqihi F, Alharthy A, Alshaya R, Papanikolaou J, Kutsogiannis DJ, Brindley PG et al. Reverse takotsubo cardiomyopathy in fulminant

COVID-19 associated with cytokine release syndrome and resolution following therapeutic plasma exchange: a case-report. BMC Cardiovasc Disord 2020; 20: 389. doi: 10.1186/s12872-020-01665-0.

27. Moradi H, Abbasi S. Hemoperfusion as a supportive treatment in a COVID-19 patient with late pulmonary thromboembolism: a case report. Int Med Case Rep J 2020; 13: 341-345. doi: 10.2147/IMCRJ.S263127.

28. Dienz O, Rud JG, Eaton SM, Lanthier PA, Burg E, Drew A et al. Essential role of IL-6 in protection against H1N1 influenza virus by promoting neutrophil survival in the lung. Mucosal Immunol 2012; 5: 258-266. doi: 10.1038/mi.2012.2.

29. Clark EG, Hiremath S, McIntyre L, Wald R, Hundemer GL, Joannidis M. Haemoperfusion should only be used for COVID-19 in the context of randomized trials. Nat Rev Nephrol 2020; 16: 697-699. doi: 10.1038/s41581-020-00352-9.

30. Kang K, Luo Y, Gao Y, Zhang J, Wang C, Fei D et al. Continuous renal replacement therapy with oXiris filter may not be an effective resolution to alleviate cytokine release syndrome in non-AKI patients with severe and critical COVID-19. Front Pharmacol 2022; 13: 817793. doi: 10.3389/fphar.2022.817793.

31. Darban M, Yarmohamadi M, Mohammadkhani MM, Jazaeri SM. Outcome and complications of hemoperfusion in patients with COVID-19 in intensive care unit: a cross-sectional study. Cardiovasc Hematol Agents Med Chem 2022. doi: 10.2174/1871525720666220514164855.

32. Clark WR, Ferrari F, La Manna G, Ronco C. Extracorporeal sorbent technologies: basic concepts and clinical application. Contrib Nephrol 2017; 190: 43-57. doi: 10.1159/000468911.

33. Chen JT, Ostermann M. Review of anti-inflammatory and antiviral therapeutics for hospitalized patients infected with severe acute respiratory syndrome coronavirus 2. Crit Care Clin 2022; 38: 587-600. doi: 10.1016/j.ccc.2022.02.002.

34. Bahmani M, Chegini R, Ghanbari E, Sheykhsaran E, Shiri Aghbash P, Leylabadlo HE et al. Severe acute respiratory syndrome coronavirus 2 infection: role of interleukin-6 and the inflammatory cascade. World J Virol 2022; 11: 113-128. doi: 10.5501/wjv.v11.i3.113.

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ORIGINAL ARTICLE

Psychometric Properties of the Method "Evaluation of Negative Mental Reactions and States of Combatants" and Experience of its Application in Short-term Psychological Recovery

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Abstract: *The article shows the development of the method of psychological evaluation called "Evaluation of Negative Mental Reactions and States of Combatants". In the study participated 1300 male servicemen (29.84% from junior lieutenant to colonel and servicemen under contract and demobilized, and 70.16% from private to senior warrant officer). The age of participants varied from 20 to 55 years. The system of evaluation developed consisted of 16 instruments that could help to determine the presence of negative psychological symptoms of servicemen related to their participation in hostilities. The results indicated that the evaluation method developed is a tool that allows determining the presence of negative psychological symptoms related to participation in combat. Likewise, it is a useful and fast method to assess the effectiveness of short-term psychological recovery programs. Unlike existing methods of diagnosing negative mental reactions and states of an individual, which arose after their participation in hostilities, the developed psychodiagnostic toolkit could consider the physical and mental fatigue of the respondents, their deterioration, and other cognitive dysfunctions*.

Keywords: *combat activity, psychological rehabilitation, psychological recovery, post-traumatic stress disorder, evaluation system*

INTRODUCTION

Long participation in hostilities depleted the psychological adaptation resources of servicemen, sharply posing the question concerning the need for psychological recovery [1,2]. This issue was complicated and comprehensive; it related both to the definition of rotation of servicemen and to the determination of the duration and development of effective programs of psychological recovery for all participants of hostilities [3] as well as to the determination of indications for medical and psychological rehabilitation of the servicemen, whose mental health and ability to readaptation was lost [4]. The aim of psychological recovery was to restore the physical and mental resources of servicemen to prolong their ability to perform tasks under the conditions of combat stress factors action [5].

Nowadays, the psychological decompression measures were directed not only to ensuring the adequacy of switching from military service to peaceful life [6], including traditional stress relief and help in civilian life realization, taking into account the acquired military experience, accepting this experience to reduce the probability of post-traumatic stress disorders (PTSD) formation [7,8], but also for the psychological restoration of mental health of servicemen who participated in hostilities to relieve the accumulated stress prolonging the possibility of adequate functioning of servicemen under combat conditions when it was impossible to realize the

massive rotations to keep their resistance – psychological stability, ability to resist negative influence from the side of combat stress factors [2]. To the institutions of psychological recovery were sent the servicemen with expressed signs of maladjustment [9], acute stressful reactions [7], significant exhaustion, devastation, and fatigue [10], and servicemen, who had difficulties in adaptation [11] while getting back in line after injuries and concussion and after their stay in hospitals.

Institutions that implemented psychological recovery programs were located in the third echelon of defense in safe places in order to form in the minds of servicemen the idea of the need to return to the performance of combat missions, and military duty, which was a way of posing the direction of recovery – the restoration of combat capacity.

Realization of activities of psychological rehabilitation and implementation of existing psychological programs of decompression on the basis of their personal professional experience and world experience of rehabilitation of servicemen was imposed on the military psychologists of the Armed Forces and the National Guard of Ukraine, as well as on the volunteer psychologists from NGOs who had appropriate training and experience. Usually, the implementation of psychological recovery programs was a combination of procedures of medical treatment orientation with the use of appropriate material and technical bases and the involvement of appropriate specialists.

Even though the system of implementation of the psychological restoration of combat servicemen was well-established and proved its effectiveness in practice, there arose a question on the development of effective psychodiagnostic tools of the mental state control of servicemen before and after a complex of actions by the program of psychological rehabilitation for individual servicemen and correction of the recovery program if required. There were distinguished the following requirements for the psychodiagnostic method:

1) convenient while conducting both individual and group psycho-diagnosis of servicemen, typical for a survey with a large number of people (100-200 people), capable of taking into account the physical and mental fatigue of the respondents, deterioration of their attention, and other cognitive dysfunctions related to stressful experience;

2) suitable for the diagnosis of negative mental reactions and conditions that occur after participation in hostilities;

3) reliable for re-diagnosis due to a minor period of time, excluding the ability to remember accurately their past answers;

4) able to clearly demonstrate changes in psychological state that occurred during their participation in the psychological recovery program;

5) convenient for summarizing data and receiving the psychologist's feedback on the effectiveness of the introduction of new actions into the programs of psychological recovery;

6) useful for obtaining information related to the effectiveness of individual consulting, providing a psychologist with a reflection on his/her professional activity. With existing pressure on psychologists, there occurred a need for supervision and their rotation in institutions that dealt with psychological recovery.

The objective of the study was the development of a psychological evaluation system of the consequences of participation in combat activities for military personnel participating in hostilities. Unlike the existing systems to diagnose the psychological consequences of combat participation, it is intended to develop a set of psychodiagnostic tools that assess the physical and mental fatigue of combatants, their deterioration, and other cognitive dysfunctions. And also, that it is capable of clearly showing the psychological changes achieved by participation in psychological recovery programs.

MATERIALS AND METHODS

Participants and Procedure

The study was conducted in 2022. The study included 1300 servicemen who underwent a psychological recovery program after taking part in a long combat mission. The tested group consisted of officers – 29.84% (from junior lieutenant to the colonel) and servicemen under the contract and mobilized – 70.16% (from private to senior warrant officer). The age of the study participants varied from 20 to 55 years.

While developing the method "Evaluation of negative mental reactions and states of combatants", there were combined the simplest procedures of conditions evaluation which were typical for the method such as "Profile of mood states" (POMS) [12,13], "Self-esteem of psychophysiological state" (Kokun) [14], "Measurement of states" used to express evaluation of emotional states of sportsmen [15]. Also, there was conducted analysis of negative mental reactions and states that often occurred in servicemen while their participation in hostilities, including those who described the ability to perform tasks and the ability to interact with others in the performance of command work [1,16]. Thus, the list of negative mental reactions and states (experience) was quite wide and contained 16 points: irritability; anxiety; aggressiveness;

anger; inattention; self-doubt; devastation; apathy; concern; sense of guilt; sense of powerlessness; lack of concentration; unwillingness to communicate; lack of trust in comrades in the service; lack of trust in commanders; inability to perform the assigned tasks. It was assumed that the use of factor analysis would give the possibility to group these points into the scale.

It was necessary to point out that the simplicity of the instructions and of the testing procedure itself was an important circumstance for effective diagnostic work with servicemen who had been experiencing the influence of combat stress factors for a long time and who had difficulty in the redistribution of attention.

However, a number of points (16) of the evaluation of negative mental states but the evaluation scale itself (from 0 to 10 points) was quite large (exceeding the amount of short-term memory 7±2 elements), which complicated their memorization and accuracy reproduction during re-testing.

The determination of psychometric indicators of the method “Evaluation of negative mental reactions and states of combatants” and its testing was carried out during the participation in a psychological recovery program by servicemen. 1300 servicemen participated at this stage.

The servicemen filled out the form of the method at the beginning of the psychological recovery program and after it. The results obtained in accordance with the method “Evaluation of negative mental reactions and states of combatants” were compared with the results of methods that were conducted with servicemen to control their condition before and after their participation in the psychological recovery program. Before participating in a psychological recovery program, servicemen were surveyed with the following methods: “Maladjustment” (Prykhodko, Matsegora, Kolesnichenko, and Baida) [17], “Mississippi Scale for Combat-Related PTSD” (Keane, Caddell, and Taylor) [18], “Diagnostics of psychological safety of an individual” (Prykhodko, 2012) [19], “Evaluation of traumatism of combat experience of servicemen” (Kolesnichenko) [20]. After participating in the psychological recovery program, servicemen were surveyed in accordance with the following psychodiagnostic methods – “Resistance to psychological traumatism of combat experience” (Kolesnichenko) [21].

All procedures in the study conformed to the ethical standards of the 1964 Helsinki Declaration and its later amendments. All participants consent for their data to be used in this research.

Instruments and Measures

To determine the constructive validity of the method "Evaluation of negative mental reactions and states of combatants" there were used methods which were standardized on the Ukrainian selection.

Method "Maladjustment" (Prykhodko, Matsegora, Kolesnichenko, and Baida) [17] was an express version of the method "Adaptability" (Maklakov) [22] which had a long tradition of use in the Armed Forces of Ukraine. The "Adaptability" method was concluded by military psychologist A.H. Maklakov [22] to determine the adaptation potential of servicemen based on the individual scales of the method "Minnesota Multiphasic Personality Inventory" (McKinley, Hathaway) [23]. The developer reported satisfaction with the psychometric characteristics of the formed methodology [22]. Since the beginning of hostilities in eastern Ukraine among military psychologists of Ukraine, there was spread a modification of the methodology proposed by Maklakov "Adaptability 200", carried out by Chermianin and Kondratiev [24]. Unlike the previous method, it was supplemented with a number of issues that allowed us to distinguish "military and professional orientation", "tendency to deviant behaviors", and "suicidal risk" and to calculate "the level of resistance to combat stress". This method included 200 questions; thus, there was a need to form a simpler and more reliable toolkit, which was the basis for the development of an express version of the method. The developed method "Maladjustment" (Prykhodko, Matsegora, Kolesnichenko, and Baida) [17] was aimed at the identification of specific violations of adaptation potential which could have a big influence on the ability to adequately perform the tasks. Thus, the method had 4 scales, each with 10 questions – "Violation of behavioral regulation", "Probability of committing suicidal attempts", "Violation of moral normativity" and "Loss of communicative potential". There was highlighted the calculation of the general indicator of "Maladjustment". This calculation was simple and convenient and could be carried out under field conditions without any additional tools. Although working with the method involved the presence of trust in psychologists, the method had a scale of sincerity. The developers provided data about the satisfactory psychometric indicators of the method.

The study used the "Mississippi Scale for Combat-Related PTSD" (Keane, Caddell, and Taylor), which was restored for the Ukrainian selection [18]. Nowadays, it was one of the most common methods used to measure the signs of PTSD. The scale included 35 statements, each of which can be estimated on a five-point scale. The total indicator which was made up in accordance with this method gave the possibility to estimate the degree of influence of the traumatic experience transferred by an individual.

"Diagnosis of Psychological Safety of an Individual" (Prykhodko), which was developed on the basis of the concept of psychological safety of an individual of specialists of extreme activities [19]. According to this concept,

psychological safety was not only a lack of danger but also an opportunity for development and self-realization. Psychological safety had a level structure. Each level in the method met a scale with a similar name. The first level was moral and communicative, it meant that knowledge and use of the rules of communication and norms of morality made interaction with the social environment controlled and predictable, formed the ability to escape potentially conflict situations, and involved external resources to overcome problematic situations. The motivational and volitional levels suggested that the developed goal setting, intensity in goal setting, and flexibility in their corrections could ensure the self-realization of an individual in difficult conditions of life. It was assumed that the ability to flexible restructuring of relations with the environment gave the possibility to be leading in these relationships, to control them. The valuable and semantic level was considered as an ability to conscious attitude to one's own life, awareness of one's own influence on the world, and responsibility for its changes. The developer believed that this conscious attitude gave the possibility for an individual to tolerate life difficulties and sufferings that arose in the process of self-realization. Moreover, due to the developer, the hierarchy of the semantic sphere gave the possibility to depreciate the experience in frustration as unimportant and to consolidate efforts to achieve important aims. The level of internal comfort was the factor that provided a change in the direction of activity. Thus, the evaluation of life as safe, and the condition as comfortable contributed to the decision to continue normal regulation. The decisions related to the changes were made in case of non-compliance of the environment with the needs and capabilities of an individual. There was highlighted the calculation of the general indicator of psychological safety of an individual, its height indicated the ability to set new goals of self-realization. When the indicators were reduced the thing was in a supportive reproduction of usual goals of life or in the arrest of development, and further impossibility of self-realization. The developed method had satisfactory psychometric indicators. The National Guard of Ukraine had been using this method for more than 10 years.

The method of "Evaluation of traumatism of combat experience of servicemen" [20] was based on the American method "Combat Exposure Scale" [25]. In the process of its development, there were considered the traumatic events and their intensity which were typical for military actions in Ukraine with the beginning of the Russian invasion in 2014. Unlike the "Combat Exposure Scale" method, the method of "Evaluating of traumatic experience of servicemen" (Kolesnichenko) had been developed; it included a list of phenomena that gave the possibility to reduce the trauma of combat stress factors influence. The method had 5 scales that met 3 groups of combat stress factors and 2 factors that described internal and external resources used to counteract stress factors. In the process of standardizing the method, there was used the procedure of regressive analysis which gave the possibility to determine the contribution of each scale to acute stress disorder which occurred due to the action of combat stress factors. It was reported that the method had satisfactory psychometric characteristics.

The method "Resistance to psychological traumatism of combat experience" (Kolesnichenko) [21] was developed on the basis of the author's concept of combat psychological traumatism of servicemen [1]. The method reflected the given in this concept three levels (stages) of realization of resistance to the action of combat stress factors, which 1) were related to the preparation for activity under the conditions of combat stress factors and under the existing expectations concerning the stress factors' activity and their ability to overcome them, 2) had the direct ability to overcome stressful influence and used adequate situational copings, and 3) had the ability to accept and realize the acquired experience under the stressful conditions. There was provided the calculations of general resistance to combat psychological traumatism. It was reported that this indicator had a reverse correlation with the "Mississippi Scale for Combat-Related PTSD" (Keane, Caddell, and Taylor) [18], $r = -0.60$, $p \leq 0.01$. Moreover, the method of the scale of the second order – "helplessness", "conscious attitude to professional training", "ability to acquire experience", "cognitive dysfunction", and "attitude to military duties". The method had satisfactory psychometric indicators.

Data Analysis

To represent the data, there was used the main descriptive statistics (arithmetic mean M and standard deviation SD). To distinguish the correlational rate between the variables there was used the correlation analysis. To determine the internal coherence of the method "Evaluation of negative mental reactions and states of combatants" there were used calculations based on Cronbach's alpha. To determine the specific negative mental reactions and states which were experienced by servicemen due to their participation in hostilities there was used regression analysis. To determine the structure of the method "Evaluation of negative mental reactions and states of combatants" there was used factor analysis with the help of the method "Principal components". Mathematical data was processed with the help of SPSS 17.0.

RESULTS

We have developed the following form of psychodiagnostic method "Assessment of negative mental reactions and states in combatants" (Table 1). The instructions are as follows:

"Please assess your psychological state at the moment on a scale from 0 - slightly expressed, 10 - strongly expressed". The internal consistency of the method was evaluated using the α-Cronbach indicator, which was 0.944 having the selection of 1300 people for 16 indicators.

Table 1: Form of the methodology "Evaluation of negative mental reactions and states of combatants"

Mental reactions and states	Evaluation of reactions and states										
Irritability	0	1	2	3	4	5	6	7	8	9	10
Anxiety	0	1	2	3	4	5	6	7	8	9	10
Aggressiveness	0	1	2	3	4	5	6	7	8	9	10
Anger	0	1	2	3	4	5	6	7	8	9	10
Inattention	0	1	2	3	4	5	6	7	8	9	10
Self -doubt	0	1	2	3	4	5	6	7	8	9	10
Devastation	0	1	2	3	4	5	6	7	8	9	10
Apathy	0	1	2	3	4	5	6	7	8	9	10
Concern	0	1	2	3	4	5	6	7	8	9	10
Sense of guilt	0	1	2	3	4	5	6	7	8	9	10
Sense of powerlessness	0	1	2	3	4	5	6	7	8	9	10
Lack of concentration	0	1	2	3	4	5	6	7	8	9	10
Unwillingness to communicate	0	1	2	3	4	5	6	7	8	9	10
Lack of trust in comrades in the service	0	1	2	3	4	5	6	7	8	9	10
Lack of trust in commanders	0	1	2	3	4	5	6	7	8	9	10
Inability to perform the assigned tasks	0	1	2	3	4	5	6	7	8	9	10

Despite the fact that the developed method included negative mental reactions and states for evaluation of PTSD, and maladjustment, and testified both negative experiences and inability to manage their behavior, its purposefulness and inability to maintain interaction and consistency in teamwork, factor analysis which was conducted in accordance with "Principal Components" presented the presence of only one factor that included all 16 variables with different factors of factor evaluation: "irritability" (0.743), "anxiety" (0.796), "aggressiveness" (0.692), "anger" (0.722), "inattention" (0.744), "self-doubt" (0.744), "devastation" (0.808), "apathy" (0.733), "concern" (0.808), "sense of guilt" (0,793), "lack of concentration " (0.801), "unwillingness to communicate" (0.714), "lack of trust in comrades in the service" (0.640), "lack of trust in commanders" (0.675), "inability to perform the assigned tasks" (0.746).

Taking into account the received data, the method included the calculations of general indicators. Experience using the method had shown that the most convenient indicator was the calculation of the average arithmetic value for all 16 indicators. Thus, the general indicator had a range from 0 to 10 points, which was convenient to perceive general results by the method and did not require memorization of additional information for manual data processing.

It was necessary to point out that the selection of a single-factor structure of the method was a certain confirmation of less regularity of negative mental reactions and states, a reflection of greater integration of mental processes while operating under stressful conditions.

The determination of the validity of the method was conducted in two stages. In the first stage, to determine the constructive validity, the data of the method "Evaluation of negative mental reactions and states of combatants" was compared with the data of methods which gave the possibility to diagnose the peculiarities of negative mental reactions and states of servicemen, proving that they were related to their participation in hostilities. First of all, the talk was about the method "Maladjustment" which gave the possibility to evaluate the violation of "behavioral regulation", "the probability of committing suicidal attempts", "violation of moral normativity" and "loss of communicative potential" by servicemen [17], and "Mississippi Scale for Combat-Related PPSD" (Keane, Caddell, and Taylor) [18], which gave the possibility to diagnose PTSD symptoms of those who had participated in hostilities and left the battlefield [24]. Moreover, there was used the method of "Evaluation of traumatic experience of servicemen" (Kolesnichenko) [20] and "Resistance to psychological traumatism" (Kolesnichenko) [21], which in this study gave the possibility to connect the experience of negative mental reactions and states with the

experience of participation in hostilities, as well as with their peculiarities and preparation for them.

Correlational relations with the method of "Diagnosis of psychological safety" (Prykhodko) [19] indicated the depth of violation of personality structures, which ensured its safety and ability to develop, which was an important factor for making a prognosis for the restoration of an individual in the process of psychological decompression and rehabilitation. The results of correlational analysis, which were obtained at this stage of validity determination were given in Table 2. Considering that the selection of the study at this stage included 1300 people, then all the correlational indicators given reached the level of statistical significance and did not require additional indicators.

Dense correlation relations of the method "Evaluation of negative mental reactions and states of combatants" and methods such as "Maladjustment" (Prykhodko et al.) [17] and "Mississippi Scale for Combat-Related PTSD" (Keane, Caddell, and Taylor) [18] pointed out that according to the data provided by the developed method, it was really possible to consider negative experience, which was connected with adaptation disorders and PTSD symptoms. The data provided by the method "Evaluation of traumatic experience of servicemen" [20] proved that negative experience was mostly related to the force of negative effects than to the existing external support.

However, the formed personality structure (according to the method "Diagnosis of Psychological Safety" [19] including the process of professional and professional-psychological training, due to the method "Evaluation of traumatism of combat experience of servicemen" [20] was able to restrain the development of negative states, providing adequate functioning of an individual under combat conditions. But at this stage, it was impossible to monitor the accumulated influence of traumatic events on the development of negative mental states while exceeding the recommended time for rotation (more than 6 months).

The second stage of determination of the method's validity was developed to determine its ability to be a tool for tracking the dynamics of changes during psychological recovery. The methods which were used at the first stage had satisfactory indicators of reliability, and, therefore, could be insensitive to the changes which occurred during the week (this was a usual term of the program of psychological recovery of servicemen). The method of "evaluation of negative mental reactions and states of combatants" was developed specifically for evaluating the control of negative states' changes before and after participation in the psychological recovery program, including the possibility to evaluate its effectiveness.

Considering such purpose, the data obtained by the method "evaluation of negative mental reactions and states of combatants" before and after the participation in the recovery program was compared to the data obtained by Lüsher's color test including the indicator of anxiety. This indicator pointed out the availability of frustrated needs and inadequacy of compensation and, unlike other indicators by this projective method, could be confused with indicators by other methods. The indicator of anxiety in accordance with Lüsher's color test was used as an integrated state evaluation since the main determinants of mental states were the ratio: firstly, conscious and unconscious needs, desires, and aspirations of an individual; secondly, the capabilities of an individual (obvious abilities and hidden potentials); thirdly, environmental conditions (objective influence and subjective perception of the current situation) [25].

40 servicemen participated at this stage of the study. Thus, the general indicator by the method "evaluation of negative mental reactions and states of combatants" correlated with anxiety before the beginning of the decompression program at a moderate level – $r = 0.41$, $p \leq 0.01$; after the decompression program the data was – $r = 0.47$, $p \leq 0.01$. These data proved that the developed method was sensitive to the changes in states and could be used to evaluate the dynamics of states during the programs of psychological recovery which were developed for short-term (up to a week).

It was figured out that the general indicator (see Table 2) had a slightly higher density than individual indicators by the method "evaluation of negative mental reactions and states of combatants" with general indicators of maladjustment, PTSD, psychological safety of an individual, traumatism of combat experience, and resistance to psychological traumatism. It was another piece of evidence that the method would be more reliable if it was used as a single scale.

Then there was used the procedure of regression analysis to determine specific negative mental reactions and states experienced in these psychological categories; thus, there were formed relevant regression equations:

Maladjustment = 3.804 + 0.216*Irritability + 0.307* Aggressiveness + 0.259*Self-doubt + 0.249*Devastation + 0,245*Concern + 0.386*Reluctance to communicate + 0.229* Lack of trust in comrades in the service + 0.350*Lack of trust in commanders +0.264* Inability to perform the assigned tasks + 0,529.

Post-traumatic stress disorder = 54.66 + 1,070*Irritability + 0.719*Aggressiveness + 0.572*Inattention + 0.557* Devastation + 1.230*Apativity + 0.794*Concern + 0.613* Unwillingness to communicate + 0.602*Lack of trust in commanders +0.941* Inability to perform the assigned tasks +0.506.

Table 2: The indicators of correlative relations between the scales of method "Evaluation of negative mental reactions and states of combatants" and the scales of other psychodiagnostics methods which were used to estimate its validity (in points).

Indicators	"Estimation of negative mental reactions and states of combatants"																			
	Irritability	Anxiety	Aggressiveness	Anger	Inattention	Self-doubt	Devastation	Apathy	Concern	Sense of guilt	Sense of powerlessness	Lack of concentration	Unwillingness to communicate	Lack of trust in comrades in the service	Lack of trust in commanders	Inability to perform the assigned tasks	General indicators due to the method			
"Maladjustment" (Prykhodko, Matsegora, Kolesnichenko, and Baida) [17]																				
Violation of behavioral regulation	0.50	0.56	0.46	0.44	0.49	0.51	0.52	0.51	0.54	0.41	0.54	0.52	0.49	0.42	0.49	0.55	0.68			
Probability of committing suicidal attempts	0.41	0.52	0.36	0.39	0.47	0.48	0.54	0.48	0.49	0.41	0.53	0.49	0.48	0.38	0.42	0.51	0.62			
Violation of moral normativity	0.34	0.24	0.37	0.33	0.20	0.16	0.25	0.18	0.23	0.14	0.22	0.23	0.29	0.28	0.36	0.19	0.34			
Loss of communicative potential	0.36	0.37	0.39	0.38	0.35	0.35	0.38	0.34	0.37	0.27	0.35	0.35	0.43	0.41	0.40	0.36	0.50			
General indicators of maladjustment	0.50	0.52	0.49	0.47	0.47	0.47	0.52	0.47	0.50	0.38	0.51	0.49	0.52	0.46	0.52	0.50	0.66			
"Mississippi Scale for Combat-Related PTSD" (Keane, Caddell, and Taylor) [18]																				
PTSD	0.54	0.56	0.51	0.48	0.50	0.50	0.57	0.53	0.54	0.44	0.54	0.53	0.50	0.44	0.48	0.55	0.69			
"Diagnostics of psychological safety of an individual" (Prykhodko) [19]																				
Trust	-0.29	-0.34	-0.25	-0.29	-0.29	-0.32	-0.38	-0.30	-0.39	-0.35	-0.39	-0.35	-0.35	-0.33	-0.30	-0.35	-0.44			
Respect	-0.25	-0.25	-0.26	-0.29	-0.22	-0.18	-0.28	-0.20	-0.30	-0.24	-0.26	-0.26	-0.32	-0.29	-0.24	-0.21	-0.34			
Moral and communicative	-0.30	-0.33	-0.28	-0.32	-0.29	-0.28	-0.37	-0.28	-0.38	-0.33	-0.36	-0.35	-0.37	-0.34	-0.31	-0.32	-0.44			
Motivational and volitional	-0.31	-0.38	-0.27	-0.31	-0.34	-0.36	-0.38	-0.33	-0.39	-0.36	-0.40	-0.41	-0.36	-0.28	-0.25	-0.34	-0.46			
Valuable and semantic	-0.28	-0.30	-0.27	-0.28	-0.28	-0.28	-0.35	-0.29	-0.32	-0.32	-0.36	-0.33	-0.36	-0.30	-0.25	-0.29	-0.41			
Internal comfort	-0.24	-0.30	-0.22	-0.25	-0.30	-0.31	-0.39	-0.33	-0.31	-0.32	-0.37	-0.34	-0.33	-0.27	-0.25	-0.29	-0.40			
General indicators of psychological safety of an individual	-0.30	-0.35	-0.28	-0.31	-0.32	-0.32	-0.39	-0.33	-0.37	-0.35	-0.39	-0.38	-0.38	-0.32	-0.28	-0.33	-0.45			
"Evaluation of traumatism of combat experience of servicemen" (Kolesnichenko) [20]																				
Unfavorable social conditions of performing service combat tasks	0.47	0.49	0.41	0.37	0.37	0.39	0.42	0.41	0.44	0.33	0.42	0.42	0.34	0.41	0.50	0.45	0.58			
Specific traumatic combat conditions	0.27	0.29	0.23	0.22	0.13	0.17	0.14	0.21	0.23	0.21	0.14	0.18	0.11	0.22	0.29	0.15	0.28			
Unfavorable social situation of participation under combat conditions	0.21	0.23	0.25	0.26	0.08	0.09	0.09	0.13	0.18	0.06	0.11	0.13	0.15	0.14	0.23	0.09	0.21			
Internal resources of resistance	-0.12	-0.14	-0.03	0.00	-0.23	-0.20	-0.24	-0.27	-0.12	-0.10	-0.24	-0.22	-0.10	-0.15	-0.07	-0.27	-0.21			
External resources of resistance	-0.11	-0.14	-0.08	-0.10	-0.16	-0.17	-0.20	-0.13	-0.17	-0.12	-0.16	-0.08	-0.07	-0.09	-0.01	-0.14	-0.16			
General indicators of traumatism of combat experience	0.32	0.37	0.25	0.24	0.32	0.32	0.38	0.37	0.34	0.23	0.36	0.31	0.17	0.28	0.24	0.36	0.42			
"Resistance to psychological traumatism of combat experience" (Kolesnichenko) [21]																				
Expectations of participation in hostilities	-0.32	-0.37	-0.25	-0.15	-0.40	-0.37	-0.39	-0.38	-0.34	-0.31	-0.43	-0.39	-0.26	-0.27	-0.34	-0.46	-0.48			
Overcoming a stressful situation	-0.38	-0.38	-0.29	-0.16	-0.40	-0.41	-0.38	-0.31	-0.30	-0.27	-0.40	-0.41	-0.28	-0.27	-0.26	-0.46	-0.46			
Implementation of the received experience	-0.36	-0.34	-0.31	-0.19	-0.39	-0.30	-0.44	-0.38	-0.30	-0.25	-0.41	-0.40	-0.30	-0.29	-0.30	-0.42	-0.47			
General indicators of resistance to traumatism	-0.40	-0.41	-0.32	-0.18	-0.45	-0.41	-0.45	-0.40	-0.36	-0.31	-0.46	-0.45	-0.32	-0.31	-0.34	-0.50	-0.53			
Helplessness	0.28	0.32	0.23	0.16	0.34	0.38	0.30	0.28	0.29	0.26	0.35	0.33	0.27	0.25	0.27	0.39	0.41			
Conscious attitude towards professional training	-0.12	-0.07	-0.10	0.01	-0.16	-0.08	-0.17	-0.16	-0.09	-0.07	-0.18	-0.18	-0.07	-0.09	-0.10	-0.17	-0.15			
The ability to get experience	-0.35	-0.36	-0.25	-0.17	-0.34	-0.28	-0.33	-0.25	-0.22	-0.23	-0.30	-0.39	-0.19	-0.27	-0.24	-0.34	-0.38			
Cognitive dysfunction	0.40	0.38	0.29	0.13	0.37	0.36	0.38	0.32	0.28	0.26	0.39	0.39	0.27	0.23	0.27	0.42	0.45			
Conscious attitude towards military duties	-0.21	-0.27	-0.20	-0.09	-0.28	-0.22	-0.34	-0.32	-0.22	-0.18	-0.35	-0.28	-0.18	-0.21	-0.25	-0.38	-0.35			

Psychological safety of an individual = 5.325 – 0.072*Irritability – 0.064*Devastation – 0,077*Sense of guilt – 0,095*Sense of powerlessness – 0.071* Reluctance to communicate + 0.775.

Traumatism of combat experience = -17.672 + 0.426*Anxiety + 0.393*Apathy + 0.502*Inability to perform the assigned tasks + 0.789.

Resistance to combat psychological traumatization = 167.165 – 2.514*Anxiety + 2.869*Anger – 1.621*Apathy – 1,510* Lack of trust in comrades in the service – 4.812*Inability to perform the assigned tasks + 0.599.

The procedure of regression analysis had to give the possibility to reduce the dimension of measurements for each state, but as it could be seen, the error of evaluation in the concluded regression equations was quite high, especially in the process of predicting traumatism of combat experience (e = 0.789) and psychological safety of an individual (e = 0.775) that made it inappropriate to use them for calculations. However, the information obtained through regression analysis gave the possibility to better understand the experience of servicemen who had different negative symptoms due to their participation in hostilities.

Moreover, a long-last period of testing and a large selection of the study had shown that the calculations made with the help of regression analysis by individual scales were less accurate than the normalized general indicator by the method (that indicated one more time the importance of using the method as a single scale). It was the regulation for different negative symptoms that prevailed in determining the ways of processing data by the method.

Thus, the obtained data showed that if the general indicator by the method "Evaluation of negative mental reactions and states of combatants" exceeded 3.5 points, then 65.45% of servicemen-participants of the psychological recovery program were likely to be symptoms of maladjustment by the same method. If the average points according to the developed method were 5 or more, then more than 85% of servicemen with this indicator were diagnosed with expressed symptoms of maladjustment.

The comparison of the general indicator by the method "evaluation of negative mental reactions and states of combatants" with the method "Mississippi Scale for Combat-Related PTSD" (Keane, Caddell, and Taylor) [18] showed that while exceeding 3.5 points according to the scale of the developed method more than 90% of servicemen with this indicator had expressed PTSD symptoms. When the average quantity of points was 5.5% – 100% of servicemen who participated in psychological recovery activities had an indicator that exceeded the norm by the "Mississippi Scale for Combat-Related PTSD" (Caddell and Taylor) [18].

The comparison with the data provided by the method "Resistance to psychological traumatism of combat experience" showed that with general points 3 or more in accordance with the method "Evaluation of negative mental reactions and conditions of combatants" 75.59% of servicemen with such quantity of points were diagnosed with an unsatisfactory indicator of resistance (from 0 to 143 points).

If the general indicator was exceeded in accordance with the method "Evaluation of negative mental reactions and states of combatants" the score of 5 points meant that low resistance to combat psychological traumatism was diagnosed in almost 86% of servicemen who participated in psychological recovery activities.

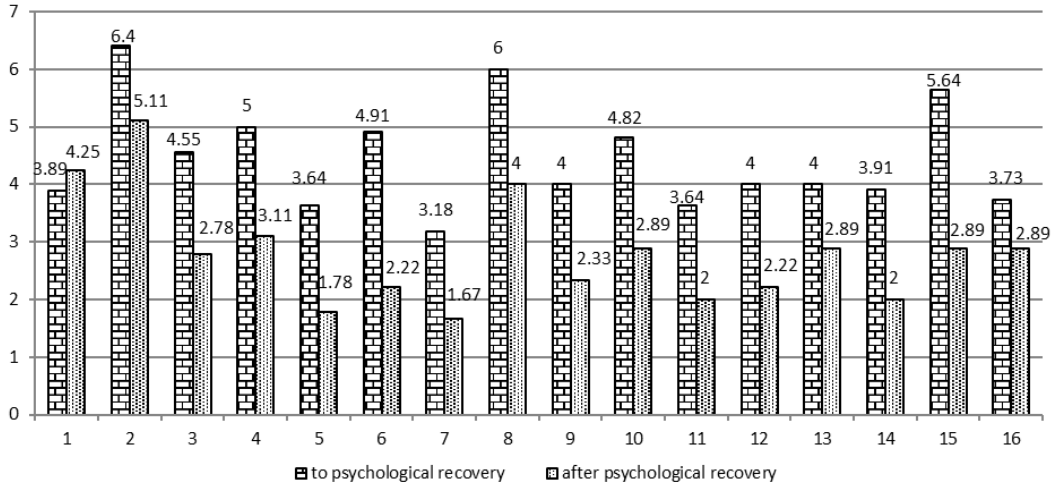
The comparison with the express method "Psychological Safety of an Individual" (Prykhodko) [19] and "Evaluation of traumatism of combat experience of servicemen" (Kolesnichenko) [20] pointed out that if the points were less than 3 by the general scale of the method "Evaluation of negative mental reactions and states of combatants" 89% of servicemen retained satisfactory indicators of psychological safety of an individual, and 85.41% were diagnosed with low trauma of combat experience.

More reliable for these two methods was a forecast concerning psychological well-being than negative symptoms.

Thus, the given data showed that for the general indicator by the method "Evaluation of negative mental reactions and states of combatants" it was normal to have a high probability of negative symptoms' absence (PTSD, maladjustment, instability to combat psychological traumatization, and psychological safety of an individual) and it also showed that high ability to recover was possible when an indicator was less than 3 points.

It was necessary to point out that the results obtained with the help of the method, both individual and group ones, were convenient to present in the form of column histograms. As an example, there was proposed the histogram of the dynamics of negative mental reactions and conditions of servicemen with signs of maladjustment (in particular, violation of behavioral regulation) in the process of one of the decompression courses (Figure 1).

Figure 1: Dynamics of negative mental reactions and conditions while participating in psychological recovery in a group of servicemen with violation of behavioral regulation (in points)



Notes: 1 – inability to perform the assigned tasks; 2 – lack of trust in commanders; 3 – lack of trust in comrades in the service; 4 – unwillingness to communicate; 5 – lack of focus; 6 – sense of impotence; 7 – sense of guilt; 8 – concern; 9 – apathy; 10 – devastation; 11 – self-doubt; 12 – inattention; 13 – anger; 14 – aggressiveness; 15 – anxiety; 16 – irritability

DISCUSSION

According to Ukrainian [14] and foreign specialists [26,27], early diagnosis of negative mental reactions and states [28], post-stress states, and determination of a group of increased psychological attention among personnel gave the possibility to identify servicemen with low personal adaptive potential and high probability of early and severe manifestations of combat psychological traumas [29] and its consequences [30]; also gave the possibility to create individual tactics and methods of prevention and restoration of each surveyed serviceman. To solve the problem of diagnosis of negative mental reactions and states of servicemen, it was suggested to use the following psychodiagnostic tools: "The Hospital Anxiety and Depression Scale (HADS) ", "Brief Scale of Anxiety, Depression, and PTSD", "The Montgomery-Asberd Depression Rating Scale (MADRS)" [31], "Beck Depression Inventory (BDI)" [32], "Primary Screening for Post-Traumatic Stress Disorder (PTSD)", "Mississippi Scale for Combat-Related PTSD" (Keane, Caddell, and Taylor) [18], "Impact of Event Scale–Revised (IES-R)" [33], "Patient Health Questionnaire (PHQ)-9" [34], "Clinical-administered PTSD Scale" [35], "Neurotization and Psychopathization (LNP) questionnaire" [14] and others. As an additional diagnostic tool, at the request of a psychologist, there was used the method "The Suicidal Behaviors Questionnaire-Revised (SBQ-R)" [36] to diagnose the suicidal inclinations of servicemen. However, this psychological study could have been placed under the conditions of medical and psychological rehabilitation which lasted not less than two weeks, but it was quite difficult to realize this tool under the conditions of psychological recovery, which lasted not more than one week.

Traditionally, in clinical practice, there had been used for a long time the projective method such as Lusher's color test, in particular after psychotherapy and training activities for self-regulation and restoration of adaptive capacity, the selection of colors could be compared with the so-called autogenic norm by Wallnöfer [37].

World tendencies in psychological studies showed that the diagnosis of mood, mental reactions, and conditions was relevant not only for the needs of the clinic but also in the workplace. The study of workers' moods and states was an important component of the psychological well-being (health) of workers. These studies were extremely large-scale and attracted thousands of working people as participants [38]. Such interest in the problem of studying the state of a working person, as an indicator of his/her psychological well-being, was quite clear since the psychological state was a holistic, systematic, integral formation of human psychological activity. The psychological state of an individual could be internally and externally observed, it acted as a regulatory function of adaptation to the external situation and environment [16]. According to the definition by Kirilenko, the psychological state was the formation of psychological activity, which reflected the moment of stability and specificity of psychological processes' duration, as a form of response, and reflected the attitude of an individual toward his/her own psychological phenomena at a certain point in time under certain conditions [39]. Varii pointed out that the psychological state was a temporary functional level of the psyche, which reflected the interaction of the influence of the internal environment of the body or external factors and determined the orientation of

psychological processes' duration at a certain moment and manifestation of psychological properties of an individual [40]. The author defined the following areas in the studies of mental states: 1) mental states were an integral characteristic of the psyche at a particular moment; 2) psychological states were the background on the bases of which operated the psychological activity and orientation of the psychological activity of an individual; 3) it was a systemic reaction of the human psyche to changes of the conditions.

Volzhentseva highlighted that the leading functions of mental states were the regulation and integration into functional units, which were formed in the hierarchy of a single, holistic set of psychological processes and properties [25]. According to the author, the adaptive function of the psychological state was to establish the correspondence between the current needs and capabilities of an individual, considering the external conditions, features of activity, and behavior.

It was likely that the integration and integrity of psychological states became the basis for reducing the dimensions of the methods which were intended for their research. Thus, in foreign scientific sources, it was reported that to determine the moods and conditions, which were important indicators of short-term effects of intervention, was also used in clinical practice, "The Profile of Mood States (POMS)" [12,41]. This scale was developed by American experts, it had the form of a self-report and included 65 elements that related to 7 different scales: depression, anxiety, fatigue, energy, irritability, tension, and confusion.

The answer scale was divided into 5 categories from "not at all" to "completely yes". However, German psychologists in the re-standardization of POMS [12,13] created a shortened version of the method that included only 35 points which belonged to the scale "Depression/anxiety", "Fatigue", "Energy" and "Irritability" [38]. Another study was intended to reduce the dimension of POMS [41]. For this purpose, the POMS scale [12,13] with the help of regression analysis correlated with "The Eight State Questionnaire" (8SQ) [42], which was formed to measure anxiety, stress, depression, regression, fatigue, guilt, extraversion, and excitement. Researchers found that the excessiveness of measurement between these two methods mainly referred to negative emotional states.

CONCLUSIONS

Thus, the developed method "evaluation of negative mental reactions and states of combatants" was a tool that gave the possibility to determine the presence of negative psychological symptoms of servicemen related to their participation in hostilities and was a convenient tool for estimation of the dynamics of the state under the conditions of short-term programs of psychological recovery without the use of complex evaluation procedures and calculation of data.

Conflicts of interest and sources of funding

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Authors' contribution

Conceptualization, O.K. and YaM.; managed the project, I.P.; conducted the research, V.K. and V.P.; contributed to the final draft of the manuscript, A.P., S.S. and N.P.; substantiated the methodology, S.L. All authors have read and agreed to the published version of the manuscript. All authors have read and agreed to the published version of the manuscript.

Patient consent for publication

Informed consent was obtained from all subjects for inclusion in the study while maintaining their confidentiality. Written informed consent has been obtained from all subjects to publish this paper.

Ethics approval and consent to participate

All procedures followed were in accordance with the ethical standards of the Helsinki Declaration of 1975, as revised in 2000.

References:

1. Kolesnichenko O.S. Zasady boiovoi psykholohichnoi travmatyzatsii viiskovosluzhbovtsiv Natsionalnoi hvardii Ukrainy [Basics of combat psychological traumatization of military personnel of the National Guard of Ukraine]. 2018; Kharkiv : National Academy of the National Guard of Ukraine. https://books.ndcnangu.co.ua/knigi/ Monograf_ bojov_psihol_travm_2018.pdf

2. Prykhodko I, Kolesnichenko O, Matsehora Ya, Aleshchenko V, Kovalchuk O, Matsevko T, Krotiuk V, Kuzina V. Effects of posttraumatic stress and combat losses on the combatants' resilience, Československá psychologie. 2022; 66(2), 157-169. https://doi.org/ 10.51561/cspsych.66.2.157

3. Roy M. J., & Francis J. L. The psychological recovery of physically wounded service members. In A. B. Adler, P. D. Bliese, & C. A. Castro (Eds.), Deployment psychology: Evidence-based strategies to promote mental health in the military. 2011. (pp. 195–216). American Psychological Association. https://doi.org/10.1037/12300-008

4. Besemann, M., Hebert, J., Thompson, J. M., Cooper, R. A., Gupta, G., Brémault-Phillips, S. B., & Dentry, S. J. Reflections on recovery, rehabilitation and reintegration of injured service members and veterans from a bio-psychosocial-spiritual perspective. Canadian journal of surgery. Journal canadien de chirurgie. 2018; 61(6), 219-231. https://doi.org/10.1503/cjs.015318

5. Prykhodko I.I. Program of psychological rehabilitation of the National Guard of Ukraine military personnel participated in combat actions. International Journal of Science Annals. 2018; 1(1-2), 34–42. https://doi.org/10.26697/ijsa.2018.1-2.05

6. Adler A. B., Castro C. A., & McGurk D. Time-driven battlemind psychological debriefing: a group-level early intervention in combat. Military medicine. 2009; 174(1), 21–28. https://doi.org/10.7205/milmed-d-00-2208

7. Deahl M., Srinivasan M., Jones N., Thomas J., Neblett C., & Jolly A. Preventing psychological trauma in soldiers: the role of operational stress training and psychological debriefing. The British journal of medical psychology. 2000; 73(1), 77–85. https://doi.org/10.1348/000711200160318

8. Kennis M., & Te Brake H. Facilitating the transition home after military deployment: a systematic literature review of post-deployment adaptation programmes. European journal of psychotraumatology. 2022; 13(1), 2073111. https://doi.org/10.1080/20008198.2022.2073111

9. Bartone, P. T. Resilience under military operational stress: can leaders influence hardiness? Military Psychology. 2006; 18(supp1.), 131–148. https://doi.org/10.1207/s15327876mp 1803s_10

10. Bonanno, G. A. Loss, trauma, and human resilience: have we underestimated the human capacity to thrive after extremely aversive events? American Psychologist. 2004; 59(1), 20–28. https://doi.org/10.1037/0003-066X.59.1.20

11. Blackburn, L., & Owens, G. P. Rumination, resilience, and posttraumatic stress disorder symptom severity among veterans of Iraq and Afghanistan. Journal of Aggression, Maltreatment & Trauma. 2016; 25(2), 197–209. https://doi.org/10.1080/10926771.2015.1107174

12. McNair, D. M., Heuchert, J. W. P., & Shillony E. (in press). Research with the Profile of Mood States (POMS), 1964-2002: A comprehensive bibliography. Toronto, Canada: Multi-Health Systems.

13. McNair, D. M., Lorr, M., & Droppleman, L. F. Manual for the Profile of Mood States. San Diego, CA: Educational and Industrial Testing Services. Educational and Industrial Testing Service, San Diego, Calif., 1971.

14. Agaev N. A, Kokun O. M, Pishko I. O, Lozinskaya N. S, Ostapchuk V. V, Tkachenko V. V. (2016). Zbirnyk metodyk dlia diahnostyky nehatyvnykh psykhichnykh staniv viiskovosluzhbovtsiv [Collection of methods for diagnostics of negative mental states of servicemen]. 2016; Kyiv: NDTs HP ZSU, 234 s. https://lib.iitta.gov.ua/107163/1/%D0%9F%D0%BE%D1%81%D1%96%D0%B1%D0%BD%D0%B8%D0%BA%20%D0%9D%D0%9F%D0%A1_16.pdf

15. Kyselov Yu.Ia. Deiaki psykholohichni aspekty optymizatsii sportyvnoi diialnosti. Psykholohichni problemy predsorevnovatelnoi pidhotovky kvalifikovanykh sportsmeniv [Some psychological aspects of optimization of sports activities. Psychological problems of pre-competition training of qualified athletes]. Sankt-Peterburh : SPNIIFK, 1997.

16. Prykhodko I. I., Kolesnichenko O. S., Matsehora Ya.V. ta in. Psykholohiia diialnosti v osoblyvykh umovakh [Psychology of activity in special conditions]. 2021. Kharkiv: NA NHU. https://books.ndcnangu.co.ua/knigi/Slovnik_psihologiya_diyalnosti.pdf

17. Prykhodko I.I., Kolesnichenko O.S., Matsehora Ya.V., Baida M.S. Ekspres-opytuvalnyk "Dezadaptyvnist" : rozroblennia, aprobatsiia, psykhometrychni pokaznyky [Express questionnaire "Maladjustment": development, testing, psychometric indicators]. Visnyk Natsionalnoi akademii Derzhavnoi prykordonnoi sluzhby Ukrainy. 2017; 3, 53–78. http://nbuv.gov.ua/UJRN/Vnadpn_2017_3_8

18. Keane TM, Caddell JM, Taylor KL. Mississippi Scale for Combat-Related Posttraumatic Stress Disorder: Three studies in reliability and validity. Journal of Consulting and Clinical Psychology. 1988; 56(1), 85–90. https://doi.org/10.1037//0022-006x.56.1.85

19. Prykhodko I.I. Rozrobka psykhodiahnostychnoho instrumentariiu vyznachennia psykholohichnoi bezpeky osobystosti fakhivtsiv ekstremalnykh vydiv diialnosti [Development of a psychodiagnostic toolkit for determining the psychological safety of an individual of specialists in extreme types of activities]. Naukovyi visnyk Lvivskoho derzhavnoho universytetu vnutrishnikh sprav. Seriia psykholohichna. 2012; 2(1), 312–322. http://nbuv.gov.ua/UJRN/Nvldu_2012_2%281%29__39

20. Kolesnichenko O.S. Metodyka "Otsinky travmatychnosti boiovoho dosvidu" u viiskovosluzhbovtsiv-uchasnykiv boiovykh dii» [The methodology "Evaluation of the traumatic experience of combat in servicemen participating in combat operations"]. Ukrainskyi psykholohichnyi zhurnal. 2018; 3, 78–95. http://nbuv.gov.ua/UJRN/ukpsj_2018_3_8

21. Kolesnichenko O.S. Struktura ta zmist metodyky "Stiikist do boiovoi psykholohichnoi tramatyzatsii" fakhivtsia ekstremalnoho vydu diialnosti [The structure and concept of the methodology "Strength to Combat Psychological Tramatization" facilitation of an extreme type of activity]. Zbirnyk naukovykh prats Natsionalnoi akademii Derzhavnoi prykordonnoi sluzhby Ukrainy. Seriia: "Psykholohichni nauky". 2018; 1 (9), 110–127.

22. Maklakov A.G. Multilevel personality questionnaire "Adaptiveness" [Multilevel personal questionnaire "Adaptiveness"]. Professional psychological selection of candidates for military educational institutions of the Ministry of Defense of the Russian Federation [Professional psychological selection of candidates for military educational institutions of the Ministry of Defense of the Russian Federation]. 1994. (pp. 164-174)

23. McKinley J. C., Hathaway S. R., & Meehl P. E. The Minnesota Multiphasic Personality Inventory: VI. The K Scale. Journal of Consulting Psychology. 1948; 12(1), 20–31. https://doi.org/10.1037/h0061377

24. Maklakov AG & Chermyanin SV. Mnogourovnevyiy lichnostnyiy oprosnik "Adaptivnost" (MLO) [Multilevel Personality Questionnaire "Adaptability" (MLO)]. In DYa Raygorodskiy (Ed.), Prakticheskaya psikhodiagnostika [Practical psychodiagnostics]. 2006. Samara: Bahrah-m', Publishing House. 549-672.

25. Volzhentseva I.V. Problema rehuliatsii psykhichnykh staniv studentiv u stresovykh sytuatsiiakh navchalnoi diialnosti [The problem of regulating mental states of students in stressful situations of educational activity]. Visnyk pisliadyplomnoi osvity. 2009; 13(2), 69–75. http://umo.edu.ua/zhurnal-pisljadiplomna-osvita-v-ukrajini-1

26. Gates M. A., Holowka D. W., Vasterling J. J., Keane T. M., Marx B. P., & Rosen R. C. Posttraumatic stress disorder in veterans and military personnel: epidemiology, screening, and case recognition. Psychological services. 2012; 9(4), 361–382. https://doi.org/10.1037/a0027649

27. Liu Y., Collins C., Wang K., Xie X., & Bie R. The prevalence and trend of depression among veterans in the United States. Journal of affective

disorders. 2019; 245, 724–727. https://doi.org/10.1016/j.jad.2018.11.031

28. Warner C. M., Warner C. H., Breitbach J., Rachal J., Matuszak T., & Grieger T. A. Depression in entry-level military personnel. Military medicine. 2007; 172(8), 795–799. https://doi.org/10.7205/milmed.172.8.795

29. Afifi T. O., Taillieu T., Zamorski M. A., Turner S., Cheung K., & Sareen J. Association of Child Abuse Exposure With Suicidal Ideation, Suicide Plans, and Suicide Attempts in Military Personnel and the General Population in Canada. JAMA psychiatry. 2016; 73(3), 229–238. https://doi.org/10.1001/jamapsychiatry.2015.2732

30. Searle A. K., Van Hooff M., Lawrence-Wood E. R., Grace B. S., Saccone E. J., Davy C. P., Lorimer M., & McFarlane A. C. The impact of antecedent trauma exposure and mental health symptoms on the post-deployment mental health of Afghanistan-deployed Australian troops. Journal of affective disorders. 2017; 220, 62–71. https://doi.org/10.1016/j.jad.2017.05.047

31. Quilty L. C., Robinson J. J., Rolland J. P., Fruyt F. D., Rouillon F., & Bagby R. M. The structure of the Montgomery-Åsberg depression rating scale over the course of treatment for depression. International journal of methods in psychiatric research. 2013; 22(3), 175–184. https://doi.org/10.1002/mpr.1388

32. Beck A. T., Steer R.A., & Garbin M.G. Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. Clinical Psychology Review. 1988; 8(1), 77-100.

33. Tiemensma J., Depaoli S., Winter S. D., Felt J. M., Rus H. M., & Arroyo A. C. The performance of the IES-R for Latinos and non-Latinos: Assessing measurement invariance. PloS one, 2018; 13(4), e0195229. https://doi.org/10.1371/journal.pone.0195229

34. Kroenke K., Spitzer R. L., & Williams J. B. W. The PHQ-9: Validity of a brief depression severity measure. Journal of General Internal Medicine. 2001; 16, 606–613. http://dx.doi.org/10.1046/j.1525-1497.2001.016009606.x

35. Tarabrina N. V. (2001). Praktykum po psykholohyy posttravmatycheskoho stressa [Workshop on psychology of post-traumatic stress]. 2001. Sankt-Peterburh: Pyter. https://nwk.su/assets/files/BOOKS/Tarabrina_Praktikum_po_psikhologii.pdf

36. Osman A., Bagge C. L., Gutierrez P. M., Konick L. C., Kopper B. A., & Barrios F. X. The Suicidal Behaviors Questionnaire-Revised (SBQ-R): validation with clinical and nonclinical samples. Assessment. 2001; 8(4), 443–454. https://doi.org/10.1177/107319110100800409

37. Wallnöfer H. Auf der Suche nach dem Ich: Psychotherapie, Meditation und seelische Gesundheit. Albert Müller Verlag. Rüschlikon-Zürich. 1986.

38. Morfeld M., Petersen C., Krüger-Bödeker A., von Mackensen S., & Bullinger M. The assessment of mood at workplace - psychometric analyses of the revised Profile of Mood States (POMS) questionnaire. Psycho-social medicine. 2007; 4, Doc06.

39. Kyrylenko T.S. Psykholohiia: emotsiina sfera osobystosti [Psychology: emotional sphere of personality]. 2007. Kyiv : Lybid. https://soc.univ.kiev.ua/en/library/psihologiya-emociyna-sfera-osobistosti-navchposibnik

40. Varii M.I. Zahalna psykholohiia [General Psychology]. 2009. Kyiv : Tsentr uchbovoi literatury. http://194.44.152.155/elib/local/r298.pdf

41. McNair, D. M., Lorr, M., & Droppleman, L. F. Manual for the Profile of Mood States. San Diego, CA: Educational and Industrial Testing Services. Educational and Industrial Testing Service, San Diego, Calif., 1971

42. Boyle G. J. Quantitative and Qualitative Intersections between the Eight State Questionnaire and the Profile of Mood States. Educational and Psychological Measurement. 1987; 47(2), 437–443. https://doi.org/10.1177/0013164487472015

43. Boyle G.J. Item analysis of the subscales in the Eight State Questionnaire (8SQ): Exploratory and confirmatory factor analyses. Multivariate Experimental Clinical Research. 1991; 10(1), 37–65. https://psycnet.apa.org/record/1992-11261-001.

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ORIGINAL ARTICLE

Associations Between Medical Students' Opinions on Usage of Internet Services and Digital Teaching Tools

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Abstract: *Currently, the educational process must integrate new tools, to keep pace with technological progress. Our paper aims to investigate the extent to which the preferences of medical students for the autonomous use of multimedia resources in the learning process are correlated with their opinions towards the Internet and the intensity of using it in their daily activities. Methods: We investigated 395 medical students from 4 medical universities in Romania, 75.9% females, and 88.8% in the 1st and 2nd years of study. Students were asked to express on Likert-scales their agreement with a list of statements about Internet services, as well as whether they like learning using multimedia tools and how intensively they use Internet services. Results: The students agree to a medium to large extent with the favorable statements about Internet services but are also aware of the negative influences that indiscriminate use of such technology can have. The intensity of Internet usage is high, although not exaggerated. With small exceptions, the students who enjoy using multimedia resources during the learning process have also favorable opinions about Internet services, and use them constantly, mainly for information and instant messaging on social networks*.

Keywords: *multimedia-based learning; blended learning; Internet services; social networks; medical students*

INTRODUCTION

Currently, digital technology has become increasingly used in everyday activities, and its intensive use in most fields of activity has attracted changes in the structure of society, and even in the psychology of individuals, who gradually change their conceptions about life, work, and education, about the ideal way of spending leisure time and about the features of an optimal work climate. In this general context, it is obvious that the educational process must integrate new tools, in an attempt to keep pace with technological progress. The protagonists of this process, students as well as teachers, are people with a fundamentally different lifestyle than 20 years ago, with different expectations and conceptions.

The most obvious changes are noticed in the case of the current generation of students. This is the so-called "Generation Z" (children born after 1997), also known as iGen, post-millennial, or digitally native. These are children who have been exposed to technology from the beginning of their lives, so using computers and gadgets has become second nature to them, as have the activities online and on social networks. Consequently, these children prefer to study independently, at their own pace, using visual or kinaesthetic didactic tools, which give them immediate feedback. It is important for them to respect the right to privacy and personal space; they are pragmatic, entrepreneurial, and generally reluctant to take risks (because they faced periods of economic recession in childhood); although they generally enjoy interaction with the teacher, Generation Z children have fewer social skills associated with face-to-face communication and the art of conversation, compensated instead by intense online activity [1].

There are currently relatively few studies in the literature concerning Generation Z issues, which usually focus on describing its characteristics [2,3], effective strategies for recruitment in the public sector [4], and individuals' attitudes towards work [5], but without focusing on the specific problems of medical students of this generation, with their own needs, preferences and learning styles.

Obviously, the learning style of Generation Z students has features that differentiate it from the learning styles preferred by other generations of students. The most preferred method is active learning (through discussion and involvement in practical projects), based on sensory stimuli (visual - images, graphics, auditory and kinetic). Knowledge is achieved through observation, practice, and quick and targeted access to the necessary information through the use of technology and online resources: e.g. YouTube for video tutorials, Facebook (for chatting with classmates and sharing projects and teaching materials), or Google (for documenting and searching for scientific references). Students prefer self-study, at their own pace, with a flexible schedule and teaching materials that intensively use multimedia resources: explanatory or demonstrative video sequences, PowerPoint presentations with audio support, simulations, collaborative projects, discussion forums, online questionnaires, and case studies in the classical environment (seminar room or practical works). In this context, the portrait of the ideal teacher has also changed significantly: firstly, he must be a good communicator, close and friendly, transparent, enthusiastic, passionate and competent in his field, able to propose realistic goals and to provide immediate and constructive feedback on their achievement, willing to provide professional and emotional support to his students, both academically and individually, to prepare them for their future careers.

In this context, the concept of blended education, based on the intensive integration of digital resources into the teaching process, is becoming increasingly popular among teaching tools.

Such education programs are usually developed in mixed regimes, online and onsite, combining as much as possible in an optimal manner the advantages of both methods. Blended courses are a current trend that provides a new and effective instructional experience to the students they address, and have several major advantages:

- Flexibility in the teaching schedule, which simplifies students' access to the course, regardless of their physical location and allows them to organize their time and pace of learning according to their own needs and availability;

- More effective teaching: Most scientific studies show that blended teaching is more effective than traditional courses, but also than full online courses. A 2009 report from the United States examined 51 studies comparing online and traditional methods and concluded that students enrolled in blended learning programs score on average better on exams than those enrolled in full-onsite programs [6]; on the other hand, blended teaching programs also perform better than fully online ones as well [7], as they still give to the students the opportunity to interact effectively with the teacher when needed.

- Clearer organization of content: It is the natural result of a well-designed blended course, which must provide students with clear and detailed indications of using the proposed resources, activities, and tests, helping them to concentrate better and proposing an optimal pace of learning, in the same way that the teacher guides students onsite in going through the exposed materials;

- Stimulation of active learning, which emphasizes the student's autonomy in effective learning communities;

- Lower costs: Reducing the number of onsite meetings frees up the teaching spaces of the institution and reduces some utility expenses. The teachers and the students will gain lower transport costs and time savings, although logistics expenses can be slightly increased (it is necessary to purchase adequate personal computers and involves additional costs for electricity consumption and telephone subscription).

Our paper aims to investigate the extent to which the preferences of students at medical faculties for the autonomous use of multimedia resources in the learning process are correlated with their opinions towards the online environment and the Internet and the intensity with which they use such resources in their daily activities, not necessarily related to the learning process.

MATERIALS AND METHODS

We conducted a case study that enrolled 395 medical students from 4 medical universities in Romania. The general features of the sample are shown in Table 1. Students are 3 quarters females (75.9%); most students are in the 1st and 2nd years of study (88.8%), aged between 18-20 years (74.4%), with an average age of 21.78 ± 3,736 years and a range of variation between 18-48 years.

Also, most students come from faculties of Dental Medicine (34.4%) or General Medicine (47.6%), mainly from the "Grigore T. Popa" University of Medicine and Pharmacy in Iasi, Romania (50.9%); 27.1% of the participating students are from University of Medicine and Pharmacy in Craiova, and 20.3% from University of Medicine and Pharmacy "Victor Babeș" in Timisoara.

Students were invited to fill in an online questionnaire in order to express their agreement degree with a list of statements about Internet services (favorable – 7 items and unfavorable – 3 items). In addition, they were asked whether they like learning using multimedia tools and resources and how intensively they use different Internet services (7 items).

The agreement degree with the proposed statements was quantified using a 5-step Likert scale, ranging from 1 – very small agreement to 5 – very large agreement.

Table 1: General features of the study sample

		n	%
Gender	masculine	95	24.1
	feminine	300	75.9
Age group	18-20 years	294	74.4
	21-24 years	78	19.7
	over 25 years	23	5.8
Year of study	1	228	57.7
	2	123	31.1
	3	44	11.1
Specialization	Dentistry	136	34.4
	General medicine	188	47.6
	Dental technique	70	17.7
	Prophylaxis assistance	1	0.3
University	UMPh Iasi	201	50.9
	UMPh Craiova	107	27.1
	UMPh Timișoara	80	20.3
	UMPh Cluj Napoca	7	1.8
Total		395	100.0

The questionnaire was presented and explained individually to each study participant.

Participation in the study was voluntary. Participants were informed about the study and the overall objectives of the research and, at the beginning of the questionnaire, were invited to give their informed consent. The questionnaires were completed anonymously.

The study was approved by the Research Ethics Commission of the "Grigore T. Popa" University of Medicine and Pharmacy, Iasi (decision no. 21/16.11.2020).

Statistical analysis

Data collected from students were recorded and processed in SPSS 29.0 (SPSS Inc., Chicago, IL) for Windows.

The responses to each item were characterized by frequency distributions and contingency tables. The numerical variables were characterized by descriptive statistics (mean, standard deviation, standard error, range of variation, and median). Comparisons between samples were made using the Kruskal-Wallis test for quantitative data, after having previously verified that they comply with the normal distribution law, using the Shapiro-Wilks normality tests. We considered the p-value ≤ 0.05 to be statistically significant (*) and the p-value ≤ 0.01 to be statistically highly significant (**).

RESULTS

The 7 favorable statements about the Internet were as follows:
- Item 1: The main advantage of the Internet is that it provides information fast;
- Item 2: The main advantage of the Internet is that it provides correct information;
- Item 3: Freedom of expression should not be restricted on the Internet;
- Item 4: Most people would not be able to cope if they no longer had access to the Internet;
- Item 5: I can't imagine my life without Internet access;
- Item 6: People who socialize on the Internet are happier than others;
- Item 7: If I didn't socialize on the Internet I would be sadder.

88.6% of students evaluate the Internet as a fast source of information (item 1) but are more reserved about its correctness (only 30.6% of them think that information on the Internet is much or very much correct – item 2).

68.9% of students believe that most people would not be able to cope if they no longer had access to the Internet (item 4) and 60.7% believe that they themselves would not be able to cope if there is no Internet (item 5). 53.9% of students believe that freedom of expression should not be limited to the Internet (item 3).

On the other hand, only a small percentage of students believe that socializing in the virtual environment ensures a comfortable psychological status, making them happier (item 6 – 10.9%, respectively item 7 – 21.5%) – Table 2.

The 3 unfavorable statements about the Internet were as follows:
- Item 8: Internet is addictive;
- Item 9: Parents should limit their children's access to Internet to at most one hour;
- Item 10: People's privacy is at risk due to social media.

A large part of students believe that the Internet can be addictive (item 8 – 76.2%). Although they generally do not consider it necessary for parents to limit their children's access to the Internet (item 9 – only 41.0% agree to a large or very large extent), they still believe that people's privacy is at risk due to social networks (item 10 – 59.5%) – Table 3.

Table 2: Favourable opinions about Internet services – students' responses

Favorable opinions about Internet services	Agreement:									
	1 – to a very small extent		2 – to a small extent		3 – in average measure		4 – to a large extent		5 – to a very large extent	
	n	%	n	%	n	%	n	%	n	%
Item 1	1	0.3	4	1.0	40	10.1	125	31.6	225	57.0
Item 2	8	2.0	49	12.4	217	54.9	93	23.5	28	7.1
Item 3	9	2.3	16	4.1	157	39.7	107	27.1	106	26.8
Item 4	7	1.8	25	6.3	91	23.0	143	36.2	129	32.7
Item 5	21	5.3	35	8.9	99	25.1	115	29.1	125	31.6
Item 6	81	20.5	121	30.6	150	38.0	34	8.6	9	2.3
Item 7	75	19.0	118	29.9	117	29.6	46	11.6	39	9.9

Table 3: Unfavourable opinions about Internet services – students' responses

Unfavorable opinions about Internet services	Agreement:									
	1 – to a very small extent		2 – to a small extent		3 – in average measure		4 – to a large extent		5 – to a very large extent	
	n	%	n	%	n	%	n	%	n	%
Item 8	3	0.8	17	4.3	74	18.7	139	35.2	162	41.0
Item 9	43	10.9	56	14.2	134	33.9	94	23.8	68	17.2
Item 10	10	2.5	44	11.1	106	26.8	118	29.9	117	29.6

The consumer of Internet services profile was outlined through another 7 questions, regarding the way, intensity, and main purposes for which students use Internet services. The recorded responses are shown in Table 4.

Most students (97.5%) say they use the Internet daily, and 70.9% of them use the Internet at least 3 hours a day. Almost 1/3 of students (29.4%) believe that they could not give up the Internet without problems even for a day - which indirectly means acknowledging an addiction to this practice. On the other hand, half of students (47.6%) indicate the one-week period as the maximum limit for opting out of the Internet, which is also a limited time frame. Most students access the Internet using their mobile phones (84.6%).

Although they use online services quite intensively, the main objective of students is not written communication – thus, almost 3 quarters of them (71.6%) say they receive/send between 1 - 10 emails per day, and 9.4% say they do not use e-mail at all. Half of students (52.4%) are active on social networks, having over 100 friends; however, there is also a significant percentage of students (20.8%) who have fewer than 10 friends online. In contrast, 74.2% of students post on social media only a few times a year or a few times a month. Therefore, students use social networks in a relatively moderate regime, mainly for instant communication and less for permanent posts.

Finally, the students were asked whether they liked learning, even autonomously, using multimedia tools and resources (Item 18). The answers to this question are generally favorable: 41.5% of students say they like much or very much to learn using multimedia tools, 38.0% of students agree on average with this statement, and only 20.5% of students show a total or partial disagreement (Table 5).

In order to express more precisely the obtained results, we quantified them as numerical scores, calculated as arithmetic averages of the responses. We calculated 2 scores, one for favorable opinions about Internet services (INTF) and one for unfavorable opinions (INTNF), with a range of variation between 1 – 5, which we interpreted as follows:

- Values between 1.00 – 1.49 = agreement to a very small extent;
- Values between 1.50 – 2.49 = agreement to a small extent;
- Values between 2.50 – 3.49 = agreement in average measure;
- Values between 3.50 – 4.49 = agreement to a large extent;
- Values between 4.50 – 5.00 = agreement to a very large extent.

Using the same procedure, we calculated also a third score, to characterize the intensity in using Internet services (INTS) – with a range of variation between 1 – 4 and interpreted accordingly:

- Values between 1.00 – 1.49 = very low intensity;
- Values between 1.50 – 2.49 = low intensity;
- Values between 2.50 – 3.49 = high intensity;
- Values between 3.50 – 4.00 = very high intensity.

The analysis of these scores reveals that students agree to a medium to large extent with the favorable statements about Internet services (INTF = 3.44 ± 0.590), but also with the unfavorable statements about these services (INTNF = 3.69 ±

0.817), being therefore aware of the negative influences that indiscriminate use of such technology can have. The intensity of Internet usage is high, although not exaggerated (INTS = 2.85 ± 0.350) – Table 6.

Table 4: Intensity and main purposes in using Internet services – students' responses

		n	%
Item 11. On average, I access the Internet:	several times a month	3	0.8
	several times a week	7	1.8
	daily	385	97.5
Item 12. On average, the amount of time I spend on the Internet during a day is:	less than 1 hour	7	1.8
	1 - 3 hours	108	27.3
	3 - 6 hours	145	36.7
	over 6 hours	135	34.2
Item 13. I could quit the Internet without problems for a time frame of:	1 year	25	6.3
	1 month	66	16.7
	1 week	188	47.6
	not even a day	116	29.4
Item 14. Generally, I access the Internet using:	a desktop	13	3.3
	a laptop	47	11.9
	a tablet	1	0.3
	a mobile phone	334	84.6
Item 15. On average, the number of emails I receive/send daily is:	none	37	9.4
	1 to 10	283	71.6
	11 to 30	58	14.7
	31 to 50	12	3.0
	over 50	5	1.3
Item 16. The number of friends (contacts) I have on the most frequently used social network is:	under 10	82	20.8
	between 11 and 50	68	17.2
	between 51 and 100	38	9.6
	between 101 and 500	109	27.6
	over 500	98	24.8
Item 17. On average, the frequency with which I post new information on my social media profile is:	none	35	8.9
	several times a year	152	38.5
	several times a month	141	35.7
	several times a week	55	13.9
	several times a day	12	3.0

Table 5: General opinion about the use of multimedia resources during the learning process – students' responses

General opinion	Agreement:									
	1 – to a very small extent		2 – to a small extent		3 – in average measure		4 – to a large extent		5 – to a very large extent	
	n	%	n	%	n	%	n	%	n	%
Item 18: I like to learn using multimedia tools and resources	19	4.8	62	15.7	150	38.0	81	20.5	83	21.0

Table 6: Internet services usage scores - descriptive statistics parameters

	n	Mean (M)	Standard deviation (SD)	Standard error of the mean (SEM)	Min	Max	Median
Favourable opinions about Internet usage (INTF)	395	3.44	0.590	0.030	1.57	5.00	3.43
Unfavourable opinions about Internet usage (INTNF)	395	3.69	0.817	0.041	1.00	5.00	3.67
Internet usage intensity (INTS)	395	2.85	0.350	0.018	1.71	3.71	2.86

We compared these scores according to the students' degree of agreement with the usage of multimedia resources during the learning process, to identify the possible links between these two elements. We started with the hypothesis that the students who enjoy using digital technologies for entertainment in leisure time should also enjoy using them professionally, respectively during the learning process.

The obtained results are presented in Table 7 and actually validate this research hypothesis.

Table 7: Internet services usage scores – compared according to the degree of agreement with the use of multimedia resources during the learning process

	Agreement:					
	1 – to a very small extent	2 – to a small extent	3 – in average measure	4 – to a large extent	5 – to a very large extent	Kruskal-Wallis test
	M ± SD	M ± SD	M ± SD	M ± SD	M ± SD	
Favorable opinions about Internet usage (INTF)	3.02 ± 0.705	3.43 ± 0.612	3.32 ± 0.545	3.53 ± 0.522	3.67 ± 0.593	H = 23.634 p < 0.001**
Unfavorable opinions about Internet usage (INTNF)	4.02 ± 0.842	3.68 ± 0.692	3.74 ± 0.807	3.58 ± 0.733	3.63 ± 0.973	H = 5.414 p = 0.247
Internet usage intensity (INTS)	2.75 ± 0.415	2.97 ± 0.325	2.81 ± 0.350	2.88 ± 0.324	2.80 ± 0.358	H = 12.310 p = 0.015*

There are statistically significant differences between the scores of favorable opinions about Internet usage, determined by the degree of agreement with the use of multimedia resources during the learning process. The lowest scores are found in students who agree to a very small extent with the use of multimedia resources (3.02 ± 0.705), and the highest in students who agree to a very large extent with the use of multimedia resources (3.67 ± 0.593), so these 2 elements are in clear correlation.

The situation is different for the scores of unfavorable opinions: the highest score of unfavorable opinions about Internet usage is found in students who strongly disagree with the use of multimedia resources in the learning process (4.02 ± 0.842). As the degree of agreement with the use of multimedia resources increases, the score of unfavorable opinions decreases, but with random fluctuations, so the observed differences are not statistically significant.

The lowest score of Internet usage intensity is also found in students who strongly disagree with the use of multimedia resources in the learning process (2.75 ± 0.415) – therefore they are fundamentally against digital technologies. On the other hand, the highest score of Internet usage intensity (2.97 ± 0.325) is observed in students with little agreement for the use of multimedia resources in the learning process – so they are obviously not against digital technologies but probably prefer to use them exclusively for leisure. Students who agree to a medium or large extent with the use of multimedia resources in the learning process have scores of Internet usage intensity between the 2 categories mentioned above, so they enjoy using digital technologies both professionally and for leisure. The differences between the investigated categories of students are statistically significant.

DISCUSSION

The data from the literature prove that multimedia resources are an effective tool for learning because they are able to stimulate the students' interest [8] and improve their cognitive skills [9], also contributing to the development of supplementary skills – like empathy [10,11] or the academic writing [12]. Such tools are preferred by medical students because they tend to be kinaesthetic learners, who use multiple ways to present a topic for a better understanding [13,14,15] – observations also confirmed by our study.

Medical students are advanced users of smartphones and laptops and easily use such devices during their daily activities and learning [15,16] – a fact also confirmed by our results. The students investigated by us are generally interested in digital technologies and their applicability during the learning process [15].

It is thus natural that our students have generally positive opinions about Internet services, without thinking that they are addicted to them. Moreover, they are even aware of the presence of such a risk, which proves realistic and mature thinking. Most students use the Internet for information, although they are also aware of the risk of not obtaining accurate data – a fact confirmed by other literature data as well [17]. We must admit that the media and entertainment tools familiar to previous generations (TV, radio, written press) have now been joined by new, equally important, or even more important partners – the smart devices, which seem to have become the most convenient ways to access virtual environments.

Almost all students use the Internet daily, from their mobile phones, and most of them for at least 3 hours – which shows a certain degree of dependence on this technology, although it is not recognized as such. The most frequently used Internet services are, according to some authors, WhatsApp (as a fast communication solution) [18,19,20], YouTube, and Blackboard [21].

It is also interesting to note that socializing in cyberspace is not very important for our students and does not replace real socialization. Only half of the students have many friends on social media, but even they don't post very frequently (only a few times a year or a few times a month, which is a moderate pace). Moreover, almost 60% of students believe that people's privacy is at risk due to social networks – a result that is questionable, because not the social networks pose a danger, but the people using them inappropriately – an aspect that seems to have been omitted by students. Literature data also confirms that the students, particularly the medical students, are not very well informed about the ethical issues regarding the use of social media resources [21].

There is an obvious and positive association between the degree of agreement expressed by students towards the use of multimedia resources during the learning process and their favorable opinions towards the use of Internet services. This means that the general openness to modern technologies is reflected by integrating them into personal life, but also professionally. On the other hand, unfavorable opinions towards the use of Internet services are associated sometimes with the general avoidance of modern technologies. We also identified a separate category of students who, although they do not like to use multimedia resources in the learning process, are instead very active on the Internet; they are especially interested in activities on social networks, without being very concerned about the other advantages provided by digital technologies. Anyway, the students who enjoy using multimedia resources during the learning process are also constant users of Internet services, which they use mainly for information, but also for activities on social networks (mainly instant messaging) – a fact also confirmed by previous studies in the literature [21,22,23].

CONCLUSIONS

Technology is only a tool that can improve the teaching process, but not only by itself. Those who are responsible for change are the teachers, who can improve the students' outcomes by using technology to convey knowledge, streamlining their methods, and perfecting themselves [24]. The concept of blended education facilitates such approaches and can trigger positive changes, satisfying for students, who will benefit from flexibility and comfort, and, consequently, also for teachers, who will have the satisfaction that their work achieves its purpose and that the information they transmit is properly heard and acquired.

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Authors' contribution

Conceptualization, C.G.D. and V.L.P.; methodology, C.G.D.; software, C.G.D. and R.S.C.; validation, R.S.C.; formal analysis, C.G.D.; investigation, M.E.A. and R.S.C.; resources, V.L.P.; data curation, C.G.D.; writing—original draft preparation, C.G.D. and M.E.A.; writing—review and editing, C.G.D. and V.L.P.; supervision, V.L.P.; project administration, C.G.D. and M.E.A. All authors have read and agreed to the published version of the manuscript.

Patient consent for publication

Informed consent was obtained from all subjects involved in the study.

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethical Committee of "Grigore T. Popa" University of Medicine and Pharmacy from Iasi, Romania (decision no. 21/16.11.2020).

References:

1. Shorey, S.; Chan, V.; Rajendran, P.; Ang, E. Learning styles, preferences and needs of generation Z healthcare students: Scoping review. Nurse Education in Practice 2021, 57, 103247. doi: 10.1016/j.nepr.2021.103247.

2. Dimock, M. Defining generations: where millennials end and generation Z begins. Pew Res. Center 2019, 1–7.

3. Seemiller, C.; Grace, M. Generation Z goes to college; John Wiley & Sons: San Francisco, 2016.

4. Acheampong, N.A. Recruiting and Retaining Generation Z into Public Sector Organizations: A Systematic Review. Doctoral dissertation, University of Maryland University College, 2019.

5. Tang, F. A critical review of research on the work-related attitudes of generation Z in China. Soc. Psychol. Soc. 2019, 10(2), 19–28. doi: 10.17759/sps.2019100203.

6. Yates, B. A.; Bakia, M.; Means, B.; Jones, K. Evaluation of evidence-based practices in online learning: A meta-analysis and review of online learning studies. US Department of Education, Office of Planning, Evaluation and Policy Development 2009. Available online: http://edicswebed.gov/edics_files_web/ 03898/Att_ReferencesandGlossary.doc (accessed on 21 05 2021).

7. Zhang, W.; Zhu, C. Impact of Blended Learning on University Students' Achievement of English as a Second Language. International Journal on E-Learning 2018, 17(2), 251–273.

8. Clark, J. PowerPoint and pedagogy: maintaining student interest

in university lectures. Coll Teach. 2008, 56(1), 39-44. doi: 10.3200/CTCH.56.1.39-46.

9. Akçayır, M.; Akçayır, G. Advantages and challenges associated with augmented reality for education: a systematic review of the literature. Educ Res Rev. 2017, 20, 1-11. doi: 10.1016/ J.Edurev.2016.11.002

10. Chen, A.M.; Kiersma, M.E.; Yehle, K.S.; Plake, K.S. Impact of the Geriatric Medication Game(R) on nursing students' empathy and attitudes toward older adults. Nurse Educ Today. 2015, 35(1), 38-43. doi: 10.1016/j.nedt.2014.05.005.

11. Chen, A.M.; Kiersma, M.E.; Yehle, K.S.; Plake, K.S. Impact of an aging simulation game on pharmacy students' empathy for older adults. Am J Pharmaceut Educ. 2015, 79(5), 65. doi: 10.5688/ ajpe79565.

12. El Tantawi, M.; Sadaf, S.; Al Humaid, J. Using gamification to develop academic writing skills in dental undergraduate students. Eur J Dent Educ. 2018, 22(1), 15-22. doi: 10.1111/eje.12238.

13. Lujan, H.L.; Sejaipe DiCarlo. First-year medical students prefer multiple learning styles. Adv Physiol Educ. 2006, 30(1), 13-16. doi: 10.1152/advan.00045.2005.

14. Baykan, Z.; Naçar, M. Learning styles of first-year medical students attending Erciyes University in Kayseri, Turkey. Adv Physiol Educ. 2007, 31(2), 158-160. doi: 10.1152/ advan.00043.2006.

15. Vagg, T.; Balta, J.Y.; Bolger, A.; Lone, M. Multimedia in Education: What do the Students Think? Health Professions Education 2020, 6, 325-333. doi: 10.1016/j.hpe.2020.04.011.

16. Trelease, R.B. Diffusion of innovations: smartphones and wireless anatomy learning resources. Anat Sci Educ. 2008, 1(6), 233-239. doi: 10.1002/ase.58.

17. Ahmad, T.; Sattar, K.; Akram, A. Medical professionalism videos on YouTube: content exploration and appraisal of user engagement. Saudi J. Biol. Sci. 2020, 27(9), 2287-2292. doi: 10.1016/j.sjbs.2020.06.007.

18. Coleman, E.; O'Connor, E. The role of WhatsApp® in medical education; A scoping review and instructional design model, BMC Med. Educ. 2019, 19, 279. doi: 10.1186/s12909-019-1706-8.

19. Jayakumar, K.M.N.; Nasimuddin, A.K.S.; Malaiyan G.S.J. Whatsapp enhances Medical education: is it the future? Int. J. Med. Sci. Publ. Health 2017, 6(2), 353-358. doi: 10.5455/ijmsph.2017.02082016622.

20. Us Salam, M.A.; Oyekwe, G.C.; Ghani, S.A.; Choudhury, R.I. How can WhatsApp® facilitate the future of medical education and clinical practice? BMC Med. Educ. 2021, 21(1), 54. doi: 10.1186/s12909-020-02440-7.

21. Nisar, S.; Alshanberi, A.M.; Mousa, A.H.; El Said, M.; Hassan, F.; Rehman, A.; Ansari, S.A. Trend of social media use by undergraduate medical students; a comparison between medical students and educators. Annals of Medicine and Surgery 2022, 81, 104420. doi: 10.1016/j.amsu.2022.104420.

22. Dar, Q.A.; Ahmad, F.; Ramzan, M.; Khan, S.H.; Ramzan, K.; Ahmed, W.; et al. Use of social media tool "WhatsApp" in medical education. Ann King Edward Med Univ 2017, 23(1). doi: 10.21649/akemu.v23i1.1497.

23. Fitzgerald, R.T.; Radmanesh, A.; Hawkins, C.M. Social media in medical education, Am. J. Neuroradiol. 2015, 36(10), 1814-5. doi: 10.3174/ajnr.A4136.

24. Whitaker, T. What great teachers do differently: 17 things that matter most. Routledge: New York, 2013.

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ORIGINAL ARTICLE

The Impact of Physical Therapy on Psychomotor Functions in a Patient with Systemic Lupus Erythematosus and Diabetes Mellitus – Case Illustrated Literature Review

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Abstract: *The scientific and medical world is making permanent efforts to study, understand, and cure the complicated pathology of Systemic Lupus Erythematosus (SLE) – the disease with 100 faces, due to the diversity and complexity of the symptoms. SLE has a devastating impact on the patient's life, causing multiple metabolic imbalances produced by both the disease itself and the necessary medication. This case report addresses the therapeutic aspects of SLE and diabetes mellitus, on a 47-year-old male with a sensitive multi-pathology and aggressive evolution, medication, and approaching psychomotor rehabilitation therapy, up to now, when SLE treatment has ended. Also, this case study report highlights the importance of flexibility in the psychomotor rehabilitation strategy, in the context of a large range of factors that influence its definition.*

Keywords: *SLE - systemic lupus erythematosus, diabetes mellitus, medication, recovery therapy, psychomotor*

INTRODUCTION

The scientific and medical staff are making permanent efforts to study, understand, and cure the complicated pathology of Systemic Lupus erythematosus (SLE) [1-3]. SLE, an inflammatory autoimmune disease, also named the disease with 100 faces due to the diversity and complexity of the symptoms, has a devastating impact on the patient's life due to the multiple metabolic imbalances produced by the disease itself and the necessary medication [4].

The etiology of SLE is unknown, as are the possible disorders (but not necessarily) – hematological, nephrological, neurological, skin, and ocular, because of cellular and tissue damage [5-7]. There is no chronological sequence of SLE manifestations, even in the same patient. It is problematic to diagnose, hard to treat (due to the various symptomatology from minimum to severe), and difficult to continuously adapt the strategy of preserving psychomotor capacity, sometimes necessary to change in an abrupt way.

Diabetes Mellitus in the case of SLE is a particular situation with the need for continuous monitoring because it can be influenced by this long-term disease and its complex medication treatment [8,9]. Administration of insulin units and/or gliclazide must be dosed by the treating physician according to the particularities of the case [9,10]. It is well known that diabetes can be controlled with careful diet and weight monitoring, and physical exercise as a supplement to medical treatment. That is why we consider the good collaboration between family, patient, doctor, and physical therapist, alongside the regular medical checkouts for blood variables of vital importance. The medical approach therapy is individualized and customized to fit each patient's need depending on the type of disease and each symptom.

Reflection of the theme in specialized literature and conceptual boundaries

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with multisystem involvement. It is triggered by deregulation of the immune system which, due to the autoantibodies produced, attacks the body's healthy cells and tissues. The clinical picture is very rich, it can affect several organs, it has an undulating evolution with periods of exacerbation and remission, and the forms of presentation are from clinical manifestations without life risk (affects the skin, and joints) to potentially severe forms (affects the patient at neurological, renal, cardiovascular level).

There are 4 types of lupus:

• Systemic lupus erythematous – is the most common form of lupus. The manifestation of the disease differs depending on the affected structures.

• Cutaneous lupus – manifests itself in the skin.

• Lupus induced by drugs – iatrogenic lupus occurs as a reaction to the administration of certain drugs.

• Neonatal lupus – is a particular form of the condition and occurs due to the transplacental transmission of anti-Ro antibodies from mother to fetus during pregnancy and can have skin, cardiac (the most serious being atrioventricular block), hematological, and neurological manifestations.

Symptoms can range from mild to very severe, and although they can be chronic, they usually come and go, with the disease having an undulating course.

The most common complaints are fatigue, altered general condition, fever, lymphadenopathy (inflammation of the lymph nodes), and joint and muscle pain. Almost any organ can be affected.

Skin-mucosal damage

It is present in approximately 70% of patients. The classic manifestation of acute lesions is the heliotrope rash, erythema in "butterfly wings" present at the level of the nasal pyramid and the cheeks (redness that extends from the nose to the cheeks, below the eye area), without affecting the nasolabial folds. Erythema can also spread to other areas exposed to UV radiation – forehead, chin, décolleté. Photosensitivity is another characteristic of lupus patients. Subacute lupus may initially present with erythematous lesions that, over time, become papulosquamous, mimicking psoriasis or lichen planus. Discoid lupus erythematosus can appear on the face, scalp, ears, arms, hands, and back, the erythema being followed by hyperkeratosis or atrophy. Discoid lupus can be a strictly dermatological lesion, without being accompanied by systemic manifestations [29].

There may also be alopecia, skin purpura, erythema, small red dots, urticarial eruptions, livedo reticularis, Raynaud's syndrome, and ulcerations of the fingers pulp. Mucous membrane lesions consist of frequently painless petechial and ulceration of the nasal, oral, and, less commonly, genital mucosa.

Musculoskeletal damage

About 90% of patients diagnosed with lupus will have joint pain, arthritis, or muscle pain at some point. The joints of the hands, fists, and then the large joints (knees, ankles, shoulders, elbows) are most frequently affected. They can be painful, swollen, or red, the damage is usually symmetrical. Unlike rheumatoid arthritis, lupus arthritis rarely causes severe joint deformities and is not erosive.

Hematological impairment

Anemia, thrombocytopenia, leukopenia with neutropenia or lymphopenia may occur within the disease or secondary to pharmacological treatment.

Cardiovascular damage

Pericarditis, myocarditis, and endocarditis can occur in this disease.

Lupus endocarditis, called Libman-Sacks endocarditis, has no infectious cause. Atherosclerosis occurs more frequently and develops more rapidly than in the general population.

Lupus patients can also associate antiphospholipid syndrome (SAFL), in which antiphospholipid antibodies are present (anti-beta 2 glycoprotein 1 antibodies, anti-cardiolipin antibodies, lupus anticoagulant).

The presence of SAFL causes thrombosis), and spontaneous abortions.

Lung damage

It can take the following forms: pleurisy, inflammation of the pleura, pleurisy, pneumonitis, interstitial lung disease, pulmonary hypertension, and pulmonary thromboembolism. These can cause coughing, dyspnea (choking hazard), chest pain, and hemoptysis.

Kidney damage (lupus nephritis)

Renal damage determines the severity of the evolution of lupus patients. One-third of patients have kidney damage, suggested by proteinuria or hematuria, serum creatinine is above the upper limit of the laboratory, and creatinine clearance is low.

Neuropsychological impairment

It is the least understood manifestation of systemic lupus erythematosus and one of the most severe. Among the neurological manifestations, we mention convulsions, severe headaches, peripheral neuropathies, cranial nerve damage, cerebral vascular accidents, acute meningitis, and chorea. Psychiatric manifestations include psychoses, cognitive dysfunction, anxiety syndrome, and mood disorders.

Gastrointestinal symptoms

The most common gastrointestinal symptoms are anorexia, nausea, vomiting, and abdominal pain, and may be manifestations of mesenteric vasculitis, peritonitis, pancreatitis, or secondary to the administered medication.

Liver damage is found in up to 60% of patients – hepatomegaly, increased liver enzymes, and hepatic steatosis. Up to 8% of patients develop retinal artery inflammation with thrombosis at this level. The conjunctiva and cornea can be affected by secondary Sjogren's syndrome [30].

Specific immunological abnormalities

The presence of autoantibodies that target their own structures. Antinuclear antibodies (ANA) occur in approximately 95% of patients but have low specificity and may be associated with other conditions (rheumatoid polyarthritis, autoimmune thyroiditis, autoimmune liver diseases, infections, neoplasms, or in healthy individuals). The most frequent antibodies encountered in SLE are the antibodies: anti-double-chain DNA (SLE specific, associated with disease activity), anti-Sm (SLE specific), anti-U1 RNP, anti-Ro, anti-La, anti-ribosomal protein P (SLE specific, appear in neurological, hepatic damage), anti-histones (occur in classical and drug-induced lupus), anti-phospholipids (characteristics of SAFL), rheumatoid factor (non-specific, occurs in many other autoimmune conditions, infections). Decreased serum complement fractions (C3, C4, CH50) are associated with disease activity.

As is the case with many chronic conditions, systemic lupus erythematosus (SLE) negatively affects the quality of life, due to factors such as depression, pain, cognitive dysfunction, and sleep disorders.

Despite a little-understood etiology, fatigue is associated with SLE in approximately 80% of cases, which leads to a decrease in the level of physical activity necessary to carry out usual daily activities and thus dramatically decreases the quality of life.

Physical medicine and recovery in Systemic Lupus Erythematous may involve physical therapy, occupational therapy, speech therapy, recreational therapy, or combinations thereof. The specialist doctor should coordinate the patient's care and be attentive to subtle changes in symptoms that may indicate periods of disease activity [32].

Ultrasound is a frequently used procedure to provide heat in the depth of the affected joint, but it should not be used in the presence of inflammation; locally applied ice is the preferred method for inflamed joints. When ultrasound is used to improve joint mobility, the application of ultrasound and joint movement should be simultaneous.

Hydrokinetic therapy is recommended for the mobilization of inflamed joints, due to the buoyancy that ensures the unloading of the joint and the soothing action of the warm water.

The cardiovascular and pulmonary systems can also be affected by lupus. We try to improve aerobic capacity through physical exercises and specific breathing exercises [31]. These exercises will also contribute to maintaining a strong bone system, as well as strengthening ligaments and joints. Regular practice of sports activities is particularly recommended for patients with lupus.

Occupational therapy has the role of helping the patient regain as much of his functional independence as possible, despite the problems caused by the disease. Activities of daily living are encouraged and may require training with special equipment, techniques, and procedures. These activities include feeding, dressing, bathing, grooming, grooming, and cooking in the home.

A safety assessment at the patient's home may be indicated. Occupational therapy can provide recommendations for equipment (for example bathtub bench, elevated toilet seat, grab bar) to increase the patient's independence and safety at home.

Patients who have neuropsychiatric complications due to lupus may have cognitive dysfunctions, with deficits in attention, language, and memory. The speech therapist can be helpful when a patient with systemic lupus erythematous has slurred speech, difficulty understanding speech, or difficulty speaking properly.

Because systemic lupus erythematosus is a condition that manifests itself episodically, through bouts of activity alternating with episodes of remission, it is important that the patient does nothing without consulting the rheumatologist who deals with his disease – thus, it will reduce the risk of triggering a set of activities.

Unfortunately, there is still no treatment that can cure lupus, but there are treatments that can improve the symptoms while prolonging the episodes of remission of the disease. Adopting a healthy lifestyle also contributes to increasing the quality of life of the lupus patient.

Other things that the lupus patient can do to improve their condition:

• To give up smoking, but also the consumption of caffeine or alcohol.

• To adopt a healthy, balanced diet, based on as many natural foods as possible.

• To rest enough.

• Follow exactly the treatment recommended by the doctor, even during periods of remission of the disease.

• To avoid exposure to the sun because ultraviolet radiation

increases the risk of triggering a flare-up of systemic lupus erythematous.

It is recommended to reduce exposure to UV rays (using creams with a minimum sun protection factor of 50, avoiding exposure to the sun), a diet adapted to the patient undergoing corticosteroid therapy (to prevent its adverse effects – diabetes, hypertension, dyslipidemia), quitting smoking.

To prescribe a drug treatment, it is essential to identify the type of organ damage and its severity.

Non-life-threatening damage (skin-mucous, musculoskeletal, serositis) is indicated for the administration of non-steroidal anti-inflammatory drugs, low-dose systemic cortico-therapy, and synthetic antimalarials.

Potentially vital damage (cardio-pulmonary, hepatic, renal, hematological, central nervous system) requires cortico-therapy in moderate or high doses, associated depending on the affected organ, with immunosuppressants, anticoagulants, anticonvulsants, or even biological therapy.

Systemic lupus erythematosus is a chronic condition with multisystem involvement that presents severe evolutionary potential. Currently, thanks to advances in the knowledge of mechanisms, diagnosis, and treatment, the 10-year survival rate of lupus patients is almost 90% [30].

MATERIALS AND METHODS

This review started with a case study and addresses the therapeutic aspects of SLE and Diabetes Mellitus of a 47-year-old male with a delicate multi-pathology and aggressive evolution, caused by both the diagnostic and the difficult approach of the psychomotor rehabilitation therapy when SLE treatment has ended. In this case study report, we approach the importance of the management of the disease combining not only the multiple therapeutic actions but also the proper medication and nutrition and the psychomotor rehabilitation [11]. The study includes stages of life-threatening biological depreciation, and treatment, until the present when the therapy is positively affecting the patient's quality of life.

We present the short version of the patient's clinical history:

- At 27 years old, he underwent surgery for Non-Hodgkin's Lymphoma, associated with polychemotherapy and radiotherapy, with good response, in remission and without any specific medication from 2003.

- No forms of SLE manifestation until 2017.

- The aggressive form of SLE debuted in September 2017, caused by an unstable lifestyle associated with many detrimental factors accumulated in the last 15 years: unbalanced alimentation (almost exclusively processed meat products/minced meats and semi-prepared products, and carbonated beverages), smoking, stress, lack of sleep, improper self-medication for diabetes mellitus, sustained effort.

- The SLE treatment itself begins in February 2018, the patient's previous treatment included only medication for his symptoms - edema, hypertension, cytopenia, etc.

- In his delicate condition, with the complex ongoing treatment, the patient beneficiated from the support of his family, nutritionist, priest, and doctors which improved his mental state of being.

- The period 2018-2019 was an equilibrated one when the patient was under observation, good nutritional plan, and 3 weekly sessions of physical therapy.

- In February 2022 the patient gets infected with SARS-CoV-2 Covid 19 Omicron Type which lead to a 10 days hospitalization in the nephrology unit medical care.

- The clinical picture of the subject presented above starts from the aggressive debut in the autumn of 2017 until 2021. We mention that multi-pathology and all associated diagnoses are not included in this presentation.

We also mention that during this period of multiple hospitalizations, there were diagnosed multiple associated pathology such as Diabetes mellitus type 2 with established Diabetic Nephropathy, Hypertensive Nephropathy with Renal Impairment, Hyperuricemia without signs of Inflammatory Arthritis or Tophaceous Disease, Vulgar Ichthyosis, Glomerular disorders in systemic connective tissue disorders, other water and electrolyte disturbances not elsewhere classified, Anemia in other chronic diseases classified elsewhere, Non-inflammatory Pericardial infusion, Medication-induced Specific Polyneuropathies, Secondary hypertension of other kidney disorders, Ascites, Hypo-osmolality and hyponatremia, Chronic nephritis syndrome, etc.

Also, here are some additional landmarks: the dietary regimen consisted of predominant vegetarian and hypoglycemic food, water management with 500 ml more than the urinary removal, medical plant tea indication, measurement of food in carbs no more than 150 per day (50/50/50 for each meal) associated with the prescribed medication; glycemic test each day before meals with calculated insulin administration (rapid and long-acting insulin) and/or gliclazide.

The multidisciplinary team of doctors (diabetologists, nephrologists, cardiologists, and Physiotherapists) [12-17] followed the patient during all the periods.

Treatment of SLE with the administration of combined diuretic treatment: high-ceiling diuretics (furosemide), Vasopressin antagonists (tolvaptan), Diuretic thiazide and potassium-sparing (amiloride hydrochloride and hydrochlorothiazide), thiazide diuretics (hydrochlorothiazide) and immune-suppressive combination (cyclophosphamide, mycophenolate mofetil), cyclosporine and corticosteroids (prednisolone).

Evaluation methods

To carry out this research from the Physiotherapists point of view, we chose the following measurements and evaluation tests:

1. to assess the level of the peripheral inflammatory stage at the level of the lower limbs as well as that of the muscle mass of the subject, we performed the anthropometric-perimetry method for the ankle and calf.

2. to evaluate the degree of mobility of the lower limb necessary for functionality, we used the goniometric method for the ankle and hip joints.

3. to assess static balance, we used the simple bipedal balance test with eyes open with several penalties for imbalance for 5 minutes.

4. to assess dynamic balance we asked the patient to walk on a drawled line of 5 meters distance, eyes open, without imbalance, dizziness, or lateral support.

5. to evaluate the subject's effort capacity, we used the ergometric bike without resistance with heart rate measurement.

Description of the used methods

1. The patient is in the supine position, and the measuring tape is applied at the level of the ankle joint including the most inflamed area, measuring an average of the right/left ankles before the physical therapy program.

2. The patient lying on his back, and the goniometer is applied according to the goniometric measurement and evaluation standards of the ankle and hip joint for the flexion movement, before the physical therapy program.

3. The patient in the standing position with bare feet on the floor for better plantar kinesthesia, eyes open, is timed for how many minutes/seconds he can stand without imbalances, dizziness, or lateral support. The evaluation was carried out at the beginning of the meeting for static balance.

4. For dynamic balance, a 5m line was marked on the floor, and the patient was asked to follow the line walking, eyes open, marking any sign of imbalance, dizziness, or lateral support, evaluated in how many meters the patient succeed to go on, at the end of the session.

5. The patient on the ergometric bicycle without lumbar support, with a distance between the hip and the pedals so that the knee is slightly flexed, without load, he pedals freely at a slow pace, following the heart rate so that it does not exceed 120 beats/min, it is marked how many minutes he can pedal up to the indicated maximum cardiac effort, or any other sign of imbalance, dizziness, numbness or pain. The test was held at the end of the physical therapy session.

Evaluation Instruments

The used instruments were a tape measure, goniometer, stopwatch, liner, ergometric bicycle, and pulse tester.

Research methods used

The research methods used in the paper were:

- the theoretical documentation method.

- pedagogical observation.

- the experimental method.

- the method of tests and evaluation samples.

- the investigation method.

- the method of recording and statistical-mathematical data processing.

- the graphic method.

Applied intervention

To streamline and synthesize the process of describing exercises applied, they are presented below (Tables 1 and 2).

The tables show the means we worked with, the exercise program proposed for every period, and their dosage.

Teaching materials used to fulfill the improvement program of motor functional skills and of balance and effort capacity were the stick, a small hand weight 1 kg, a terra band, the balance board, the inflatable balance disc, the gym ball, the small spikes ball for prehension, the bicycle, marker.

The physical therapy program no. 1 consisted of this period in: specific exercises that do not involve risks factors for strokes, bruises, or bleeding; exercises that do not present risk factors for a patient with high blood pressure; exercises and techniques for lymphatic drainage; specific techniques for tone muscle and equilibrium; specifically adapted methods for connective flexibility and joints mobility; programs for developing effort capacity; outdoor adapted program; exercises that consider the electrolyte imbalance (already existing due to the disease); breathing exercises.

Table 1: The process of describing initial exercises applied – the first program

Type of method	Exercise	Series	Reps or seconds/minutes	Pause (sec)
Mobilization	From the lying position - slow passive mobilization of the ankle in all directions	3	30 reps	30 sec
	From the lying position - slow passive mobilization of the knee for flexion and extension	3	15 reps	30 sec
	From lying position - Slow passive mobilization of the hip in all ranges of motions from simple to complex	3	15 reps	60 sec
	From lying position and sitting - Active mobilization of the upper limbs with a stick in all ranges of motions	3	15 reps	60 sec
	From lying position - Free active mobilization of the upper limb in all ranges of motions	3	15 reps	30 sec
	From lying position - Free active mobilization of lower limbs in all ranges of motion (bicycle, shears, bypasses)	3	15 reps	60 sec
	Quadrupedal position, cat forward and backward	3	10	120 sec
Tone muscle	Lying position - all range motion mobility with 1-kg hand weights	3	15	60 sec
	Sitting position - all range motion mobility with 1-kg hand weights	3	15	60 sec
	Sitting position - terra band extension between arms in abduction and extension	3	10	120 sec
	Sitting position - leg extension with a terra band resistance	3	10	120 sec
	Lying position - knee flexion and extension with terra band resistance	3	10 reps	120 sec
Static balance	Sitting position - imbalance from the shoulders in all directions with the requirement to maintain the posture from the abdomen without the help of the hands	3	10 reps	60 sec
	Standing position - Keep abduction of the hands	3	10-60 seconds	120 sec
	Standing position - maintain the balance without lateral support or movements	3	10-60 seconds	120 sec
Dynamic balance	Standing position - Raise 1 leg on a support ball	3	10-60 seconds	60 sec
	Standing position - walking with a plastic cup with water in the hand	3	10 m	60 sec
	Standing position - walking on a drawled line on the floor without lateral support or lateral deviations	3	10 m	120 sec
	Standing position - with lateral or face hand support - on a balance platform or ball - back straight, crunches	3	10 reps	120 sec
	Standing position - lateral support - kick a ball	3	10 reps	60 sec
Effort capacity	Bicycle ride - level 0	1	5 min	-
	Bicycle ride - level 0	1	15 min	-
	Claiming stairs from 1 to 3 floors	1	15-30 min	5 min
Outdoor training	Walking outdoors on a parc with support (frame, cane or crutch, or human lateral support)	1	15-30 min	-
Breathing techniques	Lying position - costal and abdominal breathing techniques, slowly and following the dizziness or pain	1	5- 10 min	-
	Sitting position - gently inhale with the extension of the trunk and arms, and exhale slowly and long with the return and withdrawal of the navel towards the spine.	1	5-10 min	-
Manual techniques	Manual lymphatic drainage and pump exercises	1	15 – 30 min	-
	Manual therapy for connective tissues	1	15-30 min	-

All exercises and techniques were adapted to the daily dynamic state of functionality of the patient from very simple basic to the maximum possible in his case. The programs were carried out on an outpatient basis at the patient's home, with a frequency of 3 sessions per week (Monday, Wednesday, Friday), the duration of the session being between 30 and 120 minutes depending on the daily state of the patient and the applied methods.

Table 2: The process of describing initial exercises applied – the second program

Type of method	Exercise	Series	Reps or seconds/minutes	Pause (sec)
Mobilization	From the lying position - slow active mobilization of the ankle in all directions	3	30 reps	30 sec
	From the lying position - slow active mobilization of the knee for flexion and extension	3	15 reps	30 sec
	From lying position - Slow active mobilization of the hip in all ranges of motions from simple to complex	3	15 reps	60 sec
	From lying position and sitting - Active mobilization of the upper limbs with a stick in all ranges of motions	3	15 reps	60 sec
	From lying position - Free active mobilization of the upper limb in all range of motions with 1 kg hand weights	3	15 reps	30 sec
	From lying position - Free active mobilization of lower limbs in all ranges of motion with 1 kg leg weights (bicycle, shears, bypasses)	3	15 reps	60 sec
	Quadrupedal position, cat forward and backward	3	10	120 sec
Tone muscle	Face lying position - all range motion mobility with terra band	3	15	60 sec
	Sitting position - all range motion mobility with 1 kg hand weights	3	15	60 sec
	Sitting position - terra band extension between arms in abduction and extension	3	10	120 sec
	Sitting position - leg extension with a terra band resistance or 1 kg leg weights	3	10	120 sec
	Lying position - knee flexion and extension with terra band resistance or 1 kg leg weights	3	10 reps	120 sec
Static balance	Sitting position - imbalance from the shoulders in all directions with the requirement to maintain the posture from the abdomen without the help of the hands or with a ball or a weight of 1 kg in the hands	3	10 reps	60 sec
	Standing position - Keep abduction from 90^{O} - 180^{O} of the hands	3	10-60 seconds	120 sec
	Standing position - maintain the balance without lateral support or movements and keep a 1 kg weight on the hands	3	10-60 seconds	120 sec
Dynamic balance	Standing position - Raise 1 leg on a support ball with 1 kg leg weight	3	10-60 seconds	60 sec
	Standing position - walking with a 1 kg weight on the hand	3	10 m	60 sec
	Standing position - walking on a drawled line on the floor without lateral support or lateral deviations with a cup of plastic water in the hand or on the head	3	10 m	120 sec
	Standing position - with lateral or face hand support- on a balance platform or ball - back straight, squats or lunges	3	10 reps	120 sec
	Standing position - lateral support - kick a ball or roll a 1 kg leg weight	3	10 reps	60 sec
Effort capacity	Bicycle ride - level 1	1	5 min	-
	Bicycle ride - level 1	1	15 min	-
	Claiming stairs from 1 to 6 floors	1	15-30 min	5 min
Outdoor training	Walking outdoors on a parc with or without support (frame, cane or crutch or human lateral support)	1	15-30 min	-
Breathing techniques	Standing position - costal and abdominal breathing techniques, slowly and following the dizziness or pain	1	5- 10 min	-
	Standing or quadrupedal position - gently inhale with the extension of the trunk, leg, and arm, and exhale slowly and long with the return and withdrawal of the navel towards the spine	1	5-10 min	-
Manual techniques	Manual lymphatic drainage and pump exercises	1	15 – 30 min	-
	Manual therapy for connective tissues	1	15-30 min	-

The program contains breathing exercises from decubitus and sitting, easy mobilization exercises for upper limbs with the stick and weights no more than 1 kg, slow exercises for lower limbs at the bedside level, lymphatic drainage, progressive passive mobilizations, progressive active spine mobilizations, static and dynamic equilibrium methods, core and leg muscle

tone exercises, home bicycle program from 0 weight, outdoor walking sessions. Monday and Wednesday were addressed to the indoor program and Friday evening (due to the ocular and skin problems in SLE) if the weather was proper and the state of the patient was a good one, was addressed to the outdoor program.

Objectives

The 1 physical therapy program followed the objectives of each period of the evolution of the patient's state.

The initial objectives of the treatment were those of:
- preserving life
- following developments in functionality and evasion of complications.

The main objectives were:
- Improve the quality of life
- Decrease in inflammation and lymph retention
- Preserve and gain flexibility
- Develop tone muscle
- Develop a functional effort capacity
- Obtain a good static and dynamic stability
- Maintain a good psychological state of mind and optimism with the patient and family.

The functional state of the patient translates into functional disability to service and personal care, unable to have an orthostatic position, seated posture, and displacement.

The physical therapy program no. 2 consisted of the same exercises as in the first period but improved and adapted to the new daily possibilities of the patient. Such as upper and lower limb mobilization in a full range motion and with resistance, static and dynamic balance improved techniques for outdoor walking without the support and on uneven terrain, effort capacity development on the bicycle with resistance, maneuverability, and coordination exercises.

The program contains breathing exercises from sitting and standing positions, mobilization, and tonus exercises for upper limbs with the stick and 1 kg weight, exercises for lower limbs at the bedside level and from standing position with terra band, abdominal and diaphragmatic exercises, equilibrium exercises with or without lateral support, progressive active mobilizations, prehension exercises, lymphatic drainage, and manual therapy, bicycle training, outdoor walking sessions.

All exercises and techniques were adapted to the daily dynamic state of functionality of the patient following the rule of "primum non nocere" [26].

Objectives

The 2 physical therapy programs followed the objectives of each period of the evolution of the patient's state.

The initial objectives of the treatment were those of:
- preserving the quality of life and existent functionality
- following developments in functionality and evasion of complications.

The main objectives were:
- Improve the quality of life
- Preserve and gain flexibility and connective tissue elasticity
- Develop tone muscle and regain muscle mass
- Gain a functional effort capacity for outdoor functionality
- Obtain good static and dynamic stability together with coordination skills
- Maintain an optimistic continuous psychological state of mind and optimism with the patient and family.

Figure 1: Representative images of the foot edema and neuropathy skin lesions

The recovery protocol consisted of tracking the functionality of each step according to the patient's evolution, following the food and drug indications and the degree of muscle and joint recovery, and also considering the equilibrium function that has been greatly affected.

During these months of complex treatment, the patient had positive or stagnant recovery moments, being affected by atmospheric pressure temperature, and climate change.

The purpose was to perform standing posture and walking with a moderate balance and state of equilibrium.

The functional state of the patient in March 2021 was that of functional and personal care integrity, the ability to perform standing posture, and walking with a moderate balance and state of equilibrium (Figure 3).

The patient continued the prescribed programs on his own at home during the pandemic period and the functional state of the patient in June 2022 was that of functional and personal care integrity, the ability to perform standing posture and walking with a moderate balance, and a state of equilibrium. (Figure 4).

RESULTS

The results concerning our patient were very promising (Table 3).

The perimetric measurements showed a constant decrease between the initial, intermediate, and final evaluations of the dimensions by 6 centimeters for the ankle joint and by 8 centimeters for the calf, relevant to a good drainage process both through the function of the kidney and through the lymphatic system, due to both effective medication and the sustained kinetic program.

Figure 2: Representative images of the foot edema and neuropathy skin lesions

Figure 3: Representative images of the foot from March 2021.

Figure 4: Representative images of the foot from June 2022.

The goniometric measurements for ankle and hip flexion had values of increased joint mobility, thus the ankle gained 10 degrees and the hip 55 degrees in a range of motion, which allowed the patient better mobility and dynamic functionality.

Table 3: Results of evaluation tests

Measurements	Initial testing Feb 2017	Intermediary testing Feb 2018	Final testing March 2019	Observations
Ankle perimeter	30 cm	27 cm	24 cm	Decreased by 6 cm
Calf perimeter	45 cm	43 cm	37 cm	Decreased by 8 cm
Ankle flexion mobility	5^{o}	10^{o}	15^{o}	Improved with 10^{o}
Hip flexion mobility	35^{o}	85^{o}	90^{o}	Improved with 55^{o}
Static stability	0	5 min	10 min	Improved 10 min
Dynamic stability	0	10 meters	30 meters	Improved 30 meters
Effort capacity	0	10 min	15 min	Improved 15 min

The evaluation of static stability recorded beneficial increases for the patient's life from the value of 0 minutes to 10 minutes without imbalance. The dynamic stability tests increased from 0 meters to 30 meters of walking without imbalance and support. Thus, the static stability gained 10 minutes without imbalances, and the dynamic one from value 0 reached a displacement of 30m without imbalances and support, which allowed the patient to go outside the house.

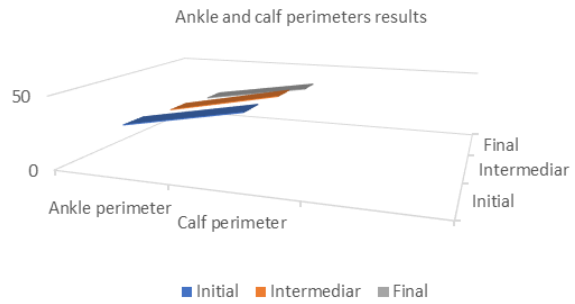

Figure 5: Ankle and calf perimeters measurements results

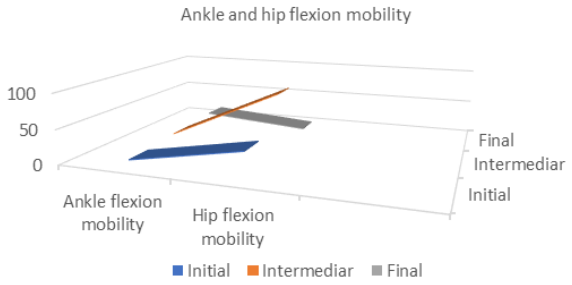

Figure 6: Ankle and hip flexion mobility results

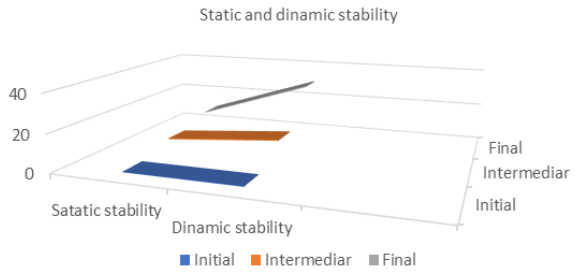

Figure 7: Static and dynamic stability evaluation results

The evaluation of the effort capacity from 0 initial value has reached 10 minutes without effort disorders so that later on the final evaluation on the best day of the patient will be 15 minutes without effort disorders. We mention that every day the patient's dynamics undergo changes from one hour to the next and the time of day matters a lot.

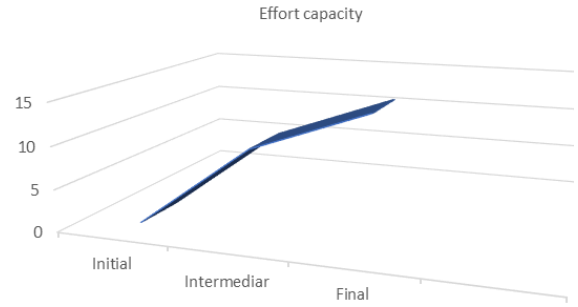

Figure 8: Effort capacity results.

DISCUSSION

The recommended strategy for addressing such a complex SLE case, for recovery of motor function, requires monitoring of at least three lines of observation:

1 Always be aware of disease progression (more in the context of risk of relapse of disease) and medication applied:

• Consulting physician recommendations, the results of medical tests, imaging investigations, etc.

• Check the treatment schedule, especially in the case of a disease involving a long-term treatment scheme with the adjustment of the substances and doses used (side effects of drugs can often have an impact on the patient's condition).

2 Use in an efficient manner the pluses of a positive psychic state (a calm, orderly mind with clear targets) and cultivate the will of the patient.

3 Permanent assessment of patient evolution, in points where difficulties were found: posture, coordination, and motricity.

Following the lines of this strategy, the physical therapist will be able:

• To work together with the patient, in a flexible system, the recovery exercises - maximum 10-30 minutes.

• To recommend to the patient a set of exercises to perform at home (immunosuppressive regimens do not recommend the presence of the SLE patient in the community over long periods of time, even more in the presence of other patients with transmissible diseases).

• And additionally, where appropriate, to apply therapeutic manual therapy and drainage sessions, as well as breathing techniques.

The recommended strategy for addressing the rehabilitation of motor function in such a complex case requires monitoring of at least these five levels of observation:

- Always be aware of the disease progression (even more in the context of risk of relapse) and medication administration, constantly consult physician recommendations, the results of medical tests, imagistic investigations, and so on. In this case, multiple impairments of the organ systems have led to chronic or acute manifestations of imbalances in the body [21-25,33, 34]. Permanently check the treatment schedule, especially in the case of a long-term treatment plan disease with the adjustment of the substances and doses used (side effects of drugs can often have an impact on the patient's condition).

- Permanent assessment of the patient’s evolution, in points where difficulties were found posture, coordination, and motricity, cause many of the associated diseases, both in the kidneys and other organs, make it difficult to choose the correct and balanced diet and medication.

- An important path leading to complete rehabilitation in this case, as in many others, was the combination of sustained social - psychological - spiritual support through faith and management with attention focused on the patient. The psychological support received from the medical staff and family, largely based on the patient’s trust in them, was even more necessary as the treatment with corticosteroids can cause changes in behavior (periods of extreme energy and activity, combined with periods of insomnia and irritability). We identified at least three main engines of the patient’s desire to recover – confidence in the attending physician and successful completion of the treatment, the desire to return to a normal life and sacred therapy.

The multi-pathology, as well as the delicate situation of the patient, have greatly raised the stakes of the entire medical staff in choosing the most suitable treatment management, which is still in progress daily.

References:

1. Ciccacci C (2017) A polymorphism upstream MIR1279 gene is associated with pericarditis development in Systemic Lupus Erythematous and contributes to definition of a genetic risk profile for this complication. Lupus 26(8): 841-848.

2. Ivan C, Popescu L (2019) Adapted training sessions - a plus for beginner athletes- Discobolul - Physical Education, Sport and

Kinetotherapy Journal Year 57(3): 31-35.

3. Petri MA, Van Vollenhoven RF, Buyon J (2013) Baseline predictors of systemic lupus erythematosus flares: data from the combined placebo groups in the phase III belimumab trials. Arthritis Rheum 65: 2143-53.

4. Yeganeh MZ, Sadeghi S (2013) Risk factors of glucocorticoid-induced diabetes mellitus in systemic lupus erythematosus. Galen Medical Journal 2: 39-43.

5. Houssiau FA, Vasconcelos C, D'cruz D (2010) The 10-year follow-up data of the Euro-Lupus nephritis trial comparing low-dose and high-dose intravenous cyclophosphamide. Ann Rheum Dis 69: 61-64.

6. Koutsonikoli A, Trachana M, Heidich AB (2015) Dissecting the damage in northern Greek patients with childhood-onset systemic lupus erythematosus: a retrospective cohort study. Rheumatol Int 35: 1225-1232.

7. Schroeder M, Russo S, Costa C, Hori J, Tiscornia I, et al. (2017) Pro-inflammatory Ca++-activated K+ channels are inhibited by hydroxychloroquine. Sci Rep 7(1): 1892.

8. Cortes S, Chambers S, Jerónimo A, Isenberg D (2008) Diabetes mellitus complicating systemic lupus erythematosus-analysis of the UCL lupus cohort and review of the literature. Lupus 17: 977-980.

9. Wahono CS, Rusmini H, Soelistyoningsih D, Hakim R, Handono K, et al. (2014) Effects of 1,25(OH)2D3 in immune response regulation of systemic lupus erithematosus (SLE) patient with hypovitamin DInt J Clin Exp Med 7(1): 22-31.

10. Stoicescu I (1999) Practice Dermato-Venerology Guide, Sitech Publishing House, Craiova, pp. 147-150.

11. Ulivieri C, Baldari CT (2014) Statins: from cholesterol-lowering drugs to novel immunomodulators for the treatment of Th17-mediated autoimmune diseases- Pharmacol Res 88: 41-52.

12. Bucur G, Opris DA (2002) Dermatoveneric Encyclopedia Diseases. (National Medical edn), Bucharest, Romania, pp. 468-471

13. Calabrese L, Resztak K (1998) Thalidomide revisited: pharmacology and clinical applications. Exp Opin Invest Drugs 7: 2043-2060.

14. Hanjani NM, Nousari CH (2002) Mycophenolate Mofetil for the Treatment of Cutaneous Lupus Erythematosus With Smoldering Systemic Involvement Arch Dermatol 138: 1616-1618.

15. Housman TS, Jorizzo JL Colab SI (2003) Low-Dose Thalidomide Therapy for Refractory Cutaneous Lesions of Lupus Erythematosus Arch Dermatol 139: 50-54.

16. Tien KJ (2013) Epidemiology and Mortality of New-Onset Diabetes after Dialysis. Diabetes care 36: 3027-3032.

17. Van Vollenhoven RF, Mosca M , Bertsias G (2014) Treat-to-target in systemic lupus erythematosus: recommendations from an international Task Force. Ann Rheum Dis 73: 958- 967.

18. Van Vollenhoven RF, Mosca M , Bertsias G (2014) Treat-to-target in systemic lupus erythematosus: recommendations from an international Task Force. Ann Rheum Dis 73: 958- 967.

19. Popescu V (2005) Clinica de Pediatrie și Neurologie pediatrică, Spitalul Clinic de copii „Dr. Victor Gomoiu", București - Criteriile revizuite pentru diagnosticul SLE (după Tass și colab, 1982); Jurnalul Medicinei Românesti 3(4): 59.

20. Ugarte-GIL MF, Wojdyla D, Pons-Estel GJ (2017) Remission and low disease activity status (LDAS) protect lupus patients from damage occurrence: data from a multiethnic, multinational Latin American lupus cohort (GLADEL). Ann Rheum Dis 76: 2071-2074.

21. Knop J, Bonsmann, G, Happle R si colab (1983) Thalidomide in the treatment of sixty cases of chronic discoid lupus erythematosus. Br J Dermatol 108: 461-466.

22. Tseng S, Pak G (1996) Rediscovering thalidomide: a review of its mechanism of action, side effects, and potential uses. J Am Acad Dermatol 35: 969-979.

23. Powell RJ (1999) Thalidomide: current uses. Bio Drugs 11(6): 409-416.

24. Werth V (2001) Current Treatment of Cutaneous Lupus Erythematosus. Dermatology Online Journal 7(1): 2.

25. http://www.csid.ro/health/sanatate/lupusul-o-boala-cu- o-mie-de-fete-10262986.

26. Geambasu, A., Therapeutic approach to Systemic Lupus Erythematosus – a case study, Discobolul – Physical Education, Sport and Kinetotherapy Journal Vol. XIV, no. 4(54), 2018, p 57

27. https://www.medlife.ro/glosar-medical/afectiuni-medicale/lupusul-eritematos-sistemic-les-cauze-simptome-tratament

28. https://www.doc.ro/lupus-cauze-simptome-tratament/medicina-fizica-si-recuperarea-in-lupusul-eritematos-sistemic

29. Ewa Kuca-Warnawin, Magdalena Plebańczyk, Marzena Ciechomska, Marzena Olesińska, Piotr Szczęsny, Ewa Kontny. Impact of Adipose-Derived Mesenchymal Stem Cells (ASCs) of Rheumatic Disease Patients on T Helper Cell Differentiation, Int. J. Mol. Sci. 2022, 23(10), 5317; https://doi.org/10.3390/ijms23105317 - 10 May 2022

30. Ahmad Haidar Ahmad, Dyhia Melbouci, Patrice Decker LiP Polymorphonuclear Neutrophils in Rheumatoid Arthritis and Systemic Lupus Erythematosus: More Complicated Than Anticipated, Immuno 2022, 2(1), 85-103; https://doi.org/10.3390/immuno2010007, 7 January 2022 (This article belongs to the Special Issue Advances in Autoimmune and Rheumatic Diseases: A Theme Issue in Honor of Prof. Dr. Yehuda Shoenfeld)

31. Teodora Wesselly Camelia Branet, Carmen Grigoroiu, Mihaela Netolitzchi, The Effect of Plyometric Training on Lower Body Strength in Preadolescent Athletes, BRAIN. Broad Research in Artificial Intelligence and Neuroscience, Vol 11, No. 4, Sup1 (2020), https://lumenpublishing.com/journals/index.php/brain/article/view/3733/2716

32. Corina Predescu, Anca Dana Popescu, Ioana Oprişescu Controlul biomedical al refacerii,. Bucureşti: Discobolul 2011

33. Periferakis A, Periferakis K, Badarau IA, Petran EM, Popa DC, Caruntu A, Costache RS, Scheau C, Caruntu C, Costache DO. Kaempferol: Antimicrobial Properties, Sources, Clinical, and Traditional Applications. International Journal of Molecular Sciences. 2022; 23(23):15054. https://doi.org/10.3390/ijms232315054

34. Caruntu A, Moraru L, Surcel M, Munteanu A, Costache DO, Tanase C, Constantin C, Scheau C, Neagu M, Caruntu C. Persistent Changes of Peripheral Blood Lymphocyte Subsets in Patients with Oral Squamous Cell Carcinoma. Healthcare. 2022; 10(2):342. https://doi.org/10.3390/healthcare10020342

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