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Evaluation of peripheral vestibular system in Hashimoto thyroiditis

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Ethics Committee Approval
The study was approved by the Başkent University Research Committee of Medical and Health Sciences and Ethics Committee (Project no: KA18/33).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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Abstract

Background/Aim: Hashimoto thyroiditis (HT) is a common autoimmune thyroid disease that may have systemic effects on any organ, including the inner ear. Increased frequency of autoimmune thyroid disease in patients with Meniere's disease and benign paroxysmal positional vertigo (BPPV) has been found, and autoimmunity was implicated in the etiopathogenesis of both diseases. The aim of this study was to evaluate vestibular functions and the effect of levothyroxine (LT4) therapy in patients with Hashimoto's thyroiditis.

Methods: The study included 61 men and women with HT diagnosis (group I: 31 patients who did not receive treatment; group II: 31 patients on LT4 treatment) and 30 healthy individuals (control group) between 18 and 60 years of age. Free T3, free T4, TSH, anti-TPO, and anti-Tg levels of all individuals were measured, and Cervical vestibular evoked myogenic potentials (cVEMPs), ocular vestibular evoked potentials (oVEMP), and video head impulse test (vHIT)tests were performed.

Results: In the cVEMP results, a 20% VEMP wave was not obtained in the group with HT on LT4 treatment. However, no significant difference was found in the statistical results between the groups. There was no significant difference in vHIT and oVEMP tests between groups. Vestibular tests of patients with hypothyroidism (TSH >4.9) were compared with those of euthyroid patients. The altered frequency in the cervical VEMP test of the left ear was higher in hypothyroid patients (P=0.042). The oVEMP test results were similar for both ears in both groups. The groups were similar in terms of VOR gain in the vHIT test.

Conclusion: In euthyroid HT patients, vestibular tests were normal. Progression of vestibular dysfunction might be induced by hypothyroidism rather than autoimmune thyroid diseases.

Keywords: Hashimoto thyroiditis, vestibular evoked myogenic potentials, video head impulse test, peripheral vestibular system

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Introduction

Autoimmune thyroid diseases are common and affect 1-5% of the general population. Hashimoto thyroiditis (HT) is the most frequent organ-specific autoimmune disorder and arises from an immune response against thyroid antigens that is triggered by environmental factors in genetically predisposed individuals [1,2]. HT is known to cluster with a wide spectrum of autoimmune disorders ranging from organ-specific diseases to systemic diseases [3]. Dizziness affects 15% to over 20% of adults yearly according to large population-based studies, and vestibular vertigo has a prevalence of 5% and an annual incidence of 1.4%. Its prevalence rises with age and is greater in women than in men. The most common vestibular diseases are Meniere's disease (MD) and benign paroxysmal peripheral vertigo (BPPV) [4].

Peripheral vestibular disorders result from vestibular labyrinth or vestibular nerve pathologies. Vestibulospinal and vestibulo-ocular reflexes are evaluated by a vestibular evoked myogenic potential (VEMP) test and the video head impulse test (vHIT). VEMP tests are non-invasive electrophysiological test methods that measure the reflex arc resulting in muscle contraction as a result of stimulation of the peripheral vestibular organs. Cervical vestibular evoked myogenic potentials (cVEMPs) involve the saccule and inferior vestibular nerve [5], and ocular vestibular evoked potentials (oVEMP) involve the utricle and superior vestibular nerve reflex arc responses [6]. The vHIT is based on the examination of eye movements that develop in response to repeated rapid head pushing movements to measure the integrity of the vestibulo-ocular reflex (VOR). It is especially useful for the differential diagnosis of peripheral vestibular diseases and diseases originating from the central nervous system.

The cochlear-vestibular system might be affected by autoimmune diseases, and vertigo could be more common in patients with autoimmune disorders [7]. Autoimmune inner ear disease is rare and is a syndrome of progressive hearing loss and/or dizziness, which is caused by antibodies or immune cells attacking the inner ear [8]. Autoimmunity may be responsible for several forms of frequently seen vestibular diseases, such as MD and BPPV [9,10]. The increased prevalence of systemic autoimmune diseases in patients with MD than the general population, the elevated levels of immunocomplexes, the association between MD and HLA-types, and good response to glucocorticoid treatment are considered to support possible autoimmune etiology in MD [11]. Although this association between autoimmune disorders and vertigo has led to the hypothesis that autoimmune mechanisms might also be involved in the pathogenesis of benign paroxysmal positional vertigo (BPPV), studies show conflicting results [12].

Based on clinical observations of increased vestibulocochlear symptoms in patients with thyroid dysfunction and possible role of autoimmunity in vestibular disorders, certain studies have investigated the relationship between vestibular disorders as MD benign paroxysmal positional vertigo [13,14]. Studies investigating the relationship between vestibular disorders and autoimmune thyroid diseases revealed inconsistent results and were unable to demonstrate a direct cause–effect relationship, and the role of thyroid dysfunction remains unclear. The aim of this study was to investigate the association between HT and vestibular function and the possible effect of levothyroxine (LT4) treatment on vestibular function.

Materials and methods

Patients

This study examined 91 adult subjects. 61 patients with HT were referred from the outpatient clinic of Başkent University, Department of Endocrinology and Metabolism. This study was approved by the Başkent University Research Committee of Medical and Health Sciences and Ethics Committee (Project no: KA18/33). Written informed consent was obtained from all the participants. The inclusion criteria were an absence of a complaint or history of vertigo, no previous use of medication that might affect the vestibular system in the last 2 weeks, no history of head trauma or previous ear surgery, absence of disorders related to cervical vertebra or the neck, absence of problems with vision or the eyes, normal ear examination, and normal spontaneous nystagmus records. Subjects not meeting any of these criteria were excluded from the study.

The study examined 3 groups. Group I comprised 31 patients who were diagnosed with HT but did not receive treatment, group II comprised 31 patients with HT who were on LT4 treatment, and the control group comprised 30 age and sex-matched healthy individuals. For power analysis, G-power 3.1 software were used. The three independent groups were compared using the power test F test and one-way ANOVA. The effect size was 0.42, type 1 error was taken as 0.05, and the power of the study was 95%.

None of the subjects had vestibular or hearing complaints. All subjects underwent a complete thyroid evaluation, including physical examination and measurement of serum free T4 (FT4), free T3 (FT3), TSH, and anti-thyroid peroxidase (anti-TPO) autoantibodies. Blood samples were drawn after an overnight fast and studied immediately. Serum concentrations of TSH (normal ranges: 0.35–4.94 μU/mL), FT4 (normal range: 0.7–1.48 ng/dL), FT3 (normal range: 2.3–4.2 pg/mL), and anti-TPO antibodies were determined by chemiluminescence immunoassay using an Abbott-Architect analyzer (Chicago, IL). Anti-TPO <35 U/mL was considered as negative.

Procedure

Pure tone audiometry, tympanometry, VEMP, and vHIT analyses were performed for all patients and the control group. Audiologic tests were conducted using an AC40 Clinical Audiometer audiometric device (Interacoustics A/S, DK-5610, Assens, Denmark). The air and bone conduction hearing thresholds were determined by routine audiologic analyses with air conduction thresholds for values between 0.125 and 8 kHz and bone conduction at 0.5, 1, 2, and 4 kHz. Hearing thresholds greater than 20 dB at two or more frequencies were accepted as sensorineural hearing loss.

Video head impulse test (vHIT)

The vHIT was performed using the Otosuite Vestibular computer program and goggles with a camera attached (GN Otometrics, Taastrup, Denmark). The head was leaned forward

30° and then thrust right and left randomly in the horizontal plane (head velocity ~100-250°/sec) to induce lateral semicircular canals. The head was thrust forward and backward randomly in the sagittal plane (head velocity ~50-250º/sec) to induce vertical semicircular canals (LARP and RALP). Twenty impulses given true were accepted for the evaluation of each canal.

The normal ranges of the VOR gain for lateral and vertical vHIT were accepted as 0.8-1.2 and 0.7-1.2, respectively. Saccade with an amplitude higher than the peak head velocity was accepted as pathological saccade. A saccade beginning before the end of the head movement was considered as a covert saccade, while a saccade beginning after head movement termination was considered as an overt saccade. In some patients, the saccade amplitude was lower than the peak head velocity in vHIT.

c/oVEMP test technique

The c/oVEMP tests were performed using a Grason-Stadler (GSI) Audera device (Grason-Stadler Inc., MN, USA). All study participants first underwent skin cleansing using alcohol and a peeling gel. Single-use Ag/AgCI (Ambu Blue Sensor N Ref No N-00-S/25) superficial electrodes were used for each test.

oVEMP

Reference electrodes were placed 5 mm below the eye sockets on the inferior oblique muscle. Active electrodes were placed 1–2 cm below the reference electrodes, and the ground electrode was placed on the forehead. Electrode resistances were kept <5 μΩ. During the recording, volunteers in a sitting position were asked to look at objects previously placed 1 m away at 30–40° angles on a horizontal plane with a neutral gaze line for the duration of sound. While giving stimuli via an insert earphone, a recording was made from the contralateral eye. During ear changeover, the individuals were asked to rest with their eyes shut. The apices of the first waveform that was formed after the introduction of the stimulus were designated as N1 and P1. The latency and amplitude values of the waves were then measured.

cVEMP

The surface electromyographic activity of the SCM muscle was recorded using an EP 25 device (Interacoustics Co., Assens, Denmark). The active electrode was put on the upper half of the ipsilateral SCM muscle, and the reference electrode was put on the suprasternal notch. During the recording, the seated patients were instructed to rotate their heads to the side opposite to the stimulated ear to activate the SCM. Background electromyographic activity was monitored visually for consistent tonic contraction.

Short tone bursts (100 dB nHL and 500 Hz each with a 1-ms rise/fall time and a 5-ms plateau time) were delivered monaurally via TDH 49P insert earphones. The stimulation rate was 5 Hz, and the analysis time was 60 ms. In total, 128 responses to stimuli were averaged, and the measurements were repeated twice to check the test wave reproducibility. The latencies of the first positive peak (p13), the next negative peak (n23), and the amplitude difference between the p13 and n23 amplitudes were measured.

Statistical analysis

Analyses were performed using SPSS version 25.0 for Windows (SPSS, Chicago, IL, USA). Continuous data were presented as the mean and standard deviation or the median [minimum–maximum] as appropriate. Comparisons of various numeric parameters among patient and control groups were analyzed with ANOVA and Kruskal–Wallis tests as necessary. Differences were considered to be statistically significant if *P*-values were <0.05.

Results

The demographic and biochemical characteristics of study subjects are presented in Table 1. Groups were similar in terms of age (*P*=0.410) and gender (*P*=0.156). As expected, serum TSH and anti-TPO levels were higher in patients with HT compared with the control group (*P*<0.001). The audiometric examinations of all study subjects were normal.

Table 1: Demographic and biochemical characteristics of study participants.

	Group I (n=31)	Group II (n=30)	Control (n=30)	*P*-value
Age (years)[a]	38.19 (10.58)	40.93 (10.39)	38.03 (7.26)	0.410
Gender (M/F)	2/29	2/28	6/24	0.156
fT3 (pg/mL)[a]	2.91 (0.52)	2.75 (0.36)	2.79 (0.33)	0.292
fT4 (ng/dL)[a]	1.51 (1.95)	1.05 (0.23)	0.99 (0.12)	0.155
TSH (μIU/mL)[b]	2.0 (0.86-7.1)	3.65 (0.03-16.83)	1.16 (0-3.36)	**<0.001**
AntiTPO (U/mL)[a]	312.96 (298.56)	582.01 (349.02)	0.46 (0.39)	**<0.001**

a: Mean (SD), b: Median (minimum-maximum), fT3: free T3, fT4: free T4, TSH: thyrotiropin stimulating hormon, anti TPO: Anti-thyroid peroxidase antibodies

There were no differences between groups for the frequencies of altered cervical and ocular VEMP tests (Table 2). There was no statistically significant difference between the groups in in terms of the absence of oVEMP and cVEMP. In cVEMP responses, the number of people with absent VEMP waves in group II was higher, but the difference was not statistically significant (*P*=0.379). In vHIT tests, there was no statistically significant difference between the groups in the mean VOR gain results in each group in all semicircular canals (Table 3).

Table 2: The cervical and ocular VEMP test results of the study participants

		Group I (n=31)	Group II (n=30)	Control (n=30)	*P*-value
cVEMP Lower case? No-hyphen?	Right Ear (A/P)	2/29	5/25	1/29	0.161
	Left Ear (A/P)	2/29	5/25	0/30	0.357
oVEMP	Right Ear P1(A/P)	4/27	5/25	5/25	0.895
	Left Ear P1 (A/P)	5/26	7/23	3/27	0.379

cVEMP: Cervical vestibular evoked myogenic potential oVEMP: Ocular vestibular evoked myogenic potentials A: absent P: positive

Table 3: The vestibulo-ocular reflex (VOR) gain results for each semicircular canal of study participants

VOR gain		Group I (n=31)	Group II (n=30)	Control (n=30)	*P*-value
Left ear	Lateral	0.9 (0-1.3)	0.9 (0.7-1.4)	0.9 (0.6-1.5)	0.998
	Posterior	0.9 (0-1.2)	0.9 (0-1.1)	0.9 (0-1.1)	0.883
	Anterior	0.8 (0-1.2)	0.8 (0.6-1)	0.8 (0-1.06)	0.694
Right ear	Lateral	1 (0-1.3)	1 (0.8-1.3)	1 (0.8-1.5)	0.985
	Posterior	0.7 (0-0.9)	0.8 (0.5-1.1)	0.8 (0-0.9)	0.152
	Anterior	0.9 (0-1.1)	0.9 (0.7-1.2)	0.9 (0-1.2)	0.554

In order to investigate the effect of TSH levels on the vestibular tests, the study subjects were grouped according to their TSH level. There were 22 hypothyroid patients with a median TSH level of 6.0 (4.2-16.4) μU/mL, and 69 were euthyroid with a median TSH level of 1.5 (0.4-3.3) μU/mL. The altered frequency in the cVEMP test of the left ear was higher in hypothyroid patients (*P*=0.042). The oVEMP test results were similar for both ears in both groups (Table 4). The groups were similar in terms of VOR gain in the vHIT (Table 5).

Table 4: The cervical and ocular VEMP test results of hypothyroid and euthyroid participants.

		Euthyroid (n=69)	Hypothyroid (n=22)	*P*-value
cVEMP	Right Ear (A/P)	4/65	4/18	0.093
	Left Ear (A/P)	1/68	3/19	**0.042**
oVEMP	Right Ear (A/P)	10/59	4/18	0.737
	Left Ear (A/P)	10/59	5/17	0.509

cVEMP: Cervical vestibular evoked myogenic potential, oVEMP: Ocular vestibular evoked myogenic potentials, A: absent, P: positive

Table 5: The vestibulo-ocular reflex (VOR) gain results for each semicircular canal hypothyroid and euthyroid participants.

VOR gain		Euthyroid (n=69)	Hypothyroid (n=22)	*P*-value
Left	Lateral	0.9 (0-1.5)	0.9 (0-1.2)	0.607
	Posterior	0.8 (0-1.2)	0.9 (0-1.1)	0.791
	Anterior	0.8 (0-1.1)	0.9 (0-1.2)	0.528
Right	Lateral	1 (0-1.5)	1 (0-1.3)	0.433
	Posterior	0.8 (0-1.1)	0.8 (0-0.9)	0.170
	Anterior	0.9 (0-1.2)	1 (0-1.1)	0.199

Discussion

This cross-sectional study showed that there was no difference in vestibular function between patients with HT and the control group in detailed vestibular tests. Studies show an increased prevalence of autoimmune thyroid disease in patients diagnosed with MD and BPPV, and autoimmunity was held responsible in the etiopathogenesis of both diseases. Most studies were designed to investigate thyroid autoimmunity or thyroid dysfunction in patients who have already been diagnosed with a vestibular disease, and some of these studies had no control group [15]. There are limited studies concerning vestibular pathologies in patients with HT.

To address the limitations in the literature, our study evaluated the peripheral vestibular system in patients with thyroid autoimmunity without vestibular complaints. The similar results of vestibular function tests in both patient and control group suggest that thyroid autoimmunity may not have a causal role in vestibular dysfunction. Our study indicates that thyroid autoimmunity might be limited to the thyroid gland alone and not have any systemic effects. However, thyroid autoantibodies are accepted as an indicator for predisposition to other autoimmune diseases [16]. Considering the possible role of autoimmunity in the pathogenesis of peripheral vestibular diseases, we may conclude that patients with HT may be potential candidates for developing peripheral vestibular diseases, especially MD. Further prospectively designed studies are needed to evaluate this.

In our study, the VEMP test results were similar in both control and patient groups. We can conclude that the endolymphatic sac, saccule macula, and inferior vestibular nerve may be affected by these results. Similar to our study, Chiarella et al. [14] found that cVEMP tests were higher in HT patients than the control group. In this study, the ratio of female patients to male patients in the HT group was significantly higher than in the control group. There is a predominance of females among those with MD, and hormonal factors may play a role in its etiopathogenesis. Therefore, the high number of female patients in the HT group in the study by Chiarella et al. [14] may have caused the higher frequency of abnormal VEMP tests. Moreover, in that study, only one SCC was evaluated using a caloric test, whereas in our study, all three SCCs were evaluated with vHIT tests. This increases the strength and reliability of our study.

There was no difference between groups in terms of gain of VOR. vHIT evaluates all three SCCs with a high-frequency impulse. McCaslin et al. [17] showed that vHIT is the most effective way of evaluating horizontal VOR in their study on MD. Chen et al. [18] demonstrated that there are normal vHIT symptoms in the early stages of the disease, but dysfunctions arise in the advanced stages. In light of the results, it was concluded that the immune response that may lead to dysfunction in the cupula in the semicircular canals, afferent cellular system, and vestibular nerve did not occur.

Our study was a cross-sectional study and was performed on asymptomatic patients who had not yet developed the autoimmune changes that cause MD or BPPV, which may be the reason behind the failure to detect the pathology in vertigo-related tests. Thus, prospective studies to investigate the association between thyroid autoimmunity and vertigo in asymptomatic HT patients are required. Approximately half of the HT patients included in our study were under LT4 treatment and were euthyroid. No significant difference was detected between HT patients under LT4 treatment and HT patients not receiving any treatment in terms of vestibular tests. There was an altered frequency in the left ears of patients with hypothyroidism in cervical VEMP tests. Since the patients did not have any symptoms and signs of vestibular dysfunction, we could not interpret the clinical importance of this result. Nevertheless, this may be an early sign of vestibular dysfunction accompanying thyroid dysfunction.

Limitations

This study had the following limitations. Firstly, due to the small number of participants (both with HT and hypothyroidism), some abnormalities in vestibular function may not have been identified, and we may not have tested the exact effect of hypothyroidism on the vestibular system. Secondly, the cross-sectional design of our study did not allow us to follow the patients for the symptoms and signs of vestibular dysfunction.

Conclusion

In conclusion, in our study, we did not find any relationship between HT and vestibular dysfunction, despite the opposite clinical observations and the findings in a relatively small number of studies. For this reason, there is a need for further studies with a prospective design to investigate the course of vestibular function in patients with HT.

References

1. McLeod DS, Cooper DS. The incidence and prevalence of thyroid autoimmunity. Endocrine. 2012;42(2):252-65. Epub 2012/05/31. doi: 10.1007/s12020-012-9703-2. PubMed PMID: 22644837.
2. Effraimidis G, Wiersinga W. Mechanisms in endocrinology: autoimmune thyroid disease: old and new players. European Journal of Endocrinology. 2014;170:R241-R52.
3. Weetman A. Diseases associated with thyroid autoimmunity: explanations for the expanding spectrum. Clinical Endocrinology. 2011;74:411-8.
4. Neuhauser HK. The epidemiology of dizziness and vertigo. Handb Clin Neurol. 2016;137:67-82. Epub 2016/09/18. doi: 10.1016/B978-0-444-63437-5.00005-4. PubMed PMID: 27638063.
5. Rosengren SM, Colebatch JG, Young AS, Govender S, Welgampola MS. Vestibular evoked myogenic potentials in practice: Methods, pitfalls and clinical applications. Clin Neurophysiol Pract. 2019;4:47-68. Epub 2019/04/06. doi: 10.1016/j.cnp.2019.01.005. PubMed PMID: 30949613; PubMed Central PMCID: PMCPMC6430081.
6. Bell SL, Barker F, Heselton H, MacKenzie E, Dewhurst D, Sanderson A. A study of the relationship between the video head impulse test and air calorics. Eur Arch Otorhinolaryngol. 2015;272(5):1287-94. Epub 2014/11/25. doi: 10.1007/s00405-014-3397-4. PubMed PMID: 25416853.
7. Gloddek B, Arnold W. Clinical and experimental studies of autoimmune inner ear disease. Acta Otolaryngol Suppl. 2002(548):10-4. Epub 2002/09/05. doi: 10.1080/00016480260094901. PubMed PMID: 12211349.
8. Roland JT. Autoimmune inner ear disease. Curr Rheumatol Rep. 2000;2(2):171-4. Epub 2000/12/21. doi: 10.1007/s11926-000-0058-y. PubMed PMID: 11123055.
9. Rossini BAA, Penido NO, Munhoz MSL, Bogaz EA, Curi RS. Sudden Sensorioneural Hearing Loss and Autoimmune Systemic Diseases. Int Arch Otorhinolaryngol. 2017;21(3):213-23. Epub 2017/07/07. doi: 10.1055/s-0036-1586162. PubMed PMID: 28680488; PubMed Central PMCID: PMCPMC5495599.

10.Fattori B, Nacci A, Dardano A, Dallan I, Grosso M, Traino C, et al. Possible association between thyroid autoimmunity and Meniere's disease. Clin Exp Immunol. 2008;152(1):28-32. Epub 2008/02/05. doi: 10.1111/j.1365-2249.2008.03595.x. PubMed PMID: 18241228; PubMed Central PMCID: PMCPMC2384067.
11.Kangasniemi E, Hietikko E. The theory of autoimmunity in Meniere's disease is lacking evidence. Auris Nasus Larynx. 2018;45(3):399-406. Epub 2017/08/09. doi: 10.1016/j.anl.2017.07.008. PubMed PMID: 28784462.
12.Yetiser S. Review of the pathology underlying benign paroxysmal positional vertigo. J Int Med Res. 2020;48(4):300060519892370. Epub 2019/12/31. doi: 10.1177/0300060519892370. PubMed PMID: 31885315; PubMed Central PMCID: PMCPMC7605005.
13.Sari K, Yildirim T, Borekci H, Akin I, Aydin R, Ozkiris M. The relationship between benign paroxysmal positional vertigo and thyroid autoimmunity. Acta Otolaryngol. 2015;135(8):754-7. Epub 2015/03/13. doi: 10.3109/00016489.2015.1021932. PubMed PMID: 25761528.
14.Chiarella G, Tognini S, Nacci A, Sieli R, Costante G, Petrolo C, et al. Vestibular disorders in euthyroid patients with Hashimoto's thyroiditis: role of thyroid autoimmunity. Clin Endocrinol (Oxf). 2014;81(4):600-5. Epub 2014/04/17. doi: 10.1111/cen.12471. PubMed PMID: 24735417.
15.Chiarella G, Russo D, Monzani F, Petrolo C, Fattori B, Pasqualetti G, et al. Hashimoto Thyroiditis and Vestibular Dysfunction. Endocr Pract. 2017;23(7):863-8. Epub 2017/05/24. doi: 10.4158/EP161635.RA. PubMed PMID: 28534686.
16.Boelaert K, Newby PR, Simmonds MJ, Holder RL, Carr-Smith JD, Heward JM, et al. Prevalence and relative risk of other autoimmune diseases in subjects with autoimmune thyroid disease. Am J Med. 2010;123(2):183 e1-9. Epub 2010/01/28. doi: 10.1016/j.amjmed.2009.06.030. PubMed PMID: 20103030.
17.McCaslin DL, Rivas A, Jacobson GP, Bennett ML. The dissociation of video head impulse test (vHIT) and bithermal caloric test results provide topological localization of vestibular system impairment in patients with "definite" Meniere's disease. Am J Audiol. 2015;24(1):1-10. Epub 2014/11/09. doi: 10.1044/2014_AJA-14-0040. PubMed PMID: 25381440.
18.Chen Y, Zhao Z, Zhuang J, Xie X, Jin Z, Li F. [The features of high and low-frequency function of horizontal, semicircular canal in Meniere's disease]. Lin Chuang Er Bi Yan Hou Tou Jing Wai Ke Za Zhi. 2015 May;29(10):882-4. Chinese. PMID: 26595999.

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Effects of mean platelet volume, mean corpuscular hemoglobin concentration and neutrophil-to-lymphocyte ratio on mortality in patients undergoing coroner artery bypass graft surgery

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Ethics Committee Approval
The study was approved by Adıyaman University Non-Invasive Clinical Research Ethics Committee (17/11/2020, 2020/10-11).
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Abstract

Background/Aim: Laboratory tests play a vital role in diagnosing, monitoring, treating, and determining the prognosis of diseases. Several parameters, including mean corpuscular hemoglobin concentration (MCHC), mean platelet volume (MPV), mean corpuscular volume (MCV), platelet distribution width (PDW), platelet count (PLT), plateletcrit (PCT), neutrophil count (NEU), platelet/lymphocyte ratio (PLR), and neutrophil/lymphocyte ratio (NLR), have been investigated in various diseases. This study aims to explore whether these parameters can predict mortality in patients undergoing coronary artery bypass graft surgery (CABG).

Methods: The study was conducted as a retrospective cohort study, analyzing 2478 patients who underwent CABG in the cardiovascular surgery clinic of our hospital between January 2013 and November 2020. Preoperative blood count parameter values (PLT, PCT, PDW, MPV, MCHC, MCV, PLR, NEU, NLR, and MCHC/MCV) were compared between 80 patients who died after the operation (Group 1) and 80 patients who were discharged from the hospital (Group 2).

Results: The analysis revealed that PLT and MCV were significantly lower in Group 1, while MPV, NEU, NLR, and MCHC/MCV were significantly higher. In the receiver operating characteristic (ROC) analysis, the positive probability rate of PLT in predicting mortality (cut-off >260.2, +LR: 2.44, 95% CI: 0.605–0.754) was higher than that of MPV (cut-off ≤7.53, +LR: 2, 95% CI: 0.584–0.735), MCV (cut-off ≤82.21, +LR: 1.26, 95% CI: 0.513–0.671), NEU (cut-off ≤68.2, +LR: 2.03, 95% CI: 0.640–0.785), NLR (cut-off ≤2.66, +LR: 2.58, 95% CI: 0.571–0.724), and MCHC/MCV (cut-off ≤0.4, +LR: 1.45, 95% CI: 0.551–0.706).

Conclusion: Preoperative PLT, MCV, MPV, NEU, NLR, and MCHC/MCV values are effective parameters for predicting mortality in CABG patients.

Keywords: coronary artery disease, coronary artery bypass graft operation, mortality, blood count parameters

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Introduction

The purpose of coronary artery bypass graft surgery (CABG).can be summarized as improving the quality and duration of life, relieving angina, and reducing the occurrence of recurrent ischemic events, such as myocardial infarction, by decreasing the need for subsequent procedures. Despite being considered one of the most life-saving surgeries, the mortality rate for CABG ranges from approximately 1.48% to 2.67%, depending on the surgical technique employed and the surgeon's experience [1,2].

By identifying and addressing preventable factors contributing to mortality, it may be feasible to further reduce this rate. In the contemporary healthcare, laboratory tests are crucial in disease diagnosis, prognostic evaluation, and treatment selection.

Hematologic parameters, including mean platelet volume (MPV), plateletcrit (PCT), platelet distribution width (PDW), platelet/lymphocyte ratio (PLR), and mean corpuscular hemoglobin concentration (MCHC), can be determined through cost-effective laboratory tests. The literature reports these parameters' utilization in the diagnosis and treatment of numerous diseases. For instance, MPV has been identified as an independent parameter associated with well-known risk factors such as dyslipidemia, hypertension, increased fibrinogen levels, and elevated white cell count. Moreover, a significant correlation has been observed between MPV and atherothrombosis [3].

Research has demonstrated the utility of PCT and PLR as markers for identifying heightened thrombotic status and inflammatory response in individuals with morbid obesity [4]. Additionally, a separate study indicated a correlation between NLR and acute coronary syndromes [5].

This study aims to examine whether MPV, PCT, PDW, PLR, MCHC, mean corpuscular volume (MCV), and MCHC/MCV can serve as predictors of mortality in CABG patients.

Materials and methods

The study commenced after obtaining approval from the Local Ethics Committee (TC. Non-Interventional Ethics Committee of Adiyaman University) on November 17, 2020, with session number 2020/10-11. A total of 3,478 patients who underwent CABGO and were diagnosed with coronary artery disease (CAD) between January 2013 and November 2020 were included in the study, along with 80 randomly selected patients who were discharged with recovery. The data were collected electronically from the hospital's data recording system. An equal number of male and female patients were randomly selected as the control group. The patients who died were categorized as Group 1, while the control patient group was referred to as Group 2. The preoperative PLT, PCT, PDW, MPV, MCHC, MCV, PLR, NEU, NLR, and MCHC/MCV values of these groups were compared. Blood samples were analyzed using the Abbott Cell-Dyn Ruby (USA) hematology analyzer.

Patients who underwent additional operations other than CABGO and emergency surgeries were excluded from the study. Furthermore, patients with hematologic diseases, active infections, and liver dysfunction were also excluded. To mitigate gender bias, an equal number of male and female patients were selected in this study, matching the number in the control group.

Statistical analysis

Statistical analysis was conducted using SPSS 15.0 for Windows (SPSS Inc.) and Medcalc v.9.4.4.0. The one-sample Kolmogorov-Smirnov test was employed to assess the normal distribution of the data. Group comparisons were performed using the Independent Two Samples t-test or the Mann-Whitney U test, as appropriate. Results were presented as mean, standard deviation and median (min-max). Non-parametric data were compared using the Chi-square test and reported as numbers or percentages. Pearson correlation coefficients were utilized for continuous variables. Multivariate binary logistic regression analysis was conducted to determine predictive factors for ex-subjects considering statistically relevant confounding variables. The receiver operating characteristics (ROC) curve was employed for evaluating clinical parameters. A *P*-value <0.05 was considered statistically significant.

Results

Randomly selected patients who underwent CABGO with a diagnosis of CAD and subsequently died after surgery were included in the study. Group 1 consisted of 40 males and 40 females, while Group 2 comprised 40 men and 40 women. The study was conducted between January 2013 and November 2020. The mean age of Group 1 was 66.49 (9.99) years, whereas Group 2 had a mean age of 63.30 (8.34) years (P=0.030). No significant differences were observed in comorbidity between the two groups (Table 1). Table 1 provides a summary of the demographic, clinical, and laboratory characteristics of the patients.

Table 1: Demographic, clinical and laboratory characteristics of the patients.

Variables		Group 1 (n=80) Exitus (Deceased)		Group 2 (n =80) Discharge		
		Mean (SD) n(%)	Median (Min-Max)	Mean (SD) n(%)	Median (Min-Max)	*P*-value
Age		66.49 (9.99)	65.00 (45.00-89.00)	63.30 (8.34)	63.00 (46.00-81.00)	0.030 Φ
Gender	Male	40 (50%)		40 (50%)		1.000 Ψ
	Female	40 (50%)		40 (50%)		
Smoking		21 (26.25%)		19 (23.75%)		0.710 Ψ
Hypertension		29 (36.25%)		26 (32.50%)		0.614 Ψ
Alcohol		11 (13.75%)		10 (12.5%)		0.807 Ψ
Diabetes Mellitus		20 (25%)		22 (27.5%)		0.715 Ψ
PLT		229.69 (64.2)	229.69 (87.32-481.0)	276.82 (92.43)	269.5 (116.2-747.1)	<0.001 ᵀ
MPV		8.40 (1.63)	8.16 (5.37-12.65)	7.50 (1.47)	7.2 5.11-11.74	<0.001 Φ
PCT		0.22 (0.1)	0.20 (0.10-0.63)	0.19 (0.06)	0.18 (0.09-0.41)	0.095 ᵀ
PDW		18.40 (3.36)	19.27 (9.60-24.84)	17.70 (3.95)	18.57 (8.50-24.70)	0.228 Φ
MCHC		33.27 (1.64)	32.90 (29.62-37.66)	32.86 (1.49)	33.04 (29.26-36.39)	0.105 Φ
MCV		85.03 (5.93)	85.7 (70.64-99.62)	86.88 (4.23)	86.72 (73.41-100.30	0.025 Φ
NEU		69.53 (11.77)	69.70 (46.63-92.40)	60.88 (8.11)	60.34 (42.81-78.39)	<0.001 Φ
LYM		26.56 (7.82)	27.75 (9.40-42.96)	29.09 (6.38)	28.50 (16.04-45.60)	0.143 Φ
NLR		3.01(1.4)	2.76 (1.30-7.37)	2.22 (0.75)	2.17 (0.14-3.93)	<0.001 ᵀ
PLR		9.71 (5.1)	8.40 (3.51-29.66)	10.07 (5.5)	9.0 (0.52-46.58)	0.187 ᵀ
MCHC/MCV		0.393 (0.03)	0.39 (0.37-0.42)	0.382 (0.02)	0.38 (0.32-0.70)	0.002 Φ

Ψ Chi-Square test was used, Φ Independent two sample t-test was used, ᵀ Mann-Whitney U test was used. SD: Standard deviation, Min: Minimum, Max: Maximum, PLT: Platelet, MPV: Mean platelet volume, MCV: Mean corpuscular, PCT: Plateletcrit, PDW: Platelet distribution width, MCHC: Mean corpuscular hemoglobin concentration, MCV: Mean corpuscular volume, NEU: Neutrophil, LYM: Lymphocyte, NLO: Neutrophil-to-lymphocyte ratio, PLO: Platelet-to-lymphocyte ratio, MCHC/MCV: Mean corpuscular hemoglobin concentration to mean corpuscular volume ratio

Based on the file scans, it was determined that all patients who experienced mortality had died prior to the follow-up period in the ward after being in the Intensive Care Unit.

Significant differences were observed between Group 1 and Group 2 in terms of PLT levels from laboratory data (P<0.001). Furthermore, Group 1 exhibited significantly higher values of MPV, MCV, NEU, NLO, and MCHV/MCV compared to Group 2 (P<0.001, P=0.025, P<0.001, P<0.001, and P=0.002, respectively). The results of the Multivariate Binary Logistic Regression Analysis are presented in Table 2. According to these findings, elevated PLR values were associated with increased mortality, whereas decreased MPV, PCT, PDW, NLR, and MCVC/MCV rates were associated with decreased mortality. The analysis revealed that MPV (OR: 0.653, 95% CI: 0.493–0.864, P=0.003), PCT (OR: 0.004, 95% CI: 0.000–1.000, P=0.003), PDW (OR: 0.885, 95% CI: 0.787–0.996, P=0.042), NLR (OR: 0.197, 95% CI: 0.102–0.381, P<0.001), and PLR (OR:1.310, 95%CI: 1.124–1.526, P=0.001) values were independent predictive factors for mortality (Table 2). Pearson Correlation Analysis was performed to examine the relationships between the predictive parameters and other variables (Table 3). In the deceased group (Group 1), PLR exhibited significant positive correlations with PLT (r=0.560, P<0.001), NEU (r=0.296, P<0.001), and NLR (r=0.778, P<0.001), while demonstrating a significant negative correlation with LYM (r=-0.724, P<0.001). NLR showed a significant positive correlation with NEU (r=0.632, P<0.001) but a negative and significant correlation with LYM (r= -0.922, P<0.001). PDW displayed a positive and significant correlation with MCHC (r=-0.224, P<0.001). No significant correlations were observed between MPV and PCT predictive parameters and other variables (P=0.095). In Group 2, PDW exhibited a negative and significant correlation with PCT (r=-0.224, P=0.05), while the other measurements were similar to those of the deceased group.

Table 2: The multivariate binary logistic regression analysis to identify predictors of mortality

Variables	B	S.E.	*P*-value	OR	95% CI	
					Lower	Upper
MPV	-0.427	0.143	0.003	0.653	0.493	0.864
PCT	-5.590	2.852	0.050	0.004	0.000	1.000
PDW	-0.122	0.060	0.042	0.885	0.787	0.996
NLR	-1.625	0.337	<0.001	0.197	0.102	0.381
PLR	0.270	0.078	0.001	1.310	1.124	1.526
MCHC/MCV	-23.555	7.684	0.002	0.000	0.000	0.000

B: Beta coefficient, SE: Standard error, OR: Odds Ratio, CI: Confidence Interval, Hosmer–Lemeshow goodness-of-fit test: X^2: 12.32, P=0.138, MPV: Mean platelet volume, PCT: Plateletcrit, PDW: Platelet Distribution Width, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet- lymphocyte ratio, MCHC/MCV: Mean corpuscular hemoglobin concentration to mean corpuscular volume ratio

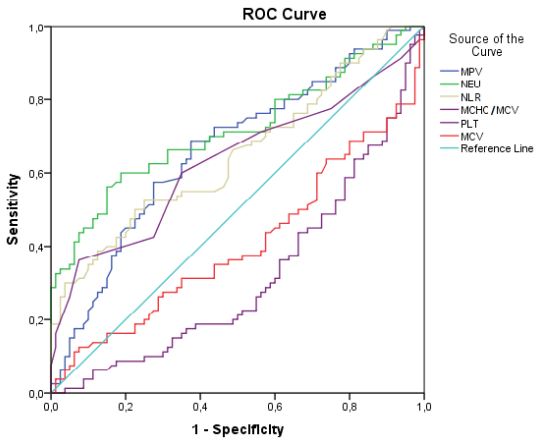
Table 3: Receiver operating characteristics curve analysis

Variables	Cut-off	Sensitivity (95% CI)	Specificity 95% CI	+LR 95% CI	-LR 95% CI	AUC (95% CI)	*P*-value
PLT	>260.2	55 (43.5 - 66.1)	77.5 (66.8 - 86.1)	2.44 (1.9 - 3.1)	0.58 (0.4 - 0.9)	0.683 (0.605 - 0.754)	<0.001
MPV	≤7.53	62.5 (51.0 - 73.1)	68.75 (57.4 - 78.6)	2 (1.6 - 2.5)	0.55 (0.4 - 0.8)	0.662 (0.584 - 0.735)	<0.001
MCV	>82.21	90 (81.2 - 95.6)	28.75 (19.2 - 40.0)	1.26 (0.9 - 1.8)	0.35 (0.2 - 0.7)	0.594 (0.513 - 0.671)	0.037
NEU	≤68.02	81.25 (71.0 - 89.1)	60 (48.4 - 70.8)	2.03 (1.7 - 2.5)	0.31 (0.2 - 0.5)	0.716 (0.640 - 0.785)	<0.001
NLR	≤2.66	75 (64.1 - 84.0)	52.5 (41.0 - 63.8)	1.58 (1.2 - 2.0)	0.48 (0.3 - 0.7)	0.651 (0.571 - 0.724)	0.001
MCHC/MCV	≤0.4	92.5 (84.4 - 97.2)	36.25 (25.8 - 47.8)	1.45 (1.1 - 2.0)	0.21 (0.09 - 0.5)	0.631 (0.551 - 0.706)	0.003

+LR: positive likelihood ratio, −LR: negative likelihood ratio, PLT: Platelet, MPV: Mean platelet volume, MCV: Mean corpuscular volume, NEU: Neutrophil, NLR: Neutrophil-to-lymphocyte ratio, MCHC/MCV: Mean corpuscular hemoglobin concentration to mean corpuscular volume ratio

ROC curve analysis was conducted to assess the diagnostic performance and characteristics of the variables found to be significant in Table 1. The results revealed that the predictive capacity of probable positivity rate in predicting mortality (cut-off >260.2, +LR: 2.44, 95% CI: 0.605–0.754) was higher compared to MPV (cut-off ≤7.53, +LR: 2, 95% CI: 0.584–0.735), MCV (cut-off ≤82.21, +LR: 1.26, 95% CI: 0.513–0.671), NEU (cut-off ≤68.2, +LR: 2.03, 95% CI: 0.640–0.785), NLR (cut-off ≤2.66, +LR: 2.58, 95% CI: 0.571–0.724), and MCHC/MCV (cut-off ≤0.4, +LR: 1.45, 95% CI: 0.551–0.706). Consequently, the PLT value with a cut-off of 260.2 exhibited a more accurate diagnostic value in predicting mortality (AUC: 0.683, 95% CI: 0.605–0.754) (Table 3). The ROC chart illustrated that MPV, NLR, and MCHC/MCV were significantly higher in Group 1 than in Group 2, as indicated by their positioning above the reference line (Figure 1). Conversely, PLT and MCV were significantly lower in Group 1 than Group 2, causing them to be situated below the reference line.

Figure 1: Receiver operating characteristic curve of group variables to estimate the likelihood of mortality



MPV: Mean platelet volume, NEU: Neutrophil, NLR: Neutrophil-to-lymphocyte ratio, MCHC/MCV: Mean corpuscular hemoglobin concentration to mean corpuscular volume ratio, PLT: Platelet, MCV: Mean corpuscular volume

Discussion

Despite advancements in cardiac surgery and cardiac anesthesia techniques, the mortality rate attributed to various complications remains around 2%, even in top-tier medical centers [2]. A thorough examination of the factors influencing mortality reveals that multiple variables, including body mass index, age, gender, aortic clamp time, and total cardiopulmonary bypass time, contribute to increased risk [6].

This study aimed to examine preoperative laboratory values and identify factors influencing mortality, excluding obvious factors. Multivariate Binary Logistic Regression Analysis was conducted to compare patients who died in the intensive care unit of cardiovascular surgery with those who were discharged, considering matching numbers and genders. The results revealed that PLT, MPV, PCT, PDW, and NLR were independent predictive factors for mortality. Specifically, low preoperative PLT and MCV levels, along with elevated MPV, NLR, and MCHC/MCV ratios, were found to significantly impact mortality.

MPV serves as an approximate indicator of platelet activation and has been utilized for risk assessment and prognostic evaluation in cardiovascular diseases [7]. However, no significant correlations were observed between Group 1 (patients who died) and Group 2 (patients who were discharged) in our study. Previous research has demonstrated that MPV is an independent risk factor in individuals with acute coronary syndrome and is closely linked to complications following acute myocardial infarction and restenosis post-stent placement in percutaneous coronary interventions [8]. Additionally, Smyth et al. conducted a separate study revealing elevated MPV levels in patients who experienced restenosis after successful single-vein angioplasty [9]. Our study found that low platelet (PLT) count and elevated MPV were associated with increased mortality.

A separate study highlighted the potential of MPV and MCHC as cost-effective and influential parameters for prognostic evaluation in three vascular coronary artery diseases [8]. MCV and MCHC were initially introduced by Wintrobe in 1929 to assess the size of red blood cells and the amount of hemoglobin. These values, referred to as red cell indices, were initially utilized solely for diagnosing specific types of anemia and understanding their underlying causes [10]. Subsequent clinical trials have emphasized that MCHC, in particular, could serve as a determinant of mortality in CAD and may also predict acute mortality in patients presenting at the emergency department [11-13].

Our study revealed that both MCV and MCHC/MCV ratios significantly impacted mortality. A low MCV value below the cut-off of 82.21, as well as an MCHC/MCV ratio below the cut-off of 0.4, were identified as significant determinants of mortality.

Atherosclerosis, diabetes mellitus, hypertension, dyslipidemia, and smoking are interconnected risk factors contributing to the complex systemic disease known as CAD [14]. Recent research findings indicate that the development of atherosclerosis involves not only passive vascular damage triggered by blood lipoproteins and other elements within the arterial wall but also a significant contribution from white blood cells in the inflammatory process [15,16]. Neutrophils, in particular, have been shown to play various roles, from atherosclerosis progression to plaque stabilization [14]. As a result, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been extensively studied as inflammation biomarkers, with NLR specifically linked to the severity and prognosis of CAD [14,17,18].

Our study evaluated the preoperatively calculated NLR using Multivariate Binary Logistic Regression and ROC Analysis. The results demonstrated that NLR independently served as a risk factor for predicting mortality in patients undergoing coronary artery bypass grafting (CABG).

Limitations

Our study had several limitations that should be acknowledged. Firstly, it was a single-center retrospective study, which inherently restricts the generalizability of the findings. The patient population included in the study was relatively small, further limiting the statistical power of the analysis. Another limitation is that most patients underwent interventional procedures such as coronary angiography, catheter insertion, and urinary probe placement at the cardiology clinic, and many were on anticoagulant and antiplatelet therapy. These procedures and medications can potentially induce inflammatory responses, which may have influenced the inflammatory parameters measured. It is important to recognize that inflammatory parameters can be influenced by various factors, and therefore, a multicenter study considering all relevant prospective influencing factors is necessary to provide a more comprehensive understanding.

The primary limitation of our study is its single-center design, which may restrict the generalizability of the findings to a broader population. Additionally, our study is retrospective in nature, which introduces inherent limitations such as potential bias and limited control over data collection. However, our study has notable strengths, including a relatively large sample size compared to similar studies and the novelty of being the first single-center study reporting on these specific findings in the literature.

Conclusion

In summary, our study demonstrated the significant impact of inflammatory parameters, including preoperative MPV, NEU, NLR, MCHC/MCV, PLT, and MCV, on mortality in patients who underwent CABG. These findings align with existing literature regarding the influence of inflammatory markers on CAD and surgical mortality. Notably, these parameters offer several advantages, such as cost-effectiveness, quick availability (results in less than 20 minutes), and ease of repeatability.

References

1. Rocha EAV. Fifty Years of Coronary Artery Bypass Graft Surgery. Braz J Cardiovasc Surg. 2017 Jul-Aug;32(4):II-III. doi: 10.21470/1678-9741-2017-0104
2. Watkins AC, Ghoreishi M, Maassel NL, Wehman B, Demirci F, Griffith BP, et al. Programmatic and Surgeon Specialization Improves Mortality in Isolated Coronary Bypass Grafting. Ann Thorac Surg. 2018 Oct;106(4):1150-8. doi: 10.1016/j.athoracsur.2018.05.032.
3. Hudzik B, Korzonek-Szlacheta I, Szkodziński J, Liszka R, Lekston A, Zubelewicz-Szkodzińska B, et al. Association between multimorbidity and mean platelet volume in diabetic patients with acute myocardial infarction. Acta Diabetol. 2018 Feb;55(2):175-83. doi: 10.1007/s00592-017-1079-6.
4. Erdal E, İnanir M. Platelet-to-lymphocyte ratio (PLR) and Plateletcrit (PCT) in young patients with morbid obesity. Rev Assoc Med Bras (1992). 2019 Oct 10;65(9):1182-7. doi: 10.1590/1806-9282.65.9.1182.
5. Duffy BK. Gurm HS. Rajagopal V. Gupta R. Ellis SG. Bhatt DL. Usefulness of an elevated neutrophil to lymphocyte ratio in predicting long-term mortality after percutaneous coronary intervention. Am J Cardiol 2006;97(7):993-6.
6. Mavili İ, Şahutoğlu C, Pestilci Z, Kocabaş S, Aşkar FZ. Etiological factors concerning the early complications that occur following coronary artery bypass graft surgery. Journal of Cardio-Vascular-Thoracic Anaesthesia and Intensive Care Society. 2016;22(1):16-23.

7. Ding L, Sun L, Wang F, Zhu L, Zhang T, Hua F. Clinical Significance of Platelet Volume and Other Platelet Parameters in Acute Myocardial Infarction and Stable Coronary Artery Disease. Arq Bras Cardiol. 2019 Jun;112(6):715-9. doi: 10.5935/abc.20190058. Epub 2019 April 1.
8. Karaman S, Coskun A. Do MCHC, MPV, and Procalcitonin Levels Determine Prognosis in Acute Coronary Syndrome? Emerg Med Int. 2019 July 18;2019:6721279. doi: 10.1155/2019/6721279
9. Smyth DW, Martin JF, Michalis L, Bucknall CA, Jewitt DE. Influence of platelet size before coronary angioplasty on subsequent restenosis. Eur J Clin Invest. 1993 Jun;23(6):361-7. doi: 10.1111/j.1365-2362.1993.tb02037.x.
10. Sarma PR. Red Cell Indices. In: Walker HK, Hall WD, Hurst JW, editors. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd ed. Boston: Butterworths; 1990. Chapter 152. PMID: 21250103.
11. Tang WH, Yeo PS. Epidemiology of anemia in heart failure. Heart Fail Clin. 2010 Jul;6(3):271-8. doi: 10.1016/j.hfc.2010.03.007. PMID: 20630401.
12. Simbaqueba C, Shrestha K, Patarroyo M, Troughton RW, Borowski AG, Klein AL, et al. Prognostic implications of relative hypochromia in ambulatory patients with chronic systolic heart failure. Congest Heart Fail. 2013 Jul-Aug;19(4):180-5. doi: 10.1111/chf.12010.
13. Brzeźniakiewicz-Janus K, Lancé MD, Tukiendorf A, Janus T, Franków M, Rupa-Matysek J, et al. Selected Hematological Biomarkers to Predict Acute Mortality in Emergency Department Patients. Recent Polish Hospital Statistics. Dis Markers. 2020 July 16;2020:8874361. doi: 10.1155/2020/8874361.
14. Serrano CV Jr, de Mattos FR, Pitta FG, Nomura CH, de Lemos J, Ramires JAF, et al. Association between Neutrophil-Lymphocyte and Platelet-Lymphocyte Ratios and Coronary Artery Calcification Score among Asymptomatic Patients: Data from a Cross-Sectional Study. Mediators Inflamm. 2019 March 26;2019:6513847. doi: 10.1155/2019/6513847.
15. Balta S, Celik T, Mikhailidis DP, Ozturk C, Demirkol S, Aparci M, et al. The Relation Between Atherosclerosis and the Neutrophil-Lymphocyte Ratio. Clin Appl Thromb Hemost. 2016 Jul;22(5):405-11. doi: 10.1177/1076029615569568.
16. Balta S, Ozturk C, Yildirim AO, Erdogan S, Celik T. The neutrophil-lymphocyte ratio and atherosclerosis. Expert Rev Cardiovasc Ther. 2016 Aug;14(8):885. doi: 10.1080/14779072.2016.1194199.
17. Kim NY, Chun DH, Kim SY, Kim NK, Baik SH, Hong JH, et al. Prognostic Value of Systemic Inflammatory Indices, NLR, PLR, and MPV, for Predicting 1-Year Survival of Patients Undergoing Cytoreductive Surgery with HIPEC. J Clin Med. 2019 April 29;8(5):589. doi: 10.3390/jcm8050589.
18. Kurtul A, Ornek E. Platelet to Lymphocyte Ratio in Cardiovascular Diseases: A Systematic Review. Angiology. 2019 Oct;70(9):802-18. doi: 10.1177/0003319719845186.

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Research article

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Does the levels of vitamin D correlate with the levels of vitamin B12 and ferritin in fibromyalgia?

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Ethics Committee Approval
The study was approved by the Eskisehir Osmangazi University Ethics Committee (14/07/20-34: E-25403353-050.99-77349). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Considering the effects of inflammation on fibromyalgia and the small intestine, we hypothesize that vitamin D deficiency may contribute to inflammation and affect vitamin B12 and ferritin levels in patients with fibromyalgia. The objectives were: 1) to compare the levels of vitamin D, vitamin B12, and ferritin in patients with fibromyalgia and patients who have local painful conditions, and 2) to evaluate the correlation of vitamin D levels with vitamin B12 and ferritin levels.
Methods: The records of 299 patients with fibromyalgia (274 female, 25 male) and 128 patients with local painful conditions (114 female, 14 male) between April 2019 and 2020 were examined, including measurements of 25-hydroxy vitamin D, vitamin B12, ferritin, erythrocyte sedimentation rate, and C-reactive protein.
Results: The levels of 25-hydroxy vitamin D were low in both groups, with levels below 30 ng/ml in 90.3% of all patients. However, there was no significant difference in vitamin B12 and ferritin levels between the two groups, and the levels of these markers were within normal limits in both groups. Correlation analysis showed that vitamin D levels were significantly correlated with vitamin B12 ($P<0.001$, r=0.211) and ferritin ($P=0.005$, r=0.337) levels in patients with fibromyalgia but not in the other group.
Conclusion: Consistent with our hypothesis, an association was found between vitamin D levels and vitamin B12 and ferritin levels in fibromyalgia. However, this correlation was not found in patients with local painful conditions.

Keywords: fibromyalgia, neuroinflammation, vitamin D

Introduction

Fibromyalgia is characterized by widespread chronic pain and fatigue [1], and its exact origin is unknown. It is speculated that vitamin deficiencies may play a role in its development, although it remains unclear whether they contribute to the underlying pathophysiology [2].

The relationship between iron and fibromyalgia has been investigated in previous studies, yielding varying results. A controlled study comparing fibromyalgia patients with healthy subjects suggested that iron, as a cofactor in the dopamine and serotonin pathways, may play a role in the etiology of fibromyalgia [3]. In contrast, another controlled study with healthy volunteers reported that patients with fibromyalgia do not have reduced iron stores [4]. Deficiency in vitamin B12 can lead to a decrease in neurotransmitter levels by affecting methylation reactions [5], and it has been associated with pain and other musculoskeletal disorders [6]. Therefore, several studies have examined the relationship between fibromyalgia and vitamin B12, finding normal serum levels of vitamin B12 [3,7].

Vitamin D has been extensively studied in relation to fibromyalgia, with many studies reporting low levels of this vitamin in individuals with the condition [8-10]. Akar et al. [8] suggested that patients with vitamin D levels below 25 ng/ml may be more prone to experiencing pain and developing fibromyalgia. Similarly, Özcan et al. [9] observed lower levels of 25-hydroxy vitamin D in 60 patients with fibromyalgia compared to 30 healthy controls. Özgen et al. [10] reported that only 11.48% of the patients with fibromyalgia had normal vitamin D levels (above 30 ng/ml).

There is evidence of both neuroinflammation and systemic inflammation in fibromyalgia [11-13]. Fibromyalgia often coexists with gastrointestinal dysbiosis and intestinal hyperpermeability [14-16], which can be attributed to the effects of systemic inflammation on the gastrointestinal tract, including barrier function, epithelial cells, villus structures, and intestinal absorptive area [17,18]. On the other hand, vitamin D has been shown to have anti-inflammatory properties [19], as well as the ability to reduce intestinal hyperpermeability [20] and improve intestinal dysbiosis [21].

Given the impact of inflammation on the small intestine, we hypothesize that vitamin D deficiency may contribute to inflammation and potentially affect vitamin B12 and ferritin levels in patients with fibromyalgia.

This study was conducted with the following objectives: 1) to investigate the levels of vitamin D, vitamin B12, and ferritin in patients with fibromyalgia, 2) to compare these results with patients who have local painful conditions, and 3) to evaluate the correlation between vitamin D levels and vitamin B12 and ferritin levels.

Materials and methods

The study involved a retrospective analysis of patients with fibromyalgia and a local painful condition at the Physical Medicine and Rehabilitation Outpatient Clinic between April 2019 and 2020. This analysis was conducted by searching the computerized database and patient files. The medical records of 956 patients diagnosed with fibromyalgia, according to the American College of Rheumatology (ACR) 1990 Criteria (ICD-10: M79 and subgroups), were reviewed, along with the records of 350 patients with a local musculoskeletal problem (experiencing pain but without a systemic musculoskeletal problem) (ICD-10: M75.1, S83, G56.0, M17). The review focused on gathering information regarding age, gender, and blood test results.

Two-hundred-ninety-nine patients with fibromyalgia (274 female, 25 male) were included in Group 1, while 128 patients (114 female, 14 male) with only a local musculoskeletal problem (Group 2) and no systemic musculoskeletal problem were also included in the study. The inclusion criteria specified that patients must be aged between 20 and 75 years, with available records of age and gender, as well as 25-hydroxy-vitamin D (25(OH)vit D) and vitamin B12 values from blood tests. Patients who did not have both 25-hydroxy-vitamin D and vitamin B12 values, those with C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels higher than twice the normal upper limit, and patients who visited the hospital for control purposes and received vitamin therapy were excluded from the study. Additionally, patients with multi-joint osteoarthritis were excluded from Group 2.

The ACR 1990 Fibromyalgia Criteria defines fibromyalgia as the presence of widespread pain accompanied by tenderness at 11 or more of the 18 tender points for a duration of at least 3 months [1].

Blood tests were conducted to gather records of 25-hydroxy-vitamin D, vitamin B12, ferritin, ESR, and CRP levels. The following reference ranges were used: serum 25(OH)vit D values of 0–19.99 ng/ml (or 50 nmol/ml) indicated vitamin D deficiency, values of 20–29.99 ng/ml (or 50–75 nmol/ml) indicated mild deficiency and values of 30 ng/ml and above were considered within the normal serum concentration range. Vitamin B12 values between 190 and 880 pg/ml, ferritin values between 5–120 ng/ml, CRP values between 0 and 5 mg/l, and ESR values between 1 and 20 mm/h were regarded as normal serum concentrations. However, for geriatric patients, the normal upper limit of ESR values was calculated using the formula (age + 10)/2 for women and age/2 for men [22].

The study obtained approval from the Eskisehir Osmangazi University Ethics Committee (14/07/20-34: E-25403353-050.99-77349).

Statistical analysis

The distribution of each continuous variable was assessed using the Shapiro-Wilk test. Non-normally distributed variables were analyzed using the Mann-Whitney U test and are reported as median values with the interquartile range (25th-75th percentile). Categorical variables were compared using chi-square statistics and are presented as numbers and percentages. Spearman correlation analysis was employed to examine the relationships between variables. A significance level of $P < 0.05$ was considered statistically significant. All statistical analyses were conducted using SPSS version 22.0 software (SPSS Inc., Chicago, IL, USA).

Results

No significant differences were found in age, gender, vitamin B12, ferritin, CRP, and ESR levels between the two

groups. The levels of these factors were within normal limits in both groups. However, both groups exhibited low vitamin D levels (Table 1). Table 2 displays the 25(OH)vit D levels for all patients. Only 11.6% of group 1 and 5.4% of group 2 had normal 25(OH)vit D levels.

Correlation analysis revealed significant correlations between vitamin D levels and vitamin B12 ($P<0.001$) as well as ferritin ($P=0.005$) levels in fibromyalgia patients. However, this correlation was not observed in patients with a local painful condition (Table 3).

Table 1: Comparison of age, gender, vitamin, c-reactive protein and erythrocyte sedimentation rate levels between groups

	Group 1		Group 2		*P*-value
Age, years, mean (range)	48.0 (40-56)		48.5(38-57)		0.857
	n	%	n	%	
Gender					
Female	274	91.63%	114	89.06%	0.212
Male	25	8.36%	14	10.93%	
	Median (IQR 25-75%)		Median (IQR 25-75%)		
25-hydroxy vitamin D	18.30 (12.90-25.10)		16.65 (9.65-22.97)		0.011
Vitamin B12	353.0 (265.25-434.0)		342.50 (265.50-412.0)		0.482
Ferritin	22.0 (6.50-44.0)		23.0 (6.0-51.0)		0.655
C-Reactive Protein	1.0 (0.10-3.10)		1.0 (0.20-2.90)		0.757
ESR	9.0 (6.0-15.0)		11.0 (5.0-17.0)		0.378

ESR: Erythrocyte Sedimentation Rate, IQR: inter quartile range

Table 2: Vitamin D levels of both groups

	Group 1 (n=299)			Group 2 (n=128)		
Vitamin D categories	<20ng/ml	20-30ng/ml	≥30ng/ml	<20ng/ml	20-30ng/ml	≥30ng/ml
n (%)	163 (54.51%)	102 (34.11%)	35 (11.70%)	82 (64.06%)	39 (30.46%)	7 (5.46%)

Table 3: Correlation of vitamin levels in all patients

	Group 1 (n=299)			Group 2 (n=128)		
	25-hidroxy-vitamin D (n=299)	**Vitamin B12 (n=299)**	**Ferritin (n=68)**	**25-hidroxy-vitamin D (n=128)**	**Vitamin B12 (n=128)**	**Ferritin (n=45)**
Vitamin B12	r=0.211 *P*<0.001	-		r=0.073 *P*=0.411	-	
Ferritin	r=0.337 *P*=0.005	r=0.128 *P*=0.295	-	r=0.223 *P*=0.141	r=0.121 *P*=0.429	-

Discussion

Vitamin deficiencies may play a role in the pathophysiology of fibromyalgia, although the mechanisms are still unclear [2]. On the other hand, many studies have compared the vitamin status of individuals with fibromyalgia to that of healthy controls, making it unclear whether vitamin deficiency is associated with fibromyalgia or simply a painful condition. To address this, we compared fibromyalgia with local painful conditions to evaluate the levels of vitamin D, ferritin, and vitamin B12. We found a deficiency in 25(OH)vit D levels but not in ferritin and vitamin B12 levels. Our results suggest that vitamin B12 and ferritin are not related to fibromyalgia. In our study, the level of 25(OH)vit D was below 30 ng/ml in 90.3% of all patients, indicating a relationship between painful conditions and vitamin D deficiency. These results are consistent with previous studies comparing patients with fibromyalgia and musculoskeletal pain. Block et al. [23] found low vitamin D levels in both patients with fibromyalgia and chronic musculoskeletal pain who do not meet the ACR criteria for fibromyalgia. These findings indicate that not only patients with fibromyalgia but also those with local painful conditions experience vitamin D deficiency. It is already known that low levels of vitamin D are associated with various musculoskeletal problems such as pain [8,24], myopathy, osteoporosis, and cognitive function [25]. Therefore, there is no doubt that vitamin D levels should be studied in general practice, physical therapy, and rehabilitation clinics, not only in relation to fibromyalgia.

According to our hypothesis, an association was found between the levels of vitamin D and the other vitamins, vitamin B12 and ferritin, in fibromyalgia. The impact of vitamin D levels on vitamin B12 and ferritin levels can be attributed to the effect of vitamin D on the gastrointestinal tract. Vitamin D receptors have been identified in various human tissues, including stomach and intestine cells [26]. Stumpf et al. [27] demonstrated the presence of vitamin D receptors in the digestive tract, including gastric glands and the absorptive epithelium of the small and large intestines. They suggest that vitamin D affects various digestive processes, such as parietal cell and intrinsic factor secretion. If a correlation were found only between vitamin D and B12 levels but not ferritin levels, it would indicate that vitamin D deficiency affects the parietal cells and intrinsic factors and reduces vitamin B12 levels.

Additionally, studies have shown a relationship between vitamin D deficiency and autoimmune gastritis [28]. However, vitamin D deficiency affects both vitamin B12 and ferritin levels. We believe that vitamin D deficiency may reduce absorption from the small intestine, which is the site of absorption for both vitamin B12 and ferritin. It is important to note that the association between vitamin D and ferritin, as well as vitamin B12 levels, was observed only in patients with fibromyalgia and not in those with a local painful condition. By examining the pathogenesis of fibromyalgia differently from local pain, we may have an opportunity for further discussion.

Evidence suggests the presence of both central neuroinflammation and neurogenic inflammation in peripheral tissues in fibromyalgia. Patients with fibromyalgia have been found to have elevated levels of neuropeptides associated with neuroinflammation, such as substance P [13], nerve growth factor [29], and brain-derived neurotrophic factor [30], in their cerebrospinal fluid (CSF). Additionally, increased levels of IL-8 have been reported in the CSF of fibromyalgia patients [31]. Furthermore, other studies have shown elevated levels of proinflammatory chemokines and cytokines in the blood of individuals with fibromyalgia [11,12]. While the exact cause of fibromyalgia remains unclear, these findings suggest a potential immune-related link to neuroinflammation. However, it is important to note that the presence of neuroinflammation alone is premature without considering the coexistence of small intestine bacterial overgrowth (SIBO), a type of gastrointestinal dysbiosis, and vitamin D deficiency.

Systemic inflammation has well-established effects on gastrointestinal function and morphology, including barrier function, epithelial cells, and the absorptive area of the intestines. Clinical and experimental evidence indicates systemic inflammation leads to reduced villus height, increased permeability, and disruptions in digestion and absorption processes [17,18]. Given the impact of inflammation on the gastrointestinal tract, it is common for neuroinflammation in fibromyalgia to coexist with gastrointestinal dysbiosis [14]. Pimentel et al. [16] reported that all 42 fibromyalgia patients in their study exhibited laboratory evidence of SIBO, and the severity of SIBO positively correlated with the severity of fibromyalgia symptoms. Additionally, Goebel et al. [15]

demonstrated that patients with fibromyalgia have increased intestinal permeability, a condition known as intestinal hyperpermeability.

Research has demonstrated that vitamin D supplementation can alleviate inflammation [19], reduce pain in fibromyalgia [32], improve intestinal hyperpermeability [20], address intestinal dysbiosis [21], and even inhibit experimental microglial activation [33], which is a crucial component of central sensitization and neuroinflammation. Furthermore, low vitamin D levels have been associated with high levels of lipopolysaccharide (LPS) [34]. LPS-induced stimulation of proinflammatory cytokines has been linked to chronic pain, and the presence of SIBO and increased intestinal permeability can lead to enhanced systemic absorption of LPS [35].

Neuroinflammation, SIBO, and vitamin D deficiency each have an additive or synergistic effect on the others [14]. Based on the aforementioned studies, we propose that in fibromyalgia, if vitamin D levels are low, the impairment of absorption for both vitamin B12 and ferritin from the small intestine may be further exacerbated by the additive inflammatory effects. Conversely, in patients with local musculoskeletal problems, low vitamin D levels may not cause absorption disorders due to the absence of SIBO and neuroinflammation. A study by Curic et al. [36] supports our hypothesis, as they found a significant association between 25(OH) vitamin D levels and vitamin B12 levels in obese middle-aged women. This study further strengthens our hypothesis, as neuroinflammation is also observed in obesity [37,38], similar to fibromyalgia.

Limitations

To our knowledge, this is the first study to investigate the relationship between levels of vitamin D and ferritin, as well as vitamin B12. This aspect represents a notable strength of our study. However, it is important to acknowledge certain limitations. First, our study has a retrospective design, which may introduce inherent biases and limitations in data collection. Additionally, a lack of a third control group consisting of healthy individuals is another limitation. This absence is because healthy individuals did not seek treatment at our clinic, thus restricting our ability to include them in the study.

Conclusion

In this study, our investigation revealed vitamin D deficiency in 90.3% of all patients with musculoskeletal problems. Additionally, we observed a positive correlation between vitamin D levels and the levels of vitamin B12 and ferritin in individuals with fibromyalgia. This finding suggests that vitamin D may play a role in the absorption of vitamin B12 and ferritin among fibromyalgia patients. However, further studies are necessary to explore this relationship in other diseases characterized by neuroinflammation and to determine the impact of vitamin D replacement therapy on vitamin B12 and ferritin levels.

References

1. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Arthritis Rheum. 1990;33(2):160-72. doi: 10.1002/art.1780330203
2. Arranz L, Canela M, Rafecas M. Fibromyalgia and nutrition, what do we know? Rheumatol Int. 2010;30(11):1417–27. doi: 10.1007/s00296-010-1443-0
3. Ortancil O, Sanli A, Eryuksel R, Basaran A, Ankarali H. Association between serum ferritin level and fibromyalgia syndrome. Eur. J. Clin. Nutr. 2010;64(3):308-12. doi: 10.1038/ejcn.2009.149
4. Mader R, Koton Y, Buskila D, Herer P, Elias M. Serum iron and iron stores in non-anemic patients with fibromyalgia. Clin. Rheumatol. 2012;31(4):595-9. doi: 10.1007/s10067-011-1888-x
5. Bottiglieri T. Homocysteine and folate metabolism in depression progress. Neuro-Psychopharmacol. Biol. Psychiatry. 2005;29(7):1103-12. doi: 10.1016/j.pnpbp.2005.06.021
6. Zhang M, Han W, Hu S, Xu H. Methylcobalamin: a potential vitamin of pain killer. Neural Plast. 2013:424651. doi: 10.1155/2013/424651
7. De Carvalho JF, Silva DNF. Serum levels of vitamin B12 (cobalamin) in fibromyalgia. Rheumatology international. 2016;36(5):741-2. doi: 10.1007/s00296-016-3454-y
8. Akar N, Çaglar NS, Aytekin E, Akar A, Aksu Ö, Öz N. Low levels of serum vitamin D3 are associated with fibromyalgia syndrome in pre-menopausal women: A pilot study. Turk J Phys Med Rehabil. 2020;66(1):67-72. doi: 10.3906/sag-1508-30
9. Ozcan DS, Oken O, Aras M, Koseoglu BF. Vitamin D levels in women with fibromyalgia and relationship between pain, depression, and sleep. Turk J Phys Med Rehabil. 2014;60(4):329-35. doi: 10.5152/tftrd.2014.45143
10. Özgen M, Aydoğan AM, Uygur A, Armağan O, Berkan F, Mutlu F. Fibromiyalji Sendromunda D Vitamin Düzeylerinin Değerlendirilmesi. OJM. 2018;41(2):161-5. doi: 10.20515/otd.459018
11. Backryd E, Tanum L, Lind AL, Larsson A, Gordh T. Evidence of both systemic inflammation and neuroinflammation in fibromyalgia patients, as assessed by a multiplex protein panel applied to the cerebrospinal fluid and to plasma. J Pain Res. 2017;10:515–25. doi: 10.2147/JPR.S128508
12. Rodriguez-Pinto I, Agmon-Levin N, Howard A, Shoenfeld Y. Fibromyalgia and cytokines. Immunol Lett. 2014;161(2):200–3. doi: 10.1016/j.imlet.2014.01.009
13. Russell IJ, Orr MD, Littman B, Vipraio GA, Alboukrek D, Michalek JE, et al. Elevated cerebrospinal fluid levels of substance P in patients with the fibromyalgia syndrome. Arthritis Rheum. 1994;37(11):1593–601.
14. Vasquez, A. Neuroinflammation in fibromyalgia and CRPS is multifactorial. Nat Rev Rheumatol. 2016;12:242. doi: 10.1038/nrrheum.2016.25
15. Goebel A, Buhner S, Schedel R, Lochs H, Sprotte G. Altered intestinal permeability in patients with primary fibromyalgia and in patients with complex regional pain syndrome. Rheumatology. 2008;47:1223–7. doi: 10.1093/rheumatology/ken140
16. Pimentel M, Wallace D, Hallegua D, Chow E, Kong Y, Park S, et al. A link between irritable bowel syndrome and fibromyalgia may be related to findings on lactulose breath testing. Ann. Rheum. Dis. 2004;63(4):450-2. doi: 10.1136/ard.2003.011502
17. Peuhkuri K, Vapaatalo H, Korpela R. Even low-grade inflammation impacts on small intestinal function. World journal of gastroenterology. 2010;16(9):1057-62. doi: 10.3748/wjg.v16.i9.1057
18. Mourad FH, Barada KA, Bou Rached NA, Khoury CI, Saadé NE, Nassar CF. Inhibitory effect of experimental colitis on fluid absorption in rat jejunum: role of the enteric nervous system, VIP, and nitric oxide. Am J Physiol Gastrointest Liver Physiol. 2006;290:262-8. doi: 10.1152/ajpgi.00271.2005
19. Timms PM, Mannan N, Hitman GA, Noonan K, Mills PG, Syndercombe-Court D, Boucher BJ. Circulating MMP9, vitamin D and variation in the TIMP-1 response with VDR genotype: mechanisms for inflammatory damage in chronic disorders? Qjm. 2002;95(12):787-96. doi: 10.1093/qjmed/95.12.787
20. RafteryT, Martineau AR, Greiller CL, Ghosh S, McNamara D, Bennett K, et al. Effects of vitamin D supplementation on intestinal permeability, cathelicidin and disease markers in Crohn's disease: results from a randomised double-blind placebo-controlled study. United European gastroenterology journal. 2015;3(3):294-302. doi: 10.1177/2050640615572176
21. Bashir M, Prietl B, Tauschmann M, Mautner SI, Kump PK, Treiber G, et al. Effects of high doses of vitamin D 3 on mucosa-associated gut microbiome vary between regions of the human gastrointestinal tract. European journal of nutrition. 2016;55(4):1479-89. doi: 10.1007/s00394-015-0966-2
22. Smith EM, Samadian S. Use of the erythrocyte sedimentation rate in the elderly. Br J Hosp Med. 1994;51:394-7. doi: 10.3906/sag-1710-81
23. Block SR. Vitamin D deficiency is not associated with nonspecific musculoskeletal pain syndromes including fibromyalgia. In Mayo Clinic Proceedings. 2004;79(12):1585-6. doi: 10.4065/79.12.1585
24. Atalay SG, Atalay R, Alkan BM, Fidan F, Bozkurt S, Aksekili H. Vitamin D deficiency in adults with musculoskeletal pain. Turk J Osteoporos. 2015;21(3):101-4.
25. Ösken S, İçağasıoğlu A, Arslan P, Eğilmez Z, Murat S. D Vitamininin Kognitif Fonksiyonlarla İlişkisi: Genç Erişkin Kadınlarda Kesitsel Bir Çalışma. Turk J Osteoporos. 2016;22:137-40.
26. Griffin MD, Xing N, Kumar R. Vitamin D and its analogs as regulators of immune activation and antigen presentation. Annu Rev Nutr. 2003;23:117-45. doi: 10.1146/annurev.nutr.23.011702.073114
27. Stumpf WE, Hayakawa N, Koike N, Hirate J, Okazaki, A. Nuclear receptors for 1, 25-dihydroxy-22-oxavitamin D 3 (OCT) and 1, 25-dihydroxyvitamin D 3 in gastric gland neck mucous cells and gastrin enteroendocrine cells. Histochem. Cell Biol. 1995;103(4):245-50.
28. Antico A, Tozzoli R, Giavarina D, Tonutti E, Bizzaro N. Hypovitaminosis D as predisposing factor for atrophic type A gastritis: a case–control study and review of the literature on the interaction of vitamin D with the immune system. Clin Rev Allergy Immunol. 2012;42(3):355-64. doi: 10.1007/s12016-011-8255-1
29. Giovengo SL, Russell IJ, Larson AA. Increased concentrations of nerve growth factor in cerebrospinal fluid of patients with fibromyalgia. J Rheumatol. 1999;26(7):1564–9.
30. Sarchielli P, Mancini ML, Floridi A, Coppola F, Rossi C, Nardi K, et al. Increased levels of neurotrophins are not specific for chronic migraine: evidence from primary fibromyalgia syndrome. J Pain. 2007;8(9):737–45. doi: 10.1016/j.jpain.2007.05.002
31. Kadetoff D, Lampa J, Westman M, Andersson M, Kosek E. Evidence of central inflammation in fibromyalgia-increased cerebrospinal fluid interleukin-8 levels. J Neuroimmunol. 2012;242(1–2):33–8. doi: 10.1016/j.jneuroim.2011.10.013
32. Wepner F, Scheuer R, Schuetz-Wieser B, Machacek P, Pieler-Bruha E, Cross HS. Effects of vitamin D on patients with fibromyalgia syndrome: a randomized placebo-controlled trial. Pain. 2014;155(2):261-8. doi: 10.1016/j.pain.2013.10.002
33. Hur J, Lee P, Kim MJ, Cho YW. Regulatory effect of 25-hydroxyvitamin D3 on nitric oxide production in activated microglia. Korean J. Physiol. Pharmacol. 2014;18:397–402. doi: 10.4196/kjpp.2014.18.5.397
34. Luthold RV, Fernandes GR, Franco-de-Moraes AC, Folchetti LG, Ferreira SR. Gut microbiota interactions with the immunomodulatory role of vitamin D in normal individuals. Metabolism. 2017;69:76-86. doi: 10.1016/j.metabol.2017.01.007
35. Littlejohn, G. Neurogenic neuroinflammation in fibromyalgia and complex regional pain syndrome. Nat. Rev. Rheumatol. 2015;11:639–48. doi: 10.1038/nrrheum.2015.100
36. Curic N, Ilincic B, Milic N, Cabarkapa V, Nikolic S, Medic-Stojanoska M. The relationship between the vitamin serum 25 (OH) D and the B12 concentrations in obese women. Minerva medica. 2018;109(2):79-87. doi: 10.23736/s0026-4806.17.05447-7
37. Miller AA, Spencer SJ. Obesity and neuroinflammation: a pathway to cognitive impairment. Brain Behav Immun. 2014;42:10-21. doi: 10.1016/j.bbi.2014.04.001
38. Aguilar-Valles A, Inoue W, Rummel C, Luheshi GN. Obesity, adipokines and neuroinflammation. Neuropharmacology. 2015;96:124-34. doi: 10.1016/j.neuropharm.2014.12.023.

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Determination of depression, anxiety, and hopelessness levels in adolescents with refractive errors after the COVID-19 pandemic

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Ethics Committee Approval
Ethical approval was obtained from Erciyes University Non-Interventional Clinical Research Ethics Committee (Decision No: 2023/575). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: The prevalence of myopia is increasing worldwide especially among adolescents. Changes in living conditions such as reduced engagement in outdoor activities as well as increased activities near the workplace like reading, writing, and screen exposure are thought to be responsible for this increase. Adolescence is a sensitive period of rapid changes in psychological, physiological, and social aspects. Mental health issues such as anxiety and depression are common during this period. During the pandemic, mental health issues among children and adolescents increased due to stress caused by the disease, social isolation, disruption of routines, and the loss of loved ones. With the rapid increase in myopia among adolescents, there is a need to investigate the effects of myopia on mental health. The aim of this study is to evaluate anxiety, depression, and hopelessness levels in adolescents with myopia after the COVID-19 pandemic and to examine the relationship between myopia and anxiety, depression, and hopelessness.

Methods: This was a case-control study that included 40 myopic adolescents aged 16-19 with a spherical refractive degree of -2 diopters (D) and above and 40 emmetropic (no refractive error). Participants who had previously undergone refractive surgery, had binocular visual acuity less than 1.0, had strabismus and amblyopia, had a diagnosis of glaucoma, had undergone ocular surgery for any reason, had retinopathy, or had an astigmatic refractive degree greater than ±0.50 were excluded from the study. The study did not include patients with chronic physiological or psychiatric diseases. Both groups were administered the Automatic Thoughts Questionnaire (ATQ), Coronavirus Anxiety Scale (CAS), Beck Hopelessness Scale (BHS), and Beck Depression Inventory (BDI). The groups were compared according to the scales. Myopic degrees were compared with mixed-effect linear models according to scale categories, and the relationship between ATS scores and myopia degrees was evaluated using the Spearman correlation coefficient.

Results: The mean (SD) spherical refractive power of myopic adolescents was -3.156 (1.40) diopters; 62.5% of participants with myopia had been exposed to COVID-19, and the anxiety rate in myopic participants compared to controls was 15% (P=0.026). However, no significant difference was found between the myopia and control groups in terms of automatic thoughts, hopelessness, and depression inventory scores when comparing the groups. No correlation was found between the CAS (F=1.098), BHS (F=1.610), BDI (F=1.699), and ATQ (r=0.151) scales and the increase in myopia when we performed linear mixed model analysis and Spearman correlation analysis. There was no significant relationship between the degree of myopia and automatic thoughts, hopelessness anxiety, and depression.

Conclusion: The results indicate that adolescents with myopia had higher levels of anxiety after the COVID-19 pandemic. There was no significant correlation between the degree of myopia and anxiety, depression, hopelessness, and automatic thoughts. It is important to monitor adolescents with myopia carefully during pandemics and provide the necessary mental health support. This is because offering mental health support to myopic young people may protect them from potential lasting emotional problems in adulthood during potential future pandemics. It may be beneficial for adolescents to increase their engagement in outdoor activities to reduce myopia and anxiety.

Keywords: COVID-19, myopia, adolescents, anxiety, depression, hopelessness

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Introduction

Myopia is a serious vision problem worldwide. The World Health Organization estimates that by 2050, half of the global population will be myopic [1]. According to other estimates, by 2050, 5 billion people will be myopic with over 1 billion having myopia exceeding -5 diopters (D) [2]. Studies have shown an increasing prevalence of myopia in adolescents, and this increase is thought to be due to changes in living conditions such as increased near work activities, reading, writing, and screen exposure [3,4].

Studies have shown that people with myopia tend to be more introverted, have fewer friends, prefer indoor activities over outdoor ones, and are often engaged in intellectual activities rather than sports [5]. Considering that the frequency of myopia in adolescents is rapidly increasing, it is crucial to understand its effects on adolescent mental health [4].

Adolescence is a vulnerable period of rapid psychological, physiological, and social changes. The most common mental health problems in adolescents are anxiety and depression [6]. Angi et al. [7] found that university students with myopia had higher levels of anxiety and somatization than controls. Another study showed that anxiety was higher in adolescent boys with myopia [4].

During the pandemic, children and adolescents experienced an increase in mental health issues due to factors such as fear of the disease's pathogenic effect, social isolation, inability to meet friends, disruption of routines, and the loss of loved ones [8,9]. Among these mental health problems, anxiety and depression were the most common [10]. Thus, this study aims to evaluate the presence of anxiety and depression in adolescents with myopia who have experienced the COVID-19 pandemic and investigate the relationship between anxiety, depression, hopelessness, and myopia.

Materials and methods

Study groups and sample size

This study was conducted between September and October 2023 and included 40 myopic adolescents aged 16-19 with a spherical refractive power of -2 diopters (D) or higher who applied to the ophthalmology clinic for eye diseases as well as 40 emmetropic adolescents with no chronic physiological or psychiatric diseases who visited the general pediatric outpatient clinic. Refractive measurements were obtained using an autorefractometer (TonoRef II, Nidek, Japan). After the ocular and systemic examinations, participants' best-corrected visual acuity was determined using the Snellen chart. In addition, intraocular pressure was measured, slit-lamp examination of the anterior segment and posterior segment was performed, and color vision was assessed using the Ishihara test. Participants who had previously undergone refractive surgery, had binocular visual acuity less than 1.0, had strabismus and amblyopia, had a diagnosis of glaucoma, had undergone ocular surgery for any reason, had retinopathy, or had an astigmatic refractive degree greater than ±0.50 were excluded. The study did not include patients with chronic physiological or psychiatric diseases in the emmetropic group. To reduce bias during patient selection, comprehensive pre-defined criteria were used to identify individuals for inclusion in the study. These criteria were set in accordance with the main aims and hypotheses of the research. In addition, methods such as random assignment or the creation of balanced groups were used to minimize potential bias between groups. Each step in this selection process was carefully planned and implemented to increase the reliability and internal validity of the research.

Sample size and power analysis were performed using G*Power 3.1 software. A minimum of 39 participants in each group was required to detect a moderate or higher difference in the studied variables between the groups (Cohen's d=0.65) with 80% power and a 5% Type-I error rate. Ethical approval for the study was obtained from the Erciyes University Non-Interventional Clinical Research Ethics Committee (Decision No: 2023/575). Participants were administered The Automatic Thoughts Questionnaire (ATQ), the Coronavirus Anxiety Scale (CAS), the Beck Hopelessness Scale (BHS), and the Beck Depression Inventory (BDI).

Data Collection Tools

Automatic Thoughts Questionnaire (ATQ): This scale was developed by Hollon and Kendall and consists of 30 items. The scale is a 5-point Likert type. The lowest score is 30, and the highest score is 150. Higher scores indicate that the individual's automatic thoughts occur frequently [11].

Coronavirus Anxiety Scale (CAS): This was developed by Lee [12] to identify possible dysfunctional anxiety cases related to the COVID-19 crisis. It is a one-dimensional Likert-type scale consisting of five questions and is scored from 0 to 4. The lowest possible score is 0, while the highest is 20. A score of nine and above indicates a high level of anxiety. Scores of 9 and above indicate anxiety, while scores below 9 suggest no anxiety.

Beck Hopelessness Scale (BHS): Developed by Beck, Weissman, Lester, and Trexler, this scale is used to determine the level of future-oriented pessimism in adolescents and adults. The scale assesses three sub-dimensions of the future: Feelings about the future, loss of motivation, and expectations about the future. The scale consists of 20 items, and the score ranges from 0 to 20. Questions are answered with "Yes" or "No," and 0 points are given for negative answers, and one point is given for positive answers. The score ranges from 0 to 20. A higher score implies more hopelessness [13]. People who score between 4-8 points have mild hopelessness symptoms, those who score between 9-14 points have moderate hopelessness symptoms, and those who score 15 points and above have severe symptoms of hopelessness [14].

Beck Depression Inventory (BDI): Developed by Beck, Ward, Mendelson, Mock, and Erbaugh, this inventory is a multiple-choice self-report inventory used to assess the severity of depression in adolescents and adults [15]. The BDI contains 21 items with four choices each. A score of 0-9 indicates minimal depression, 10-18 indicates mild depression, 19-29 indicates moderate depression, and 30-63 indicates severe depression [16].

Statistical analysis

Data were analyzed using the statistical package program IBM SPSS Statistics Standard Concurrent User V 29 (IBM Corp., Armonk, New York, USA). Descriptive statistics

were given as number of units (n), percentage (%), mean (standard deviation), median and inter-quartile range values. The normal distribution of the numerical variables was evaluated with the Shapiro-Wilk normality test. Variance homogeneity of the groups was analyzed by Levene's test. Two-group comparisons for numerical variables were performed by an independent sample t-test if the data were normally distributed and by the Mann-Whitney U test if the data were not normally distributed. Chi-square analyses (Pearson chi-square, Yates chi-square, Fisher exact test) were used to compare the groups with categorical variables. Myopia degrees were compared with mixed-effect linear models based on scale categories, and the relationship between ATS scores and myopia degrees was evaluated using the Spearman correlation coefficient. A *P*-value <0.05 was considered statistically significant.

Results

The study comprised of 40 adolescents with myopia and 40 healthy controls aged between 16 and 19 years. All myopic participants had a visual acuity of 1.0, normal intraocular pressure, and normal anterior and posterior segment findings. Their mean (SD) spherical refractive error was -3.156 (1.40) diopters (Table 1). The myopic group consisted of 47.5% of males and 52.5% of females; 62.5% of whom had been diagnosed with COVID-19. Between those with and without myopia, there was a significant difference in the CAS (*P*=0.048). When compared with the control group according to the cut-off point of the scale, 15% of those with myopia were anxious and the difference was significant (*P*=0.026). No differences were found between the groups on the ATQ, BHS, and BDI (Table 2).

Table 1: Mean spherical equivalent of the right and left eyes in the myopia group

	Degree of myopia in right eye	Degree of myopia in left eye	Mean Spherical Equivalent
Mean diopters	-3.1437	-3.1687	-3.1562
Standard deviation	1.42200	1.48323	1.40162
Minimum	-2	-1.25	-1.75
Maximum	-7.75	-7.25	-7.5

Table 2: Comparison of groups according to demographic data and scales

	Groups		Test Statistics	
	Myopic	Control	Test results	*P*-value
Sex	n (%)	n (%)		
Boy	19 (47.5)	20 (50.0)	0.001	1.000
Girl	21 (52.5)	20 (50.0)		
Age year, mean (SD)	17.6 (1.1)	17.2 (1.1)	1.782	0.079†
COVID-19 infection history	n (%)	n (%)		
No	15 (37.5)	20 (50.0)	0.813	0.367‡
Yes	25 (62.5)	20 (50.0)		
ATQ	60.50 (37.75)	55.50 (34.50)	0.977	0.329&
CAS	0.50 (1.00)	0.00 (0.00)	**1.974**	**0.048**&
BHS	5.50 (8.75)	4.00 (6.50)	0.126	0.900&
BDI	13.00 (21.25)	13.50 (14.00)	0.520	0.603&
CAS	n (%)	n (%)		
Absence of anxiety	34 (85.0)	40 (100.0)	**6.486**	**0.026**‡
Presence of anxiety	6 (15.0)	0 (0.0)		
BHS	n (%)	n (%)		
Minimal	15 (37.5)	16 (40.0)		
Mild	12 (30.0)	14 (35.0)	1.457	0.742‡
Moderate	8 (20.0)	8 (20.0)		
Severe	5 (12.5)	2 (5.0)		
BDI	n (%)	n (%)		
Absence of depression	21 (52.5)	24 (60.0)	0.203	0.652‡
Presence of depression	19 (47.5)	16 (40.0)		

SD: standard deviation, n: number of patients, %: Column percentage, numerical data presented as mean (SD) or median (interquartile range) values, †: Independent samples t-test, &: Mann-Whitney U test, ATQ: Automatic Thoughts Questionnaire CAS: Coronavirus Anxiety Scale, BHS: Beck Hopelessness Scale, BDI: Beck Depression Inventory

No correlation found between the CAS (*F*=1.098), BHS (*F*=1.610), BDI (*F*=1.699), and ATQ (*r*=0.151) scales and the increase in myopia when we performed linear mixed model analysis and Spearman correlation analysis. There was no significant relationship between the degree of myopia and scores on automatic thoughts anxiety, depression, and hopelessness (Table 3).

Table 3: Correlation between scales based on the severity of myopia

	Degree of myopia Mean (SD)	Test results	*P*-value
CAS			
Absence of anxiety	-3.059 (0.240)	*F*=1.098	0.301
Presence of anxiety	-3.708 (0.571)		
BHS			
Minimal	-3.675 (0.354)		
Mild	-2.760 (0.395)	*F*=1.610	0.204
Moderate	-3.266 (0.484)		
Severe	-2.375 (0.613)		
BDI			
Absence of depression	-3.429 (0.303)	*F*=1.699	0.200
Presence of depression	-2.855 (0.316)		
ATQ		*r*=0.151	0.183

SD: standard deviation, *F*: Linear mixed model analysis, *r*: Spearman correlation coefficient, CAS: Coronavirus Anxiety Scale, BHS: Beck Hopelessness Scale, BDI: Beck Depression Inventory, ATQ: Automatic Thoughts Questionnaire

Discussion

Adolescence denotes the transition from childhood to adulthood. Amidst the pandemic, adolescents, who are among vulnerable groups, faced numerous mental health problems because of several factors such as stressful life events, quarantines, the loss of family members due to illness, and the subsequent mourning process. Furthermore, excessive use of the Internet and social media was common since they couldn't socialize with their peers [17]. As per recent studies, anxiety and depression emerged as the most prevalent mental health issues among adolescents who contracted COVID-19 [10]. Anxiety and depression are prevalent mental health conditions in young individuals which can persist into adulthood as anxiety disorders [6]. The closure of schools, shift to online education, prolonged near-work, and reduced engagement in outdoor activities due to the COVID-19 pandemic have been associated with an elevated incidence of myopia [18,19]. One study [20] found a higher incidence of separation and castration anxiety in myopia patients, while anxiety and somatization disorder were more prevalent in university students with myopia versus those without vision problems in another [7].

Consistent with prior research, patients diagnosed with myopia exhibited higher levels of coronavirus-related anxiety, although there was no observable escalation in anxiety with a greater degree of myopia. A previous investigation indicated that increased myopia amongst young people corresponded to heightened anxiety levels [21]. Nonetheless, other studies have so far been unable to corroborate these findings, which is consistent with the outcomes of our study. Adolescents with myopia who wear glasses may experience peer bullying at school, thus leading to a victim mentality [22]. Furthermore, Horwood et al. [23] suggest that a victim mentality beginning in early life may result in psychosocial maladjustment, increased anxiety, depression, and loneliness; lower self-esteem and behavioral problems may also be observed. A study conducted by Rosanes and colleagues [24] demonstrated a rise in non-specific anxiety disorders amongst myopic and hypermetropic patients who are required to wear glasses relative to healthy volunteers. Furthermore, people with myopia—particularly those with high myopia—exhibit lower quality of life which serves as another contributing factor to anxiety [21,25].

Limitations

Self-assessment questionnaires were used here to evaluate anxiety levels among adolescents. However, relying solely on scale scores to determine the presence of anxiety can lead to misconceptions. To obtain more accurate results in future studies, it may be beneficial to supplement self-assessment questionnaires with a complete psychiatric evaluation

Conclusion

We found that myopic adolescents had higher levels of coronavirus anxiety, as expected, but no differences were found between the groups in terms of automatic thoughts, hopelessness, and depression. As part of the pandemic measures, adolescents in particular were not allowed to leave their homes. Thus, near vision became mandatory for adolescents who had to socialize at home and communicate with computers via the Internet for their education. It should not be forgotten that myopia, and therefore anxiety, may increase if people are unable to leave their homes during pandemic periods. Therefore, during possible future pandemics, it may be beneficial for this age group to have the opportunity to go out and also to limit the time they spend on the computer. Mental health support for myopic adolescents may protect them from emotional problems that may persist into adulthood.

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References

1. Sankaridurg P, Tahhan N, Kandel H, Naduvilath T, Zou H, Frick KD, et al. IMI Impact of Myopia. Invest Ophthalmol Vis Sci. 2021;62:2–2.
2. Holden BA, Fricke TR, Wilson DA, Jong M, Naidoo KS, Sankaridurg P, et al. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology. 2016;123:1036–42.
3. Lv L, Zhang Z. Pattern of myopia progression in Chinese medical students: a two-year follow-up study. Graefes Arch Clin Exp Ophthalmol. 2013;251:163–8.
4. Łazarczyk JB, Urban B, Konarzewska B, Szulc A, Bakunowicz-Łazarczyk A, Żmudzka E, et al. The differences in level of trait anxiety among girls and boys aged 13-17 years with myopia and emmetropia. BMC Ophthalmol. 2016;16:1–7.
5. Lanyon RI, Giddings JW. Psychological approaches to myopia: a review. Am J Optom Physiol Opt. 1974;51:271–81.
6. Stapinski LA, Bowes L, Wolke D, Pearson RM, Mahedy L, Button KS, et al. Peer victimization during adolescence and risk for anxiety disorders in adulthood: a prospective cohort study. Depress Anxiety. 2014;31:574–82.
7. Angi M, Rupolo G, De Bertolini C, Bisantis C. Personality, psychophysical stress and myopia progression. A prospective study on 57 university students. Graefes Arch Clin Exp Ophthalmol. 1993;231:136–40.
8. Branje S, Morris AS. The Impact of the COVID-19 Pandemic on Adolescent Emotional, Social, and Academic Adjustment. J Res Adolesc. 2021;31:486–99.
9. Ravens-Sieberer U, Kaman A, Otto C, Adedeji A, Napp AK, Becker M, et al. [Mental health and psychological burden of children and adolescents during the first wave of the COVID-19 pandemic-results of the COPSY study]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2021;64:1512–21.
10. Pasha H, Omidvar S, Faramarzi M, Bakhtiari A. Depression, anxiety, stress, and PTSD symptoms during the first and second COVID-19 waves: a comparison of elderly, middle-aged, and young people in Iran. BMC Psychiatry. 2023;23.
11. Hollon SD, Kendall PC. Cognitive self-statements in depression: Development of an automatic thoughts questionnaire. Cognit Ther Res. 1980;4:383–95.
12. Lee SA, Mathis AA, Jobe MC, Pappalardo EA. Clinically significant fear and anxiety of COVID-19: A psychometric examination of the Coronavirus Anxiety Scale. Psychiatry Res. 2020;290. https://doi.org/10.1016/J.PSYCHRES.2020.113112.
13. Beck AT, Weissman A, Lester D, Trexler L. The measurement of pessimism: the hopelessness scale. J Consult Clin Psychol. 1974;42:861–5.
14. Seber G, Dilbaz N, Kaptanoğlu C, Tekin D. The scale of desperation: Validity and reliability. Crisis Journal. 1993;1:139–42.
15. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry. 1961;4:561–71.
16. Hisli N. A reliability and validity study of Beck Depression Inventory in a university student sample. J Psychol. 1989;7:3–13.
17. Guessoum SB, Lachal J, Radjack R, Carretier E, Minassian S, Benoit L, et al. Adolescent psychiatric disorders during the COVID-19 pandemic and lockdown. Psychiatry Res. 2020;291:113264.
18. Chang P, Zhang B, Lin L, Chen R, Chen S, Zhao Y, et al. Comparison of Myopic Progression before, during, and after COVID-19 Lockdown. Ophthalmology. 2021;128:1655–7.
19. Liu J, Li B, Chen Q, Dang J. Student Health Implications of School Closures during the COVID-19 Pandemic: New Evidence on the Association of e-Learning, Outdoor Exercise, and Myopia. Healthcare (Basel). 2021;9(5):500.
20. Seitler BN. Separation-individuation issues and castration anxiety: their curious influence on the epigenesis of myopia. Am J Psychoanal. 2009;69:221–37.
21. Zhang H, Gao H, Zhu Y, Zhu Y, Dang W, Wei R, et al. Relationship Between Myopia and Other Risk Factors With Anxiety and Depression Among Chinese University Freshmen During the COVID-19 Pandemic. Front Public Health. 2021;9:774237.
22. Juvonen J, Graham S, Schuster MA. Bullying among young adolescents: the strong, the weak, and the troubled. Pediatrics. 2003;112:1231–7.
23. Horwood J, Waylen A, Herrick D, Williams C, Wolke D. Common visual defects and peer victimization in children. Invest Ophthalmol Vis Sci. 2005;46:1177–81.
24. Rosanes MB. Psychological correlates to myopia compared to hyperopia and emmetropia. J Proj Tech Pers Assess. 1967;31:31–5.
25. Rose K, Harper R, Tromans C, Waterman C, Goldberg D, Haggerty C, et al. Quality of life in myopia. Br J Ophthalmol. 2000;84:1031–4.

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Cross-sectional and descriptive study of centrofacial fractures at the Cocody University Hospital Center from 2016 to 2020

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Ethics Committee Approval
The study was approved by comité national d'éthique des sciences de la vie et de la santé (CNESVS), National Ethics Committee for Health and Life Sciences (CNESVS) (January 26, 2022, 0019-22/MSHPCMU/CNESVS-km).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Centrofacial fractures resulting from high-impact violence can be considered mild traumatic brain injuries. Given the complexities and associated risks, a comprehensive examination of these fractures is warranted. These fractures are increasingly prevalent among young adult patients and are commonly associated with road traffic accidents. In the literature, only a few studies have focused on this particular type of facial bone lesion. In Ivory Coast, no studies have been conducted on these fractures, which highlights the importance of our research aimed at describing the epidemiological and anatomical-clinical characteristics of centrofacial fractures in the stomatology and maxillofacial surgery department of the Cocody Teaching Hospital.
Methods: This descriptive cross-sectional study was conducted in the Stomatology and Maxillofacial Surgery Department of the Cocody University Hospital Center from January 2016 to December 2020.
Results: The prevalence of these fractures was 24.20%, with a predominance of male subjects. The age group most affected was 20 to 40 years old, accounting for 70.96% of cases, and most patients resided in Abidjan (59%). All socio-economic categories were represented, with a higher proportion of individuals in liberal professions (91.4%). Road traffic accidents involving two-wheeled vehicles were the primary cause of these fractures (76.8%), with the most common injury site being the naso-ethmoido-maxillo-fronto-orbital complex (NEMFOC) (32.5%).
Conclusion: The epidemiological characteristics of centrofacial fractures associated with two-wheeled vehicles in the Abidjan metropolis of Côte d'Ivoire suggest the need for increased accountability among motor vehicle drivers and stricter enforcement of traffic laws.

Keywords: fracture, centrofacial, NEMFOC, motor vehicle

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Introduction

Facial trauma is a common occurrence in urban areas due to population growth and increased transportation options. Its prevalence remains high in Africa, particularly in underserved communities, resulting in many clinical injuries [1].

Centrofacial fractures refer to discontinuities in the central part of the face. While they were once rare, they have become more frequent and often result from violent incidents. These fractures can be severe as they are often associated with fractures of the anterior part of the skull base. Therefore, meticulous radioclinical exploration is necessary. Failure to recognize these fractures can lead to infectious complications (such as post-traumatic meningitis, which is particularly concerning), functional complications (such as anosmia or blindness), and aesthetic complications [2,3].

In the existing literature, very few studies have focused on this specific type of facial bone injury. Moreover, in Côte d'Ivoire, no studies have been conducted on these fractures. This motivated us to initiate this research project to describe the epidemiological and anatomical-clinical aspects of these fractures.

Materials and methods

This descriptive cross-sectional study was conducted at the Stomatology and Maxillofacial Surgery Department of the Cocody University Hospital Center from January 2016 to December 2020. The study included patients of all ages who were admitted to the department with a central facial fracture.

Patients with maxillofacial trauma who underwent a complete clinical examination and radiological assessment revealing a central facial bone lesion were included. Patients with incomplete exploration were excluded from the study.

The following variables were examined: epidemiological [gender, age categorized in 20-year intervals, profession of the traumatized individual (student, worker, professional, middle manager, executive, unemployed), date and location of the occurrence, cause of the trauma (road accident, work accident, assault, domestic accident, altercation), role of the injured person at the time of the trauma (driver of wheeled vehicles, motorcyclist, pedestrian), and compliance or non-compliance with safety measures (wearing a helmet or seat belt)] and clinical and paraclinical [observed clinical signs (including nosebleeds, cerebrospinal fluid rhinorrhea, telecanthus, nasal pyramid flattening, tearing, enophthalmos, diplopia, anosmia, and others), centrofacial skeletal lesions (including naso-ethmoidal-maxillo-front-orbital (NEMFO) complex, maxillary, nasal, and naso-ethmoidal fractures), and associations with other facial and extra-facial fractures (including mandible, zygomatic bone, anterior floor, skull, lower and upper limbs, pelvis, and spine)].

Sampling methodology

A non-probabilistic sampling method was used to select patients admitted to the stomatology and maxillofacial surgery department during the study period.

Sample size

The sample size (n) was determined using the following formula:

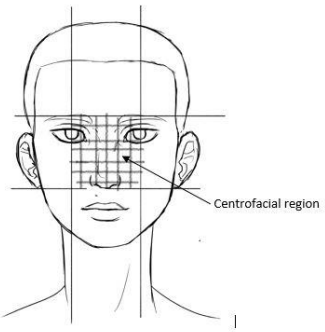
$N=[Ɛ2 \times P \times (1-P)] / m2=[(1.96)2 \times 0.08 \times (1-0.08)] / 0.052 \approx 113$

Where N is the sample size, P is the prevalence (8%), m is the margin of error of 5%, and Ɛ is 1.96.

Operational definitions

The operational definitions used were: centrofacial region [the middle third of the face between the horizontal line passing through the glabella (upper part) and the horizontal line passing through the nostril wings (lower part)] (Figure 1); upper frame (patients working in companies with a minimum education level of BAC+5); middle frame (patients working in companies with a maximum education level of BAC+2); and liberal profession (patients working independently, regardless of the nature of their activity).

Figure 1: Centrofacial region



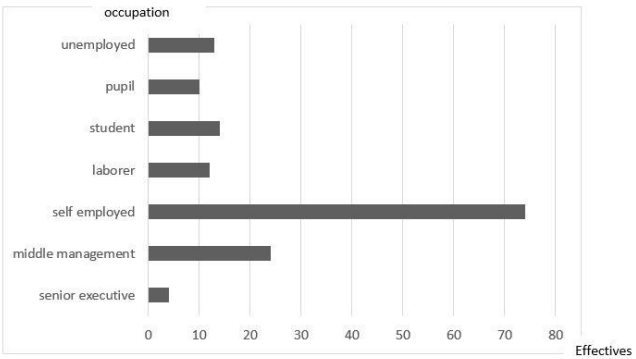
Statistical analysis

The data was entered into Excel 2016, and tables and graphs were generated using the same software version. Descriptive statistics were calculated for quantitative variables, including mean and standard deviations. For certain variables, median values and extremes were also specified. Proportions were calculated for qualitative variables.

Results

We identified a total of 151 patients, with centrofacial fractures accounting for 24.20% of all facial fractures. The average age of the patients was 30 (8) years, and the highest incidence was observed in the third and fourth decades of life. The male-to-female ratio was 9:1. Patients in liberal professions represented 49% (n=74) of the cases (Figure 2).

Figure 2: Distribution by occupation



Among the different municipalities, Abobo had the highest number of centrofacial fractures, accounting for 17% (n=25) of the cases (Figure 3). Road traffic accidents were the leading cause, accounting for 76.80% of cases (Table 1). Two-wheeled vehicles were involved in 44% of accidents, and in 78.44% of cases, the victims were not wearing seatbelts (Table 2). Among victims from four-wheeled vehicles, 69% were not wearing seatbelts. Nosebleeds were present in all patients, with 53% (n=80) experiencing nasal pyramid flattening and 20% (n=30) experiencing cerebrospinal fluid leakage (Figure 4).

Table 1: Distribution by causes

Causes	Number	Percentage
AVP	116	76.80%
ACC work	10	6.60%
Attack	11	7.30%
ACC domestic	6	4%
Brawl	4	2.60%
Others	4	2.60%

AVP: Road accidents, ACC work: work accidents, ACC domestic: domestic accidents

Table 2: Distribution by type of engine

Occupation of the victim	Number	Percentage
Two-wheeler driver	51	44%
Four-wheel driver	48	41%
Pedestrian	17	15%

Figure 3: Distribution by location

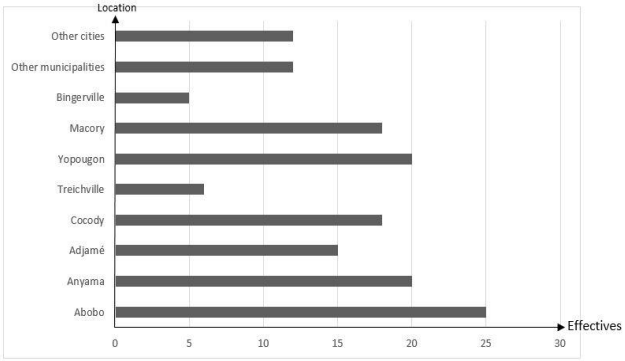
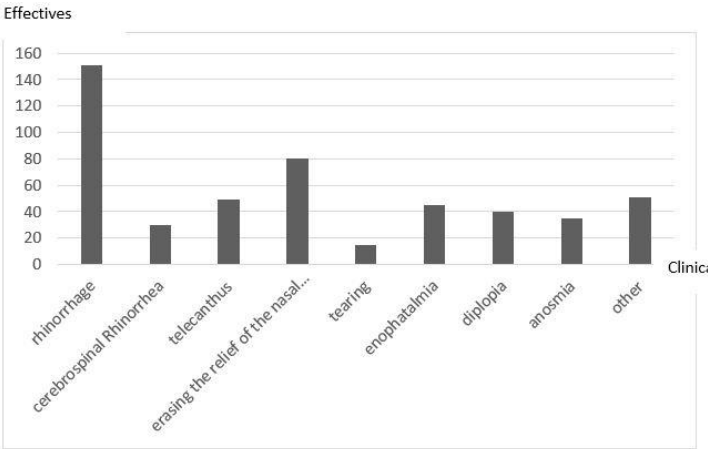


Figure 4: Distribution according to clinical signs



Regarding specific fractures, the most common form was the NEMFO complex fracture, accounting for 32.50% of cases. Additionally, 36.4% of centrofacial fractures were associated with zygomatic bone fractures (Table 3). Most of these fractures occurred in December and January, with rates of 17% (n=25) and 13% (n=19), respectively. Monday and Thursday had the highest number of cases, with 31 and 28 recorded, respectively. Most traumas occurred between 12 PM and 4 PM (Figure 5, 6, 7).

Table 3: Distribution according to maxillofacial and extra-maxillofacial fractures

Treatment of centro-facial fractures	Number	Percentage
NEMFOC	49	32.50%
Maxilla	40	26.45%
Nasal	33	21.85%
Naso ethomodal	29	19.20%
	Facials fracture association	
Mandible	43	28.50%
Os zygomatic	55	36.40%
Fracture front floor	30	19.87%
No	23	15.23%
	Extra-facial fracture association	
Skull	23	15.20%
Lower limb	9	6%
Senior limb	9	6%
Spine	1	7%
Basin	0	0%

NEMFOC: naso-ethmoido-maxillo-fronto-orbital complex

Figure 5: Distribution by month

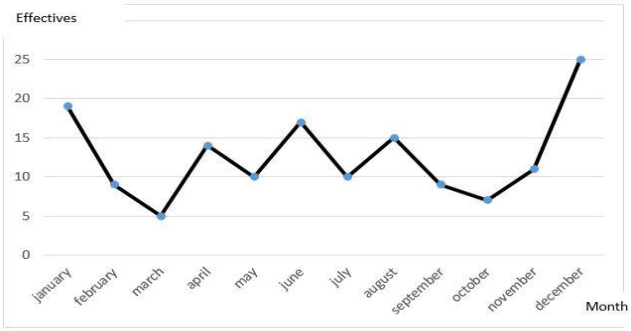


Figure 6: Distribution according to the days of the week

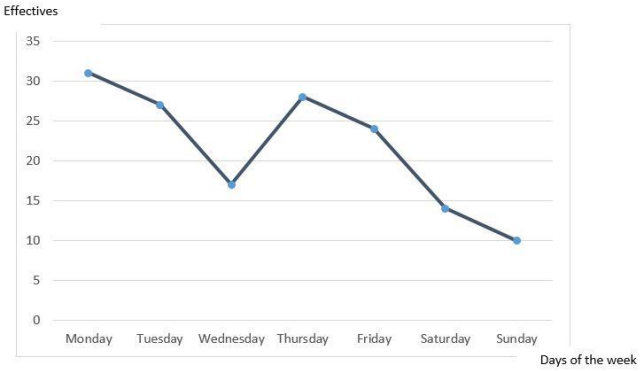
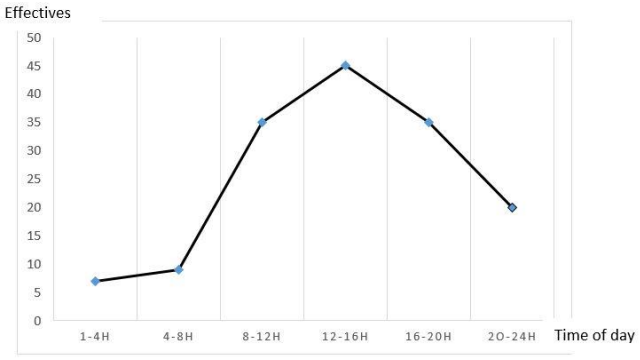


Figure 7: Distribution by time of day



Discussion

Centrofacial fractures accounted for 24.20% of all facial fractures in our study. Our findings show a higher prevalence than Bourguila et al. [5], who reported a prevalence of 8% in Tunis. The mean age of our patients was 30 years old, with a median of 28 years old. Bourguila et al. also found similar mean and median ages of 29 and 27 years old, respectively.

A notable sex ratio of 9:1 was observed, indicating a clear male predominance, which aligns with findings from other studies. This male predominance can be attributed to factors such as engagement in risky behaviors, participation in dangerous

games, violent contact sports, and a propensity for risk-taking. In Western series, although the male predominance is less pronounced, it typically ranges around 2-3 males per female [6,7].

The peak occurrence of centrofacial fractures was between the third and fourth decades of life, a finding consistent with several other studies. The higher incidence during these decades in our study can be attributed to the fact that this age group represents the most active population and, therefore, the most exposed to potential risks. Additionally, this population may exhibit a certain carelessness and engage in dangerous practices. These fractures can have significant socio-economic impacts.

In a Japanese series, Lida et al. [8] reported the peak occurrence of centrofacial fractures between the ages of 10 and 20 years. In our study, the most affected individuals were freelancers, accounting for 74 out of 151 cases. These results are similar to those reported by Rabenandrasana et al. [9] in Antananarivo and exceed those reported by Ngaba et al. [10] in Yaoundé. Freelancers typically belong to the low-income bracket and work in the informal sector, constantly on the move and seeking subsidies.

Our series' primary cause of fractures was public road accidents, accounting for 76.8% of cases. This aligns with the findings of other African authors [11]. Several factors contribute to this trend: rapid urban population growth, leading to a younger population, increased production of faster-motorized equipment, non-compliance with or disregard for traffic regulations, poor road conditions, lack of vehicle maintenance, and the emergence of new means of transport with limited or no safety measures.

In the context of the socio-economic crisis, there has been a rise in the “moto-taxi phenomenon”. These motorcycles are used for transporting people and goods, driven by young individuals who lack knowledge of traffic regulations due to a lack of driving licenses. Moreover, these individuals often use psychoactive substances while performing their activities. Furthermore, these motorcycles are frequently overloaded, sometimes carrying three or four passengers, making them unstable.

According to Bourguila [5], “this high frequency of public road accidents requires public health reflection and political efforts to improve prevention”. In Western series, sports accidents account for 25.8%, followed by public road accidents at 23.1%, as reported by Lebeau [6]. The causes of maxillofacial trauma vary depending on the habits and practices of different populations.

In our series, the peak occurrence of fractures was observed in December with 25 cases, followed by January with 19 cases and June with 17 cases. This can be explained by the fact that December, corresponding to the end-of-year celebrations, involves significant population movements. During this period, vigilance tends to decrease due to the festive atmosphere. Additionally, the young population generally tends to consume alcohol and psychoactive substances during this month.

Monday had the highest number of patients, while Sunday had the least. This could be attributed to the fact that Monday marks the beginning of the workweek after the weekend break, resulting in increased traffic density and higher accident risks.

Most accidents occurred between 12 PM and 4 PM, coinciding with the lunch break for formal sector workers. However, this period also corresponds to the peak activity hours for certain categories of self-employed workers, particularly “motorcycle deliverymen”.

Clinically, all of our patients exhibited rhinorrhea, and 80 out of 151 cases showed flattening of the nasal pyramid. The clinical presentation of centrofacial fractures can vary, ranging from benign to severe deformities. The clinical examination of these fractures should be conducted meticulously and systematically to avoid overlooking any underlying serious injuries. In the presence of rhinorrhea, healthcare practitioners should be concerned about cerebrospinal fluid (CSF) leakage and actively seek its presence. CSF leakage indicates a breach in the meninges and can lead to serious complications such as post-traumatic meningitis, which is challenging to treat and can rapidly become fatal.

Fractures of the nasal-ethmoid-fronto-orbital complex were the most frequent, accounting for 32.50% of cases, followed by maxillary fractures at 26.45%. Additionally, facial fracture associations were noted, particularly involving the zygomatic bone (36.4%). Furthermore, we observed 23 cases (15.2%) of skull fracture associations on the extra-facial level. Our findings differ from those of Lebeau, who reported lower numbers. The predominance of NEMFO fractures and associated cranial vault fractures reflects the extreme violence of the impacts in our context. These fractures present significant functional, aesthetic, and life-threatening implications, highlighting the urgent public health challenge they pose in tropical regions.

Limitations

During our literature review, we encountered insufficient data on centrofacial fractures in the African literature. Additionally, it should be noted that a significant number of medical records were unusable at the time of data collection, resulting in a reduced sample size. Despite these limitations, we could still obtain a representative population sample.

Conclusion

Centrofacial fractures are inadequately described in the existing literature, and it is crucial for both specialists and general practitioners to be aware of them. Failure to recognize these fractures can lead to severe and potentially fatal complications. As these fractures primarily affect young adults, who are part of the most productive segment of the population, they present a significant public health concern. Authorities should address this issue through awareness campaigns, education, and training.

Further prospective studies are warranted to comprehensively assess the epidemiological, clinical, and anatomical aspects of centrofacial fractures.

References

1. Diallo AO, Itiere Odzili FA, Keita A, Bah ML, Alloh HM, Kourouma A, et al. Traumatismes isolés de la face à Conakry: considérations épidémiologiques et prise en charge. Health Sci Dis. 2017;18(4):44-7.
2. Koffi KM, Kouakou KB, Assini Eyogbo S, Ory OADM, Harding-Kaba MB, Bissa HC, et al. Fractures de l’étage antérieur de la base du crane au Chu de Cocody(Abidjan): à propos de 47 cas. Bul Med Owendo. 2010;12(34):22-5.

3. Anzouan-Kacou E, Assouan C, Milogo M, N'Guessan N, Angoh P, Salami A, et al. Difficultés thérapeutiques des traumatismes centro-faciaux par arme à feu en période de guerre: cas de la Cote d'Ivoire. Rev Int Ser San For Arm. 2016;89(2):17-21.
4. Assouan C, Milogo M, Anzouan KE, N'Guessan N, Salami A, Diomande A, et al. Traumatismes maxillo-faciaux au CHU de Treichville d'Abidjan en Côte d'Ivoire. Etude épidémiologique de 1066 dossiers. Rev Col Odonto-Stomatol Afr Chir Maxillo-fac. 2014;21(4):31-4.
5. Bourguila J, Zairi I, Konsari RH, Jablaoui Y, Hellali M, Adouani A. Etude de la traumatologie maxillofaciale à Tunis. Rev Stomatol Chir Maxillofac. 2008;109:353-7.
6. Lebeau J, Kanku V, Duroure F, Morand B, Sadek H, Raphael B. Traumatisme faciaux au CHU de Grenoble. Rev Stomatol Chir Maxillofac. 2006;107:23-9.
7. Renier MA, Raux M, Asencio Y, Gaillard J, Ettalhaoui N, Riou B, et al. Que prédisent les valeurs de lactates d'un polytraumatisé en centre spécialisé? Congrès de la SFAR. 2011:R183
8. Lida S, Kogo M, Suguira T, Mima T, Matsuya T. Retrospective analysis of 1502 patients with facial fractures. Int Oral Maxillo-fac Surg. 2001;30:286-90.
9. Ranbenandrasana FV, Ndrianarivony SC, Matovoarisoa D, Razafindrade JAB, Rjoarivony AE, Rakotoarison RA. Etude épidémiologique des traumatismes maxillo-faciaux au CENHOSOA. Revue Odonto Mal en ligne. 2019;16:29-34.
10. Ngaba MPOMN, Youssef MD, Zing S, Bengondo MC. Fractures maxillo-faciales dues aux accidents de la circulation routière: aspects épidémiologiques et cliniques dans les trois hopitaux de la ville de Yaoundé. Int J of innov scientific res and rev. 2021;03(07):1529-33.
11. Rakotoarisoa AHN, Rakotoarimanana FVA, Randriamanantena T, Rasolongatovo TY, Randriamiarisoa NH, Raotoson HS, et al. Epidémiologie des fractures observées au service de chirurgie maxillo-faciale du CHU d'Antananarivo. Rev Odonto Mal en ligne. 2014;9:20-32.

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Spontaneous posterior cervical epidural hematoma: A case report

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The authors stated that the written consent was obtained from the patient presented with images in the study.

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Abstract

Spontaneous spinal epidural hematoma (SSEH) is a rare neurological emergency affecting the spinal cord. The etiology of SSEH is unknown, but it may occur due to using anticoagulants and antiplatelet agents, which are commonly used to treat vascular diseases. Because of its rarity and non-specific initial symptoms, early and accurate diagnosis can be difficult, potentially negatively impacting a patient's survival and quality of life. In this report, we present the case of a young male patient with SSEH who had no comorbidities, did not use anticoagulants, and presented with sudden-onset neck pain without predisposing factors. Regarding survival and prognosis, postoperative patient follow-up is equally important as prompt diagnosis and treatment of SSEH.

Keywords: posterior cervical, laminectomy, neck pain, spontaneous, re-bleeding

Introduction

Spontaneous spinal epidural hematoma (SSEH) is a hemorrhage in the spinal epidural space without evident traumatic or iatrogenic causes [9]. SSEH requires prompt diagnosis and treatment, as its risk of morbidity and mortality is high despite its estimated frequency of only 1 in 100,000 population [7]. SSEH is a rare condition with an unknown origin that may occur secondary to using anticoagulant and antiplatelet agents, primarily prescribed for vascular disease treatment. Due to its extreme rarity and initial non-specific symptoms, early and accurate diagnosis can be challenging, potentially impacting the patient's clinical course and quality of life [1].

While the pathogenesis of SSEH is not yet fully understood, coagulation disorders, vascular malformations, hypertension, cancer, pregnancy, and anticoagulant and antiplatelet therapies are believed to be the primary causes of SSEH [4]. Nevertheless, in 40% of cases reported in the literature, no predisposing factor has been identified [5].

The most common clinical symptoms of SSEH include sudden-onset spinal pain, followed by nerve root and spinal cord compression symptoms [8]. While the severity of its symptoms is variable, they are often atypical, and the extent and duration of bleeding are significantly related to the severity of the clinical presentation [6]. SSEH is most commonly located between the lower cervical and upper thoracic levels but can occur throughout the entire spine. Prompt and accurate diagnosis and emergency surgical intervention can yield positive neurological and functional outcomes [10,11].

This report presents the case of a young male patient with SSEH who had no comorbidities, did not use anticoagulants, presented with sudden-onset neck pain, and had no known predisposing factors.

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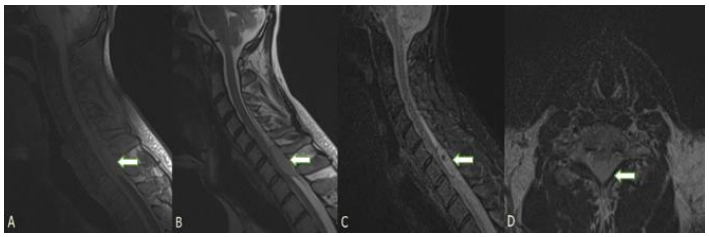
Case presentation

A 36-year-old male patient presented to our emergency department with severe neck pain that had started three days earlier. Ethics approval and participation consent were not required as this report presents our clinical experiences and observations regarding a single individual. The patient exhibited no motor or sensory deficits or neurological issues on examination. The patient had not experienced recent head or spinal trauma, undergone surgical treatment, or smoked. Routine blood parameters, including bleeding time, platelet count, and biochemical tests, were normal. Contrast-enhanced cervical magnetic resonance imaging (MRI) revealed a posterior SSEH at the C6-T1 level. The patient underwent emergency surgery (Figure 1).

Figure 1: Preoperative MRI showing a posterior SSEH located at C6-T1 level. (A) T1-weighted images showing isointensity, (B) T2-weighted sagittal images showing heterogeneous signal intensity, (C) contrast-enhanced T2-weighted sagittal images showing heterogeneous signal intensity, and (D) T2-weighted axial images showing spinal cord compression on dorsal and left lateral sides.



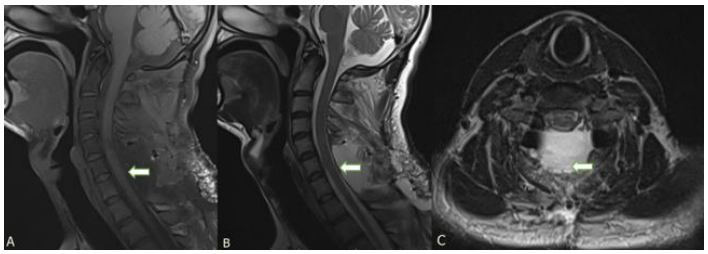
Under general anesthesia, the patient was placed in a supine position. The surgical site was disinfected with a tincture of iodine and covered with sterile drapes. The skin was incised using the classical posterior cervical approach, and the hematoma was completely evacuated via a left-sided C7-T1 hemilaminectomy. The surgical site was closed to fit the anatomy, and a Hemovac drain was inserted. Following surgery, the patient was awakened and taken to the postoperative neurosurgery clinic.

On the first postoperative day, although the pain had decreased, a significant regression was observed in neurological functions. On examination, there was hypoesthesia below C7, and finger flexion and extension had a motor strength of 2/5, with all lower extremity muscles having a strength of 2/5 as well. The American Spinal Cord Injury Association Impairment grade was C. An urgent repeat cervical MRI revealed C6-T1 epidural re-bleeding (Figure 2).

Figure 2: Postoperative MRI showing a recurrent posterior SSEH at C6-T1 level. (A) T1-weighted images showing isointensity, (B) T2-weighted sagittal images heterogeneous signal intensity suggestive of spinal cord compression, and (C) T2-weighted axial images showing spinal cord compression in dorsal and left lateral sides in the laminectomy area.

Due to the patient's symptoms and MRI findings, a second surgery was performed. This time, the patient underwent C6-C7 total laminectomy, followed by posterior cervical instrumentation involving C5-6 lateral mass screw fixation and C7 pedicle screw fixation. On the second postoperative day, the pain subsided, and motor strength improved. By the first postoperative week, lower extremity motor strength had reached 4/5; by the second postoperative week, it had returned to 5/5. A follow-up MRI showed complete evacuation of the hematoma (Figure 3).

Figure 3: MRI images showing the spinal cord following hematoma evacuation in the second surgery. (A) T1-weighted sagittal images, (B) T2-weighted sagittal images, and (C) T2-weighted axial images.



The sutures were removed in the second postoperative week, and the patient was transferred to the physical therapy department for rehabilitation.

Discussion

SSEH is a rare but significant neurological emergency that can occur at any age, although it primarily affects those over 40 years old [12]. The use of anticoagulants and antiplatelet drugs in treating vascular diseases is among the most common factors contributing to the development of SSEH [13].

It is estimated that 25% to 70% of SSEH patients have a history of anticoagulant use. The first cases of SSEH were described by Jackson in 1869, and since then, approximately 900 cases have been reported, with 40% to 60% lacking an identifiable etiology. After the onset of SSEH, the pathophysiologic process involves mechanical compression and hemodynamic variation. An epidural hematoma can directly damage the spinal cord structure or lead to spinal cord hypoxia [2]. Multiple studies have shown that prompt surgical intervention can result in rapid recovery within 12–36 h. Therefore, timely decompression surgery is paramount for SSEH [11]. However, many studies have also reported favorable outcomes with conservative treatment in patients with mild clinical symptoms [3].

Conclusion

Although SSEH is rare, its clinical symptoms can rapidly progress. In addition to early diagnosis and prompt treatment, patient follow-up is crucial. SSEH clinical outcomes are closely related to its symptoms, and surgical options are determined based on the patient's clinical condition and MRI findings. Close monitoring of the patient following surgery is critical for the prognosis.

References

1. Çorum M, Uysal İ, Afşin A, Aksoy C. A spontaneous cervical spinal epidural hematoma in a male patient receiving treatment for acute coronary syndrome: A case report. Turk J Phys Med Rehabil. 2020;66(3):360.
2. Dolan EJ, Tator CH, Endrenyi L. The value of decompression for acute experimental spinal cord compression injury. J Neurosurg. 1980;53(6):749-55.
3. Kim T, Lee C-H, Hyun S-J, Yoon S-H, Kim K-J, Kim H-J. Clinical outcomes of spontaneous spinal epidural hematoma: a comparative study between conservative and surgical treatment. J Korean Neurosurg Society. 2012;52(6):523.
4. Kirazli Y, Akkoc Y, Kanyilmaz S. Spinal epidural hematoma associated with oral anticoagulation therapy. Am J Phys Med Rehabil. 2004;83(3):220-3.
5. Kreppel D, Antoniadis G, Seeling W. Spinal hematoma: a literature survey with meta-analysis of 613 patients. Neurosurg Rev. 2003;26(1):1-49.
6. Liao C-C, Lee S-T, Hsu W-C, Chen I-R, Liu T-N, Lee S-C. Experience in the surgical management of spontaneous spinal epidural hematoma. J Neurosurg Spine. 2004;100(1):38-45.
7. Liu Z, Jiao Q, Xu J, Wang X, Li S, You C. Spontaneous spinal epidural hematoma: analysis of 23 cases. Surgl neurol. 2008;69(3):253-60.
8. Matsumura A, Namikawa T, Hashimoto R, Okomoto T, Yanagida I, Hoshi M, et al. Clinical management for spontaneous spinal epidural hematoma: diagnosis and treatment. Spine J. 2008;8(3):534-7.
9. Messerer M, Dubourg J, Diabira S, Robert T, Hamlat A. Spinal epidural hematoma: not always an obvious diagnosis. Eur J Emerg Med. 2012;19(1):2-8.
10. New PW. Functional outcomes and disability after nontraumatic spinal cord injury rehabilitation: results from a retrospective study. Arch Phys Med Rehabil. 2005;86(2):250-61.

11. Rajz G, Cohen JE, Harnof S, Knoller N, Goren O, Shoshan Y, et al. Spontaneous spinal epidural hematoma: the importance of preoperative neurological status and rapid intervention. J Clin Neurosci. 2015;22(1):123-8.
12. Ravid S, Schneider S, Maytal J. Spontaneous spinal epidural hematoma: an uncommon presentation of a rare disease. Child's Nervs Syst. 2002;18(6-7):345-7.
13. Vayá A, Resurección M, Ma Ricart J, Ortuno C, Ripoll F, Mira Y, et al. Spontaneous cervical epidural hematoma associated with oral anticoagulant therapy. Clin Appl Thromb Hemost. 2001;7(2):166-8.