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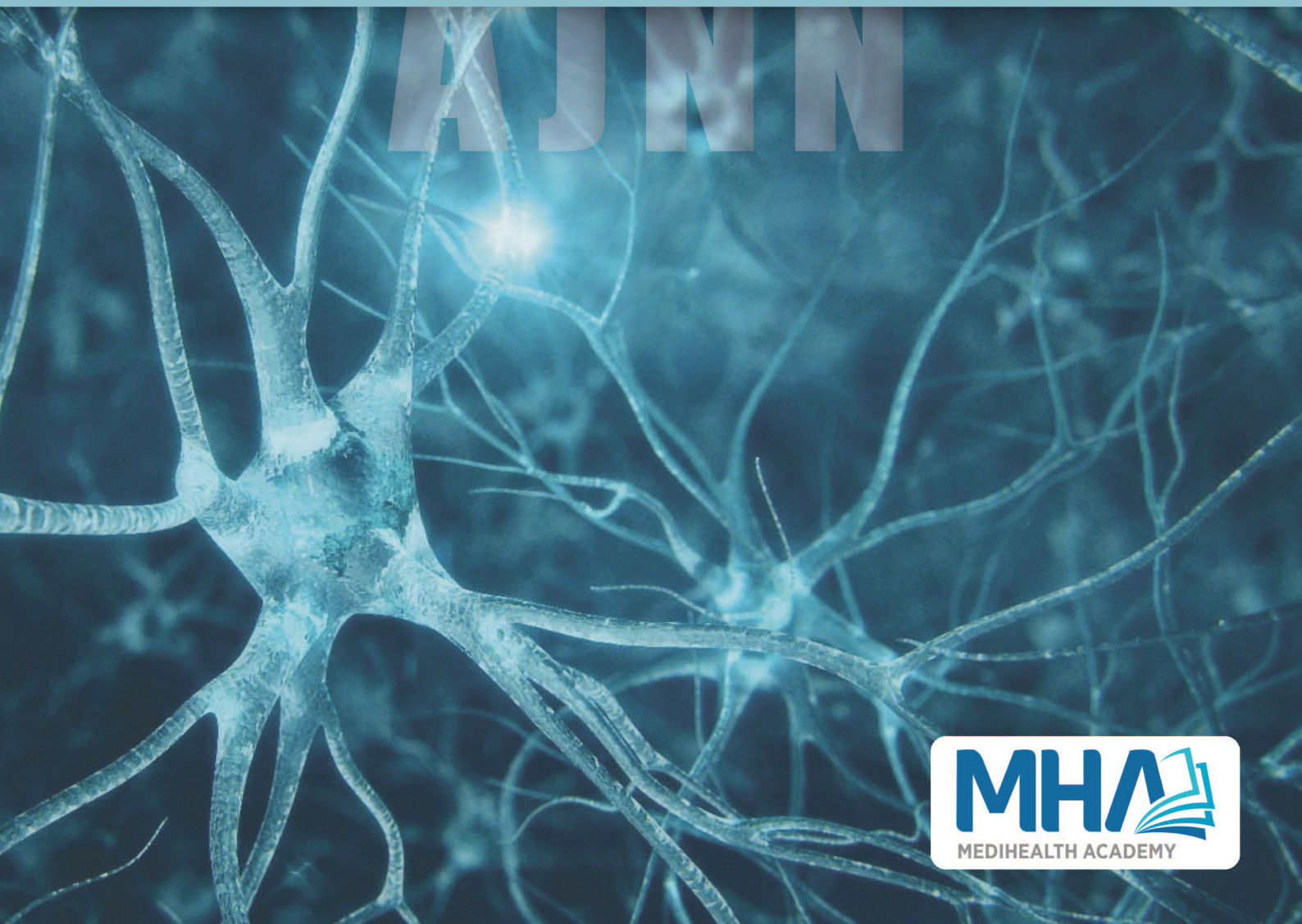

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Evaluation of the knowledge and attitudes on stroke among family medicine residents in Ankara province

Kübra Kaplan Kasar[1], Mustafa Çelik[2]

[1]*Department of Family Medicine, Kırıkkale Provincial Health Directorate, Kırıkkale, Turkiye*
[2]*Department of Family Medicine, Gülhane Faculty of Medicine, University of Health Sciences, Ankara, Turkiye*

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Corresponding Author: Kübra Kaplan Kasar, kbrakpln@gmail.com

ABSTRACT

Aims: Stroke is a major cause of morbidity and mortality worldwide and in Turkiye. A significant proportion of patients in family medicine practice are individuals at risk for stroke. This study aimed to assess the knowledge and attitudes regarding stroke among family medicine residents working in medical faculties and training and research hospitals in Ankara.

Methods: This descriptive cross-sectional study included 241 family medicine residents working in Ankara. Sociodemographic characteristics, knowledge, attitudes, and training status related to stroke were collected using a structured questionnaire. Data were analyzed using IBM SPSS version 25.0.

Results: Of the participants, 140 (58.1%) were female and 101 (41.9%) were male. The mean knowledge score was 79.63±7.89, and the mean attitude score was 86.78±5.94. Only 31 participants (12.9%) had completed a neurology rotation. Forty-seven participants (19.5%) had previously received training on stroke; 34 (14.1%) considered themselves sufficient in stroke management, while 131 (54.4%) considered themselves partially sufficient. Seventy-one participants (29.5%) reported adequate knowledge of stroke risk factors. Knowledge scores were significantly higher among those who had completed a neurology rotation ($p=0.027$). Participants who had received stroke-related training felt more competent in the subject ($p<0.001$). No significant correlation was found between age, years in practice, or duration of residency and knowledge or attitude scores.
Conclusion: Although family medicine residents demonstrated generally adequate knowledge about stroke, there were gaps in training and practical experience. The rates of participation in neurology rotations and stroke-related educational programs were low. Completing a neurology rotation was associated with higher knowledge scores. Incorporating neurology rotations into residency training may positively enhance residents' knowledge and attitudes toward stroke, which is crucial for public health.

Keywords: Family medicine, stroke, cerebrovascular disease, knowledge, attitude

INTRODUCTION

Stroke is a major cause of morbidity and mortality worldwide and in Turkiye. According to World Health Organisation (WHO) data, stroke ranks second among causes of death worldwide and affects approximately 15 million people each year. Of these, approximately 5 million die, while 5 million continue to live with permanent disabilities.[1] It is the fourth leading cause of death in the United States.[2] According to 2023 data from the Turkish Statistical Institute (TÜİK), cerebrovascular diseases account for approximately 6.8% of all deaths in Turkiye, making it the third leading cause of death.[3]

Stroke not only reduces an individual's quality of life but also imposes a significant economic burden on the healthcare system and society. Therefore, early recognition, prevention of risk factors, and effective management of stroke are of great importance at both the individual and societal levels. Primary healthcare services, and particularly family physicians, play a critical role in stroke prevention.[4]

The most important risk factors for stroke include preventable conditions such as hypertension, diabetes, dyslipidaemia, atrial fibrillation, smoking, and obesity.[5,6] Family physicians' ability to recognise and manage these risk factors may be decisive in reducing the incidence of stroke.[7]

Additionally, stroke is a clinical condition that requires a race against time in terms of diagnosis and treatment. Therefore,

early detection, appropriate management, and prompt referral are of great importance.[8] In this process, the role of primary care providers, especially family physicians and family medicine residents undergoing specialised training, is critical.

The literature indicates that healthcare professionals' knowledge of stroke symptoms and their ability to respond appropriately directly affect the success of the intervention process.[9,10] However, various studies have shown that family physicians and primary care healthcare professionals do not have sufficient knowledge about stroke and that their level of knowledge in this area varies.[11-13]

Research on the knowledge levels and attitudes of family medicine residents regarding stroke in Turkiye is limited. Most of the existing studies in the literature focus on groups such as nurses, medical students, or emergency department staff.[14]

In our study, the knowledge and attitudes of family medicine residents regarding stroke will be evaluated. This will help increase the awareness of family physicians, who will provide primary care, regarding stroke.

METHODS

Prior to the start of the study, approval was obtained from the Clinical Researches Ethics Committee of Ankara Training and Research Hospital, University of Health Sciences (Date: 28.12.2022, Decision No: 1171/2022). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study is a cross-sectional descriptive study. A face-to-face survey was conducted with family medicine resident doctors actively working in Ankara between 28 December 2022 and 25 June 2023. There were a total of 604 family medicine residents studying in Ankara province. The sample size was calculated as at least 236 people at a 95% confidence level, based on a population of 604 and a margin of error of 5%. A total of 241 individuals were included in the study. Of the 285 individuals invited, 28 refused to participate and 16 provided incomplete questionnaires; therefore, the final participation rate was 84.6%.

The questionnaire includes 5 questions on sociodemographic characteristics and 6 questions on participants' education, behaviour, and experiences related to stroke. The knowledge and attitude questions were developed by reviewing questions used in previous similar studies. There are 24 knowledge questions and 15 attitude questions, and the scores obtained from each were converted to a 100-point system. Symptom knowledge and risk factor knowledge were calculated as one point each, while statements were calculated as two points each.

Statistical Analysis

IBM SPSS 25.0 (IBM Statistical Package for Social Sciences, version 25) software was used for data analysis in the study. The normality of distribution was tested using the Kolmogorov-Smirnov and Shapiro-Wilk tests. To examine the difference between group means, the Student t-test and ANOVA variance analysis were used for variables showing normal distribution, while the Mann-Whitney U test and Kruskal Wallis test were used for variables not showing normal distribution. The Chi-square test was used to examine the relationships between nominal variables, and the Pearson correlation test and Spearman correlation test were used to examine the degree of relationship between numerical variables. The significance level was set at $p<0.05$ for all tests.

RESULTS

A total of 241 family medicine residents working in family medicine clinics at medical faculties and training and research hospitals in Ankara province were included in the study. Of the participants, 140 (58.1%) were female and 101 (41.9%) were male; 204 (84.6%) of the residents worked full-time, and 37 (15.4%) worked on a contractual basis. When the distribution by year of residency was examined, 121 (50.2%) of the participants were in their first year, 36 (14.9%) were in their second year, and 84 (34.9%) were in their third year of residency. The sociodemographic characteristics of the participants are presented in Table 1.

Table 1. Sociodemographic characteristics of participants (n=241)

Sociodemographic characteristics		n	%
Gender	Female	140	58.1
	Male	101	41.9
Assistant status	Full-time	204	84.6
	Contractual	37	15.4
Assistant period	1	121	50.2
	2	36	14.9
	3	84	34.9

Only 31 participants (12.9%) had completed a neurology rotation. The number of participants who had previously received training on stroke was 47 (19.5%). Male gender ($p=0.025$), full-time assistants ($p=0.015$), and those who had received stroke training ($p<0.001$) had statistically significantly higher perceptions of competence. On the other hand, no significant difference was found between having completed a neurology rotation and perceived competence ($p=0.077$). A comparison of participants' characteristics and their perceived competence in stroke care is presented in Table 2.

Participants were found to have answered statements containing stroke risk factors correctly at a high rate. The most commonly known stroke risk factors were, in order, 'previous history of stroke' (97.9%), "smoking" (96.7%) and 'atrial fibrillation'. Among the risk factors presented to participants, only the statement 'Female gender is a risk factor for stroke' was incorrect, and 31.5% of participants answered 'yes' to this statement, indicating that they had provided an incorrect response. The participants' responses to statements containing information about stroke risk factors are presented in Table 3.

Most participants correctly identified stroke symptoms. The most commonly recognised stroke symptom was 'speech impairment' (98.8%), followed by 'consciousness impairment' (98.3%) and 'loss of balance' (95.9%). It was found that

Table 2. Comparison of participants' self-perceived competence in stroke care with certain characteristics (n=241)

Characteristics		The state of considering oneself competent about the subject of stroke			p*
		Yes n (%)	No n (%)	In part n (%)	
Gender	Female (n=140)	13 (9.3)	50 (35.7)	77 (55.0)	0.025
	Male (n=101)	21 (20.8)	26 (25.7)	54 (53.5)	
Assistant status	Full-time (n=204)	29 (14.2)	57 (27.9)	118 (57.8)	0.015
	Contractual (n=37)	5 (13.5)	19 (51.4)	13 (35.1)	
Neurology rotation completed	Yes (n=31)	8 (25.8)	6 (19.4)	17 (54.8)	0.077
	No (n=210)	26 (12.4)	70 (33.3)	114 (54.3)	
Stroke training received	Yes (n=47)	15 (31.9)	6 (12.8)	26 (55.3)	<0.001
	No (n=194)	19 (9.8)	70 (36.1)	105 (54.1)	

Chi-square test, p<0.05 is statistically significant

Table 3. Distribution of participants' responses to statements containing information about stroke risk factors

Statements about stroke risk factors	Answers	
	Yes n (%)	No n (%)
A history of stroke is a risk factor for stroke. (C)	236 (97.9)	5 (2.1)
Smoking is a risk factor for stroke. (C)	233 (96.7)	8 (3.3)
Atrial fibrillation is a risk factor for stroke. (C)	232 (96.3)	9 (3.7)
Hypertension is a risk factor for stroke. (C)	228 (94.6)	13 (5.4)
A history of transient ischaemic attack is a risk factor for stroke. (C)	224 (92.9)	17 (7.1)
Advanced age is a risk factor for stroke. (C)	224 (92.9)	17 (7.1)
Diabetes is a risk factor for stroke. (C)	218 (90.5)	23 (9.5)
Dyslipidaemia is a risk factor for stroke. (C)	216 (89.6)	25 (10.4)
Female gender is a risk factor for stroke. (I)	76 (31.5)	165 (68.5)

C: Correct, I: Incorrect

participants incorrectly identified 'facial flushing' (19.5%) and 'coldness in the extremities' (36.9%) as stroke symptoms. The distribution of responses to information-based statements about stroke symptoms is presented in Table 4.

Table 4. Distribution of participants' responses to statements containing information about stroke symptoms

Statements about stroke symptoms	Answers	
	Yes n (%)	No n (%)
Speech impairment is a symptom of stroke. (C)	238 (98.8)	3 (1.2)
Consciousness impairment is a symptom of stroke. (C)	237 (98.3)	4 (1.7)
Loss of balance is a symptom of stroke. (C)	231 (95.9)	10 (4.1)
Blurred vision/double vision is a symptom of stroke. (C)	229 (95.0)	12 (5.0)
Dizziness is a symptom of stroke. (C)	211 (87.6)	30 (12.4)
Headache is a symptom of stroke. (C)	205 (85.1)	36 (14.9)
Facial flushing is a symptom of stroke. (I)	57 (19.5)	194 (80.5)
Coldness in the extremities is a symptom of stroke. (I)	89 (36.9)	152 (63.1)

C: Correct, I: Incorrect

The majority of participants demonstrated a positive attitude by responding "I agree" to statements related to prevention of stroke. All participants responded "I agree" to the statement "Smoking cessation is recommended", followed by 'Regular physical activity is recommended' (99.2%), 'Weight reduction is recommended for patients with a high body mass index' (99.2%), and 'Blood pressure levels should be monitored, and treatment should be arranged for patients with high blood pressure' (99.1%). Regarding the single incorrect statement, 'Antioxidant vitamin supplements have been proven to reduce the risk of stroke.' 43.2% responded with 'I agree,' giving an incorrect answer, while 8.7% responded with 'I disagree,' giving the correct answer, and 48.1% indicated 'I am undecided.' The distribution of participants' agreement with statements related to stroke prevention is presented in Table 5.

Table 5. Distribution of participants' agreement with statements related to fall prevention

Statements related to prevention of stroke	Answers		
	Agree n (%)	Disagree n (%)	Undecided n (%)
Quitting smoking is recommended. (C)	241 (100)	-	-
Regular physical activity is recommended. (C)	239 (99.2)	1 (0.4)	1 (0.4)
Weight reduction is recommended for patients with a high body-mass index. (C)	239 (99.2)	-	2 (0.8)
Blood pressure levels should be monitored, and treatment should be arranged for patients with high blood pressure. (C)	240 (99.1)	-	1 (0.4)
Appropriate treatment should be arranged for patients with high cholesterol levels. (C)	237 (98.3)	2 (0.8)	2 (0.8)
Blood sugar levels should be monitored, and treatment is recommended for patients diagnosed with diabetes. (C)	233 (96.7)	-	8 (3.3)
Antioxidant vitamin supplements have been proven to reduce the risk of stroke. (e.g., vitamin D supplements) (I)	104 (43.2)	21 (8.7)	116 (48.1)
In primary care, pulse assessment followed by active atrial fibrillation screening with electrocardiography may be beneficial in patients over 65 years of age. (C)	223 (92.5)	2 (0.8)	16 (6.6)

C: Correct, I: Incorrect

As a result of the assessment measuring the participants' knowledge levels, the average knowledge score was determined to be 79.63 (min. 48.39-max. 100). In the section evaluating attitude levels, the average attitude score was calculated to be 86.78 (min. 66.67-max. 100).

When examining the relationship between sociodemographic characteristics and knowledge scores, only those who had completed a neurology rotation had statistically significantly higher stroke knowledge scores (p=0.027). No significant differences were observed for other variables (p>0.05). No statistically significant relationship was found between gender, residency status, neurology rotation, and stroke education status and attitude scores (p>0.05). The comparison

of sociodemographic variables with knowledge and attitude scores is shown in Table 6.

Table 6. Comparison of sociodemographic variables with knowledge and attitude scores

Sociodemographic characteristics		Knowledge score		Attitude score	
		Mean±SD	p	Mean±SD	p
Gender	Female	79.74±7.27	0.084	87.09±5.83	0.583
	Male	79.46±8.73		86.33±6.00	
Assistant status	Full-time	79.80±7.91	0.931	87.07±5.75	0.054
	Contractual	78.63±7.84		85.13±6.50	
Neurology rotation completed	Yes	80.02±10.00	0.027	84.51±6.47	0.497
	No	79.51±7.54		87.11±5.75	
Stroke training received	Yes	80.02±6.94	0.297	86.52±5.38	0.223
	No	79.41±8.09		86.80±6.06	

SD: Standard deviation. *Student's t-test, p<0.05 is statistically significant

No significant correlation was found between knowledge and attitude scores and age, years of professional experience and length of assistantship (p>0.05). The results of the correlation analysis between participants' age, years of professional experience and length of assistantship and their knowledge and attitude scores are presented in Table 7.

Table 7. Correlation analysis results between participants' age, years of professional experience, and duration of assistantship and their knowledge and attitude scores

Sociodemographic characteristics		Knowledge score	Attitude score
Age	r	0.042	0.001
	p	0.518	0.986
Years of experience	r	0.027	-0.011
	p	0.681	0.862
Duration of residency	r	0.036	0.086
	p	0.577	0.185

Pearson correlation test, p<0.05 is statistically significant

DISCUSSION

It was determined that 19.5% of family medicine residents working in Ankara who participated in the study had previously received training on stroke. Ding et al.[13] reported that 67.8% of primary care workers had participated in stroke training. In a study conducted by Traynelis[15] with 63 participants, 70% of the participants stated that they had completed a training programme on stroke. According to the data in the literature, it is seen that the rate of family physicians in Ankara participating in training on stroke is low. This indicates that training in this area is not sufficiently systematic during specialist training. This is a problem that is frequently highlighted in the literature. In a study by Albart et al.,[16] it was emphasised that primary care physicians have significant gaps in their knowledge about stroke and that training programmes are necessary.

Only 12.9% of family medicine residents participating in the study were found to have completed a neurology rotation. The reason for the low number of physicians completing a neurology rotation may be explained by the fact that neurology rotation is an elective rotation and is not frequently chosen by residency students. In our study, the fact that the knowledge scores of participants who completed a neurology rotation were statistically significantly higher indicates that clinical experience has a positive effect on knowledge levels. This finding is consistent with studies supporting the impact of experiential learning on knowledge acquisition.[7,9] It highlights the importance of including these rotations in educational programmes to increase stroke awareness.

Our study showed that male residents, full-time employees, and those who had previously received stroke training felt more competent in stroke care. In particular, the statistically significant increase in perceived competence following stroke training underscores the importance of such education in this field. This finding is consistent with other studies showing that healthcare workers' self-confidence and sense of competence increase through education.[12] However, it is noteworthy that the competence perceptions of residents who completed a neurology rotation were not significantly different from those who did not. This finding may indicate that the content and effectiveness of rotation programmes need to be reviewed. It is possible that the theoretical and practical knowledge acquired during the neurology rotation does not sufficiently reflect the residents' perceptions of clinical competence. Integrating more structured training focused on standardised and evidence-based clinical guidelines for stroke management and prevention into family medicine residency programmes may be beneficial.

The average knowledge score of participants was 79.63, which indicates a medium-high level of knowledge when compared to similar studies in the literature. A study conducted in India to assess the knowledge level of primary healthcare workers found a lower level of knowledge.[11] This suggests that medical education in Turkiye has a relatively stronger theoretical foundation in stroke. However, the fact that 31.5% of participants answered incorrectly to the statement 'female gender is a risk factor for stroke' indicates that misconceptions in this area are still widespread. While it is known that advanced age increases the risk of stroke in women, current international guidelines emphasise that gender alone is not an independent risk factor, and that the risk increases as a result of the interaction between age and other factors.[17] Family physicians play an important role in conveying such nuanced information to their patients to enable accurate risk assessment.

One of the most notable findings of the study is the significant difference in knowledge levels between those who have completed a neurology rotation and those who have not. This supports the notion that clinical experience directly influences stroke knowledge. Similarly, Pandian et al.[9] reported that healthcare workers' knowledge levels regarding stroke are directly related to their on-the-ground experience. In this context, it can be said that structured clinical rotations and practical training aimed at increasing stroke awareness among physicians working in primary care are particularly important. However, the fact that 87.1% of the participants had not completed a neurology rotation and 80.5% had not received formal training in this area indicates that there is significant room for improvement in terms of increasing knowledge levels. As emphasised in the literature, healthcare professionals working in primary care in particular are

reported to need training in rapid diagnosis, emergency referral and awareness of risk factors for stroke.[10]

Participants were found to have answered statements containing stroke risk factors correctly at a high rate. The most common risk factors for stroke were, in order, 'history of stroke' (97.9%), "smoking" (96.7%), and 'atrial fibrillation' (96.3%). Among the risk factors presented to participants, only the statement 'female gender is a risk factor for stroke' was incorrect, and 31.5% of participants answered 'yes' to this statement, indicating an incorrect response. In a study involving 173 participants investigating patients' knowledge of stroke, smoking was found to be the most commonly known risk factor, and none of the participants were aware that male gender was a risk factor.[18] All participants recommended quitting smoking to prevent stroke. Based on these results, smoking is one of the most well-known risk factors for stroke, both in our own study and in the literature.

Most participants correctly identified stroke symptoms. The most commonly recognised stroke symptom was 'speech impairment' (98.8%), followed by 'consciousness impairment' (98.3%) and 'loss of balance' (95.9%). It was found that participants incorrectly identified 'facial flushing' (19.5%) and 'coldness in the extremities' (36.9%) as stroke symptoms. In a study examining nursing students' misconceptions about stroke, it was observed that many students limited the neurological assessment for stroke to impaired consciousness.[19] In a study by Ramírez-Moreno et al.[20] investigating the general population's knowledge of stroke, it was found that 73% of the general population knew at least one symptom, with the most commonly known symptoms being sudden weakness, dizziness, and headache. In a study by Pérez-Lázaro et al.,[21] it was observed that 63.5% of the population did not recognise stroke symptoms. These results show that family medicine residents in Ankara have a relatively high level of knowledge in this area, but also indicate that some misconceptions still persist and that awareness of stroke symptoms needs to be further improved.

The high percentage of participants who responded 'agree' to statements related to stroke prevention indicates that they generally have a positive attitude. The high average attitude score (86.78) indicates that family physicians are willing and prepared to play a key role in primary and secondary stroke prevention.[14] In particular, their awareness of the importance of managing known risk factors such as hypertension, diabetes, and smoking in stroke prevention was found to be high.

All participants agreed with the statement 'Quitting smoking is recommended.' for stroke prevention, followed by 'Regular physical activity is recommended' (99.2%), 'Weight reduction is recommended for patients with a high body-mass index' (99.2%), and 'Blood pressure levels should be monitored, and treatment should be arranged for patients with high blood pressure' (99.1%). The majority of participants responded 'I agree' to statements related to stroke prevention at a high rate, demonstrating a positive attitude towards stroke prevention. However, although the statement 'Antioxidant vitamin supplements have been proven to reduce the risk of stroke.' is incorrect, 43.2% of participants accepted it as true. In fact, there is no scientific evidence to support the claim that antioxidants reduce the risk. Current guidelines and meta-analyses indicate that antioxidant supplements (especially vitamins C and E, beta-carotene) do not reduce the risk of stroke and may even have potential harmful effects in some cases.[22] Additionally, there is evidence that vitamin E supplements may increase the risk of haemorrhagic stroke.[23] This lack of information poses a significant problem for evidence-based medical practice. Family physicians must provide accurate guidance on popular but unproven treatment methods during patient consultations. Emphasising such current and evidence-based information in family medicine residency training programmes is critical for patient safety and effective treatment management.

In our study, a statistically significant difference was found between participants' neurology rotation status and their knowledge scores. In a study conducted by Traynelis,[15] participants who attended a continuing education programme on stroke scored significantly higher on a test prepared on stroke knowledge than those who did not participate. In a study conducted by Rababah et al.[24] involving doctors, registered nurses, and healthcare workers, a randomised test study was designed after a single-session stroke education programme was presented, and it was observed that the education programme had a positive effect on the stroke knowledge level of healthcare providers. Another study also showed that the knowledge level of emergency department staff increased after they were included in an education programme.[25] Based on these data, we believe that the participation rate of family medicine residents in Ankara in stroke education and the increase in the number of residents completing a neurology rotation will lead to an improvement in their knowledge and attitudes.

In our study, other sociodemographic variables such as gender, duration of residency, age, and years of professional experience did not show a significant relationship with either knowledge or attitude scores. This finding suggests that knowledge and attitude levels are shaped more by individual effort, clinical experience, and education.[26]

The fact that the average attitude score of the participants was higher than the average knowledge score indicates that residents have a high level of sensitivity towards stroke, but this positive attitude does not always translate into knowledge. This situation is defined in the literature as the 'knowledge-attitude gap,' and it is recommended that primary care physicians adopt methods to reduce this gap in their educational strategies.[27]

Limitations

This study is important as one of the few studies evaluating the knowledge and attitudes of family medicine residents in Turkiye regarding stroke. However, the fact that the study was conducted only in Ankara limits the generalisability of the findings. Additionally, the fact that the data were collected through self-reporting increases the likelihood that the responses are based on perception. Finally, due to some knowledge questions remaining at a theoretical level, clinical practice competence may not have been fully reflected.

CONCLUSION

The study showed that family medicine residents generally had sufficient knowledge about stroke, but there were gaps in their practical skills. The rates of family medicine residents in Ankara who completed a neurology rotation and participated in a training programme on stroke were low. Those who completed a neurology rotation had higher knowledge scores than those who did not. We believe that family medicine residents completing a neurology rotation will positively improve their knowledge and attitudes regarding stroke, which is important for public health.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted after obtaining approval from the Clinical Researches Ethics Committee of Ankara Training and Research Hospital, University of Health Sciences (Date: 28.12.2022, Decision No: 1171/2022).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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The role of hemogram parameters in predicting diabetic neuropathy risk in patients follow-up with type 2 diabetes mellitus

Güneş Seda Albayrak[1], Duygu Felek[2]

[1]Department of Neurology, Faculty of Medicine, Yozgat Bozok University, Yozgat, Turkiye
[2]Department of Internal Medicine, Faculty of Medicine, Yozgat Bozok University, Yozgat, Turkiye

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Corresponding Author: Güneş Seda Albayrak, drgunesalbayrak@yahoo.com

ABSTRACT

Aims: Neuropathy, which develops during the course of diabetes mellitus (DM), significantly affects patients' quality of life, making its early diagnosis and detection crucial. Furthermore, it is thought that the impact of neuropathy developing in the course of DM is not localized but has systemic effects. In our study, we will investigate the role of evaluating hemogram parameters and systemic effects in predicting the risk and monitoring the course of diabetic neuropathy in patients followed up with DM.

Methods: Data from patients who presented to the Yozgat Bozok University Neurology Outpatient Clinic between 2024 and 2025 will be scanned. This will include patients diagnosed with diabetic neuropathy and DM, as well as those investigated for but not found to have neuropathy. One hundred individuals will be included in each group. Group 1 was defined as 50 individuals with a diagnosis of diabetic neuropathy, and group 2 as 50 individuals without a diagnosis of diabetic neuropathy. Within the scope of the study, the following data will be recorded from the hospital data system: patients' age, gender, past medical histories, diagnoses, treatments received, and laboratory test results including hemogram, HbA1c, glucose, sedimentation, CRP, ALT, AST, BUN, serum creatinine, B12, vitamin D, folic acid, ferritin, and electrolyte levels. The ratios of neutrophil, platelet, and monocyte counts to lymphocytes will be calculated and analyzed to assess their association with neuropathy. The data will be analyzed using SPSS, with the significance level set at 0.005.

Results: Of the 100 individuals included in the study, 61 (55.5%) were female and 39 (35.5%) were male; the mean age was calculated as 45.77±17.48. The 50 individuals with diabetic polyneuropathy and the 50 individuals in the healthy control group were analyzed as two groups. Among the 100 patient individuals, 44 (48.9%) were within the target HbA1c range, while 46 (51.1%) individuals were observed to have uncontrolled DM. No statistically significant difference was observed between the groups in terms of fasting blood glucose and HbA1c levels (p=0.657). While no statistically significant difference was observed in NLR and PLR, calculated from the same hemogram data in group 1 and group 2 (p=0.647 and p=0.242, respectively), the difference in MLR was found to be statistically significant (p=0.0024).

Conclusion: Although diabetic neuropathy presents with localized symptoms, its effects are systemic. The monocyte-to-lymphocyte ratio (MLR) was evaluated as a usable parameter for the early detection of developing neuropathy and for determining neuropathy risk. Its correlation with next-generation inflammatory biomarkers may be required. As hemogram data is a test that is available and feasible to perform in most medical centers, it could be a suitable tool for monitoring the development of neuropathy in DM patients, and potentially for post-treatment follow-up.

Keywords: Diabetes mellitus, diabetic neuropathy, neutrophil, lymphocyte, monocyte

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a disease characterized by hyperglycemia and associated with microvascular (retinopathy, neuropathy, and nephropathy), macrovascular (coronary artery disease, peripheral artery disease), and neuropathic (autonomic and peripheral) complications.[1,2] Neuropathy, one of the complications of T2DM, holds particular importance due to the subsequent health problems it causes (diabetic foot ulcers, foot amputations, etc.).[3] When these complications occur, they can become a significant source of morbidity and mortality. Furthermore, the economic burden this condition places on national economies is equally important. It has been reported that

in 2002, approximately 20% of healthcare expenditures in the U.S. were allocated to preventing and treating DM and its complications, and this figure is observed to be steadily increasing.[4] For this reason, the early detection of chronic complications of DM, identification of accompanying risk factors, and their prevention have gained even greater importance. Typically, diabetic patients are referred for neurological examination to detect diabetic neuropathy only if they present with neuropathic symptoms. Patients without neuropathic complaints are merely monitored and followed up by clinicians.

Diabetic peripheral neuropathy is one of the common complications of diabetes that can affect almost every tissue in the body and is a significant cause of morbidity and mortality.[5] Early detection of neuropathy and identification of predisposing risk factors in individuals is crucial. The prevalence of neuropathy in diabetic patients is observed to be around 67.6%. The coexistence of complications and their association with morbidity and mortality is also quite high.[6] It is thought that this rate is significantly high since many patients remain undiagnosed. In a recent cross-sectional study aimed at identifying subclinical diabetic neuropathy, the rate of neuropathy was found to be 44.6%.[7] There are various factors that influence the development of neuropathy in diabetic individuals. Glycemic control, duration of diabetes, smoking, alcohol consumption, hypertension, weight, hyperlipidemia, and plasma homocysteine levels have been shown to be potentially influential in different studies.[8-10]

Since neuropathy that develops during the course of diabetes mellitus (DM) affects patients' quality of life, its early diagnosis and detection are highly important. Özütemiz and colleagues[11] proposed that neutrophil, lymphocyte, and platelet values could be used to assess the complications of diabetes. Similarly, Tuncer and colleagues[12] conducted a clinical study to detect increased inflammation in diabetic neuropathy using hemogram data. Çelikdelen and colleagues[13] evaluated the explainability of the relationship between neutrophil/lymphocyte ratio and systemic inflammation in diabetic nephropathy.

The aim of this study is to investigate whether hemogram parameters can be useful in predicting the risk of diabetic neuropathy in patients followed up with T2DM. Unlike previous studies, our research will concurrently evaluate the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR). These ratios will be compared between individuals with DM who have not been diagnosed with neuropathy and those who have, in order to assess their utility in predicting neuropathy risk. It is thought that neuropathy, which occurs as a complication of DM, has systemic effects rather than being merely a localized complication. We will examine whether the underlying cause for this is increased inflammation by investigating the neutrophil-to-lymphocyte, platelet-to-lymphocyte, and MLRs, which can serve as indicators of inflammation.

METHODS

Ethics

The study was initiated after obtaining approval from the Yozgat Bozok University Non-interventional Clinical Researches Ethics Committee (Date: 02.07.2025, Decision No: 2025-GOKAEK-2513_2025.07.02_531). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Patients who presented to the Yozgat Bozok University Neurology outpatient clinic between 2024 and 2025, including those diagnosed with diabetic neuropathy, those with a diagnosis of DM who were investigated for neuropathy, and those in whom neuropathy was not detected, were included in the study. A total of 100 individuals were to be included in the study, divided into two groups: Group 1 consisted of 50 individuals diagnosed with diabetic neuropathy, and group 2 consisted of 50 individuals without a diagnosis of diabetic neuropathy.

Definitions of DM and Diabetic Neuropathy

Individuals who met the diagnostic criteria for DM, as defined by the Turkish Society of Endocrinology and Metabolism (SEMT), were included in the study. The diagnosis of neuropathy is made through physical examination, which includes an assessment of nerve fiber function by applying 10 grams of pressure. In the clinic, a monofilament test and a vibration sensation test can be performed. However, in cases where typical symptoms are not present or the diagnosis is unclear, electrophysiological tests may be necessary. The diagnosis of diabetic neuropathy is established in all patients only after excluding other causes of neuropathy, such as toxins (e.g., alcohol), neurotoxic drugs (e.g., chemotherapy), vitamin B12 deficiency, hypothyroidism, kidney disease, malignancies (e.g., multiple myeloma, bronchogenic carcinoma), infections (e.g., HIV), chronic inflammatory demyelinating polyneuropathies, hereditary neuropathies, and vasculitis.[1,2]

Data Collection

Within the scope of the study, the following data were recorded from the hospital data system: patients' age, gender, past medical histories, diagnoses, and treatments they received, along with their blood test results including hemogram, HbA1c, glucose, sedimentation, CRP, ALT, AST, BUN, serum creatinine, B12, vitamin D, folic acid, ferritin, and electrolyte levels. The ratios of neutrophil, platelet, and monocyte counts to lymphocytes were examined and their relationship with neuropathy was evaluated. Individuals under the age of 18, those without a DM diagnosis, those without diabetic polyneuropathy, those using anti-inflammatory drugs, those with a diagnosis of myeloproliferative disease, those with electrolyte imbalance, and those with existing vitamin deficiency were excluded from the study.

Statistical Analysis

The data analyses were performed using the SPSS 20.00 (Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL) software. Descriptive statistics are presented as

mean±standard deviation for continuous variables and as percentages for categorical variables. Whether the groups had a normal distribution or not was determined using the Kolmogorov-Smirnov test. For comparing measurement values between groups, Independent samples t-test and ANOVA tests were used, while categorical variables were assessed using the Chi-square test. However, in cases where the groups were not normally distributed, the Mann-Whitney U and Kruskal-Wallis tests were employed. The relationship between quantitative variables was evaluated using correlation analysis (Pearson, Spearman). A p-value below 0.05 was considered the criterion for statistical significance.

RESULTS

Of the 100 individuals included in the study, 61 (61%) were female and 39 (39%) were male. The minimum age was 21, the maximum age was 80, and the mean age was calculated as 45.77±17.48. The 50 individuals with diabetic polyneuropathy and the 50 individuals in the healthy control group were analyzed as two separate groups.

The results obtained simultaneously from the hemogram data of the groups were evaluated. A statistically significant difference was observed between the groups in white blood cell count, neutrophil count, neutrophil percentage, and monocyte count (p=0.008, 0.037, 0.001, and 0.002, respectively). In contrast, no difference was observed in lymphocyte count, lymphocyte percentage, and platelet levels (p=0.182, 0.169, and 0.682, respectively) (Table 1).

While no statistically significant difference was observed in the NLR and PLR—calculated based on the same hemogram data between group 1 and group 2 (p=0.647 and p=0.242, respectively)—the difference in MLR was found to be statistically significant (p=0.0024) (Table 2).

The HbA1c distribution of the patient individuals included in the study was observed across a wide scale. It was found that 44 out of 100 individuals (44.9%) were within the target HbA1c range, while 46 individuals (51.1%) were identified as having uncontrolled DM based on the age-specific target ranges set by the SEMT (Figure).

An analysis of NLR, PLR, and MLR between the groups achieving and not achieving target HbA1c remission showed no significant difference (p=0.108, p=0.114, and p=0.287, respectively) (Table 3).

Table 2. Analysis of NLR, PLR, and MLR between the groups

	Group 1 (patient)		Group 2 (control)		
	Mean	SD	Mean	SD	p
NLR	5.23	2.18	14.67	2.36	0.647
PLR	295.14	117.78	356.86	130.53	0.242
MLR	0.83	0.26	0.65	0.21	0.024

NLR: Neutrophil-lymphocyte ratio, PLR: Platelet- lymphocyte ratio, MLR: Monocyte- lymphocyte ratio, SD: Standard deviation

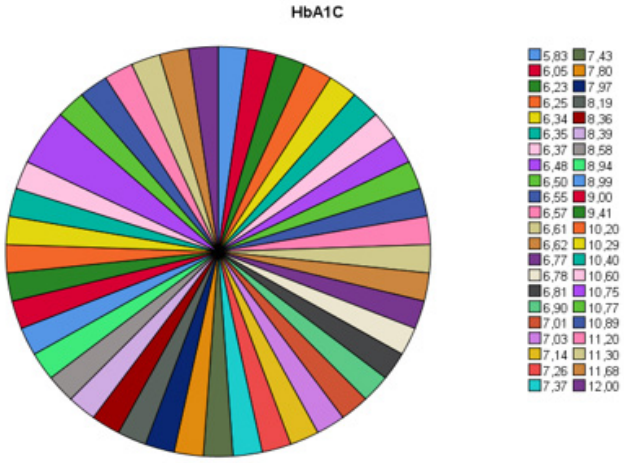

Figure. HbA1c distribution

Table 3. Analysis of NLR, PLR, and MLR according to target HbA1c

	In remission		Not in remission		
	Mean	SD	Mean	SD	p
NLR	1.94	0.67	2.39	1.13	0.108
PLR	108.22	23.25	129.73	59.39	0.114
MLR	0.245	0.073	0.284	0.152	0.287

NLR: Neutrophil-lymphocyte ratio, PLR: Platelet- lymphocyte ratio, MLR: Monocyte- lymphocyte ratio, SD: Standard deviation

The monocyte count showed a correlation with the lymphocyte and neutrophil counts (p=0.001 and p=0.002, respectively). However, no direct correlation was observed for NLR, PLR, or MLR. Furthermore, neutrophil, lymphocyte, and monocyte levels were not found to correlate with the calculations of NLR, PLR, and MLR. A significant correlation was observed between HbA1c and monocyte level (p=0.009), and between glucose level and lymphocyte count (p=0.006) (Table 4).

Table 1. Hemogram parameters of the groups

	Group 1 (patient)				Group 2 (control)				
	Min	Max	Mean	SD	Min	Max	Mean	SD	p
WBC (10^3/mm^3)	3.9	14.90	7.79	2.31	3.72	10.07	6.66	1.79	0.008
Neu #	1.58	10.60	4.70	1.77	1.86	7.48	3.99	1.60	0.037
Neu %	38.8	76.80	59.41	8.59	41.60	88.90	58.30	10.61	0.567
Mono #	0.28	1.13	0.56	0.18	0.24	0.83	0.39	0.13	0.001
Mono %	4.2	16.90	7.37	2.24	3.60	11.30	6.05	1.87	0.002
Lym #	1.02	6.03	2.30	0.82	0.51	3.41	2.11	0.64	0.183
Lym %	14.7	49.40	30.23	7.71	6.00	47.60	32.56	9.06	0.169
PLT (10^3/mm^3)	89	425.00	247.72	60.10	158.00	321.00	243.20	49.27	0.682

Min: Minimum, Max: Maximum, SD: Standard deviation, WBC: White blood cell, Neu: Neutrophil, Mono: Monocyte, Lym: Lymphocyte, PLT: Platelet

Table 4. Correlation between blood glucose levels and hemogram parameters

	HbA1C	Glucose	Hb	WBC	Neu#	Mono#	Lenf#	PLT	NLR	PLR
Glucose	.810**	1								
Hb	0.018	0.171	1							
WBC	0.132	0.177	0.156	1						
Neu#	0.077	0.083	0.118	.924**	1					
Mono#	.268**	0.171	0.124	.581**	.454**	1				
Lenf#	0.121	.271**	0.158	.558**	.217*	.313**	1			
PLT	0.018	0.027	-0.188	0.105	0.089	-0.060	0.128	1		
NLR	-0.110	-0.112	0.049	.251*	.516**	0.003	-.457**	-0.100	1	
PLR	-0.165	-0.160	-0.119	-.226*	0.072	-.254*	-.716**	.321**	.730**	1
MLR	0.057	-0.012	0.051	0.103	.287**	.488**	-.505**	-0.175	.664**	.566**

Hb: Hemoglobin, WBC: White blood count, Neu: Neutrophil, Mono: Monocyte, PLT: Platelet, NLR: Neutrophil-lymphocyte ratio PLR: Platelet- lymphocyte ratio, MLR: Monocyte- lymphocyte ratio

DISCUSSION

In our study, among individuals with T2DM who were diagnosed with diabetic neuropathy, a statistically significant difference was observed between groups in terms of white blood cell count, neutrophil count, neutrophil percentage, and monocyte count (p=0.008, 0.037, 0.001, and 0.002, respectively). In contrast, no significant difference was found in lymphocyte count, lymphocyte percentage, and platelet levels (p=0.182, 0.169, and 0.682, respectively). While no statistically significant difference was observed in the NLR and PLR, calculated from the same hemogram data in group 1 and group 2 (p=0.647 and p=0.242, respectively), the difference in MLR was found to be statistically significant (p=0.0024). The MLR was considered a usable parameter, as it was associated with diabetic neuropathy in diabetic patients. It was postulated that an autoimmunity-mediated condition might be involved, as there is strong evidence for this, particularly in rheumatological diseases. In the study conducted by Hao et al.,[14] hemogram-derived ratios were observed to be usable as diagnostic tools in autoimmune rheumatological diseases, demonstrating the clinical importance of their strong association. Similarly, Yang et al.[15] also demonstrated that hemogram parameters (eosinophil, basophil, and lymphocyte ratios) are valuable in indicating autoimmunity and highlighted their role in rheumatological diseases with a well-established autoimmune pathogenesis. The utility of hematological indices has also been observed in the disease course of systemic conditions that are both rheumatological and involve systemic involvement, such as systemic lupus erythematosus.[16,17] Clinical studies exist that have examined the relationship of proportional evaluation of hemogram data in malignant diseases with both systemic side effects and increased inflammation, as well as with survival.[18,19] Although a disease may be local, it is important to investigate its systemic effects and the adverse outcomes they bring. In our study, it was possible to observe these systemic effects in a highly prevalent disease with significant complications, such as diabetes. The suppression of inflammation in diabetic neuropathy has been identified as highly important for treatment and has become a therapeutic target.[20] Our study highlights that the significant value of proportional evaluations, particularly those based on monocyte levels which were associated with diabetic neuropathy, points to increased inflammation in diabetic neuropathy and suggests a potential role of autoimmunity, even in type 2 diabetes. Our study observed the utility of hemogram data for detecting inflammation and monitoring treatment response. Liu et al.[21] conducted a similar study on diabetic retinopathy, evaluating its association with the NLR and platelet levels. Likewise, Tuncer et al.[12] also investigated hemogram parameters in diabetic neuropathy, as in our study. The difference of our study from the existing one is that it allows for a comparison with a group of DM patients in whom neuropathy was not detected, thus providing results directly related to the complication.

The HbA1c distribution of the patient individuals included in the study was observed across a wide scale. Of the 50 patients, 22 (48.9%) were within the target HbA1c range, while 23 (51.1%) individuals were considered to have uncontrolled DM based on the age-specific target ranges set by the SEMT. This situation indicates that more than half of the individuals are still not regulated, are highly susceptible to complications, and demonstrates how high the risk remains. When NLR, PLR, and MLR were analyzed between the groups in remission and not in remission based on the target HbA1c level for diabetes regulation, no difference was observed (p=0.108; 0.114; 0.287). However, in unregulated individuals, the fact that NLR, PLR, and MLR averages were detected as higher—although the difference was not statistically significant—could be evaluated as being associated with increased inflammation in DM not in remission. Increased inflammation in cases of poor glycemic control was investigated by Hofmann et al.,[22] who also highlighted its detectability in peripheral blood mononuclear cells. This condition has been studied for many years, with a similar study conducted on type 1 DM as early as 2001.[23] While type 1 DM has a well-established autoimmune association, studies have been conducted on undefined autoimmunity underlying the family history in T2DM.[24] It is suggested that poor glycemic control, complicated by an autoimmune background, may bring about numerous complications. Increased microalbuminemia in unregulated DM was associated with the NLR in a study conducted by Öztürk.[25] Furthermore, the fact that the inflammation caused by dyslipidemia in diabetes has also been investigated in diabetic neuropathy using the NLR and PLR demonstrates the utility of these tools in yet another microvascular complication.[26] In our study, although inflammation was found to be somewhat higher when remission was not

achieved, the lack of statistical significance indicates the need for a larger-scale study, suggesting that a clear final result can only be provided in this way.

Based on the data, aside from proportional parameters in peripheral blood, a direct correlation was observed between glucose toxicity and the following: HbA1c showed a correlation with monocyte levels (p=0.009), and glucose levels showed a correlation with lymphocyte count (p=0.006). This result was interpreted as indicating that glucose has adverse effects on bone marrow or on the process of cellular transformation in peripheral blood. A clinical study exists on the effect of insulin resistance on lymphocyte morphology.[27] However, studies generally focus on proportional evaluations. Although Sözel et al.[28] also address glucose toxicity that begins with impaired glucose tolerance, their study likewise discusses proportional hemogram data. The fact that monocyte and lymphocyte levels, which are not directly evaluated in relation to inflammation, are affected by glucose toxicity was considered to be in favor of glucose's adverse effects on the developmental pathway of blood cells. However, obtaining sufficient evidence for this would likely only be possible through bone marrow sampling or by investigating stem cells in peripheral blood.

CONCLUSION

As a result, diabetic neuropathy is an undesirable complication of diabetes, and in individuals currently in remission, it may have occurred as a result of previous long-term glucose toxicity. Early detection and diagnosis of diabetic neuropathy is expected to reduce morbidity and mortality and increase the quality of life of individuals. The MLR was observed to be a usable parameter in this process and was evaluated as a clinically applicable tool, particularly as it was noted not to be directly influenced by raw hemogram data.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was initiated after obtaining approval from the Yozgat Bozok University Non-interventional Clinical Researches Ethics Committee (Date: 02.07.2025, Decision No: 2025-GOKAEK-2513_2025.07.02_531).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Evaluation of cerebrospinal fluid opening pressure and protein levels in relation to clinical profile and recovery in idiopathic intracranial hypertension

İlkin İyigündoğdu

Department of Neurology, Faculty of Medicine, Başkent University, Ankara, Turkiye

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Corresponding Author: İlkin İyigündoğdu, ilkiniyigundogdu@hotmail.com

ABSTRACT

Aims: Idiopathic intracranial hypertension (IIH) is an increase in CSF pressure without any other primary cause such as hydrocephalus, mass lesion, or meningeal abnormality. Evaluation of the severity of the disease and management of the treatment in patients are important for clinicians, and different parameters such as blood biomarkers and cerebrospinal fluid (CSF) opening pressure or protein levels are investigated. This study aimed to review the cases with IIH and evaluate the relationship between CSF opening pressure and protein levels obtained at the first presentation and the patient's clinical findings.

Methods: The data of patients diagnosed with IIH between 2012 and 2024 were retrospectively reviewed in the hospital electronic database, and demographic, clinical findings, neuroimaging results, and CSF analysis results were documented. The association between CSF opening pressure and protein levels obtained at the first presentation and the patient's clinical profile was analyzed. SPSS version 25 program was used in the statistical analysis of the data. $p<0.05$ was found to be statistically significant.

Results: Among 56 cases, 47 patients (83.9%) were female. The median age was 35 years. Visual impairment was the most common symptom (n=42, 75.0%). The mean of the CSF opening pressure was 332.68 mmH_2O, and patients had protein levels with a median of 27.05 mg/dl. Median CSF protein levels were found to be statistically significantly higher in patients presenting with decreased vision compared to those without (p=0.031). The number of patients with severe papilledema and decreased visual acuity was found to be significantly higher in the high CSF pressure group (p=0.041, p=0.042). Also, the number of patients with recurrent symptoms during the follow-up period was found to be significantly higher in high-pressure group (p=0.045).

Conclusion: In this retrospective study, clinical, laboratory, and radiological profiles of IIH patients were examined. Elevated CSF opening pressure in patients was found to be associated with visual impairment, increased symptom recurrence during follow-up, and severe papilledema; however, no association was observed with overall clinical recovery. CSF protein level was found to be associated only with improvement in visual acuity during follow-up. These findings underscore the need for multicenter studies to be conducted on this subject with a larger patient population to define the parameters and associations with the clinical course and prognosis.

Keywords: Idiopathic intracranial hypertension, headache, cerebrospinal fluid, protein, opening pressure

INTRODUCTION

Idiopathic intracranial hypertension (IIH), which was previously named benign intracranial hypertension or pseudotumor cerebral syndrome, is a disorder characterized by isolated increased intracranial pressure without any other primary cause.[1-3] Therefore, other primary causes of increased intracranial pressure, such as intracranial mass, cerebral venous thrombosis, or obstructive hydrocephalus, must be ruled out in patients with IIH.[3] Patients can have favorable outcomes with early diagnosis and management but permanent visual loss can be seen in patients, especially with anemia, obesity, high-grade papilledema, or rapid onset of disease and patients with severe symptoms can need invasive procedures.[1,2] Evaluating the severity of the disease and managing the treatment in patients is important

for clinicians as the prevalence of the disease increases worldwide.[1] However, differences in characteristics of the patients at presentation can vary between patients and make it hard to predict prognosis or plan the treatment and follow-up strategies.[1] Therefore, considering different parameters such as blood biomarkers, cerebrospinal fluid (CSF) opening pressure, or protein levels, is investigating.

There are only a few studies evaluating the associations between these parameters and symptoms or signs in patients with IIH. The aim of this study was to review the cases investigated in the neurology department with a diagnosis of IIH and evaluate the relationship between clinical symptoms and the profile of patients with CSF opening pressure and protein levels.

METHODS

The study was conducted with the permission of the Ethics Committee of Başkent University Faculty of Medicine and Health Sciences (Date: 04.06.2025, Decision No: KA25/218). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients evaluated with IIH in the neurology department in Başkent University Hospital between 2012 and 2024 were retrospectively investigated. The diagnosis of IIH was made according to the modified Dandy criteria (Table 1).[4] Patients who have cerebral venous thrombosis, intracranial mass, central nervous system inflammatory diseases, other diseases including optic nerve, or other primary causes that can cause increased intracranial pressure were excluded. Patients with results of CSF and imaging evaluated in other centers were not included in the study. Patients with inadequate information about the diagnosis or incomplete imaging or laboratory test results were also excluded.

Table 1. Modified Dandy criteria

1. Awake and alert patients
2. Symptoms and signs of increased intracranial pressure
3. Absence of focal signs on neurologic examination (6^{th} and 7^{th} cranial nerve palsies are permitted)
4. Normal diagnostic studies (neuroimaging and CSF analysis) except evidence for increased intracranial pressure
5.No other etiology for increased intracranial pressure identified

CSF: Cerebrospinal fluid

Baseline demographic data of the patients, including patients' sex, age at onset, and body-mass index (BMI), were recorded. Past medical history, presence of endocrine diseases, migraine, polycystic ovarian syndrome, and drugs that are used, such as levothyroxine, tetracycline, steroids, or vitamin A derivatives, were listed. Duration and characteristics of the symptoms, clinical presentation of the disease at onset, and clinical examination findings were retrospectively evaluated, and papilledema grade, severity, visual acuity, and visual field test results were recorded. Papilledema was classified according to the Frisén Scale,[5] and papilledema grade ≥2 was determined as severe papilledema.

Brain magnetic resonance (MR) images and cerebral MR venography images of patients were examined. Baseline hematological and biochemical blood test results were recorded. All patients underwent lumbar puncture (LP). CSF opening pressure which was measured during LP in lateral decubitis position with a manometer was recorded. CSF protein concentrations were measured using a standardized turbidimetric method, which is routinely employed in this center. The analysis was performed with an automated biochemistry analyzer (Abbott Alinity c-Series) and compatible reagent kits were used. All measurements were conducted in accordance with the laboratory's internal quality control protocols. The laboratory reference range for CSF protein was 15-45 mg/dl.

In this study, patients were further divided into two subgroups according to CSF opening pressure. A data-driven approach was adopted, using the median CSF opening pressure value of 340 mmH_2O within this population as the cut-off point. Accordingly, patients with CSF opening pressures ≤340 mmH_2O were classified as low-pressure group, while those with pressures above >340 mmH_2O were classified as the high-pressure group.

Medical and surgical treatment procedures were reviewed. Dosage and types of medical treatments were listed. The duration of follow-up period and advancements, and course of the disease during the follow-up period were investigated.

Outcome during the follow-up period with treatment modalities was reviewed and divided into four groups: "total regression", "partial regression", "unchanged", and "progressed" according to the course of headache, visual field defects, papilledema or visual acuity. For the visual outcome, the worst eye of the patients was chosen.

Statistical Analysis

The data analyses were performed using SPSS (Version 25.0). Numerical data with normal distribution were presented as mean±standard deviation, while data with skewed distribution were reported as median (interquartile range (IQR)). Categorical variables were presented as numbers and percentage values. For the comparison of categorical data, Pearson's Chi-square test and Fisher's exact test were performed. The Mann-Whitney U, Kruskal-Wallis, and independent samples t-test were used for the comparison of numerical data. p values <0.05 were considered statistically significant.

RESULTS

After exclusion criteria, data of 56 patients were analyzed. The majority of patients were female (n=47, 83.9%), and patients had a median age of 35 (IQR: 15) years. Nineteen patients (33.9%) had increased BMI (overweight or obese), and 6 patients (10.7%) had thyroid dysfunction and were using levothyroxine. Only 1 patient (1.8%) was using oral contraceptive drugs. No patient was using tetracycline, steroids, or vitamin A derivatives. One patient was pregnant at the time of diagnosis, and one patient was in the postpartum period. Median duration of the symptoms was 2 (IQR: 4.50) months in patients, and visual impairment was the most common symptom in patients (n=42, 75.0%). Headache was observed in 36 patients (64.3%) at admission. Demographic data of the patients and symptoms at admission were listed in Table 2.

Table 2. Demographic and clinical data of the patients

	n=56
Age, years, median (IQR)	35 (15)
Female gender, n (%)	47 (83.9%)
Comorbid diseases, n (%) Thyroid dysfunction Hypertension Diabetes mellitus	 6 (10.7%) 5 (8.9%) 3 (5.4%)
Migraine history, n (%)	4 (7.1%)
Patients with increased BMI, n (%)	19 (33.9%)
Symptoms of the patients	
Headache, n (%)	36 (64.3%)
Visual impairment, n (%)	42 (75.0%)
Tinnitus, n (%)	12 (21.4%)
Diplopia, n (%)	4 (7.1%)
Nausea, n (%)	8 (14.3%)
Dizziness, n (%)	3 (5.4%)
Duration of symptoms, months, median (IQR)	2 (4.50)
Features of headache, n(%)	
Unilateral	13 (23.2%)
Bilateral	23 (41.1%)
Throbbing	16 (28.6%)
Pressing or tightening Daily headache	20 (35.7%) 25 (44.6%)

IQR: Interquartile range, n: Number, BMI: Body-mass index

Papilledema was the most common examination finding and was found in 96.4% of the patients, mostly as bilateral. Nineteen patients had severe papilledema. Thirty-three patients (58.9%) had visual field defects. Signs and types of ocular examination findings of the patients were shown in Table 3.

Table 3. Frequency of ocular findings in patients with IIH

	n=56
Decreased visual acuity, n (%)	13 (23.2%)
Papilledema, n (%)	
Bilateral symmetrical	35 (62.5%)
Bilateral asymmetrical	15 (26.8%)
Unilateral	4 (7.1%)
Friesen scale, n (%)	
Grade 0	2 (3.6%)
Grade 1	35(62.5%)
Grade 2	11 (19.6%)
Grade 3	6(10.7%)
Grade 4	1(1.8%)
Grade 5	1(1.8%)
Visual field defect, n (%)	33 (58.9%)
Central scotoma	20 (35.7%)
Constriction of peripheral fields	10 (17.9%)
Arcuate field defect	3 (5.4%)
Abducens nerve palsy, (%)	2 (3.6%)

IIH: Idiopathic intracranial hypertension

All patients had cranial MR imaging, and 42 patients (75.0%) had cerebral MR venography. The major cranial MR imaging finding was perioptic subarachnoid space distension (POSD) with or without optic nerve tortuosity. According to the MR imaging findings: fifteen patients (26.8%) had POSD with or without optic nerve tortuosity, 14 patients (25.0%) had transverse sinus stenosis (TSS), 6 patients (10.7%) had POSD and partial empty sella sign (PES), 4 patients (7.1%) had TSS and POSD, and 1 patient (1.8%) had PES.

All patients underwent the LP procedure. The mean of the CSF opening pressure was 332.68 mmH_2O and patients had protein levels with a median of 27.05 (16.03) mg/dl. CSF cell counts were within normal limits, and CSF culture results were negative in all patients.

All patients were given medical treatment. Acetazolamide and topiramate were the most common options for medical treatment, either used alone or as multiple therapy. Thirty-seven patients (66.1%) were given acetazolamide as a monotherapy, 2 patients (3.6%) were given only topiramate, and 17 patients (30.4 %) were using both. The dose of diazomide was changing between 250 -1500 mg/day (median: 750 mg/day (IQR: 375)) in patients and topiramate was used in a range of 25-200 mg/day (median: 100 mg/day (IQR: 13)). Invasive procedures were suggested to 5 patients. Two patients had undergone ventriculoperitoneal shunt surgery, and one patient had optic nerve fenestration.

The median of the duration for the follow-up period was 9 months (IQR: 32). During the follow up period, 19 patients had repetitive LP. The median of the CSF pressure of the second LP was 250 mmH_2O (IQR: 90). During the follow-up no change was observed in the papilledema of 9 patients. While progression was observed in the papilledema findings of 3 patients (5.4%), total regression was observed in 17 patients (30.4%), and partial regression was observed in 25 patients (44.6%), respectively. When the change in headaches of the patients was evaluated during the follow-up period, partial improvement was observed in 21 patients (37.5%), total improvement was observed in 14 patients (25%), while no change was observed in the frequency or type of pain in 1 patient (1.8%). Improvement in visual acuity was observed at a lower rate during follow-up. While the decrease in visual acuity was completely resolved in only 3 patients (5.4%), partial improvement was observed in 2 patients (3.6%). No change was detected in visual acuity in 6 patients (10.7%). Progression and a decrease in visual acuity levels were observed during follow-up in 2 patients (3.6%).

The median CSF protein values were found to be significantly higher in men than in women (p=0.004). There was no significant difference in CSF protein levels with comorbid conditions, migraine history, or increased BMI. When the symptoms were evaluated, median CSF protein levels were only found to be statistically significantly higher in patients presenting with decreased vision compared to those without (p=0.031). No significant difference was observed between the groups in terms of decreased visual acuity, visual field defect, papilledema, or severity of papilledema in examination findings. No significant difference was observed between the groups in terms of median CSF protein values between treatment options or recurrence of complaints under treatment. When the clinical findings of the patients were evaluated during the follow-up period, no significant difference was observed in patients with headache and papilledema change, while CSF protein median

values were found to be significantly higher in patients with complete visual acuity recovery compared to those with no or partial recovery (p=0.022). Also in correlation analyses, no correlation was observed between CSF protein levels and age, duration of symptoms, and number of days with pain in patients with headache.

The CSF pressure was investigated in two groups as: the high-pressure group (>340 mmH_2O) and low-pressure group (≤340 mmH_2O). No difference was observed between the groups in terms of gender, age, and comorbid conditions. Only the number of patients presenting with visual impairment was found to be significantly higher in the high-pressure group (p=0.044). No difference was observed between the groups in terms of other symptoms at admission. In the examination findings, the number of patients with a decrease in visual acuity was found to be statistically significantly higher in the high-pressure group (p=0.042). No significant relationship was found between the presence of visual field defect, type of visual field defect, or the type of papilledema, but the number of patients with severe papilledema was found to be significantly higher in the high-pressure group (p=0.041). No difference was observed between the groups in cranial MRI findings or treatment options. The number of patients who underwent repeated LP and the number of patients who were recommended to have invasive procedures were found to be similar between the groups. The number of patients whose papilledema or headache improved during the follow-up period was higher in the first group, although the difference was not found to be statistically significant. Also, the number of patients with recurrent symptoms during the follow-up period was found to be significantly higher in high-pressure group (p=0.045) (Table 4).

Table 4. Comparison of patient characteristics and outcomes in low vs. high CSF opening pressure groups

	<340 (n=31)	>340 (n=25)	p value
Age, years, median (IQR)	32(14)	37(20)	0.282
Female, n (%)	27 (87.1%)	20 (80.0%)	0.472
Headache, n (%)	19 (61.3%)	17 (68.0%)	0.602
Visual impairment, n (%)	20 (64.5%)	22 (88%)	0.044
Decreased visual acuity, n (%)	4 (12.9%)	9 (36.0%)	0.042
Visual field defect, n (%)	17 (54.8%)	16(64.0%)	0.488
Bilateral papilledema, n (%)	23 (74.2%)	12 (48.0%)	0.073
Severe papilledema, n (%)	7 (23.3%)	12 (50.0%)	0.041
Regression of papilledema, n (%)	26 (86.7%)	16 (66.7%)	0.079
Total relief of headache, n (%)	9 (47.4%)	5 (29.4%)	0.352
Recurrence of symptoms, n (%)	5 (16.1%)	10 (40.0%)	0.045

CSF: Cerebrospinal fluid, IQR: Interquartile range

DISCUSSION

IIH is a rare disease with unknown etiology, and the disease is important for clinicians, as delayed access to care, diagnosis, and management can cause severe disability with permanent visual impairment and chronic headache.[1,6,7] Therefore, correct diagnosis and evaluation of the patients and early management are essential in patients.[7]

The recognition of the disorder has increased in recent years.[7] Both the increased recognition and increasing prevalence of obesity lead to an increase in the prevalence of IIH worldwide.[6] The incidence of IIH varies between regions across the world, with 0.5-2 per 100.000 people in the general population.[7] Western countries usually have higher incidence than Asian countries.[7] The disease is generally seen in young adults and is rare in patients with an age of >50 years.[3] Similarly, in this study, only 12.5% of the patients were older than 50 years. Most of the patients were found to be female, and the median age was found to be 35 years in this study, in accordance with the literature data from both Turkey and other countries.[6,8-10]

The pathogenesis of IIH remains poorly understood, and different mechanisms for the disease have been proposed.[3,11] One of the mechanisms is blockage of CSF absorption at arachnoid villi, which is caused by cerebral venous hypertension secondary to venous sinus stenosis.[3] The hyperemic hydrocephalus hypothesis, which is characterized by cerebral blood flow fluctuations, is another theory.[11] In addition, hormones and adipose tissue were suggested to play a role as a result of the increased incidence of disease in obese women.[3] The pathogenesis was also suggested to differ according to age or gender.[8] Since obesity is less common in Turkish and Asian populations compared to patients in Western countries.[8]

Thyroid dysfunction was the most common comorbid condition in this study. Similarly, Keskin et al.[8] reported that diabetes or thyroidopathy were the most frequent comorbid diseases (18.6%) in IIH patients in a study from Turkiye. However, Tian et al.[7] found anemia as the most common comorbid condition in patients.

Transient visual obscuration, visual impairment, or double vision are the visual symptoms that can be seen in IIH patients. Blurred vision or visual impairment was observed as the most common symptom of the patients in this study. In different studies approximately half of the patients were reported to have visual impairment,[2,10] however, in this study the symptom was detected more commonly, and 75% of the patients were observed to be admitted to the hospital with visual symptoms.

Headache is the second most common symptom in IIH in this study, with 64.3%. In the IIH Treatment trial, it was reported that 84% of the patients had headaches,[12] and in a study from Turkiye, Keskin et al.[8] reported that 78% of the patients had headache. Nausea and vomiting can accompany headache.[3] Generally, pain is aggravated with positions that increase intracranial pressure and increases in severity in the morning, however, different headache features can also be seen in IIH patients.[2,3] Most patients have bilateral headaches, although patients with unilateral headaches were also observed in this study (23.2%) which is consistent with other studies reported previously.[13] The frequency of the days with headache can vary between patients, but in this study, 44.6% of the patients were found to have daily headaches. However, in two different studies, it was more commonly reported as 75% and 78.95% of the patients.[10,13]

Pulsatile tinnitus is another common symptom of IIH and is observed in approximately 52-60% of the patients.[3] Both unilateral and bilateral tinnitus can be seen.[3] In this

study, 21.4% of the patients were found to have tinnitus, and in another study %8.5 of the patients were reported.[8] The frequency of occurrence can be different between studies since the patients do not report spontaneously or underestimate the symptom in mild cases.

The most common and important sign of IIH is papilledema.[3,14] Mostly it is bilateral symmetric, although rare cases with unilateral papilledema can be seen.[3,10,14] Only four patients were observed to have unilateral papilledema in this study. Also, in some cases, papilledema might not be observed, and this is suggested to be as a result of anatomical divisions of the subarachnoid space and prevention of the CSF pressure from reaching the retrolaminar part of the optic nerve.[3] In a study by Cho et al.[2] fundus examinations were found normal in 37.3% of the patients, and Sharma et al.[10] reported 5.74% of the patients had no papilledema. The severity of papilledema can be changed in patients. In this study most of the patients had grade 1 papilledema according to the Frisén Scale. However, in other studies, papilledema grade ≥2 was more commonly detected.[10,14]

Empty sella sign, posterior globe flattening, POSD with or without optic nerve tortuosity, and TSS are different MR imaging signs that are seen in IIH patients.[2,15] The presence of at least three signs could be sensitive for IIH, but the absence of MR imaging signs does not rule out IIH, and 71.4% of the patients were observed to have MR changes in this study.[15] Also, Bsteh et al.[15] found that at least one MRI sign is present in 78.6% of the patients. No significant association was found between MRI features and symptoms at initial presentation or examination findings in this study, similar to literature data.[15]

The mean opening CSF pressure was calculated as 332.68 mmH_2O in this study. There was no significant difference between male and female patients in terms of CSF opening pressure, consistent with other studies.[8] The data about CSF opening pressure and clinical evaluation or outcomes of patients with IIH are limited and vary between studies. Kattah et al.[16] reported a mild correlation between baseline CSF pressure and papilledema grade. Opening CSF pressure was not found to be associated with headache frequency, severity of headache, visual acuity, or presence of tinnitus. In this study severity of papilledema was found associated with CSF opening pressure similar to data reported previously.[10,16] Also, CSF opening pressure was found to be associated with decreased visual acuity in examinations of the patients. Only visual impairment was found significantly associated with increased opening CSF pressure. Similarly, Sharma et al.[10] also found an association between CSF opening pressure and visual impairment in literature data. Moreover, no other association was observed between CSF pressure and the presence and frequency of headache or other symptoms at admission in this study. In a different study comparing lower (200-250 mm) and higher (>250 mm) CSF opening pressure, patients with higher levels were observed to have more bilateral headaches, TVO, and horizontal diplopia with abducens palsy.[17] However, BMI, headache frequency, and other clinical features were not different.[17] Data about CSF opening pressure and MR imaging features are controversial. Sharma et al.[10] reported a significant correlation between CSF opening pressure and MR imaging signs except empty sella but in this study CSF opening pressure was not found to be associated with MR imaging signs or the number of MR imaging features, which is consistent with a study by Bsteh et al.[15]

In a study 64% of the patients were found to be stable or improved during the follow-up period.[8] Delay in treatment and generalized constriction in the visual field were observed to be associated with poor prognosis.[8] Cho et al.[2] reported that 61.5% of the patients who had 3-6 months of follow-up showed remission or improvement in over 50% of the headache status.

Age was not found associated with the visual prognosis;[9] similarly, in this study, no association was found between outcomes and age or gender. Although CSF total protein and increased opening pressure were independently associated with Humphrey visual field mean deviation in the worst eye on follow-up in a study, no significant association was observed between visual field defects or course of the defect and CSF protein or opening pressure in this study.[18]

For the follow-up period, CSF protein median values were only found to be significantly associated with complete visual acuity recovery compared to those with no or partial recovery. Also for the outcomes, no relationship was shown between regression of papilledema or headache and opening CSF pressure or CSF protein levels. Similarly, Takkar et al.[14] reported opening CSF pressure showed significant association with visual outcomes, but after adjusting for the vision at admission, no association was observed.

There are different data in the literature regarding the association between CSF protein levels and CSF opening pressure values.[18] In a study it was found that CSF total protein and CSF opening pressure have a negative linear association regardless of age, sex, and BMI in both pediatric and adult patients[18] but no significant correlation was found in this study.

Limitations

This study has several limitations that should be acknowledged. First, due to its retrospective design, the study relied on previously recorded data. Additionally, the study was conducted in a single center and sample size was relatively small that could potentially limit the generalizability of the findings to large populations. Also, the criteria for diagnosis of IIH have been revised over years, and cut-off values for opening CSF pressure can change between different classifications. This can cause discrepancies between studies. Moreover the variability in follow-up durations among patients may have influenced the assesment of clinical outcomes. Future prospective studies with larger cohorts and standardized follow-up periods are needed to elucidate the relationships between CSF characteristics and clinical features in IIH.

CONCLUSION

In this study, IIH patients who applied to a tertiary health institution were evaluated retrospectively and their clinical, laboratory, and radiological profiles were examined. Data on CSF pressure and clinical findings in the literature

show differences between regions. CSF opening pressure in patients was found to be associated with decreased vision clinically and increased frequency of symptom recurrence during follow-up and severe papilledema as a finding. While no relationship was observed between clinical recovery rates and opening CSF pressure, CSF protein level was found to be associated only with improvement in visual acuity during follow-up. The lack of a significant relationship between clinical recovery parameters and other examination parameters emphasizes the importance of individualized treatment and follow-up strategies. In order for CSF protein and opening pressure levels in IIH patients to be a guiding parameter for the clinician regarding the clinical course during the follow-up process, multicenter studies should be conducted on this subject with a larger patient population.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of the Ethics Committee of Başkent University Faculty of Medicine and Health Sciences (Date: 04.06.2025, Decision No: KA25/218).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The author has no conflicts of interest to declare.

Financial Disclosure

The author declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Case Report

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Spontaneously resorbed lumbar disc herniation: two case reports

Ulaş Yüksel, Alemiddin Özdemir, Özge Aydın

Department of Neurosurgery, Faculty of Medicine, Kırıkkale University, Kırıkkale, Turkiye

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Corresponding Author: Ulaş Yüksel, ulasyks@hotmail.com

ABSTRACT

It has been reported that patients with lumbar disc herniation, particularly those without severe symptoms, may benefit from conservative treatment, and spontaneous resorption of the herniated disc can occur in the natural course of some cases of lumbar disc herniation. In this study, two patients with intervertebral disc herniation were discussed: one with a right lateral recess at the lumbar 3-4 level, causing compression of the right lumbar 4 nerve root, and the other with a left lateral recess at the lumbar 2-3 level, causing compression of the left lumbar 3 nerve root. Both patients exhibited no significant neurologic or functional deficits, except for radicular pain. Magnetic resonance images of both patients revealed that the herniated disc material had migrated within the spinal canal, and the T2 signal intensity was increased; therefore, these herniated discs were considered to be soft. Both patients underwent conservative treatment. Follow-up magnetic resonance images showed the complete disappearance of the herniated disc material at five months for one patient and at nine months for the other. In conclusion, conservative treatment methods should be preferred for lumbar disc herniation patients without severe symptoms. Furthermore, the herniated disc material may undergo resorption and even completely disappear with close follow-up of this patient group.

Keywords: Lumbar disk herniation, spontaneous disk resorption, extrusion, magnetic resonance imaging

INTRODUCTION

Deciding whether to perform surgery for lumbar disc herniation (LDH) and selecting the appropriate procedure depends on the severity of the symptoms and the relationship between the clinical, physio-pathological, and radiological findings. However, the choice of treatment also takes into account the patient's and/or the surgeon's preferences.[1]

In the literature, the presence of disc extrusion, "cauda equina" syndrome, severe motor deficits/disabilities, and persistent pain is reported as absolute indications for surgical intervention. Although surgical intervention has advantages such as rapid symptom relief, increased stability, facilitated bone healing, and restoration of alignment, several randomized controlled trials have shown that the clinical findings between conservative and surgical treatment in LDH patients with radiculopathy were similar one year after diagnosis.[1] Some patients with LDH, particularly those without severe symptoms, may benefit from conservative treatment. Some of the patient's clinical symptoms will soon subside or completely resolve. In fact, given that spontaneous resorption of herniated discs is often present in the natural history of some LDH, symptoms will resolve spontaneously in some patients.[2] In the literature, there is no optimal treatment scheme for massive LDH, which is only associated with pain, and clear indications for surgical treatment have not been established yet.

This study discussed two patients with LDH who underwent conservative treatment and experienced rapid, spontaneous disc resorption by the end of the treatment period.

CASE 1

A 57-year-old man was admitted to the neurosurgery outpatient clinic complaining of pain in his right leg. He had pain in his right buttock that radiated to the front of his thigh. His neurogenic claudication threshold was 500 meters, and he had no urinary or fecal incontinence. On examination, there was no motor deficit, the right Lasègue's sign was positive, and the Faber and Fadir tests were negative. The patient had hypoesthesia in and below the dermatome from which he experienced pain. Deep tendon reflexes were normal. Lumbar T2-weighted magnetic resonance (MR) imaging showed an extruded, downward-migrated disc herniation at the lumbar (L) L3-4 level. This was located in the right lateral recess and was compressing the right L4 nerve root (Figure 1). Surgery

was not considered as the patient had no motor deficit and the herniated disc fragment appeared as an edematous soft disc on MR images.

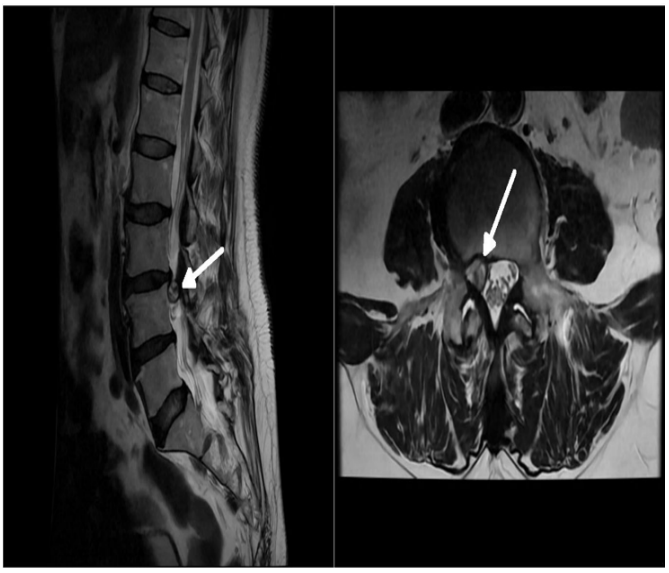

Figure 1. Lumbar T2-weighted MR imaging of a 57-year-old man showed an extruded and downward-migrated disc herniation at the L3-4 level, which was located in the right lateral recess and compressed the right L4 nerve root (indicated with a white arrow).

The patient attended a follow-up appointment two months later. His symptoms were ongoing. Repeated examination revealed no motor deficit; however, the Lasègue sign remained positive, and hypoesthesia persisted. Lumbar MR scan showed that the shape and location of the disc fragment had not changed (Figure 2A). Because MR images with gadolinium, which were used to differentiate between a possible facet or ligamentum flavum cyst and other masses, revealed an extruded soft disc herniation with dense edema, conservative treatment was continued.

When the patient attended a follow-up appointment five months later, it was established that his symptoms and hypoesthesia had improved. Neurological examination revealed complete muscle strength and a negative Lasègue's sign. Control lumbar MR scan with gadolinium showed that the disc fragment had completely disappeared and that the right nerve root had been relieved (Figure 2B).

CASE 2

A 42-year-old man attended the neurosurgery outpatient clinic complaining of worsening low back pain over the previous two weeks. The pain radiated from his lower back down through his left buttock and into his left toe. His neurogenic claudication threshold was 500 meters. There was no urinary or fecal incontinence. Lasègue's sign was negative, and the left Faber test was positive. The muscle strength evaluation revealed that left hip flexion and extension were 4+/5, and left foot dorsiflexion was 4+/5. The patient's lumbar MR images revealed an extruded and upward-migrated disc herniation at the L2–L3 level. This was located in the left lateral recess, severely compressing the left L3 nerve root. The herniated part was soft and swollen (Figure 3A). Surgery was not considered initially because the patient did not have severe motor deficits and had a soft herniated disc with dense oedema.

Ten months later, at the follow-up appointment, it was found that the patient's symptoms had improved significantly. Neurological examination revealed complete muscle strength, normoactive deep tendon reflexes, and negative Lasègue's, Faber's, and Fadir's tests. The patient had no urinary or fecal incontinence. Control lumbar MR images showed that the herniated disc had disappeared completely and that the left nerve root was free through its neural foramen (Figure 3B).

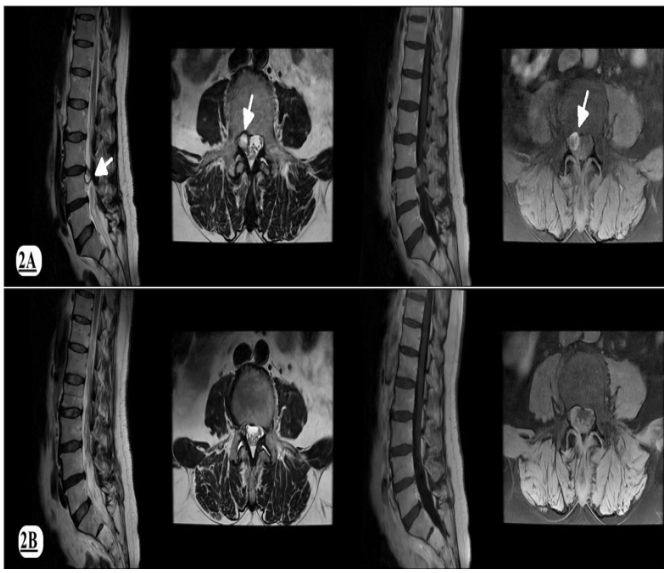

Figure 2. Lumbar MR images of a 57-year-old man scanned at a follow-up visit two months later showed the same shape and the location of the soft disc fragment with dense edema. MR images with gadolinium revealed that this extruded disc fragment showed high contrast enhancement (indicated with a white arrow) **(2A)**. T2-weighted MR and MR images with gadolinium checked five months later revealed that the disc fragment in the patient had completely disappeared, and the right root was relieved **(2B)**.

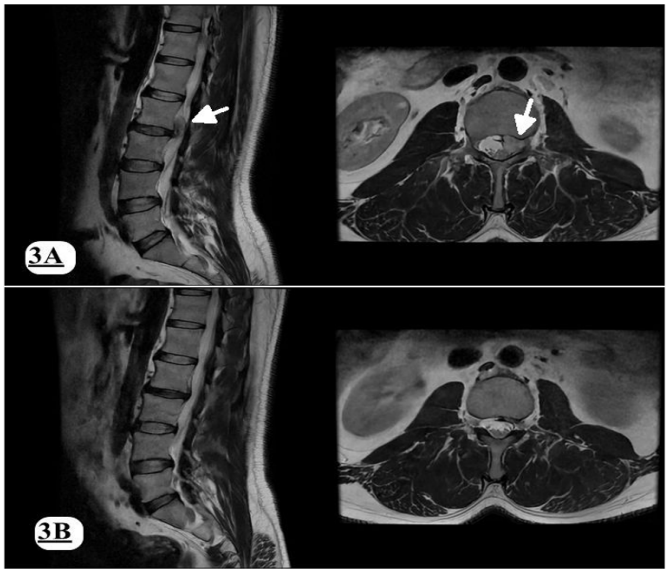

Figure 3. T2-weighted MR images of a 42-year-old man showed an extruded and upward migrated disc herniation at the L2-3 level, and it was located in the left lateral recess with severe compression of the left L3 nerve root. The herniated part was observed as soft and edematous (indicated with white arrow) **(3A)**. Control T2-weighted MR images of the patient examined nine months later showed that the herniated disc had disappeared completely, and the left nerve root was free throughout its foramen **(3B)**.

DISCUSSION

The choice of treatment strategy for LDH should be based on the severity of the disease and the patient's general condition. Choosing the non-surgical or surgical treatment depends on the severity of symptoms and the clinicopathologic correlation. However, the decision on the treatment strategy is partly preference-sensitive, depending on the surgeon's preference, which is influenced by the physician's experience and patients' expectations.[3] On the other hand, the natural history of LDH is not fully understood, but it is well-known that herniated disc fragments can spontaneously resolve over time. Cribb et al.[4] reported that repeated MR scans performed on average 24 months later showed dramatic resolution of massive LDH in 14 out of 15 patients. In both of our patients, MR scans showed that the herniated disc was severely edematous in soft nature, but despite this, there was no significant neurological loss. Since the patients did not have severe neurologic loss and did not have pain or loss of function (such as drop foot, incontinence, neurologic claudication, or erectile dysfunction) that severely affected their quality of life, surgical treatment was not considered as a treatment option. Therefore, conservative treatment methods (such as using analgesics and muscle relaxants, absolute bed rest for at least one week followed by physiotherapy, weight loss, exercises including walking, and swimming) were preferred. Indeed, these conservative treatment method results showed that the patient's complaints were completely resolved within an average of one year, and there was no additional neurologic deterioration during this period.

Recently, Chiu et al.[5] reported that the predictive factors for spontaneous regression of herniated disc were extruded and sequestered herniation types, migrated disc, transligamentous herniation, herniation showing contrast enhancement, and high T2 signal intensity of the herniated disc on MR images. They also reported that the spontaneous regression rate was 96% for disc sequestration, 70% for disc extrusion, 41% for disc protrusion, and 13% for disc bulging. In another study, a decrease in disc size was observed in 7 of 8 patients with migrated discs, suggesting that migrated discs are a strong predictive factor for spontaneous regression of LDH.[6]

On the other hand, the literature suggests three potential hypotheses for the process of disc resorption: "retraction", "dehydration and shrinkage", and "inflammatory response and neovascularization". In particular, it has been argued that an inflammatory response and neovascularization lead to the gradual resorption of cartilage tissue through enzymatic degradation and phagocytosis. Intervertebral disc tissue possesses antigenic properties and is separated from the human immune system by the annulus fibrosus. When this tissue detaches from the annulus, it behaves like a foreign body, prompting an autoimmune reaction. Tumor necrosis factor-α is present in the area following disc herniation and triggers significant interleukin secretion. This can facilitate the absorption of herniated disc tissue by promoting aggregation of the macrophages. This process involves crucial apoptosis-related factor ligands that induce apoptosis and mediate inflammation. They induce apoptosis and mediate inflammation.[7] In this context, Kobayashi et al.[8] examined the intervertebral disc herniation tissue obtained from patients who underwent surgery for LDH, using light microscopy and electron microscopy. They found that new microvessels had penetrated the epidural space and emerged around the tissue of the intervertebral disc, causing localized inflammatory reactions and intense infiltration of macrophages.

Our patients had extruded and migrated discs, and these herniated discs exhibited high T2 signal intensity on MR images. Especially in the first case, the contrast-enhanced lumbar MR images revealed that the disc herniation persisted, the T2 signal intensity remained high, and the extruded disc showed intense contrast enhancement following the administration of gadolinium intravenously. We hypothesized that this intense contrast enhancement and high T2 signal intensity were secondary to neovascularization and inflammatory reactions against the extruded disc. For this reason, we concluded that the reason for the complete disappearance of the herniated discs in the MR images of both patients was not due to "retraction", "dehydration, and shrinkage", but rather a foreign body reaction (phagocytosis by macrophages migrating into the environment after neovascularization) against the herniated discs.

Autio et al.[9] reported that the 41–50 age group was associated with a higher resorption ratio of the herniated discs. The authors suggested that herniated discs in older patients are harder, more fibrotic, and drier than those in younger patients. They also found that the presence of less nucleus pulposus tissue and more annulus fibrosus and cartilaginous endplate material in herniated discs inhibits neovascularization around the disc. Conversely, Seo et al.[10] reported that the extent of LDH resorption was not associated with age, and the volumetric increase was higher in older patients than in younger patients. Our patients were aged 40-60 years. Additionally, MR images revealed high T2 signal intensity and significant contrast enhancement in the herniated disc tissue. Therefore, the intervertebral disc material in our patients was soft and, more importantly, edematous with increased vascularity. For this reason, it was thought that the water content of the intervertebral disc material may still be high in the young middle-aged patients. Furthermore, the absence or minimal neurological deficit in patients supported the idea that the disc material compressing the neural tissues may have a soft consistency.

CONCLUSION

This study found that conservative treatment methods could be preferable for patients with LDH who do not experience severe symptoms such as persistent pain, "cauda equina" syndrome, or motor/functional loss. Furthermore, close monitoring of this patient group revealed that the herniated disc material may undergo resorption or even disappear completely. In conclusion, these observations suggest that conservative treatment options could achieve similar clinical results to surgery for this patient group, while avoiding the various early and late complications that surgery may cause.

ETHICAL DECLARATIONS

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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Author Contributions

All authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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Letter to the Editor

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Letter to "Investigation of cognitive decline in patients with COVID-19 syndrome within 12 weeks after infection"

Edip Varan

Department of Neurology, Beypazarı State Hospital, Ankara, Turkiye

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Corresponding Author: Edip Varan, edp1990@hotmail.com

Keywords: COVID-19 syndrome, cognitive decline, cognitive test, post-acut COVID syndrome

Dear Author,

I had the pleasure of reading and reviewing your study titled "investigation of cognitive decline in patients with COVID-19 syndrome within 12 weeks after infection." This research addresses a critical area of concern, as the cognitive effects of COVID-19 have become increasingly recognized in the medical community.

A substantial amount of literature exists regarding the examination of cognitive functions in patients who have experienced COVID-19. For instance, in a study conducted by Colvin et al.[1] involving 574 patients, the cognitive functions of those recovering from COVID-19 were assessed. The findings highlighted significant differences in cognitive abilities among groups with varying academic performances, suggesting that educational background may play a role in cognitive recovery. The study emphasized the importance of ensuring that patients have similar educational levels to accurately assess cognitive decline.

Similarly, Becker et al.[2] conducted a study with 740 participants, where they evaluated the cognitive functions of COVID-19 patients. Their findings indicated that cognitive decline was less pronounced in patients who experienced mild COVID-19 while receiving outpatient treatment. This suggests that the severity of the infection may be correlated with the extent of cognitive impairment experienced.

In a large-scale randomized study by Tang et al.,[3] which included 32.494 cases of SARS-CoV-2 infection, 8,316 hospitalized COVID-19 patients, and 4.792 severe COVID-19 cases, it was found that cognitive decline was more significant in those who were hospitalized and experienced severe symptoms compared to those with mild infections. This further underscores the need to differentiate between varying severities of COVID-19 when assessing cognitive outcomes.

Additionally, Hampshire et al.[4] conducted research in the UK with 112.964 participants, focusing on cognitive functions associated with COVID-19 infection. Their findings revealed that cognitive decline was more pronounced during the early stages of the pandemic compared to later phases. They also noted that individuals who experienced severe COVID-19 demonstrated greater cognitive decline than those who had mild infections or did not contract the virus at all.

Your study raises an important point regarding the necessity of evaluating cognitive functions prior to COVID-19 infection, as this could help determine whether the observed cognitive decline is indeed attributable to the virus. Many prior studies lack pre-COVID assessments using tools such as the Montreal Cognitive Assessment (MoCA) test, which could provide crucial baseline data.

There are still numerous unknowns associated with COVID-19, and your research contributes significantly to clarifying the cognitive implications of the infection. This study serves as an important piece of work that illuminates the complexities surrounding cognitive effects in COVID-19 patients. Previous studies have established that cognitive function is influenced by academic performance in patients who have contracted COVID-19. Therefore, increasing the patient sample size and conducting the study within a more homogeneous group could enhance the robustness of the findings.

Furthermore, separating the analysis of patients who experienced mild COVID-19 infections from those who

were hospitalized and faced severe illness would provide deeper insights into the cognitive outcomes related to varying severities of the disease.

Thank you for your contribution to this important field of research.

Sincerely yours,

ETHICAL DECLARATIONS

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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