Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Evaluation of the Frequency of Patent Foramen Ovale in Children with Migraine: A Prospective Case-Control Study

Delil Ekinci
Dicle University Medical Faculty
Alper Akın
alperakin1@hotmail.com
Dicle University Medical Faculty
Rojan İpek
Dicle University Medical Faculty
Mehmet Ture
Dicle University Medical Faculty
Duygu Uç
Dicle University Medical Faculty

Research Article

Keywords: Migraine, Patent Foramen Ovale, Electroencephalography, Child

Posted Date: February 26th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-8817540/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Objective: To evaluate the frequency of patent foramen ovale (PFO) in children with migraine and to assess its association with clinical characteristics, heart rate, and electroencephalography (EEG) findings. This prospective study included children aged 5-18 years diagnosed with migraine according to the International Classification of Headache Disorders criteria, and a control group of age-and sex-matched healthy children. Transthoracic echocardiography was performed to determine the presence of PFO. Electroencephalography was conducted in the migraine group. Clinical and laboratory data were compared between migraine patients with and without PFO. PFO was detected in 15 of 71 children with migraine (21.1%) compared with 2 of 71 control subjects (2.8%), demonstrating a significantly higher prevalence in the migraine group ($p<0.003$). The migraine patients with PFO had a significantly higher mean resting heart rate than those without PFO ($p<0.001$), although all values were within age-appropriate physiological limits. EEG evaluation was performed in 59 migraine patients and revealed epileptiform abnormalities in 9 patients (15.3%). The frequency of pathological EEG findings did not differ significantly between migraine patients with and without PFO ($p<0.261$). None of the patients had clinical epilepsy, and cranial MRI findings were normal in all cases. Children with migraine exhibit a higher prevalence of patent foramen ovale compared with healthy peers. Notably, migraine patients with PFO showed higher resting heart rates than those without PFO, suggesting potential involvement of autonomic regulation. The lack of association between PFO and EEG abnormalities indicates that the migraine–PFO relationship in childhood is most likely indirect and multifactorial. These findings indicate the need for larger studies on neurocardiac interactions in patients with migraine and PFO.

Introduction

Migraine is known to be a common neurological disease usually characterized in children by a bilateral, recurrent, severe, compressive, throbbing headache. Although these attacks are often accompanied by photophobia and phonophobia, sensory disorders such as nausea and vomiting may also be seen and this can seriously affect the quality of life of the individual [1–3]. As migraine in childhood represents one of the primary types of headache most frequently seen in the paediatric population, it is an important public health problem. The prevalence of migraine in children and adolescents, most of which are migraine without aura, has been reported at rates varying between 4% and 11%, depending on age and demographic factors [4].

Patent foramen ovale (PFO) is known to be a common congenital cardiac anomaly characterized by a permanent opening between the right and left atriums. Although this opening typically closes a short time after birth, it remains open throughout life in approximately 25% of the general population, and studies have drawn attention to the relationship with different diseases, primarily migraine. Many studies in the literature have suggested that individuals with PFO have a higher prevalence of migraine attacks than those without PFO [5–9]. From the filtering effect of pulmonary circulation because of shunt from right to left in the presence of PFO, microembolic particles and vasoactive substances can escape and reach systemic circulation and cerebral circulation, and it has been suggested that this can trigger

neurovascular processes such as cortical spreading depression which contribute to migraine pathogenesis [10]. The aim of this study was to contribute to the literature about the effects of PFO on migraine in children by investigating PFO frequency in paediatric patients with migraine.

Methods

Study Design

This prospctive study included patients aged 5–18 years who were diagnosed with migraine in the Paediatric Neurology Polyclinic of Dicle University Medical Faculty Hospital between 1 September 2023 and 1 September 2024. The diagnosis of migraine was made as a result of a detailed clinical evaluation performed by a paediatric neurology specialist, based on the International Classification of Headache Disorders, 3rd edition (ICHD-3) diagnostic criteria published by the International Headache Society (IHS) [11]. A detailed neurological examination was performed to discount secondary headache causes with the application of neuro-imaging and additional tests.

To evaluate the presence of PFO in the children diagnosed with migraine, 12-channel surface electrocardiography (ECG) was performed and evaluated by a paediatric cardiology specialist. Transthoracic echocardiography (TTE) performed by a paediatric cardiology specialist was evaluated for the presence of PFO. Contrast echocardiography was not routinely applied, but was only used in cases where it was seen to be clinically necessary.

Echocardiography evaluations were performed independently of clinical data by two experienced paediatric cardiology specialists to decrease observer-dependent differences, and in cases with a difference of opinion, a consensus was reached. The echocardiographic examinations were made according to the American Echocardiography Society and paediatric echocardiography guidelines [12]. During the examination, the parasternal long and short axes, apical four chamber, and especially the subcostal four chamber windows were used. In the interatrial septum evaluation, the fossa ovalis region was examined in detail with high resolution two-dimensional imaging. The presence of PFO was evaluated based on the echocardiographic findings below:

- Observation of a thin flap-like septal structure at the level of the fossa ovalis
- On colour Doppler examination, visualisation of temporary and phasic current passage from the interatrial septum
- The current is from right to left or biphasic at rest or with provocation

A control group was formed of children of similar age and gender to the patient group, who were not diagnosed with migraine. Echocardiography and ECG examinations were made of all the control group subjects and the findings were compared with those of the patient group.

Study Inclusion Criteria

1. A diagnosis of migraine according to the ICHD classification for headache diagnosis between 1 September 2023 and 1 September 2024,
2. Age between 5 and 18 years,
3. Acceptance of participation in the study provided by the patient and parents,
4. No other disease determined which could cause the symptoms.

Study Exclusion Criteria

1. Diagnosis other than migraine or the presence of clinical neurological findings suggesting secondary headache,
2. Age younger than 5 years or older than 18 years,
3. Unwillingness to participate in the study of the patient or parents.

Approval for the study was granted by the Clinical Research Ethics Committee of Dicle University (protocol no: 345, dated:13.09.2023). All the study procedures were in compliance with the Helsinki Declaration.

Statistical Analysis

Data obtained in the study were analyzed statistically using SPSS vn. 24.0 software (SPSS Inc., Chicago, IL, USA). Conformity of numerical variables to normal distribution was assessed with the Kolmogorov-Smirnov test. Continuous variables were stated as mean ± standard deviation (SD) values when normal distribution was seen and as median, minimum-maximum values when distribution was not normal. Categorical variables were stated as number (n) and percentage (%). In the comparisons of two groups of continuous variables, the Student's t-test or the Mann Whitney U-test was used. The Chi-square test was applied in the comparisons of categorical data. To determine correlations between measured variables, the Pearson correlation test was applied to variables with normal distribution and Spearman correlation analysis to variables not showing normal distribution, and correlation coefficients were calculated. A value of $p < 0.05$ was accepted as the level of statistical signficance.

Results

Evaluations were made of the patient group of 71 children diagnosed with migraine (Group 1) and the control group of 71 children not diagnosed with migraine (Group 2). The patient group comprised 39 (55%) females and 32 (45%) males with a mean age of 13.23 ± 3.08 years (range, 6–17 years) and the control group comprised 30 (42%) females and 41 (58%) males with a mean age of 11.87 ± 3.47 years. There was no statistically significant difference between the groups in respect of age and gender ($p = 0.131$, $p = 0.156$). The anthropometric measurements of all the study participants, the systolic and diastolic blood pressure values, transcutaneous oxygen saturation and heart beats per minute are shown in Table 1.

Table 1
The anthropometric, blood pressure, heart rate and oxygen saturation values of the patients with migraine (n:71)

	Mean ± SD	**Min-max**
Age (years)	13.23 ± 3.08	6.00–17
Body weight (kg)	45.69 ± 13.37	20–83
Height (cm)	152.85 ± 15.04	115–182
Body Mass Index (kg/m^2)	19.20 ± 3.55	11.84–28.89
Systolic blood pressure (mmHg)	113.24 ± 7.69	90–125
Diastolic blood pressure (mmHg)	69.96 ± 6.50	60–85
Heart rate (beats/min)	85.11 ± 11.38	60–112
Oxygen saturation (%)	95.82 ± 1.17	94–98

In the examinations of the laboratory data of the patients the mean serum Vitamin B12 level was determined to be 250.39 ± 191.14 (14.33–1278.00) pg/mL, mean serum ferritin level 24.11 ± 18.41 (2.84–117.40) ng/mL, mean serum folate level 8.87 ± 2.97 (3.40-18.05) ng/mL, mean thyroid stimulating hormone (TSH) level 2.18 ± 1.65 (0.50–13.40) μIU/mL, mean thyroxin (T4) level 0.97 ± 0.18 (0.62–1.66) μg/dL, and mean serum Vitamin D level 15.06 ± 9.03 (3.55–57.82) ng/mL.

Of the 71 patients in Group 1, 70 were diagnosed with migraine without aura, and 1 with aura. Cranial magnetic resonance imaging (MRI) was performed on all 71 patients in Group 1, and electroencephalographic (EEG) evaluation was made of 59. The cranial MRI findings of all the patients were evaluated as normal. Of the 59 patients who underwent EEG examination, the EEG findings were determined to be normal in 50 (84.75%) and showed epileptiform activity in 9 (15.25%). No clinical epilepsy was determined in any of the patients with epileptiform EEG findings (Table 2).

Table 2
Cranial MRI and EEG results of the migraine patients.

		n	**%**
MRI	Normal	71	100
EEG	Normal EEG	50	84.7
	Pathological EEG (epileptiform)	9	15.2
MRI: Magnetic resonance imaging, EEG: Electroencephalography			

The ECG findings of all the children in both groups were evaluated as normal. In the echocardiographic examination, 55 (77.5%) patients in Group 1, and 68 (95.8%) control group subjects in Group 2 were

evaluated as normal, and PFO was determined in 15 (21.1%) patients in Group 1 and in 2 (2.8%) children in Group 2. A secundum atrial septal defect (ASD) was determined in one case in each group. The frequency of PFO was determined to be statistically signiificantly higher in the patient group with migraine ($p = 0.003$).

The patients with migraine in Group 1 were separated into two sub-groups as those with PFO (Group 1a) and those without PFO (Group 1b). The mean heart rate was determined to be 93.93 ± 11.62 bpm in Group 1a and 82.87 ± 10.23 bpm in Group 1b. The difference was found to be statistically significant ($p < 0.001$). Other examination and laboratory data showed no significant differences between Groups 1a and 1b (Table 3).

Table 3
Comparisons of the physical examination and laboratory data of the migraine patients determined with PFO (Group 1a) and without PFO (Group 1b)

	ECHO	n	Mean + SD	P*
BMI (kg/cm^2)	Group 1b	55	19.35 ± 3.66	0.354
	Group1a	15	18.38 ± 3.11	
Oxygen saturation (%)	Group 1b	55	95.69 ± 1.06	0.190
	Group1a	15	96.13 ± 1.40	
SBP (mmHg)	Group 1b	55	113.31 ± 7.69	0.732
	Group1a	15	112.53 ± 7.99	
DBP (mmHg)	Group 1b	55	70.22 ± 6.91	0.418
	Group1a	15	68.67 ± 4.86	
Heart rate (beats/min)	Group 1b	55	82.87 ± 10,23	**< 0.001***
	Group1a	15	93.93 ± 11.62	
Vitamin B12 (pg/mL)	Group 1b	55	245.04 ± 200.59	0.563
	Group1a	15	277.73 ± 160.04	
Ferritin (ng/mL)	Group 1b	55	25.24 ± 20.29	0.278
	Group1a	15	19.35 ± 8,51	
Folate (ng/mL)	Group 1b	54	8.69 ± 2.97	0.249
	Group1a	15	9.70 ± 2.93	
TSH (µIU/mL)	Group 1b	54	2.02 ± 0.97	0.417
	Group1a	15	2.70 ± 3.09	
T4 (µg/dL)	Group 1b	54	0.96 ± 0.18	0.539
	Group1a	15	0,99 ± 0.18	
Vitamin D (ng/mL)	Group 1b	51	14.08 ± 6.56	0.284
	Group1a	13	18.88 ± 15.13	

n: number of patients, SD: Standard deviation, BMI: body mass index, kg/cm²: kilogram/centimetres squared, SBP: Systolic blood pressure, DBP: Dyastolic blood pressure, TSH: Thyroid Stimulating Hormone, T4: Thyroxin, ECHO: Echocardiography, PFO: Patent Foramen Ovale.

**comparisons between groups were performed with the Student's t-test. A value of p < 0.05 was accepted as statistically significant.*

In the comparisons of other data between Group 1a and Group 1b, the female/male ratio was determined to be 6/9 in Group 1a and 32/33 in Group 1b ($p = 0.210$). The pathological EEG/normal EEG ratio was 3/9 in Group 1a and 6/41 in Group 1b ($p = 0.261$). No statistically significant difference was determined between the two groups in respect of gender distribution ($p = 0.210$) and EEG findings ($p = 0.261$).

Discussion

Migraine is a headache type that seriously affects daily life. Management and treatment are difficult, so the importance of comorbidities is increased. Patent foramen ovale (PFO) is a frequently seen congenital heart disease known to be associated with cerebrovascular events. Although many adult studies have been conducted about the relationship between the presence of PFO and migraine, very few studies have evaluated this relationship in children [7, 9, 13].

The vast majority of studies in literature that have evaluated the relationship between migraine and PFO have reported that female gender was more frequent in the group with migraine and PFO together [7, 14–16]. However, a significant proportion of those studies were of the adult population. Although the majority of the paediatric patients in the current study were female, no statistically significant difference was determined between males and females. The predominance of female gender in the current study was consistent with findings in the literature.

The frequency of PFO in the current study patients with migraine was determined to be higher than in the control subjects without migraine. Przemyslaw W. et al. [15] screened 816 adult patients in respect of ischaemic cerebrovascular event or transitory ischaemic attack, and PFO was determined in 224, of which 55% were also found to have migraine symptoms. Dalla et al. [17] reported PFO frequency of 61.9% in patients with migraine with aura, 16.2% in those with migraine without aura, and 36.8% in the group with cluster headache. The reason for the low number of cases of migraine with aura in the current study was thought to be that parents in our region are not aware of aura and therefore do not take their children to hospital at the time of an attack. In another study by Fu et al. [18], the PFO frequency was investigated in 170 migraine patients (85 with aura, 85 without aura) and a healthy control group of 85 subjects. Although no significant difference was determined in PFO frequency between the migraine groups with and without aura ($p = 0.427$), both groups were determined to have PFO at a statistically significantly higher rate than the control group ($p = 0.002$). There are few studies in the literature that have directly examined the relationship between PFO and migraine in children, and most of those studies have been conducted on small samples. Moreover, in a few studies there has been found to be no statistically significant relationship or there has been seen to be insufficient evidence supporting the relationship. This demonstrates that the evidence of a relationship between migraine and PFO is limited and inconsistent.

While the relationship between PFO and migraine in children is much more evident with the presence of aura, the PFO prevalence in migraine cases without aura has not shown a significant difference when

compared with the general population [16, 9]. McCandless RT et al. [16] investigated PFO in 109 children with migraine in the 6–18 years age range, and determined PFO prevalence of 35% in these children. PFO was found to be as high as 50% in children with migraine with aura and this rate was significantly different from that of the general population, but the prevalence was found to be similar in cases without aura. In another study of 32 children with migraine, Cho DY et al. [9] reported that although PFO prevalence was higher in the migraine group, no statistically significant difference was seen between the overall migraine group and the control group (46.9% vs. 25.8%, p = 0.084). The PFO prevalence was found to be significantly higher only in the migraine with aura sub-group.

In the current study, PFO frequency was determined to be 21.1% in the migraine group and 2.8% in the control group. When it is considered that PFO frequency has been reported to be 20–25% in the general population in literature, the low rate determined in the control group seems to be noteworthy. However, the PFO prevalence reported in community-based autopsy studies and the prevalence determined in clinical studies using transthoracic echocardiography (TTE) are known not to overlap. Small shunts from right to left that emerge only with provocation in asymptomatic individuals may be difficult to determine with TTE. The children forming the control group in the current study were selected from clinically healthy individuals with no cardiac or neurological symptoms, but this raises the possibility that some small, clinically silent PFOs could have been overlooked. Therefore, the low frequency of PFO determined in the control group could be due to the predominant nature of clinically significant PFO emerging from the diagnostic method used rather than a methodological error of the study.

There are conflicting results in the literature on the subject of the efficacy of PFO closure in adults with migraine and PFO together. Mas et al. [14] determined migraine in 30.6% of 473 adult patients with PFO. In the patients determined with PFO in that study, no difference was found between closure of PFO with a transcatheter device and follow-up with medical treatment in terms of cessation of migraine attacks, migraine-related disability status, and the frequency of use of migraine preventative drugs during follow up. In another study of adult patients with stroke or TIA-related migraine, a statistically significant decrease in the frequency of migraine attacks and the use of migraine preventative drugs was experienced by patients during a 12-month follow up after PFO closure [15]. Although transcatheter PFO closure interventions have been reported for migraine in adults, there is insufficient evidence supporting this approach in children. The lack of paediatric randomised studies and that adult data cannot be generalised to children are significant limitations. The current paediatric guidelines do not recommend PFO closure in migraine cases with no history of cryptogenic stroke or systemic emboli. Therefore, PFO closure was not performed on any patient in the current study.

EEG findings of an epileptiform nature were determined in 15.25% of the current study paediatric patients diagnosed with migraine. This rate is consistent with previous paediatric studies that have indicated a clinical and pathophysiological overlap between migraine and epilepsy. Both migraine and epilepsy are neurological diseases with a paroxysmal course, which share common mechanisms such as cortical neuronal over-stimulation and ion channel dysfunctions [19, 20]. The prevalence of epileptiform EEG findings in children with migraine has been reported to be 5%-25% in the literature, and

it has been emphasized that the vast majority of these findings do not progress to clinical epilepsy [21–23]. In the current study, a diagnosis of clinical epilepsy was not made for any patient determined with epileptiform EEG findings, suggesting that these EEG abnormalities could be subclinical and non-specific. The fact that no significant relationship was determined between the presence of PFO and EEG findings in this study supports the view that EEG abnormalities are associated with central neurological mechanisms rather than cardiac shunt. Consequently, epileptiform EEG findings determined in children with migraine should be evaluated not so much as a reflection of clinical epilepsy but as a sign of the neurophysiological overlap between migraine and epilepsy.

There are studies in the literature that have reported that migraine, which is a disorder characterised by both neurological and vascular degeneration, is not a specific risk factor for cardiac arrhythmia, and other studies have stated that there may be ECG changes in migraine patients even in the attack-free period [24, 25]. Aygün et al. [26] reported that in addition to electrophysiological changes such as prolonged QT during a migraine attack, there could also be sinus arrhythmia and sinus tachycardia. In the current study, the ECG results of all the patients were evaluated as normal. However, mean heart rate was determined to be statistically significantly higher in the children with migraine and PFO compared to the migraine patients without PFO. Although the heart rate values of both groups were within the normal physiological limits for age, this finding may be associated with differences in the autonomic nerve system regulation in the combination of migraine and PFO. Migraine is a neurovascular disease which is seen with disruption of the sympathetic-parasympathetic balance in particular, and has been previously shown to be associated with autonomic dysfunction. The leakage of microembolic or vasoactive substances into the systemic circulation from the filtering effect of pulmonary circulation because of the shunt from right to left in the presence of PFO may contribute to a slight increase in heart rate which has an effect on central autonomic regulation [27, 28]. In another study of children with migraine, parasympathetic hyperfunction was determined with an increase in the frequency of Valsalva manoeuvres in the patients, and there was observed to be hypofunction in the parasympathetic system with an increase in the frequency of attacks and severity of headaches [29]. However, that pathological arrhythmia was not determined in the current study and that the heart rate values were withinn normal limits suggest that this finding could reflect a subclinical and compensatory autonomic response rather than indicating a clinically significant arrhythmia. There is a need for further studies of larger patient series and including autonomc function evaluations to clarify the mechanism of this relationship.

The serum Vitamin D, ferritin, folate, Vitamin D levels, and thyroid function tests were evaluated in the paediatric patients with migraine in this study. No significant difference in these parameters was determined in the comparisons made according to the presence of PFO. It has been suggested in the literature that there could be a relationship between the frequency and severity of headaches and iron deficiency, thyroid function tests, and low levels of Vitamin B12 and folate in individuals with migraine, but the majority of these studies have been conducted on adult populations and the results are inconsistent [30–32]. In the current study, Vitamin D levels were found to be relatively low in both groups, which is frequently seen in childhood and was attributed to regional/seasonal factors. Although it has been suggested that Vitamin D deficiency could play a role in migraine pathogenesis, it was not seen as

a specific determinant related to PFO presence in the current study [33]. Consequently, the laboratory parameters evaluated in this study were not determined to be explanatory biomarkers or predictive of the presence of PFO in children with migraine. This suggests that the migraine-PFO relationship could be associated with functional, neurovascular, and autonomic mechanisms rather than biochemical changes.

İn conclusion, the results of ths study demonstrated a higher frequency of PFO in paediatric patients diagnosed with migraine than in the control group. This finding contributes to the limited paediatric literature about the migraine-PFO relationship and indicates the need for evaluation of this relationship in childhood independently of adult data. Although the heart rate values were within the normal physiological limits for age, they were found to be higher in the migraine patients with PFO. This finding could be related to differences in autonomic nerve system regulation in cases with PFO and migraine combined. The laboratory parameters in this study were evaluated as secondary variables in respect of explaining the relationship of PFO with migraine, and it was not possible to draw any causal implications from these data.

In conclusion, although PFO is seen more frequently in children with migraine, the current findings are insufficient to support interventional approaches to PFO. To be able to better understand the relationship between migraine, PFO, and the underlying neurophysiological mechanisms, there is a need for further prospective paediatric studies with larger samples and longer follow-up periods.

Strengths and Limitations

One of the strongest aspects of this study was that it is one of a limited number of paediatric studies to have evaluated the frequency of PFO in children with migraine compared to a healthy control group. The important components increasing the internal validity of the study included identification of cases according to standard clinical criteria, echocardiographic evaluation of PFO performed by experienced paediatric cardiologists, and that the EEG findings were interpreted together with the presence of clinical epilepsy.

However, the single-centre design of the study and the relatively limited sample size restrict the generalisability of the results. A further limitation was that the low number of patients with migraine with aura prevented analysis of this sub-group. The cross-sectional design did not allow a causal relationship to be established between migraine, PFO, and EEG findings. Finally, the PFO evaluation made with TTE could have led to small or temporary shunts from right to left being overlooked.

Declarations

Acknowledgments: This manuscript is produced from the first author's thesis under the supervision of coauthors.

Authors' Contributions: All authors fulfill the criteria for authorship; DE, Rİ and AA: initiated the study, DE, Rİ, MT, and AA: collected the data, DE, Rİ, AA and DU: analyzed the data, DE, AA, Rİ, MT, DU: interpreted the data, DE, Rİ, AA, MT, and DU: drafted the report. All authors commented on the drafts and have seen and approved the final version.

Funding: This research received no external funding.

Availability of data and material: Data will be disclosed only if required and subject to further authorization by the ethics committee.

Conflict of Interest: The authors declare no conflict of interest.

Ethics approval: Ethical committee approval has been obtained from the Non-Interventional Ethics Committee of Dicle University (number 345, dated 13 September 2023

Consent to participate: Consent has been obtained from the participants.

References

1. Wang L, Wang Q, Diao H, Liu X, Zhao Y. The evolving landscape and research trend of calcitonin gene-related peptide in migraine: A bibliometric analysis and visualization. Front Neurol. 2024, 15:1415760.
2. Tanaka M, Tuka B, Vécsei L. Navigating the Neurobiology of Migraine: From Pathways to Potential Therapies. Cells. 2024; 3(13):1098.
3. Naguit N, Laeeq S, Jakkoju R, et al. Acupuncture Safe and Effective Treatment for Migraine? A Systematic Review of Randomized Controlled Trials. Cureus. 2022 Jan 3;14(1):e20888.
4. Onofri A, Pensato U, Rosignoli C, et al. European Headache Federation School of Advanced Studies (EHF-SAS). Primary headache epidemiology in children and adolescents: a systematic review and meta-analysis. J Headache Pain. 2023 Feb 14;24(1):8.
5. Yan, G.Xue Y, Xing Z. Efficacy and safety of percutaneous closure in patients with patent foramen ovale and migraine. Cardiovascular Reviews. 2023; 1(2), 20-25.
6. Noble S. PFO Closure and Migraine: Does Residual Shunt Matter? JACC Cardiovasc Interv. 2020 Feb 10;13(3):303-305.
7. Mi Z, He G, Li C, et al. Efficacy and safety of transesophageal ultrasound-guided patent foramen ovale closure for migraine in adolescents. Front Pediatr. 2023 Nov 15;11:1296825.
8. Sadrameli SS, Gadhia RR, Kabir R, Volpi JJ. Patent Foramen Ovale in Cryptogenic Stroke and Migraine with Aura: Does Size Matter? Cureus. 2018 Aug 27;10(8):e3213.
9. Choi DY, Shin DH, Cho KH, Lee SP, Park S. Migraine with aura: a predictor of patent foramen ovale in children and adolescents. Cephalalgia. 2013 May;33(7):463-8.

10. Liu K, Wang BZ, Hao Y, Song S, Pan M. The Correlation Between Migraine and Patent Foramen Ovale. Front Neurol. 2020 Dec 1;11:543485.
11. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018 Jan;38(1):1-211.
12. Silvestry FE, Cohen MS, Armsby LB, et al. American Society of Echocardiography; Society for Cardiac Angiography and Interventions. Guidelines for the Echocardiographic Assessment of Atrial Septal Defect and Patent Foramen Ovale: From the American Society of Echocardiography and Society for Cardiac Angiography and Interventions. J Am Soc Echocardiogr. 2015 Aug;28(8):910-58.
13. Zou R, Wang S, Liu P, Chen D, Yan J, Cai H, Wang Y, Wang C. The association between patent foramen ovale and unexplained syncope in pediatric patients. Ital J Pediatr. 2024 Jan 7;50(1):2.
14. Mas JL, Guillon B, Charles-Nelson A, et al. Patent foramen ovale closure in stroke patients with migraine in the CLOSE trial. The CLOSE-MIG study. Eur J Neurol. 2021 Aug;28(8):2700-2707.
15. Przemysław W, Spisak-Borowska K, Bochenek T, et al. Impact of percutaneous patent foramen ovale closure on migraine headaches in patients with history of ischemic neurological events. Postepy Kardiol Interwencyjnej. 2020 Sep;16(3):315-320.
16. McCandless RT, Arrington CB, Nielsen DC, Bale JF Jr, Minich LL. Patent foramen ovale in children with migraine headaches. J Pediatr. 2011 Aug;159(2):243-7
17. Dalla Volta G, Guindani M, Zavarise P, Griffini S, Pezzini A, Padovani A. Prevalence of patent foramen ovale in a large series of patients with migraine with aura, migraine without aura and cluster headache, and relationship with clinical phenotype. J Headache Pain. 2005 Sep;6(4):328-30.
18. Fu X, Li M. Relationship between Migraine and Patent Foramen Ovale Observed by Contrast-enhanced Transthoracic Echocardiography. J Coll Physicians Surg Pak. 2023 Mar;33(3):352-354.
19. Pietrobon D, Moskowitz MA. Pathophysiology of migraine. Annu Rev Physiol. 2013;75:365-91.
20. Hamed SA. The vascular risk associations with migraine: relation to migraine susceptibility and progression. Atherosclerosis. 2009 Jul;205(1):15-22.
21. Panayiotopoulos CP. The Epilepsies: Seizures, Syndromes and Management. Oxfordshire (UK): Bladon Medical Publishing; 2005. PMID: 20821848.
22. Uyur E, Hacıfazlıoğlu NE. Clinical features and EEG findings in pediatric migraine: A retrospective analysis of 148 patients .Cephalalgia Reports. 2025;8: 1–9
23. Guidetti, V., Matricardi, M., Di Sabato, M., Brinciotti, M. Electroclinical Features in Children and Adolescents with Epilepsy and/or Migraine, and Occipital Epileptiform EEG Abnormalities. Clinical EEG and Neuroscience. 2000;31(2), 76–82.
24. Tosun O, Karatoprak E. Increased QT and P-wave dispersion during attack-free period in pediatric patients with migraine attacks. Cardiol Young. 2019 Apr;29(4):488-491.
25. Torun A, Güldiken YC, Kılıç Ş, Budak EF, Selekler HM. Changes in Cardiac Electrophysiology and Predisposition to Arrhythmia in Migraine Patients. Bull Cardiovasc Acad. 2024;2(2):43-46.

26. Aygun D, Altintop L, Doganay Z, Guven H, Baydin A. Electrocardiographic changes during migraine attacks. Headache. 2003 Sep;43(8):861-6.
27. Peroutka SJ. Migraine: a chronic sympathetic nervous system disorder. Headache. 2004 Jan;44(1):53-64.
28. Elmenshawy E, Sherif Sakr S. Autonomic dysfunction in migraine; what do we need to know? The Egyptian Journal of Neurology Psychiatry and Neurosurgery. 46(2):489-496
29. Akyol D, Demir N, Polat Aİ, Öztura İ, Yiş U, Hız AS. Evaluation of Autonomic Dysfunction in Pediatric Migraine Patients J Dr Behcet Uz Child Hosp. 2024;14(2):81-90.
30. Al-Qassab ZM, Ahmed O, Kannan V, Ullah N, Geddada S, Ibrahiam AT, Nwosu M. Iron Deficiency Anemia and Migraine: A Literature Review of the Prevalence, Pathophysiology, and Therapeutic Potential. Cureus. 2024 Sep 18;16(9):e69652.
31. Acar A, Evliyaoğlu O, Uzar E, et al. Serum Vitamin B12, Folic Acid and Ferritin Levels in Patients with Migraine .Turk Norol Derg. 2011;17:90-95
32. Jeffrey R. Garber, Rhoda H. Cobin, Hossein Gharib, et al. Clinical Practice Guidelines for Hypothyroidism in Adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Thyroid. 2022; 22(12): 1200-1236
33. Bhuya MSI, Saiduzzaman M, Linckon K, et al. Association of Serum Vitamin D Level in Patients with Migraine. Mymensingh Med J. 2025 Apr;34(2):312-318.