Exploring the Relationship Between Migraine and Blood Pressure in Pediatric Patients: A Case-Control Study

Saba Rezazadeh[1], Amirabbas Faridpour[1]*, Fakhreddin Shariatmadari[2], Yazdan Ghandi[3], Seyed Mojtaba Hashemi[4], Parsa Yousefichaijan[5]

[1] *Student Research Committee, Arak University of Medical Sciences, Arak, Iran*

[2] *Department of Pediatric Nourology, Clinical Research Development Center of Amirkabir Hospital, Arak University of Medical Sciences, Arak, Iran*

[3] *Department of Pediatric Cardiology, Clinical Research Development Center of Amirkabir Hospital, Arak University of Medical Sciences, Arak, Iran*

[4] *Departement of Pediatric Gastroenterology, Clinical Research Development Center of Amirkabir Hospital, Arak University of Medical Sciences, Arak, Iran*

[5] *Department of Pediatric Nephrology, Clinical Research Development Center of Amirkabir Hospital, Arak University of Medical Sciences, Arak, Iran*

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Abstract- Migraine headaches are a significant concern for both parents and primary care providers due to their frequency and impact on the child's quality of life. Studies in the adult population have shown that migraines are linked to cardiovascular disease. This study aimed to compare blood pressure in children with and without Migraine. In this case-control study, we evaluated blood pressure in patients with Migraine and a control group. Blood pressure was evaluated during three clinic visits. Systolic, diastolic, pulse, and mean arterial blood pressure were compared between the two groups, and the association between blood pressure and Migraine was evaluated using the odds ratio. The mean systolic and diastolic pressures, pulse pressure, and mean arterial pressure were not significantly different between the two groups (P>0.05). Twenty-three children with Migraine had abnormal blood pressure, and the adjusted odds ratio was 1.32 (95% CI: 0.68-2.57). There was no significant relationship between prehypertension, stage 1 hypertension, and stage 2 hypertension and Migraine in children (P>0.05). The prevalence of prehypertension in children with bilateral Migraine was higher compared to unilateral Migraine, although this difference was not statistically significant (P>0.05). Our results did not confirm blood pressure as an etiological factor in children with Migraine. These findings suggest that further research is needed to explore the relationship between Migraine and blood pressure in pediatric populations.

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Introduction

Migraine is a prevalent type of primary headache commonly observed in childhood, characterized by intense headache episodes often accompanied by various neurological symptoms. These recurrent headaches are a significant concern for both parents and primary care providers due to their frequency and impact on the child's quality of life (1). The prevalence of Migraine in pediatric populations ranges from 3% to 20%, varying by age and gender (2-4).

Despite their high occurrence and associated disability, the precise pathophysiological mechanisms and comorbid conditions of migraines remain

Corresponding Author: A. Faridpour
Student Research Committee, Arak University of Medical Sciences, Arak, Iran
Tel: +98 8633838268, E-mail address: Faridpouram@gmail.com

inadequately understood. Previous studies have implicated vascular pathologies, autonomic dysfunction, and ischemic vascular disorders in the etiology of migraines (5,6). There is also evidence linking migraines to cardiovascular disease and related risk factors, such as hypertension (5,7-9). Additional studies have identified associations between migraines and elevated blood pressure, stroke, epilepsy, and psychiatric disorders (10).

The potential interplay between migraines and blood pressure may involve several mechanisms, including the renin-angiotensin system, although definitive evidence is still lacking (11). Community-based research, primarily involving adults, suggests that individuals with migraines may exhibit higher blood pressure levels (5,9). Conversely, some studies indicate that migraines are specifically associated with increased diastolic blood pressure, while others suggest an inverse relationship with hypertension (12).

Currently, there is no consensus on the correlation between blood pressure and migraines in pediatric populations. Although migraines represent a significant health issue during childhood, research exploring the relationship between migraines and blood pressure in this demographic is scarce. Therefore, this study aims to investigate the correlation between blood pressure and migraines in children and adolescents, addressing a critical gap in the existing literature.

Materials and Methods

Study design

This case-control study aimed to evaluate blood pressure differences in pediatric patients with and without Migraine. Data were collected from children attending the pediatric clinic at Amir Kabir Hospital in Arak, Iran, between January 2021 and December 2021.

Setting

The study was conducted in Arak University of Medical Sciences, involving pediatric patients from Amir Kabir Hospital's clinic.

Eligibility criteria

The criteria for including participants in the case group were as follows: (I) children and adolescents aged 5 to 18 years diagnosed with migraine headaches, (II) no history of chronic hypertension, (III) not currently on antihypertensive medications, and (IV) no prior treatment with beta blockers. Participants without migraine headaches in the same age range were included if they had no history of systemic diseases that could influence blood pressure. Both groups were excluded if participants (I) had a history of high blood pressure, (II) were classified as overweight or obese, or (III) did not provide informed consent to participate in the study. Additionally, participants in the case group were excluded if they presented during an acute headache attack.

Participants in the case and control groups were matched based on age and gender to ensure comparability between the two groups.

Clinical and biochemical assessments

Diagnosis of Migraine was confirmed by a board-certified pediatric neurologist (FS) according to the International Classification of Headache Disorders-3 (ICHD-3) (13).

All participants had their blood pressure measured in an office setting on three separate occasions, following standardized protocols (14). Briefly, they were instructed to remain seated and relaxed for at least 15 minutes prior to measurement. A trained medical student used a standard pediatric sphygmomanometer for the measurements. To ensure proper fit, the arm circumference of each child was measured, and appropriately sized cuffs were selected.

High blood pressure was diagnosed based on specific criteria: for children under 13 years old, if their blood pressure readings exceeded the 95th percentile on three consecutive occasions (as determined by the MSD MANUAL software), they were classified as having high blood pressure. For those aged 13 and older, a diagnosis of hypertension was made if their blood pressure was consistently at or above 130/80 mmHg across three separate measurements. Normal blood pressure was defined as below the 90th percentile and less than 130/80 for participants younger and older than 13 years, respectively (15).

Prehypertension was identified as readings between the 90th and 95th percentiles. First-stage high blood pressure was classified as being between the 95th and 99th percentiles, plus an additional 5 mmHg. Second-stage high blood pressure was defined as readings above the 99th percentile, with an additional 5 mmHg threshold that accounted for factors including sex, age, and height (16).

Finally, systolic and diastolic blood pressure values were recorded and categorized according to established guidelines. To analyze the data, the average of the three measurements was calculated. Additionally, pulse pressure was calculated as the difference between systolic and diastolic blood pressures (17). Mean arterial pressure (MAP) was calculated using the formula:

MAP=[(2×diastolic BP) + systolic BP]/3 (18).

Sampling

The control group was matched to the migraine group based on age, gender, and height. This matching was conducted prospectively to ensure comparability between the groups and to minimize confounding variables. By controlling for age, gender, and height, we aimed to isolate the relationship between migraine and blood pressure more effectively.

To prevent any bias, data collection was done as follows. The diagnosis of Migraine and group allocation were determined by a pediatric neurologist (FS), and blood pressure was measured by a trained medical student supervised by a pediatric cardiologist (SR and YG). In the end, our data analyst (AAH) gathered the final data with patients' IDs and analyzed them. In this way, data collection and analysis were blinded.

The sample size for this case-control study was calculated to determine the relationship between blood pressure and Migraine in children. The calculation was based on findings from Yılmaz *et al*., (19), who reported that 45.9% of children with migraines and 16.6% of children in the control group were diagnosed with either prehypertension or hypertension. Using the following formula for sample size estimation in case-control studies:

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 \cdot [p_1(1-p_1) + p_2(1-p_2)]}{(p_1 - p_2)^2}$$

The calculated sample size per group was approximately 36 participants to achieve 80% power and a 95% confidence level. However, to ensure greater precision and account for potential subgroup analyses, the sample size was increased to 200 participants per group, for a total of 400 participants. This adjustment enhances the reliability of the results and allows for robust statistical analysis.

Statistical analysis

The Shapiro-Wilk test was used to test normality. The results indicated normal distribution of the data (W=0.98, *P*=0.55). Descriptive indices (mean and standard deviation) were used to describe quantitative variables, and count and percent were used to describe qualitative variables. The independent t-test was used to compare the means of continuous variables between the migraine and control groups, as the groups were matched prospectively by age, gender, and height during participant selection and analyzed as independent samples. Categorical variables were compared using the chi-square test, and logistic regression was employed to calculate odds ratios. Statistical analyses were performed using Stata version 11 (StataCorp, College Station, TX, USA) at a 95% confidence level.

Results

The study included 189 participants, with an average age of 10.02 years (±3.01). The control group had an average age of 9.99 years (±3.07), while the migraine group had an average age of 10.06 years (±2.95).

The overall average age of the children was 10.02±3.01 years. The age difference between the two groups was not statistically significant (*P*=0.803).

There was no significant difference in gender distribution between the groups (girls: 48.5% in the healthy group vs. 46% in the migraine group, *P*=0.617). The average BMI was similar between groups (healthy: 23.29±3.31 vs. Migraine: 23.12±3.29, *P*=0.917), and none of the participants were classified as obese, overweight, or underweight.

Table 1 presents the comparison of average blood pressure between the two groups. The findings indicate that there were no statistically significant differences in average blood pressure measurements—systolic, diastolic, pulse pressure, and mean arterial pressure—between the groups (*P*>0.05).

Table 1. Blood pressure measurements in the group of pediatric patients with migraine and healthy pediatric patients

Variable	Case (n=92), mean (SD)	Control (n=97), mean (SD)	*P**
Systolic blood pressure	102.1 (10.15)	101.27 (10.04)	0.406
Diastolic blood pressure	67.29 (8.64)	67.2 (8.35)	0.915
Pulse pressure	34.81 (7.56)	34.06 (7.59)	0.322
Mean arterial blood pressure	78.9 (8.45)	78.56 (8.2)	0.683

* According to the independent t-test

In total, 19 healthy children (9.5%) and 23 children with migraines (11.5%) exhibited abnormal blood pressure. Table 2 shows the prevalence of abnormal blood pressure in each group, classified by hypertension type.

The odds ratio was calculated and adjusted for age and gender. The findings indicate no statistically significant differences in hypertension prevalence across prehypertensive, stage 1 hypertension, and stage 2 hypertension categories (P>0.05). Additionally, no significant association was found between migraines and hypertension in children.

Table 2. The relationship between blood pressure and parental migraine history with children's migraine

Variable		Case	Control	OR (95%CI)	*P**
Blood pressure	Normotensive	177 (88.5%)	181 (90.5%)	Reference	Reference
	Prehypertension	11 (5.5%)	9 (4.5%)	1.17 (0.46-2.96)	0.725
	Stage 1 hypertension	7 (3.5%)	5 (2.5%)	1.77 (0.53-5.85)	0.346
	Stage 2 hypertension	5 (2.5%)	5 (2.5%)	1.18 (0.32-4.29)	0.792
History of migraine in parents	No	86 (43%)	119 (59.5%)	Reference	Reference
	Yes	144 (57%)	81 (40.5%)	1.98 (1.32-2.96)	0.001

Case (n=92); n(%) and Control (n=97); n(%)
*P and odds ratio were calculated by logistic regression test adjusted for age and gender.
OR: Odds ratio, 95%CI: 95% confidence interval

A history of migraines was more common among parents of children with migraines (57%) than among those of healthy children (40.5%, P=0.001). Children with a parental migraine history were 1.98 times more likely to develop migraines (95% CI: 1.32–2.96).

Among children with migraines, 56.5% had bilateral migraines. There were no significant differences between unilateral and bilateral migraines in terms of average age (10.2±2.90 vs. 10.11±3 years, P=0.392) or gender distribution (girls: 47.13% vs. 45.13%, P=0.779).

Table 3 presents the comparison of blood pressure between children with unilateral and bilateral migraines. The average blood pressure in children with bilateral migraines was slightly higher than that of those with unilateral migraines; however, these differences were not statistically significant (P<0.05).

Table 3. Blood pressure measurements in unilateral versus bilateral migraine

Variable	Unilateral (n=77), mean (SD)	Bilateral (n=15), mean (SD)	*P**
Systolic blood pressure	101.29 (10.23)	102.73 (10.09)	0.161
Diastolic blood pressure	66.75 (8.66)	67.7 (8.63)	0.221
Pulse pressure	34.54 (7.22)	35.02 (7.84)	0.326
Mean arterial blood pressure	78.27 (8.56)	79.38 (8.36)	0.179

*According to the independent t-test

Table 4 outlines the frequency of abnormal blood pressure categorized by migraine type and blood pressure levels. The results showed that the prevalence of prehypertension was higher in children with bilateral migraines compared to those with unilateral migraines, although this difference was not statistically significant (P=0.107). The odds ratio did not indicate significance for prehypertension, hypertension, or parental migraine history.

Table 4. The relationship between blood pressure and parental migraine history with children's migraine type

Variable		Group		OR (95%CI)	*P**
		Unilateral (n=77)	Bilateral (n=15)		
Blood pressure	Normotensive	79 (90.8%)	98 (86.73%)	Reference	Reference
	Prehypertension	2 (2.3%)	9 (7.96%)	3.63 (0.75-17.44)	0.107
	Hypertension	6 (6.9%)	6 (5.31%)	1.3 (0.064-1.88)	0.652
History of migraine in parents	No	40 (45.98%)	46 (40.71%)	Reference	Reference
	Yes	47 (54.02%)	67 (59.29%)	1.15 (0.64-2.06)	0.627

Unilateral (n=77); n(%) and Bilateral (n=15); n(%)
**P* and odds ratio were calculated by logistic regression test adjusted for age and gender.
OR: Odds ratio, 95%CI: 95% confidence interval

Discussion

Key results

In this study, we observed that systolic, diastolic, pulse, and mean arterial pressures were marginally elevated in children with migraines compared with healthy peers, but these differences did not reach statistical significance. Additionally, the odds ratio analysis suggested that children with prehypertension, stage 1 hypertension, and stage 2 hypertension had a greater likelihood of experiencing migraines compared to those with normal blood pressure. However, these odds ratios were not statistically significant, indicating only a potential link between abnormal blood pressure and migraines. Moreover, the average blood pressure readings for children with bilateral migraines were slightly higher than those for children with unilateral migraines across all measured parameters—systolic, diastolic, pulse, and mean arterial pressure—yet these differences were also not statistically significant. The odds ratio analysis further suggested an increased likelihood of bilateral migraines in children with abnormal blood pressure compared to those with normal readings. Another aspect of this study involved examining the relationship between parental migraine history and the occurrence of migraines in their children. The findings suggest a possible connection between parental migraines and the development of migraines in offspring; however, this warrants further investigation. Importantly, the results indicated no correlation between parental migraine history and the specific type of migraines (unilateral or bilateral) experienced by their children.

Existing literature

The link between high blood pressure and migraines has raised concerns for many years, with various studies investigating this relationship in adults (5,7,9,11). One population-based study assessed 6,102 individuals with migraines alongside 5,243 healthy participants, revealing that those with migraines had a 1.6 times greater likelihood of developing high blood pressure (5). Additionally, another study tracking 13,426 individuals without pre-existing hypertension over five years found a significantly higher incidence of hypertension among migraine sufferers (P=0.003) (20). Changes in mean blood pressure have also been noted in migraine patients (12,20,21). For instance, Gudmunsson *et al*., (12) conducted a study involving 21,537 participants and found no direct link between hypertension and migraines. However, they did observe that migraine patients exhibited lower systolic blood pressure but higher diastolic blood pressure. Furthermore, the study indicated that a one standard deviation increase in diastolic blood pressure was associated with a 30% higher risk of migraines in women and a 14% higher risk in men. In contrast, an 11-year prospective study examining the connection between headaches and blood pressure suggested that high systolic blood pressure might actually reduce the risk of migraines in women (21).

The current literature on the relationship between Migraine and hypertension in the pediatric population is limited. A study by Yılmaz *et al*., (19) explored the connection between blood pressure and migraines in children. Their research focused on ambulatory blood pressure in young migraine sufferers and found that nearly half exhibited abnormalities in their readings. While the overall rate of high blood pressure did not differ significantly, the occurrence of unusual ambulatory blood pressure patterns was notably higher in the migraine group (45.9% vs. 16.7% in controls; P=0.018). Furthermore, the average nocturnal arterial blood pressure in children with migraines was significantly elevated compared to the control group (P<0.05), supporting our own findings. It is important to note that the lack of significant results in our study may be due to a limited sample size.

The relationship between Migraine and hypertension

remains controversial, and definitive conclusions are challenging due to the heterogeneity in study methods and populations. It is still uncertain whether high blood pressure is a predictor of migraines. More research is essential to clarify the complex interplay between blood pressure and migraines, particularly in pediatric populations.

Limitations

This study has several strengths, including its novelty as the first investigation of the relationship between blood pressure and migraines in pediatric populations in Iran. Additionally, the thorough evaluation of blood pressure during multiple clinic visits enhances the reliability of the findings, and the assessment of family history provides valuable insights into its potential influence on migraines. However, classifying migraines as unilateral or bilateral did not significantly improve the study's outcomes. The most notable limitation is the relatively small sample size, which complicates comparisons of variables and limits the generalizability of the results. Furthermore, potential confounding factors, such as lifestyle, diet, and psychological stressors, were not assessed, which may impact the relationship between migraines and blood pressure. Future research with larger cohorts is needed to address these limitations and further explore these associations.

Based on our study, although the average arterial pressure in children with migraines was higher than in healthy children, the likelihood of developing pressure in children with migraines was higher than in healthy children; these differences were not statistically significant. However, more studies are needed to confirm the effects of blood pressure. On the other hand, there is a tangible need to conduct studies on the impact of other factors on children's migraine headaches.

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