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Association Between Migraine and Diabetes in Pregnancy

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Abstract

Background: Migraine ranks as the eighth most disabling condition and one of the most common causes of headache in Pakistan.
Objectives: In this study, we aimed to determine the association between migraine and diabetes in pregnant women.
Patients and Methods: This cross-sectional study recruited 498 pregnant women, grouped into pregnant without diabetes (n = 300) and pregnant with diabetes (n = 198) according to the International Association of the Diabetes and Pregnancy Study criteria. Seventy-five women with known migraine were also recruited as positive controls. After confirming that the study subjects had headache at least once a month, the researcher filled out a comprehensive form based on the International Classification of Headache Disorders version II. Migraine disability score was used to assess severity. Fasting blood glucose levels were measured by using the enzymatic method. Data were presented as mean ± SD and frequencies, where applicable. Chi-square test and Spearman correlation test were performed. A P value of <0.05 was considered significant.
Results: The headache prevalence during pregnancy was 69% in the women with diabetes and 64% in the women without diabetes. A positive unilateral distribution was observed in 51% of the cases and 36.3% of the controls (P < 0.01). However, 94.7% of the pregnant cohort reported not having experienced aura. Of the pregnant women with diabetes, 19% fell within the mild to moderate disability score as compared with the 10.3% of the pregnant women without diabetes (P < 0.01). High fasting blood glucose levels showed a significant association with headache scores (r = 0.144; P < 0.01).
Conclusions: Headaches, particularly migraine without aura, are a common occurrence in pregnancy in our population. Migraine severity is positively associated with high blood glucose levels.

Keywords: Diabetes Mellitus, Migraine Without Aura, Migraine With Aura, Pregnancy

1. Background

Headaches are among the most common disorders of the nervous system and are associated with significant disability. According to the World Health Organization, the estimated prevalence of current headache disorder among adults is 47%. Among the primary headache disorders, the most common ones are tension-type headaches and migraines. Migraine ranks as the eighth most disabling condition according to the years lived with disability (1). It is a chronic neurological disease characterized by recurring episodes of headache often associated with nausea, vomiting, vision disturbances, and other neurological symptoms. It is prevalent by up to 6% in males and 18% in females, with the highest prevalence at the age from 25 to 55 years (2).

Migraine is one of the most common causes of headaches in Pakistan. A study reported that almost 81% of patients who visited a specialist headache clinic in Karachi, Pakistan, were diagnosed with migraine (3). Migraine has been shown to be associated with a number of conditions such as obesity and high blood glucose levels (4). A previous study reported a correlation between insulin resistance and chronic migraine (5). Moreover, the frequency and duration of headaches can also change during pregnancy. Studies have shown that the frequency and duration of all headaches, including migraine, decrease during pregnancy (6, 7). Contrary to the general belief, we found the opposite to be true in our study population.

2. Objectives

In this study, we aimed to determine the prevalence of migraine in pregnant women and to identify possible risk factors such as increased body mass index (BMI) and fasting blood glucose (FBG) level.

3. Patients and Methods

This cross-sectional study was conducted from March 2014 to February 2015. A total of 498 pregnant women were recruited. The sample size was calculated by using the online software OpenEpi (http://www.openepi.com/), with the overall prevalence of 16%, an alpha of 95%, and power of 80%. Women with hypertension, known psychiatric illness, systemic infections, and twin pregnancy were excluded from the study. The study subjects were classified according to the International Association of the Diabetes and Pregnancy Study criteria as follows: pregnant with diabetes mellitus (DM; n = 198), having a FBG level of $\geq$ 92 mg/dL (5.1 mmol/L) and/or $\geq$ 180 mg/dL (10.0 mmol/L) at 1 hour and/or $\geq$ 153 mg/dL (8.5 mmol/L) at 2 hours (when any of the following plasma glucose values are exceeded) (8), and pregnant without DM (n = 300), having a FBG level below the cutoff values. In addition, 75 subjects with known migraine were also selected as positive controls in order to compare the characteristics of the headache reported in the pregnant women. The study subjects were recruited from Memon Hospital Karachi and United Medical and Dental College Karachi, Pakistan. All the study subjects received a brief explanation about the study. They provided written informed consent for participation in the study, which was approved by the institutional ethical review committee (Ref#12-10-14-ERC-UMDC).

Researcher filled out a detailed and comprehensive form based on the International Classification of Headache Disorders version 2 (ICHD-II) (9). Anthropometric data and FBG levels were collected from all the study subjects. FBG level was measured by using the glucose oxidase-phenol-aminophenazone method (Merck, France). The weight (kg) and height (m) of the known cases (n = 75) were measured by using a stadiometer (ZT-120 Health Scale, made in China). The subjects were asked to stand in an erect posture, wearing light clothing. Data on the weights (kg) and heights (m) of the pregnant women at the time of their first visit to the clinic were obtained from their medical record cards. BMI was then calculated by using the formula (weight in kg/height in m^2) (10).

3.1. Statistical Analysis

Data were entered and analyzed by using SPSS version 19 (IBM, Chicago, USA). Data were presented as mean $\pm$ SD and frequencies, where applicable. Chi-square test was used to test differences in categorical variables. Spearman correlation test was used to identify the relationship of age, BMI, and FBG with headache scores. A P value of <0.05 was considered significant.

4. Results

The study findings are summarized in Tables 1 - 3. Briefly, the mean age of the pregnant women with DM was 27.51 $\pm$ 5.56 years, and that of those pregnant without DM was 25.78 $\pm$ 4.73 years. The BMI of the pregnant women with DM was 24.83 $\pm$ 5.13 kg/m^2, and that of the pregnant women without DM was 22.38 $\pm$ 3.93 kg/m^2. The mean FBG level of the pregnant without DM was 79.60 $\pm$ 5.83 mg/dL, and that of the pregnant with DM was 108.29 $\pm$ 26.05 mg/dL (P < 0.05).

Table 1 shows the prevalence of headache along with its associated features in the study subjects. A total of 69.2% (n = 137) of the pregnant women with DM and 64% (n = 192) of those without DM complained of headaches during pregnancy. A positive unilateral distribution was found in 51% (n = 101) and 36.3% (n = 109) of the pregnant women with DM and those without DM, respectively, when compared with 62% (n = 47) of the subjects with known migraine (P < 0.01). This resulted in the overall prevalence of migraine to be 66% (n = 329) in the pregnant cohort. However, 94.7% (n = 471) of the pregnant cohort reported to have not experienced aura. Overall, 13.6% (n = 41) of the pregnant women without DM and 14.1% (n = 28) of those with DM complained of nausea/vomiting during the attacks, as compared with 14.6% (n = 11) of those with known migraine. It is interesting that only 7% (n = 21) of the pregnant women without DM and 4.5% (n = 9) of those with DM reported a family history of migraine, as compared with 40% (n = 30) of the subjects with known migraine (P < 0.01). When stratified according to disability score, 19.7% (n = 59) of the pregnant women with DM and 10.3% (n = 65) of those without DM fell within the mild to moderate disability score, as compared with 53.3% (n = 40) of the women with known migraine (P < 0.01; Table 2).

Table 3 shows the Spearman correlation of age, BMI, and FBG level with headache severity score. The results show that age and BMI did not depict any significant association with headache severity. However, high FBG level was significantly positively associated with headache score (R = 0.144; P < 0.01).

5. Discussion

The results of this study show that 66% of the study subjects complained of having a migraine attack during the course of their pregnancy. The migraine attacks were accompanied by symptoms such as blurred vision in 12.6% of cases and decreased hearing in 5.6% of cases when compared with those in the controls (4.3% and 1.7%, respectively) (P < 0.05). However, most (53%) of the controls did not experience muscular derangements, unlike most (34%)

Table 1. Headache Prevalence Scale of the Study Subjects

Question on Headache	Pregnant Without DM (n = 300)[a]	Pregnant With DM (n = 198)[a]	Positive Control (n = 75)[a]	P Value, Compared With the Controls
Headache				< 0.01[b]
Yes	192 (64)	137 (69.2)	75 (100)	
No	108 (36)	61 (30.8)	0	
Unilateral	109 (36.3)	101 (51.0)	47 (62.6)	
Bilateral	34 (11.3)	31 (15.7)	28 (37.3)	
None	157 (52.3)	66 (33.3)	0	
Aura				< 0.01[b]
Yes	18 (6)	9 (4.5)	16 (21.3)	
No	282 (94)	189 (95.5)	59 (78.7)	
General symptoms				< 0.01[b]
Nausea/vomiting	41(13.6)	28 (14.1)	11(14.6)	
Vertigo	21 (7.0)	20 (10.1)	5 (6.7)	
Photophobia	5 (1.6)	7 (3.5)	10 (13)	
Combination	55 (18.3)	45 (22.7)	26 (34.7)	
None	178 (59.3)	98 (49.5)	23 (30.7)	
Vision				< 0.01[b]
Blurred	13 (4.3)	25 (12.6)	15 (20)	
Blindness	24 (8.0)	24 (12.1)	1 (1.3)	
Combination	14 (4.3)	15 (7.5)	4 (5.3)	
None	249 (83.0)	134 (67.7)	55 (73.3)	
Hearing				< 0.01[b]
Ringing	21 (7.0)	18 (9.1)	9 (12.0)	
Decreased	5 (1.7)	11 (5.6)	1 (1.3)	
Speech difficulty	1 (0.3)	2 (1.0)	5 (6.7)	
None	273 (91.0)	167 (84.3)	60 (80.0)	
History of epilepsy				0.197
Yes	2 (0.7)	1 (0.5)	2 (2.7)	
No	298 (99.3)	197 (99.5)	73 (97.3)	
Muscular symptoms				< 0.01[b]
Weakness	45 (15)	33 (16.7)	19 (25.3)	
Numbness	17 (5.7)	9 (4.5)	1 (1.3)	
Tingling	1 (0.3)	3 (1.5)	1 (1.3)	
Loss of consciousness	0	2 (1)	1 (1.3)	
Abdominal pain	3 (1)	4 (2)	3 (4)	
Combination	75 (25)	79 (39.9)	50 (66.7)	
None	159 (53)	68 (34.3)	0	
Family history of migraine				< 0.01[b]
Yes	21 (7)	9 (4.5)	30 (40)	
No	279 (93)	189 (95.5)	45 (60)	

[a] values are presented as No. (%).
[b] P < 0.05 when compared with the controls.

of the cases (Table 1). When classified according to migraine severity scale, 26.1% participants fell in the mild to moderate disability range during pregnancy, as compared with 53.3% (n = 40) of the subjects with known migraine (P < 0.01; Table 2). Similar findings were reported by a study conducted by Frederick et al. (11), who reported that moderate to severe disability due to migraine headache was prevalent at 26% in pregnant women. Migraine is a significant health issue among women. About 27% of women in childbearing age have migraine (12, 13). Lack of sleep, low blood glucose level, dehydration, and stress contribute to the occurrence of migraine attacks (14). Most epidemiological studies demonstrated that pregnant women who experience headaches before pregnancy report to have a 55 - 90% improvement in the severity of the attack after they become pregnant (15-17). A large-scale MIGRA study

Table 2. Headache Severity Scale of the Diabetic and Non-diabetic Study Subjects

Headache Severity Scale	Pregnant Without DM (n = 300)[a]	Pregnant With DM (n = 208)[a]	Positive Control (n = 75)[a]	P Value
Headache				< 0.01[b]
Little or no disability	239 (79.7)	129 (65.2)	35 (46.7)	
Mild disability	28 (9.3)	26 (13.1)	18 (24)	
Moderate disability	31 (10.3)	39 (19.7)	13 (17.3)	
Severe disability	2 (0.7)	4 (2)	9 (12)	

[a] values are presented as No. (%).
[b] P < 0.05 when compared with the controls.

Table 3. Correlation of Age, Body Mass Index, and Fasting Blood Glucose Level with Headache Severity

Variables	r	P Value
Age	0.041	0.323
Body mass index	0.035	0.399
Fasting blood glucose level	0.144	0.001

also revealed a significant decrease in the frequency of migraine during pregnancy (18). This could be attributed to stable levels of estrogen and progesterone, along with an increase in beta-endorphin. Beta endorphin is known for its anti-nociceptive effect during pregnancy, which might be a possible reason for the changing course of migraine during pregnancy (18, 19).

An interesting finding in this study was that the prevalence of migraine attacks without aura was high in the study subjects and did not subside during pregnancy. A recent study reported that women having migraine without aura are more likely to recover than women having migraine with aura (18), but this trend was not observed in our study. It is easy to understand that physical and social problems arising during pregnancy can play a role in the course of migraine during pregnancy. Pakistan being a developing country bears many challenges, and perhaps the anxiety and stress levels play a part in these episodes. However, pregnancy being a stressful condition in itself, we were limited to rule out stress factor in this study.

We found no association of headache with age, BMI, and socioeconomic status (P > 0.05). However, high blood glucose levels during pregnancy had a significant positive correlation (R = 0.144; P <0.01) with headache severity. Migraine headache is a neurovascular headache that is likely to be aggravated with certain risk factors such as diabetes, hypertension, and tobacco smoking (20). The influence of blood glucose concentrations on migraine attack might be linked to an anomaly in the carbohydrate metabolism. Excess blood glucose but reduced glucose supply to organs might lead to a neurogenic attack and aggravate migraine in diabetic patients (21). Perhaps the high frequency of migraine attacks in our population can be attributed to the uncontrolled blood glucose levels. Future longitudinal studies that focus on the biochemical aspect related to both migraine and diabetes are required for a better understanding.

Untreated migraine can cause an increased risk of preterm delivery, and migraine attacks can lead to poor nutritional intake, stress, and depression, which will cause negative effects on the maternal and fetal well-being (22, 23). Hence, this health risks should be dealt with properly. Pregnant patients must be made aware of the effects of migraine on their fetus and prompt treatment must be initiated. Non-pharmacological therapies (massage, ice packs, sleep, etc.) should be tried first to treat migraine in pregnant women because many of the drugs normally used are teratogenic and abortifacient, particularly in the first trimester. Moreover, weight management and lifestyle modifications are advised to reduce feto-maternal complications (24, 25). Our study is limited in terms of its sample size. In addition, we could not follow up the subjects post pregnancy in order to compare the migraine status during and after pregnancy. Further studies must be conducted on a larger scale to confirm the relationship between increased migraine and pregnancy, and then to determine the level of awareness, disease severity, and treatment goals in this regard.

5.1. Conclusions

This study reports that headaches, particularly migraine without aura, were a common occurrence in preg-

nancy in our study population. Migraine severity is positively associated with high blood glucose levels. Further longitudinal studies should be conducted to identify the causal relationship of this condition.

Footnote

Authors' Contribution: Syeda Zain was involved in the conception and design of the study, and drafting of the article. Syed Farrukh Mustafa, Hamza Abdur Rahim Khan and Muhammad Faraz Raghib were equally involved in data acquisition, performing experiments, and drafting the article. Syeda Sadia Fatima was responsible for the analysis and interpretation of data, and drafting and revision of the manuscript for critically important intellectual content. All the authors gave final approval of the submitted version of the manuscript.

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