Scientific Research Publishing

Open Journal of Medical Psychology, 2023, 12, 82-93
https://www.scirp.org/journal/ojmp
ISSN Online: 2165-9389
ISSN Print: 2165-9370

Risk Factors Associated with Cephalalgia during Pregnancy and Postpartum in a Sample of Greek Women

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How to cite this paper: Giaxi, P., Bala, C., Maniatelli, E., Charos, D. and Vivilaki, V. (2023) Risk Factors Associated with Cephalalgia during Pregnancy and Postpartum in a Sample of Greek Women. *Open Journal of Medical Psychology*, **12**, 82-93.
https://doi.org/10.4236/ojmp.2023.122005

Received: August 7, 2022
Accepted: April 25, 2023
Published: April 28, 2023

Abstract

Background: The two most common types of cephalalgia in women are migraine and tension-type cephalalgia. Cephalalgia is associated with an increased risk of developing pregnancy complications or psychological difficulties. **Objectives:** To investigate the prevalence and the characteristics of maternal cephalalgia during pregnancy and early postpartum and identify associated risk factors. **Study Design:** This study was conducted between May 2012 and August 2012. The study population comprised 170 mothers. The interviews were conducted in a postnatal ward during the first postpartum week and information on the characteristics of maternal cephalalgia before and during pregnancy was collected. Data regarding previous history of cephalalgia, pregnancy and postpartum health history, as well as the mode of delivery were also recorded. Mothers were given a cephalalgia diary in order to record medication use, as well as cephalalgia attack frequency, severity (5-level scale) and duration. The following surveys were administered: Edinburgh Postnatal Depression Scale (EPDS), Mediterranean Diet Score (Medi Score), International Physical Activity Questionnaire (IPAQ) and Women Abuse Screening Tool (WAST) within the first week postpartum. Statistical analyses were performed using SPSS 19. The level of statistical significance was set at $p < 0.05$. **Results:** Maternal self-reported cephalalgia in pregnancy and early postpartum was significantly associated with scores in EPDS (depressive symptoms) ($p = 0.005$), hypertension ($p < 0.004$), thyroid pathology ($p < 0.003$), IVF ($p < 0.006$) and psychological abuse ($p < 0.001$). Mothers with a previous history of cephalalgia (51.8%) did not experience any worsening or even experience improvement of symptoms during pregnancy or early postpartum. A significant pro-

portion of pregnant women who did experience cephalalgia used paracetamol/acetaminophen (56.5%), aspirin (32.3%), or triptans (6.5%), while 36.8% did not use any medication. **Conclusion:** Pregnancy and early postpartum is a graceful period in women with cephalalgia. However, cephalalgia is associated with an increased risk of developing pregnancy complications or psychological difficulties. Further studies should elucidate the safety and recommended use of cephalalgia medication during pregnancy and breastfeeding.

Keywords

Cephalalgia, Pregnancy, Postpartum, EPDS, WAST

1. Introduction

Cephalalgia is one of the most common reasons for office and emergency room visits (1% of all visits) and the number one referral for neurological consultation in the outpatient setting [1] [2]. The two most common types of cephalalgia in women are migraine and Tension-Type headache (TTH) cephalalgia with lifetime prevalence rates of 25% and 88%, respectively.

Extensive studies have been published on the relationship between female sex hormone levels and cephalalgia, particularly migraine [3] [4] [5]. In women, migraine has been extensively studied in relation to reproductive milestones (menarche, pregnancy and menopause) [6]. Migraine has not been proven to affect fertility or the course of pregnancy [7], but pregnancy substantially alters migraine.

Few studies focusing on cephalalgia during pregnancy have been cited in the literature [8] and little is known about other factors influencing its occurrence in pregnant women. Hormonal changes, fatigue, tension, hunger, as well as physical and emotional stress can be listed as predisposing factors during this period [9]. Data are available regarding the effect of pregnancy on cephalalgia and in particular on migraine, which has been reported to improve during pregnancy in a high percentage of patients [10] [11]. TTH does not show any improvement during pregnancy [12] [13]. The normal amelioration of primary cephalalgias during pregnancy varies greatly among women [14]. Adverse perinatal outcomes associated with ischemic placental disorders are noted to be increased among pregnant women suffering from migraine [15].

Pregnancies complicated by preterm delivery, low birth weight, placental abruption and hypertensive disorders of pregnancy including preeclampsia are now recognised to be more common among pregnant migraineurs. Moreover, migraine has been reported to be associated with Intimate Partner Violence (IPV) [16] [17] and depressive symptoms [8] [18].

Consequently, the objectives of this study were: 1) to determine rates of cephalalgia symptomatology during pregnancy and after birth in a sample of Greek

women, and 2) to explore the potential relationship between cephalalgia and predictors of depressive symptoms, psychological abuse, diet, exercise, as well as pathologic conditions during the perinatal period.

2. Materials and Methods

2.1. Sample Characteristics and Data Collection

A University Maternity Hospital, which serves the population of Athens, was selected for the recruitment process. Demographic questionnaire and the translated, culturally adapted Greek versions of EPDS, WAST, MediScore and IPAQ were administered to mothers who delivered their babies between May 2012 and August 2012. Completed questionnaires were retrieved daily from each recruitment site. In order to be eligible for participation, mothers had to: 1) be 18 to 45 years old; 2) have delivered a healthy infant; 3) be able to complete the questionnaires in a private room by themselves; 4) be fluent in spoken and written Greek; and 5) be able to provide informed consent. Women were excluded if they had had an episode of depression in the previous 2 years or if they had received pharmacological or psychotherapeutic treatments for depression that lasted 3 consecutive months (minimum treatment of once per week). The study flow diagram is shown in Figure 1.

Of the 201 women who were eligible to participate, 22 were excluded for reasons such as refusal, language difficultiesandother. The total sample recruited from the perinatal care registers of the Maternity Departments of the Maternity Hospital comprised 170 women. Participants were randomly selected by clinic or shift. The midwife researcher created a calendar to ensure balance across shifts and days of the week. More specifically, the women were recruited at a steady rate, on a different day each week (*i.e.* on Monday one week, on Tuesday the

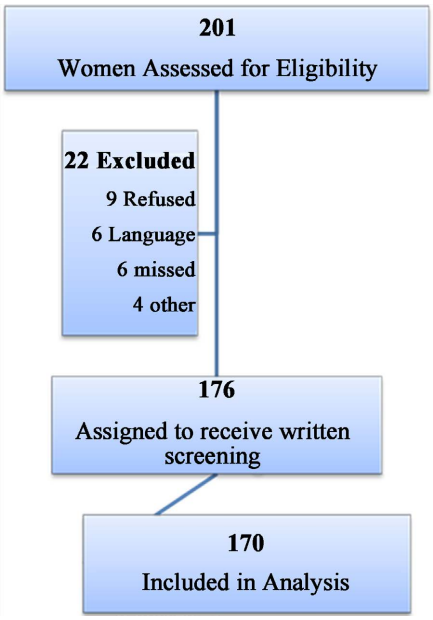

Figure 1. Study flow diagram

following week, on Wednesday the week after that, and so on), so as to avoid bias connected to possible seasonality. Each recruitment day was split into three shifts (8 a.m., 4 p.m., 12 a.m.), and we chose the first 4 women who had given birth after 8 a.m., the following week after 4 p.m., etc., so as to eliminate possible bias, such as delivery mode. The study was conducted in Athens from May 2012 to August 2012.

In addition to standard demographic questions, women completed the EPDS, WAST, MediScore and IPAQ questionnaires in the presence of a midwife during their stay at the postnatal ward. The order of completion of the four above-mentioned questionnaires was counterbalanced. For safety reasons, no reference to "abuse" or "violence" was made until women were taken to a private room where oral informed consent was given. Mothers were encouraged to discuss any concerns they might have and were told that their midwife would be informed of their responses during the screening process. All participants were informed verbally about health services in the community and of the opportunity to destroy any study material they felt might put them at risk.

2.2. Measures

Instruments

A demographic questionnaire was constructed to collect basic sociodemographic information such as income, employment status, ethnicity and education, as well as reproductive history including history of miscarriage or pregnancy termination, family planning, mode of delivery and prenatal/postnatal complications.

Edinburgh Postnatal Depression Scale (EPDS) [19]

The EPDS is a 10-item self-report scale consisting of statements describing depressive and anxiety symptoms. Each item is scored on a point scale ranging from 0 - 3, depending on the severity or duration of each symptom. The Greek version of EPDS used in this study was validated and showed high internal consistency (Cronbach's alpha = 0.804 and Guttman split-half coefficient 0.742). The Greek EPDS was significantly correlated (Pearson $r = 0.66$ $p < 0.0005$) with the validated Greek version of BDI-II (Beck Depression Inventory II [20]. A threshold score of 8/9 fitted the model sensitivity at 76.7% and model specificity at 68.3% [21].

Women Abuse Screening Tool (WAST) [22]

The original English version of WAST consists of 8 short questions and it is a self-report scale consisting of statements describing forms of abuse (physical, sexual and emotional). Each question has three possible graded answers, depending on the severity or duration of each form of abuse. It has good internal consistency (Cronbach's α coefficient of 0.95), and is well accepted by women [22] [23]. The first 2 questions of WAST form the WAST-Short, which has been very useful for screening for abuse, since those questions are more convenient to answer, from the women's point of view [22]. The remaining questions contribute to the final assessment of emotional abuse. In the validation study, signifi-

cant differences were found between the abused and non-abused women regarding the mean total WAST scores (18 vs 8.8, respectively; $p < 0.001$) [22]. A threshold score of 0/1 fitted the model sensitivity at 99.7% and model specificity at 64.4% [24].

Mediterranean Diet Score **[25]**

MediScore includes the consumption of the following nutritional groups in the diet: non-refined cereals (whole bread, pasta, rice, other grain, biscuits, etc.), fruit, vegetables, legumes, potatoes, fish, meat and meat products, poultry, full fat dairy products (like cheese, yoghurt and milk), as well as olive oil and alcohol intake. The point scale ranges from 0 - 5, depending on consumption per week and the score ranges from 0 to 55. Higher values of this diet score indicate greater adherence to the Mediterranean diet.

International Physical Activity Questionnaire **(*IPAQ*) [26]**

We used the IPAQ-short version, which consists of a 9-item questionnaire. The purpose of the IPAQ is to sum up vigorous, moderate and walking Physical Activities (PAs) over the previous seven-day period and generate a total PA score, expressed in MET-minutes per week. PA status is classified into three categories (PA classes): 1) low, 2) moderate and 3) high PA class. The Greek version presented with acceptable reliability [27] and validity [28] properties in young Greek adults.

2.3. Procedure

2.3.1. Ethics

The study was approved by the Research Ethics Board of the Maternity Hospital. All participants provided verbal informed consent prior to enrolment. Along with the questionnaires there was a cover letter explaining the purpose of the study, providing the researchers' affiliation and contact information, and clearly stating that answers would be confidential and anonymity would be guaranteed in the final data reports.

2.3.2. Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics version 19. Descriptive characteristics (including means, standard deviations, frequencies and percentages) were calculated for the sociodemographic variables. Group comparisons were examined using chi-square analyses or Fisher's exact test (depending on expected cell counts) for categorical outcome variables and one-way ANOVA for continuous outcome variables between mothers who experienced cephalalgia and the mothers who didn't experience cephalalgia during perinatal period. The assumptions of normality, homogeneity and independent cases of the sample were checked. An alpha level of 0.05 was used for all statistical tests. However, due to the exploratory nature of this study, only predictors with odds ratios above 1.5 or below 0.5 were considered relevant to the findings.

Exploratory Structural Equation Modelling **(*ESEM*)**

ESEM was performed to investigate the factor structure and to test the in-

variance of structure in the two groups (cephalalgia and no cephalalgia). ESEM differs from traditional Confirmatory Factor Analysis (CFA) in terms of factor loading estimations. Simple structures are tested by CFA (each indicator is influenced by only one factor) and rely on strong hypotheses about the factor structure; ESEM is less restrictive and allows loading matrix rotation and therefore loading variation across factors, as in Exploratory Factor Analysis (EFA). ESEM provides more flexibility in a complex measurement structure. It also allows multiple-group EFA with measurement invariance, which is needed to test for structural invariance between the two groups of mothers (cephalalgia and no cephalalgia group). To assess the adequacy of the model, the following fit indices were used:

- The Root Mean Square Error of Approximation (RMSEA), which is an approximation of the fit in the population. A value of 0.05 or less can be considered a good fit, whereas a RMSEA between 0.05 and 0.08 can be interpreted as an acceptable fit [29];
- The Comparative Fit Index (CFI), which compares the result to the independence model. Values greater than 0.95 are considered a good fit, and those between 0.90 and 0.95 an acceptable fit [30];
- The Standardised Root Mean Square Residual (SRMR) for EFA and the Weighted Root Mean Square Residual (WRMR) for ESEM calculated the difference between observed and predicted correlations. Values under 0.10 for SRMR and 0.90 for WRMR are interpreted as good fits [31].

***Structural Equation Modelling* (*SEM*)**

SEM was then conducted on the different models to test their predictive accuracy effects on cephalalgia, depressive symptoms measured by EPDS, physical, sexual and emotional abuse measured by WAST, diet intake (vegetables and diary), thyroid pathology and IVF. The model considered the effects of the above latent variables on cephalalgia during the 1st, 2nd and 3rd trimester of pregnancy and the early postpartum period. This time, we constrained the loading of experiences related to the other factor to zero in order to see the pure effect of each latent variable on cephalalgia. The fit indices described above were used to assess which model was best. SEM was performed controlling for socio-demographic variables and other significant variables as found by the ESEM analysis correlated with cephalalgia during pregnancy.

3. Descriptive Results

The sociodemographic characteristics of participants are presented in **Table 1**. The age of women ranged from 20 to 42 years (mean 31.21 years, Standard Deviation 5.95). The cephalalgia rate was 25.4%, 13.7%, 19.5% and 20.8% during the first, second, third trimesters and early postpartum, respectively. The more prevalent related symptoms of mothers experiencing cephalalgia included nausea (65.9%), vomiting (61.3%), photophobia (50%), vertigo (56%), sweating (44.4%), disruption of speaking (35.2%) and dizziness (64.3%). Maternal self-reported

Table 1. Characteristics of the study sample.

	All Women No (%)	Cephalgia No (%)	No Cephalgia No (%)	P-value
Nationality				0.54
Greek	136 (80)	58 (43.4)	69 (51.0)	
Other	27 (16.1)	2 (1.0)	10 (4.3)	
Education				0.03
Elementary & Junior High	18 (10.3)	11 (6.5)	7 (3.8)	
High School	50 (29.9)	27 (17)	23 (12.9)	
University/College Education	64 (38.5)	27 (14.2)	37 (24.1)	
Postgraduate Studies	29 (16.7)	2 (1.2)	27 (15.5)	
Work Status				0.95
Housewife	35 (20.5)	18 (19.5)	14 (15.2)	
Unemployed	40 (23.5)	4 (4.3)	3 (3.2)	
Student	2 (1.1)	1 (0.5)	1 (0.5)	
Public Sector	15 (8.8)	5 (2.9)	10 (5.9)	
Private Sector	54 (31.8)	25 (14.7)	29 (17.1)	
Independent	15 (8.8)	4 (3.2)	11 (9.7)	
Other	9 (5.3)	1 (0.6)	8 (4.7)	
Family Income per Month				0.49
500 - 1000 Euros	40 (23.2)	14 (10.4)	26 (12.7)	
1000 - 2000 Euros	57 (33.7)	30 (17.4)	27 (16.2)	
2000 - 3000 Euros	40 (23.2)	14 (8.1)	26 (15.1)	
>3000	33 (19.7)	11 (5.8)	22 (13.9)	
Religion				0.06
Christian Orthodox	168 (98.9)	76 (44.5)	92 (54.3)	
Catholic	0 (0.0)	0 (0.0)	0 (0.0)	
Muslim	2 (1.0)	0 (0.0)	2 (1.0)	
Atheist	0 (0.0)	0 (0.0)	0 (0.0)	
Other	0 (0.0)	0 (0.0)	0 (0)	
Gravida				0.53
Primigravida	84 (49.4)	37 (21.9)	46 (27.4)	
Multigravida	85 (50.5)	40 (23.0)	46 (27.4)	
Marital Status				0.37
Married	168 (98.9)	73 (42.8)	95 (56.0)	
Single	2 (1.1)	2 (1.1)	0 (0.0)	

Continued

Divorced	0 (0.0)	0 (0.0)	0 (0.0)	
Mode of Delivery				0.09
Vaginal Birth	78 (45.7)	28 (16.3)	48 (29.4)	
Caesarean Section	90 (54.3)	48 (28.2)	44 (26.1)	
Abortions				0.73
No	159 (90.0)	67 (42.2)	92 (47.7)	
Yes	10 (10.0)	2 (2.2)	8 (7.7)	
Miscarriages				0.19
No	140 (78.8)	57 (36.6)	83 (42.2)	
Yes	25 (21.1)	7 (6.6)	18 (14.4)	

cephalalgia in pregnancy and early postpartum was significantly associated with scores on EPDS (no depressive symptoms 55.4%, depressive symptoms 44.6%), hypertension, thyroid pathology, IVF and psychological abuse. No mother experienced a worsening of cephalalgia during pregnancy or early postpartum (51.8% before pregnancy). A significant proportion of women used paracetamol/acetaminophen (56.5%), aspirin (32.3%) and triptans (6.5%), while 36.8% did not receive any medication.

Univariate independent t tests and chi-square tests revealed that non-responders did not differ significantly from the respondents in age, educational level, working status, marital status or parity.

***Exploratory Structural Equation Modelling* (*ESEM*)**

The exploratory factor analysis revealed three orthogonal factors (KMO measure of sampling adequacy = 0.60 and Bartlett's test of sphericity = 70.021, df = 21, $p < 0.0005$).The first factor (F1) includes mothers who undergo IVF and experience thyroid pathology. These are specific questions for high-risk pregnancy; therefore, this subscale was named "High Risk". The second factor (F2) is composed of items that report depressive symptoms and psychological abuse. These are specific questions regarding maternal psychological status of the mother; therefore, we named this subscale "Psychology". The third factor (F3) is composed of the items "Physical Activity" and "Dairy Intake". These are specific questions regarding physical activity and diet; therefore, we named this subscale "Physical Activity and Diet".

***Structural Equation Modelling* (*SEM*)**

The fit indices for the model: RMSEA = 0.039, CFI = 0.977, WRMR = 1.478. Goodness of Fit Statistics was also estimated. Minimum Fit Function Chi-Square = 628.96, p = 0.05; Root Mean Square Error of Approximation (RMSEA) = 0.107.

4. Discussion

To the best of our knowledge, this is the first study to report the associations of

maternal cephalalgia with physical activity and diet. We found that women with cephalalgia had increased levels of depressive symptoms measured by EPDS [32]. Since this study may be one of the first to investigate whether maternal cephalalgia status is associated with physical, sexual and emotional abuse measured by WAST, diet intake (vegetables and diary), thyroid pathology and IVF, our findings can only tentatively be compared with studies that have separately investigated these perinatal predictors.

This study aimed to explore the factor structure by comparing two groups of mothers (cephalalgia and no cephalalgia). Both the EFA and ESEM showed that the model could fit the results quite well. The predictive accuracy of the model was then tested using SEM, with the latent variables [depressive symptoms measured by EPDS [32], the physical, sexual and emotional abuse measured by WAST, diet intake (vegetables and diary), thyroid pathology and IVF] considered as predictors of maternal cephalalgia.

Our findings are generally consistent with other studies reporting associations of cephalalgia with hypertensive disorders, including preeclampsia [33]. To summarise, the three-factor model did not only seem to be the best model from a statistical point of view, but also from a clinical point of view, as it could differentiate how the specific variables predict maternal cephalalgia. A significant proportion of mothers who experienced cephalalgia didn't use any medication (36.8%), however (56.5%) used paracetamol/acetaminophen, aspirin (32.3%) and triptans (6.5%). The safety of Cephalalgia treatment has been discussed and is associated with adverse outcomes [33] [34].

This study presents some limitations. First, the study design and our reliance on self-reported signs and symptoms of cephalalgias (using a questionnaire that was not validated in the specific study population) raise concerns about recall bias. To help mitigate the likelihood of systematic reporting errors, a well-trained interviewer-midwife used a standard questionnaire to collect information from the study participants. Moreover, neither the interviewer nor the participants were aware of any of the specific study hypotheses. Second, we didn't include the information about maternal use of medications to treat cephalalgia in the statistical analysis. Future studies will have to include this information so that independent and joint effects of maternal cephalalgia and medication use can be evaluated.

Nevertheless, participants in our study had similar sociodemographic and medical characteristics to those reported in other previous relevant Greek studies [22]. Furthermore, efforts were made to recruit a representative sample and rapid socioeconomic changes over the last three decades have led to a relatively homogenous cultural background in Greece. The vast majority of women from rural areas are routinely transferred to deliver in Athens and more specifically to the large metropolitan university hospital of our study. Finally, in spite of the above concerns, the size of our sample was satisfactory for the statistical analysis [34] [35].

Our results suggest that the risk of pathology is increased in women having cephalalgia during pregnancy. However, prospective cohort studies are needed to elucidate the possible association of cephalalgia and/or its treatments with the occurrence of physical, sexual and emotional pathology. Results from studies that allow for characterising cephalalgia history according to the age of onset, frequency, and triggers will likely yield new information that can be used to develop strategies for the prevention and control of cephalalgia in reproductive-aged women. Our results add to the evolving literature, which suggests that pregnant women with cephalalgia should be considered at high risk for developing complications. Preconception counseling, important for women with any medical conditions including cephalalgia, may provide opportunities for optimising control of cephalalgia symptoms with the lowest effective doses of the lowest number of medications; or if appropriate, with non-pharmacological treatment including biofeedback-assisted relaxation, hydration, improved sleep hygiene and reductions in occupational and home activities.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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