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Depressive Symptoms and Migraine Comorbidity among Pregnant Peruvian Women

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Abstract

Background—Migraine and depression are known to be comorbid conditions in non-pregnant women and men. However, the migraine-depression comorbidity among pregnant women, particularly women in developing countries has not been evaluated. Therefore, we evaluated the migraine-depressive symptom relationship in a large cohort of pregnant Peruvian women.

Methods—Women who delivered singleton infants (N=2,293) at the Instituto Nacional Materno Perinatal, Lima, Peru were interviewed during the postpartum hospital stay. Women were asked questions related to their lifetime and pregnancy experiences with headaches and migraines. Responses to these questions enabled the classification of “probable” and “strict” migraines according to the International Headache Society diagnostic criteria. Depressive symptoms were assessed using the nine-item Patient Health Questionnaire Depression Subset. Logistic regression procedures were used to estimate adjusted odds ratios (AORs) and 95% confidence intervals (CIs).

Results—Approximately 32% of the women reported a history of migraine, while 41% reported experiencing moderate to severe depressive symptoms during pregnancy. Compared with women without a history of migraine, women with strict migraine had AORs of 2.12 (95% CI 1.54–2.93), 1.85 (95% CI 1.16–2.96) and 2.23 (95% CI 1.08–4.62) for moderate, moderately severe and severe depressive symptoms, respectively.

Conclusion—This is the first report of a cross-sectional association between migraine and depressive symptoms in pregnant women. If our findings are confirmed, pregnant women with a history of migraine may benefit from increased vigilance for screening and treating depressive symptoms.

Keywords

Migraine; Depressive symptoms; Pregnant women; Peru

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1. Introduction

Migraine, a recurrent primary headache disorder, is characterized by episodes of severe throbbing, pulsatile headache associated with nausea, vomiting, photophobia, phonophobia, and aversion to physical activity (Menon and Bushnell, 2008). Migraines are particularly common among women of childbearing age (Lipton et al., 2007). Age-specific prevalence of migraine in women of childbearing age has been reported to range between 5% and 45% (Lipton et al., 2007; Morillo et al., 2005). Reviews of migraine during pregnancy have found that preexisting migraine may diminish or disappear in majority of pregnant women, or remain unchanged, worsen or appear for the first time during pregnancy (Adeney and Williams, 2006; Menon and Bushnell, 2008). Moreover, several investigators have reported associations between a history of migraine and an increased risk of preeclampsia (Adeney and Williams, 2006; Sanchez et al., 2008) and stroke during pregnancy (James et al., 2005; Kittner et al., 1996).

Perinatal depression encompasses major and minor depressive episodes that occur either during pregnancy or within 1 year postpartum (Bennett et al., 2004). Meta-analyses of perinatal depression reported point prevalence estimates between 6% and 13% (Gavin et al., 2005). Perinatal depression is of concern because it has been linked to negative health-related behaviors and outcomes, including poor nutrition, increased use of alcohol, tobacco and illicit drugs, inadequate prenatal care, impaired fetal growth, preeclampsia, preterm delivery, postpartum postnatal depression, and suicide (Barrio and Burt, 2000; Hoffman and Hatch, 2000; Horrigan et al., 2000; Kurki et al., 2000; Llewellyn et al., 1997; Najman et al., 2000).

Clinic and community-based studies have documented associations between depression and migraine (Breslau et al., 1994; Breslau et al., 2003; Breslau et al., 2000; Jette et al., 2008; Kalaydjian and Merikangas, 2008; Merikangas et al., 1990; Swartz et al., 2000; Zwart et al., 2003). Some of these studies have demonstrated bi-directional relationships between migraine and depression, with each disorder increasing the relative risk for the subsequent first onset of the other (Breslau et al., 1994; Breslau et al., 2003; Breslau et al., 2000; Swartz et al., 2000). To our knowledge, there is no published study on the association between migraine and depression in pregnant women.

Both migraine and depression are prevalent among women in Lima, Peru (Adeney et al., 2006; Peru, 2002). A survey conducted in the metropolitan areas of Lima and Callao documented a high prevalence of lifetime depressive disorders (23%) (Peru, 2002). Additionally, lifetime prevalence of migraine among reproductive age women in Lima were reported to be 29% (Adeney et al., 2006) and 17% (Sanchez et al., 2008). The high prevalence of migraine and depressive disorders, together with the potential for co-occurrence of these disorders are a concern because a diagnosis of one should lead to increased vigilance for screening and treating the other. There are no published reports on the co-occurrence of migraine and depressive symptoms in pregnant women. We, therefore, examined the relationship between migraine and depressive symptoms in a large cohort of pregnant Peruvian women who participated in a postpartum interview study.

2. Methods

2.1 Subjects

Participants were 2,394 women who delivered at the Instituto Nacional Materno Perinatal (INMP) in Lima between August, 2005 and June, 2006. Study subjects were recruited within 4 days of delivery, and the participation rate was 99%. Written consent was obtained from all participants. Of the 2,394 participants, women who delivered twins (n=31), had infants with

gross malformation (n=43), and with missing information on key variables such as migraine status or depressive symptoms (n=27) were excluded, leaving 2,293 (95.8%) women for analyses. Institutional review boards of INMP, Lima and the University of Washington, Seattle approved this study.

2.2 Data collection procedures and measurement

Women were interviewed using a structured questionnaire during the postpartum delivery stay. Participants' age were categorized as follows: <20, 20–29, 30–34, and ≥35 years. Educational attainment was categorized as ≤6, 7–12, and >12 years of education. Other sociodemographic variables were categorized as follows: marital status (married, living with husband, and others); parity (nulliparous vs. multiparous); race (Mestizo vs. others); housing status (home owner vs. other); access to basic foods and medical care (limited vs. somewhat limited); employment, prenatal care, consumption of prenatal care vitamins, unintended pregnancy (unplanned index pregnancy), and any intimate partner violence (physical, sexual or emotional) during lifetime and during pregnancy (yes vs. no); delayed prenatal care (during vs. after first trimester), and frequency of prenatal care visit (≥7, 1–6, none).

All women were asked if they suffered headaches repeatedly the past four to five years, and if yes, whether they suffered from headache everyday. Headache classification was determined using the modified International Headache Society (IHS) criteria for migraine without aura (IHS, 2004). “Strict migraine” (IHS category 1.1) was defined by at least five lifetime headache attacks lasting 4–72 hours, with at least two of the qualifying pain characteristics (unilateral location, pulsating quality, moderate or severe pain intensity, aggravation by routine physical exertion), at least one of the associated symptoms (nausea and/or vomiting, photo/phonophobia), and not readily attributable to another central nervous system disorder or head trauma (according to subject self-report). “Probable migraine” (IHS category 1.6.1) was designated if all but one of the migraine without aura criteria were fulfilled, excluding headaches attributable to another disorder.

Depressive symptomatology during pregnancy was evaluated using the Patient Health Questionnaire-9 (PHQ-9) (Kroenke et al., 2001). The instrument has been demonstrated to be a reliable tool for assessing recent psychosocial stressors among obstetrics-gynecology patients (Spitzer et al., 2000) and in Spanish-speaking women (Wulsin et al., 2002). The PHQ-9 scale includes nine items, and choices for responses were a) never; b) several weeks, over the pregnancy; c) more than half the pregnancy; or d) nearly the whole pregnancy. The PHQ-9 total score is the sum of scores for the nine items for each woman, and ranged from 0–27. We defined two sets of categorical variables using these data. First, women were assigned to one of four depressive symptom categories based on total PHQ-9 score, (a) no depressive disorder (0–9), (b) moderate (10–14), (c) moderately severe (15–19) and (d) severe (20–27). Second, women were assigned into one of two categories of depressive disorder based on total PHQ-9 score, (a) no depressive disorder (0–9) and (b) major or other depressive disorder (10–27) (Kroenke et al., 2001). The headache and migraine questions and PHQ-9 have been used successfully in other studies of pregnant Peruvian women (Adeney et al., 2006; Sanchez et al., 2008).

2.3 Statistical analyses

Frequency distributions of maternal socio-demographic characteristics, medical and reproductive histories were examined. Logistic regression procedures were used to calculate maximum likelihood estimates of odds ratios (ORs) and 95% confidence intervals (CIs), adjusted for potential confounders (Rothman and Greenland, 1998). To assess confounding, variables were entered into the logistic regression model one at a time, and adjusted ORs were compared to unadjusted ORs. Final logistic regression models included covariates that altered

unadjusted ORs by 10%, (Maldonado and Greenland, 1993) as well as maternal age and race. All reported p-values are 2-tailed with statistical significance set at 0.05.

3. Results

The majority of the women were between 20 and 29 years of age, unmarried, had low levels of education, and limited access to basic foods and medical care. Approximately 32% of the sample reported a history of migraine while 41% of the sample reported moderate to severe depressive symptoms (PHQ-9 score ≥ 10) during pregnancy (Table 1). Our results indicate that 55.1% of women with strict migraine and 48.0% of women with probable migraine experienced moderate to severe depressive symptoms during pregnancy. Adjusted odds ratios (AORs) and 95% CI for each level of depression severity associated with history of strict migraine were: moderate 2.12 (1.54–2.93); moderately severe 1.85 (1.16–2.96); and severe 2.23 (1.08–4.62). We report an increased risk for moderate to severe depressive symptoms in women with probable migraine (AOR=1.58, 95% CI 1.29–1.93) and strict migraine (AOR=2.06, 95% CI 1.54–2.76) when compared with women without migraine (Table 2). All reported risks were adjusted for maternal age and race.

4. Discussion

Women with a history of migraine had statistically significantly higher odds of moderate to severe depressive symptoms when compared with women without migraine. To the best of our knowledge, this is the first study examining the relationship between migraine and depressive symptoms in pregnant women. Although there are no published findings for this relationship specific to pregnant woman, our findings are consistent with the following cross-sectional studies reporting associations between migraine and depression at the population level. Merikangas et al. (1990) reported a strong association between major depression and migraine (OR=2.2, 95% CI 1.1–4.8) for men and women in Zurich, Switzerland. In the United States, Swartz et al. (2000) reported a 3-fold increased odds (OR=3.1, 95% CI 2.0–4.0) for migraine among individuals with major depression. Zwart et al. (2003) found that the OR for depression was significantly higher in Norwegians with migraine compared with headache-free Norwegians (OR=1.9, 95% CI 1.6–2.3), while McWilliams et al reported an OR of 2.8 (95% CI 2.2–3.7) in US adults (McWilliams et al., 2004). Other investigators (Patel et al., 2004) who conducted a study in a health maintenance organization reported an increased odds for major depression in individuals with strict (OR=2.7, 95% CI 2.2–3.3) and probable migraine (OR=1.9, 95% CI 1.5– 2.4) when compared with those without migraine.

The pathogenesis for comorbid migraine and depression remains unknown. However, investigators have speculated that migraine may share some common etiologic factor (genetic, biochemical or environmental factor) with depression or that a causal relationship exists between the two disorders (Kalaydjian and Merikangas, 2008; Torelli et al., 2006). Findings of a bi-directional influence between migraine and major depression (Breslau et al., 1994; Breslau et al., 2003) suggest a common neuropathology with a hypothesis that migraines and major depression may be linked through dysfunction of the serotonergic and dopaminergic systems (D'Andrea et al., 1989; Frediani and Villani, 2007; Meltzer and Lowy, 1987). The depletion of 5-hydroxytryptamine (5-HT) has been shown to induce migraine, while reserpine can initiate a migraine attack (Curzon et al., 1969). Low levels of platelet 5-HT and presence of reserpine have also been found in depressed individuals (Weiner, 1980). Longitudinal studies are needed to clarify the temporal relation of the symptoms and diagnoses of each disorder.

Several important limitations should be considered when interpreting our study results. First, our cross-sectional study design prohibits clarification of the temporal relationship of migraine

and depression onset in the cohort. Second, participants did not receive formal clinical evaluation and diagnosis for migraine and depression. However, instruments used to characterize these disorders have well established psychometric properties in diverse study populations (Adeney et al., 2006; Wulsin et al., 2002). Third, maternal depressive symptoms and migraine were assessed after delivery; and thus may be subject to recall bias. Finally, despite controlling for potential confounders, residual confounding by factors not measured in our study (e.g., smoking, and alcohol use) may have influenced reported risk estimates. However, the prevalence of these behaviors among pregnant women in Lima are reported to be <5% (Sanchez et al., 2006). Nevertheless, we cannot rule out residual confounding by these unmeasured covariates.

In summary, we found associations between independent disorders of migraine and depressive symptoms in this sample of Peruvian women. The comorbidity of migraine and depressive symptoms supports the need for integration of both migraine and mental disorders in clinical evaluation and treatment of patients with these disorders (Bigal and Lipton, 2006; Breslau et al., 2003; Frediani and Villani, 2007). Women with migraine should be carefully screened for depression.

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Table 1

Frequency distribution of maternal characteristics, Lima, Peru.

Characteristic	Frequency (n=2,293)	%
Maternal age (year \pm SD; continuous)	27.0 \pm 6.0	
Maternal age (years)		
< 20	161	7.0
20 – 29	1,414	61.7
30 – 34	402	17.5
35 and older	316	13.8
Education		
More than 12 years	267	13.0
7 – 12 years	284	12.4
Less than or equal to 6 years	1,708	74.5
Missing	4	0.2
Unmarried	1,951	85.1
Unemployed	1,263	55.1
Multiparous	1,322	57.7
Mestizo	2,064	90.0
Limited access to basic foods	1,606	70.0
Limited access to medical care	1,821	79.4
No prenatal care	65	2.8
Delayed first prenatal care visit (after first trimester)	842	36.7
Frequency of prenatal care visit		
\geq 7	1,301	56.7
1 – 6	915	39.9
None	65	2.8
Missing	12	0.5
Unintended pregnancy	1,482	64.6
Any lifetime intimate partner abuse	1,030	44.9
Any pregnancy intimate partner abuse	490	21.4
Migraine status		
No	1,560	68.0
Probably	519	22.6
Strict	214	9.3
Depressive symptoms		
Mild and minimal	1,353	59.0
Moderate to severe	940	41.0

Table 2

Depressive symptoms and migraine comorbidity among women, Lima, Peru.

Depressive symptoms (PHQ-9 total score)	No migraine (n=1,560)		Probable migraine (n=519)		Strict migraine (n=214)	
	n (%)	n (%)	n (%)	Adjusted OR ^{*a} (95% confidence interval)	n (%)	Adjusted OR ^{*b} (95% confidence interval)
Mild and minimal (<10)	987 (63.3)	270 (52.0)	1.00 (Referent)	96 (44.9)	1.00 (Referent)	
Moderate (10–14)	386 (24.7)	157 (30.3)	1.48 (1.18–1.87)	81 (37.9)	2.12 (1.54–2.93)	
Moderately severe (15–19)	145 (9.3)	67 (12.9)	1.69 (1.23–2.33)	26 (12.1)	1.85 (1.16–2.96)	
Severe (20–27)	42 (2.7)	25 (4.8)	2.04 (1.22–3.42)	11 (5.1)	2.23 (1.08–4.62)	
Mild and minimal (<10)	63.3	270 (52.0)	1.00 (Referent)	44.9	1.00 (Referent)	
Moderate to severe (10–27)	36.7	249 (48.0)	1.58 (1.29–1.93)	55.1	2.06 (1.54–2.76)	

* Adjusted for age and race.

^a Comparison between probable migraine and no migraine.

^b Comparison between strict migraine and no migraine.