Migraine and the risk of post-traumatic stress disorder among a cohort of pregnant women

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Abstract

Background: Individually both migraine and post-traumatic stress disorder (PTSD) prevalence estimates are higher among women. However, there is limited data on the association of migraine and PTSD in women during pregnancy.

Methods: We examined the association between migraine and PTSD among women attending prenatal clinics in Peru. Migraine was characterized using the International Classification of Headache Disorders (ICHD)-III beta criteria. PTSD was assessed using the PTSD Checklist-Civilian Version (PCL-C). Multivariable logistic regression analyses were performed to estimate odds ratios (OR) and 95% confidence intervals (CI) after adjusting for confounders.

Results: Of the 2922 pregnant women included, 33.5% fulfilled criteria for any migraine (migraine 12.5%; probable migraine 21.0%) and 37.4% fulfilled PTSD criteria. Even when controlling for depression, women with any migraine had almost a 2-fold increased odds of PTSD (OR: 1.97; 95% CI: 1.64–2.37) as compared to women without migraine. Specifically, women with migraine alone (i.e. excluding probable migraine) had a 2.85-fold increased odds of PTSD (95% CI: 2.18–3.74), and women with probable migraine alone had a 1.61-fold increased odds of PTSD (95% CI: 1.30–1.99) as compared to those without migraine, even after controlling for depression. In those women with both migraine and comorbid depression, the odds of PTSD in all migraine categories were even further increased as compared to those women without migraine.

Conclusion: In a cohort of pregnant women, irrespective of the presence or absence of depression, the odds of PTSD is increased in those with migraine. Our findings suggest the importance of screening for PTSD, specifically in pregnant women with migraine.

Keywords: Migraine, Post-traumatic stress disorder, PTSD, Pregnancy

Background

According to the National Health Interview Survey in 2011, 26.1% of women 18–44 years of age reported migraines or severe headaches in the last 3 months [1]. Migraine is more prevalent among reproductive-aged women as compared to men [2] and from early to middle adulthood as compared to younger or older individuals [1]. Migraine also often adversely affects the health of large populations [3]. Further, migraine in pregnancy is associated with an increased risk of perinatal complications including preeclampsia [4, 5], preterm delivery [6], placental abruption [7], hypertensive disorders [6], as well as cardiovascular disease and stroke [8–11].

Maternal mood and anxiety disorders have been implicated as important risk factors for migraine [12–16]. Migraine during pregnancy is associated with an increased risk of depression [17, 18] and suicidal ideation [19]. Additionally, both migraine and PTSD are more prevalent in reproductive-aged women as compared to men [2, 3]. Although increasing data supports an association between posttraumatic stress disorder (PTSD) and migraine in U.S. cohorts [3, 20, 21], no prior study has examined the risk
of PTSD in pregnant women. Further there is little evidence for the association between migraine and PTSD in women from low income countries or the impact of depression on this association. To fill in these gaps in the literature, we examined the association between migraine and PTSD among a cohort of pregnant women in Lima, Peru.

**Methods**

**Study population**

The study population for this cross-sectional study was drawn from participants of the Pregnancy Outcomes, Maternal and Infant Study (PrOMIS) cohort. The PrOMIS cohort has been described previously [22–25]. The cohort was designed to examine maternal social and behavioral risk factors on the development of preterm birth and other adverse pregnancy outcomes among Peruvian women. The PrOMIS cohort was comprised of women attending prenatal care clinics at the Instituto Nacional Materno Perinatal (INMP) in Lima, Peru. INMP is operated by the Peruvian government and is the primary reference establishment for maternal and perinatal care. Women were eligible for inclusion if they initiated prenatal care before 16 weeks of gestation, were at least 18 years of age, and could speak and read Spanish. Pregnant women were excluded if they have mental retardation, twins, fetal malformation or a history of chronic hypertension, diabetes mellitus, sepsis or renal failure. Participants provided written informed consent. All study procedures were approved by the INMP in Lima, Peru, and the Office of Human Research Administration at the Harvard T.H. Chan School of Public Health, Boston, MA.

**Analytical population**

Information was collected from participants enrolled in the PrOMIS cohort from February 2012 to March 2014. After excluding 20 women due to missing information on migraine, a total of 2922 women were included in our analysis. The excluded participants were not different from the rest of the cohort in regards to sociodemographic or lifestyle characteristics.

**Migraine assessment**

Trained interviewers administered a Spanish-language questionnaire to determine migraine classification. Migraine and probable migraine status were classified based on the International Classification of Headache Disorders (ICHD)-III beta criteria [26]. Migraine was classified as participants fulfilling all 5 migraine diagnostic criteria. Probable migraine was designated if all 5 but one of the diagnostic criteria were fulfilled. Women fulfilling ICHD-III beta criteria for migraine or probable migraine when combined were classified as “any migraine.”

**PTSD assessment**

PTSD was assessed using the PTSD Checklist-Civilian Version (PCL-C), a self-report measure with 17 items reflecting Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria [27]. For each item, participants were asked how bothered they were by a symptom over the past month on a 5-point Likert scale in regards to their most significant life event stressor. The total score on the PCL-C ranges from 17 to 85. Recent data from our team support that a PCL-C score of 26 or higher on the Spanish-language version is associated with an 86% sensitivity and 63% specificity in diagnosing PTSD in a Peruvian population [28]. Further, we also examined PTSD using the established cutoff score of 44 or higher [20, 29, 30].

**Other covariates**

Sociodemographic characteristics and information pertaining to depression status were collected from participants through structured questionnaires. Participants’ age was classified as: 18–19, 20–29, 30–34, or ≥35 years old. Other sociodemographic covariates included: body mass index (BMI) based on self-reported pre-pregnancy weight and measured early pregnancy BMI (<18.5, 18.5–24.9, 25–29.9, >30 kg/m²), educational attainment (≤6, 7–12, >12 years), maternal ethnicity (Mestizos of mixed Amerindian and European descent vs. others), employment status (employed vs. not employed), marital status (married or living with partner vs. other), difficulty paying for medical care (hard vs. not very hard), difficulty paying for the very basics (hard vs. not very hard), planned pregnancy (yes vs. no), parity (nulliparous vs. multiparous), lifetime intimate partner violence (yes vs. no), childhood abuse (no abuse, physical abuse only, sexual abuse only, both physical and sexual abuse), and gestational age in weeks at the time of interview. The presence of antepartum depression was ascertained using the 9 item Spanish-language Patient Health Questionnaire—9 (PHQ-9) that has been validated in this population [31–33]. The PHQ-9 assesses depressive symptoms over the previous 14 days. The PHQ-9 score is calculated by assigning a score of 0–3 to the following response categories: “not at all,” “several days,” “more than half the days,” “nearly every day.” We defined presence of depression if participants had a PHQ-9 score ≥ 10 [34]. Lifetime intimate partner violence was ascertained through questions adapted from the Demographic Health Survey Questionnaires and Modules: Domestic Violence Module [35] and the WHO Multi-Country Study on Violence Against Women [36], respectively.
Statistical analysis
Sociodemographic and reproductive characteristics were examined using number (percent, %) for categorical variables and mean (± standard deviation [SD]) for continuous variables. Chi-square tests were used to evaluate differences in distribution of categorical variables, and analysis of variance (ANOVA) was used to evaluate mean differences for continuous variables. Multivariable logistic regressions were used to estimate odds ratios (OR) and 95% confidence intervals (CI) of migraine in relation to PTSD.

Confounding factors were examined based on their hypothesized relationship with migraine and PTSD. Confounding was evaluated by entering potential confounders into a logistic regression model sequentially and comparing adjusted and unadjusted ORs. Final multivariable regression models included covariates that altered ORs by at least 10% or were considered a priori as potential confounders in the association between migraine and PTSD [37]. We examined the following covariates as potential confounders in the analyses: age, education, BMI, Mestizo ethnicity, marital status, employment, difficulty paying for the basics or for medical care, parity, planned pregnancy, gestational age, childhood abuse, lifetime intimate partner violence, and depression. Prior studies have reported the comorbidity of depression and migraine [38, 39], including during pregnancy [18]. Given this, we repeated the analyses stratifying by maternal depression. In addition, some studies have used a PCL-C cutoff score of 44 to identify PTSD. Thus, we performed a sensitivity analysis using a PCL-C cutoff score of 44 or higher to diagnose PTSD. Reported P-values were two-sided and were statistically significant at P ≤ 0.05. All analyses were performed using SPSS Statistics, Version 23.0 (IBM SPSS v23.0, Armonk, NY, USA).

Results
Sociodemographic and reproductive characteristics
The sociodemographic and reproductive characteristics of the study population are shown in Table 1. A total of 2922 pregnant women between 18 to 35 years old (mean = 28.12 years; standard deviation (SD) = 6.31) were included in the analysis. The average gestational age at time of the interview was 9.23 weeks (SD = 3.46). The majority of the participants were married or living with a partner (81.1%), Mestizos (a race/ethnicity of mixed Amerindian and European descent; 75.2%), unemployed (53.7%), and with less than 12 years of education (59%). The prevalence of any migraine was 33.5% (migraine 12.5%; probable migraine 21.0%). Those with migraine were more likely to be unemployed, have difficulties paying for basic necessities and medical care, identify as Mestizo, and have a history of child abuse and lifetime intimate partner violence (Table 1). Of the 2922 participants, 37.4% of the participants fulfilled criteria for PTSD. Participants with PTSD were less likely to identify as Mestizo and were more likely to have difficulties paying for the basics, have difficulties paying for medical care, have a history of lifetime intimate partner violence, and suffer from depression than those without a PTSD diagnosis (Additional file 1: Table S1).

Migraine and PTSD
A history of any migraine (migraine and probable migraine) was statistically significantly associated with increased odds of PTSD (OR = 2.50; 95% CI: 2.14–2.93) (Table 2). After adjusting for sociodemographic confounders, women who suffered from any migraine had a 3.74-fold increased odds of PTSD (95% CI: 3.00–4.82) as compared to non-migraineurs, and the association remained significant after adjusting for lifetime intimate partner violence and depression status attenuated the magnitude of association but it remained significant (OR = 1.97; 95% CI: 1.64–2.37). After adjusting for sociodemographic confounders, women with migraine had a 3.81-fold increased odds of PTSD (95% CI: 3.00–4.82) as compared to non-migraineurs, and the association remained significant after adjusting for lifetime intimate partner violence and depression status (OR = 2.85; 95% CI: 2.18–3.74). Participants with probable migraine had a 1.80-fold increased odds of PTSD (95% CI: 1.49–2.18) as compared to non-migraineurs after adjusting for potential confounders. Further adjustment for depression status and lifetime intimate partner violence slightly attenuated the magnitude of association (OR = 1.61; 95% CI: 1.30–1.99) (Table 1).

Migraine and PTSD stratified by depression
Finally, we explored the association of migraine and PTSD stratified by depression status (Table 3). In a multivariable adjusted model, women with any migraine (migraine and probable migraine) but without depression had a 1.93-fold increased odds of PTSD (95% CI: 1.55–2.40) (Table 3) compared with the reference group (women without migraine or depression). Women with migraine but no depression had a 2.76-fold increased odds of PTSD (OR = 2.76; 95% CI: 1.99–3.82) after adjusting for sociodemographic confounders compared with women who had neither condition. Pregnant women with probable migraine and no depression had a 1.62-fold increased odds of PTSD (OR = 1.62, 95% CI: 1.99–3.82) compared with the reference. Compared to the reference group, participants suffering from depression and any migraine had an approximately 2.1-fold increased odds of PTSD (OR = 2.09; 95% CI: 1.49–2.92) after adjusting for potential confounders. Women with migraine or probable migraine stratified by depression had a similar increase in likelihood of PTSD compared to non-migraineurs (migraine: OR = 3.13; 95% CI: 1.91–5.11;
Table 1 Socio-demographic and reproductive characteristics of the study population according to types of migraine in Lima, Peru (N = 2922)

| Characteristics                        | All participants (N = 2922) | No migraine (N = 1943) | Probable migraine (N = 613) | Migraine (N = 366) | P-value |
|----------------------------------------|-----------------------------|------------------------|-----------------------------|-------------------|---------|
| Age (years) a                         | 28.12 ± 6.31                | 28.30 ± 6.31           | 27.76 ± 6.30                | 27.76 ± 6.27      | 0.093   |
| Age (years)                            |                             |                        |                             |                   |         |
| 18–19                                  | 154 5.3                     | 102 5.2                | 33 5.4                      | 19 5.2            | 0.549   |
| 20–29                                  | 1642 56.2                   | 1068 55.0              | 359 58.6                    | 215 58.7          |         |
| 30–34                                  | 602 20.6                    | 411 21.2               | 115 18.8                    | 76 20.8           |         |
| ≥ 35                                   | 524 17.9                    | 362 18.6               | 106 17.3                    | 56 15.3           |         |
| Education (years)                      |                             |                        |                             |                   |         |
| ≤ 6                                    | 123 4.2                     | 77 4.0                 | 27 4.4                      | 19 5.2            | 0.142   |
| 7–12                                   | 1599 54.8                   | 1058 54.5              | 356 58.4                    | 185 50.7          |         |
| > 12                                   | 1194 40.9                   | 806 41.5               | 227 37.2                    | 161 44.1          |         |
| Pre-pregnancy self-reported BMI        |                             |                        |                             |                   |         |
| < 18.5                                 | 30 1.2                      | 18 1.1                 | 9 1.7                       | 3 1.0             | 0.777   |
| 18.5–24.9                              | 1298 53.3                   | 865 54.1               | 270 51.8                    | 163 51.9          |         |
| 25–29.9                                | 851 34.9                    | 545 34.1               | 189 36.3                    | 117 37.3          |         |
| > 30                                   | 256 10.5                    | 172 10.8               | 53 10.2                     | 31 9.9            |         |
| Early pregnancy measured BMI           |                             |                        |                             |                   |         |
| < 18.5                                 | 54 1.9                      | 26 1.4                 | 23 3.8                      | 5 1.4             | 0.001   |
| 18.5–24.9                              | 1405 48.6                   | 935 48.8               | 278 45.9                    | 192 53.0          |         |
| 25–29.9                                | 1073 37.1                   | 707 36.7               | 240 39.6                    | 126 34.8          |         |
| > 30                                   | 361 12.5                    | 257 13.4               | 65 10.7                     | 39 10.8           |         |
| Mestizo ethnicity                      | 2194 75.2                   | 1454 74.9              | 491 80.1                    | 249 68.2          | <0.001  |
| Married/living with a partner          | 2360 81.1                   | 1566 80.9              | 498 81.6                    | 296 81.1          | 0.927   |
| Employed                               | 1351 46.3                   | 953 49.1               | 244 39.8                    | 154 42.1          | <0.001  |
| Difficulty paying for basics           |                             |                        |                             |                   |         |
| Hard                                   | 1449 49.6                   | 905 46.6               | 340 55.5                    | 204 55.7          | <0.001  |
| Not very hard                          | 1471 50.4                   | 1036 53.4              | 273 44.5                    | 162 44.3          |         |
| Difficulty paying for medical care     |                             |                        |                             |                   |         |
| Hard                                   | 1532 52.6                   | 937 48.4               | 372 60.7                    | 223 61.1          | <0.001  |
| Not very hard                          | 1382 47.4                   | 999 51.6               | 241 39.3                    | 142 38.9          |         |
| Nulliparous                            | 1425 48.9                   | 971 50.2               | 289 47.2                    | 165 45.1          | 0.129   |
| Planned pregnancy                      | 1206 41.6                   | 823 42.6               | 252 41.4                    | 131 36.1          | 0.067   |
| Gestational age at interview a          | 9.23 ± 3.46                 | 9.28 ± 3.49            | 9.14 ± 3.40                 | 9.11 ± 3.42       | 0.545   |
| Intimate partner violence b            | 1064 36.5                   | 648 33.4               | 243 39.8                    | 173 47.7          | <0.001  |
| Childhood abuse                        |                             |                        |                             |                   |         |
| No abuse                               | 827 28.3                    | 590 30.4               | 161 26.3                    | 76 20.8           | <0.001  |
| Physical only                          | 1135 38.8                   | 761 39.2               | 237 38.7                    | 137 37.4          |         |
| Sexual only                            | 230 7.9                     | 155 8.0                | 41 6.7                      | 34 9.3            |         |
| Both physical and sexual               | 730 25.0                    | 437 22.5               | 174 28.4                    | 119 32.5          |         |
| PTSD (PCL-C ≥26)                       | 1093 37.4                   | 585 30.1               | 276 45.0                    | 232 63.4          | <0.001  |
| Depression (PHQ-9)                     | 799 27.6                    | 435 22.6               | 193 31.7                    | 171 47.2          | <0.001  |

Due to missing data, percentages may not add up to 100%

* mean ± SD (standard deviation); How many weeks pregnant were you during your first prenatal care visit?

b Lifetime intimate partner violence

For continuous variables, P-value was calculated using the one-way ANOVA; for categorical variables, P-value was calculated using the Chi-square test

P-values that are italicized are all <0.05
probable migraine: OR = 1.59; 95% CI: 1.07–2.35) (Table 3).

The results remained similar using a PCL-C cut-off score of 44 to identify PTSD (Additional file 2: Table S2). For example, after adjusting for confounders, women who suffered from any migraine had a 3.81-fold increased odds of PTSD (95% CI: 2.14–2.93) as compared to women with no history of migraine. Further adjustment for lifetime intimate partner violence and depression status attenuated the magnitude of association, but it remained significant (OR: 2.67; 95% CI: 1.87–3.82).

**Discussion**

In our cross-sectional study of pregnant Peruvian women, migraine (whether any migraine [migraine and probable migraine], migraine alone, or probable migraine alone) was associated with increased odds of PTSD. After adjusting for confounders including antepartum depression, women who reported any migraine had a 1.97-fold increased odds of PTSD (95% CI: 1.64–2.37) compared to women with no history of migraine. In a multivariable adjusted model, women with probable migraine had a 1.61-fold increased odds of PTSD (95% CI: 1.30–1.99), and women with migraine had a 2.85-fold increased odds of PTSD (95% CI: 2.18–3.74), compared to women without migraine (Table 2). In the presence of antepartum depression, women with probable migraine or migraine had increased odds of PTSD (probable migraine: OR = 1.59; 95% CI: 1.07–2.35; migraine: OR = 3.13; 95% CI: 1.91–5.11) compared to non-migraineurs (Table 3).

Previous studies have shown significant comorbidities between migraine and PTSD. However, to our knowledge, this study is the first to evaluate the association between migraine and PTSD in pregnant women. Our current findings are comparable with prior studies of adult men and non-pregnant women. In a small clinic-based study of headache patients (including migraine or tension type headache; N = 80), prevalence of PTSD-like symptomatology was similar to a comparison group of patients with masticatory muscle pain [40]. However, Peterlin et al. (2008) in their study of migraineurs attending an outpatient headache center demonstrated that PTSD was more frequently reported among chronic migraineurs than episodic migraineurs (42.9% vs. 9.4%, p = 0.0059) [20]. In a general population study in 2011, Peterlin et al. reported that those with episodic migraine had a 3- to 4-fold increased odds of PTSD as compared to those without headaches after adjusting for confounders (lifetime prevalence: OR = 3.07, 95%CI: 2.12–4.46; 12-month prevalence: OR = 4.34, 95%CI: 2.73–6.89) [41]. In a cross-sectional study in Turkey, migraine was associated with PTSD among university students (OR = 10.16, 95%CI: 3.16–32.71, p = 0.001) [42]. A recent study by Smitherman and Kolivas similarly found that those with migraine were almost twice as likely to fulfill diagnostic criteria for PTSD than non-migraineurs (25.7% vs. 14.2%, p < 0.0001). Further, compared to those without migraine, migraineurs reported more traumatic events (3.0 vs. 2.4, p < 0.0001) [21]. Despite differences in geographic location, population characteristics, and sociodemographics, previous findings consistently show comorbidity between migraine and PTSD.

Several potential biological and neurochemical mechanisms have been postulated for the association between migraine and PTSD. These include the biochemical markers serotonin, cortisol, and norepinephrine. Migraineurs have been shown to have imbalances of serotonin, a regulator of pain in the nervous system [43]. Serotonin levels decrease during a migraine attack, causing the trigeminal nerve to release neuropeptides and cause severe migraine pain [44]. PTSD has been previously associated with serotonin function [45, 46]. The hypothalamic–pituitary–adrenal axis and

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**Table 2** Association between migraine and PTSD ^a^ assessed by the PCL-C during pregnancy (N = 2922)

| Migraine Status | No PTSD (N = 1829) | PTSD (N = 1093) |
|----------------|-------------------|-----------------|
|                | n    | %    | n    | %    | Unadjusted OR (95% CI) | Adjusted OR (95% CI) b | Adjusted OR (95% CI) c | Adjusted OR (95% CI) d |
| No migraine    | 1358 | 74.2 | 585  | 53.5 | Reference               | Reference              | Reference              | Reference              |
| Any migraine   | 471  | 25.8 | 508  | 46.5 | 2.50 (2.14–2.93)        | 2.37 (2.02–2.79)       | 2.30 (1.95–2.71)       | 1.97 (1.64–2.37)       |
| Types of migraine |     |      |      |      | Adjusted OR (95% CI) b | Adjusted OR (95% CI) c | Adjusted OR (95% CI) d |
| No migraine    | 1358 | 74.2 | 585  | 53.5 | Reference               | Reference              | Reference              | Reference              |
| Probable migraine | 337 | 18.4 | 276  | 25.3 | 1.90 (1.58–2.29)        | 1.80 (1.49–2.18)       | 1.76 (1.45–2.14)       | 1.61 (1.30–1.99)       |
| Migraine       | 134  | 7.3  | 232  | 21.2 | 4.02 (3.18–4.82)        | 3.81 (3.00–4.82)       | 3.65 (2.86–4.66)       | 2.85 (2.18–3.74)       |

Abbreviations: OR odds ratio, CI confidence interval

^a^ PTSD is defined as PCL-C score ≥ 26

^b^ Adjusted for age, marital status, difficulty paying for the very basics, and difficulty paying for medical care

^c^ Adjusted for age, marital status, difficulty paying for the very basics, difficulty paying for medical care, and lifetime intimate partner violence

^d^ Adjusted for age, marital status, difficulty paying for the very basics, difficulty paying for medical care, lifetime intimate partner violence, and depression status
related cortisol levels have also been associated with migraine and PTSD [3, 47–49]. Additionally, decreased levels of cortisol and elevated levels of pro-inflammatory cytokines (e.g. tumor necrosis factor-alpha, interleukin-6) in patients with PTSD have been suggested to be linked to migraine [50, 51]. Videlock et al. (2008) found that noradrenaline plasma levels are lower in those with PTSD when compared to individuals without PTSD [52]. Migraine patients also may have lower levels of plasma and platelet norepinephrine [53]. Mental health during pregnancy is of particular interest given the high burden of violence in this population [24, 54]. A previous study in the same cohort found 70% of participants had a history of childhood abuse and 36.7% had a history of intimate partner violence, and their abuse history was associated with an increased risk of migraine [54]. PTSD is prevalent during pregnancy and may increase postpartum if it is not identified [55]. Although a large percentage of the population suffers from migraines, particularly those of reproductive age, the mechanisms underlying the development of migraines and PTSD have yet to be fully understood [56].

Our study has several strengths, including a large sample size and a population with a high prevalence of migraine and PTSD. However, some limitations should also be considered. First, this cross-sectional study does not establish temporal relationships between migraine and PTSD. Second, the study was conducted among low-income pregnant women in Peru; thereby, warranting caution when generalizing our study to other pregnant women. Lastly, migraine and PTSD diagnoses were established using self-reported questionnaires. Thus, we cannot exclude the possibility that PTSD and migraine status were underreported in our study. Studies that systematically use screening and confirmatory diagnostic evaluations will greatly attenuate concerns about misclassification of PTSD and migraine diagnoses in epidemiological studies [20, 21].

Conclusions

Individually, migraine [57–59] and PTSD [60, 61] each carry a high individual, societal, and economic burden. Our study found an association between migraine and PTSD, even after adjusting for antepartum depression. Furthermore, our findings extend the body of literature on the increased risk of PTSD in those with migraine to include those with probable migraine and pregnant women. Taken together, these findings support the need for additional research on the association between migraine and PTSD, including in pregnant women, as well

### Table 3 Association between migraine and PTSD $^a$ during pregnancy ($N = 2922$) stratified by depression status

| Migraine Without Depression | No PTSD ($N = 1587$) | PTSD ($N = 507$) | Unadjusted OR (95% CI) | Adjusted OR (95% CI) $^b$ | Adjusted OR (95% CI) $^c$ |
|----------------------------|----------------------|------------------|-----------------------|---------------------------|---------------------------|
| No migraine                | 1191 75.0            | 297 58.6         | Reference             | Reference                  | Reference                  |
| Any migraine               | 396 25.0             | 210 41.4         | 2.13 (1.72–2.62)      | 1.99 (1.61–2.46)           | 1.93 (1.55–2.40)           |
| Types of migraine          |                      |                  |                       |                           |                           |
| No migraine                | 1191 75.0            | 297 58.6         | Reference             | Reference                  | Reference                  |
| Probable migraine          | 286 18.0             | 129 25.4         | 1.81 (1.42–2.31)      | 1.67 (1.31–2.15)           | 1.62 (1.25–2.08)           |
| Migraine                   | 110 6.9              | 81 16.0          | 2.95 (2.16–4.04)      | 2.81 (2.04–3.86)           | 2.76 (1.99–3.82)           |
| Migraine With Depression   |                      |                  |                       |                           |                           |
| No migraine                | 152 67.9             | 283 49.2         | Reference             | Reference                  | Reference                  |
| Any migraine               | 72 32.1              | 292 50.8         | 2.18 (1.57–3.01)      | 2.13 (1.53–2.96)           | 2.09 (1.49–2.92)           |
| Types of migraine          |                      |                  |                       |                           |                           |
| No migraine                | 152 67.9             | 283 49.2         | Reference             | Reference                  | Reference                  |
| Probable migraine          | 49 21.9              | 144 25.0         | 1.58 (1.08–2.31)      | 1.58 (1.07–2.32)           | 1.59 (1.07–2.35)           |
| Migraine                   | 23 10.3              | 148 25.7         | 3.46 (2.14–5.59)      | 3.29 (2.03–5.34)           | 3.13 (1.91–5.11)           |

Abbreviations: OR odds ratio, CI confidence interval

$^a$ PTSD is defined as PCL-C score $\geq 26$

$^b$ Adjusted for age, marital status, difficulty paying for the very basics, and difficulty paying for medical care

$^c$ Adjusted for age, marital status, difficulty paying for the very basics, difficulty paying for medical care, and lifetime intimate partner violence
as the need for research evaluating potential treatment implications of this comorbidity.

Additional files

Additional file 1: Table S1. Socio-demographic and representative characteristics of the study population according to PTSD a in Lima, Peru (N = 2922). (DOCX 36 kb)

Additional file 2: Table S2. Association between migraine and PTSD a during pregnancy (N = 2922). (DOCX 31 kb)

Abbreviations
ANOVA: Analysis of variance; BMI: Body mass index; CI: Confidence interval; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders; ICHD: International Classification of Headache Disorders; IL: Interleukin; INMP: Instituto Nacional Materno Perinatal; OR: Odds ratio; PCL-C: PTSD Checklist-Civilian Version; PHQ-9: Patient Health Questionnaire-9; PROMIS: Pregnancy Outcomes, Maternal and Infant Study; PTSD: Post-traumatic stress disorder; SD: Standard deviation

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Authors’ contributions
BLP, BG, LEF, and MAW conceived and designed the study. RPH, CA, and LEF analyzed data and drafted the manuscript. All authors interpreted the data, BLP, BG, LEF, and MAW conceived and designed the study. RPH, CA, and LEF critically revised the draft for important intellectual content, and gave final approval of the manuscript to be published.

Competing interests
Dr. Gelaye has consulted for Egalet Corporation for an unrelated project. Dr. Peterlin has unrelated investigator-initiated grant support from Egalet Corporation and the Landenberger Foundation. The other authors have no conflicts of interest to disclose.

Ethics approval and consent to participate
Participants provided written informed consent. All study procedures were approved by the INMP in Lima, Peru, and the Office of Human Research Administration at the Harvard T.H. Chan School of Public Health, Boston, MA.

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