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# Comorbidities of Primary Headaches During Pregnancy and the Perinatal Period: An Integrative Review

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## ABSTRACT

**Introduction: This article provides an overview of available information regarding Primary Headaches (PH) during pregnancy and the postpartum period with a focus on their comorbidities such as psychiatric disorders (depression, anxiety, stress, post-traumatic stress disorder), sleep disorders, abuse and potential trigger factors such as assisted reproductive techniques and smoking. Methods: A systematic search was conducted on five electronic databases, PubMed, Embase, Web of sciences, Scopus and Cochrane Library, spanning from January 1983 to August 2024, for pertinent manuscripts. The collected datasets were summarized and synthesized descriptively. Results: Nineteen manuscripts were incorporated into the analysis. Among them, half employed self-report methods to classify headaches, while 14 utilized validated questionnaires and scales to evaluate psychiatric and sleep disorders, as well as intimate partner violence. Additionally, the results of a case study and a letter to the editor were also included in the compilation. Primary Headaches are associated with psychiatric and sleep disorders, intimate partner violence and assisted reproductive techniques during perinatal period. Depression,**

**anxiety and stress are more prevalent among pregnant individuals suffering from migraines compared to those without the condition. Discussion: Accurate diagnosis is crucial for the effective management of headaches experienced by pregnant and postpartum women. This review underscores the necessity for research studies evaluating headaches and their correlated conditions at various points around the perinatal period. The implementation of early screening protocols and crafting customized treatment strategies can greatly improve the quality of care offered to women during the perinatal period.**

**Keywords:** Headache, comorbidities, pregnancy, postpartum

## INTRODUCTION

Headache is one of the most common disorders of the nervous system [1]. Primary headaches are classified into four types: migraine, tension type headache (TTH), trigeminal autonomic cephalgia's (TACs), and other primary headache disorders [2]. Worldwide, migraine affects 11 % of adults, with a three-times higher rate in women, which is hormonally-driven, and TTH appears with an average of 42 % in adults, higher in women than in men [1].

Primary headaches can thus be pre-existing (i.e., they begin before pregnancy) or can occur for the first-time during pregnancy, during the postpartum, or while breastfeeding [3]. Among women seeking medical consultation for headache disorders during pregnancy, migraine and TTH are the most prevalent conditions [4]. Migraine is by far the most common primary headache for which pregnant women seek care, accounting for about 60% of visits for primary headaches [5].

Roughly 50% to 75% of women with migraines observe a substantial improvement in their condition during pregnancy, marked by a significant decrease in the frequency and intensity of attacks, and in some cases, complete resolution [4]. On the contrary, the majority of TTH patients reported no change in the headache burden during pregnancy [4]. While pre-existing headaches often show improvement during pregnancy, about one-third of mothers experience headaches within the initial week after delivery [6,7]. Breast feeding seemed to protect from migraine recurrence during postpartum6 ($P = 0.0006$), positioning headaches as one of the three most common reasons for acute care visits during the puerperium [4,8].

Comorbidities of primary headache disorders include neurological, metabolic and cardiovascular conditions, e.g., stroke, epilepsy, multiple sclerosis, obesity, diabetes, hypertension and sleep disorders [9]. Furthermore, mental health conditions like depression or anxiety have also been identified as comorbidities [9]; nevertheless, these comorbidities are occasionally inadequately defined and treated merely as symptoms of depression or anxiety [9]. Wood et al. [10], found that during pregnancy, common comorbidities of migraines included hypertension (10.8%), obesity (10.7%), smoking (5.8%), epilepsy (4.7%), depression (14.0%), anxiety (15.6%), and other pain conditions (54.6% with musculoskeletal pain).

Nevertheless, there is a lack of studies understanding these social and psychological factors in perinatal period. Most of the available research on comorbidities of primary headaches is focused on migraine. The objective of the present study was to gain an overview of the existing

data on the comorbidities associated with primary headaches during pregnancy and the postpartum period and discuss its impact on the health and well-being of women.

## METHODS

### Searches

We conducted a literature review by retrieving relevant papers from five electronic database, PubMed, Embase, Web of sciences, Scopus and Cochrane Library, spanning from January 1983 to August 2024. Various key terms deemed pertinent were simultaneously entered into these databases. The Mesh terms were used in the following format: pregnancy 'or' puerperium 'or' gestation 'and' headache 'or' cephalalgia 'or' migraine 'and' sleep disorders 'or' sleep 'and' infertility treatment 'or' assisted reproductive techniques 'or' IVF 'and' smoking cessation 'or' tobacco 'and' intimate partner violence 'or' domestic violence 'or women abuse 'and' depression 'and' anxiety 'and' stress 'and' post-traumatic stress disorder (PTSD). The final literature search was performed on the 31st of August 2024.

### Eligibility Criteria

Manuscripts were eligible for inclusion if they met the following criteria: (1) women during pregnancy or the postpartum period and (2) reporting on primary headaches including migraine, TTH and cluster headache. No language restrictions were applied on manuscripts. Studies that focused on secondary headaches and on specific pathologies during perinatal period (e.g., diabetes, hypertension) were excluded.

### Data Collection, Synthesis & Analysis

Data was systematically extracted from the selected manuscripts, including details on the country in which each study was conducted, the specific time points at which data collection occurred, and the total number of participants involved in each study. Additionally, the methods employed for data collection, such as quantitative surveys, qualitative interviews, or other observational techniques, were carefully recorded. Data regarding any comorbidities, defined as medical conditions co-occurring with the primary health condition under investigation, were also obtained. Furthermore, outcome measures, referring to the specific criteria or indicators used to assess the effectiveness or impact of the interventions being studied, were comprehensively collected and documented.

The datasets were summarized and synthesized in a descriptive way. (Table 1).

## RESULTS

We The databases search identified 28648 manuscripts. We subsequently and screened 3302 titles and abstracts for eligibility after duplicate removal. We screened the full text of 61 manuscripts and excluded 40 that did not fulfil the eligibility criteria for inclusion. Our final sample comprised nineteen manuscripts (Figure 1). Almost all studies were carried out in Western countries. Half of them used self-report for the classification of headaches, fourteen studies used relevant validated questionnaires and scales for assessing psychiatric and sleep disorders and intimate partner violence. We also included the results of a case study [27] and of a letter to editor [19].


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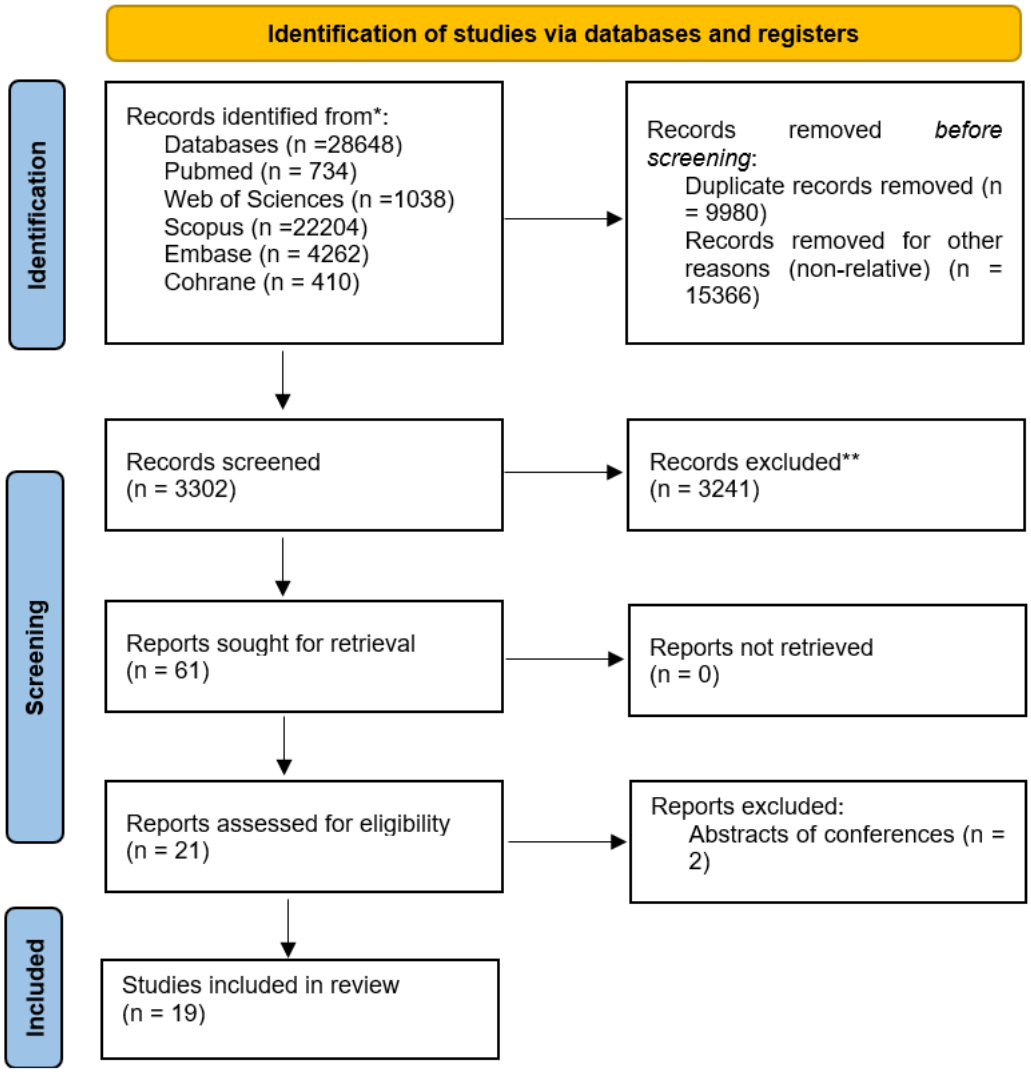


**Figure 1: Flowchart of study selection based on PRISMA-guidelines [11]**

## Psychiatric Disorders

### Depression:

Six studies provided information on depression in pregnant women with migraines. The first population study that found an association between migraine and depressive symptoms took place in Peru [12] during the postpartum hospital stay. They utilized the Patient Health Questionnaire-9 (PHQ-9) as their screening tool. Their results revealed a noteworthy correlation between migraine and depressive symptoms. For each level of depression severity, the odds of experiencing that level of depression were higher among women with a history of strict migraine compared to those without. Specifically, for moderate depression, the odds ratio was approximately 2.12 (CI: 95% CI 1.54–2.93), for moderately severe (AORs=1.85, 95% CI 1.16–2.96), and for severe depression (AORs=2.23.95% CI 1.08–4.62). 32% of the women reported a history of migraines, while 41% reported experiencing moderate to severe depressive symptoms during pregnancy. The second study, conducted by Orta et al. [13], reported on the co-occurrence of migraine and psychiatric disorders in the first trimester of pregnancy. The study revealed heightened odds of unipolar mood disorders in pregnant migraineurs compared to non-migraineurs, with particularly elevated odds observed among

migraineurs with aura. Migraineurs with aura, as compared with non-migraineurs, were more likely to have moderate depression (AOR=1.76; 95% CI: 0.99–3.11) and severe depression (AOR=3.28; 95% CI: 1.13–9.50). Thirdly, in a cohort study by Welander et al. [14] at three distinct time points during pregnancy (gestational weeks 17 and 32) and postpartum week 6, it was observed that a history of migraine appears to be a more robust predictor of depressive symptoms during pregnancy compared to the postpartum period. In a fourth study, migraine was associated with depressive symptoms during pregnancy at 17 and 32 weeks, and at postpartum period, at six weeks and at six months after birth (AOR=1.7, 95% CI 1.2–2.6) [15]. The fifth study by Katon et al.16, screened women at 4 and 8 months of pregnancy, and at 6 weeks after birth and found that there is no significant association between migraines and women with postpartum depression (PPD), AOR=1.40, 95% CI 0.93–2.11. Both studies used self-report for headache status. Finally, F.F. Erdoğan et al, found an association between higher depression score and higher headache risk [17].

**Anxiety and Stress:**

The search yielded four papers on anxiety and stress in pregnant women with migraines. A study by Orta et al. [13] reported that migraineurs, as compared with non-migraineurs, had higher odds of severe anxiety (AOR=1.38, 95% CI: 0.66–2.90) and severe stress symptoms (AOR=2.01, 95% CI: 0.98–4.12) as measured with the DASS-21 questionnaire. Associations were also notably stronger for migraineurs with aura as compared with non-migraineurs. The questionnaires were administered in the first trimester of pregnancy. Similarly, Welander et al. [14] used the Edinburgh Postnatal Depression Scale (EPDS) at gestational weeks 17 and 32 and postpartum week 6. In their findings, migraine was statistically significantly associated with anxiety at week 17 (AOR: 1.69; 95% CI: 1.11–2.54) and with mixed depression and anxiety at week 32 (AOR: 1.45; 95% CI: 1.06–1.99). The associations between migraine and either depression, anxiety or mixed depression and anxiety were not significant at 6 weeks postpartum. Higher levels of stress were positively associated with headaches during pregnancy according to the study of Lopes BCS et al [18]. A last study shows no correlation between diminution of migraine and stress during pregnancy [19].

Ozdemir et al. observed that there is no difference between women with and without headache in terms of prevalence of distress (distress is defined as depression, anxiety and/or stress) [20,21].

**Post-traumatic Stress Disorder (PTSD)**

Friedman et al. [22] is the only study which researches the PTSD among pregnant migraineurs. Women with any type of migraine but without depression have increased risk of PTSD, (OR=1,93, 95% CI:1,55-2,40). In those women with migraine and comorbid depression, the odds of PTSD in all migraine categories, during pregnancy, were even further increased as compared to those women without migraine (AOR=1,97, 95% CI:1,64-2,37).

**Sleep Disorders**

Two papers reported on sleep disorders among pregnant women. Williams et al. [23], observed heightened risks among pregnant women with migraines, including increased odds of short sleep duration (AOR = 1.57, 95% CI:1.11-2.23), excessive daytime sleepiness (AOR = 1.46, 95% CI:0.94-2.26), vital exhaustion (AOR = 2.04, 95% CI:1.52-2.76) and elevated perceived stress during pregnancy (AOR = 1.57,95% CI:1.06-2.31). However, only the latter two conditions



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reached statistical significance, and these associations were notably pronounced among overweight migraineurs. The study by Qui et al. [24] showed that migraineurs, regardless of the presence or absence of aura, were more likely than non-migraineurs to report short (AOR=1.47, 95% CI:1.07–2.02) or long sleep durations, daytime dysfunction (AOR=1.51, 95% CI:1.12–2.02), sleep medication use (AOR=1.71, 95% CI:1.20–2.42), snoring during pregnancy (AOR= 1.32, 95% CI:1.02–1.71), and overall poor sleep quality (AOR=1.73, 95% CI:1.35–2.23). The odds of sleep disturbances were particularly elevated among pre-pregnancy overweight migraineurs.

**Intimate Partner Violence (IPV)**

There were 3 papers reporting on the relationship between headaches and IPV. Gelaye et al. [25] found that women with a history of IPV had 43% increased odds of any migraine as compared to women without IPV (OR=1.43, 95%CI:1.02-2.02). Another study observed that psychological violence increased the risk of headache (OR 1.75, 95% CI:1.25–2.40) during pregnancy, along with other socioeconomic and lifestyle variables [26]. Over half of the women reported migraine during pregnancy, and those who experienced some type of insult, humiliation or threat (psychological violence) from their intimate partners had 81% more chance of having this symptom [26]. Finally, Cripe et al. [12] found that compared with pregnant women without a history of IPV, women with experience of IPV were associated with 1.44-fold increased odds (aOR=1.44, 95% CI:1.19–1.75) of any migraine. The relationship between IPV and any migraine was strongest among women with depressive symptoms [12]

**Relevant Trigger Factors**

**Assisted Reproductive Technology (ART):**

The search resulted in 2 papers that reported on IVF (in vitro fertilization), headaches and pregnancy. A first case study documented a woman experiencing cluster headaches triggered by hormone treatment linked to in vitro fertilization (IVF). Despite no family history of cluster headaches (her mother had migraine without aura), the recurrence of cluster attacks during progesterone therapy and their remission at the end of each treatment period strongly suggest a causal connection. The most prolonged and frequent attacks took place after successful IVF. Upon discontinuation of progesterone intake at 10 weeks of gestation, the headaches gradually diminished and disappeared within a week, with no subsequent recurrences [27]. Giaxi et al. [28] on the other hand found that headaches in pregnancy and the early postpartum was significantly associated with higher scores on EPDS scale (depressive symptoms) ($p = 0.005$), with hypertension ($p < 0.004$), thyroid pathology ($p < 0.003$), IVF ($p < 0.006$) and psychological abuse ($p < 0.001$).

**Smoking:**

The search resulted in 3 papers that reported on the relationship of smoking and headaches during pregnancy. One of the most significant factors experienced headaches among pregnant women was the smoke status [17]. The probability of having headaches during pregnancy was 2.2 times lower for women who had never smoked and 1.9 times lower for women who were ex-smokers than it was for smokers [17]. Turner et al. [29] found that during the perinatal period, smoking prior to pregnancy (AOR 1.50,95% CI: 1.05 to 2.13) is associated with increased odds of experiencing headache during pregnancy. According to another study, smokers were more likely to report symptoms of severe headache in the last 3 months of pregnancy relative to non-smokers [30].

## DISCUSSION

Worldwide, headaches are the second most frequent/serious public health problem which causes disability with dramatic effects on personal and public life [9,10], making them many economically damaging situations for the economies of the states. Globally, an active headache disorder of any type was estimated at 52.0% (95%CI 48.9–55.4) of the populations studied (males 44.4%, females 57.8%), migraine in 14.0% (95%CI 12.9–15.2) (males 8.6%, females 17.0%) and TTH in 26.0% (95%CI 22.7–29.5) (males 23.4%, females 27.1%) [11]. The prevalence of headache in gravid women has been described to be as high as 35% [14,15]. At least 5% of pregnancies are affected by de novo headache, meaning either new onset or new type of headache [14,16].

The complex hormonal and psychological changes during pregnancy and the postpartum period make reaching a proper diagnosis for headaches challenging. It has been acknowledged that all the aforementioned disorders, such as depression, anxiety, stress, insomnia and intimate partner violence, are associated to one another [13,31-34]. In 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 [22]. The combination of depression, anxiety and stress is more likely to pregnant migraineurs [13]. Two recent meta-analyses revealed that both insomnia and poor sleep quality during gestation are associated with an increased risk of depression in pregnant mothers [31,32]. Moreover, Maghami et al. [33], found a significant relationship between sleep disturbances during pregnancy and PPD. Women with sleep disorders are at an increased risk of developing PPD, which warrants screening pregnant mothers for sleep disturbances [33]. Perinatal depression is also associated with general, physical, sexual, and psychological IPV [34].

### Psychiatric Disorders

It is essential to consider the role of mental health in dealing with patients with headache disorder because they are potential triggers of headache attacks as well as important causes of emotional burden for affected people. It is known that the presence of psychiatric disorders predicts a worse prognosis for every headache subtype [35].

Comorbidity between headaches and psychiatric disorders is a broad and, in some respects, still unexplored subject. The headache subtype that has most extensively been investigated for psychiatric comorbidity is migraine [36]. In a meta-analysis, Caponetto et al. [9] found that the most frequent psychiatric comorbidities in subjects with primary headaches were anxiety and depression, followed by post-traumatic stress disorder: these comorbidities were found, respectively, in 25% (95%CI: 22–28%), 23% (95%CI: 20–26%) and 15% (95%CI: 6–28%) of the subjects in the general population. In the perinatal period, women with migraine had higher rates of depression, anxiety and mixed depression and anxiety than women without migraine [14].

### Depression:

Depression is a common mental disorder. Globally it is estimated that 5% of adults suffer from the disorder [37]. Depression is a leading cause of disability worldwide and is a major contributor to the overall global burden of disease [37]. More women (5.1%) are affected by depression than men (3.6%) [37]. During pregnancy and the postpartum period, women are especially susceptible to depression, which at this period is referred to as peripartum



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depression. In a meta-analysis, the pooled prevalence of peripartum depression was 11.9% [14,38]. Depression is often comorbid with anxiety disorders in patients with migraine [39]. Despite the limited studies during pregnancy, three of them indicated the association between migraine and depressive symptoms when they are combined with anxiety [14-16].

**Anxiety and Stress:**

Anxiety disorders are two to five times more prevalent in patients with migraine than in the general population, up to two times more common in patients with migraine than in patients with depression, and much more common in patients with chronic migraine (CM) than in patients with episodic migraine (EM) [39].

Generalized anxiety disorder (GAD) is characterized by emotionally unpleasant, developmentally inappropriate states of unfocused uneasiness and worry, usually about objectively unthreatening situations [40]. The systematic review of Karimi et al. [40] showed a strong and consistent positive relationship between migraine and anxiety. The prevalence of anxiety disorders among migraineurs is double that associated with depression.

A review by Ross et al. [41] showed that anxiety disorders are common during the perinatal period, with reported rates of obsessive-compulsive disorder and generalized anxiety disorder being higher in postpartum women than in the general population.

The existing studies among pregnant women are limited, one of them found that migraineurs were more likely to have unipolar depression, anxiety, and stress, which is accordance with studies at non pregnant adult populations [13]. In another study, migraineurs are more likely to experience anxiety in mid-pregnancy (week 17) and mixed depression and anxiety at later stages of pregnancy (week 32). This study did not demonstrate an association between migraine and symptoms of either depression or anxiety in postpartum week 6 [14].

Stress is a prevalent migraine trigger. Stressful events, especially early in life, increase the incidence and susceptibility of major depressive disorder and other psychiatric disorders [39]. During pregnancy approximately 84% of women report some form of psychosocial stress [42]. Both mental/cognitive stress and daily stress (perceived) were related to an increase in pain perception and related to the development of headache or enhanced transient pain intensity in migraine and TTH patients [43].

**Post-traumatic Stress Disorder (PTSD):**

PTSD during pregnancy is a significant global mental health concern, affecting up to 1 in 5 trauma-exposed pregnant women, and is linked to increased risks for adverse maternal and infant health outcomes [45]. Overall, it affects between 4% and 6% of women during pregnancy and at postpartum period [46]. The onset of PTSD can precede pregnancy or occur during the perinatal period [45] and could arise due to traumatic incidents like accidents, interpersonal violence, or natural disasters [46]. The overall mean prevalence of prenatal PTSD is 4.6% (k=35, 95% CI, 3.42–6.14) while postnatal PTSD is 5.44% (k=28, 95% CI, 3.62–8.1) [46]. In patients with migraine, the prevalence of PTSD is higher compared to the general population (14–25% vs 1–12%), and it is even more pronounced in patients with CM compared to those with EM (43% vs 9%), despite similar rates of trauma exposure between the groups [39].

## Sleep Disorders

Chronic sleep deprivation and poor-quality, fragmented sleep result in excessive daytime sleepiness, neurocognitive dysfunction, memory impairment, depression, anxiety and cardiovascular diseases [47,48].

While healthy women appear to have objectively better-quality sleep than men, women of all adult age groups report more sleep problems, including inadequate sleep time and insomnia [49]. Reproductive hormones play important roles in sleep physiology for women at different ages and times of their lives. Especially in pregnancy the prevalence of sleep apnea and restless leg syndrome increases from hormonal effect [50].

In general population poor quality or short duration of sleep is reported as a trigger factor for acute attacks of Tension Type Headache [51] and migraine attacks [52]. In primary headaches the prevalence of sleep disorder is (48%, 95% CI: 42–54%) and of RLS (20%, 95%CI: 13–27%) [9].

Although, little is known about sleep disorders among pregnant women with headaches. Two studies were retrieved focused on migraineurs pregnant women, where their findings were similar to those from previous population-based studies of men and non-pregnant women [23,24,53-55].

## Intimate Partner Violence

Overall, 35% of women worldwide have experienced either physical and/or sexual intimate partner violence or non-partner sexual violence and are 2.6 times more likely to experience depression or anxiety [56]. Intimate partner violence (IPV) includes physical violence, sexual violence, threats of physical or sexual violence and emotional abuse. The prevalence of IPV in pregnancy is estimated to be between 4% and 20% [39] and in 5.9% of cases, the abuse started during pregnancy [57]. Patients with headache with a history of emotional abuse, emotional neglect and/or sexual abuse are more likely to suffer from migraines than tension headaches [39]. IPV was largely associated with perinatal depression and PTSD [34].

It is worthwhile to mention that in January 2012, the American Academy of Neurology (AAN) position statement on abuse and violence also recommended screening all neurological patients with referral as appropriate [58,59].

## Relevant Trigger Factors

### Assisted Reproductive Technology (ART):

Infertility affects 72.4 million women worldwide, the majority of whom will seek medical care60. Most forms of medically assisted reproduction (MAR) require using hormonal medication for: (i) induction of pituitary quiescence, (ii) ovarian stimulation, (iii) ovulation triggering, and/or (iv) luteal support. Headache is a common side effect (i.e., 11–19%) of many medications for ovarian stimulation [61]. Amir et al. [62] observed that during the IVF-ET protocol (long, mid-luteal protocol), the associated headache attacks occur not only among migraine patients, but also in a substantial percentage (17.8%) of non-migraine patients. Moreover, a relatively high frequency of headache was reported at phase 1 and 3. There are not enough studies linking primary headaches with ART. The study by Giaxi et al. [28] observed an association between IVF and headaches during pregnancy and early postpartum. A case study


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reported on a woman suffering from cluster headaches indicated that the longest and most frequent attacks occurred after successful IVF until the end of the first trimester of pregnancy. Further studies are needed to validate these observations.

**Smoking:**

Smoking in pregnancy is a serious health issue, since both mother and fetus are subject to the toxic substances present in cigarettes. In a cohort study of women with migraine during pregnancy, smoking is included as a comorbidity [10]. It is also associated with some psychological effects, including high levels of anxiety, depression, and perceived stress [63]. The absence of depression (aOR=2,65, 95% CI :1.62-4.30) and low stress (aOR=0,58, 95% CI :0.44-0.77) is associated with smoking cessation during pregnancy [64]. The systematic review of Albers et al. [65], found that the effect size of smoking on headaches could not be verified due to the small size of results in general population. Another study showed no significant associations between smoking and headache disorders [66]. Chen et al. [67] could not provide definitive evidence either supporting or rejecting the hypothesis that smoking and migraine are independent of each other. Regardless of smoking classification, more migraineurs consumed tranquilizers, amphetamines, and sleeping pills than headache-free women [67].

## STRENGTHS AND LIMITATIONS

This review represents the first comprehensive summary of research on risk factors for primary headaches during pregnancy and the perinatal period. The included studies exhibited variability in terms of the trimester during pregnancy, providing a diverse perspective on the subject matter. However, the predominant reliance on self-report for headache classification poses a limitation, potentially impacting the precision of the findings. The geographical concentration of studies in Western countries constitutes another limitation, limiting the generalizability of the results to low-income settings.

Moreover, while migraine received more extensive attention, other types of headaches were comparatively less explored. Despite these limitations, the report serves as a crucial starting point, emphasizing the scarcity of available data and advocating for further research to illuminate the intricate relationships between these factors and headaches in the perinatal population.

## RECOMMENDATIONS FOR FUTURE PRACTICE AND RESEARCH

More research should focus on longitudinal studies tracking headache patterns, hormonal influences, and the long-term impact of comorbidities on maternal health. Implementing early screening protocols and developing tailored treatment plans can significantly enhance the quality of care provided to pregnant and postpartum individuals. Collaborative efforts between obstetricians, neurologists, and other relevant specialists can contribute to a more comprehensive approach to managing headaches during pregnancy and the postpartum period. Additionally, standardized screening protocols for associated comorbidities and enhanced patient education on headache management are recommended. Providing information about lifestyle modifications, stress reduction techniques, and available support services can contribute to proactive self-care. Overall, the study highlights the necessity for an integrated approach to maternal healthcare to support the physical and mental well-being of mothers and their infants.

## CONCLUSION

Pregnancy and the postpartum period bring significant physical and emotional changes, and it's crucial to recognize the comorbidities associated with headaches during this time. A holistic and individualized approach is essential for understanding and addressing these challenges. Healthcare providers must recognize the interconnected nature of factors like anxiety, insomnia, depression, and abuse, which can contribute to headaches during pregnancy and postpartum. Early detection, proactive management, and ongoing support from healthcare providers are vital for expectant and new mothers. Adequate postpartum care is essential to address evolving dynamics in headache management and the unique needs of new mothers and their infants.

Timely medical advice should be sought for persistent or severe headaches during the perinatal period, as they could indicate underlying complications requiring immediate attention. Open communication, regular check-ups, and personalized strategies are crucial components in the continuum of care for both the mother and the newborn. Future research is needed to estimate the prevalence of these disorders, identify potential implications, and contribute to improved guidelines and approaches for the well-being of mothers and their newborns. Collaborative efforts between obstetricians, neurologists, midwives, and other specialists are necessary for a comprehensive approach to managing headaches during pregnancy and the postpartum period.

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## Abbreviations

tension-type headache (TTH)
Primary Headache Disorders (PHDs)
trigeminal autonomic cephalgia's (TACs)
chronic migraine (CM)
episodic migraine (EM)
Generalized anxiety disorder (GAD)
Assisted reproductive technology (ART)
Post Partum Depression (PPD)
In Vitro Fertilization (IVF)
Intimate partner violence (IPV)
Post-traumatic stress disorder (PTSD)

**Table 1: Characteristics of studies included in the literature review**

| Study | Sample size | Data collection method | Associated comorbidity | Study time point | Results | Pooled proportion 95%CI |
|---|---|---|---|---|---|---|
| Williams et al., USA, 2010 | 1334 | Epsworth Sleepiness Scale (ESS), self report for mignaine status | Sleep disorders | Before and early pregnancy (until 20 weeks) | Increased risks of short sleep duration, excessive daytime sleepiness among migraineurs. | OR = 1.46; 95% CI 0.94-2.26 |



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|---|---|---|---|---|---|---|
| Qiu et al., USA, 2015 | 1324 | Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), migraine diagnoses were based on the International Classification of Headache Disorders-II criteria, deCODE Migraine Questionnaire (DMQ3) | Sleep disorders | Early pregnancy (14 weeks on average) | Migraineurs (regardless of the presence or absence of aura) were more likely than nonmigraineurs to report short or long sleep durations, daytime dysfunction, sleep medication use, snoring during pregnancy, and overall poor sleep quality | OR=1.79; 95% CI 1.39–2.32 |
| Orta et al., USA, 2014 | 1321 | Patient Health Questionnaire Depression Module-9 (PHQ-9), Depression Anxiety Stress Scales 21-item Short Form (DASS-21), International Classification of Headache Disorders diagnostic criteria (ICHD-II) | Psychiatric disorders | First trimester | Migraineurs were more likely to have unipolar depression, anxiety, and stress | Unipolar depression AOR=1.60; 95% CI: 1.12–2.31 Severe stress AOR=2.01; 95% CI: 0.98–4.12 Severe anxiety AOR=1.38; 95% CI: 0.66–2.90 |
| Welander et al., Sweden, 2021 | 4831 | Edinburgh Postnatal Depression Scale (EPDS), self report for mignaine status | Psychiatric disorders | Gestational weeks 17 and 32 and at 6 weeks postpartum | Migraineurs are more likely to experience anxiety in mid-pregnancy (week 17) and mixed depression and anxiety at later stages of pregnancy (week 32). | Anxiety at week 17 AOR: 1.69; 95% CI: 1.11–2.54 mixed depression and anxiety at week 32 AOR: 1.45; 95% CI: 1.06–1.99 |
| Passchier et al., Netherlands, 1996 | 37 | Migraine diagnoses were based on IHS criteria | Psychiatric disorders | First trimester, second trimester, third trimester, 1 year after birth | No correlation between diminution of migraine and stress during pregnancy. | |
| Lopes BCS et al., Brazil,2023 | 1279 | State-Trait Anxiety Inventory (STAI), Perceived Stress Scale (PSS-14), self report for headache status | Psychiatric disorders | During pregnancy | High level of stress are associated with headaches during pregnancy. | |
| OZDEMIR et al., Turkey, 2022 | 600 | Tilburg Pregnancy Distress Scale, self report for headache status | Psychiatric disorders | During pregnancy | No difference was found between women with and without headache in terms of prevalence of distress. | |

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|---|---|---|---|---|---|---|
| Giaxi et al., Greece, 2023 | 170 | Self report for headache status, EPDS, WAST (Women Abuse Screening Tool), MediScore (Mediterranean Diet Score) and IPAQ (International Physical Activity Questionnaire) | IVF, depression, abuse | First postpartum week | 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 ($p < 0.001$). | |
| Gaul et al., Switzerland, 2007 | case study | | IVF | First trimester | Cluster headache worsed until the end of first trimister | |
| Cripe et al., USA, 2010 | 2293 | Classification by International Headache Society (IHS) criteria, Patient Health Questionnaire-9 (PHQ-9) | Psychiatric disorders | First postpartum week | Increased risk for moderate to severe depressive symptoms in women with migraine | 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 |
| Wikman et al., Sweden, 2020 | 2466 | Self report for headache status, EPDS, Stressful Life Events Scale SLES, Lifetime Incidence of Traumatic Events LITE | Psychiatric disorders | Gestational weeks 17 and 32, at six weeks and at six months postpartum | Migraine was associated with peripartum depression at gestational weeks 17 and 32, and at six weeks and at six months postpartum | During pregnancy AOR=1.7, 95% CI 1.2–2.6, early postpartum AOR=1.7, 95% CI 1.2–2.4 |
| Katon et al., USA, 2014 | 1423 | Patient Health Questionnaire-9 PHQ-9, Prenatal Psychosocial Profile Stress Scale, Abuse Assessment Screen, Alcohol screening questionnaire the T-ACE, self report for headache status | Psychiatric disorders | Second or third trimester | No significant association between women with PPD and migraines | Migraines AOR=1.40, 95% CI 0.93–2.11 |



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|---|---|---|---|---|---|---|
| F.F. Erdoğan et al., Turkey, 2012 | 1357 | Zung depression score, self report for headache status | Psychiatric disorders, smoking | During pregnancy | Higher depressive scores associated with higher headache risk. The prevalence of headaches is greater among smokers than among nonsmoker | |
| Friedman et al., USA, 2017 | 2922 | International Classification of Headache Disorders (ICHD)-III beta criteria, PTSD Checklist-Civilian Version (PCL-C), Patient Health Questionnaire-9 (PHQ-9) | PSTD | During pregnancy | Increased risk for PSTD among migraineurs pregnant women | OR=1,93, 95% CI:1,55-2,40 |
| Audi et al., Brazil, 2012 | 1379 | Alcohol Use Disorders Identification Test, WHO VAW instrument for violence against women | IVP | During pregnancy and 40 days postpartum | Psychological violence increased the risk of headache | OR 1.75, 95% CI 1.25–2.40 |
| Cripe et al., USA, 2011 | 2066 | Demographic Health Survey Questionnaires and Modules: Domestic Violence Module and the World Health Organization (WHO) Multi-Country Study on Violence against Women, Headache classification by using the modified ICHD-2 criteria, Patient Health Questionnaire-9 (PHQ-9) | IVP | First week of postpartum | Women with experience of IPV were associated with any migraine | aOR=1.44, 95% CI 1.19–1.75 |
| Gelaye et al., USA, 2016 | 2970 | Childhood Physical and Sexual Abuse Questionnaire, Demographic Health Survey Questionnaires and Modules: Domestic Violence Module and the WHO Multi-Country Study on Violence Against Women, International Classification of Headache Disorders (ICHD)-III beta criteria | IVP | During pregnancy | Migraine was associated with history of IPV | OR=1.43; 95%CI 1.02-2.02 |

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|---|---|---|---|---|---|---|
| Turner et al., USA, 2012 | 2434 | Delivery Information Questionnaire, Entrance questionnaire | Smoking | During pregnancy, within 72 hours after delivery, and at 8 weeks after delivery. | Smoking prior to pregnancy is associated with increased odds of experiencing headache during pregnancy. | AOR 1.50, 95% CI: 1.05 -2.13 |
| Cristian et al., USA, 2004 | 17767 | | Smoking | During pregnancy | Smokers were more likely to report symptoms of severe headache in the last 3 months of pregnancy relative to nonsmokers | |



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