

Review article

Panic disorder during pregnancy: A scoping review

Eman Al-Awabdeh^{a,c,*}, Lubna Abu Shaikha^b, Abdelrahman Salameh^c,
Jafar Alasad Alshraideh^b^a University of Jordan, Amman, Jordan^b School of Nursing, The University of Jordan, Amman, Jordan^c Fatima College of Health Sciences, Abu Dhabi-UAE, United Arab Emirates

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ABSTRACT

Background: Panic Disorder is a serious anxiety disorder, and one of the severe mental problems that impacts mothers' mental health and fetal health as well.

Aim: The current scoping review aims to provide a wide overview of the literature regarding panic disorder during pregnancy.

Methods: Twenty-five eligible articles were selected for full review from SAGE, CINAHL, PubMed, Medline, Research Gate, Science Direct, and Google Scholar literature searches. This review followed the framework suggested by Arksey and O'Malley for a scoping review.

Results: Content analysis of the studies was done, and five categories have been identified: Panic disorder course during pregnancy; prevalence of panic disorder during pregnancy; factors associated with pregnancy panic disorder; impact of panic disorder during pregnancy; and treatment of panic disorder during pregnancy.

Conclusion: A significant gap in the literature, and inconsistent and mixed findings regarding prevalence, impact, associated factors, and treatment of PD during pregnancy exist. This scoping review revealed that more studies need to be conducted to further understand and examine PD during pregnancy.

1. Introduction

Panic Disorder (PD) is a chronic mental illness that affects the individual's quality of life and elevates the risk of comorbid medical problems [1]. According to the Diagnostic and Statistical Manual of Mental Health Disorders/fifth edition (DSM5), PD is a serious anxiety disorder with recurrent, unexpected panic attacks followed by at least one month or more of persistent fear about having additional attacks, fear about the attack's consequences, and a significant modification of the individual's behavior to avoid perceived predisposing situations [2].

PD was formally classified as a specific diagnostic disorder in 1980, in the DSM/third edition [3]. Although the cause of PD is still unknown [4], multiple theories suggest some factors that may have a role in the etiology of PD, for example: chemical imbalance as a major factor, adverse childhood conditions, and genetic and environmental factors [1].

It is estimated that the prevalence of PD among population is 1.7% [5], and it is double in women than in men [6].

Pregnancy is a sensitive period for women, and remarkable psychological and physiological changes occur during this time [7].

* Corresponding author.

E-mail addresses: eawabdeh@gmail.com (E. Al-Awabdeh), l.abushaikha@ju.edu.jo (L. Abu Shaikha), abdelrahmansalameh@gmail.com (A. Salameh), jalasad@ju.edu.jo (J.A. Alshraideh).

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According to the World Health Organization (WHO) around 10%–16% of women worldwide experience psychological problems during their pregnancy [8].

The importance of studying PD during pregnancy lies in the higher prevalence rates across various studies. Furthermore, there is a tendency to focus on mothers' physical health during pregnancy rather than mental health [9]. This review will focus and provide a better understanding regarding PD during pregnancy and increase awareness among healthcare providers.

1.1. Purpose

This scoping review's aim is to summarize research findings and provide a wide overview of the literature regarding PD during pregnancy.

2. Methods

2.1. Protocol and registration

In this review, the researchers followed the guidelines defined by Arksey and O'Malley for scoping review [10]. This scoping review is registered at Open Science Framework (OSF) ([11]).

2.2. Methodological framework

A scoping review aims at finding research gaps in the existing literature and summarize and disseminate research results [10]. Furthermore, it assesses the potential breadth and scope of the available research literature [12]. The current scoping review was done utilizing the methodological framework defined by Arksey and O'Malley for scoping review [10]. This methodological framework comprises five stages (Table 1).

1 Identify the research question.

The research question of the current scoping review was: What is known about PD during pregnancy from the existing literature?

2 Identify the relevant studies.

2.3. Literature search

A literature search was done via electronic databases: SAGE, CINAHL, PubMed, Medline, Research Gate, Science Direct, and Google Scholar. The search included free text keywords. Primary search terms included: PD during pregnancy, antenatal anxiety disorders, antenatal PD, antenatal mental disorders, and risk factors of antenatal PD. Conjunctions like 'AND' and 'OR' were used to combine search terms. Further, relevant studies mentioned in the references of selected articles were considered for the review.

3 Selection of the study

2.4. Eligibility criteria

Studies published between 2000 and 2023, published research reports, quantitative studies, qualitative studies, literature reviews, full-text publications, studies written in the English language, and studies related to PD during pregnancy were included in this scoping literature review. While unpublished studies, editorials, gray literature, peer discussion, student thesis and dissertations were excluded from the search.

4 Charting the data

Two reviewers (EA and LAS) conducted a comprehensive review of the included studies. They extracted and summarized the

Table (1)

Summary of the methodological framework according to Arksey and O'Malley (2007).

Stage	Description
1. Identify the research question	It is the beginning point. Question should be wide in nature as it aims to provide a wide description.
2. Identify the relevant studies	Identify the relevant studies via different sources (electronic databases and reference lists). Further, identify where to search, which keywords to use, which sources to search, duration, and in what language.
3. Selection of the study	Selection of the studies include inclusion and exclusion criteria.
4. Charting the data	Sorting materials according to key issues, categories, and themes.
5. Collating, summarizing, reporting results	Content analysis is used to present a narrative description of existing literature.

studies' information in an organized electronic and paper datasheet (Appendix A) for ease of review and interpretation of findings. The electronic datasheet was organized into seven sections, that includes: author(s)/year/country, title, aim of study, design, setting/sample, intervention, and findings.

5 .Collating, summarizing, and reporting results.

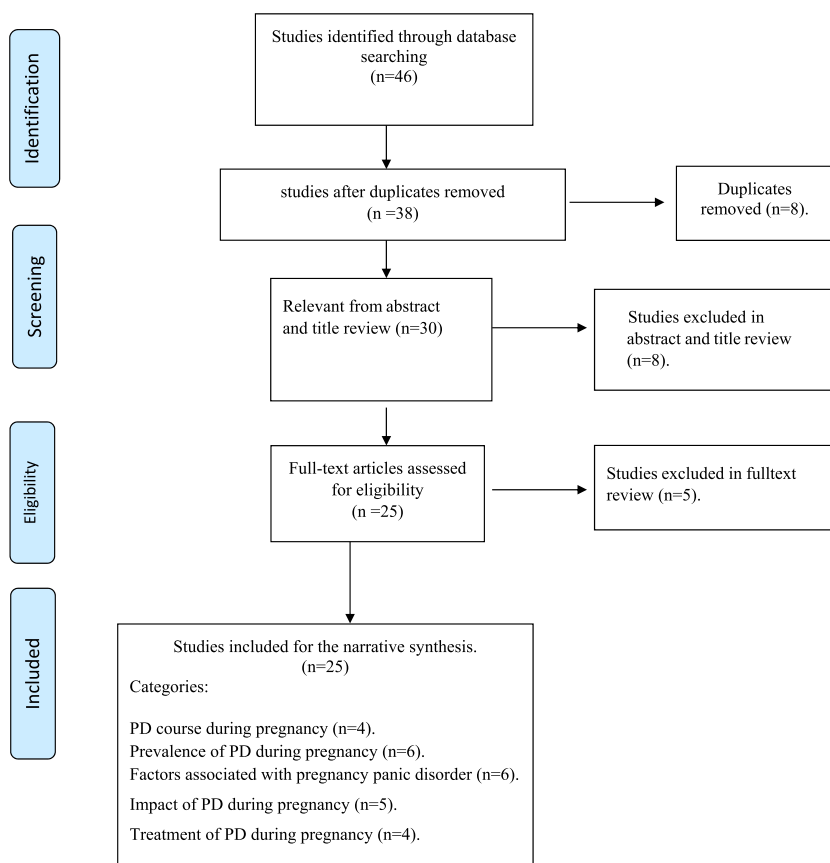
Content analysis was applied to analyze the data and report the results in a narrative style. The reviewers discussed the implications for practice, policy, and future research.

3. Results

A total of 46 studies were collected. After the removal of duplicates, 38 studies were screened for titles and abstracts. There were 30 relevant studies that underwent full-text screening, of which 25 met the eligible criteria to be included in the review. The search process and studies' selection are shown in Fig. 1 (PRISMA flow diagram).

The current scoping review yielded 25 articles published between 2003 and 2021 from 18 countries. Six articles were conducted in Turkey, two in the United State of America, two in Germany, one in each of the following countries: the United Kingdom, Taiwan, Korea, Japan, Australia, Hungary, Sweden, Italy, Greece, Israel, Qatar, Saudi Arabia, Gaza Strip, Jordan, Egypt. There was an absence of literature from Africa. Most of the studies were of a quantitative approach ($n = 19$) (76%), followed by two systematic reviews (8%) and two research reports (8%), one study was a narrative review (4%), and one study was a qualitative study (4%).

Content analysis was done to analyze the results and draw conclusions. The reviewers first read the included studies carefully more than once until they became familiar with the studies' contents. Then, they categorized the contents into the following five categories: PD course during pregnancy; prevalence of PD during pregnancy; factors associated with pregnancy panic disorder; impact of PD during pregnancy; and treatment of PD during pregnancy. The reviewers organized the five categories and their related studies using the content map. After that they analyzed, revised, and evaluated the categories to ensure that they had sufficient evidence behind them. Finally, the findings were presented in narrative form.



*Some studies addressed multiple categories

Figure (1). PRISMA flow diagram of the process of studies' selection.

4. Discussion

As far as we know, it is the first scoping review to focus on and discuss PD during pregnancy. The aim of this review was to summarize research findings and provide a wide overview of the literature regarding PD during pregnancy in terms of; PD course during pregnancy; prevalence of PD during pregnancy; factors associated with pregnancy panic disorder; impact of PD during pregnancy; and treatment of PD during pregnancy.

4.1. PD course during pregnancy

The effect of pregnancy on pre-existing PD showed mixed results. While some studies found that pregnant women with a pre-existing panic disorder had a decrease in symptoms during pregnancy, other studies concluded that symptoms did not decrease, but on the contrary that severe panic attacks occurred during pregnancy.

For example, in a naturalistic study with a follow-up of seven years that aimed to examine the effect of pregnancy on a pre-existing panic disorder, the researchers recruited eighty-five women with PD and found that pregnancy might increase the risk of PD relapse, and pregnant women had a more severe PD relapse as compared with nonpregnant women [13]. Furthermore, in a systematic review that goes with this finding, the researchers concluded that pregnancy can be a risk factor for the incidence and/or worsening of PD [14].

Contrary to these studies, a prospective study that was conducted in Turkey showed that the severity of panic disorder symptoms declined from pregnancy to 6 weeks after birth, which could be explained by psychosocial influences (E.g., financial problems, an increased workload, or reduced sleeping) and hormonal changes mainly estrogen, progesterone, and cortisol [15].

In another study that was conducted in Germany, the researchers recruited 128 women with PD and demonstrated that PD symptoms during pregnancy are fewer, while the postnatal period seems to increase the risk for the onset or worsening of PD symptoms [16]. These results were inconsistent with another study findings, that pregnant women with a short period of panic disorder may experience significant relief in the severity of panic disorder symptoms during the postnatal duration [17].

4.2. Prevalence of PD during pregnancy

There is no uniform worldwide prevalence of PD during pregnancy. Therefore, the estimated prevalence of PD during pregnancy varies between studies, and it ranges from 0.2 % to 7.0 %. For example, in Sweden it was 0.2% [18], in Hungary it was 0.5% [19], in Italy it was 7.0% [20], and 1.3% among Turkish pregnant women [15]. This discrepancy in prevalence may be due to different assessment tools used by the researchers, different settings, and cultural differences. Furthermore, it was found that the prevalence of PD was more in pregnant women (3%) compared with the general population (1.6%), which indicates that PD is common among pregnant women [14].

Studies found in this aspect were in high income countries, while no studies were found in low-and middle-income countries. Instead, in low- and middle-income countries the studies found related to the prevalence of anxiety disorder in general during pregnancy.

In the Arab countries, for example, no prevalence rate was found for PD among pregnant women. Instead, there were some studies investigating the prevalence of anxiety disorders in general during pregnancy. For example, the prevalence of pregnancy-related anxiety in Saudi Arabia using state-anxiety scale was 23.6% [21], in Qatar it was 26.5% [22], 11.4 % in Egypt [23], and in the Gaza Strip 4.3% of pregnant women had moderate anxiety, and 8.8% had a severe form of anxiety [24]. In Jordan, in a cross-sectional study that was conducted to study the prevalence of anxiety among pregnant women attending routine obstetric care clinics, the researchers found that among 200 participants, 32 (16.0%) women had minimal symptoms, 60 (30.0%) had mild symptoms, 66 (33.0%) had moderate symptoms, and 42 (21.0%) had severe symptoms of anxiety [25].

4.3. Factors associated with pregnancy panic disorder

According to a systematic review that was conducted in 2016, the most important factors associated with anxiety disorders, including PD, were: Absence of partner and/or social support; abuse history; history of mental disorder; unplanned or unwanted pregnancy; high perceived stress; complications during pregnancy; and abortion [26]. These findings confirm other study's findings, that high level of anticipated social support and resilience showed a reduction in generalized and pregnancy-related anxiety [22].

Furthermore, the risk is more among non-working women who have a history of unplanned pregnancy and miscarriage (21; 25), lower education level, more childbirths, and less family support [20], and there is a strong association with exposure to intimate partner violence [23].

In addition, psychological factors play an essential role in the anxiety disorders development during pregnancy, including mother's concerns over the health of the child, being able to be a good mother, the change in lifestyle, and finances [27]. Furthermore, the existence of major depression and/or any anxiety disorder at the beginning of pregnancy was a valid factor in predicting the occurrence of pregnancy-onset panic disorder during pregnancy [15].

4.4. Impact of PD during pregnancy

Panic disorder during pregnancy is ambiguous, and few studies were found regarding this issue. While some studies indicated that

there was no relation between PD during pregnancy and adverse effects on the mothers and/or their babies, other studies did not.

For example, research was conducted to examine the possible relationship between pregnancy panic disorder and complications during pregnancy, the researchers found that PD during pregnancy was connected with anemia, a shorter gestational age, and a larger ratio of preterm births [19]. In concordance with another study, the researchers concluded that prenatal PD was connected with neonates being born preterm and small for gestational age [28]. Moreover, the highest percentage of preterm birth, low birthweight, and the need for neonatal care was found in infants of untreated mothers with panic disorder [29]. Furthermore, in a prospective-longitudinal multi-wave study, the researchers demonstrated that women with peripartum PD presented with lower social and partner support, and a shorter period of breastfeeding [6].

Astonishingly, in a population-based case-control study that was conducted in 2006 in Hungary to examine the possible connection between maternal PD during pregnancy and congenital abnormalities, a higher prevalence of pregnancy panic disorder was found in the groups of babies with cleft lip/palate [30].

Contrary to these findings, a cohort study was carried out between July 2005, and July 2009 in Connecticut and Southern Massachusetts in the United States of America (USA) to examine if panic disorder or generalized anxiety disorder (GAD) in pregnancy related to adverse maternal or neonatal pregnancy outcomes. In this study, 2654 women were longitudinally followed up during pregnancy and the postnatal period. The researchers demonstrated that neither generalized anxiety disorder nor panic disorder was connected with maternal or neonatal adverse outcomes [31].

4.5. Treatment of PD during pregnancy

The main methods of PD treatment include both psychological and pharmacological treatment [1]. The first-line drug of choice is Selective Serotonin Reuptake Inhibitors (SSRI), and short duration of regular benzodiazepine along with antidepressants [32].

Given the fact that psychotropic drugs could cause serious complications for the developing fetus, the possible effects of the drugs must be weighed against the potential effects on the mother and fetus if the PD is not treated [27].

For example, in a retrospective study, the researcher examined 33 pregnant women with panic disorder using The Hamilton Depression Rating Scale and the Hamilton Rating Scale for Anxiety to examine citalopram's efficacy, the researcher found that efficacy of citalopram at 20 mg/d was beneficial for treating pregnant women with PD [33].

Furthermore, Acs et al. (2006) found that drugs, mainly benzodiazepines, used for PD treatment, were effective in treating pregnant women with PD. On the other hand, use of a benzodiazepine during pregnancy was connected to the delivery of a low-birth-weight infant, cesarean delivery, and use of neonatal ventilatory support [31].

As a substitute to pharmacological treatment, nonpharmacologic therapy, such as cognitive behavioral therapy, can be first choice treatment approach in pregnant women with PD [34] to avoid drugs complications. Furthermore, complementary, and alternative medicine (Acupuncture, Herb extract granules, and Korean medicine psychotherapy) may be safe and effective to control the symptoms of PD among pregnant women [35].

Therefore, when discussing treatment of pregnant women with PD, it is important to take into consideration some aspects when selecting the treatment approach, for example, previous response to treatment, treatment cost and availability, patient-clinician relationship, presence of comorbid psychological disorders, patient beliefs and preferences [36], and above all mother and fetus possible complications.

4.6. Research gaps and future perspectives

The course of PD during pregnancy is variable. As a result of this variability, a conclusion cannot be drawn about the usual course of PD during pregnancy. Research is needed to determine if symptoms of PD improve or deteriorate during pregnancy. Furthermore, the studies that were found and reviewed focused on the impact of pre-existing PD on pregnant women, while no studies were found regarding the impact of PD as a first onset during pregnancy on pregnant women. Which indicated a gap in the literature that revealed a need for more research in this aspect. Finally, there is a need for studies to be conducted in Arab countries to examine the prevalence rate and the impact of PD during pregnancy due to the lack of such studies in this region.

5. Clinical implications

- Inspire researchers in the medical field, who are interested in studying this issue to further understand and examine PD during pregnancy.
- Help healthcare providers in the prevention, early detection, and treatment, since PD during pregnancy can have serious adverse effects on both mothers and babies.
- Increase mental health awareness and shed some light on the importance of women's mental health during pregnancy.
- The findings of this review can assist the health care policy makers to develop policies to integrate maternal mental health with pregnancy care.

6. Limitations

Scoping reviews' limitations are in their rigor and duration, meaning that they hold the potential for bias [12]. Further, the quality of the included articles was not assessed. Therefore, the findings of this review may have limited reliability. Our review was also

limited by review only English-language studies.

7. Conclusion

The main purpose of this scoping review was to review and summarize the existing research evidence regarding PD during pregnancy. The results of the current review revealed that there is a gap in the literature, and inconsistent and mixed findings regarding the prevalence, impact, associated factors, and treatment of PD during pregnancy. The findings of this review found that more studies need to be conducted to further understand and examine PD during pregnancy.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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Availability of data and material

There is no data associated with this review.

CRedit authorship contribution statement

Eman Al-Awabdeh: Writing – original draft, Methodology, Conceptualization. **Lubna Abu Shaikha:** Visualization, Validation. **Abdelrahman Salameh:** Data curation, Conceptualization. **Jafar Alasad Alshraideh:** Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

Not applicable.

List of abbreviations

Abbreviation Meaning

CBT	Cognitive Behavioral Therapy
DSM	Diagnostic and Statistical Manual of Mental Health
GAD	Generalized Anxiety Disorder
PD	Panic Disorder
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
SSRI	Selective Serotonin Reuptake Inhibitors
USA	United States of America
WHO	World Health Organization

Appendix (A)

Summary of Studies Datasheet

Authors, year & country	Title	Objective	Study design	Setting& Sample (participant characteristics)	Intervention	Findings
Basha, A., Sabanekeh, C., Shlash, L., Dawod, L.,	Prevalence of Anxiety among Pregnant Women	To study the prevalence of anxiety among	A cross sectional study	Jordan University Hospital. 200 women with	The participants were interviewed using the Generalized Anxiety	32 (16.0%) women had minimal symptoms, 60

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Appendix (A) (continued)

Authors, year & country	Title	Objective	Study design	Setting& Sample (participant characteristics)	Intervention	Findings
Dweik, M., Obeidat, N., Malkawi, L., Alryalat, Saif A. (2021). Jordan	Attending Antenatal care in Jordan: A Single Center Study.	pregnant women attending routine antenatal care clinics.		mean age between 15 and 45.	Disorder –7 (GAD-7) questionnaire.	(30.0%) had mild symptoms, 66 (33.0%) had moderate symptoms while 42 (21.0%) had severe symptoms. Recurrent miscarriage can affect women's psychological well-being; with an increase in the possibility of experiencing anxiety.
Faruk Uguz (2020) Turkey	Citalopram in Treatment of Pregnant Women With Panic Disorder	To investigate efficacy of citalopram in pregnant women with panic disorder	A Retrospective Study	Psychiatry Outpatient Clinic of a University Hospital. 33 pregnant women with panic.	The Clinical Global Impression-Improvement Scale. The Hamilton Depression Rating Scale, and the Hamilton Rating Scale for Anxiety.	Citalopram may be beneficial for in pregnant women with panic disorder.
Marchesi, C., Ampollini, P., Paraggio, C., Giaracuni, G., Ossola, P., De Panfilis, C., Tonna, M., Viviani, D. (2014). Italy	Risk factors for panic disorder in pregnancy: A cohort study	To investigate the prevalence of PD with or without comorbid depression at several times during pregnancy.	A cohort study. Prospective	Two Centers for Prenatal Care of the Public Health Service in Italy. 277 pregnant women	The Italian translation of the Primary Care Evaluation of Mental Disorders (PRIME-MD)	The prevalence of PD during pregnancy was 7.0 %.
Murtaja, F., Thabet, A. (2017). Gaza Strip	Anxiety and depression among pregnant women in the Gaza Strip	To examine the levels of anxiety and depression among pregnant women attending primary healthcare clinics in Gaza Strip.	A cross-sectional study	Primary healthcare clinics in the Gaza Strip 400 pregnant women were randomly selected	The participants were interviewed using the sociodemographic scale, Hamilton Anxiety Rating Scale (HAM-A), and Beck Depression Inventory (BDI).	The study showed that 33.3% of the pregnant women showed moderate and 18.5% showed severe depression. Women living in refugee camps more often reported clinical cases of depression. 14.3% of these women showed moderate and 8.8% showed severe symptoms of anxiety.
Abdelhai, R., Mosleh, H. (2015). Egypt	Screening for antepartum anxiety and depression and their association with domestic violence among Egyptian pregnant women.	To screen for anxiety and/or depression among pregnant women, as well as identify the frequency and association of exposure to DV.	A cross-sectional study	The antenatal care outpatient clinic at the largest university hospital in Egypt A systematic random sample of 376 pregnant women	Participants were interviewed using a structured questionnaire including three components: sociodemographic characteristics of the participants, the Hospital Anxiety and Depression Scale questionnaire (HADS), and the Hurt, Insulted, Threaten, Scream (HITS) inventory for screening for DV.	Women who expressed simultaneous anxiety and depressive manifestations accounted for 63%, whereas 11.4% and 10.4% of them expressed only anxiety and only depression, respectively. Exposure to DV was detected in 30.6% of all participants. Symptoms of anxiety and depression were highly reported among this sample of

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Appendix (A) (continued)

Authors, year & country	Title	Objective	Study design	Setting& Sample (participant characteristics)	Intervention	Findings
Uguz, F., Yuksel, G., Sahmelikoglu Onur, O., Karsidag, C., Gezginc, K., Arpaci, N. (2018).	Neonatal outcomes in pregnant women with untreated and treated panic disorder	To compare neonatal outcomes including gestational age, birth weight and hospitalization of newborns of pregnant women with treated with antidepressants and untreated panic disorder.	Naturalistic observational	The study sample included 146 pregnant women (44 patients with panic disorder treated with antidepressants, 52 patients with untreated panic disorder, and 50 healthy controls).	Panic disorder was diagnosed by means of the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.	pregnant Egyptian women and were significantly associated with exposure to intimate partner violence. The highest proportions of preterm birth (28.8%), low birthweight (34.6%) and requirement of neonatal care (25.0%) was observed in infants of untreated patients with panic disorder. Treatment with pharmacotherapy of panic disorder during pregnancy may have beneficial effects on the risk of negative neonatal outcomes due to maternal panic disorder in the infants.
Matsumoto, K., Sato, K., Hamatani, S., Shirayama, Y., Shimizu, E. (2019). Japan	Cognitive behavioral therapy for postpartum panic disorder: a case series	To investigate the adaptability of CBT for postpartum PD of Japanese patients.	A case series	Psychiatry unit in Teikyo, University Chiba Medical Center Three women aged 36–38 years	Mini International Neuropsychiatric Interview, for PD diagnosis. Panic Disorder Severity Scale to evaluate patients' panic symptoms and their severity.	CBT provides a therapeutic effect and is a feasible method for treating postpartum PD
Güler, Ö., Koken, G., Emul, M., Ozbulut, O., Gecici, O., Uguz, F., Gezginc, K., Zeytinci, I., Karatayli, S., Askin, R. (2008). Turkey	Course of panic disorder during the early postpartum period: a prospective analysis	To examine prospectively the clinical course of 13 pregnant women with a diagnosis of PD across pregnancy and the early postpartum period.	Prospective study	2 medical research centers: the Meram Medical School of Selcuk University in Konya, Turkey, and the Medical School of Kocatepe University in Afyon, Turkey. 13 women	The authors who are psychiatrists individually interviewed all subjects by using valid and reliable psychiatric instruments. Panic and Agoraphobia Scale was used to determine the severity of PD.	Pregnant women with PD may experience a marked improvement in PD symptoms in the early postpartum period.
Rubinchik, S., Kablinger, A., Gardner, J. (2005). United States	Medications for Panic Disorder and Generalized Anxiety Disorder During Pregnancy.	To reviews the literature on the course of generalized anxiety disorder (GAD) and panic disorder during pregnancy and the postpartum period and presents guidelines for management.	Narrative literature review	An English language electronic search of relevant studies using PubMed (January 1, 1985–January 2004) was performed. 21 articles	The researchers reviewed the articles and primary pharmacologic treatment trials were analyzed and incorporated into the review based on adequate methodology, completeness of data, and information on pregnancy outcome.	The goal of treatment during pregnancy and lactation is sufficient treatment for syndrome remission. nonpharmacologic treatment, such as cognitive behavioral therapy, should be first line treatment. in pregnant women with GAD or panic disorder
Papakostas, Y., Eftychiadis, A., Papakostas, G., Christodoulou,	A Historical Inquiry into the Appropriateness of	To examine critically the rationale and the appropriateness of	A historical perspective reports.	_____	The author presented a Brief historical account of anxiety that comes in the	The introduced term 'panic' appropriately and successfully

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Appendix (A) (continued)

Authors, year & country	Title	Objective	Study design	Setting& Sample (participant characteristics)	Intervention	Findings
G. (2003). Greece	the Term 'panic disorder'	this term from a historical perspective.			episodic form, and the medical and psychiatric terminology that emerged during the last two centuries regarding this condition. Next, the origins of the concept of panic as a collective or individual fear reaction are traced from a mythological and historical standpoint, up to its current, almost accidental, introduction into the official psychiatric diagnostic systems.	replaced the old ones.
Alqahtani, A., Al-Khedair, K., Al-Jeheiman, R., Al-Turki, H., Al-Qahtani, N. (2018). Saudi Arabia	Anxiety and depression during pregnancy in women attending clinics in a University Hospital in Eastern province of Saudi Arabia: Prevalence and associated factors.	To assess the prevalence of anxiety and depression during pregnancy in women attending the hospital for antenatal care and assess the associated factors.	Prospective cohort study	University Hospital of Imam Abdulrahman Bin Faisal University 575 women	Anxiety was evaluated using the State Trait Anxiety Inventory. Depression was assessed using Edinburgh Postnatal Depression Scale (EPDS).	The prevalence of anxiety using state-anxiety scale was 23.6%, while using the trait scale it was 23.9%. The risk is higher among unemployed women with history of miscarriage and unplanned pregnancy
Vythilingum, B. (2008). South Africa	Anxiety disorders in pregnancy	To discuss the epidemiology of anxiety disorders in pregnancy, clinical presentation of these disorders, and management issues specific to pregnancy	A report	—	—	Anxiety symptoms in pregnancy have been associated with adverse fetal and infant outcomes. Furthermore, having an anxiety disorder during pregnancy is one of the strongest risk factors for postnatal depression.
Biaggi, A., Conroy, S., Pawlby, S., Pariante, C. (2015). United Kingdom	Identifying the women at risk of antenatal anxiety and depression: A systematic review	to identify the main risk factors involved in the onset of antenatal anxiety and depression.	A systematic review	97 papers were selected.	This systematic review was conducted using PubMed, PsychINFO, and the Cochrane Library. Original papers were included if they were written in English and published between January 1, 2003 and August 31, 2015.	The most relevant factors associated with antenatal depression or anxiety were: lack of partner or of social support; history of abuse or of domestic violence; personal history of mental illness; unplanned or unwanted pregnancy; adverse events in life and high perceived stress; present/past pregnancy complications; and pregnancy loss.
Andersson, L., Sundström-Poromaa, I., Bixo, Marie.,	Point prevalence of psychiatric disorders during the second	To determine the point prevalence of psychiatric disorders during	A population-based study	Two obstetric clinics in Northern Sweden.	Participants were evaluated for 1 year. The Primary Care Evaluation of Mental	Major depression was prevalent in 3.3% of patients and minor depression in

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Appendix (A) (continued)

Authors, year & country	Title	Objective	Study design	Setting& Sample (participant characteristics)	Intervention	Findings
Wulff, M., Bondestam, K., Åström, M. (2003). Sweden	trimester of pregnancy.	the second trimester of pregnancy in a population-based sample of pregnant women.		1795 consecutive pregnant women	Disorders (PRIME-MD) was used for evaluating.	6.9% of patients. Anxiety disorders were encountered in 6.6% of patients. Women with psychiatric disorders displayed significantly more somatic symptoms and more pronounced fear of childbirth. Among diagnosed patients, only 5.5% had some form of treatment
Güler, Ö., Sahin, F., Emul, M., Ozbulut, O., Gecici, O., Uguz, F., Gezginc, K., Zeytinci, I., Karatayli, S., Askin, R. (2008). Turkey	The prevalence of panic disorder in pregnant women during the third trimester of pregnancy	To investigate the clinical characteristics of PD in pregnant and nonpregnant women. To assess the current prevalence rate of panic disorder (PD) in pregnant women during the third trimester of pregnancy	Cohort study	The obstetric outpatient clinics of 2 university research centers (the Meram Medical School of Selçuk University in Konya, Turkey, and the Medical School of Kocatepe University in Afyon, Turkey) 512 consecutive women in the third trimester of pregnancy	The authors who are psychiatrists individually interviewed all subjects by using valid and reliable psychiatric instruments. Diagnosis of PD was determined by means of the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) Axis I disorders (SCID-I) and the severity of PD was assessed by the Panic and Agoraphobia Scale (PAS)	The prevalence rate of PD was found to be 2.5% (n = 13) among the subjects in the third trimester of pregnancy. Study's findings suggests that PD may be common among pregnant females during the third trimester of pregnancy and seems to be associated with similar clinical features during gestation and non-gestation.
Naja, S., Alkubisi, N., Singh, R., Bougmiza, I. (2020) Qatar	Generalized and pregnancy-related anxiety prevalence and predictors among pregnant women attending primary health care in Qatar, 2018–2019	To measure the prevalence and determinants of generalized and pregnancy-related anxiety among pregnant women	Analytical cross-sectional study	Nine primary healthcare centers distributed across Qatar. 800 pregnant women	800 pregnant women completed a structured interview and self-administrated questionnaires after being selected through probability sampling.	26.5% reported high pregnancy-related anxiety. high level of perceived social support and resilience was shown to mitigate generalized and pregnancy-related anxiety.
Jonge, P., Roest, A., Lim, C., Florescu, S., Bromet, E., Stein, D., Harris, M., Nakov, V., Caldas de Almeida, J., Levinson, D., Al-Hamzawi, A., Haro, J., Viana, M., Borges, G., O'Neill, S., de Girolamo, G., Demyttenaere, K., Gureje, O., Iwata, N., Scott, K. (2016). 25 countries	Cross-national epidemiology of panic disorder and panic attacks in the world mental health surveys.	To present representative data about the cross-national epidemiology of PD and PAs in accordance with DSM-5 definitions.	Nationally representative cross-sectional surveys of 25 countries which were: Colombia, Iraq, Nigeria, Peru, the People's Republic of China (Beijing and Shanghai), and Ukraine, the upper-middle income countries of Brazil, Bulgaria, Colombia (Medellin), Lebanon,	Data collection took place between 2001 and 2012, and response rates ranged from 45.9 to 97.2%, with an average of 68.6%. Respondents (n = 142,949) from 25 high, middle, and lower-middle income countries across the world aged 18 years or older.	Data from the World Mental Health Surveys were used. The presence of mental disorders was assessed using the World Health Organization Composite International Diagnostic Interview version 3.0. was used.	Lifetime prevalence of PAs for all countries combined was 13.2%. Of the persons with lifetime PA, 12.8% had lifetime PD, for a population-level lifetime prevalence of PD of 1.7%. Of persons with lifetime PA without PD, about two thirds (66.5%) had recurrent PAs. Significant differences in prevalence rates of PAs and PD were observed between

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Appendix (A) (continued)

Authors, year & country	Title	Objective	Study design	Setting& Sample (participant characteristics)	Intervention	Findings
			Mexico, and Romania, and the high-income countries of Australia, Belgium, France, Germany, Israel, Italy, Japan, New Zealand, Northern Ireland, Poland, Portugal, Spain, Spain (Murcia), the Netherlands, and the United States			country groups based on income level and on WHO regions, with higher prevalence rates in high-income countries and countries in the region of the Americas, Western Pacific, and Western Europe.
Acs, N., Bánhidly, F., Horváth-Puhó, f., Czeizel, A. (2006). Hungary	Maternal panic disorder and congenital abnormalities: A population-based case-control study.	To investigate the possible association between maternal panic disorder during pregnancy and structural birth defects (congenital abnormalities).	A population-based case-control study	38,151 controls represented 1.8% of all Hungarian births, and among those controls, 187 (0.5%) were born to mothers with panic disorder.	First, The first step was the selection of cases from the dataset of the Hungarian Congenital Abnormality Registry (HCAR), 1980–1996. second step was to ascertain appropriate controls from the National Birth Registry of the Central Statistical Office for the HCCSCA. obtain the necessary maternal, particularly exposure data from 3 sources (Retrospective self-reported maternal information, Prospective medically recorded data, and Supplementary data collection). The fourth step was the evaluation of maternal panic disorder. The fifth step was the statistical analysis of data	A higher prevalence of maternal panic disorder was found in the groups of offspring with cleft lip/palate (CL/P) and multiple congenital abnormalities. However, drugs, mainly benzodiazepines used for the treatment of panic disorder, were associated with a significant reduction in risk for the above 2 congenital abnormalities groups in the offspring of pregnant women with panic disorders. Thus, panic disorder itself seems to be teratogenic.
Dannon, P., Iancu, I., Lowengrub, K., Grunhaus, L., Kotler, M. (2006). Israel	Recurrence of Panic Disorder During Pregnancy: A 7-Year Naturalistic Follow-up Study.	To examine the effect of pregnancy as a predicting factor of relapse in patients with panic disorder (PD).	Naturalistic Follow-up Study.	Outpatient clinics of either the Chaim Sheba Medical Center or the Rehovot Community Mental Health Clinic 85 female patients with PD between the ages of 20 and 35 years.	All patients underwent a comprehensive, psychiatric semi-structured diagnostic evaluation performed by a senior psychiatrist. Treatment with paroxetine,	Pregnancy might confer an increased risk of relapse in PD. Subjects who relapsed during pregnancy had a more severe relapse as compared with nonpregnant relapses.
Viswasam, K., Eslick, G., Starcevic, V. (2019). Australia	Prevalence, onset and course of anxiety disorders during pregnancy: A systematic	To shed more light on the prevalence, onset and course of anxiety disorders and related conditions	systematic review	Thirty-six studies were included	A comprehensive literature search was performed on a wide range of databases. And a random effect	Pregnancy may be a specific risk factor for the occurrence and/or exacerbation of PD and OCD and underscore the

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Appendix (A) (continued)

Authors, year & country	Title	Objective	Study design	Setting& Sample (participant characteristics)	Intervention	Findings
Chen, Y., Lin, H., Lee, H. (2010). Taiwan	review and meta-analysis. Pregnancy outcomes among women with panic disorder - Do panic attacks during pregnancy matter?	during pregnancy, with implications for clinical practice. To assess whether maternal PD during pregnancy contributes to risks of adverse pregnancy outcomes, when compared to mothers with no history of this chronic disease	A report/cohort comparison. nationwide population-based study	1956 participants. 371 women who gave birth from 2001 to 2003, who had been diagnosed with PD within 2 years prior to the index delivery, together with 1585 matched women without this chronic disease as a comparison cohort	model was used for the meta-analysis. The researchers linked two nationwide population-based datasets: the birth certificate registry and the Taiwan National Health Insurance Research Dataset.	importance of their early diagnosis and management. We conclude that prenatal PD, particularly the occurrence of panic attacks during pregnancy, was associated with adverse birth outcomes. PD mothers with panic attacks were linked to the highest risks of neonates being born preterm and SGA, while a less-strong association was identified between maternal PD without a panic attack and having SGA infants. During pregnancy panic manifestations are fewer, while the postpartum period seems to increase the risk for onset or exacerbation of panic disorder.
Bandelow, B., Sojka, F., Broocks, A., Hajak, G., Bleich, S., R��ther, E. (2006). Germany	Panic disorder during pregnancy and postpartum period	To quantify panic manifestations in pregnancy and postpartum period in large sample of women.	Single blind retrospective design.	Anxiety Disorders Outpatient Unit at the Department of Psychiatry, University of G��ttingen. 128 women with panic disorder, 93 of whom had had 195 pregnancies.	128 women with panic disorder were interviewed personally or by telephone. To exclude other relevant psychiatric disorders, a SCID (Structured clinical interview for DSM-IV was performed. All women completed a questionnaire about panic symptoms, and women with pregnancies were asked an additional set of 16 questions about panic manifestations during pregnancies and postpartum period.	During pregnancy panic manifestations are fewer, while the postpartum period seems to increase the risk for onset or exacerbation of panic disorder.
Yonkers, K., Gilstad-Hayden, K., Furray, A., Lipkind, H. (2017) USA	Association of Panic Disorder, Generalized Anxiety Disorder, and Benzodiazepine Treatment During Pregnancy with Risk of Adverse Birth Outcomes	To determine whether panic disorder or generalized anxiety disorder (GAD) in pregnancy are associated with adverse maternal or neonatal pregnancy outcomes.	Cohort study	The Yale University School of Medicine, New Haven, Connecticut, and 137 collaborating hospitals and private practices throughout Connecticut and southern Massachusetts 2654 pregnant women Mean age was 30 years. Most were non-Hispanic white. 98 had panic disorder, 252 had	2654 women in the final analysis were longitudinally followed up through pregnancy and the postpartum period between July 1, 2005, and July 14, 2009.	neither panic disorder nor generalized anxiety disorder was associated with maternal or neonatal outcomes of interest. Furthermore, the authors found that the maternal use of a benzodiazepine connected to delivery of a low-birth-weight infant, cesarean delivery, and use of neonatal ventilatory support. While use of an SRI was connected to preterm birth, use of

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Appendix (A) (continued)

Authors, year & country	Title	Objective	Study design	Setting& Sample (participant characteristics)	Intervention	Findings
				GAD, 67 were treated with a benzodiazepine, and 293 were treated with a serotonin reuptake inhibitor Serotonin Reuptake Inhibitors (SRI) during pregnancy.		minor neonatal respiratory interventions, and hypertensive diseases of pregnancy
Martini, J., Beesdo-Baum, K., Garthus-Niegel, S., Wittchen, H. (2020) Germany	The course of panic disorder during the peripartum period and the risk for adverse child development: A prospective-longitudinal study	To investigate the course of PD and comorbid MD during the peripartum period in more detail distinguishing incident and recurrent cases and the occurrence of PD during pregnancy and the postpartum period.	Prospective-longitudinal multi-wave design.	Gynecological outpatient settings in Dresden (Germany). 306 pregnant women.	306 women were repeatedly interviewed with the Composite International Diagnostic Interview for Women. Social support and partnership quality, gestational outcomes, duration of breastfeeding, regulatory disorders, maternal bonding, and parenting style were assessed via medical and maternal reports. Standardized observations of neuropsychological development, infant temperament and attachment were conducted 4 and 16 months after delivery.	Panic disorders were commonly observed during the early stages of pregnancy. Women with peripartum PD presented with a worse psychosocial situation, Clear behavioral differences, differences concerning gestational outcomes, duration of breastfeeding, maternal parenting, and bonding as well as regulatory problems in infants were identified.
Güler, Ö., Kaya, V., Gezginc, K., Kayhan, F., Cicek, E., & Sonmez, O., Uguz, F. (2015) Turkey	Pregnancy-Onset Panic Disorder: Incidence, Comorbidity and Associated Factors	To investigate the incidence rate of pregnancy-onset panic disorder (POPD) among Turkish pregnant women using a diagnostic interview.	Case report	Obstetric outpatient clinic of two research centers in Turkey. 1475 consecutive pregnant women.	Panic disorder and other anxiety or mood disorders were determined by means of the Structured Clinical Interview for DSM-IV. Comorbid Axis II disorders were diagnosed with the Structured Clinical Interview for DSM-III-R Personality Disorders.	The existence of any anxiety disorder and major depression at the onset of gestation was a strong factor in predicting the occurrence of POPD during pregnancy
Seo, S., Song, S., Koo, B., Kim, G. (2017) Korea	A Case of Korean Medicine Treatment for Pregnant Woman with Panic Disorder - From Early Pregnancy to Delivery.	To evaluate the efficacy and safety of Korean medicine treatment (Acupuncture, Herb extract granules, and Korean medicine psychotherapy) for pregnant women with panic disorder.	Case study	Female, 37 years old with panic disorder.	From November 24, 2016, to August 4, 2017 (for 254 days), the patient was instructed to visit the clinic regularly once a week, and was encouraged to visit the hospital at any time when symptoms are severe to endure. She has treated with Acupuncture, Herb extract granules, and Korean medicine psychotherapy	Mental and body symptoms were reduced. Both mother and the baby were healthy after delivery. Korean medicine treatment may be effective and safe to control symptoms of pregnant women with panic disorder.

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Appendix (A) (continued)

Authors, year & country	Title	Objective	Study design	Setting& Sample (participant characteristics)	Intervention	Findings
Aydogan, S., Uguz, F., Yakut, E., & Bayman, M., Gezginc, K. (2020) Turkey	The course and clinical correlates of panic disorder during the postpartum period: A naturalistic observational study.	To investigate the course of panic disorder and its demographic and clinical correlates during the postpartum period.	A naturalistic observational study.	Obstetric inpatient clinic of a university hospital 38 consecutive postpartum women diagnosed with panic disorder.	Psychiatric assessments were carried out on the first day after delivery and at 6–8 weeks postpartum.	Patients with a short duration of illness may experience significant alleviation in the severity of panic symptoms during the postpartum period.

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