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Anxiety, depression and stress in pregnancy: implications for mothers, children, research, and practice

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Abstract

Purpose of review—To briefly review results of the latest research on the contributions of depression, anxiety, and stress exposures in pregnancy to adverse maternal and child outcomes, and to direct attention to new findings on pregnancy anxiety, a potent maternal risk factor.

Recent findings—Anxiety, depression, and stress in pregnancy are risk factors for adverse outcomes for mothers and children. Anxiety in pregnancy is associated with shorter gestation and has adverse implications for fetal neurodevelopment and child outcomes. Anxiety about a particular pregnancy is especially potent. Chronic strain, exposure to racism, and depressive symptoms in mothers during pregnancy are associated with lower birth weight infants with consequences for infant development. These distinguishable risk factors and related pathways to distinct birth outcomes merit further investigation.

Summary—This body of evidence, and the developing consensus regarding biological and behavioral mechanisms, sets the stage for a next era of psychiatric and collaborative interdisciplinary research on pregnancy to reduce the burden of maternal stress, depression, and anxiety in the perinatal period. It is critical to identify the signs, symptoms, and diagnostic thresholds that warrant prenatal intervention and to develop efficient, effective and ecologically valid screening and intervention strategies to be used widely.

Keywords

anxiety; depression; pregnancy; prenatal stress; stress

INTRODUCTION

For more than a decade, psychiatry and related disciplines have been concerned about women experiencing symptoms of anxiety and depression during pregnancy and in the months following a birth. *Current Opinion in Psychiatry* alone published relevant reviews in 1998, 2000, 2004, 2007, 2008, 2009, and 2011, usually addressing the clinical management of postpartum depression or the effects of antidepressant use on mothers and their babies. Meanwhile, a parallel literature has grown rapidly in other health disciplines, especially

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behavioral medicine, health psychology, and social epidemiology, regarding stress in pregnancy and the implications for mothers, infants, and development over the life course. The purpose of this article is to briefly review results of the latest research on effects of negative affective states (referring throughout to anxiety and depression) and stress exposures in pregnancy, mainly regarding effects on birth outcomes. We direct attention specifically to recent research on pregnancy anxiety, a newer concept that is among the most potent maternal risk factors for adverse maternal and child outcomes [1■■]. By highlighting these developments, we hope to encourage synthesis and new directions in research and to facilitate evidence-based practices in screening and clinical protocols.

Psychiatric research on pregnancy focuses mostly on diagnosable mental disorders, primarily anxiety, and depressive disorders [2,3] and somewhat on posttraumatic stress disorder following adverse life events or childbirth experiences. However, a large body of scientific research outside psychiatry provides extensive information on a wide range of clinical symptoms during pregnancy, as measured with screening tools such as the Edinburgh Postpartum Depression Scale (EPDS), for example, the Beck Depression Inventory, or the Center for Epidemiological Studies Depression Scale. Scores on these measures are sometimes dichotomized in order to create depressed/nondepressed groups of women as a proxy for diagnostic categories, but continuous scores of symptom severity are more often used in research. Symptoms typically show linear or dose–response associations with outcomes such as preterm birth (PTB), low birth weight (LBW), or infant abnormalities. Our current understanding of negative affective states in pregnancy is based largely on these studies of symptomatology, not investigations of confirmed diagnoses, perhaps because investigators lacked clinical expertise or funding to conduct diagnostic interviews. More studies of confirmed diagnoses would be helpful, particularly with larger samples and controlling for antidepressant medications and other relevant variables. Nonetheless, research findings on symptoms of anxiety and depression in pregnancy are informative for clinicians regarding prenatal screening, early detection, prevention, and treatment of perinatal mood disturbances among expecting and new mothers.

Estimates of the prevalence of depression during pregnancy vary depending on the criteria used, but can be as high as 16% or more women symptomatic and 5% with major depression [2]. Firm estimates for prenatal anxiety do not exist, nor is there agreement about appropriate screening tools, but past studies suggest that a significant portion of women experience prenatal anxiety both in general and about their pregnancy [1■■,3]. Evidence of high exposure to stress in pregnancy is more widely available, at least for certain subgroups of women. For example, a recent study of a diverse urban sample found that 78% experienced low-to-moderate antenatal psychosocial stress and 6% experienced high levels [4]. Some of the stressors that commonly affect women in pregnancy around the globe are low material resources, unfavorable employment conditions, heavy family and household responsibilities, strain in intimate relationships, and pregnancy complications.

A large body of research is now available regarding stress and affective states during pregnancy as predictors of specific pregnancy conditions and birth outcomes [5,6]. The most commonly studied are PTB (<37 weeks gestation) and LBW (< 2500 g). Both are of US and international significance due to high incidence in many parts of the world and also

consequences for infant mortality and morbidity. It has been estimated that two-thirds of LBW infants are born preterm. Thus, there are likely to be both common and unique etiological pathways [1■■,7■■]. Current theoretical models emphasize biopsychosocial and cultural determinants and interactions of multiple determinants in understanding these birth outcomes [8,9■■,10–12].

STRESS IN PREGNANCY

The literature on stress in pregnancy and birth outcomes is reviewed in two subsections, one on PTB and the other on LBW.

Stress and preterm birth

More than 80 scientific investigations on stress and PTB were recently reviewed by Dunkel Schetter and Glynn [7■■], of which a majority had prospective designs, large samples, and validated measures, and were fairly well controlled for confounds such as medical risks, smoking, education, income, and parity. These studies can be grouped by the type of stress examined. Of the more than a dozen published studies assessing 'major life events in pregnancy', a majority found significant effects; women who experienced major life events such as the death of a family member were at 1.4 to 1.8 times greater risk of PTB, with strongest effects when events occurred early in pregnancy. The majority of a second, smaller group of studies on catastrophic, community-wide disasters (e.g., earthquakes or terrorist attacks) also showed significant effects on gestational age at birth or PTB. A third small set of studies on chronic stressors, such as household strain or homelessness, all reported significant effects on PTB. Finally, a majority of past investigations on neighborhood stressors such as poverty and crime indicated significant effects on gestational age or PTB. In comparison, studies on daily hassles and perceived stress did not consistently predict PTB. Thus, of the many distinguishable forms of stress, many (but not all) contribute to the risk of PTB.

Stress and low birth weight

A second area of developing convergence concerns the effects of stress on infant birth weight and/or LBW, reviewed recently by Dunkel Schetter and Lobel [9■■]. Again these studies can be organized by type of stressor. Evidence suggests that 'major life events' somewhat consistently predicted fetal growth or birth weight, whereas measures of 'perceived stress' had small or nonsignificant effects. 'Chronic stressors', however, have been even more robust predictors of birth weight. For example, unemployment and crowding predicted 2.0 to 3.8 times the risk of LBW among low-income women in one study [13]. An important source of chronic stress is 'racism or discrimination' occurring both during the pregnancy and over a woman's lifetime [14]. Racism and discrimination contribute to birth outcomes independently of other types of stress [15]. A growing number of studies have demonstrated that racism and discrimination prospectively predict birth weight, particularly in African-American women [16]. Although this literature has focused mainly on women in the USA, it is relevant to minority women in other countries [17].

In summary, chronic strain, racism, and related factors such as neighborhood segregation are significant risk factors for LBW [18]. Of note, investigations of chronic stress and racism do not usually take into account depressive symptoms. Yet, depression may be an important mechanism whereby the effects of exposure to chronic stress and racism influence fetal growth and birth weight, likely via downstream physiological and behavioral mechanisms [9■].

ANXIOUS AND DEPRESSED AFFECT IN PREGNANCY

Recent research on symptoms of anxiety and depression during pregnancy is reviewed similarly within two subsections distinguishing findings on PTB from those on LBW.

Affect and preterm birth

State anxiety during pregnancy significantly predicted gestational age and/or PTB in seven of 11 studies recently reviewed [7■], but only in combination with other measures or in subgroups of the sample. More consistent effects have been found for 'pregnancy anxiety' (also known as 'pregnancy-specific anxiety' and similar to 'pregnancy distress'). Pregnancy anxiety appears to be a distinct and definable syndrome reflecting fears about the health and well being of one's baby, of hospital and health-care experiences (including one's own health and survival in pregnancy), of impending childbirth and its aftermath, and of parenting or the maternal role [1■,19]. It represents a particular emotional state that is closely associated with state anxiety but more contextually based, that is, tied *specifically* to concerns about a current pregnancy. Assessment of pregnancy anxiety has entailed ratings of four adjectives combined into an index ('feeling anxious, concerned, afraid, or panicky about the pregnancy [20]' or use of a 10-item scale reflecting anxiety about the baby's growth, loss of the baby, and harm during delivery, as well as a few reverse-coded items concerning confidence in having a normal childbirth) [21]. Other measures exist as well.

There is remarkably convergent empirical evidence across studies of diverse populations regarding the adverse effects of pregnancy anxiety on PTB or gestational age at birth [7■, 19]. More than 10 prospective studies have been conducted on this topic, all of which report significant effects on the timing of birth. An early study found that the 10-item scale scores combined with a standard measure of state anxiety predicted gestational age of the infant at birth, controlling for medical risk factors, ethnicity, education, and income; these results were also independent of the effects of a woman's personal resources (sense of mastery, self-esteem, and dispositional optimism) [21]. Use of multidimensional modeling techniques later revealed that state anxiety, pregnancy anxiety, and perceived stress all predicted the length of gestation, but pregnancy anxiety (as early as 18 weeks into pregnancy) was the only significant predictor when all three indicators were tested together with medical and demographic risks controlled [20]. At least three large, well controlled, prospective studies have replicated these results using similar pregnancy anxiety measures [22–24]. The largest of these was a prospective study of 4 885 births finding that women with high pregnancy anxiety were at 1.5 times greater risk of a PTB, controlling for socio-demographic covariates, medical and obstetric risks, and specific worries over a high-risk condition in pregnancy [23].

In sum, recent evidence is remarkably convergent, indicating that pregnancy anxiety predicts the timing of delivery in a linear manner. Further, pregnancy anxiety predicts risk of spontaneous PTB with meaningful effect sizes across studies, comparable to or larger than effects of known risk factors such as smoking and medical risk. These effects hold for diverse income and ethnic groups in the USA and in Canada. The consistency of these findings paves the way for investigating the antecedents and correlates of pregnancy anxiety, mechanisms of effects, and available treatments.

In contrast, relatively few of the more than a dozen studies on depressed mood or symptoms of trauma found significant effects on gestational age or PTB [9■■■]. A Swedish study found that elevated antenatal depressive symptoms predicted increased risk for PTB [odds ratio (OR) = 1.56] [25], and a recent meta-analysis concluded that PTB was associated with depression across 11 studies. However, in general, effect sizes were relatively small across studies with an average OR of 1.13 [confidence interval (CI 1.07–1.30)] [26].

Affect and low birth weight

Recent evidence points more often to the role of maternal depressive symptoms in the etiology of LBW as compared with the etiology of PTB [27■■■]. The recent meta-analysis on depression in pregnancy, cited earlier, evaluated 20 studies and found that high depressive symptoms were associated with 1.4 to 2.9 times higher risk of LBW in undeveloped countries, and 1.2 times higher risk on average in the USA [26]. Another recent review found relatively large effects of maternal depressive symptoms on infant birth weight across several studies, with the largest effects for low-income or low social status women and women of color [9■■■]. Furthermore, although there are few studies on diagnosed disorders, one study reported that mothers with a depressive disorder had 1.8 times greater risk of giving birth to a LBW infant [28]. Thus, evidence appears to be stronger for contributions of depressive symptoms or disorder to slower growth of the fetus and LBW than to the timing of delivery or PTB, and these effects are pronounced for disadvantaged women [29]. In contrast, very few studies have demonstrated any effects of anxiety on LBW, with rare exceptions [30].

STRESS AND NEGATIVE AFFECTIVE STATES IN PREGNANCY AND INFANT OR CHILD OUTCOMES

Evidence for effects of maternal stress, depression, and anxiety in pregnancy on adverse neurodevelopmental outcomes for the child is substantial [31], through a process known as 'fetal programming' [5,32]. Research utilizing animal models indicates that maternal distress negatively influences long-term learning, motor development, and behavior in offspring [33,34]. Evidence suggests that this occurs via effects on development of the fetal nervous system and alterations in functioning of the maternal and fetal hypothalamic pituitary adrenal (HPA) axes [34–36]. Maternal mood disorders have also been shown to activate the maternal HPA axis and program the HPA axis and physiology of the fetus [37,38]. In short, a mother's stress exposure and her affective states in pregnancy may have significant consequences for her child's subsequent development and health [5,39–43]. This evidence has been reviewed in many articles and spans effects on attention regulation, cognitive and

motor development, fearful temperament, and negative reactivity to novelty in the first year of life; behavioral and emotional problems and decreased gray matter density in childhood; and impulsivity, externalizing, and processing speed in adolescents [44–47]. Of note, many of these findings involve the effects of prenatal pregnancy anxiety on infant, child, or adolescent outcomes. Maternal stress has also been linked to major mental disorders in offspring [40,47].

SUMMARY AND KEY ISSUES

In summary, there is substantial evidence that anxiety, depression, and stress in pregnancy are risk factors for adverse outcomes for mothers and children. More specifically, anxiety in pregnancy is associated with shorter gestation and has adverse implications for fetal neurodevelopment and child outcomes. Furthermore, anxiety about a particular pregnancy seems to be especially potent. Finally, chronic strain, exposure to racism, and depressive symptoms in mothers during pregnancy are associated with lower birth weight infants with consequences for development as well. These differential risk factors and related pathways to PTB and LBW deserve further investigation. Beyond this, women with high stress, anxiety, and depressive symptoms in pregnancy are more likely to be impaired during the postpartum period. Postpartum affective disturbance and stress in turn impair parenting quality and effectiveness [48]. Figure 1 summarizes the evidence that has been briefly reviewed in a simple schematic with connections in bold representing those with notably stronger and more consistent evidence. This simple diagram can be elaborated further to include associations among the various types or forms of stress and to include mediated pathways to birth outcomes. For example, major life events or community catastrophes can be hypothesized to increase pregnancy anxiety, and long-term chronic strain to increase risk of depression. The effects of chronic strain on LBW via depression are also not depicted but are worthy of further research. Together, the evidence and developing consensus that biological and behavioral mechanisms explain these findings lay the groundwork for a next era of psychiatric and collaborative interdisciplinary research on pregnancy.

Why pregnancy anxiety?

It is not clear why 'pregnancy anxiety' has such powerful effects on mothers and their babies. In fact, the nature of this concept has not yet received sufficient attention to be fully explicated. Possibly what makes it potent is that measures of pregnancy anxiety capture both dispositional characteristics, or traits, and environmentally influenced states. For example, women who are most anxious about a pregnancy seem to be more insecurely attached, of certain cultural backgrounds, more likely to have a history of infertility or to be carrying unplanned pregnancies, and have fewer psychosocial resources [49]. These results suggest that existing vulnerabilities that predate pregnancy may interact with the social, familial, cultural, societal, and environmental conditions of pregnancy to increase levels of pregnancy anxiety, producing effects on the maternal–fetal–placental systems, especially during sensitive periods such as early pregnancy. This process can then adversely influence fetal development by programming the fetus's HPA axis and also have effects on the initiation of labor via maternal, fetal, and placental hormonal exchanges. Although there is much we do not know, a worthwhile future goal for clinical researchers may be to identify women high

in anxiety before conception, as well as women high in anxiety during pregnancy, and especially those women who are anxious about specific aspects of their pregnancies – about *this* child and *this* birth, and about competently parenting with *this* partner. These women would appear to be targets for early intervention such as evidence-based interventions for stress reduction, mood regulation treatments such as cognitive behavioral therapies, pharmacological treatments, and follow-up care during postpartum to prevent a range of adverse outcomes for mother, child, and family.

Clinical screening for affective symptoms in pregnancy

Clinical screening for depression or anxiety in prenatal and postpartum healthcare has been widely recommended but is also potentially problematic. The issues concern what screening tools to use; what cutoffs to adopt for identifying women at risk; the need for expert clinicians to follow up on those women who score above thresholds to make diagnoses; and, for those who have established diagnoses, the availability of affordable and efficacious treatments [50]. These issues must be resolved for prenatal (and postpartum) clinical screening to be recommended widely. For example, the EPDS, which is a gold standard used widely in clinic settings for depression screening both prepartum and postpartum, actually measures both depressive and anxiety symptoms, which may contribute to confusion about risks [51]. In addition, experts have questioned the validity of a diagnosis of depressive disorders using standard diagnostic criteria for mood disturbance because they include typical somatic symptoms of pregnancy such as fatigue, sleep disturbance, and appetite changes [52]. Also relevant is one recent study reporting that women with both depression and anxiety disorders were at highest risk of LBW, as compared with those with only depressive or anxious symptoms or none [53]. Combinations of symptoms have received very little research attention. Furthermore, little research thus far has examined the feasibility and utility of screening for prenatal stress or pregnancy anxiety.

If broad screening for affective symptoms during pregnancy results in high rates of false-positive results, low rates of clinical follow-up and referral, insufficient or ineffective education for women about the meaning of screening results, lack of treatment, and/or absence of proven evidence-based interventions, then clinical screening as a standard procedure in specific prenatal settings is of questionable value. Nonetheless, if important preconditions can be met, screening for pregnancy anxiety, state anxiety, depressive symptoms, and stress in pregnancy stands to provide potentially important clinical benefits for mothers and their children [54,55].

The broader context of pregnancy

An essential consideration in implementing widespread effective prenatal screening, diagnosis, and treatment is the context of a woman's pregnancy. The context includes her partner, family, friends, neighborhood, and larger community, all of which are known to influence a woman's mental health and responses to a diagnosis of disorder. Therefore, attention must be paid to these levels of influence in any attempts to screen and treat depression, anxiety, pregnancy anxiety, or stress in pregnancy. For example, a woman's ability to understand or respond to a diagnosis of a mood or anxiety disorder and accept treatment may be facilitated by involving her partner, closest relative, or friend in follow-up

after screening. Families and communities can undermine or enhance efforts to screen and treat women in pregnancy as a result of their beliefs, values, and level of information (or misinformation). Although these issues are known barriers to community mental health treatment in diverse populations, they have not yet been addressed in establishing appropriate clinical procedures in pregnancy for follow-up of widespread screening for affective disorders. It may also be useful to identify a range of protective and resilience factors such as mastery, self-efficacy and social support in women for the purpose of intervention planning [2,56[■]]. If efforts are directed to strengthening women's psychosocial resources as early as possible, ideally before conception, it is possible that prenatal health and outcomes could be better optimized.

CONCLUSION

In conclusion, although considerable, rigorous research now demonstrates the potential deleterious effects of negative affective states and stress during pregnancy on birth outcomes, fetal and infant development, and family health, we do not yet have a clear grasp on the specific implications of these facts. Key issues for the next wave of research are as follows: disentangling the independent and comorbid effects of depressive symptoms, anxiety symptoms, pregnancy anxiety, and various forms of stress on maternal and infant outcomes; better understanding the concept of pregnancy anxiety and how to address it clinically; and further investigating effects of clinically significant affective disturbances on maternal and child outcomes, taking into account a mother's broad socio-environmental context. As our knowledge increases, it will be critical to identify the signs, symptoms, and diagnostic thresholds that warrant prenatal intervention and to develop efficient, effective, and ecologically valid screening and intervention strategies to be used widely. If risk factors can be identified prior to pregnancy and interventions designed for preconception, many believe this window of opportunity is our best bet [57]. Interdisciplinary research and collaboration will be crucial, however, to meeting these objectives and in order to reduce the burden of maternal stress, depression, and anxiety in the perinatal period.

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KEY POINTS

- Anxiety, depression, and stress in pregnancy are risk factors for adverse outcomes for mothers and children.
- Anxiety regarding a current pregnancy ('pregnancy anxiety') is associated with shorter gestation and has adverse implications for preterm birth, fetal neurodevelopment and child outcomes.
- Chronic strain (including long-term exposure to racism) and depressive symptoms in mothers during pregnancy are associated with lower birth weight with many potential adverse consequences.
- These distinguishable risk factors and related pathways to distinct birth outcomes merit further investigation.
- It is critical to agree upon the signs, symptoms and diagnostic thresholds that warrant prenatal intervention and to develop efficient, effective, and ecologically valid screening and intervention strategies that can be used widely.

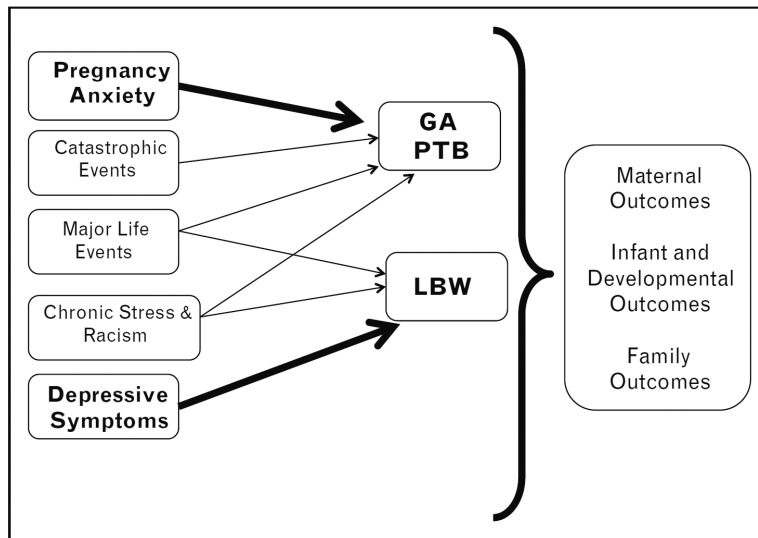


Figure 1. Summary of evidence on depression, anxiety and stress. GA, gestational age at birth; LBW, low birth weight; PTB, preterm birth.