Predictors of Postpartum Depression: A Comprehensive Review of the Last Decade of Evidence

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Abstract: Postpartum depression (PPD) is one of the most frequent complications of childbirth affecting ~500,000 women annually (prevalence 10% to 15%). Despite the documented adverse outcomes for mother and child, there remains a great need to develop prospective approaches to identify women at risk. This review examines some of the best-characterized molecular and clinical risk factors for PPD. We illustrate that this is a growing literature but there remains a lack of reliable molecular predictors for PPD. Current best predictors are clinical assessments for psychiatric history and adverse life events, highlighting the need for increased depression screening across the perinatal period.

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Introduction and Background

Postpartum depression (PPD) is a perinatal form of major depressive disorder (MDD) and affects ~500,000 women annually in the United States (prevalence 10% to 15%).[1] PPD is one of the most frequent complications of childbirth[2] and is associated with many adverse outcomes for both mother and offspring including, maternal mortality and morbidity,[1] increased risk for infanticide,[3] poorer maternal-infant attachment, and impaired parenting behaviors.[2] There is a great need for prospective approaches that identify women at risk for PPD. This is a growing

TABLE 1. Reported Risk Factors for PPD

	Evidence Level
Inherent/prepregnancy risk factors	
Genetics	Positive
Epigenetics	Mixed
Neuroactive molecules	Mixed
Psychiatric history	Positive
Other health history	Mixed
Adverse life events	Positive
Social support	Positive
Substance use	Mixed
Perinatal risk factors	
Demographic information	Mixed
Fertility history	Null
Nutrition	Mixed
Obstetrical outcomes	Mixed

Evidence level indicates if there are positive associations with PPD, mixed associations, or null findings (no associations).
PPD indicates postpartum depression.

field of research that seeks to predict those women at risk for PPD so that prevention and early detection are possible.

The purpose of this review is to examine some of the best-characterized molecular and clinical risk factors for PPD (Table 1). These risk factors are divided into 2 categories: inherent or prepregnancy risk factors and perinatal risk factors. It is important to recognize that there is no single predictor of PPD that currently exists. What we present here are the risk factors that represent the largest increases in the odds for developing PPD, measured using prospective studies.

Inherent or Prepregnancy Risk Factors

In this section, we highlight an individual's putative risk factors that exist before pregnancy. These areas of risk are important to note because they can significantly contribute to an individual's risk and may not be assessed during routine screening for PPD.

GENETICS

DNA provides every individual with a baseline risk of disease. It is the unique combination of all genetic variants that predisposes an individual to any given disorder. The heritability of PPD is ~50%[4] which means that half of the phenotypic variation seen in PPD is due to genetic variation. This is higher than the heritability of MDD (32%) suggesting that PPD may be a more homogenous subtype of depression. These recent heritability findings represent a leap in our understanding of the genetics of PPD. However, our ability to use patient DNA sequences to estimate individual risk for PPD is not currently feasible. Much of the published research into the genetic associations with PPD focuses on candidate genes. Although the evidence may appear convincing for any one study, candidate genes overall have shown they are not a reliable mechanism to predict PPD risk. First, candidate gene studies often rely on small sample sizes and are not able to be replicated. Second, they often do not account for population differences in genetic variation. Using the commonly studied BDNF Val66Met polymorphism as an example, those of European ancestry are homozygous for the G allele 60% of the time. This is compared with those of African ancestry who are homozygous for the G allele > 80% of the time. These drastic changes may appear as significant differences between PPD cases and controls when they are actually just measures of population structure. Candidate gene studies are typically not able to account for these changes in genetic ancestry. There has been a single study that looks at the effect of genetic ancestry on predictors of PPD.[5] They showed that genetic ancestry was not a predictor of PPD and did not modify the predictive value of other risk factors. Lastly, candidate gene studies, by definition, do not take into account the variation of individuals across the genome. No single gene or variant works alone in terms of biological function. These reasons are perhaps why no candidate gene has been shown to explain the variation associated with PPD or any other psychiatric disorder. Current genomics approaches, such as genetic risk score prediction, use variation across the genome to provide risk estimates

for various psychiatric disorders. However, genetic risk scores for PPD have not yet been established and are an area of current research. This method has allowed for initial investigations into the genetic overlap between PPD and other mood disorders.[6] Ultimately, the goal of genetic risk scores is to provide a clinical risk assessment for PPD based on an individual's unique genetic background. However, this goal is not immediately feasible and is reliant on very large sample sizes.

EPIGENETICS

Epigenetics refers to changes in gene function that do not alter the DNA sequence itself. The PPD literature focuses mainly on DNA methylation, which is the addition of methyl groups to the DNA that regulate gene transcription and cell specificity. This type of epigenetic modification is of particular interest in psychiatry because DNA methylation is altered by stress, medication, and reproductive hormones. The identification of DNA methylation biomarkers has been particularly successful in PPD. Using blood drawn at any point during pregnancy, DNA methylation at 2 genomic locations, along with complete blood count data, was able to prospectively predict PPD case status (determined using clinician diagnosis) with 96% accuracy (area under the receiver operating characteristic curve, AUC = 0.96).[7] This prediction is irrespective of maternal antenatal depression status. These biomarkers were first identified in a relatively small sample of women (n = 52), but have been since replicated in 2 additional cohorts with 81% accuracy (AUC = 0.81).[8] In addition, DNA methylation at the oxytocin receptor gene (*OXTR*) was found to reflect changes in inflammatory cell types and can be used as a proxy for complete blood count data in the PPD prediction model.[9] These epigenetic biomarkers are promising and would require a more large-scale clinical trial before implementation in the clinic. Although the literature on PPD-related epigenetics is currently small, it shows promise as a way to develop a clinically meaningful biomarker.

NEUROACTIVE MOLECULES

Much of the biological literature associated with PPD focuses on the association with neuroactive molecules, such as hormones and neuropeptides. The recent literature shows a focus on reproductive hormones, BDNF,[10] γ-aminobutyric acid,[11] and ghrelin.[12] When examining these studies through the lens of predicting PPD, it is important to note that these are reporting on cross-sectional associations and should not be interpreted as predictive without more longitudinal follow-up. However, there are several longitudinal studies examining the predictive ability of neuroactive molecules that we discuss next.

Allopregnanolone

A metabolite of progesterone, allopregnanolone is a positive allosteric modulator of the γ-aminobutyric acid-A receptor. Recent work has shown positive treatment effects in clinical trials as a novel treatment for PPD using a proprietary intravenous formulation of allopregnanolone, brexanolone.[13] However, its potential as a predictor of PPD onset has not been completely evaluated. A single exploratory study has been published looking at plasma allopregnanalone in the second and third trimesters as a predictor of PPD.[14] Their relatively small sample size of 60 women found that lower second trimester allopregnanalone increased the odds of developing subsequent PPD. More work will need to be conducted to replicate and refine the predictive ability of antepartum allopregnanalone, but this work is encouraging and aligns with the recent therapeutic findings.

β-endorphin

β-endorphin is an endogenous opioid neuropeptide created by the metabolism of proopiomelanocortin (POMC). It has associated function within the hypothalamic-pituitary-adrenal axis (HPA) making it an attractive candidate for association with PPD. In a

sample of 307 pregnant women, Yim et al[15] took blood samples at multiple timepoints during gestation and a 9-week postpartum visit. Upon analyses, β-endorphin levels and depression status [using edinburgh postnatal depression scale (EPDS) score > 10] at 25 weeks' gestation predicted PPD status at the 9-week postpartum visit. Although other antepartum timepoints were assessed, only the 25-week assessment was significantly predictive of future PPD. Compared with other biomarkers in this review, this predictive model only requires a single assessment and biological sampling to determine case status. However, this finding needs to be replicated before implementing in clinical practice.

Cortisol

The stress hormone cortisol has been widely investigated in psychiatric disorder etiology. However, longitudinal studies into the role of cortisol with PPD onset have yielded largely null results. The single study which identified predictive value for cortisol also examined the role of several inflammatory molecules across 7 timepoints.[16] The final predictive model requires measures of salivary cortisol and plasma-derived inflammatory markers [interleukin (IL)-8 and IL-10] at day 14 postpartum to predict PPD through 6-month postpartum. These constitute multiple measures from multiple tissues, making the clinical implementation challenging, but not impossible. However, 1 limitation of this study is that it will miss any PPD onset that occurs within the first 2 weeks following childbirth. However, this interesting study should be compared with the other studies[17,18] that did not find predictive power in cortisol measurements. The lack of other positive findings may be a result of differing sample sources, diagnostic definitions, and collection times.

Corticotropin-releasing Hormone (CRH)

Similar to cortisol, CRH is investigated in psychiatric disorders for its role in HPA-axis function and stress response. During pregnancy, the placenta produces CRH, which is followed by an abrupt drop postdelivery mirroring the milieu of reproductive hormones. Unlike reproductive hormone levels which have been shown not to be predictive of PPD, CRH has shown positive results. Work by Yim et al[19] and Iliadis et al[20] independently used longitudinal studies during pregnancy and into the postpartum period. Yim and colleagues used week 25 CRH to predict PPD at 4-week postpartum using an EPDS threshold of ≥ 10 to define PPD case status. Using a similar experimental model, Iliadis and colleagues used week 17 CRH to predict PPD at 6-week postpartum defining PPD cases with a more stringent EPDS threshold of ≥ 13. Although these findings are similar and point to the same outcome of CRH prediction of PPD, the differences may be driven by small differences in study design, most notably follow-up period and EPDS thresholds for PPD case status. A follow-up study, or possibly a reanalysis, could harmonize these results. However, another large study found no association between pregnancy levels of CRH and subsequent PPD onset.[21] This may also be an artifact of differences in study design with the null findings using less specific windows for sampling during pregnancy (< 20 wk and 24 to 29 wk), EPDS thresholds (≥ 12), and PPD follow-up (12-wk and 1-y postpartum). This work is supported by another study by Hahn-Holbrook et al[22] which found greater increases between 29 weeks and 37 weeks' gestation in CRH associated with later PPD symptoms. Despite these 3 studies highlighting CRH as a predictor of PPD, work by Glynn and Sandman did not find CRH to be predictive of PPD in a similar longitudinal sampling of CRH and mood across pregnancy and up to 6-month postpartum.[23] Overall, CRH may be a viable biomarker in the future if more work is conducted to replicate previous findings using consensus sampling and measurement protocols.

Oxytocin

The oxytocin signaling network has been of great interest to perinatal mental health researchers for many years due to its role in bonding and mother-infant interactions. Recent work has begun to identify the trajectories of oxytocin through pregnancy and into the postpartum period, with a focus on how PPD onset potentially alters these trajectories. The first of these studies came in 2011 when Skrundz et al[24] measured plasma oxytocin levels during the third trimester of pregnancy in 74 women. Depression status was assessed at baseline and 2-week postpartum. They found that plasma oxytocin levels during the third trimester can predict PPD symptoms at 2-week postpartum. Moreover, their findings showed that those with EPDS scores ≥ 10 at baseline were characterized by lower oxytocin concentrations. These initial findings were followed-up in 2 studies in 2016. First, Jobst et al[25] evaluated 100 women for depression symptoms and plasma oxytocin levels at 2 timepoints during pregnancy (35 and 38 wk) and 3 times postpartum (2 d, 7 wk, 6 mo). With multiple timepoints they showed plasma oxytocin levels increased from week 35 of pregnancy to 6-month postpartum in all women. However, those women who developed PPD showed a characteristic drop in oxytocin levels from week 38 of gestation to 2 days after delivery, where those without PPD continuously increase. This finding supports work by Skrundz and colleagues proposing that oxytocin may be a predictor of PPD in the immediate postpartum period (within 2 weeks). This window may be critical for prediction because when measuring PPD status at 6-week postpartum, Massey et al[26] were unable to find differences in third trimester oxytocin levels alone that predict PPD status. However, using past history of MDD in their prediction model shows an interaction with oxytocin levels to significantly predict PPD symptom severity. Briefly, they found that higher levels of oxytocin predicted PPD severity in women with a history of MDD, but not in women without such history. Overall, these 3 studies show that the transition from gestation to postpartum may be a critical window for oxytocin prediction of PPD. In addition, oxytocin trajectory may be altered by previous MDD history, which should be accounted for in future studies evaluating the predictive ability of serum oxytocin as a biomarker for PPD.

Thyroid Function

During pregnancy several thyroid hormone levels are altered and have been investigated in relation to perinatal mood previously.[27] Tests that measure various aspects of thyroid function are readily available and widely used, specifically measuring thyroid-stimulating hormone (TSH), thyroxine (T4), and triiodothyronine (T3). In addition, thyroid peroxidase (TPO) and thyroid-binding globulin are other indicators of thyroid function. However, when examining the role of thyroid hormones in predicting PPD, timing is key given thyroid function is reacting to the constant changes in other hormones across pregnancy. Albacar et al[28] performed some of the first investigations into whether thyroid function can prospectively predict PPD. In a large cohort ($n = 1053$), they were not able to identify any indications that thyroid function at 2 days after birth could predict future depression at 8- or 32-week postpartum. To illustrate the issue of timing, Sylven et al[29] found that TSH levels at childbirth over the clinical threshold of 4.0 mU/L was associated with increased risk for PPD (EPDS ≥ 12) at 6-month postpartum [odds ratio (OR), 11.30; 95% confidence interval (CI), 1.93-66.11). This work by Sylven and colleagues examined 227 women, of which 26 (11.5%) developed PPD and 21 had TSH over the clinical threshold. Although this is an encouraging finding, it is a small

sample that requires replication in larger cohorts with more women with PPD. Predictors assayed at the time of childbirth are less practical than those drawn earlier in pregnancy, when there is ample opportunity for prevention and intervention. Groer and Vaughan[30] found that TPO-positive women measured between 16 and 25 weeks gestation were more likely to have PPD symptoms 6 months after delivery. In a complimentary study, Wesseloo et al[31] recently found that screening positive for TPO-antibodies at 10 to 12 weeks gestation was associated with a nearly 4-fold increased risk (adjusted OR, 3.8; 95% CI, 1.3-11.6) for first-onset depression at 4-month postpartum. Taken together, this work suggests that recognizing the presence of thyroid-related immune markers may also predict PPD. Increased TSH indicates hypothyroidism, whereas TPO-positive tests suggest autoimmune disorders. If these findings are replicated, it could implicate thyroid dysfunction as a mechanism contributing to PPD, in addition to providing a prospective biomarker for PPD.

Inflammatory Markers

MDD, including PPD, has been associated with increased inflammation suggesting a shared molecular mechanism for mood disorders and inflammation processes. Identifying this mechanism is a relatively difficult task given the degree of cell specificity and number of markers that indicate immune activation. Two studies suggest that inflammatory markers can be more than just associated with PPD and prospectively predict PPD. First, Krause et al[32] found that regulatory T cells were increased 34 to 38 weeks prenatally in mothers who develop PPD and are able to significantly predict PPD onset. Second, Liu et al[33] demonstrate that 2 inflammatory markers, IL-6 and high-sensitivity C-reactive protein, each are independently capable of predicting PPD using serum at delivery. IL-6 and high-sensitivity C-reactive protein had an accuracy of 86% (AUC = 0.86; 95% CI, 0.80-0.92) and 83% (AUC = 0.83; 95% CI, 0.78-0.89), respectively in their study of 296 women. However, several other studies with larger sample sizes have reported lack of evidence supporting inflammatory markers as PPD biomarkers.[34] These studies reporting null findings used a wide range of sample sizes and racial/ethnic diversity, as well as looking across several types of inflammatory markers. In 1 study of note, their molecular predictor did not perform better than using previous MDD diagnoses as a predictor.[34] This illustrates that while associations may be significant, the ability of inflammatory markers to predict PPD require much more investigation.

PSYCHIATRIC HISTORY

Perhaps the current greatest predictor of PPD is the assessment of psychiatric disorders both before and during pregnancy. The literature has many examples that illustrate this using both retrospective and prospective measures. Practically, this abundance of information can be distilled into 1 take-home message: it is imperative to screen patients for psychiatric history to better evaluate PPD risk.

The literature strongly shows that various lifetime histories of MDD,[5,25,35,36] anxiety,[5] PPD,[35,37] PMS/PMDD,[37] other mood disorders,[38] personality disorders, or any psychiatric disorders[37,39–41] all significantly predict increase risk for PPD onset. Moreover, there is a wealth of literature showing that antenatal MDD,[25,37,42–44] anxiety,[5] or other psychiatric disorder[40] also significantly increase risk for PPD. Lastly, there is a great amount of power in self-reported family history of MDD,[45] family history of bipolar disorder, and any psychiatric illness.[39,46] Unlike many other predictors of PPD outlined in this review, assessments of psychiatric history are validated repeatedly. There is a high degree of confidence in generating risk prediction models using these data for several reasons. First, the literature represents findings that are globally recognized,

encompassing women from all genetic and cultural backgrounds. Second, many of these studies used multifactorial methods to look at the effect of psychiatric history on PPD onset, with most studies finding psychiatric history as the most significant predictor associated with prospective case status. For many nonpsychiatry clinicians, screening for psychiatric history, either through diagnostic interview, chart review, or self-report, is often missed or neglected. However, this small addition to screening can improve quality of care for PPD which is currently underdiagnosed and undertreated.

ADVERSE LIFE EVENTS

If we consider a history of psychiatric disorders as the best current predictor for PPD, adverse life events may account for the next largest source of variation associated with the disorder. Many studies find a dose response between adverse life events and risk for PPD.[5] These environmental risk factors will contribute to an individual's existing vulnerability to PPD. Many studies report cumulative measures of adverse life events,[5] also referred to stressful life events.[36,47] These reports often use summary measures to capture cumulative life events and their effect on PPD risk. In addition, researchers have attempted to tease out specific adverse life events that contribute increased risk.

Evidence has shown in multiple populations that physical, psychological, or sexual abuse[37,39–41,45,48] significantly increases a woman's risk to PPD. There is a single report that shows lifetime trauma exposure is not associated with PPD[49] identified among the many positive associations. Moreover, given the critical role partners play during the perinatal period, intimate partner violence (IPV) is especially relevant to PPD risk.[36,43,44,50–52] It should be noted that 1 study did not identify IPV as a significant risk factor for PPD,[53] though this could be due to their assessment at 1-month postpartum. Overall, IPV, as well as more general forms of physical, psychological, or sexual abuse, has been shown to increase PPD risk whether it occurs prenatally or perinatally.

Perhaps often overlooked adverse life events in PPD research are issues of immigration and discrimination. These are important topics to cover because they represent chronic stressors compared with singular adverse life events. Albeit small, the literature shows that both immigration[43,54] and discrimination[35] increase PPD risk. Issues of immigration and discrimination may account for the variation in prevalence of PPD across racial/ethnic groups, especially where increased prevalence is observed among immigrants or other groups experiencing discrimination. Overall, the current literature shows specific adverse life events, such as IPV, childhood trauma, or military deployment, increase risk for PPD. This increased risk for PPD is also observed for many other forms of adverse life events not reported in this review, including divorce, financial hardship, death of a loved one, natural disasters, and mass conflict. However, careful assessment of cumulative life events provides greater power for assessing an individual's risk for PPD.

Perinatal Risk Factors

During pregnancy and delivery, the mother and baby are carefully monitored for many medical outcomes. With this comes a lot of information to make sure developmental trajectories are met, including variables that may aid in assessing risk for PPD. This section reviews risk factors that may be identified during perinatal care visits and delivery.

DEMOGRAPHIC INFORMATION

The most widely studied risk factors for PPD are derived from demographic information. In many cases, these data are accessible from population level data collected a large number of people at one time, making demographic data easily accessible to investigate

associations with PPD. Some studies interrogate a wide range of demographic variables and report no associations with PPD risk.[42] There are also many demographic factors reported in the literature with mixed results.

Maternal Age

Much of the literature implicating age as a risk factor for PPD does so in very general terms.[55] Other studies show maternal age of PPD onset appears to have a U-shaped curve of increased risk as age increases. That is, risk for PPD is higher under the age of ~24,[38,45,48,51,52,56] decreasing between the ages of 24 to 35,[57] and increasing again over the age of 35.[45] These age specific changes in PPD risk may reflect periods of stress and degrees of social support. However, there are also multiple studies that do not find such associations between age and PPD risk.[41,50,54,58]

Race

The topic of race and ethnicity in the area of biomedical research is a complicated one. There are studies that find associations with PPD risk and race,[59] and those that do not.[5,50,54,58,60] Discrepancies here may be due to the fact that race/ethnicity may be proxies for environmental rather than biological factors. Race is typically associated with one's skin color, whereas ethnicity correlates with language. The preferred measure to examine the biological relatedness between individuals is genetic ancestry. There has been a single study investigating the role of genetic ancestry with PPD risk and found no association.[5] This study also found that self-reported race/ethnicity did not correlate well with genetic ancestry. Other studies have identified socioeconomic status (SES), community of residence, and immigrant status as moderating factors for discrepancies between PPD risk and race.[60] In addition, differences observed in race may be attributable to discrimination[61] (see the Adverse Life Events section). Although these issues of racial disparities are best summed up by the findings of Ertel et al[47] which states: "Black and Hispanic depressed mothers were more likely to experience multiple adversities and less likely to receive services than white depressed mothers."

SES

SES refers to a summary measure that measures a person's economic and social position relative to others. Many individual factors contribute to the measurement of SES, including education, income, employment, and insurance status. Overall, SES has been reported as a significant contributor to PPD risk.[41,48] Specifically, it is low SES that seems to contribute the greatest risk to PPD.[39,60,62] Indicators of low SES in the United States are qualifying for the WIC Program (Special Supplemental Food Program for Women, Infants, and Children) and SNAP (Supplemental Nutrition Assistance Program). As a potential surrogate marker of low SES, women who reported being on WIC[51,63] and SNAP[64] have shown increased PPD risk. However, it is important to note that not every study finds SES as a risk factor for PPD.[42]

Educational attainment is one contributing factor in determining SES. There are many examples in the literature that show lower levels of education are associated with increased risk for PPD.[45,47,51,52,55,56,59,62] This may be an effect of lower literacy, which also has been reported to increase risk.[41] In contrast, there are also findings of increased levels of education increasing PPD risk.[38] The differences in associations should also be noted with the negative findings observed between level of education and risk for PPD.[50,54,58]

One of the main drivers of SES is income. Low household income increases the odds of developing PPD,[36,47,51,55,56,62] though not all studies find this association.[58] Just as individual income is negatively associated with PPD risk, so is domestic economic performance.[65] Employment status is a more direct influence on an individual's income. Therefore, it makes sense that employment

status also has been associated with PPD risk,[44,56,62] though not always.[50]

OBSTETRICAL OUTCOMES

Preterm Birth

Preterm neonates (born before 37 completed weeks' gestation) account for 70% of neonatal morbidity, 50% of infant hospitalization costs, and carry a 40× increased risk of neonatal death compared with their term counterparts.[66] Surviving neonates also carry a disproportionate share of lifelong complications, including cerebral palsy, respiratory illness, blindness, and deafness.[67] Preterm birth is triggered by multiple mechanisms, including hormonal mediation, inflammation and infection, and genetic factors, converging in a final common pathway of delivery earlier than 37 weeks.[68]

Despite the multiple underlying etiologies, there are clear links between stress, depression, and preterm birth. Traditionally, studies evaluating the association between depression and preterm birth in particular have been challenging to interpret due to potential confounding effects of antidepressant use. A recent systematic review of 14 studies including 25,663 women found that those with untreated depression during pregnancy have a significantly elevated risk for preterm birth (adjusted OR, 1.56; 95% CI, 1.25-1.94) compared with women without depression.[69] Further, there was a trend towards an even greater preterm birth risk in women with severe depression.[69] Another study of 2208 women showed that women with MDD and posttraumatic stress disorder have a >4-fold increased risk for preterm birth (adjusted OR, 4.08; 95% CI, 1.3-13.2); this risk is greater than—and independent of—antidepressant use and not a function of acute mood or anxiety symptoms.[70] Cumulative psychosocial stress was also found to be a significant risk factor for preterm delivery <37 weeks' gestation among 3021 women in Canada (OR, 1.73; 95% CI, 1.07-2.81). Importantly, in this cohort, preterm birth risk was highest among those with low levels of social support or optimism.[71] Higher general levels of stress[72] and higher perceived racial discrimination[73]—which may be linked with depression—have also been associated with elevated risk for spontaneous preterm birth.

Similarly, as expected, preterm birth is associated with an elevated risk for PPD in multiple studies, including population-based studies, with the magnitude of the effect ranging from OR, 1.35 to 1.74.[74–76] One systematic review found rates of PPD as high as 40% among women who delivered preterm.[77] However, studies in this area should be interpreted with caution because many do not control for depression and other psychiatric illnesses during pregnancy.

Putative Molecular Mechanisms for PPD

When we examine the risk factors that contribute most to risk for PPD, it seems to strongly support a gene-environment interaction model. Genetic studies show there is a large heritable component to PPD (~50%). An individual's genes are deterministic for developing PPD, but it provides an inherent level of risk that is ever present. This level of risk is only exacerbated by environmental factors that significantly increase risk: previous psychiatric history, adverse life events, decreased SES, and negative obstetrical outcomes. What these environmental risk factors have in common is that they increase stress levels and alter the HPA-axis. This is significant because increased levels of stress only exacerbate underlying genetic levels of risk. In summary, manifestation of PPD is a result of inherent genetic risk plus environmental insults reaching a threshold level of risk.

Clinical Implications

Biomarkers for PPD show a lot of promise but none are ready for clinical use yet. Work in genetics and epigenetics show a

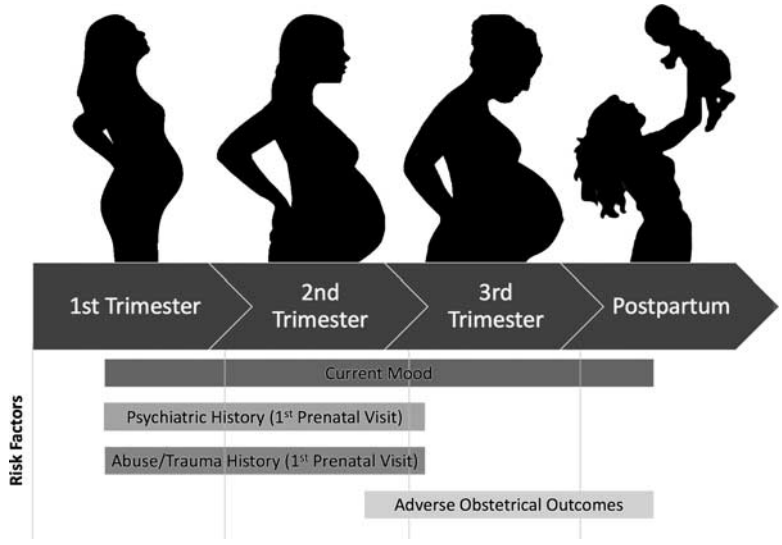

FIGURE 1. Recommended assessments during the perinatal period.

lot of promise for personal risk prediction. There are several hormonal and neurosteroids that are predictive in preliminary studies, but require further replication for clinical use. Although there is not an established prediction method for PPD, the literature shows there are practical steps a provider can take to assess who is at increased risk for PPD. In 2016, the US Preventive Services Task Force released recommendations for increased depression screening during the perinatal period.[78] This is to monitor mood symptoms in mothers at multiple timepoints through pregnancy, as they increase risk for subsequent PPD. However, we recommend performing assessments for psychiatric history and adverse life events at a single timepoint during routine perinatal care, while also monitoring for adverse obstetrical outcomes as they may occur. These single assessments can take place at any time before childbirth to assess prospective risk for PPD. Figure 1 illustrates the recommended assessments and the timeframes when they should take place. The addition of these short assessments will allow providers a better evaluation of an individual's risk for PPD. In addition, monitoring of any adverse obstetrical outcomes is critical as this also increases the odds of developing PPD. Future work will need to be conducted to formalize this process and evaluate metrics for efficacy, though this should not prevent clinicians from using these methods. Ongoing research will hopefully replicate some of the biomarker findings and lead to novel ways of predicting those at risk to prevent unnecessary suffering for women, their children and families.

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