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Perinatal Depression: An Update and Overview

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Abstract Over the last 3 years there have been notable developments in the screening and treatment of perinatal depression. Most importantly, the DSM-V has made only minor changes in the diagnostic criteria for perinatal depression as compared to the DSM-IV; "perinatal," as opposed to "postpartum," is a specifier for depression with a requirement that the depression onset occurs during pregnancy or the first 4 weeks postpartum. Advances in the treatment of perinatal depression have been made over the last 3 years, including both prevention and acute interventions. Additional support has emerged confirming the primary risk factors for perinatal depression: a personal or family history, low SES and poor interpersonal support. There is general agreement that universal screening be conducted for all perinatal women, by both the woman's obstetrician and the baby's pediatrician.

Keywords Perinatal · Depression · Review · Prenatal · Postpartum · Medication · Screening · Treatment

Introduction

The purpose of this article is to build on the previous literature [1, 2] reviewing research on perinatal depression including its associated risk factors, its impact on mother and child, and current screening recommendations. We also review treatment and prevention studies published during the last 3 years. In this review, the term perinatal depression encompasses depressive symptoms that occur during pregnancy as well as those that continue during or begin in the first year postpartum.

The most important update on the topic is that while the diagnosis of depression during the postpartum period has not changed, the specifier involving the time period for the relevant symptoms has been extended. Indeed, despite lengthy discussion engendering a great deal of controversy, the criteria for postpartum depression in DSM-5 [3] remain the same as those in DSM-IV [4]: five of nine symptoms are required for at least a 2-week period. However, the DMS-5 introduces a new "peripartum" specifier for depression in DSM-5, which requires that the depression onset occur during pregnancy or within the first 4 weeks postpartum. This peripartum specifier replaces the DSM-IV "postpartum onset" specifier, but the requirement that the onset occur within the 4 weeks of the postpartum period remains the same.

Despite these DSM-5 criteria, most experts in the field continue to define postpartum depression as occurring anytime within the first year postpartum, irrespective of the time of onset. While the biological factors influencing mood early in the postpartum period may be less relevant later, the first year after delivery is replete with many unique psychosocial stressors. Moreover, the data are clear that peak time of new onset depression in the postpartum is from 2-3 months after delivery [2, 5, 6, 7•]. For instance, Gavin et al. (2005) [1] report a period prevalence of 19.2 % for major and minor depression in the first 3 months postpartum, an obvious contrast with the DSM-5 peripartum criteria.

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Epidemiology and Risk Factors

Depressive symptoms affect more than 25 % of perinatal women [1], with a general consensus that the rates of major depressive disorder during the perinatal period range from 10-15 % [2, 1]. There is also consensus that more research on depression and anxiety rates across different underserved and minority groups is critical.

Many risk factors for perinatal depression have been identified. Recent research can be summarized succinctly as providing additional support for those that are already well established [8, 2]. These include psychosocial stressors such as low socioeconomic status, being a single mother, poor social support and general life stress [9]. Unwanted and unplanned pregnancies are also risk factors [10]. Stress in the relationship with one's partner is also a major risk factor for perinatal depression, specifically domestic violence and lack of social support [9, 11].

Medical and obstetrical factors include previous stillbirth or miscarriage [10]. New research suggests a strong association between moderate to severe premenstrual symptoms, particularly premenstrual dysphoric disorder (PMDD) and postpartum depression [12], although no association between PMDD and depression during pregnancy has been found. Lower levels of oxytocin during pregnancy have been associated with a higher score on the Edinburgh Postnatal Depression Scale (EPDS) [13], as has breastfeeding status, with women who do not breastfeed at higher risk for postpartum depression [12]. It is unclear, however, whether this finding is due to biological/hormonal factors or whether, as most experts speculate, it is due to differences in education, income and ethnicity and their association with lower breastfeeding rates [14].

Impact of Perinatal Depression on Mothers and Infants

It is acknowledged that postpartum depression has a negative impact on infant development and mother-child interactions [15–17]. For example, a recent meta-analysis by Goodman et al. [18] demonstrated a small but significant association between maternal depression and a range of childhood problems including both internalizing and externalizing psychopathology and both negative and positive emotionality. A meta-analysis by Beck also demonstrated a small, significant effect of postpartum depression on children's cognitive and emotional development [Beck 1998]. Some research has suggested that chronic and/or recurrent maternal depression may be more deleterious than depression occurring only in the postpartum period [Grace et al. 2003].

Recent studies have addressed specific elements of neurodevelopment and investigated potential biological links. Infants of mothers who are depressed during the prenatal period have been found to be less responsive to stimuli than other infants and have more difficult temperaments [19•]. In addition, effects present from birth such as a lower vagal tone, which has been linked to attentiveness and greater relative right frontal EEG activity (related to withdrawal behavior), have been found to persist at least as far as the preschool years [19•]. Depression in the postpartum period has been linked to poor quality mother-child interactions, including mutual touching, smiling and vocalizations [20]. Negative outcomes for infants of mothers with postpartum depression may also include cognitive, emotional, motor and neural functioning and development [20].

Although previous research focused on the impact of depression during the postpartum period on the developing infant, more recent work has suggests that depression during pregnancy may have marked deleterious consequences for the fetus, delivery and mother-child bonding [10]. For example, specific biological markers, such as increased fetal heart rate and decreased fetal movement in response to stimuli, have been associated with depression during pregnancy [19•]. Although the direct causal links are less clear, women who are depressed during pregnancy have greater risk for premature delivery and low birth weight infants as well as greater risk of adverse obstetrical outcomes generally [19•, 21•]. Low oxytocin levels during pregnancy have been associated with higher EPDS scores and may be associated with impaired maternal bonding [22].

Screening Recommendations

The American College of Obstetrics and Gynecology (ACOG) [23] recommends routine screening for all perinatal women. The ACOG does not however endorse specific instruments nor specify times at which screening should be done. Recognizing the impact of postpartum depression on the developing child and the critical role of pediatricians, the American Academy of Pediatrics (AAP) recommends that pediatricians screen mothers for postpartum depression at the baby's 1-, 2- and 4-month visits [24]. The AAP recommends using either the EPDS or a two-question screen.[1]

It is generally recognized that universal screening of perinatal women does improve depression outcomes [25–27] when it is coupled with accessible care. A recent cluster randomized trial [28] compared a condition that included a regimen of screening, further assessment, medication management or referral, and follow-up to a usual care condition for

[1] The two-item screen "have you felt down, depressed, or hopeless" and "have you lost interest or pleasure in things" does not have well-established sensitivity and specificity metrics. It also lacks utility as a clinical screening instrument because it does not screen for infrequent but potentially life-threatening thoughts such as self-harm or thoughts of harming the baby.

women who screened positively (at least 10 on the EPDS and at least 10 on the Patient Health Questionnaire-9, PHQ-9 [29]). A total of 2,343 women were enrolled between 5 and 12 weeks postpartum. Although there was only a trend-level effect (p=0.07) at 6 months, there was a significant effect in favor of the intervention at 12 months. The authors concluded that the results were likely due to the two-stage process: screening followed by management within primary care practices.

The most commonly used perinatal screening instruments are the EPDS [13] and the PHQ-9 [30], both of which are endorsed for their brevity, sensitivity and specificity [31, 32]. The PHQ-9, which is widely used for depression screening in general medical populations, has been validated for postpartum use [30]. Both the EPDS and the PHQ-9 have also been validated for screening use during pregnancy [33–35]. Bergink et al. (2011) [34] recommend using different cutoff scores during each trimester and emphasize screening all pregnant women during each trimester.

Tandon et al. (2012) [36] compared the EPDS to the Beck Depression Inventory [37] and the CES-D [38] in a minority population and found that the EPDS was superior to the other two as a screening instrument. They emphasize, however, that simply conducting universal screening is critical; the specific instrument to be used is secondary. Milgrom et al. (2011) [39] demonstrated that screening with the EPDS not only leads to greater identification of depression but also increases rates of treatment uptake when it is used as a universal screening instrument.

Data from the Pregnancy Risk Assessment Monitoring System (PRAMS) have been examined in several recent studies. The PRAMS is a self-report instrument developed by the Center for Disease Control for State Public Health Departments to assess risk factors for adverse maternal and infant health outcomes [32]. Many states have included three optional items that assess depressive symptoms during pregnancy; these items have been demonstrated to detect and screen for perinatal depression accurately [32, 31].[2]

Treatment of Antenatal Depression

To date, there have been no randomized antidepressant medication treatment studies for depression during pregnancy. In contrast, several recent treatment trials examining psychosocial and other non-psychopharmacologic interventions have been published.

Structured psychotherapy interventions include a trial by Grote et al. [40] who utilized Interpersonal Psychotherapy (IPT) [41] in a randomized trial comparing "culturally relevant" brief IPT to usual care for 53 depressed pregnant women who screened positively on the EPDS. The IPT consisted of an engagement session modeled on ethnographic interviewing followed by 8 sessions of weekly IPT. Maintenance treatment with IPT was also provided up to 6 months postpartum. The IPT group had significantly greater reductions in depression as measured by the EPDS and the BDI.

In addition to structured psychotherapies, several other forms of therapy or treatment have been found to be effective in treating antenatal depression. Roman et al. [42] compared standard community care to a Nurse-Community Health Worker intervention during pregnancy and the first year postpartum. Subjects were drawn from at-risk low SES populations; 530 pregnant women were randomized. Women in the intervention group had significantly lower CES-D scores at the conclusion of the intervention, although the clinical difference between groups was small (2.4 points on the CES-D).

Field et al. [43] conducted a study in which 84 depressed pregnant women were randomized to massage therapy, twice weekly yoga or a control group over 12 weeks. The massage and yoga groups evidenced significantly greater improvement in depression than the control group, but did not differ from one another.

Freeman and Davis [44] reported results from a study examining the use of supportive psychotherapy. Their primary goal was to compare the use of omega-3 fatty acids to placebo for depression; both pregnant and postpartum women (n=59) were included in the study. All women also received six 30-min sessions of supportive psychotherapy. No differences were found between the omega-3 and placebo groups. Women who attended more supportive psychotherapy sessions and those who were less depressed at baseline had lower levels of depression after 8 weeks.

Acupuncture and light therapy have also been used to treat antenatal depression.[3] Manber et al. [46] randomized 150 women to one of three conditions: depression-specific acupuncture, control acupuncture or massage. Subjects received 12 treatments over 8 weeks in all conditions. Hamilton Rating Scale for Depression (HRSD) [47] scores were significantly lower in the depression-specific acupuncture group than in the controls, although again of limited clinical significance (HRSD scores differed by 2 points).

A small study investigating light therapy for antenatal depression was conducted by Wirz-Justice et al. [48] who compared 7,000 lux white light to 70 lux placebo light in a 5-week double-blinded trial; they found that the active

[2] The three-item Prams screen includes the items: "I have felt down, depressed, or sad," "I have felt hopeless," and "I have felt slowed down physically" rated on a 1-5 scale from never to always.

[3] Please see Deligiannidis and Freeman (2014) "Complementary and alternative treatments for perinatal depression" for a detailed description of these therapies [45]. Deligiannidis, K.M. and M.P. Freeman, *Complementary and alternative medicine therapies for perinatal depression.* Best Practice Research in Clinical Obstetrics and Gynaecology, 2014. **28**(1): p. 85-95.

treatment was superior as measured by the HRSD. Parry et al. [49] examined the manipulation of sleep-wake cycles for perinatal depression in a cross-over design comparing early-wake and late-wake sleep. Seven of the 21 women were pregnant; the remainder were postpartum. Both early- and late-wake sleep had significant effects on improving mood in both groups of women on the HRSD, but not on the self-reported EPDS or BDI. There was a trend for greater improvement in the early-wake groups.

Treatment of Postpartum Depression

Much of the new research over the last 3 years involves postpartum depression prevention [50•, 51•]. There is an increasing emphasis on the use of home visitors and nursing interventions, and most of the interventions are targeted—i.e., they focus on woman at risk for depression. Many have specifically targeted minorities and the underserved because these populations are at higher risk for depression.

Prevention of Postpartum Depression

Universal prevention studies target all women as opposed to only those at high risk. This is an area that has expanded substantially within the past several years. Brugha et al. [52] tested the impact of a universal prevention intervention provided by health care visitors for women who did *not* screen positively for postnatal depression 6 weeks after delivery. Health visitors were trained to identify postpartum depression and were also trained to deliver either a cognitive-behavioral approach to counseling or a person-centered approach if needed. Counseling visits lasted 1 hour once a week for a maximum of 8 weeks. At 6 months following childbirth, 83 out of 767 (10.8 %) of the women in the control (CAU) group and 113 of 1474 (7.7 %) of women in the identification and treatment group scored more than a 12 on the EPDS, a significant difference.

Ho et al. [53] randomized 200 Taiwanese women to either a hospital depression education program prior to maternity discharge or to a control group. EPDS scores were significantly different between groups at 3 months, but the scores were not clinically significantly different (EPDS mean 5.3 compared to 7.1 in the control group).

Gao et al. [54] evaluated a childbirth education program consisting of two psychoeducation classes and a telephone follow-up within 2 weeks postpartum, comparing 100 women receiving the intervention to 100 in a control group. EPDS scores were lower in the education group at 2 weeks postpartum, but the difference between scores was negligible with a mean EPDS score of 5.6 in the education group and 6.9 in the control group.

A number of studies have examined the prevention of depression in women at risk because they are from low SES environments. Tandon et al. (2011) treated low-income women at risk for depression with either a 6-week cognitive-behavioral intervention or usual home visiting [55]. Sixty-one pregnant or postpartum women were randomized; 9 of 27 (33 %) women receiving usual care met clinical cutoff scores for depression post-treatment compared with 3 of 32 (9 %) in the control group.

Surkan et al. [56] tested a health promotion intervention to prevent postpartum depression with low SES women. A total of 679 women income-eligible for the Special Supplemental Nutrition Program for Women, Infants and Children (WIC) were randomized at 6-20 weeks postpartum to Usual WIC Care or the experimental intervention. The intensive treatment included five home visits delivered by paraprofessionals from USDA's Expanded Food and Nutrition Education Program (EFNEP) and monthly phone calls for a year. Women randomized to the intensive intervention had CES-D scores (P=0.046) 2.5 points lower than those receiving usual care alone, but the absolute difference in CES-D scores was of minimal clinical significance (12.4 to 14.8).

A more intensive approach was used by Lara et al. [57] in a randomized trial with low-income Mexican women. In a 377 women, those participating in eight 2-h weekly group sessions including educational information about postpartum depression and problem-solving work were compared to a control group. There were significantly fewer new depression cases in the intervention group (6 of 56; 10.7 %) than in the control group (15 of 60; 25 %), although attrition was very high in both groups.

Cupples et al. [58] studied the effects of peer support and mentoring during pregnancy in a trial involving 343 high-risk women in early pregnancy. Phone or in-person visits were provided by non-health professionals; on average, 8.5 visits were provided during pregnancy. The intervention results, however, proved no better in impacting depression than those in the control group.

Tripathy et al. [59] worked with poor and disadvantaged postpartum women in India, comparing a control group to monthly group treatment designed to support participatory action and learning for women, particularly maternal and newborn health problems. No differences in depression scores were noted between the two groups at the conclusion of the intervention.

Women from high-risk ethnic groups have also been studied. Howell et al. (2012) recruited 540 African-American and Latina women from the maternity ward to receive either a two-step educational program consisting of a review of a depression education pamphlet prior to discharge and a phone call by a social worker 2 weeks later [60]. Mothers in the intervention

arm were significantly less likely to screen positively for depression at 3 weeks (8.8 % compared with 15.3 %) but not at 3 or 6 months.

Le et al. [61] used eight sessions of CBT during pregnancy and three postpartum boosters with high-risk Latinas. BDI scores were significantly lower immediately after the eight sessions during pregnancy in the CBT group, but the difference did not persist into the postpartum period even with booster sessions.

Women at risk because of high scores on screening instruments were included in a study by Milgrom et al. [62]. The intervention, entitled "Towards Parenthood," consisted of a self-help workbook with eight units to be completed during pregnancy and one following birth. About one third of the 143 women enrolled in the study had EPDS scores above 12 at baseline. Women in the intervention read the material each week and then discussed the content with a psychologist in a weekly telephone support session. Participants in the intervention reported significantly lower levels of depression post-treatment than those in routine care, although absolute BDI scores were not reported.

Silverstein et al. [63] targeted women with babies in the NICU who were 33 weeks of gestation or less and tested a problem-solving education intervention consisting of four weekly or bi-weekly sessions. Fifty women were randomized to the two groups. Although no results were statistically significant, those in the intervention trended toward being less likely to experience an episode of moderately severe depression symptoms over the 6-month follow-up period (24 % vs. 44 %).

In summary, the findings from the prevention trials support conclusions extant for some time. Universal interventions are generally not of significant clinical benefit; those targeting at-risk women fare better if they are more structured and target the depression specifically. However, the cost-benefit ratio of the more intensive interventions is not clear and needs to be examined before widespread implementation can be advocated.

Non-Pharmacologic Treatment of Postpartum Depression

Two meta-analyses examining psychological treatments for postpartum depression have been published recently. Sockol et al. [64] included both pregnant and postpartum women, analyzing data from 27 studies (9 open trials, 2 quasi-randomized and 16 randomized controlled trials). Both pharmacological and psychological interventions were represented. Across all studies, post-treatment levels of depressive symptoms were significantly reduced (overall effect size 0.65). Individual therapy was significantly more efficacious than group therapy, and among all therapies, cognitive behavior therapy (CBT) [65] and IPT had the greatest effect sizes compared to control conditions, with a slight but statistically insignificant advantage for IPT. There were insufficient head-to-head comparisons to reliably separate the relative effects of psychotherapy and medication. These findings are similar to previous meta-analyses by Bledsoe and Grote [66] and Dennis and Hodnett [67].

Cuijpers et al. [68] also conducted a recent meta-analysis of 17 psychological treatment trials for postpartum depression. Compared to controls, psychological treatments led to moderate improvement (effect size 0.61). Those trials that compared psychosocial interventions to wait-list control groups had higher effect sizes than those that were compared to treatment-as-usual (effect size 0.96 vs. 0.41). There were only small differences between psychotherapy modalities, suggesting that common nonspecific factors may mediate improvement for all psychosocial interventions for postpartum depression. The authors were unable to draw conclusions about the long-term effects of psychotherapy because of the lack of data beyond 6-12 months postpartum. This limitation was also noted by Sockol et al. (2011) [64].

Recent psychotherapy treatment studies include a randomized trial by Morrell et al. [69]. The investigators randomized 101 general practices to deliver usual care or to deliver CBT-based counseling or listening visits. Health visitors were trained to identify PPD and deliver the counseling interventions to 595 women who scored >11 on the EPDS at 6 weeks postpartum. There was a significant benefit with treatment at 6 and 12 months, but no differences between the two active interventions.

Mulcahy et al. [70] conducted a randomized controlled trial for the effectiveness of group IPT for postnatal depression. Fifty women were randomized to 8 weeks of group IPT or treatment as usual. Both groups significantly improved in depression severity: HRSD scores improved from 15.82 to 9.52 in the IPT group and from 16.03 to 12.81 for TAU; the between-group difference was significant ($p=0.03$). Depression scores improved from end of treatment to the 3-month follow-up only for the IPT condition.

Several Internet-based cognitive behavioral interventions have been developed and tested, all showing promising results for the feasibility, acceptability and effectiveness of such a treatment for perinatal depression [71–73]. Sheeber et al. (2012) [71] found that mothers who participated in the intervention reported higher parental satisfaction and efficacy and lower negative parenting behaviors. Phone-based therapies have gathered additional preliminary support as potentially viable treatments for maternal depression [50•, 67].

Research on the use of alternative treatments for perinatal depression include light therapy [74] and fish oil supplementation [75, 76]. More research is needed in all of these areas given their beneficial potential and low risk.

Antidepressant Treatment of Postpartum Depression

One of the few recent studies examining antidepressant medication usage during the postpartum period is that of Hantsoo et al. [77], who compared sertraline to placebo in 38 women. Sertraline dosed from 50-200 mg produced a significantly greater response rate (59 % to 26 %) and remission rate (53 % to 21 %) than placebo.

Bloch et al. [78] did not find an additional benefit when sertraline was added to brief psychodynamic psychotherapy. Their study included 42 women with mild-to-moderate postpartum depression in an 8-week, randomized, double-blind, placebo-controlled study. A significant improvement over time was observed for both groups, but no time-by-group effect was found. Response rates were 70 % and 55 % for the drug and placebo groups, respectively, and remission rates were 65 % and 50 %, respectively, with no significant difference between groups.

While many mothers strongly prefer not to use medications in the perinatal period, the risk to offspring when maternal depression goes untreated suggests that lack of treatment may actually be the most detrimental outcome for infants [79]. This theme is echoed by other researchers who support the idea that, especially in the case of severe depression, it is more problematic for the depression to go untreated than to be treated using medication [80–82]. If effective structured psychotherapies such as IPT or CBT are not available, medication is a recommended treatment option.

Opinions on the Current State of the Literature

While numerous studies regarding perinatal depression have been added to the literature over the last few years, basic questions remain to be answered. First and foremost is more precisely determining the prevalence of perinatal depression and anxiety in minority and underserved populations, a gap that was emphasized by Gaynes et al. [5] in 2005. While universal screening is advocated, we still know little about how to disseminate and implement screening effectively. Most experts agree that both structural changes (such as reimbursement for screening) and additional education are critical, but these changes have generally not occurred.

The treatment literature for depression during pregnancy is incomplete. Most clinicians continue to use antidepressant medication without clear data regarding the efficacy and long-term effects for the exposed child [83]. While it is unrealistic to expect that any randomized antidepressant trials will be conducted during pregnancy, observational cohort studies, case control studies and case series would provide some of the needed data. More psychotherapy studies during pregnancy are also needed, especially for patients and providers who prefer a non-pharmacologic intervention.

It is clear that interventions that target women at risk are generally effective in the prevention of postpartum depression; those that are universal generally are not. The cost-effectiveness of prevention measures remains to be determined before widespread implementation can be recommended. For acute treatment of depression, there are sufficient data to recommend antidepressant treatment of postpartum depression even during breastfeeding; the structured psychotherapeutic interventions such as IPT and CBT are also effective treatments if they are accessible.

Conclusion

A number of interesting studies regarding perinatal depression have been published over the last 3 years. They have reinforced the conclusions that perinatal depression is prevalent, under-recognized and undertreated. We have effective means to screen and treat women who are depressed or at risk for depression. The greatest impact in the future will come from ensuring that screening becomes universal and that the preventive and acute treatments we already know work well are implemented and accessible.

Compliance with Ethics Guidelines

Conflict of Interest Kaela Stuart-Parrigon declares no conflict of interest.

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