POSTPARTUM DEPRESSION AND THE EFFECT ON CHILD DEVELOPMENT

By

NAIMISHA SATYASREE MALLIKA BADRI

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Approved by:

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Dr. Jeanmarie Bianchi

Department of Psychology

Abstract

This literature review provides an overview on postpartum depression and the effect on child development. Postpartum depression is incredibly common and often gets mistaken for "baby blues," though the effects of postpartum depression are more severe. Several risk factors have been identified and include prenatal attachment, length of labor, prenatal anxiety, and romantic relationship quality. Another study discussed the importance of the mother having a confidant, whether that relationship is romantic or not. Several pathophysiological mechanisms have been implicated in relation to postpartum depression but the pathways often overlap with stress and major depression. Postpartum depression has many detrimental effects on the children of the affected mothers. Short term effects at one year of age include lower motor and mental developmental skills. Long term effects at four years of age include increase in chronic and acute diseases and lower scores in communication, gross motor, and personal social skills. Mothers who have been treated for postpartum depression showed lower levels of parenting stress but had no change in how they view their child two years post-treatment. As of now, there is only one medication that is FDA approved which treats PPD and it was recently approved in 2019. Further research must be conducted on other treatments and the long-term effects of them.

Introduction

Postpartum depression (PPD) is a mood disorder that is a subset of major depressive disorder (MDD) that refers to a time during or after pregnancy. From the Diagnostic and Statistical Manual of Mental Disorders (DSM) IV to the DSM V, the term postpartum depression was changed to peripartum depression. The main difference between the two is the specific time periods. While the term "postpartum" refers to after delivery, "peripartum" includes the time during pregnancy. Postpartum depression can often be mistaken for "baby blues", which only lasts for a few weeks after delivery. However, the symptoms of postpartum depression last longer and are more severe and can even lead to postpartum psychosis. Severe cases of peripartum depression can put the mother and baby at severe health risk. The effects of postpartum depression can be extensive both on the mother and child. Maternal depression can affect the child from infancy to adolescence. It often leads to lower cognitive performance as an infant to learning disorders in adolescence. Some behavioral effects include passivity and withdrawal in infancy to anxiety disorders, phobias, panic disorders, conduct disorders, substance abuse, and alcohol dependence as an adolescent.

Postpartum depression is far more prevalent than is reported. While postpartum blues can occur in around 15-85% of women within the first 10 days after birth, the peak prevalence occurs at around three months after birth and the reported rate of postpartum depression in new mothers is 15% (Pearlstein et al., 2009). Often the symptoms of postpartum depression are minimized by mothers and healthcare providers alike as a common side effect of birth, which in turn decreases the number of cases reported (Anokye et al., 2018). Studies in this area are generally lacking. Most comprehensive trials and studies were conducted from the 1960s to the 1990s. Often, the most recent works are literature reviews or data analyses. Several studies show that

psychopathological studies, quality of the relationship/marital struggles, socioeconomic status, maternal depression before pregnancy, and family size can predict the prevalence of postpartum depression. Prenatal attachment to the child is also indicative of postpartum depression. Depressed mothers are also more aggressive towards their children, which leads to more issues with the development of the child.

Postpartum Depression

In a study performed by Smorti, Ponti, & Pancetti (2019), risk factors for postpartum depression were analyzed. The main goal of this study was to consider different sociodemographic, individual, relational, and other characteristics concerning postpartum depression and to see which had the most influence when they were all combined. It was hypothesized that women who were: younger, of lower levels of education, of lower employment status, and with unplanned pregnancies positively predict postpartum depression; prenatal anxiety and depression positively predict postpartum depression; caring prenatal attachment and quality relationships with romantic partners and parents negatively predict postpartum depression; more complicated labor, delivery type, and worse newborn index scores positively predict postpartum depression. 161 participants were selected and a longitudinal study was conducted. All participants were greater than 18 years of age, were psychologically and physically healthy, and had low-risk pregnancies with gestational ages of greater than 31 weeks. Participants with twin pregnancies, gestational pathologies, fetal pathologies, planned c-sections, and documented presence of depressive pathologies were excluded.

Data were collected via several questionnaires given at 3 different data points: 31-32 weeks of gestation, the day of delivery, and 1 month after delivery. Questionnaires given at the 31-32 weeks of gestation included psychological measures of anxiety and depression, relational

measures of relationship with mothers, fathers, romantic partners, and prenatal attachment, and sociodemographic and clinical measures. During the time of delivery, hospital records were obtained to collect information on deliveries including the type of labor (induced vs spontaneous), duration of labor in hours, mode of delivery (vaginal delivery vs emergency c-section), birth outcomes, and administration of epidural anesthetic. Birth outcomes were measured via Apgar scores. Apgar scores are assigned to babies and they are given a score up to 10, where 7-10 is the normal range, based on color, muscle tone, heart rate, reflexes, and respiration. 1 month after delivery, a psychological questionnaire was given to measure the degree of postnatal depression symptoms.

Data were analyzed using regression analysis. The severity of postpartum depression was positively correlated to the age of women. It was not correlated to the length of partner relationship, planned pregnancies, level of education, or employment status. High levels of prenatal anxiety and depression and postpartum depression levels were positively correlated. The scores on the questionnaires about the quality of relationships with mothers and fathers were very similar and combined into one score. The quality of romantic relationships and attachment to the child negatively affects the level of postpartum depression. Women who were induced or had emergency c-sections had a higher level of postpartum depression compared to those who had spontaneous and vaginal deliveries. The duration of labor positively correlated with the administration of epidural anesthesia, which then positively correlated with the level of postpartum depression. There were no significant differences in levels of postpartum depression with babies with different Apgar scores. This study, though, had no babies with Apgar scores less than 6. The study concluded that 61% of the postpartum depression score is explained by prenatal attachment, duration of anesthetic epidural administration, prenatal anxiety score, and

romantic relationship quality. Understanding what affects postpartum depression is incredibly important for the future development of treatment.

A systematic review of pathophysiological mechanisms associated with postpartum depression conducted by Payne, J. L., & Maguire, J. (2019) had incredibly mixed results. This study reviewed biomarkers, hormone levels, genetic and epigenetic factors, neuroendocrine, neurosteroids, neurotransmitters, neuroinflammatory levels, and circuit-level studies. Biomarker identification proved to be a great challenge due to the variation of the population and limited access to samples. Levels of hormones were observed in association with postpartum depression. One study showed evidence that withdrawal from above normal levels of estradiol and progesterone increases depressive symptoms. High levels of beta-endorphins, reduction in platelet serotonin levels, increased monoamine oxidase-A levels, low omega-3 levels, and lower vitamin D levels have all been associated with postpartum depression but have yet to be replicated in other studies. High levels of allopregnanolone, a metabolite of progesterone, were found in people with depression and postpartum depression. Though in other studies, this was not the case and may be due to the timing differences where blood was drawn in the second trimester of pregnancy in some studies and the third trimester in other studies.

Genome studies examined genes that have been previously implicated in major depressive disorder. Estrogen receptor alpha gene (ESR1) mediates hormonal changes during the peripartum period and it is clear that estrogen is implicated but further examination needs to be done. Polymorphisms in the serotonin transport receptor (5HTT) were correlated with postpartum depression but some studies say that this is only the case in patients with previous adverse life experiences. Polymorphisms in the gene encoding for monoamine oxidase A (MAOA) are associated with postpartum depression and the different variants of MOMA are

associated with the severity of postpartum depression scores. Conflicting results are found with interactions of catechol-O-methyltransferase (COMT) and postpartum depression. Polymorphisms in the gene encoding for COMT are associated with a risk factor for developing postpartum depression in a study but other similar studies showed that the polymorphisms are also associated with MDD. Tryptophan hydroxylase 2 (TPH2) is involved in the catalysis of serotonin. Genetic variants of TPH2 have been associated with postpartum depression symptoms at different times during the peripartum period, though further studies are required to study the interaction between stress, adverse life events, the HPA axis, and TPH2 expression. A single nucleotide polymorphism (SNP) in the gene encoding for oxytocin (OXT) was associated with variation in breastfeeding duration and postpartum depression scores. The strongest association was found with the hemicentin 1 gene (HMNC1) but the association was not significant after correlation. The exact function of hemicentin 1 is unknown but it is highly expressed in the hippocampus, and in rats, was shown to be altered by a postpartum decrease in estrogen levels. Hypothalamic-pituitary-adrenal (HPA) axis has been thought to be implicated in postpartum depression in multiple studies. Variants in MAOA and COMT genes have been associated with sex-specific cortisol differences in response to a social stressor. Protein Kinase C beta type (PRKCB) regulates the HPA axis indirectly through CRH signaling and glucocorticoid receptors. Mutations in PRKCB have been associated with postpartum depression.

Epigenetic mechanisms have been investigated as well. A study looked at DNA methylation profiles in a cross-species design in association with postpartum depression and compared them with estradiol-induced DNA methylation profiles in the hippocampus of estrogen-treated mice. Two genes in particular, heterochromatin protein 1, binding protein 3 (HP1 BP3) and tetratricopeptide repeat domain 9B (TTC9B), were found in this overlap and

have ties to estrogen signaling and synaptic plasticity. The results of this experiment were replicated in another study. An experiment was designed with HP1 BP3 knock-out mice and the mice had deficits in maternal care. Epigenetic modifications in the oxytocin receptor (OXTR) genes were also investigated and demonstrated an interaction with the genetic modifications and DNA methylation in women with postpartum depression. There was also an interaction between DNA methylation variation in the OXTR gene and previous adverse life events. A negative correlation was found between DNA methylation in the OXTR gene in patients with postpartum depression and serum estradiol levels. There was also an interaction between estradiol, OXTR DNA methylation, and the ratio of allopregnanolone to progesterone.

Neuroendocrine abnormalities have been implicated in postpartum mood disorders. Fluctuations in the reproductive hormones during the peripartum period may play a role in this. As stated earlier, withdrawal from supraphysiological levels of reproductive hormones increases depression scores in women with prior history of postpartum depression. Estrogen levels rise before giving birth and drop after delivery. Women with postpartum depression may have increased sensitivity to estrogen signaling, though changes in estradiol levels are not consistently reported. Several studies suggest that treatment with estrogen may reduce the risk of developing postpartum depression. In animal models, withdrawal from estrogen has similar effects as in humans. Rats with their ovaries removed have increased depressive behaviors which are reversed with estradiol treatment. Pseudopregnancy experiments were also performed on rats to mimic the hormone fluctuations of the peripartum period. Depressive behaviors in this experiment were also reversed with estradiol treatment. Progesterone increases the risk of postpartum depression and worsens depression scores in women postpartum. Studies have demonstrated that treatment with progesterone decreases postpartum depression recurrence in women with prior history of

prenatal depressive episodes. In mice, progesterone was administered after 3 days of withdrawal from it which increased depressive-like behaviors. This was also mimicked by blocking progesterone metabolism which decreased the levels of allopregnanolone in mediating depression-like effects of progesterone withdrawal. Oxytocin levels were more associated with maternal behaviors and breastfeeding rather than directly being related to postpartum depression. High oxytocin levels during breastfeeding correlated with decreased depressive symptoms. Decreased oxytocin levels are predictive of the future development of postpartum depression. Prolactin is also related to breastfeeding and in women with postpartum depression who are breastfeeding, prolactin levels are low. Decreased prolactin levels are found in women who are at risk for developing postpartum depression and who have higher postpartum depression scores. It was suggested that failed lactation and postpartum depression may have similar pathways as both may be related to prolactin. Prolactin knockout mice, however, had decreased anxiety and maternal behaviors but no change in depressive behaviors.

Stress hormone levels including cortisol, adrenocorticotropic hormone (ACTH), and corticotrophin-releasing hormone (CRH), have been shown to be altered in those with postpartum depression. Stress is also related to the HPA axis which is mentioned repeatedly in postpartum depression articles as a possible underlying neuropathology, though this is controversial as it remains unproven. This is because stress is a prominent risk factor for postpartum depression and also leads to neuroendocrine disruptions, which are also commonly implicated in Major Depressive Disorder. CRH in particular has been suggested to be a diagnostic criterion for postpartum depression. Supportive evidence for the HPA axis comes from evidence that chronic stressors during pregnancy can be sufficient to induce postpartum

depressive behaviors. This may be due to corticosterone because, in postpartum animals, exogenous corticosterone induces depressive-like behaviors.

Allopregnanolone, a neurosteroid and neuroactive metabolite of progesterone, has antianxiety and antidepressant effects. Decreased levels of allopregnanolone have been correlated with increased depression scores in late pregnancy. A polymorphism in a gene involved in allopregnanolone synthesis, aldo-keto reductase family 1 C2 (AKR1C2), which results in decreased allopregnanolone, has been associated with an increase in depression scores. In a double-blind, randomized, placebo trial, antidepressant treatments increased allopregnanolone levels, and treatment with brexanolone improved postpartum depression scores.

Several neurotransmitters have been examined in relation to postpartum depression. GABA, an inhibitory neurotransmitter, levels are inversely correlated with depression scores. Glutamate, an excitatory neurotransmitter, levels are increased in the medial prefrontal cortex and decreased in the dorsolateral prefrontal cortex in postpartum depression patients. Treatment with progesterone restores glutamate levels in the dorsolateral prefrontal cortex. Large reductions were seen in the anterior cingulate and mesiotemporal cortices in serotonin binding potential. Mutations in dopamine receptors (DR) have interesting resulting behaviors. Mutations in DR1 are associated with mothers orienting away from infants while mutations in DR2 are associated with maternal infant-directed vocalizing.

While neuroinflammatory mechanisms were evaluated, results were conflicting and further studies are required. Few studies have examined the role of the immune system on postpartum depression. There are conflicting reports of interleukin-6 but kynurenine, a tryptophan metabolite, levels are positively correlated with postpartum depression. Imaging

studies show that postpartum depression can cause circuit-level changes. fMRI studies showed such alterations in resting-state connectivity. There was decreased activity in the anterior cingulate cortex, amygdala, hippocampus, and dorsolateral prefrontal cortex. There was also decreased corticocortical and corticolimbic connectivity. There are many pathways and mechanisms involved in postpartum depression though it is difficult to pinpoint a specific one because these mechanisms often overlap with pathways for general depression and stress.

Effect on Child Development

The experiment conducted by Lyons-Ruth, K., Zoll, D., Connell, D., & Grunebaum, H. U. (1986) answered the following questions: What proportion of the group of multi-risk mothers with infants referred for clinical intervention services can be characterized as suffering from depression? Or is maternal depression not a frequent characteristic of the most at-risk mother-infant dyads? What is the ecological context of maternal depression in this sample? How does depression relate to the mother's past and present family context? How does the mother's depression after her maternal behavior and her infant's development and security of attachment at twelve months of age? Half of the mothers were referred to a clinical intervention service due to poor infant relationships and socioeconomic stressors. Mothers from the same neighborhood were chosen for the other half of the participants. These mothers had never received social services for their parenting skills and underwent psychiatric hospitalization. These two groups were matched based on family income, mother’s education and race, child’s age, sex, and birth order. They also did not differ on infant birth weight, mother’s age at birth, and mean number of siblings.

Participants were given a 20-item questionnaire (CES-D) that asked about depressive symptoms in the past week. There were also assessments for maternal depression, maternal

family history (treatment of mom as a child), maternal behavior at home, infant development (Bayley scales of infant development, mental, and motor scales), maternal intelligence, and infant attachment security (Ainsworth strange situation). Mothers who were previously hospitalized in a psychiatric unit had the highest CES-D scores.

Maternal depression and infant development at 1 year were analyzed. Depression was negatively related to infant scores on the mental developmental index and physical developmental index. Maternal depression had a negative effect on infant motor and mental development in that first year. When moms reported clinically significant levels of depression of 16-23, infants had average levels of development. When that level exceeded 23, the developmental scores dropped. Interestingly, mothers who deny that they are depressed had infants that were within the normal or above the normal range of development. Mothers with the least and highest depressive symptoms were equally likely to show insecure attachment and mothers with mild to moderate depressive scores showed secure attachment. Some mothers with the highest depressive scores showed avoidant or unstable avoidance attachment, which has also been associated with infant maltreatment. High infant avoidance was also frequent in infants of depressed mothers. The relationship between attachment styles and depression was consistent with maternal behaviors when infants were observed at 12 months of age but it was not completely explained by maternal behaviors. Short-term consequences were also apparent for the infants of depressed mothers, specifically at one year of age. These infants had lowered mental and motor development scores, even with maternal IQ scores controlled for.

The study conducted by Abdollahi, F., Abhari, F. R., & Zarghami, M. (2017) aimed to investigate 4-year-old children of depressed mothers and the presence of developmental disabilities. Pregnant women in the Mazandaran province of northern Iran were given the

Edinburgh Postnatal Depression Scale (EPDS) 2-12 weeks postpartum where a score of 12 or higher indicated depression. 4 years after the initial questionnaire was given, the women who agreed to participate and not excluded due to other factors were given the EPDS and the 48-month adapted Ages and Stages Questionnaire (ASQ). The ASQ assessed fine motor, problem solving, communication, gross motor, and personal-social skills of the children. The mothers were also given small questionnaires regarding the child's medical illnesses, both acute and chronic, daily medications, and height and weight. Mothers were split into 4 groups based on their depression levels: no depression (60.5 % of participants), postpartum depression only (18.8%), current depression only (9.1 %), and both current and postpartum depression (11.6 %).

All questionnaires were analyzed using chi square analysis. Women with postpartum depression only or both current and postpartum depression were less likely to breast feed. Children with postpartum depression only mothers had more children suffering developmental disabilities in two categories of ASQ – gross motor skills and personal-social skills. This result was found using a simple logistic regression though in multiple regression models, PPD predicted developmental disabilities if women had both current and postpartum depression. Women with depression, either current, postpartum, or both, had children with acute or chronic illness. Women in the current depression and both postpartum and current depression categories had children with significant scores that represent defects in communication, gross motor, and personal social domains of the ASQ. The investigators explained this in one of two possible ways – depressed women have lower maternal confidence and therefore are a poor role model or data or the data was collected based not on observation but on maternal self-estimation. Women who experienced depression at the postpartum period and 4 years later were more likely to rate their child's behavior as problematic. Though much about the long-term effects of postpartum

depression was concluded from this study, there were several limitations. Sociodemographic factors were not considered. Other factors that affect the development of disabilities in the children (e.g. lack of healthy lifestyle, psychosocial conflicts, financial or family problems, etc.) were not analyzed. This study excluded mothers who were being treated for postpartum depression and did not examine the effects of treatment on child development.

Effect of treatment

Forman and others (2007) aimed to answer the question that had gone unanswered previously in literature: is successful treatment for maternal depression sufficient to improve parenting and child outcomes? Their first goal was to test the effects of treatment in the first year on infant emotionality and parenting. The second goal was to test whether, over time, children of depressed mothers continue to be at risk and whether recovery during treatment reduces that risk. The third and final goal of this trial was to test whether the formed views that depressed mothers had of their children as difficult predicts negative child outcomes despite receiving treatment.

Participants were recruited from birth records from 4 Iowa counties. The women were at least 18 years of age, married or living with a partner for 6 months, and were screened for depression with the Inventory to Diagnose Depression (IDD). 120 mothers were enrolled in the treatment trial where 39 were experiencing their first episode of major depression and 81 had had a previous depression history. A third of the participants started with depression during pregnancy, another third during the first month postpartum, and the last third between the second and sixth month postpartum. 56 women were recruited and served as control as they scored below the IDD screening cut-off and had no other psychiatric disorder history. Education was controlled for in the analyses and two-thirds of the participants were employed outside of their

homes. The mean age of mothers was 30.6 and since maternal age did not predict outcomes, maternal age was not covaried.

Half of the women experiencing randomly assigned to a treatment team and received 12 weeks of interpersonal psychotherapy and the other half were assigned to a waitlist control. They were all instructed to not use any outside psychotherapeutic treatment. Treatment and first at-home infancy visits were conducted at 6 months of age of the children. A Structured Clinical Interview (SCID) for DSM-IV and the Hamilton Rating Scale for Depression were used to verify the presence or absence of major depressive episodes. The mothers and infants were videotaped participating in several natural mother-child tasks (e.g. bath time, diaper change, etc.) that were designed to measure infant emotionality and parenting. After 12 weeks of treatment for the intervention group, mothers and infants underwent another at-home visit. At 18 months after the end of the treatment phase, mothers were given questionnaires to report on their children's temperament, behavior problems, and attachment relationships. The differences at the 12-week and 18-month stage are evidence of the effect of treatment. The videotaped tasks were then analyzed by coders who were unaware of the mothers' depression and treatment status.

Results showed that depressed mothers were less responsive to their infants and often reported more parenting stress. After treatment, there was no change in maternal responsiveness. While there was initially no change in parenting stress after treatment, differences started appearing 3 months post-treatment. Mothers who were treated reported lower levels of parenting stress. Depressed mothers reported higher negative affectivity regarding their children, which was significant at both 6 and 9 months of age in comparison to non-depressed mothers. There was no difference after treatment. 18 months after treatment, children of treated depressed mothers scored lower in attachment security and higher in negative affect. Overall after

treatment, there was no effect on child outcomes. Mothers who viewed their children as high in the negative affect remained this way even after 2 years. This study thus concluded that treating depressed mothers was not enough to combat the effects of postpartum depression on their children.

Discussion

Majority of postpartum depression was shown to be explained by 4 different factors: prenatal attachment to the child, duration of epidural administration, prenatal anxiety, and romantic relationship quality (Smorti et al., 2019). Duration of anesthetic administration can further be linked to duration of labor. The idea of mothers and relationship quality was also mentioned in Lyons-Ruth et al., (1986) though this study discussed the importance of having a confidant whether the relationship was romantic or not. A person with whom the mother can have a quality relationship can protect against the development of maternal depression as well.

The mother-child relationship is one that is delicate and important for physical, psychological, and social development of the child. Postpartum depression can alter this relationship drastically. Short term consequences of having a depressed mother are apparent within the first year of life. Lyons-Ruth et al., (1986) found that infants at 1 year of age had lower developmental scores compared to infants with nondepressed mothers. This developmental difference persists even at 4 years of age, as found by Abdollahi et al., (2017). The presence of postpartum depression significantly increases the risk of developing maternal depression which in turn also has an effect on child development (Beck 1998). Mothers who were currently depressed at the time of the study and had a history of postpartum depression had children who were more likely to be chronically ill and have developmental disabilities, specifically with defects in communication, gross motor, and personal social skills. Regarding infant security,

Lyons-Ruth et al., (1986) found that mothers with mild to moderate depression had no effect on their child's attachment security. Interestingly, this only changes with mothers who have either very high or very low depression scores.

Several rat experiments showed reversal of increased depressive behaviors with estradiol treatment (Payne et al., 2019). While this could be a promising treatment, additional trials and testing need to be performed. Another factor that would need to be considered would be the long-term effects of estradiol treatment (Moses-Kolko et al., 2009). Another treatment would be a physiologically metabolite of progesterone. Progesterone has been to increase glutamate levels and Brexanolone was shown to improve postpartum depression scores (Payne et al., 2019). Thus far, Brexanolone is the first and only drug that has been approved by the FDA specifically to treat postpartum depression and it was approved very recently in 2019 (Powell et al., 2020). Forman et al., (2007) showed that treatment only had an effect on parenting stress. Mothers showed no change in maternal responsiveness after treatment and viewed their children in a negative affect even 2 years post treatment. Since the approval of Brexanolone is so recent, studies have not yet been conducted to show the longer-term effects of the drug. Further research is required in this area and for new drug development.

It is clear is that just more research overall needs to be conducted on postpartum depression. While attempting to look for studies to review, most of the studies that were recent were literature reviews of older studies. Looking at this body of research, it is evident that the next step for further research in postpartum depression is the effect of treatment and new treatments. This could also be helped further along by more research that could be conducted on mechanisms implicated specifically with postpartum depression compared to mechanisms that are implicated in multiple conditions. Future research should be directed to the development of

new medications and therapies that show a significant decrease in postpartum depressive symptoms.

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