Quiñones F, Winters C, Hu L, Suvarnakar A. Untreated Major Depression During Gestation: The Physical and Mental Implications in Women and Their Offspring. *Georgetown Medical Review*. 2023;7(1). doi:10.52504/001c.83340

REVIEWS

Untreated Major Depression During Gestation: The Physical and Mental Implications in Women and Their Offspring

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Keywords: preeclampsia, cesarean section, high risk behavior, preterm birth, mental health, neurodevelopment, birth weight

https://doi.org/10.52504/001c.83340

Georgetown Medical Review

Vol. 7, Issue 1, 2023

While postpartum depression has been extensively studied and is a concern surrounding major depression in women, the effects of major depression during pregnancy alone should also be considered. The purpose of this review article was to explore in longitudinal fashion, from neonate to adulthood, the lasting physical and mental implications that depression during gestation can present in offspring. Consideration of various sources pulled from the OVID Medline database yielded findings consistent with negative associations between gestational depression and offspring outcomes. In mothers, gestational depression presents with physical implications, such as preeclampsia and preterm delivery, leading to low birth weight and neurodevelopmental complications in neonates. As the children grow older, these complexities manifest as socioemotional, behavioral, and linguistic development delays presenting as increased incidence in attention-deficit/hyperactivity disorder diagnoses, parental attachment issues, and lower emotional and verbal IQ. Research regarding adolescents and adults is sparse in comparison with that of earlier stages, but there are studies that examine the developmental outcomes of certain mood disorders, such as generational depression, in the offspring of birthing parents with prenatal depression. This review presents an extended timeline of the effects of gestational major depression in offspring, and it provides suggestions for future research regarding underlying biological explanations and certain risk outcomes.

Introduction

Major depression is a common but serious medical mood disorder that is the most common mental condition to affect individuals of child-bearing age, especially around the time of pregnancy.[1] About 17% of perinatal birthing parents experience various degrees and types of depression and within that group, new experience the highest prevalence of postpartum depression.[1,2] Typical symptoms include, but are not limited to, the characterized feelings of sadness, anxiety, hopelessness, restlessness, and lack of energy, with the individual experiencing abnormal sleep schedules and decreased sleep quality. Major depression can be a debilitating condition that affects an individual's capacity to carry out daily activities and ultimately impact their life and the lives of those around them. The effects of maternal depression can permeate throughout all aspects of a pregnancy, with studies showing that maternal depression has lasting impacts on the mental, emotional, behavioral, and physical development of the neonates up to adulthood.[3]

Current treatment options for gestational depression include both pharmacologic and nonpharmacologic approaches. Nonpharmacologic approaches, which are not as effective at reducing long-term sequelae compared with pharmacologic approaches, include cognitive behavioral therapy,

supportive psychotherapy, conjoint therapy with a partner, and removal of stressors.[4] Pharmacologic approaches, of which selective serotonin reuptake inhibitors are used most frequently, increase the risk of preterm delivery and delay motor development in children.[5]

Many studies have examined pregnancy complications and birth outcomes in mothers that who experienced untreated prenatal depression. The studies showed that untreated maternal depression was a predictor for poor outcomes surrounding birth, such as preeclampsia, a potentially life-threatening uterine complication associated with high blood pressure and improper vascular development in the placenta,[6,7]; higher incidence of cesarean delivery[7-9]; prolonged labor[8]; and low birth weights .[10]As they grow older, the offspring experience complications associated with their mother's untreated maternal depression, such as higher incidence of depression,[11-13] externalizing and internalizing disorders, and decreases in verbal IQ.[14,15] There is currently a need to further investigate the long-term physical effects of prenatal maternal depression on the offspring, such as obesity and brain development, as children may be more prone to social isolation from their peers and subsequent feelings of emotional inadequacy.[2]

Additionally, the biological undergrounding of the cause between prenatal maternal depression and negative offspring outcomes needs to be explored further. There are hypotheses that marked elevations in inflammation[6,16] and hypothalamic-pituitary-adrenal (HPA) axis dysregulation mediate mother and offspring's poor outcomes, although the role of cortisol is controversial and not fully understood.[6,17] Even though it is well understood that prenatal maternal depression affects both the mother and offspring, more work is needed to confirm a biological explanation for these associations. The purpose of this review article is to explore the physical and mental implications in longitudinal fashion and highlight where further research of biologic mechanisms is needed to potentially drive novel treatment interventions.

Methods

An initial search was undertaken to identify English-language articles and a maximum of 2 systematic reviews published between 2010 and 2023. An electronic search in OVID Medline was performed using the keywords: "depression," "pregnancy," "postpartum," "developmental disabilities," and "childhood development." Four investigators independently evaluated the titles and abstracts in a first stage and the full text in a second stage review. Thirty three studies were selected and included as part of the review.

Complications of Untreated Depression in Birthing Parents

Previous studies have researched the extensive physical and mental implications of untreated major depression on a birthing parent during pregnancy. These problems, mostly stemming during the antenatal and labor periods, manifest in forms such as prolonged labor,[8,9] preeclampsia,[6,7] greater incidence of cesarean delivery,[7-9] and a greater likelihood of partaking in high-risk health behavior.[18]

Two studies examined the effects of untreated depression and its associated complications in causing prolonged labor. Weobong et al[9] used a population-based cohort study of 20679 pregnant individuals in Ghana and looked patients' Patient Health Questionnaire (PHQ) to assess the severity of untreated depression and various complications, including prolonged labor. The PHQ asked about the 9 symptom-based criteria for a diagnosis of depression according to the *DSM-IV*. After defining prolonged labor as greater than 24 hours, the researchers found that there was a 25% greater chance (adjusted relitive risk (RR), 1.25 [95% CI, 1.02-1.53]; $P = .03$) of a birthing parent undergoing prolonged labor if they had untreated depression.[9] Subsequently, a birthing parent undergoing prolonged labor can experience physical complications, such as chorioamnionitis that can lead to fetal meningitis, pneumonia, and maternal sepsis, as well as mental complications such as negative, painful associations with future pregnancies.[19]

Al Rawahi et al[8] studied the subsequent psychological distress experienced by women with untreated depression and its relationship to the prolongation of labor. Using a prospective cohort study of 959 participants in Iran, Al Rawahi et al[8] found that women birthing parents experiencing untreated depression may have had other related psychological distress that reduced uterine contractility.[8] Further, women classified with depression during the latter stages of their pregnancy reported greater anxiety and fear of childbirth; consequently leading to decreased pain threshold and an increase in the incidence of using epidural (33% vs 19%, $P = .01$; adjusted RR, 2.56 [95% CI, 1.24-5.30]) that prolonged labor. A pattern of both anxiety and fear leading to prolonged labor was consistent with both studies.[8]

Another study examined the antenatal incidence of preeclampsia on birthing parents with untreated major depression. Preeclampsia, normally associated with high blood pressure and improper vascular development in the placenta, is a potentially life-threatening uterine complication that is significantly enhanced in birthing parents with depression.[7] In a cohort study of 394 women in Iran, Khanghah et al[7] found that of the cohort, 212 were diagnosed as having untreated depression and the incidence of preeclampsia was 6.13% compared with the incidence of preeclampsia in birthing parents with no depression at 2.20% ($P < .01$).[7]

The link between untreated depression and preeclampsia may lie in the inflammatory response of the human immune system. Through reasons that are still being researched, depression during pregnancy may adversely affect and exasperate the body's immune and inflammatory response, which could lead to an inflammation of vascular endothelium, possibly leading to preeclampsia.[6] Compared with healthy pregnancies, complicated pregnancies due to depression showed elevated levels of macrophages and natural killer cells, particularly natural killer cells of the Th1 cytokine type.[6] Further evidence has shown that depression and psychological stress may stimulate the HPA axis to overproduce cortisol (adjusted RR , 1.42 [95% CI, 1.09-1.86]; P = .009), ultimately leading to endothelial dysfunction. hypertension, and preeclampsia.[20] These studies indicate that a possible inflammatory process induced by depression may increase the incidence of preeclampsia.

The prevalence of cesarean deliveries, a surgical procedure used for the delivery of babies, has been increasing in the past 20 years.[8] Compared with spontaneous vaginal deliveries, cesarean deliveries are associated with higher mortality due to postpartum hemorrhage and complications of anesthesia.[21] Cesarean deliveries may either be elective or necessary if there are prenatal complications. In particular, women with untreated depression are more likely to undergo the surgery during labor compared with those with no depression during pregnancy (adjusted RR, 1.19 [95% CI, 1.02-1.40]; P = .03).[9] This is because untreated depression is associated with increased levels of adrenocorticotropic hormone and subsequent uterine artery resistance. Consequently, this leads to antenatal difficulties such as premature membrane rupture, intrauterine fetal death, preeclampsia, and decreased uterine contractions.[7,8] In all 3 of these studies, cesarean deliveries were implemented to curb postpartum complications as much as possible due to their swiftness and compliance towards international obstetric and gynecologic governing bodies.[7-9]

In addition to physical complications, untreated depression during pregnancy can yield mental strains on individuals.[18] Chan et al[18] reported that pregnant individuals with depression are more likely to engage in high-risk behavior including drinking alcohol, smoking, and partaking in substance abuse.[18] These activities are considered high risk because, although they may increase the chances of miscarriage during pregnancy and maternal addiction post pregnancy, they significantly increase neonatal morbidity and mortality.[22] For example, engaging in high-risk behavior increases the chances of fetal growth restriction, fetal alcohol syndrome, and attention-deficit/hyperactivity disorder (ADHD) in childhood.[22] Furthermore, using the Likert scale to measure the extent of depression, individuals who scored higher, or were more depressed, reported lower self-esteem, suicidal thoughts, guilt, and appetite loss.[7] However, more research needs to be done to correlate negative self-worth and pregnancy complications.

Current options of treatment include both medical and complementary and alternative medicine therapies. The most common prescribed medicines that effectively treat depression in pregnancy belong to the selective serotonin reuptake inhibitor and serotonin and norepinephrine reuptake inhibitor drug classes.[23] Despite the numerous medical options available, medication compliance declines during pregnancy. A study conducted by Bennett et al[24] found that compliance rates declined by 39% (RR, 0.44 [95% CI, 0.41-0.46]; $P < .05$) during pregnancy primarily due to fear of the potential teratogenic effects of the medication. Complementary and alternative medicine therapies, such as bright light therapy, massage, and St John Wort, are increasingly sought out as more natural remedies; however, there is no conclusive evidence of their efficacy.[25] For pregnant patients to safely and confidently consider their options, they should receive evidence-based education regarding the risks and benefits of treatment options from their treating clinicians.[25]

Complications of Untreated Maternal Depression in Offspring: Neonatal Outcomes

Many of the effects of untreated major depression in pregnancy develop throughout the course of the gestational period, and they are evident at the onset of birth through changes to the physical characteristics and the neurodevelopment of the offspring.

Individuals experiencing untreated major depression during pregnancy have been linked to giving birth to children with abnormal characteristics such as preterm births and low birth weights.[10] Numerous associations have been found between poor mental health of pregnant individuals and an earlier gestational age at birth of their children; however, major depression during pregnancy has been connected to some of the highest risks of preterm births.[26] One study, focused on a population of patients who participated in Medi-Cal (California's Medicaid program), found that, compared with women without a mental illness, the relative risk of preterm births in mothers with major depression was 2.0 (95% CI, 1.3-3), while other maternal mental illnesses barely increased the relative risk of a preterm birth above 1.2 (95% CI, 1.1-1.3) when compared with women without a mental illness.[26] Some studies have shown that pregnant individuals with major depression may buffer the impacts of their depression through social support, which the participants in the Medi-Cal study mostly lacked.[10,26] Nevertheless, there is also strong evidence to refute these claims, suggesting that gestational major depression increases the risk of preterm births, and even spontaneous abortion, regardless of the mother's perceived social support.[10,27] As a result of major depression of the gestating individuals and its associated preterm births, newborns can also have lower birth weights as compared with infants born to mothers without untreated major depression.[10] Results from a comparative study of patients in the perinatal period in outpatient clinics in Turkey confirmed that major depression in mothers could decrease neonatal birth weight by an average of 10% compared with a mentally healthy control group.[27] It is necessary to

consider the impact of untreated major depression in pregnancy on preterm births and lower birth weights because preterm births and lower birth weights can increase the risk of infant mortality, neonatal respiratory issues, and other developmental neurologic issues.[28]

The effects of untreated major depression in pregnancy are not limited to physical outcomes because the neurologic development of the infant is often impacted by the mother's depression. Untreated maternal major depression in pregnancy can determine neurologic outcomes of the infant through the developing infant's regulation of inflammation and cortisol produced by the birthing parent's depression.[17] The increased levels of cortisol produced by birthing parents are generally inactivated to cortisone through the enzyme 11-β-hydroxysteroid dehydrogenase-2; however, these protective effects are subdued by the end of the second trimester when 11- β -hydroxysteroid dehydrogenase-1 in the fetus begins to function and reverse the inactivation of cortisol by 11-β-hydroxysteroid dehydrogenase-2.[17,29] Exposure to higher-than-normal levels of cortisol in utero is associated with an impaired ability for neurons of the central nervous system to develop properly.[17,29] As a result, developing children of birthing parents with major depressive disorder can have abnormally regulated fetal heart rate variability (FHRV), which manifests as a low FHRV.[17] Low FHRV is linked to poor regulation of temperament and ability to filter relevant information from central sensory inputs as measured by Infant Behavior Questionnaire-Revised and p50 inhibitory sensory gating repectively.[17]

Increased cortisol levels are not the only modulators of irregular fetal neurodevelopment in a pregnant individual with major depression. There are also environmental factors in utero, such as glutamate receptor and SNARE complex activity, that can affect changes to the developing fetus' genomic profile to reflect the mother's genomic profile risk score for major depressive disorder.[30] Although its mechanism is not fully understood, untreated major depression in pregnancy has been associated with environmental changes to a fetus' genome that lead to improper growth of the amygdala, hippocampus, orbitofrontal cortex, and ventromedial prefrontal cortex.[30] The changes to the developing fetus' genomic profile in these locations can include increased activity of glutamate receptors and improper SNARE complex expression, which together have been linked to abnormal fetal development of the right amygdala and the right hippocampus.[30] Abnormal development of these corticolimbic structures in utero can perpetuate the genomic profile predisposition for major depressive disorder from an untreated mother to the child; however, the symptoms themselves may not develop until later in the child's life even though the predisposition for major depressive disorder is passed in utero.[30] Although the recent evidence linking genomic and hormonal regulation to neurodevelopmental issues offers a concrete mechanism of understanding the effects of maternal major depression on fetal development, studies with larger, more diverse sample groups are needed to

confirm this mechanism of action. It is also necessary to further study potential postpartum environmental effects, such as the effects of the stability of a birthing parent–infant's strength of attachment after birth, that can also affect an infant's neurodevelopment.[29,30]

Complications of Untreated Maternal Depression in Offspring: Early Childhood Development

The consequences of maternal depression are long-reaching and can be felt beyond the womb.[2] Early childhood is a critical period for children, where many foundational skills are learned and developed. In current literature, many studies have defined a strong correlation between maternal depression and early childhood developmental delay in all aspects.[1,2,31,32] Specifically, maternal depression has been demonstrated to adversely affect the offspring's mental, emotional, social, behavioral, linguistic, and physical development.[1,2,31,32]

Maternal depression and offspring emotional development are intimately related. A longitudinal population-based study by Chorbadjian et al,[2] which included a diverse patient population of 2679 mothers with depression in the Los Angeles area, found that the offspring had a greater chance of experiencing social-emotional delays by 2.5 years. These social-emotional delays manifest in various ways during different stages of the child's life, but are overall defined by the ability of the child to properly portray feelings or emotions and how well they are able to connect and socialize with other people.[2] During infancy, these social-emotional delays put the offspring at higher risk of developing poor attachment styles, which in turn influence the child to exhibit poor emotional control, poor social skills, and more aggressive behavior as they progress through childhood.[2]

However, emotional development encompasses not only mood regulation, but also mood disorders. A study done by Goodman et al[31] found that the children of birthing parents with depression demonstrated higher risks of developing mood disorders, such as depression and anxiety, as well as issues with properly processing emotional challenges both internally and externally as well as developmental delays.[32] This is notable because these mood disorders can further contribute to the dysregulation of the offspring's emotional development and, furthermore, have notable interplay with other social and behavioral issues. Consequently, these emotional and behavioral issues that stem from early childhood could burgeon into more complex and adverse emotional, social, and behavioral issues of the children later in life.[2,31]

Additionally, there is significant evidence showing maternal depression throughout pregnancy is associated with ADHD.[33] Wolford et al[33] conducted a study including 1779 birthing parent and offspring (3 and 6 years old) dyads from the Prediction and Prevention of Pre-eclampsia and Intrauterine Growth Restriction (PREDO) Study. Interestingly, they found that higher-scoring compared with lower-scoring prenatal maternal depression was associated with

a higher likelihood of clinically significant ADHD symptoms in children at aged 3 and 6 years.[33] Furthermore, this study further clarified that postnatal maternal depression specifically added to this effect rather than was explained by this effect. These studies on offspring depression and ADHD thereby provide further support to the hypothesis that untreated maternal major depression plays a significant role in the neurodevelopment of the offspring.

Children of birthing parents with depression also demonstrate deficiencies in problem-solving skills.[32] Although many factors can influence a child's growth and development, how a birthing parent cares for their child during early childhood greatly influences how the offspring will respond to life events and experiences.[32] A study by Vameghi et al[32] demonstrated that children of mothers with depression had delayed problem-solving skills compared with children of mothers without depression, with a significant association (P = .015).[32] The inability of the offspring to demonstrate adequate problem-solving skills notably impacts their ability to respond to new or unfamiliar situations.[32] Thus, the delay in problem-solving skills and inability to adapt to new experiences can further contribute and complicate the socioemotional delays that could also be present or develop in the child as well.[2,32]

Linguistics and language development make up the process by which children learn how to properly understand and use language, which importantly takes place during early childhood. Language development aids in children's neurodevelopment and is a good predictor of intelligence and intellectual development.[1] A study conducted with more than 157 mother child dyads from Washington, DC, noted that not only did the offspring of mothers with depression retain understanding of fewer words than their peers at 15 months, but they also failed to demonstrate comparable growth in language development between the ages of 15 and 24 months compared with the offspring of mothers without depression.[1] The study by Chorbadjian et al[2] confirmed this linguistic impact of maternal depression when it also demonstrated that the offspring of mothers with depression had more difficulty retaining the use of "2-word phrases" and had difficulty "following simple instructions."[2] This communication barrier can further hinder other aspects of offspring's development because it can affect how the child can properly express themself to others.

The children of birthing parents wth depression are also affected physically. A study by Raposa et al[34] included 815 Australian mother-child dyads and concluded that many factors can contribute to the negative physical development of the offspring, notably that mothers with depression often are more prone to negative health behaviors such as "substance use and poor nutrition." A study by Wang et al[35] postulated that these negative health behaviors could consequently impact the health and growth of the child due to inadequate and unbalanced nutrition possibly because the mother is not only unable to properly model proper self-care/healthy habits, but also struggles to

provide and adequately encourage a wholesome diet and lifestyle. In turn, these poor lifestyle habits increase the risks of developing certain—possibly lifelong affective—conditions such as childhood obesity, type 2 diabetes, hypertension, and high cholesterol.[35] The study by Wang et al[35] that included 1364 families through the National Institute of Child Health and Human Development and Study of Early Child Care and Youth Development demonstrated a notable relationship between maternal depression and specifically the development of "overweight children from grades one to six." Wang et al[35] proposed that changes in maternal behavior due to depression, such as choosing more negative health behaviors like disordered feeding, could be one of the main contributors explaining the strong correlation between maternal depression with increased childhood body mass index. However, Wang et al[35] also noted that this finding of weight gain was in contradiction with other literature exploring the relationship between childhood body mass index and maternal depression, as other studies actually demonstrated the opposite—with weight loss being the positive correlation instead. One possible explanation for this discrepancy could be that depending on the population of mothers and their specifically affected maternal depression behaviors, negative health behaviors such as poor nutrition can result in the offspring being either over or underweight, depending on the type of disordered feeding demonstrated.[34,35]

To further add to the physical developmental impairment, an Iranian study of 1053 mother–child dyads discovered a statistically significant positive relationship between maternal depression and delay of gross-motor skills (P = .001).[32] Chorbadjian et al[2] also found that maternal depression contributed to gross-motor skill delay by noting that children of mothers with depression had more difficulty walking compared with children of mothers without depression.[2] The delay in physical development can further isolate the child and contribute to their social-emotional development as well because the offspring is unable to properly play and interact with their peers.[2]

Furthermore, there have been links between maternal depression during fetal development and the dysregulation of inflammation and the HPA axis.[34] This dysfunction and dysregulation later contribute to poorer overall physical health outcomes for the offspring because these physiological changes can affect the development of the offspring's immune system, consequently leading to increased risk of developing chronic illness and other health complications.[34] It is important to note, however, that more research is needed in this specific area of study to fully expound the impacts of these biochemical and physiological dysregulations on the offspring of maternal depression.[34]

Strong evidence in the literature demonstrates the relationship between maternal depression and various areas of early childhood development delay, notably in the socioemotional, behavioral, linguistic, and physical aspects. It is known that there is some interplay between all of these factors, but further research is needed to fully elucidate the relationship between them and the

extent to which one is affected while another aspect is delayed. Furthermore, even though the breadth of current literature is notable, the relationship between maternal depression and the outcomes of childhood developmental delays remains a prime topic for further research. Breakthroughs in this subject may yield better understanding on this condition and consequently lead to improved health benefits to these mothers with depression and their children.

Complications of Untreated Maternal Depression in Offspring: Late Childhood and Adult Development

In comparison with the extensive research showing the effects of untreated maternal depression in infancy and early childhood, there is less research on the effects in late childhood and adulthood. When evaluating mental health, some studies have shown an association between maternal prenatal depression and offspring depression from ages 16 to 24 years using sample populations from the Avon Longitudinal Study of Parents and Children (ALSPAC) in Avon, England.[11,13] ALSPAC is a 30-year longitudinal study based at the University of Bristol that recruited more than 14000 pregnant individuals from South West England between 1991 and 1992. By following these Individuals and their children, ALSPAC's goal is to assess how genetics and environmental factors influence parent and child development. A study by Whelan et al[13] used ALSPAC data and showed that prenatal maternal depression put both male and female offspring at risk for depressive symptoms at age 16 years.Click or tap here to enter text. Similarly, Pearson et al[11] performed a longitudinal cohort study on 2 generations of mothers and their pregnant daughters who participated in ALSPAC between the ages of 19 and 24 years. The study showed that maternal prenatal depression put their daughters at significantly higher risk of prenatal depression.[11] These studies together demonstrate an association between untreated prenatal maternal depression and depression seen in offspring.

There is also strong evidence showing that untreated prenatal maternal depression affects the offsprings' behavior in later childhood and adolescence.[14,15] Including 3298 mother and offspring pairs from the ALSPAC, Barker et al[14] looked at the risks of various child maladjustments at ages 7 and 8 years associated with prenatal and postnatal maternal depression and/or anxiety. Of note, this study showed that prenatal and postnatal maternal depression showed significantly more risk of *DSM-IV* externalizing disorders (ie, oppositional defiant disorder, conduct disorder, ADHD), internalizing disorders (ie, anxiety and depression), and decrease in verbal IQ.[14] Importantly, prenatal maternal depression was specifically associated with *DSM-IV* externalizing disorders and lower verbal IQ when compared with the postnatal period.[14] Additionally, a review by Morgan et al[15] supported this study's conclusion by showing that prenatal maternal depression was associated with antisocial behavior, specifically externalizing behavioral problems. Of the 20 studies Morgan et al[15] reviewed, 14 displayed a significant association between prenatal maternal depression and antisocial behavior of

offspring from early childhood into adolescence. The researchers also determined that cumulative exposure to maternal depression, especially beginning in the perinatal period, put offspring at greater risk for antisocial behavior.[15] In conclusion, prenatal maternal depression affects not only the mental health of their offspring, but also their behavior.

While there has been some evidence that untreated prenatal maternal depression alters the growth of certain brain structures in the fetus,[30] more studies looking at anatomical neurodevelopment continuing into adolescence and adulthood are still needed. These studies are necessary to better understand the biological mechanics behind the association of prenatal maternal depression and offspring outcomes. Of note, a study by Plant et al[16] looked at prenatal maternal depression and inflammation in the offspring at 25 years of age to look at this association. They found that prenatal maternal depression predicted significantly high-sensitivity C-reactive protein in the 25-year-old offspring, but awakening cortisol was not predictive as hypothesized by the investigators.[16] Plant et al[16] concluded that while their findings supported the developmental origins of the health and disease hypothesis, they did not show the grounding for this biological connection to be HPA axis dysregulation.Click or tap here to enter text. This study is in contrast to evidence showing that HPA axis dysregulation appears to play an important role in pregnancy complications, such as preeclampsia, as previously mentioned.[6] Further studies are needed to provide a more in-depth analysis of the biological basis for physical and psychopathology in offspring associated with prenatal maternal depression.

Discussion

The increased risks of preeclampsia, prolonged labor, cesarean delivery, and partaking in high-risk health behavior indicate that the risks of untreated depression in Childbearing and postpartum individuals is extends further than its historic portrayal as a mental illness. Although many of the tests, such as the PHQ, are subjective to diagnose major depression—giving rise to the possibility of inaccurate results—Bansil et al[6] found that there may be a greater inflammatory response in individuals with untreated depression, enabling the possibility of future objective tests.[9]

Untreated depression in pregnancy has deleterious physical effects on not only the mother, but also on the offspring for years to come. For example, Nylen et al[10] found that, physically, newborns born to mothers with gestational depression have an average lower birth weight than newborns born to mothers without gestational depression.[10] Additionally, their neurodevelopment is hindered by a possible epigenetic connection and corticolimbic improvement. However, further larger studies are needed to link these modulators and environmental stress more accurately.

The neurodevelopmental delays continue because these children are more prone to mood disorders, leading to a marked reduction in processing verbal, emotional, and social cues with other children their age as well as developing antisocial behavior.[15] Further, although the effects of maternal depression on preadult to adult offspring have not been thoroughly studied, there is evidence of a possible generational link between maternal depression and female offspring becoming depressed during their pregnancy.[11]

Going forward, the focus of new research should keep these hormonal and possible genetic mechanisms in mind when determining whether someone with a history of physical and psychological sequelae indicative of depression were born to a mother with major depression in pregnancy.

Limitations

This review article included studies that were conducted in non-US countries such as Iran, Canada, Turkey, Australia, and England. By using these studies, there may be limitations and differences in long-term sequelae due to potential variations in cultural contexts, health care systems, and research methodologies, which may affect the generalizability of findings for patients in the US.

Conclusions

Gestational depression has profound physical and biological implications for both the birthing parent and children. Studies have revealed that maternal stress during pregnancy can lead to adverse outcomes such as preterm birth, low birth weight, and developmental delays in children. Additionally, the biological changes triggered by gestational depression, such as altered cortisol levels and disrupted neurodevelopmental function, can have long-lasting effects on the child's health, increasing the risk for mental health disorders. Moving forward, it is crucial for future research to delve deeper into the underlying mechanisms linking gestational depression to these physical and biological consequences and to explore effective interventions and support systems that can mitigate these effects and promote the well-being of both birthing parents and their children.

Disclaimers

None.

Conflict of Interests

None.

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