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Hypertension During Pregnancy: A Link to Post-Partum Depression and Anxiety?

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Abstract

Hypertension during pregnancy is a common occurrence affecting 3-10% of pregnancies, while depression and anxiety in different stages of pregnancy are at a higher yield with almost 30-70% of women reporting depressive like symptoms. This mini review seeks to explore the correlation between hypertensive disorders during pregnancy such as preeclampsia and HELLP syndrome and prevalence of postpartum depression (PPD) or postpartum anxiety (PPA). Studies show women with PPD and or PPA with a history of Preeclampsia, HELLP or Normal pregnancies have no statistical differences. The review of literature identifies a clear lack of prospective trials. This is a limiting factor that could lead to the misrepresentation of statistical differences. Also the way these women are evaluated further compounds the problem in that only three recognized instruments are designed to assess PPD while several studies use the self-report and recall test which yields less than accurate results. Systemic inflammation is common in depression and anxiety in both sexes is also prevalent in pregnant women with hypertension, also suggesting a correlation. Neuroinflammation has been shown to cause cerebral autoregulation dysfunction which may cause disruption of the blood-brain barrier leading to temporary or permanent neurological changes. These neuronal changes could be the cause of depression and anxiety in pregnancy. While there is currently no definitive association between hypertensive disorders, PPD and PPA the same underlying factors that cause neuronal damages and neuroinflammation are common between all three conditions.

Keywords: Anxiety; Blood-brain barrier; Hypertension; Inflammation Post-partum depression; Pregnancy

Abbreviations: BBB: Blood Brain Barrier; HELLP: Hemolysis Elevated Liver Enzyme and Low Platelets; PPA: Post-Partum Anxiety; PPD: Post-Partum Depression; PreE: Preeclampsia; PTSD: Post-traumatic Stress Disorder

Introduction

Depression during the childbearing years is the 2nd leading cause of disability among women with an increased risk during the perinatal period [1,2]. During the prenatal period almost 70% of women have reported symptoms of depression during pregnancy [3,4] while 10-43% of women meet the criteria for depression [5,6]. Stress and anxiety are also often linked to depression especially in the postpartum period and is thought to affect between 5-20% of women [7,8]. Hypertension affects 3-10% of pregnancies [9,10] and is most commonly manifested as either preeclampsia (PreE) or HELLP (Hemolysis Elevated Liver enzyme Low Platelet) syndrome. HELLP occurs in 10-20% of women with PreE and in 0.5% of women without PreE [11-13].

Discussion

Hypertensive pregnancies and post-partum depression and post-partum anxiety

Hypertensive disorders during pregnancy are associated with adverse birth outcomes, many of which have been found to be associated with perinatal depression. As described in a meta-analysis by Grote et al [14] preterm birth and low birth weight were found to be significantly associated with depression in some of the studies examined. Despite these associations, studies have reported conflicting data as to whether women with a history of high risk pregnancies such as PreE and HELLP syndrome experience PPD or PPA. If the mental health disturbances they experience are due to their maternal disorders or with having

babies admitted to the neonatal intensive care unit or possibly who have died [15].

A systematic review by Delahaije et al discusses the findings from six studies (4 retrospective and 2 prospective) which examined the prevalence of PPD and PPA (either anxiety or post-traumatic stress disorder; PTSD) in women with a history of PreE, HELLP vs women with normal pregnancies [16]. They concluded that there was not a clear statistical indication of PPD among women with PreE and HELLP despite positive associations with depressive symptoms. However, similar to what Grote et al reported there is a clear relationship between depression and having a preterm vs term baby. Having a pregnancy complicated by either PreE or HELLP syndrome was statistically associated with PTSD and while women with a PreE pregnancy had more traits for anxiety it was not statistically significant compared to normal pregnant women.

One of the more pressing problems with identifying a relationship between hypertensive pregnancies and PPD/PPA is the lack of prospective clinical trials. Currently there are 5 trials listed in clinical trials.gov that have hypertension as a direct or indirect factor associated with PPD and/or PPA and fewer have been published. Adding to this conundrum are the mixed survey instruments that are performed across retrospective and prospective studies. The Bromley Postnatal Depression Scale, Edinburgh Postnatal Depression Scale and the Postpartum Depression Screening Scale are the only three instruments that are designed to assess PPD [17]. However, several studies have used self-report and recall to assess PPD or PPA which can yield less than accurate results.

Inflammation,hypertensive pregnancieanddepression and anxiety

Systemic inflammation has long been associated with major depression and with anxiety in both men and women [18,19]. Inflammation has also been associated with the progression of symptoms and in contributing to hypertension in both PreE and HELLP syndrome [20-22]. Additionally during pregnancy the brain is particularly susceptible to inflammatory changes in the peripheral circulation which may make it vulnerable to neuroinflammation. While the exact etiology of HELLP and PreE remain unknown, they are most commonly thought to originate from abnormal remodeling of the uterine spiral arteries, which creates an ischemic placenta that secretes and stimulates factors leading to the pathophysiology of these disorders [23,24]. The neurological symptoms include headaches and visual impairments and upon neuroimaging can include evidence of white matter lesions, hemorrhage and cerebral edema [25-29].

One mechanism thought to play a role in the development of these neurological complications is impaired cerebral autoregulation [30,31]. Cerebral autoregulation is a vital physiologic process that allows the maintenance of cerebral perfusion pressure despite fluctuations in blood pressure, maintained in part by vasoconstriction and vasodilation of cerebral vessels [30-32]. The BBB is a highly complex neurological structure that plays a crucial role in maintaining neuronal homeostasis and cerebral autoregulation [33]. Disruption of the BBB may allow for the transfer of harmful chemicals into the brain and negatively affect neuronal homeostasis and its disruptied BBB can be detrimental to the CNS leading to temporary or permanent neurological changes.

Interestingly, BBB disruption has been implicated in the hypertensive disorders of pregnancy [33-35]. Disruption in women with hypertensive disorders of pregnancy suffer not only immediate consequences from this disorder but also long term sequelae [36], thereby highlighting the importance of BBB disruption and ultimately these neurological events. The exact underlying mechanisms causing BBB dysfunction seen in women with PreE and HELLP remain unknown; however, the acute hypertension and peripheral inflammation either alone or in combination is thought to alter BBB permeability and contribute to the varying neurological complications [37-39]. It is also well established in both human and animal studies that circulating factors, potentially inflammatory factors, in subjects with PE or HELLP syndrome contribute to BBB disruption and neuroinflammation [20,34,35,39,40]. Therefore one could postulate that the increase in BBB permeability or decrease in BBB function could contribute to changes in the neural environment during pregnancy or the immediate post-partum period.

Conclusion

In conclusion, as untreated and unrecognized perinatal depression is still one of the best predictors for PPD and/or PPA it is important for women and their health providers to discuss mental health during their prenatal care and post-partum care [41]. Additionally, as pharmacologic therapy, primarily anti-depressants, during pregnancy have been associated with an increased risk for preterm birth and low birth weight as well as potentially developmental problems in the offspring it is important to understand some of the mechanisms that might contribute to PPD and/or PPA [42,43]. The data thus far only allows for us to make a causal association regarding the likelihood women with PreE or HELLP syndrome develop PPD and/or PPA. It is also recommended that future prospective studies utilize one of the three approved post-partum instruments to help with future translation.728)

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