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A COMPREHENSIVE REVIEW OF HYPERTENSIVE DISORDERS IN PREGNANCY: CURRENT PERSPECTIVES AND FUTURE DIRECTIONS

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ABSTRACT Hypertensive disorders during pregnancy encompass various conditions, including preeclampsia, gestational hypertension, chronic hypertension, and preeclampsia superimposed on chronic hypertension. Accurate diagnosis is crucial for management decisions, timing of delivery, and assessing maternal prognosis. Healthcare providers must consider other medical disorders with similar features. PlGF-based tests can aid in ruling in or ruling out preeclampsia between 20+0 and 36+6 weeks of gestation, offering improved prediction capabilities. Differentiating between these disorders can be challenging, but careful examination of blood pressure trends, proteinuria, and end-organ dysfunction signs can help. Recurrence rates of preeclampsia in subsequent pregnancies are significant, and it is associated with long-term maternal cardiovascular risks and diseases. Personalized management strategies and biomarkers hold promise for future research in preeclampsia, providing better prediction and intervention strategies for improved maternal and offspring outcomes.

KEYWORDS : Hypertension, Pregnancy, Preeclampsia.

INTRODUCTION

Hypertensive disorders during pregnancy encompass a range of conditions, including preeclampsia, gestational hypertension, chronic hypertension, and preeclampsia superimposed on chronic hypertension. Accurate diagnosis is crucial for making management decisions, such as the timing of delivery and the need for antiseizure prophylaxis, as well as assessing maternal prognosis and long-term health risks. Additionally, healthcare providers must consider other medical disorders, such as glomerulonephritis or thrombotic microangiopathies, which may present with similar clinical and laboratory features. In some regions, PlGF-based tests are recommended as adjuncts to standard clinical assessment for ruling in or ruling out preeclampsia between 20+0 and 36+6 weeks of gestation, offering improved prediction capabilities for the condition. The US FDA has also approved a PlGF-based test for pregnant patients hospitalized with hypertension to predict progression to severe preeclampsia within two weeks (1,2).

Methods

To conduct a narrative review on hypertensive disorders during pregnancy, an exhaustive and systematic search strategy would be implemented in scientific databases such as PubMed, Scopus, and Web of Science. Relevant search terms would include "preeclampsia," "gestational hypertension," "chronic hypertension," "eclampsia," "HELLP syndrome," and other related terms. Additionally, key phrases such as "pregnancy," "obstetric complications," and "hypertension" would be included. The strategy would also involve manually searching references in relevant articles and exploring gray literature. Careful evaluation of studies would be conducted, and only those providing solid and pertinent information to address the research question of the narrative review would be selected.

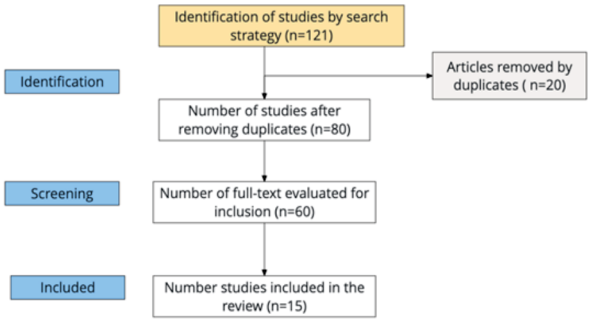

Figure 1. PRISMA.

Distinguishing Hypertensive Disorders During Pregnancy

Hypertensive disorders during pregnancy can pose significant challenges in accurate diagnosis and appropriate management. This article delves into the differential diagnosis among patients presenting with hypertension as the primary finding during pregnancy. It explores key distinctions between chronic hypertension, preeclampsia, superimposed preeclampsia, and gestational hypertension, offering crucial insights for obstetric providers (3).

Distinguishing between different hypertensive disorders during pregnancy is crucial for appropriate management. Chronic hypertension and preeclampsia can have overlapping features, but assessing blood pressure trends throughout pregnancy can help differentiate them. Chronic hypertension is characterized by an early reduction in blood pressure followed by a gradual increase to pre-pregnancy levels. However, since preeclampsia can rapidly progress, close monitoring is essential (4).

In individuals with chronic hypertension, identifying superimposed preeclampsia is critical. New-onset proteinuria and elevated serum urate levels indicate superimposed preeclampsia. For patients with chronic kidney disease, distinguishing between disease exacerbation and preeclampsia is important. Specific laboratory evidence, timing of hypertension, and proteinuria patterns aid in establishing a definitive diagnosis. Gestational hypertension and preeclampsia can also be challenging to differentiate. Careful examination of hypertension onset, urine protein excretion, and absence of end-organ dysfunction signs is necessary. Both conditions are managed similarly, given similar complication rates (5).

Hypertension combined with thrombocytopenia or elevated transaminases in pregnant patients is often indicative of preeclampsia with severe features. However, alternative diagnoses must be considered to ensure accurate and timely management. This article presents key distinctions among various conditions to aid in the differential diagnosis and facilitate appropriate clinical decisions (6).

HELLP Versus Preeclampsia With Severe Features

HELLP syndrome presents with hemolysis, elevated liver enzymes, and thrombocytopenia as prominent features, distinguishing it from preeclampsia with severe features. Although hypertension may be present in HELLP, it is not the main characteristic, and the correlation between blood pressure elevation and liver dysfunction may be limited. On

the other hand, most cases of preeclampsia with severe features display severe hypertension, with less marked abnormalities in thrombocytopenia and liver function (7).

While preeclampsia with severe features/HELLP is the most common cause of hypertension, thrombocytopenia, and abnormal liver and renal chemistries in pregnant patients, other conditions should be taken into account and excluded if possible. Among these are acute fatty liver of pregnancy (AFLP), thrombotic microangiopathy (TTP and HUS), systemic lupus erythematosus (SLE), and antiphospholipid syndrome (APS). Distinguishing AFLP from preeclampsia with severe features/HELLP can be challenging due to overlapping clinical and histological features. However, some key differences exist, such as serum fibrinogen levels below 300 mg/dL in AFLP, whereas in preeclampsia with severe features/HELLP, levels usually remain above this threshold. Other factors, including time of onset, hypertension prevalence, liver dysfunction severity, and kidney involvement, can aid in differentiation (8).

TTP and HUS present with thrombocytopenia and hemolysis, akin to preeclampsia with severe features/HELLP. However, differentiating factors include the presence of kidney injury in HUS, the severity of platelet consumption in TTP, and the levels of aspartate aminotransferase, alanine aminotransferase, and LDH. Timely differentiation is essential, as plasma exchange is life-saving in acquired TTP but not useful in preeclampsia with severe features/HELLP (9).

SLE flares can be mistaken for preeclampsia with severe features/HELLP, particularly in cases involving lupus hepatitis or nephritis. Differentiating features may include hypocomplementemia and increased anti-DNA antibody titers in SLE, whereas hemolytic anemia is more common in preeclampsia with severe features/HELLP. APS, characterized by hypertension, proteinuria, thrombocytopenia, and end-organ dysfunction, can mimic preeclampsia with severe features. Testing for antiphospholipid antibodies may be indicated in specific cases. Accurate diagnosis is vital for appropriate management (10).

Preeclampsia: Future Directions And Long-term Risks In Subsequent Pregnancies

Preeclampsia is a serious pregnancy complication characterized by high blood pressure and organ damage, particularly affecting the liver and kidneys. It remains a leading cause of maternal and perinatal morbidity and mortality worldwide. While the management of preeclampsia during pregnancy has improved over the years, there is still a need to address its long-term consequences and develop strategies for subsequent pregnancies (11).

Long-term Risks

Preeclampsia has far-reaching effects beyond the immediate pregnancy period. Studies have shown that the risk of preeclampsia recurrence in subsequent pregnancies is significant, particularly if the previous preeclampsia was of early onset or complicated by severe features. A meta-analysis of individual participant data from various studies revealed that around 15% of women with a history of preeclampsia experience gestational hypertension, and another 15% develop preeclampsia in their subsequent pregnancies. The recurrence rate can be as high as 50% in certain cases. Beyond the realm of subsequent pregnancies, strong epidemiological evidence links preeclampsia with long-term maternal cardiovascular risks and diseases. Cardiovascular disease is the leading cause of death among women, and preeclampsia appears to be a significant risk factor. Compared to women with normotensive pregnancies, those who experienced preeclampsia during pregnancy have a four-fold increased risk of developing hypertension, particularly within two years postpartum. Additionally, they are approximately twice as likely to develop type 2 diabetes and dyslipidemia (12).

The association between preeclampsia and cardiovascular risk is complex. While some risk factors are shared between preeclampsia and cardiovascular disease, other underlying mechanisms may be unique to each condition. Women with preeclampsia may have pre-existing subclinical cardiac or vascular abnormalities that predispose them to vascular or metabolic diseases during pregnancy. Moreover, it is theorized that preeclampsia itself may damage the maternal cardiovascular system. However, adjusting for conventional cardiovascular risk factors eliminates or significantly reduces any observed association between hypertension during pregnancy (including preeclampsia) and cardiovascular disease. Despite these findings, some studies have reported inconsistent estimates of the effect of prolonged maternal exposure to preeclampsia due to expectant management on cardiovascular disease (13).

Future Directions

The identification of biomarkers (maternal, fetal, or placental) and the development of dynamic multivariable models hold promise for future research in preeclampsia. Such biomarkers and models have the potential to provide novel insights into preeclampsia phenotypes, enhance prediction and management of the condition, and personalize care during and after pregnancy (14).

A personalized approach to managing cardiovascular risk in women with a history of preeclampsia is essential. The use of biomarkers and multivariable models can help identify high-risk individuals, enabling targeted interventions. Moreover, investigating the role of lifestyle modifications, such as dietary interventions, exercise programs, and weight management, in reducing long-term cardiovascular risks associated with preeclampsia will be crucial. The American Heart Association recommends that women with a history of hypertension during pregnancy, including preeclampsia, undergo cardiovascular risk screening within three months after delivery. However, current prediction models have limitations in accurately assessing cardiovascular risks over a 10-year period for young women. Therefore, developing a personalized risk prediction model based on a large population cohort remains a challenge (15).

In conclusion, understanding the long-term risks of preeclampsia and implementing personalized management strategies are vital for improving maternal and offspring outcomes. The exploration of biomarkers and dynamic models presents an exciting avenue for more effective prediction, prevention, and intervention strategies for women with a history of preeclampsia in subsequent pregnancies and beyond. By addressing the long-term consequences of preeclampsia, researchers and healthcare professionals can contribute to healthier pregnancies and improved cardiovascular outcomes for women in the future.

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