

The Role of Maternal Hypertension in the Development of Preeclampsia : A Literature Review

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ABSTRACT

Maternal hypertension is a critical factor in the development of preeclampsia, a pregnancy-related condition characterized by high blood pressure and potential complications for both the mother and fetus. This literature review explores the complex interplay of genetic, immunological, and environmental factors leading to preeclampsia, with a focus on the role of maternal hypertension. The condition can be categorized into preeclampsia with and without severe features, impacting both maternal and fetal health. The pathophysiology of preeclampsia involves insufficient placental blood flow and a cascade of inflammatory responses that disrupt normal blood vessel function. Diagnosis hinges on blood pressure measurements and proteinuria, with severe cases marked by additional clinical symptoms such as organ dysfunction and neurological issues. Managing preeclampsia involves careful monitoring and, in severe cases, delivery to prevent worsening conditions. Long-term risks include cardiovascular complications for affected mothers. This review highlights the importance of early detection and management to reduce adverse outcomes for both mothers and newborns.

Keywords: maternal hypertension; preeclampsia; pregnancy; high blood pressure.

INTRODUCTION

Maternal hypertension is vital in the onset of preeclampsia, a complicated pregnancy condition that poses serious dangers to both the mother and the fetus [1]. Preeclampsia is marked by elevated blood pressure and is often seen with protein in the urine, which can result in serious issues like organ failure, eclampsia, and early delivery [2]. Hypertension, whether it exists before pregnancy or arises during it, is a significant factor in developing preeclampsia and can worsen its intensity [3]. Preeclampsia is a complex condition linked to pregnancy, and its underlying mechanisms are still not completely clear. Additionally, it is referred to as a placental disorder since it is caused by a lack of proper placental function [4].

Preeclampsia with complications is commonly called the "disease of theory" because, so far, no individual theory has completely clarified its causes and development [5]. The complications associated with preeclampsia can be categorized into those that impact the mother and those that impact the fetus.

Maternal complications consist of eclampsia, placental detachment, subcapsular bleeding, blood clotting issues (DIC), and HELLP syndrome (hemolysis, elevated liver enzymes, and a low platelet count) [6]. Fetal complications may involve inhibited growth within the uterus, early delivery, newborn asphyxia, and stillbirth, along with higher rates of perinatal illness and death [7]. Preeclampsia itself poses a considerable threat to both maternal and newborn health. Several risk factors lead to the development of preeclampsia, such as maternal age, number of pregnancies, body mass index (BMI), past preeclampsia incidents, diabetes, high blood pressure, and levels of work and exercise. Preeclampsia itself is a significant risk factor for both maternal and neonatal problems. Various risk factors contribute to the occurrence of preeclampsia, including maternal age, parity, BMI, a history of preeclampsia, diabetes mellitus, hypertension, as well as occupational and physical activity levels [8]. Preeclampsia frequently happens in mothers with a background of several existing health issues. These preexisting medical problems can lead to higher blood pressure while pregnant, potentially initiating the development of preeclampsia [9].

Grasping the physiological processes that connect maternal hypertension to preeclampsia is important for timely diagnosis and treatment, aiding in the reduction of possible health risks. This condition is shaped by numerous genetic, environmental, and immune factors, presenting a complex challenge that needs thorough medical attention. By investigating the detailed influence of maternal hypertension on the advancement of preeclampsia, healthcare providers can more effectively recognize populations at risk, take preventive action, and refine treatment plans to safeguard both maternal and fetal well-being.

RESULTS AND DISCUSSION

1. Preeclampsia

1.1 Definition and Classification of Preeclampsia

Preeclampsia is hypertension that occurs during pregnancy after the 20th week and is accompanied by significant proteinuria. High blood pressure or hypertension is characterized by a systolic blood pressure ≥ 140 mmHg or a diastolic blood pressure ≥ 90 mmHg [10]. Proteinuria can also occur as a result of hypertension, although the onset of this symptom is slower than weight gain. During pregnancy, weight gain in pregnant women is normal. However, if there is a weight gain of 1 kg or more each week, it is important to be alert to the possibility of preeclampsia [11].

Preeclampsia often occurs in pregnant women who have hypertension [12]. Preeclampsia is a condition characterized by high blood pressure, elevated levels of protein in the urine (proteinuria), and fluid retention in the body [13]. The prevalence of preeclampsia varies between countries and is more common in developing countries than in developed ones, due to better prenatal care in developed countries [14]. The occurrence of preeclampsia is influenced by several factors such as parity, race, genetic factors, and the environment.

The latest classification for preeclampsia no longer divides it into 'mild' and 'severe' categories but instead into preeclampsia 'with severe features' and 'without severe features'. This change aims to enhance awareness of all cases of preeclampsia (PE) that could suddenly worsen [15].

- Signs and symptoms of PE: a. Blood pressure measured at 140/90 mmHg or higher after being checked twice at one-hour intervals over six hours while in a lying position. b. Protein levels in the urine exceeding 0.3 g/liter or showing a 2+ result. c. General swelling in the feet, hands, and face, or a weight gain of 1 kilogram per week [16].
- Criteria for diagnosing severe preeclampsia (PEB): a. Systolic BP ≥ 160 mmHg, diastolic BP ≥ 110 mmHg. b. Serum creatinine level > 1.1 mg/dl. c. Pulmonary edema. d. Platelet count $< 100,000/\mu\text{L}$. e. Liver function elevated (more than twice normal). f. Symptoms such as headache, vision disturbances, and epigastric pain (impending eclampsia). g. Fetal growth restriction [15].

1.2 Diagnosis of Preeclampsia

To confirm the diagnosis of preeclampsia, the systolic blood pressure must increase by 30 mmHg or more from the normal level or reach 140 mmHg or higher. An increase in diastolic blood pressure is

considered more reliable if it rises by 15 mmHg or more or reaches 90 mmHg or higher, thus confirming a diagnosis of hypertension [17]. Blood pressure measurements should be taken at least twice, with a 6-hour interval, while at rest. Additionally, detecting protein in the urine is crucial for diagnosing and managing hypertension during pregnancy. High protein levels in the urine in preeclampsia can be a warning sign for fetal health, increase the risk of low birth weight, and raise the likelihood of perinatal death [18]. If proteinuria is not detected, other signs and symptoms can be used to diagnose preeclampsia [19].

- Basic criteria for preeclampsia are:
 - (1) Blood pressure higher than 140/90 mmHg occurring after 20 weeks of pregnancy in a woman who previously had normal blood pressure.
 - (2) Protein levels in the urine exceeding 300 mg within 24 hours or a urine dipstick test greater than +1.
- Criteria for diagnosing severe preeclampsia include any of the following clinical conditions:
 - (1) Blood pressure higher than 160/100 mmHg.
 - (2) Proteinuria: a dipstick test showing greater than +2 or 2.0 g/24 hours.
 - (3) Kidney dysfunction: serum creatinine ≥ 1.2 mg/dL or an increase in serum creatinine without other kidney abnormalities.
 - (4) Pulmonary edema.
 - (5) Liver dysfunction: an increase in transaminase levels more than twice normal and/or pain in the epigastric area or upper right abdomen.
 - (6) Thrombocytopenia: platelets less than 100,000/microliter.
 - (7) Neurological symptoms such as headaches, stroke, and vision disturbances.
 - (8) Fetal growth restriction (FGR) and signs of uteroplacental circulation impairment, such as oligohydramnios [19].

• Pathophysiology of Preeclampsia

The pathophysiology of preeclampsia is highly complex, involving interrelated genetic, immunological, and environmental factors. There are two stages of preeclampsia, which depend on the signs that appear. The first stage is asymptomatic and is characterized by abnormal placental growth during the first trimester. Abnormal placental growth, particularly angiogenesis, leads to inadequate blood supply to the placenta and the release of placental material into the maternal circulation. This release of placental material triggers the second stage of preeclampsia, which is marked by symptoms such as high blood pressure, kidney problems, proteinuria, and the risk of developing HELLP syndrome, eclampsia, and other organ damage. Preeclampsia is thought to occur due to inadequate trophoblast invasion of the placenta, followed by widespread maternal endothelial dysfunction. The placenta plays a crucial role in the development and resolution of preeclampsia [20]

2. Hypertension in Pregnancy

Any pregnancy-related high blood pressure issue can lead to preeclampsia. This condition appears in as many as 35% of women who have gestational hypertension and in up to 25% of those with chronic hypertension. The specific processes that cause the development of preeclampsia are not fully understood, but it is believed to involve a reduction

in blood flow to the placenta, which leads to problems with blood vessel lining across the body. This issue stems from a less efficient invasion of the uterine spiral arteries by the cytotrophoblasts. The resulting lack of oxygen in the placenta triggers a series of inflammatory reactions, causing an imbalance of factors that promote blood vessel growth, and leads to the clumping of platelets, all contributing to blood vessel lining issues that are clinically recognized as the preeclampsia syndrome [21].

A history of high blood pressure increases the risk of severe preeclampsia. According to research analysis, all mothers with a history of hypertension experienced severe preeclampsia (PEB) [22]. Hypertension occurring before pregnancy can damage vital organs. Additionally, during pregnancy, weight gain can lead to more serious complications, as indicated by edema and proteinuria [23]. In studies on chronic hypertension, it was found that 19.83% of recurrent preeclampsia cases were due to this condition. Most pregnancies with essential hypertension proceed normally until full term. About one-third of women with high blood pressure after 30 weeks do not show any other symptoms. However, around 20% of them experience a more significant increase in blood pressure, which may be accompanied by one or more preeclampsia symptoms, such as edema, proteinuria, headaches, upper abdominal pain, nausea, and vision disturbances (superimposed preeclampsia), and can even lead to eclampsia and brain hemorrhage [24].

2.1 Management

A diagnosis of pre-eclampsia necessitates hospitalization due to the condition's ability to deteriorate quickly and the higher chance of placental abruption, particularly when it occurs alongside chronic hypertension. The only recognized 'treatment' is delivery. At term, either induction of labor or delivery is required. In cases where the pregnancy is <34 weeks and there is a positive clinical response to treatment, efforts should be made to extend the gestation to lower the chances of neonatal health issues by managing blood pressure effectively. Gestation may continue as long as blood pressure is adequately managed, there are no indications of severe maternal complications (such as DIC, HELLP, eclampsia), and fetal monitoring shows reassuring results [25]. The goal of controlling high blood pressure during pregnancy is to lessen health problems and deaths for both the mother and baby. This means avoiding the dangers linked to high blood pressure, stopping the illness from worsening, preventing seizures, and considering ending the pregnancy if the mother or baby is in a life-threatening condition [26].

There is inconsistency in the criteria for starting antihypertensive therapy due to doubts regarding the advantages for the mother from lowering blood pressure and the possible risks to the fetus from reduced blood flow caused by medications and from exposure to these medications during pregnancy [27]. Antihypertensive therapy in pregnancy lessens the incidence of serious hypertension (blood pressure of $\geq 160/110$ mm Hg) but does not appear to enhance maternal, fetal, or neonatal results and is linked to a higher chance of low birth weight for gestational age. Consequently, guidelines for treating pregnant women with chronic hypertension differ among global health organizations.

There is agreement on treating those with severe hypertension, but for patients with mild chronic hypertension (typically considered as blood pressure under 160/110 mm Hg), it remains uncertain whether to stop antihypertensive drugs until the blood pressure becomes severe or to maintain the patient's prior treatment plan [28].

2.2 Future Risk

Hypertensive conditions during pregnancy (HDP) affect 5% to 10% of pregnancies and are becoming more common as cardiometabolic diseases rise among younger women [29]. Numerous research projects have shown that women experiencing preeclampsia exhibit issues such as segmental heart muscle impairment, dysfunction in both heart chambers, and enlargement, along with a weakened blood flow state and indirect ultrasound indicators of localized heart tissue damage and scarring [30]. Women in stage 1 hypertension face a higher chance of experiencing pregnancy-related hypertensive issues at younger gestational ages than women with normal blood pressure; however, those with stage 1 hypertension generally encounter less severe hypertensive pregnancy complications compared to women with stage 2 hypertension [31].

CONCLUSIONS

Maternal hypertension plays a significant role in the development of preeclampsia, which can have severe consequences for both the mother and fetus. The condition is complex, influenced by multiple interrelated factors, and its pathophysiology remains a subject of ongoing research. Understanding the role of maternal hypertension in preeclampsia development is essential for early diagnosis and intervention, which can mitigate potential complications and improve maternal and fetal outcomes. Proper management, including blood pressure control and timely delivery when necessary, is crucial to minimize risks. Future research should focus on refining diagnostic criteria and treatment strategies to enhance patient care and long-term health, as women with a history of preeclampsia are at higher risk of cardiovascular issues later in life.

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REFERENCES

- [1] Chang, K. I., Seow, K. M., & Chen, K. H. (2023). Preeclampsia: Recent advances in predicting, preventing, and managing the maternal and fetal life-threatening condition. *International journal of environmental research and public health*, 20(4), 2994.
- [2] Narkhede, A. M., & Karnad, D. R. (2021). Preeclampsia and related problems. *Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine*, 25(Suppl 3), S261.
- [3] Ramos, I. G. L., Sass, N., & Costa, S. H. M. (2017). Preeclampsia. *Revista Brasileira de Ginecologia e Obstetrícia/RBGO Gynecology and Obstetrics*, 39(09), 496-512.

- [4] Nirupama, R., Divyashree, S., Janhavi, P., Muthukumar, S. P., & Ravindra, P. V. (2021). Preeclampsia: Pathophysiology and management. *Journal of gynecology obstetrics and human reproduction*, 50(2), 101975.
- [5] Martadiansyah, A., Qalbi, A., Santoso, B., Obstetri Dan Ginekologi, B., Kedokteran, F., Sriwijaya, U., & Mohammad Hoesin, R. (2019). Sriwijaya Journal Of Medicine. Kejadian Preeklampsia Dengan Komplikasi Dan Faktor Risiko Yang Mempengaruhinya Di RSUD Mohammad Hoesin Palembang.
- [6] Hiregoudar, P. (2017). *Clinical Study of Maternal and Fetal Outcome in Preeclampsia with Thrombocytopenia* (Master's thesis, Rajiv Gandhi University of Health Sciences (India).
- [7] Kathuria, K. (2023). Impact of Maternal Health and Disease on Neonatal Outcome. In *Clinical Anesthesia for the Newborn and the Neonate* (pp. 11-27). Singapore: Springer Nature Singapore.
- [8] Fox, R., Kitt, J., Leeson, P., Aye, C. Y. L., & Lewandowski, A. J. (2019). Preeclampsia: Risk Factors, Diagnosis, Management, and the Cardiovascular Impact on the Offspring. *Journal of clinical medicine*, 8(10), 1625. <https://doi.org/10.3390/jcm8101625>
- [9] Bokslag, A., van Weissenbruch, M., Mol, B. W., & de Groot, C. J. (2016). Preeclampsia; short and long-term consequences for mother and neonate. *Early human development*, 102, 47-50.
- [10] Lambert, G., Brichant, J. F., Hartstein, G., Bonhomme, V., & Dewandre, P. Y. (2014). Preeclampsia: an update. *Acta Anaesthesiol Belg*, 65(4), 137-49.
- [11] Spradley, F. T., Palei, A. C., & Granger, J. P. (2015). Increased risk for the development of preeclampsia in obese pregnancies: weighing in on the mechanisms. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, 309(11), R1326-R1343.
- [12] Ramos, J. G. L., Sass, N., & Costa, S. H. M. (2017). Preeclampsia. *Revista Brasileira de Ginecologia e Obstetrícia/RBGO Gynecology and Obstetrics*, 39(09), 496-512.
- [13] August, P., & Sibai, B. M. (2017). Preeclampsia: Clinical features and diagnosis. *Post TW, UpToDate. Waltham, MA: UpToDate.*
- [14] Zhang, N., Tan, J., Yang, H., & Khalil, R. A. (2020). Comparative risks and predictors of preeclamptic pregnancy in the Eastern, Western and developing world. *Biochemical pharmacology*, 182, 114247.
- [15] Akbar M, Wardhana, Annas, Dharmawan (2018). Gawat Darurat Medis dan Bedah, pp 193- 198.
- [16] Rizki Rahmawati (2020). Faktor Faktor Yang Mempengaruhi Preeklampsia: Literature Review. <http://repository.unimus.ac.id/4597/5>
- [17] Ni Komang Ayu Puspitasari (2019). Hubungan Usia Dengan Derajat Preeklampsia Pada Ibu Hamil Di RSUD Wangaya Tahun 2019.
- [18] Santoso, A. P. R., Masruroh, N., Amalia, I. N., & Santy, W. H. (2020). Relationship Between Blood Pressure and Urine Protein in Preeclampsia at Prima Husada Hospital Sidoarjo. *Medicra (Journal of Medical Laboratory Science/Technology)*, 3(2), 54-58. <https://doi.org/10.21070/Medicra.V3i2.1081>
- [19] Erna Handayani (2021). Faktor-Faktor Yang Mempengaruhi Kejadian Preeklampsia Di Rsd Wates Kabupaten Kulon Progo DIY Tahun 2019. <http://eprints.poltekkesjogja.ac.id/2187/1>
- [20] Dwi Erawati (2022). Hubungan Faktor Usia Ibu Hamil Dengan Kejadian Pre Eklampsia-Di Puskesmas Kesongo Kecamatan Kedungadem Kabupaten Bojonegoro. <http://repo.stikesicme-jbg.ac.id/id/eprint/6384>
- [21] Braunthal S, Brateanu A. Hypertension in pregnancy: Pathophysiology and treatment. *SAGE Open Medicine*. 2019;7. doi:10.1177/2050312119843700
- [22] Zakiyah, N., Tuytten, R., Baker, P. N., Kenny, L. C., Postma, M. J., van Asselt, A. D., & IMPROVED Consortium. (2022). Early cost-effectiveness analysis of screening for preeclampsia in nulliparous women: A modelling approach in European high-income settings. *PLoS One*, 17(4), e0267313.
- [23] Moussa, H. N., Arian, S. E., & Sibai, B. M. (2014). Management of hypertensive disorders in pregnancy. *Women's health*, 10(4), 385-404.
- [24] Septiasih (2017). Faktor Risiko Kejadian Preeklampsia Ibu Bersalin Di Rsd Wonosari Kabupaten Gunungkidul Tahun 2017. <http://eprints.poltekkesjogja.ac.id/1679/1>
- [25] Foo, L., Tay, J., Lees, C. C., McEniery, C. M., & Wilkinson, I. B. (2015). Hypertension in pregnancy: natural history and treatment options. *Current hypertension reports*, 17, 1-18.
- [26] Reddy, S., & Jim, B. (2019). Hypertension and pregnancy: management and future risks. *Advances in chronic kidney disease*, 26(2), 137-145.
- [27] Garovic, V. D., Dechend, R., Easterling, T., Karumanchi, S. A., McMurtry Baird, S., Magee, L. A., ... & August, P. (2022). Hypertension in pregnancy: diagnosis, blood pressure goals, and pharmacotherapy: a scientific statement from the American Heart Association. *Hypertension*, 79(2), e21-e41.
- [28] Tita, A. T., Szychowski, J. M., Boggess, K., Dugoff, L., Sibai, B., Lawrence, K., ... & Andrews, W. W. (2022). Treatment for mild chronic hypertension during pregnancy. *New England Journal of Medicine*, 386(19), 1781-1792.

- [29] Ying, W., Catov, J. M., & Ouyang, P. (2018). Hypertensive disorders of pregnancy and future maternal cardiovascular risk. *Journal of the American Heart Association*, 7(17), e009382.
- [30] Melchiorre, K., Thilaganathan, B., Giorgione, V., Ridder, A., Memmo, A., & Khalil, A. (2020). Hypertensive disorders of pregnancy and future cardiovascular health. *Frontiers in cardiovascular medicine*, 7, 59.
- [31] Sabol, B. A., Porcelli, B., Diveley, E., Meyenburg, K., Woolfolk, C., Rosenbloom, J. I., ... & Stout, M. J. (2021). Defining the risk profile of women with stage 1 hypertension: a time to event analysis. *American journal of obstetrics & gynecology MFM*, 3(4), 100376.