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Prediction of Preeclampsia Using Maternal Factors, Biochemical Markers, and Uterine Artery Doppler

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Abstract
Pregnancy-related hypertensive diseases are a major global cause of maternal and perinatal death. Preeclampsia (PE) is a pregnancy disease that often manifests after 20 weeks of gestation and generally occurs close to term.Our aim of work was to achieve early prediction of preeclampsia using maternal factors, biochemical markers, and uterine artery doppler. This review was conducted following a narrative review approach via searching many databases such as PubMed, Scopus and Google Scholar. We came to the conclusion that early diagnosis, timely medical management, and adequate surveillance and monitoring are imperative to decreasing both maternal and fetal morbidity and mortality associated with preeclampsia. The early prediction of preeclampsia can be achieved using an integrated model involving analysis of the maternal factors, biochemical markers, and uterine artery doppler. Further studies must be done to analyze all aspects of this issue.

Keywords: Preeclampsia; Uterine Artery Doppler; Obstetrics..

Introduction

Pregnancy-related hypertensive diseases are a major global cause of maternal and perinatal death. Preeclampsia (PE) is a pregnancy disease that often manifests after 20 weeks of gestation and generally occurs close to term. It is characterized by new-onset hypertension and proteinuria [1]. This condition is a spectrum of pregnancy-related hypertensive sickness that starts with gestational hypertension and develops into more severe symptoms, including eclampsia and HELLP syndrome.Over 50,000 maternal deaths, over 500,000 fetal deaths, and 2% to 8% of pregnancy-related problems are caused by this condition globally. In order to prevent difficulties for both mothers and newborns through symptomatic management and delivery planning, early diagnosis and timely treatment are crucial [2].

A systolic blood pressure (SBP) of 140 mm Hg or more or a diastolic blood pressure (DBP) of 90 mm Hg or more on two occasions spaced at least 4 hours apart are the specific criteria for the initial identification of hypertension in the context of pregnancy-induced hypertension that constitutes the "mild range"; shorter interval timing in cases of "severe range" hypertension with SBP of 160 mm Hg or more, all of which must be detected after 20 weeks of gestation [3]. These conditions would be classified as "chronic hypertension" or pre-existing essential hypertension if they were discovered prior to 20 weeks of pregnancy.Preeclampsia usually first manifests in near-term pregnancies.Pregnancy-induced hypertension (PIH) is now thought to evolve from gestational hypertension, which is characterized by new-onset hypertension, to more severe types of hypertensions with particular laboratory and clinical criteria that will be covered in greater detail [2, 4]. The traditional triad of hypertension, edema, and proteinuria has changed to hypertension and organ dysfunction (e.g., renal, hepatic, neurologic, hematological, or uteroplacental) as a result of advances in our understanding of the pathophysiology of PIH and the evolution of its diagnostic criteria [5].

Aim of work

To achieve earlyprediction of preeclampsia using maternal factors, biochemical markers, and uterine artery doppler.

Methodology

This review was conducted following a narrative review approach via searching many databases suchas PubMed, Scopus and Google Scholar.

Trending concepts of preeclampsia

The underlying etiology of preeclampsia is poorly understood, despite the fact that the clinical appearance, diagnostic criteria, and treatment of preeclampsia are well understood. Uteroplacental ischemia is the main pathogenic mechanism linked to the genesis of preeclampsia and eclampsia [6]. The observation of placental infarctions in eclampsia patients and animal studies demonstrating that subcutaneous injections of autolyzed human placental extracts into guinea pigs caused convulsions, hepatic focal necrosis, and renal lesions, similar to those seen in eclampsia-related deaths in women, served as the basis for this theory [2, 3,7].Therefore, the pathophysiology of preeclampsia can be compared to the release and progression of a specific toxin, which results in a diffuse vasculopathy. If this condition persists, it might eventually lead to serious consequences including the development of seizures seen in eclampsia [8]. Although there is some agreement regarding this suggested fundamental etiology, more investigation is needed to elucidate the underlying mechanism of uteroplacental ischemia linked to preeclampsia and PIH [4, 5, 8].

Early-onset (also known as placental) and late-onset (also known as maternal) preeclampsia are the two main subtypes of preeclampsia. Both seem to have different phenotypic and etiologies. The development of preeclampsia is linked to the faulty placenta in the early-onset variety [9]. Numerous placental infarcts and arterial sclerosis are found when the preeclamptic placenta is examined. This is accompanied by placental ischemia and hypoperfusion as a result of altered trophoblast invasion.A healthy placenta and maternal variables that eventually result in microvascular damage combine to induce maternal preeclampsia [5, 8]. Maternal endothelial dysfunction may be the cause of this. Maternal preeclampsia can be treated expectantly until 37 weeks of gestation since it develops later in the gestational period. Placental perfusion is preserved because maternal preeclampsia, which develops in the later stages of pregnancy, causes little to no change in arterial conversion [10].

Preeclampsiafrom the histopathological basisto diagnosis

Maternal and placental variables interact intricately in the histopathology of preeclampsia. Maternal vascular malperfusion (MVM) lesions, which are characterized by anomalies in the maternal blood flow to the placenta, are among the distinctive features that are frequently seen when placental tissue from patients with preeclampsia is examined [11]. These lesions can show up as increased syncytial knots, fibrinoid necrosis, and atherosis. Trophoblast abnormalities are frequently seen, such as decreased invasion into the mother's spiral arteries and increased syncytial knot development.There are clear signs of inflammatory reactions, including as immune cell infiltration and changes to the placental vasculature [7, 12].

A thorough investigation found a greater frequency of MVM lesions and placental weight <10th percentile with the initial beginning of preeclampsia compared to subsequent occurrences, even if categorical histopathologic links between the placenta and preeclampsia are still developing [6, 9]. Furthermore, during the initial episode of preeclampsia, the frequency of small for gestational age neonates and composite poor neonatal outcomes was significantly higher. If diffuse vasculopathy persists, it can eventually result in serious consequences like the onset of seizures, which are common in eclampsia. Therefore, delivery is the only effective way to stop the advancement of preeclampsia by removing the causes that cause the faulty placenta [13, 14].

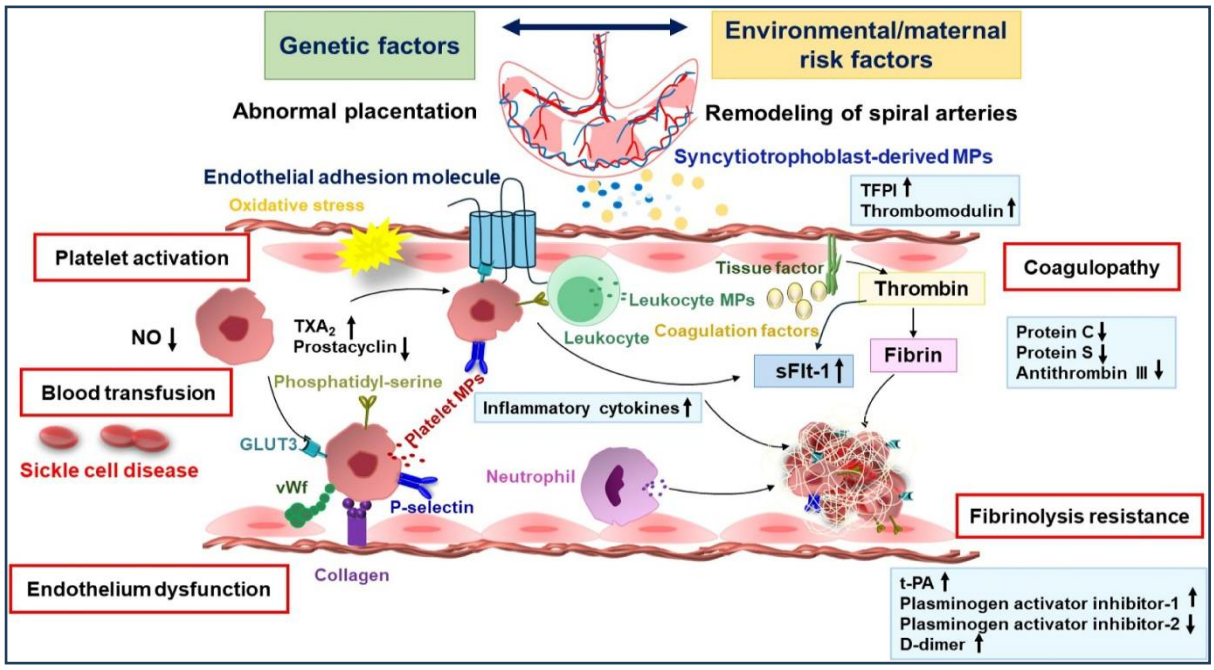

Figure (1): Pathophysiology of Preeclampsia [1].

Prediction of Preeclampsia Using Maternal Factors

Reducing maternal and fetal morbidity and death related to preeclampsia requires early diagnosis, prompt medical intervention, and sufficient surveillance and monitoring. Finding patient-specific obstacles to receiving care and educating patients are crucial components of delivering quality patient care [9]. The first step in this process is for medical personnel to properly inform patients about the diagnosis of preeclampsia, related "red-flag" signs and symptoms, and patient-specific circumstances that put them at high risk.Preeclampsia-related maternal mortality is substantially greater in groups with lower levels of education and socioeconomic status [2, 5, 6]. Understanding the distinctive features of the community they serve, developing close relationships with high-risk patients for preeclampsia, and adjusting the delivery of complex medical education on related complications to each patient's comprehension level are all responsibilities of the clinician [12, 14].

Following a detailed history and physical examination, patients with signs and symptoms of preeclampsia should undergo timely diagnostic testing [1]. This includes pregnancy-induced hypertension laboratory testing, consisting of a urinalysis to evaluate the presence of proteinuria (either with a urine dipstick result ≥2+ if other methods are not readily available, a 24-hour urine collection sample significant for ≥300 mg, or a urine protein to creatinine ratio significant of 0.3 or greater), complete blood count to evaluation for thrombocytopenia (defined as a platelet count <100 K/mm), a complete metabolic panel to assess for impaired liver function (with liver enzymes more than 2 times the upper limit of normal), and renal insufficiency (defined as a serum concentration ≥1.1 mg/dL, or levels 2 times greater than baseline). All abnormal laboratory findings must exclude any preexisting aberrations or secondary causes for abnormalities to be significant for diagnosis [2].

While it is generally believed that the diagnosis of preeclampsia requires increased blood pressure and accompanying proteinuria, this may not always be the case. Other new-onset symptoms such thrombocytopenia, renal insufficiency, pulmonary edema, poor liver function, or new-onset headache with or without visual disturbance may be used for diagnosis in such circumstances where proteinuria and new-onset hypertension are not found. Without severe signs, such as new-onset severe blood pressure (SBP ≥160 mmHg, DBP ≥110 mmHg on two readings at least 4 hours apart), this is usually referred to as preeclampsia [2, 5, 10, 13].

Prediction of Preeclampsia Using Biochemical Markers

Techniques like proteomics, metabolomics, and genomes have become increasingly accessible for clinical research in the past ten years. These methods have been used to describe a number of new routes and factors in the hunt for the etiology of PE [15]. Since many of the identified etiological variables can be measured in maternal

blood, they have been assessed as biochemical indicators for PE diagnosis and prediction. Serum/plasma markers for renal failure, endothelial dysfunction, metabolic state, oxidative stress, placenta-derived factors, hemolysis, and inflammatory markers are among them [16].

- Pregnancy-associated protein A (PAPP-A)

For nearly 30 years, researchers have been studying PAPP-A, a glycoprotein produced in the placenta, as a biochemical marker during pregnancy. During pregnancy, the concentration of maternal plasma rises. PAPP-A has been used to screen for trisomy 21, 13, and 18 at 11 ½ 0 to 13 ½ 6 weeks of gestation in conjunction with b-human chorionic gonadotropin (b-hCG) and nucal translucency thickness [17]. Reduced PAPP-A levels in the first trimester have been linked to a higher risk of PE, fetal growth restriction (FGR), small for gestational age (SGA), and premature birth in fetuses with normal chromosomes.Although PAPP-A has been assessed as a predictive and diagnostic biochemical sign for PE, its screening performance as a single biochemical marker is only 10% to 20%. PAPP-A is a potent predictive biochemical marker of PE when used with Doppler ultrasonography, with 70% prediction rates and 5% false positive rates. Although it has been demonstrated that pregnancies complicated by PE and HELLP had higher plasma PAPP-A concentrations at term, this concentration is still not indicative of the severity of the condition [15-17].

- Fetal hemoglobin and a1-microglobulin

According to recent research, the pathophysiology of PE may involve free, extracellular fetal hemoglobin (HbF). Additionally, the physiological defense against HbF involves the hemeand radical scavenger a1-microglobulin (A1M). As early predictive biochemical markers, their amounts in maternal serum or plasma can be utilized. Women with PE were shown to have higher levels of HbF mRNA in the placental tissue and free HbF protein in the placental vascular lumen.Hemoglobin is a highly reactive molecule that can bind and inactivate nitric oxide (NO), causing vasoconstriction [15]. It can also damage and disrupt cell membranes. It has recently been demonstrated that the plasma and tissue protein A1M binds to and breaks down heme, has the ability to scavenge radicals, and shields cells and tissues from extracellular Hb, heme, and ROS. Hb, heme, and ROS have been demonstrated to increase A1M expression in liver and placental cells. Ex vivo placenta perfusion studies support the pathogenic role of Hb and the protective effect of A1M in PE [18].

- Placental protein 13 (PP13)

Placental trophoblast cells produce PP13, which belongs to the galectin family. PP13 is important in proper placentation, albeit its role or functions are currently unclear. Serum PP13 levels gradually increase with gestational age in healthy pregnancies. Lowered serum levels in the first trimester of fetuses that later had PE have been seen in several investigations. PP13 exhibits varying prediction rates in several trials as a first trimester screening marker for PE [15].

- Soluble fms-like tyrosine kinase 1(sFlt-1) and soluble endoglin (sEng)

Soluble fms-like tyrosine kinase (sFlt-1), a soluble VEGF receptor, and soluble endoglin (s-Eng), a co-receptor for TGF-beta, are two angiogenesis-related factors that have been extensively researched. Maternal plasma levels of both are higher in PE patients than in healthy pregnancies. Prior to the onset of clinical signs, sFlt-1 levels are elevated. The levels are partially correlated with the severity of the disease and with the time at which clinically evident PE first appears. Higher levels of sFlt-1 are seen in early-onset PE [19].

- Placental growth factor (PlGF) and sFlt-1

A promising collection of biochemical indicators for PE prediction is the well-described PlGF/sFlt-1 ratio. Although automated quick analysis techniques have been established for these proteins, it is unclear how they function as first trimester indicators. The prognostic power of the PlGF/sFlt-1 ratio from the second trimester has been demonstrated in a number of investigations [20].

- Metabolomics

An effective method for examining the metabolites left over from a particular biological event is metabolic profiling. The pathophysiological pathways behind a disease like PE can be uncovered using metabolic profiling [15].

- Cystatin C

Clinicians frequently employ the protease inhibitor cystatin C as a sensitive indicator of renal function and glomerular filtration rate. Women with PE had higher maternal plasma levels of cystatin C, and research has shown that this level is a valid diagnostic marker for PE. It has been proposed that either enhanced placental synthesis or reduced renal function are the causes of elevated levels of cystatin C. Recently, cystatin C has been proposed as a first-trimester prognostic marker for PE [21].

- Other biochemical markers

There will be more possible biochemical indicators when genomes, proteomics, and metabolomics are created and made more accessible. The biochemical indicators should ideally provide fresh insights into the pathophysiology of PE [17, 19]. Many of the biochemical markers listed above have been identified by these new methods, and free mRNAs and miRNAs in maternal blood are noteworthy. Both kinds of RNAs are present in the mother's bloodstream and are expressed in the placenta. Profiling these RNAs may show promise in predicting pregnancy outcomes, but more research is required [18-21].

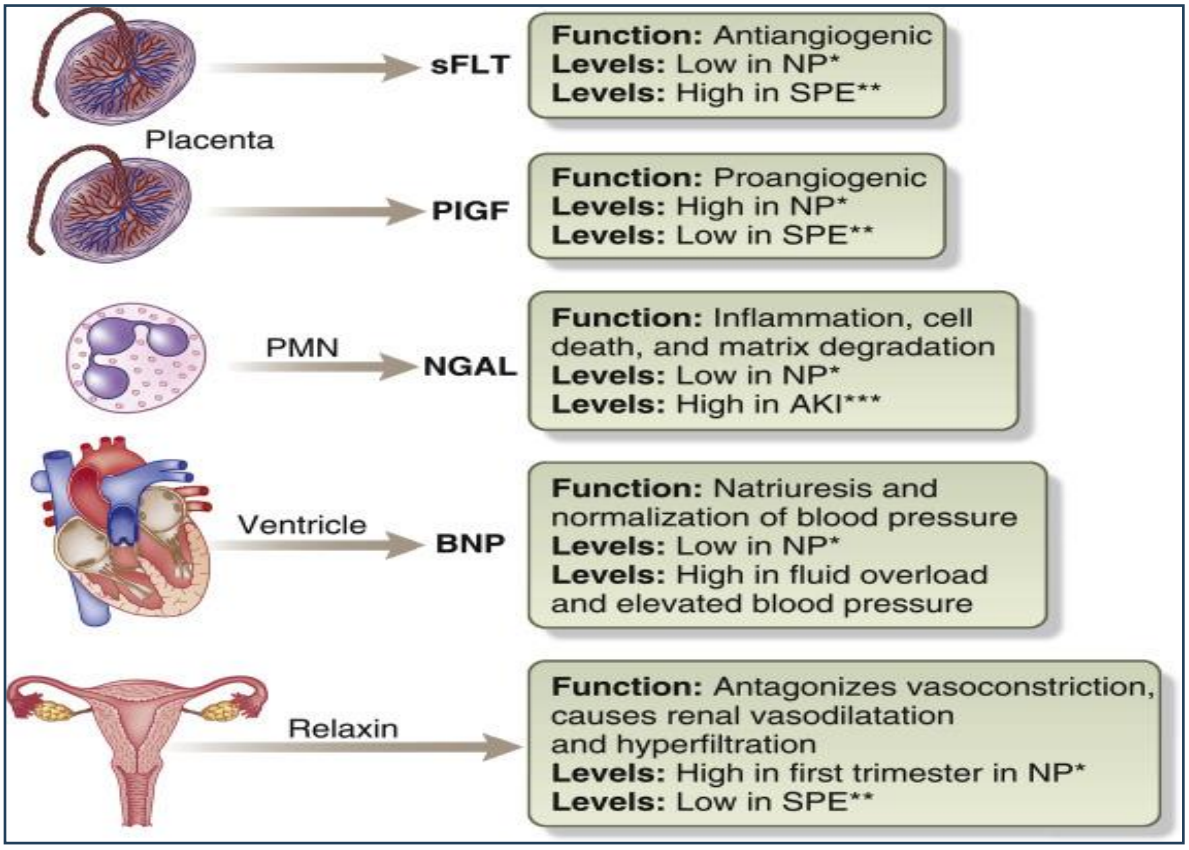

Figure (2): Promising biomarkersfor Preeclampsia [22].

Prediction of Preeclampsia Using Uterine Artery Doppler

There have also been reports of a drop in uterine artery vascular resistance during the second trimester of healthy pregnancies. The second wave of trophoblastic invasion of spiral arteries, which is finished between 16 and 18 weeks of gestation, may be reflected in this pattern, which is significantly different from that of women who are not pregnant or who are in the first trimester of pregnancy [23]. Resistance often does not decrease in pregnancies complicated by PE and/or fetal growth restriction (FGR), resulting in markedly elevated peak systolic velocity, resistance, and pulsatility indices (RI and PI, respectively).Since there is no conclusive evidence of defective placentation, it is hypothesized that the mechanism of disease in late-onset PE and FGR is different [24]. This suggests that the maternal cardiovascular system may be involved in these cases, and that the clinical manifestations may result from the placenta's inability to meet the fetus's greatest needs for oxygen and nutrients [25].

To get reliable and consistent measurements, the Doppler ultrasonography assessment of the uterine arteries should be carried out using a standardized method. Both transvaginal and abdominal ultrasounds can be used for this. A sagittal view of the cervix should be taken during the first trimester (11 to 13+6 weeks of gestation) in order to identify the internal cervical os and the cervical canal [26]. In order to identify both uterine arteries at the level of the internal os, the ultrasound transducer is then slightly angulated laterally while the color Doppler is applied.A similar method is used in the second and third trimesters, but as the cervical internal os becomes harder to see as gestational age increases, the uterine arteries should be located at the point where they intersect the external iliac artery. Next, a pulsed wave Doppler is used with an insonation angle of less than 30° and a sampling volume of 2 mm [25, 26].

In order to confirm that the insonated vessel is the uterine artery in its proximal section, it is advised to acquire at least three identical waves and to have a peak systolic velocity greater than 60 cm/s after adjusting the insonation angle.The average pulsatility index (PI) of the right and left arteries is then used to calculate the mean uterine artery PI [23]. Cervical branches overestimate the risk of pregnancy issues due to their higher PI values, while measurements taken in distal parts of the vasculature often have a lower PI. Similar procedures are used for transvaginal measurements when the transducer is placed in the anterior vaginal fornix. However, transabdominal ultrasonography is favored since this method results in higher PI values [24].

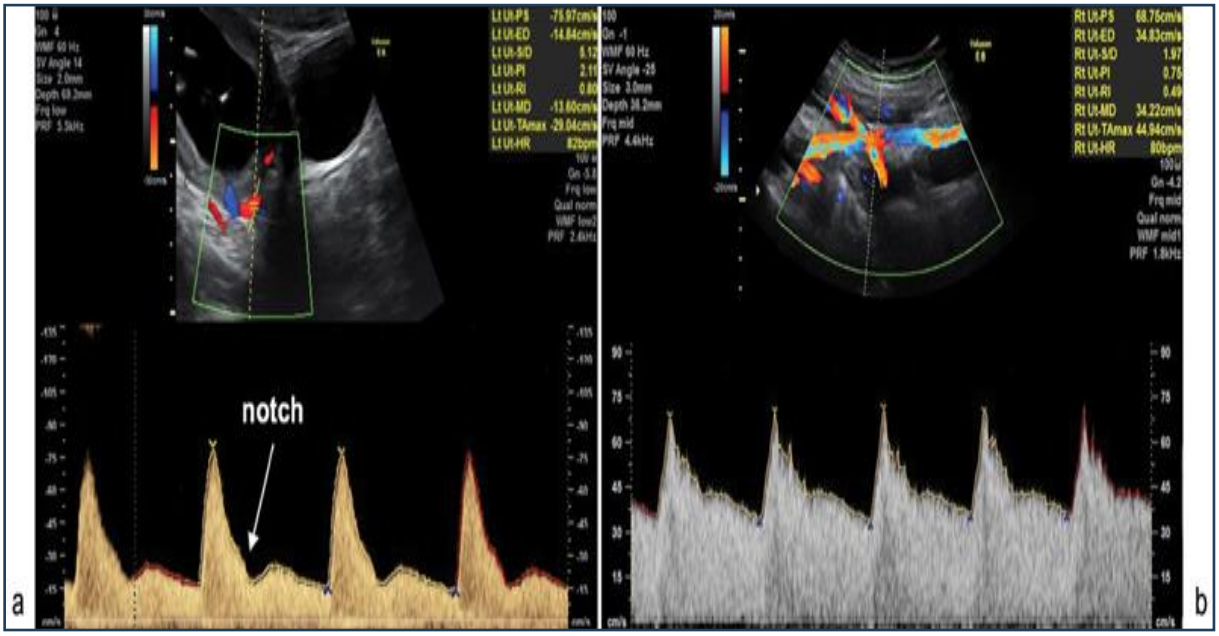

Figure (3): Doppler velocimetry of the uterine arteries showing a high resistance pattern with notching between the systolic and the diastolic components of the wave (A), characteristic of the first trimester, and a low resistance pattern (B), characteristic of the second trimester [23].

High resistance to blood flow in the uterine arteries has been clearly linked to an increased risk of pregnancy difficulties, according to recent studies, and reference ranges have already been established. However, the test's sensitivity and positive predictive value were not very good at predicting unfavorable pregnancy outcomes [23, 25]. Despite the fact that patients who would develop early and severe forms of PE or FGR have much higher mean uterine artery PI as determined by Doppler, this test's accuracy as a stand-alone screening tool is modest, with low sensitivity and positive predictive value. With greater detection rates and acceptable false-positive rates, its application in predictive algorithms that incorporate maternal traits, maternal history, and additional biophysical and biochemical indicators becomes more promising [26].

Conclusion and recommendations:

We came to the conclusion that early diagnosis, timely medical management, and adequate surveillance and monitoring are imperative to decreasing both maternal and fetal morbidity and mortality associated with

preeclampsia. The early prediction of preeclampsia can be achieved using an integrated model involving analysis of the maternal factors, biochemical markers, and uterine artery doppler. Further studies must be done to analyze all aspects of this issue.

References:

1. Martini, C., Saeed, Z., Simeone, P., Palma, S., Ricci, M., Arata, A., ... & Renda, G. (2025). Preeclampsia: Insights into pathophysiological mechanisms and preventive strategies. American Journal of Preventive Cardiology, 23, 101054.
2. Karrar, S. A., Martingano, D. J., & Hong, P. L. (2024). Preeclampsia. In StatPearls. StatPearls Publishing.
3. Magee, L. A., Nicolaides, K. H., & Von Dadelszen, P. (2022). Preeclampsia. New England Journal of Medicine, 386(19), 1817-1832.
4. Jung, E., Romero, R., Yeo, L., Gomez-Lopez, N., Chaemsaithong, P., Jaovisidha, A., ... & Erez, O. (2022). The etiology of preeclampsia. American journal of obstetrics and gynecology, 226(2), S844-S866.
5. 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.
6. Ma'ayeh, M., & Costantine, M. M. (2020, October). Prevention of preeclampsia. In Seminars in Fetal and Neonatal Medicine (Vol. 25, No. 5, p. 101123). WB Saunders.
7. Overton, E., Tobes, D., & Lee, A. (2022). Preeclampsia diagnosis and management. Best practice & research Clinical anaesthesiology, 36(1), 107-121.
8. Brownfoot, F., & Rolnik, D. L. (2024). Prevention of preeclampsia. Best Practice & Research Clinical Obstetrics & Gynaecology, 93, 102481.
9. Roberts, J. M. (2024). Preeclampsia epidemiology (ies) and pathophysiology (ies). Best practice & research Clinical obstetrics & gynaecology, 94, 102480.
10. Torres-Torres, J., Espino-y-Sosa, S., Martinez-Portilla, R., Borboa-Olivares, H., Estrada-Gutierrez, G., Acevedo-Gallegos, S., ... & Rojas-Zepeda, L. (2024). A narrative review on the pathophysiology of preeclampsia. International Journal of Molecular Sciences, 25(14), 7569.
11. Deer, E., Herrock, O., Campbell, N., Cornelius, D., Fitzgerald, S., Amaral, L. M., & LaMarca, B. (2023). The role of immune cells and mediators in preeclampsia. Nature Reviews Nephrology, 19(4), 257-270.
12. Ali, M., Ahmed, M., Memon, M., Chandio, F., Shaikh, Q., Parveen, A., & Phull, A. R. (2024). Preeclampsia: A comprehensive review. Clinica Chimica Acta, 563, 119922.
13. Bokuda, K., & Ichihara, A. (2023). Preeclampsia up to date—What's going on?. Hypertension Research, 46(8), 1900-1907.
14. Boulanger, H., Bounan, S., Mahdhi, A., Drouin, D., Ahriz-Saksi, S., Guimiot, F., & Rouas-Freiss, N. (2024). Immunologic aspects of preeclampsia. AJOG Global Reports, 4(1), 100321.
15. Anderson, U. D., Olsson, M. G., Kristensen, K. H., Åkerström, B., & Hansson, S. R. (2012). Biochemical markers to predict preeclampsia. Placenta, 33, S42-S47.
16. Tzanaki, I., Makrigiannakis, A., Lymperopoulou, C., Al-Jazrawi, Z., & Agouridis, A. P. (2025). Pregnancy-associated plasma protein A (PAPP-A) as a first trimester serum biomarker for preeclampsia screening: a systematic review and meta-analysis. The Journal of Maternal-Fetal & Neonatal Medicine, 38(1), 2448502.
17. Uriel, M., Romero Infante, X. C., Rincón Franco, S., Ibáñez Pinilla, E. A., & Rojas, N. A. (2023). Higher PAPP-A values in pregnant women complicated with preeclampsia than with gestational hypertension. Reproductive Sciences, 30(8), 2503-2511.
18. Bellos, I., Pergialiotis, V., Loutradis, D., Papapanagiotou, A., & Daskalakis, G. (2020). The role of hemoglobin degradation pathway in preeclampsia: A systematic review and meta-analysis. Placenta, 92, 9-16.
19. Palei, A., Johnson, V., Everman, S., & Kutcher, M. (2025). Soluble FMS-Like Tyrosine Kinase-1 (sFLT-1) and Soluble Endoglin (sEng) Induce Platelet Hyperfunction in a Rat Model of Severe Preeclampsia. Physiology, 40(S1), 0286.
20. Droge, L. A., Perschel, F. H., Stütz, N., Gafron, A., Frank, L., Busjahn, A., ... & Verlohren, S. (2021). Prediction of preeclampsia-related adverse outcomes with the sFlt-1 (soluble fms-like tyrosine kinase 1)/PlGF (placental growth factor)-ratio in the clinical routine: a real-world study. Hypertension, 77(2), 461-471.
21. Alshannag, F., Zaki, R. M., Hemida, E., ElBakry, M. M., & Noureldeen, A. F. (2023). Endostatin and cystatin C as potential biomarkers for early prediction of preeclampsia. ACS omega, 8(45), 42776-42786.

22. Acharya, A. (2016). Promising biomarkers for superimposed pre-eclampsia in pregnant women with established hypertension and chronic kidney disease. Kidney International, 89(4), 743-746.
23. Pedroso, M. A., Palmer, K. R., Hodges, R. J., da Silva Costa, F., & Rolnik, D. L. (2018). Uterine artery Doppler in screening for preeclampsia and fetal growth restriction. Revista Brasileira de Ginecologia e Obstetrícia/RBGO Gynecology and Obstetrics, 40(05), 287-293.
24. Oancea, M., Grigore, M., Ciortea, R., Diculescu, D., Bodean, D., Bucuri, C., ... & Mihu, D. (2020). Uterine artery Doppler ultrasonography for first trimester prediction of preeclampsia in individuals at risk from low-resource settings. Medicina, 56(9), 428.
25. Cnossen, J. S., Morris, R. K., Ter Riet, G., Mol, B. W., Van Der Post, J. A., Coomarasamy, A., ... & Khan, K. S. (2008). Use of uterine artery Doppler ultrasonography to predict pre-eclampsia and intrauterine growth restriction: a systematic review and bivariable meta-analysis. Cmaj, 178(6), 701-711.
26. Napolitano, R., Rajakulasingam, R., Memmo, A., Bhide, A., & Thilaganathan, B. (2011). Uterine artery Doppler screening for pre-eclampsia: comparison of the lower, mean and higher first-trimester pulsatility indices. Ultrasound in obstetrics & gynecology, 37(5), 534-537.