

# Updates on The Diagnosis and Management of Pre-eclampsia

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**Received:**  
05-04-2024.

**Accepted:**  
25-06-2024.

**Published:**  
30-06-2024

## Abstract

**Background:** Preeclampsia is a significant multifactorial, multi-organ disease affecting 5% to 8% of all pregnancies in the United States, where it is the third leading cause of maternal mortality. The risk factors of preeclampsia include First pregnancy, new paternity, age, race, obesity, multiple pregnancies, the interval between pregnancies, and history of certain conditions. Despite improvements in the diagnosis and management of preeclampsia, severe complications can occur in both the mother and fetus, and there is no practical method of prevention. Early detection and identification of pregnant women most at risk of developing the disease have proven challenging because the diagnosis of preeclampsia is complex, particularly on a background of medical comorbidities. Hypertension, proteinuria, and biochemical and hematological abnormalities are tertiary, downstream features of established disease, which may be absent in women presenting eclampsia. However, recent efforts combining biochemical and biophysical markers are promising. The criteria for the diagnosis of preeclampsia are evolving, and proteinuria is no longer a prerequisite to making a diagnosis. Angiogenic biomarker testing accelerates diagnosis as well as minimizes adverse maternal outcomes.

**Keywords:** Preeclampsia, Recent advances, Diagnosis, Pregnancy

## INTRODUCTION

Preeclampsia is an elusive condition to diagnose and a complex disease to manage. Recent developments have been in prediction, prevention, diagnosis, and management. Hypertensive disorders of pregnancy complicate 10% of all pregnancies and are one of the leading causes of maternal and fetal deaths worldwide and a threat to maternal and infant death (1). Pregnancy is also known as gestation or gravidity. A time during which one or more babies develop inside a woman (2).

Pregnancies complicated by preeclampsia show an increase in maternal and perinatal morbidity and mortality. The International Society for the Study of Hypertension in Pregnancy published updated guidance on the diagnosis and management of hypertensive disorders of pregnancy in 2018. The revised definition of preeclampsia is Lenovo hypertension after 20 weeks gestation with one or more proteinuria, maternal organ dysfunction (including renal hepatic, hematological, or neurological features), or fetal growth restriction (3). However, it is challenging to estimate the number of women presenting with suspected preeclampsia, but this has been estimated at 10% of the pregnant population (4).

Diagnosing preeclampsia remains a challenge. The maternal phenotype of preeclampsia is associated with inflammation and endothelial cell activation. The more severe early-onset placental phenotype is associated with foetal growth restriction. Women may present with late-onset hypertension and proteinuria, with an absence of foetal growth

restriction near term. This appears to have a few long-term consequences for the mother or infant. Conversely, early-onset, severe maternal disease is often associated with foetal intra-uterine growth restriction (4).

Even in the presence of severe preterm disease, a woman can be asymptomatic. Douglas and Redman reported an absence of hypertension and proteinuria in 38% of women who presented with an eclamptic fit, demonstrating that severe maternal adverse events occur even when the traditional clinical definition of preeclampsia is not met. Unrecognized fetal compromise contributes to the rate of fetal demise, and 1 in 20 stillbirths without congenital abnormality is complicated by or attributable to preeclampsia. It can also lead to an increased incidence of placental abruption, fetal growth restriction, and preterm delivery. Given its frequent occurrence and potential severity, early diagnosis and appropriate management are essential (4).

Preeclampsia is also known as pregnancy-induced hypertension (PIH), toxemia (PET), or gestational hypertension. It occurs when a woman's blood pressure rises above 140/90mmHg, measured twice after the 20th week of gestation (5). Another sign of PIH is a protein in the urine (>300mg) in a 24-hour urine sample. In urinalysis, a trace or 1 plus (+) protein is not uncommon in pregnancy, 2 pluses (2+) protein or higher is abnormal. When blood pressure is greater than 160/110 with other medical signs and symptoms, preeclampsia is said to be severe. For example, Haemolysis, Elevated Liver Enzymes, and Low Platelet count (HELLP) syndrome have been reported to occur in about 0.5 to 0.9 percent of all pregnancies and is a type of preeclampsia, whereas Eclampsia is when the pregnant woman develops seizures with high blood pressure and proteinuria. Both preeclampsia and eclampsia are treated at times as components of a common syndrome (6).

The risk factors of preeclampsia are obesity, new paternity, chronic hypertension, multiple pregnancies, and mothers under 20 and over 40 years of age (7). No diagnostic test is currently used to predict the likelihood of developing preeclampsia. Still, the primary signs are high blood pressure and proteinuria, which is a crucial indicator of preeclampsia (6). Some women may not have any symptoms, but the symptoms associated with preeclampsia are oedema, blurred vision, nausea and vomiting, persistent headaches, sudden weight

gain, and increased blood pressure. However, there is no specific treatment for preeclampsia, but close monitoring to quickly identify preeclampsia and its complications, which could be life-threatening (HELLP syndrome and Eclampsia), is done (5).

## Symptoms of preeclampsia

Preeclampsia develops without symptoms sometimes, but high blood pressure may grow slowly, or it may have a sudden onset. The first sign of preeclampsia is commonly a rise in blood pressure. Blood pressure that exceeds 140/90 millimeters of mercury (mmHg) or greater documented on two occasions, at least four hours apart, is abnormal. Other signs and symptoms of preeclampsia may include: Excess protein in the urine (proteinuria), severe headaches, vision changes, including temporary loss of vision, blurred vision or light sensitivity, upper abdominal pain, usually under the right side of the ribs, nausea and vomiting, decreased urine output, reduced levels of platelets in the blood, shortness of breath, caused by fluid in the lungs, sudden gain of weight and swelling (oedema) particularly in the face and hands may occur with preeclampsia (8).

Proteinuria occurs when the kidney's filtering function malfunctions, spilling protein into the urine. This is because the filter is temporarily damaged by preeclampsia. Albumins, as well as other proteins, are lost through this process.

**Headaches** – Dull or severe and throbbing headaches, often described as migraine-like, are a major cause for concern. If the headache is painful, accompanied by vision changes, it might indicate preeclampsia.

**Vision changes** – One of the most severe symptoms of preeclampsia is vision changes. These may be associated with irritation of the central nervous system or indicate brain swelling (cerebral edema). Typical changes in vision include a sensation of flashing lights, auras, light sensitivity, or blurry vision or spots.

**Abdominal (stomach area) and shoulder pain** – This type of abdominal pain, often called epigastric or upper right quadrant (URQ) pain, is usually under the ribs on the right side. It can be confused with heartburn, gall bladder problems, or pain from the baby kicking.

**Lower back pain** – This is a widespread problem that may indicate a problem with the liver, especially when accompanied by other preeclampsia symptoms.

**Nausea and vomiting**—This is particularly significant when the onset is sudden and after mid-pregnancy. Morning sickness should disappear after the first trimester, and when it suddenly appears after mid-pregnancy, it may be likened to preeclampsia.

**Swelling (edema):** An average amount of swelling occurs during pregnancy. Oedema, on the other hand, is the accumulation of excess fluid and can be a concern when it occurs in the face, around the eyes, or hands.

**Shortness of breath, anxiety** – A racing pulse, mental confusion, a heightened sense of anxiety, and a sense of impending doom can be symptoms of preeclampsia. These symptoms could indicate elevated blood pressure or, more rarely, fluid collecting in the lungs (Pulmonary oedema ).

**Sudden weight gain**—When a person gains more than 3-5 pounds in a week, this may indicate preeclampsia. When the blood vessels are damaged, more water leaks into and stays in the body's tissue and does not pass through the kidneys to be excreted (8).

## Causes of preeclampsia

The exact cause of preeclampsia involves several factors. Experts believe it begins in the placenta – the organ that nourishes the fetus throughout pregnancy. Early in pregnancy, new blood vessels develop and evolve to efficiently send blood to the placenta (9).

In women with The blood vessels don't seem to develop or function in preeclampsia. They are narrower than normal blood vessels and react differently to hormonal signaling, which limits the amount of blood that can flow through them. The causes of the abnormal development may include Insufficient blood flow to the uterus, damage to the blood vessels, a problem with the immune system, or specific genes. Also, environmental factors, e.g., air pollution, can be a possible cause (10). Other high blood pressure disorders during preeclampsia pregnancy are classified as one of four high blood pressure disorders that can occur during

pregnancy. The other three are Gestational, chronic, and chronic hypertension with superimposed preeclampsia.

**Gestational hypertension:** Women with gestational hypertension have high blood pressure with no excess protein in their urine or other signs of organ damage. Some women with this type of hypertension eventually develop preeclampsia.

**Chronic hypertension with superimposed preeclampsia:** This condition occurs in women with chronic hypertension before pregnancy who develop worsening high blood pressure and protein in the urine or other blood pressure-related complications during pregnancy. Those with high BP have a risk 7-8 times higher than those without (11).

## Risk factors of preeclampsia

Preeclampsia develops as a complication of pregnancy. Risk factors include:

**History of preeclampsia:** A personal or family history of preeclampsia significantly raises the risk of preeclampsia.

**Chronic hypertension:** Those with chronic hypertension have a higher risk of developing preeclampsia. First pregnancy: The risk of developing preeclampsia is highest during the first pregnancy.

**New paternity:** Each pregnancy with a new partner increases the risk of preeclampsia more than does a second or third pregnancy with the same partner.

**Age:** The risk of preeclampsia is higher for very young pregnant women as well as pregnant women older than 40 years of age.

**Race:** Black women have a higher risk of developing preeclampsia than women of other races.

**Obesity:** The risk of preeclampsia is higher in obese women.

**Multiple pregnancies:** Preeclampsia is more common in women who are carrying twins, triplets, or other multiples.

**The interval between pregnancies:** Having babies less than two years or more than 10 years apart leads to a higher risk of preeclampsia.

**History of particular conditions:** Having certain

conditions before becoming pregnant, such as chronic high blood pressure, migraines, type 1 or type 2 diabetes, kidney disease, and a tendency to develop blood clots or lupus – increases the risk of preeclampsia.

*In vitro* fertilization: The risk of preeclampsia increases if the baby is conceived with *in vitro* fertilization (12, 13).

## Complications of preeclampsia

The more severe the preeclampsia and the earlier it occurs in pregnancy, the greater the risks for both mother and baby. Preeclampsia may require induced labor and delivery. If there are clinical or obstetric conditions that require a speedy delivery, cesarean delivery (C-section) may be necessary (14). Complications of preeclampsia may include Foetal growth restriction, preterm birth, placental abruption, HELLP syndrome, eclampsia, damage to other organs, and cardiovascular disease.

**Fetal growth restriction:** Preeclampsia affects the arteries carrying blood to the placenta. If the placenta does not get enough blood, the baby may receive inadequate blood and oxygen and fewer nutrients. This can lead to slow growth, known as fetal growth restriction, low birth weight, or preterm birth.

**Preterm birth:** If preeclampsia with severe features occurs, the baby may be delivered early to save the life of both mother and baby. Prematurity can lead to breathing and other problems for the baby (15).

**Placental abruption:** Preeclampsia increases the risk of placental abruption, a condition in which the placenta separates from the inner wall of the uterus before delivery. Severe abruption can cause heavy bleeding, which can be life-threatening for both the mother and the baby.

**HELLP syndrome:** Haemolysis, elevated liver enzyme, and low platelet count (HELLP) is a more severe form of preeclampsia and can rapidly become life-threatening for both mother and baby. Symptoms of HELLP syndromes include Nausea and vomiting, headache, and upper right abdominal pain. It represents damage to several organ systems. It may develop suddenly, even before high blood pressure is detected, or without any symptoms.

**Eclampsia:** When preeclampsia is not controlled, Eclampsia, which is essentially preeclampsia with

seizures, can develop. It is challenging to predict which patient will have preeclampsia that is severe enough to result in eclampsia. Often, there are no symptoms or warning signs to predict eclampsia because it is serious. With consequences for both mother and baby, delivery becomes necessary regardless of how far along the pregnancy is.

**Damage to other organs:** Preeclampsia may damage the kidneys, liver, lung, heart, or eyes and cause a stroke or other brain injury. The amount of injury to other organs depends on the severity of preeclampsia.

**Cardiovascular disease:** Having preeclampsia may increase the risk of future heart and blood vessel (cardiovascular) disease. The risk is even greater if the woman has had preeclampsia more than once or she has had preterm delivery.

To minimize this risk, ideal weight should be maintained after delivery, a variety of fruits and vegetables should be eaten, regular exercise should be adopted, and smoking should be avoided (11, 16).

## Conventional methods of diagnosis, prevention and management

### Diagnosis

Preeclampsia is diagnosed by high blood pressure and one or more of the following complications after the 20th week of pregnancy.

- (1) Protein in the urine (proteinuria)
- (2) Low platelet count
- (3) Impaired liver function
- (4) New-onset headaches or visual disturbances

Previously, preeclampsia was only diagnosed if high blood pressure and protein in the urine were present. Experts now know that it is possible to have preeclampsia yet never have protein in the urine (17).

A blood pressure reading of more than 140/90mmHg is abnormal in pregnancy. However, a single high blood pressure reading does not mean one has preeclampsia. If the blood pressure reading is abnormally high, a second abnormal reading four hours after the first may confirm preeclampsia. When preeclampsia is suspected, certain tests may be done, including blood tests, urine analysis, foetal ultrasound, and a nonstress or biophysical profile

(18).

**Blood tests:** These include Liver function tests, Kidney function tests, and also measure platelets.

**Urine analysis:** 24-hour urine measurement will measure the protein in urine.

**Fetal ultrasound:** This ensures close monitoring of the baby's growth. Here, fetal weight and the amount of fluid in the uterus (amniotic fluid) are estimated (19).

**Non-stress test or biophysical profile:** This checks the baby's heart rate as it moves. A biophysical profile uses ultrasound to measure the baby's breathing, muscle tone, movement, and uterine fluid volume (18).

## Prevention of preeclampsia

Preeclampsia prevention may be primary, secondary, or tertiary (19). Primary prevention involves avoiding pregnancy in women at high risk of PE, modifying lifestyles, or improving nutrient intake in the whole population to decrease the incidence of the disease. Therefore, most cases of preeclampsia are unpreventable (12). Secondary prevention is based on the interruption of known pathophysiological mechanisms of the disease before its establishment. Recent efforts have focused on the selection of high-risk women and have proposed an effective intervention as early as it is possible to avoid the disease or its severe complications (21). Tertiary prevention relies on using

treatment to avoid preeclampsia complications. Achieving it can be challenging without exposing many to unnecessary risks (12). The prevention of preeclampsia is more likely to be successful by identifying women at high risk and scheduling them to proper antenatal care (22).

However, in some instances, low-dose aspirin and calcium supplements may reduce the risk of preeclampsia.

**Low dose aspirin:** Certain risk factors, including a history of preeclampsia, multiple pregnancies, chronic high blood pressure, kidney disease, diabetes, or autoimmune disease, a daily dose of aspirin (81 milligrams) beginning after 12 weeks of pregnancy (20).

**Calcium supplements:** Women who have calcium

deficiency before pregnancy and who don't get enough calcium during pregnancy through their diets might benefit from calcium supplements to prevent preeclampsia (23).

## Management of preeclampsia

The most effective treatment for preeclampsia is delivery. Preeclamptic patients are at increased risk of seizures, placental abruption, stroke, and possibly severe bleeding until the blood pressure decreases (24). The possible management of preeclampsia may include Medications, bed rest, hospitalization, and delivery.

**Medications to lower blood pressure:** Anti-hypertensive lowers abnormally high blood pressure (21). **Corticosteroids:** For severe preeclampsia or HELLP syndrome, corticosteroid medications can temporarily improve liver and platelet function to help prolong the pregnancy. They can help the baby's lungs mature for as little as 48 hours.

**Anticonvulsant medications:** If preeclampsia is severe, an anticonvulsant medication such as magnesium sulfate may be given to prevent the first seizure.

**Bed rest:** It was routinely recommended for women with preeclampsia, but research has not shown a benefit from this practice, and it can increase the risk of blood clots.

**Hospitalization:** In severe preeclampsia, the patient may be hospitalized, and several tests may be done to monitor the baby's well-being and the volume of amniotic fluid. Lack of amniotic fluid is a sign of poor blood supply to the baby.

**Delivery:** When a person is diagnosed with preeclampsia, induction of labor may be recommended towards the end of pregnancy. If labor is not possible, a cesarean section may be recommended right away (25).

## Novel methods for the diagnosis, prevention, and management

### New development in diagnosis

Preeclampsia is elusive to diagnose. Preeclampsia is Lenovo hypertension after 20 weeks gestation with one or more proteinuria, maternal organ dysfunction

(including renal, hepatic, hematological, or neurological features), or fetal growth restriction.

Hypertension is classified as systolic blood pressure of 140mmHg or higher and diastolic blood pressure of 90mmHg or higher at or after 20 weeks gestation (4).

Recent research focused on whether ambulatory or home blood pressure impacts maternal outcomes in preeclampsia. A systemic review recommended adequately powered randomized trials to evaluate this. Also, optimum (optimizing titration and monitoring) maternal blood pressure is a randomized controlled trial of blood pressure self-monitoring during pregnancy, which aims to assess the feasibility and most appropriate outcome measures for a larger trial (26). The Bump trial (blood pressure monitoring) in high-risk pregnancies to improve the detection and monitoring of hypertension is a randomized control trial to determine whether self-monitoring leads to earlier diagnosis of raised blood pressure and lower mean systolic blood pressure between baseline and delivery (27). Additionally, the assessment of proteinuria is variable. The gold standard for evaluation of proteinuria was previously a 24 hours urine collection. However, this was logistically challenging and prone to error (28). The DAPPS study (diagnostic accuracy in preeclampsia using proteinuria assessment) compared spot protein: Creatinine ratio (PCR) and spot albumin: Creatinine ratio (ACR) against the reference standard of 24-hour urine collection (28). They found that the diagnostic accuracy of PCR and ACR was similar to a 24-hour urine collection and that ACR had a higher sensitivity of 99% compared to 90% with PCR. Therefore, the National Institute for Health and Care Excellence (NICE) recommends dipstick screening for proteinuria, and if positive (1+ or more), the ACR or PCR should be used to quantify proteinuria (29).

## Novel methods of diagnosis

The diagnosis of preeclampsia is complex, particularly on a background of medical comorbidities. Hypertension, proteinuria, and biochemical and hematological abnormalities are tertiary, downstream features of established disease, which may be absent in women presenting eclampsia (30). There is a need for better methods of diagnosis and risk stratification of women at risk of preeclampsia. Angiogenic biomarkers are closely

linked to the pathophysiology of preeclampsia, and abnormalities in angiogenic biomarker concentrations such as PIGF and sFlt-1 have been identified up to 10 weeks before the clinical onset of the disease (31). There have been recent developments.

The diagnostic accuracy of PIGF was investigated by Chappell and colleagues, who found that low PIGF concentrations demonstrated high sensitivity and a high negative predictive value. The authors proposed that in women in whom preeclampsia is suspected clinically, an sFlt-1: PLGF ratio of less than 38 can be used to rule out the short-term development of the syndrome. In the placental growth factor in assessing and diagnosing hypertensive pregnant women, a stepped wedge trial (PARROT) is used to determine whether the addition of PIGF testing to the current management of women with preeclampsia will reduce the time taken to reach a diagnosis and, thus, improve maternal and perinatal outcomes (32). Chappell and colleagues investigated the diagnostic accuracy of PIGF in a study. Low PIGF concentrations demonstrated high sensitivity and negative predictive value for preeclampsia, necessitating delivery within 14 days in women with suspected preeclampsia before 35 weeks gestation (30). PIGF outperformed all other tests commonly used to diagnose preeclampsia, such as blood pressure, alanine transaminase, urate, and dipstick proteinuria).

More recently, the PIGF tests and sFlt-1 ratio have been assessed in further studies. The PETRA study (Preeclampsia triage by rapid assay) found that a low PIGF concentration of <100pg/ml was associated with preterm delivery and adverse neonatal outcomes. This implies that PIGF may be helpful in risk stratification for women presenting with suspected preeclampsia. The PARROT trial (PIGF) to assess and diagnose hypertensive pregnant women. This trial demonstrated a reduction in diagnosis time from 4.1 to 1.9 days and reduced severe maternal outcomes from 5.4 to 3.8%. Finally, the INSPIRE trial (a prospective, randomized) interventional study evaluates the short-term prediction of preeclampsia in pregnant women with suspected preeclampsia. This assessed the use of the sFlt-1: PIGF ratio (32).

## Novel methods of risk prediction

Externally validated risk prediction models predict adverse maternal outcomes once preeclampsia has been diagnosed to guide clinical management, including the timing of delivery, antenatal steroids, magnesium sulfate, and transfer to high-level care. Placental exosomes have been highlighted for use in the diagnosis of preeclampsia. They are extracellular vesicles that can transfer micro-RNA to target cells, influencing their function (4).

It was also reported that the levels of circulating exosomes are increased in pregnancies complicated by preeclampsia, and the difference is seen across gestations (33). This suggests a potential role for exosomal micro-RNA in predicting and diagnosing preeclampsia. The full PLIERS model is intended for use at any time in pregnancy and predicts adverse outcomes in the next 48 hours (34). This is based on gestational age, chest pain, dyspnoea, oxygen saturation, creatinine, platelets, and aspartate aminotransaminase (AST) or alanine aminotransaminase (ALT).

The PREPS prediction model is intended for use up to 34 weeks gestation and estimates the overall risk of adverse maternal outcomes (35). The PREPS model requires maternal age, gestational age, medical comorbidities, protein creatinine ratio (PCR), Urea, creatinine, platelets, systolic blood pressure, pulse oximetry, exaggerated tendon reflexes, and anti-hypertensive drugs or magnesium sulfate treatment. However, neither of these models predicts adverse perinatal outcomes.

## Prevention of preeclampsia

Given the significant morbidity and mortality associated with preeclampsia, especially with early onset, obstetric management has been directed at disease prevention. Prophylactic use of aspirin and calcium has been studied. Recently, appreciation of the role of obesity as a risk factor for preeclampsia has prompted interest in measuring the impact of bariatric surgery to decrease this risk (36).

**Aspirin:** Taken in low doses, it decreases platelet production of thromboxane relative to prostacyclin since an imbalance between thromboxane and

prostacyclin levels is considered a significant factor in the development of preeclampsia (36).

**Calcium:** Supplementing calcium helps reduce hypertension and preeclampsia in populations with low baseline dietary calcium intake. It also reduces the risk of preterm delivery (36).

## Bariatric surgery

Obesity is recognized as a contributing factor in a wide range of diseases, but its importance as a modifiable risk factor for preeclampsia may have been overlooked. Bariatric surgery is proven to mitigate the pathophysiologic effects of obesity on the cardiovascular and endocrine systems (37, 38). The relationship between obesity and pregnancy-related complications is a complex one, involving the increased inflammatory state associated with obesity and increased risk of other comorbidities such as diabetes, hypertension, and preeclampsia. Just as bariatric surgery is a proven way to improve overall health in obese patients, there is also evidence that it decreases the rate of preeclampsia in some obese women of childbearing age (39).

## Management of preeclampsia

### Blood pressure

The revised National Institute for Health and Care Excellence (NICE) guideline recommends treating hypertension in pregnancy if systolic blood pressure is above 140mmHg or diastolic blood pressure is above 90mmHg. Once anti-hypertensive treatment has been started, the target blood pressure is 135/85mmHg (29). This is an important change from previous practice when treatment was recommended if blood pressure exceeded 150/100mmHg, and reflects evidence from the control of hypertension in pregnancy study (CHIPS) (40).

The revised NICE guidance recommends labetalol as the first-line treatment for hypertension in pregnancy, with nifedipine recommended if labetalol is not suitable and methyldopa recommended if neither labetalol nor nifedipine is suitable or tolerated (29). Women must be provided with information on the benefits of treatment and the side effects of the various treatment options to enable shared decision-making and informed choice.

## Delivery

Both NICE in the United Kingdom and the American College of Obstetricians and Gynaecologists recommended delivery at 37 weeks gestation for women with confirmed preeclampsia. Before 34 weeks gestation, expectant management is advised, as iatrogenic preterm delivery before 34 weeks gestation is associated with worse neonatal adverse outcomes (40).

## Methods of delivery

Vaginal or cesarean depends on the severity of the disease, gestational age of the baby, and fetal lung maturity. After delivery, there should be close monitoring for high blood pressure and other signs of preeclampsia.

## Obstetric management

Obstetric management of preeclampsia relies on a high index of suspicion, careful observation, and early intervention. The intervention method is logically a function of the severity of the disease but ultimately the only definitive treatment is the delivery of the foetus and placenta (3).

The ACOG practice bulletin on hypertensive disorders unique to pregnancy suggests monitoring according to the recommendations of the national high blood pressure education programme. These are foetal monitoring with daily foetal movement counts, weekly non-stress tests or biophysical profiles, or both, ultrasound examination for foetal growth and amniotic fluid assessment every 3 to 4 weeks, maternal tests to check haematocrit and platelet count, liver enzymes, renal function and 12- or 24-hours urine protein collections at least weekly (3). Doppler flow velocimetry may also be used to assess fetal status. The goal of monitoring these women is to identify patients with evidence of increasing disease severity—the progression of the disease warrants hospitalization for closer observation and medical management.

## Anaesthetic management

These play an essential role in the peripartum period. The anesthesiologist performs a thorough pre-anesthetic evaluation, including a history and physical. Examination, with careful attention to the airway examination due to the increased risk of

pharyngolaryngeal edema, assessment of the patient's cardiopulmonary fluid, and coagulation status (41). Laboratory values should be obtained, including urine protein, platelet counts, liver enzymes, and possibly a coagulation panel. The ACOG and American Society of Anaesthesiologists (ASA) recommend that regional anesthesia be used in preeclamptic patients without coagulopathy to decrease the need for general anesthesia should an emergent procedure become necessary (3).

However, general anesthesia may increase the risk of complications such as cerebral hemorrhage due to blood pressure changes associated with rapid sequence induction of anesthesia (42).

Preeclampsia is a severe disease, and early identification of those at risk would likely allow targeted surveillance and intervention to improve pregnancy outcomes for both mother and foetus. Low-dose aspirin started in the first trimester in high-risk women may reduce the risk of preeclampsia by up to 50% and may improve associated fetal and maternal outcomes (43).

Calcium supplementation reduces the risk only in women deficient in dietary calcium (44). With the introduction of aspirin as a prophylactic agent, there is a package of interventions — aspirin, increased ultrasound, and blood pressure monitoring can reduce the risk of preeclampsia and increase the chances of early detection in women at high risk. Historically, the screening took the form of regular blood pressure and urine checks throughout pregnancy for all women. Today in the United Kingdom, NICE recommends using maternal history, age, body mass index, and the number of fetuses to select women for treatment with aspirin (45). Unfortunately, for a population prevalence of 4%, the positive predictive value of this model is low and would lead to nearly half of all women being screened positive (29). With a sensitivity of only 77%, a significant number of women who will develop preeclampsia are not detected with this model, so routine antenatal care still has to include regular blood pressure monitoring throughout later pregnancy.

However, new diagnostic tests are evaluated to address some of the current tests' inadequacies and presentation obscurities. Urinary Albumin/creatinine ratios are used outside of pregnancy to detect proteinuria. They may be superior to protein creatinine ratio (PCR) but have not



been validated yet in pregnancy and preeclampsia (45).

As the pathogenesis of preeclampsia relates to an imbalance in the control of angiogenesis, several factors might be outside the normal range in the weeks leading up to the presentation of preeclampsia. Placental growth factor (PIGF) is a proangiogenic factor, and from as early as 11 to 13 weeks gestation, low levels are associated with the later development of preeclampsia (30). Soluble forms like trypsin kinase-1 (sFLt-1) are antiangiogenic, and levels are elevated as much as five weeks before the clinical onset of the disease (30).

Both have been evaluated as diagnostic tests, but neither has sufficient sensitivity for clinical practice. Studies have evaluated the use of the sFLt-1/PIGF ratio as a diagnostic screening test and have found a high specificity and sensitivity, particularly for early-onset disease (30). The approach provides the possibility of rapid testing to clarify a diagnosis of preeclampsia. Furthermore, the International Society for the Study of Hypertension in Pregnancy (ISSHP) recommends admitting all women at diagnosis of preeclampsia to complete a full maternal and fetal assessment, stabilize blood pressure, and finalize a plan of care before the patient's follow-up and management (3). This is also recommended in the preeclampsia community guideline (PRECOG) day-assessment unit guideline in use, which also lays out suggested investigation pathways for women with hypertension who have not yet been diagnosed with preeclampsia and in the WHO

and ACOG guidelines (46). Maternal monitoring should include regular blood pressure measurements. Again, laboratory tests of biochemical and hematological parameters should be repeated two to three times a week, according to the severity and progression of the disease (27).

## Conclusion

Tight blood pressure control of hypertension in pregnancy (CHIPS trial) is reported to improve outcomes. Angiogenic biomarkers accelerate diagnosis and minimize adverse maternal outcomes when used in the assessment of preeclampsia. Their use also enables risk stratification. Timing of delivery is vital to improving perinatal and neonatal outcomes.

## Conflict of interest

The authors declare no conflict of interests of interest related to this article

**Source of funding:** There was no external source of funding

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How to cite this paper: Etura JE, Okpokam DC, Emeribe AO, Akpan UO, Jeremiah ZA. Updates on The Diagnosis and Management of Preeclampsia. *Annals of Medical Laboratory Science* 2024; 3(1): 76-86

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