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Preeclampsia: From Etiopathology to Organ Dysfunction

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Abstract

Preeclampsia is a hypertensive disorder of pregnancy affecting 6–12% of the population. There are various risk factors for the development of preeclampsia, ranging from advanced maternal age to genetics. The proposed etiologies for preeclampsia are abnormal placentation, immunological intolerance, endothelial damage, and genetic inheritance. The pathogenesis includes endothelial activation and dysfunction leading to vasospasm. Preeclampsia is divided into two stages: asymptomatic and symptomatic stages. Preeclampsia causes multiple organ involvement, namely central nervous system, respiratory, cardiovascular, hematological dysfunction, HELLP (hemolysis elevated liver enzymes, low platelets) syndrome, endocrine, renal, hepatic, and uteroplacental dysfunction. These organ dysfunctions increase morbidity and mortality in preeclamptic pregnant patients.

Keywords: abnormal placentation, etiology, endothelial dysfunction, epidemiology, hypertensive disorders of pregnancy, HELLP syndrome, long-term impact, multiple organ dysfunction, preeclampsia, risk factors, uteroplacental malfunction

1. Introduction

Hypertension is a common pregnancy-specific medical disorder, which is a significant cause of maternal and perinatal mortality [1]. There is disproportionate risk to the mother and fetus for further complications and long-term sequelae.

Preeclampsia is a hypertensive disorder of pregnancy causing multi-organ dysfunction syndrome with placental dysfunction occurring in the latter half of pregnancy, with major cause of maternal morbidity, maternal intensive care admissions, Cesarean section, end-organ damage, and fetal complications.

2. Definition

Preeclampsia is defined as new onset of hypertension with or without proteinuria or new onset hypertension with evidence of end organ dysfunction after 20 weeks gestation or postpartum in a previously normotensive woman [2].

Classification of hypertension in pregnancy by ACOG (American College of Obstetrician and Gynecologist) 2013 task force:

- Preeclampsia
 - Preeclampsia without severe features
 - Severe preeclampsia with severe features

Progress of preeclampsia is divided into two stages:

2.1 Asymptomatic first stage

It occurs early in pregnancy with impaired remodeling of the spiral arteries and abnormal placentation. This failure of normal angiogenesis results in superficial placentation.

2.2 Symptomatic second stage

It presents in late second or third trimester and is characterized by signs and symptoms distinguished by the release of excess of antiangiogenic factor from intervillous space into the maternal circulation, which causes widespread maternal endothelial dysfunction and accentuated systemic inflammatory response specific to each organ system.

3. Epidemiology

It affects 6–12% of all pregnant women worldwide, with preeclampsia in 5–8% of pregnancy [3, 4]. The WHO (World Health Organization) has identified hypertension as the second most common cause of maternal death among the triad of hemorrhage and sepsis [5]. It is responsible for 70,000 maternal deaths (major cause of maternal morbidity and mortality) and 500,000 fetal deaths worldwide every year [5]. Nulliparous women are prone to develop preeclampsia, while older women are at higher risk of chronic hypertension with superimposed preeclampsia.

Hypertension is well known in pregnancy worldwide, including chronic, gestational, and possible dangerous preeclampsia [6]. It is considered as high-risk pregnancy when unfavorable conditions prevail for the well-being of mother, fetus, or both.

Effective antenatal care with good surveillance minimizes the risk of complications. Hypertensive disorders of pregnancy can result in life-threatening multisystem pathology, affecting nervous, hematological, renal, hepatic, and respiratory systems.

Preeclampsia presents with maternal features of hypertension, proteinuria, and systemic dysfunction with or without fetal syndrome. Thus, proteinuria is an objective marker and reflects the system-wide endothelial leak that characterizes the preeclampsia syndrome.

There has been an alarming 30% increase in incidence of hypertensive disorders of pregnancy [7], which is explained by the demographics of increase in maternal age, obesity, and increase in use of assisted reproductive techniques, which alters the maternal-fetal immune response. It is also influenced by genetic predisposition, race, and ethnicity.

4. Risk factors

Numerous preconceptional and pregnancy-related risk factors are identified and classified in development of preeclampsia.

4.1 Advanced maternal age

There has been variation of maternal age of pregnancy from teenage to women who are 40 years or older, as compared with women between 20 and 29 years [8] of age, with approximately twofold increase in risk of preeclampsia. Hispanic ethnicity may be at increased risk of developing preeclampsia [9]. Women with advancing age and delayed childbirth show a substantial increase in chronic hypertension during pregnancy and are at increased risk of preeclampsia.

4.2 Genetic factors

Maternal and fetal genetic factors carry strong risk for preeclampsia, with one-third attributable to maternal genetic factors [10]. Women are twice as likely to develop the disorder if they have a family history of preeclampsia, [11] and the risk increases with multiple affected pregnancies [12], potentially carrying high-risk outcomes of placental abruption and fetal growth restriction. Women with history of preeclampsia in previous pregnancy are at increased risk in subsequent pregnancy, particularly in the early onset of preeclampsia.

Partner-related risk factors are long considered a disease of primigravida in women due to limited paternal sperm antigens exposure before conception, which suggests an immunological role in pathophysiology of preeclampsia, with its incidence approximately threefold higher as compared to parous women [13]. A significant contribution of paternal genes (in the fetus) was identified as risk, with one-fifth of the variance in liability conferred through fetal genes in preeclampsia [14].

4.3 Metabolic factors

With worldwide increase in prevalence of obesity, risk of preeclampsia escalates with increasing body mass index (BMI) [15]. A systemic review found that an increase in BMI of 5–7 Kg/m was associated with a twofold increased risk of preeclampsia; it also has strong association with insulin resistance and chronic hypertension, elevating the risk of preeclampsia [16].

Other maternal medical conditions with recognized risk factors for preeclampsia are chronic renal disease, antiphospholipid antibody syndrome, and systemic lupus erythematosus [17] and pregnancy-related conditions with increased placental mass, including multiple fetal gestation and hydatidiform mole, are associated with higher rates of preeclampsia as well [18].

Associated metabolic syndrome, chronic disorders hypertension, preexisting diabetes, and renal diseases that cause endothelial injury are risk factors for preeclampsia. This explains the similar tendency of endothelial dysfunction and

common factor for association of preeclampsia with increased future cardiovascular diseases [19].

4.4 Behavioral factors

Cigarette smoking during pregnancy decreases the risk of preeclampsia [20] by 30–40% as compared to women who do not smoke although biological mechanism remains unknown but probable mechanism may include nicotine inhibition of thromboxane A2 synthesis [21], simulation of nitric oxide release, or combination of both.

4.5 Recreational physical activity

Physical activity during pregnancy is associated with decreased risk for preeclampsia in non-obese women [22]. This occurs by decreasing oxidative stress, enhancing endothelial function, and modulating the immune and inflammatory response.

5. Etiology

The exact cause of initiation and progress of the disease process is not known, with placenta being the focus in pathogenesis.

Following theories have been proposed to explain mechanics causing preeclampsia.

- Abnormal placentation with failure of trophoblast invasion of uterine vessels.
- Immunological intolerance between maternal, paternal (placental), and fetal tissues.
- Vascular endothelial damage.
- Genetic-inherited predisposition and polygenic disorders.

5.1 Abnormal placentation

In physiological pregnancy, embryo-derived endovascular cytotrophoblast invades the decidual (10–12 weeks) and myometrial (16–18 weeks) segment of spiral arterioles of uteroplacental bed, replacing endothelial lining [23] and causing remodeling of vascular smooth muscles and inner elastic lamina (**Figure 1**). These physiological changes lead the maternal spiral arterioles to distend the luminal diameter fourfold, resulting in creation of tortuous and funnel-shaped flaccid [23] tubes that provide a low-resistance, low-pressure, high-capacitance, high-flow pathway into intervillous space, which gets further remodeled and unresponsive to vasoactive stimuli. These alterations in maternal vasculature ensure adequate blood flow to nourish the growing fetus and placenta.

In preeclampsia, endovascular cytotrophoblast invasion may be incomplete [24] and only the decidual vessels undergo change, while the deeper myometrial arterioles do not lose their endothelial lining and musculoelastic tissue, resulting in narrowing of maternal spiral arterioles (**Figure 1**), thus impairing placental blood flow and remaining hyperresponsive to vasomotor stimuli. Inadequate spiral arteriolar remodeling leads to narrowing of maternal vessels and relative placental ischemia.

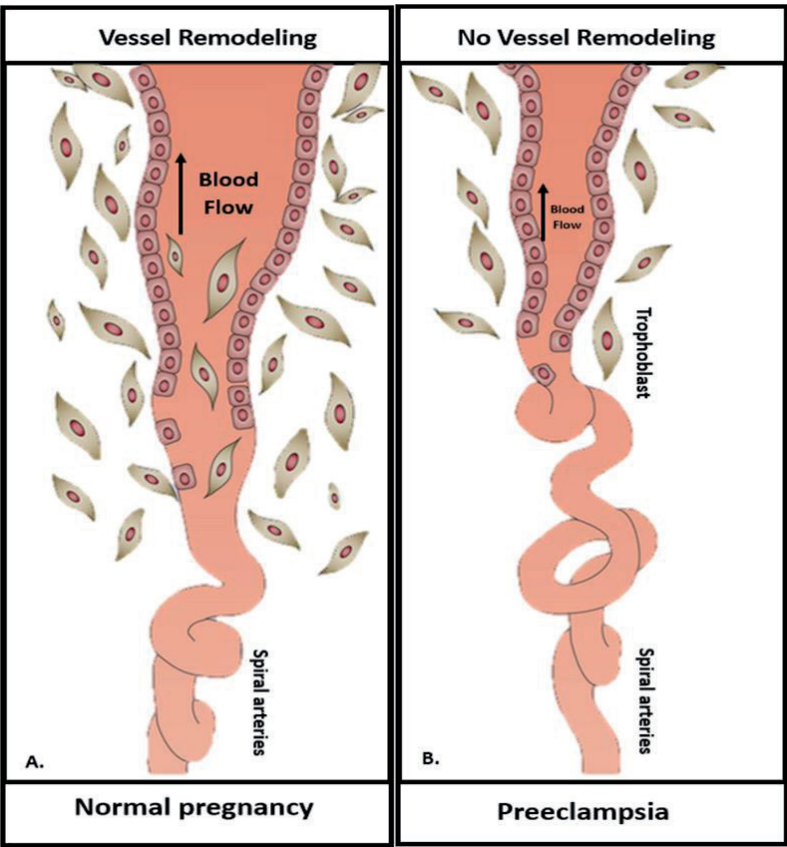


Figure 1.
A-Normal pregnancy uterine spiral arteries are wide open and remodeled by endovascular trophoblast, thereby increasing blood flow B-Preeclampsia women spiral arteries fail to remodel due to defective trophoblast invasion.

The severity of the disease correlates with the magnitude of defective trophoblastic invasion [25]. Atherosclerotic changes in maternal radial arteries that supply decidua are observed in preeclampsia. Decidual vasculopathy lesions have high association in preeclampsia with placental insufficiency, including intrauterine growth restriction and small for gestational age [26]. These changes correspond to symptomatic second stage of the preeclampsia syndrome with systemic inflammatory response [27].

In association with defective remodeling of uteroplacental vasculature, there may be presence of agonistic autoantibodies to the angiotensin receptor-1 (AT1) [28]. These autoantibodies activate AT1 receptors, endothelial cells, and vascular smooth muscle cells [29]. The autoantibodies appear to block trophoblastic invasion and may induce the production of reactive oxygen species that plays a significant role in the pathogenesis of preeclampsia at several different stages [29].

5.2 Immunological factors

Maternal immune tolerance to parentally derived placental and fetal antigens is lost at maternal-placental interface, which is suggestive of acute graft rejection. The abnormal uteroplacental development is not clearly understood but is likely due to complex interaction of immunologic, vascular, environmental, and genetic factors. The theory of immune maladaptation may play a central role in predisposition to abnormal placentation and subsequent preeclampsia, suggesting that long-term exposure to paternal antigens in sperm is protective.

In preeclamptic women, extravillous trophoblast in early pregnancy expresses reduced amounts of immunosuppressive non-classic human leukocyte antigen G (HLA G). These changes contribute to defective placental vascularization in stage 1 of preeclampsia syndrome [30].

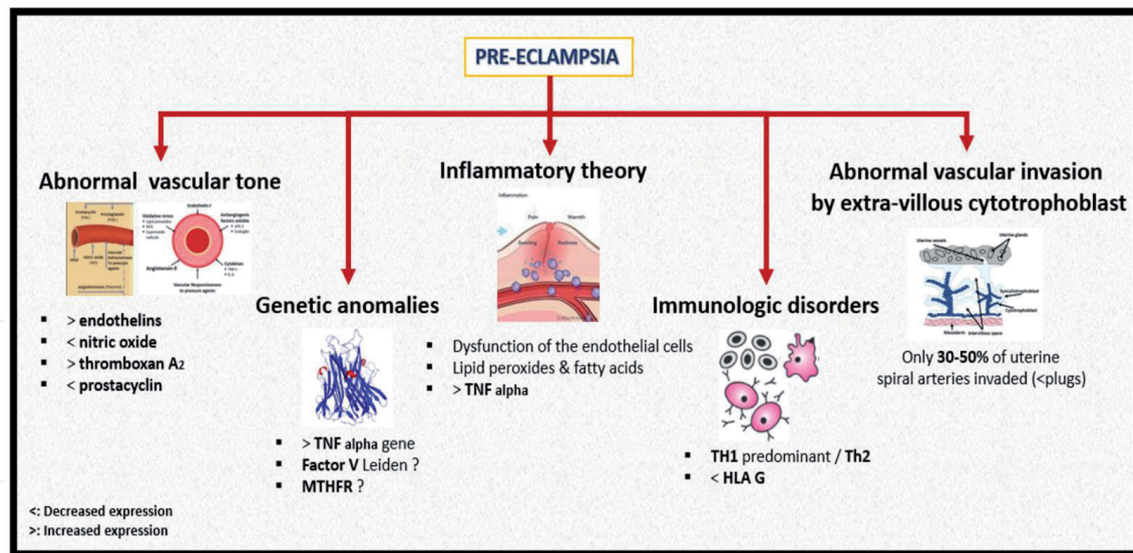


Figure 2.
Etiology of preeclampsia.

Excess macrophages in the decidua are associated with impaired trophoblast invasion and impaired placentation, signifying excess inflammation. NK cells interact with fetal trophoblast cell markers *via* killer immunoglobulin receptors (KIR) to influence trophoblastic invasion. Specific genotypic combinations of maternal KIR and trophoblastic human leukocyte antigen C (HLA-C) may increase the risk for preeclampsia. Systemic review of 22 studies examining association between HLA type and risk of preeclampsia suggests that HLA-DR correlates with preeclampsia, but it is unclear if this or any other HLA genotype is casually related to preeclampsia risk; further large sample size studies are called to examine maternal-fetal HLA combinations and risk of preeclampsia [30].

Etiology of preeclampsia is summarized in **Figure 2**.

6. Pathogenesis

6.1 Endothelial activation or dysfunction causing vasospasm

Inflammatory changes are said to be a continuation of stage 1 alternation. Placental factors are released in response to ischemia, and a cascade of events is provoked in response to antiangiogenic and metabolic factors and other inflammatory leukocyte mediators, commonly called endothelial cell activation or dysfunction. Systemic endothelial cell injury with intense vasospasm is from imbalance of vasodilators (PGI, NO), vasoconstrictors (Angiotensin-II, Thromboxane A₂, and Endothelin-II), oxidative stress, and inflammatory mediators (**Figure 3**). Vasospasm exerts a damaging effect on blood vessels and causes endothelial cells to contract and, together with hypoxia, leads to hemorrhage, necrosis, and compromised end-organ function.

In preeclampsia, inflammatory mediators contributed by systemic oxidative stress are tumor necrosis factor [31] alpha (TNF-Alpha) and interleukins that in turn lead to formation of lipid peroxidases [32], producing toxic radicals that injure systemic vascular endothelial cells.

Mechanisms are precisely understood but proposed theory discussed are as follows:

- Increase in circulatory pressor substances.

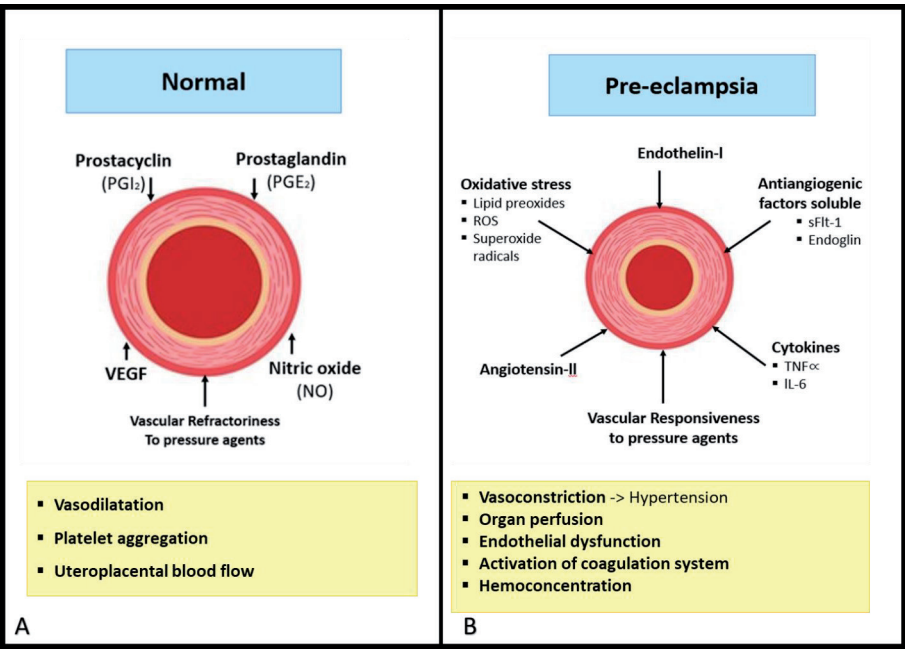


Figure 3.
A: In normal pregnancy. B: Vasoconstriction in preeclampsia.

- Increased sensitivity of the vascular system to normally circulating pressor substance.
- First-time exposure to chorionic villi.
- Superabundance of chorionic villi, exposed as with multifetal gestation or hydatidiform mole.
- Have preexisting vascular diseases associated with endothelial cell activation or inflammation such as diabetes, obesity, cardiovascular or renal, immunological disorders, or hereditary influences.
- Genetically predisposed to hypertension developing during pregnancy.
- Imbalance of angiogenic and antiangiogenic proteins.

6.2 Endothelial cell injury

Injury to systemic endothelial cell is crucial in pathogenesis of preeclampsia and likely secretes placental protein factors into maternal circulation, which provokes activation and dysfunction of systemic vascular endothelium, producing less nitric oxide contributing to vasoconstriction, and promotes coagulation and greater sensitivity to vasopressors.

6.3 Increased pressor responses

Normal pregnant women develop blunted vascular pressor response selectively to pressor agent angiotensin II, mediated by synthesis of endothelial prostaglandin and nitric oxide, which is a potent vasodilator. Following preeclampsia, angiotensinase activity is depressed, and the presence of autoantibodies to angiotensin AT1 receptor increases the vascular sensitivity to pressor agent angiotensin-II (Figure 4).

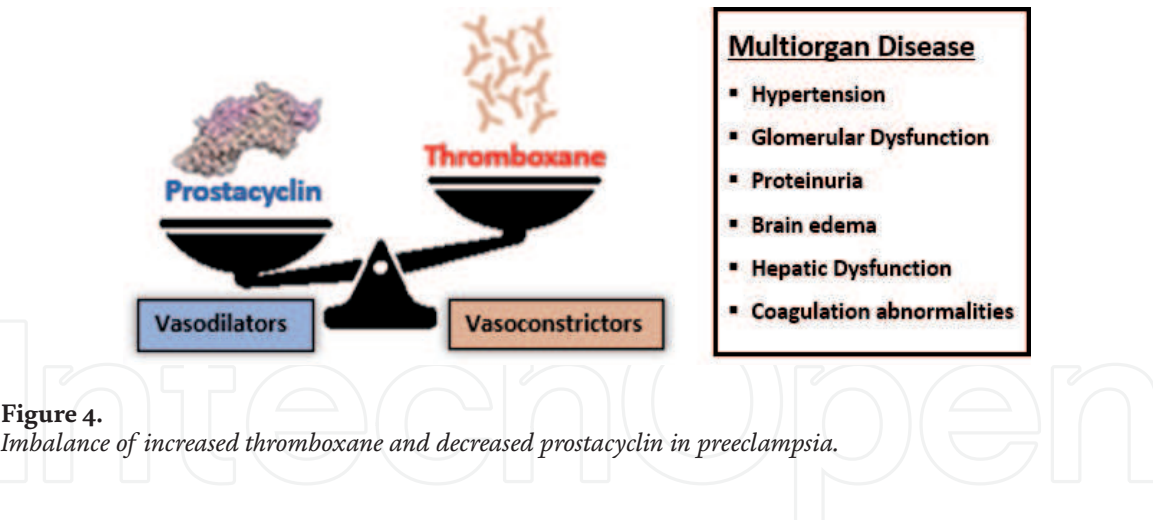


Figure 4.
Imbalance of increased thromboxane and decreased prostacyclin in preeclampsia.

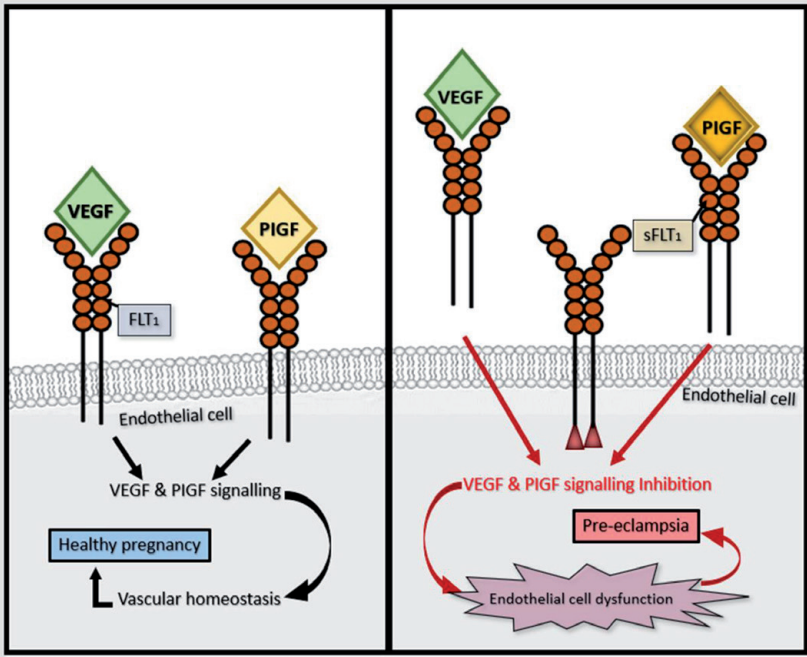


Figure 5.
Normal pregnancy: signaling of vascular hemostasis is maintained by physiological level of Vascular endothelial growth factor (VEGF) and Transforming growth factor (TGF). (B) In preeclampsia: excess secretion of Sflt1 (soluble fms-like tyrosine kinase) and sEng (soluble endoglin protein) inhibits VEGF (Vascular endothelial growth factor) and TGF (transforming growth factor) signaling of vasculature.

6.4 Angiogenic and antiangiogenic proteins

There is an imbalance of proangiogenic (VEGF) [33] and antiangiogenic (soluble fms-like tyrosine kinase sFlt-I) proteins in placental vascular bed. Soluble fms-like tyrosine kinase 1 (sFlt-1) has a receptor for VEGF (**Figure 5**).

With the progress of pregnancy, the placenta becomes relatively hypoxic at uteroplacental interface and results in an overexpression and release of placentally derived antiangiogenic peptide factors from the trophoblastic tissue, including sFlt-1 and soluble endoglin protein (sEng) into the maternal circulation, which appears to be important in pathogenesis of preeclampsia and remains the underlying theory [34]. Endothelin-I is synthesized by endothelial cells and is a potent vasoconstrictor causing hypertension (**Figure 5**).

In preeclampsia, sFlt-1 is a soluble antiangiogenic protein that is elevated, which binds and inactivates or reduces biological activity of free-circulating proangiogenic proteins, vascular endothelial growth factor (VEGF), and placental growth factor (PIGF), causing endothelial dysfunction [35].

7. Systemic organ dysfunction and complications

Severe manifestations of preeclampsia occur in all body systems because of widespread endothelial dysfunction, making diagnosis difficult due to similar clinical presentation despite complex differences in their underlying pathophysiology and prognosis.

Numerous factors combine to exert vasoactive effects in preeclampsia [36], causing resistance to blood flow and accounts for the development of arterial hypertension. Systemic organ dysfunction is explained in Figure 6.

7.1 Central nervous system dysfunction

Two marked cerebral pathologies are gross hemorrhage and ischemia, with other common variable lesions noted are edema, hyperemia, and thrombosis.

Manifestations of the central nervous system are severe headache, hyperexcitability, hyperreflexia, and coma attributable to hypoxia. Reversible vasogenic cerebral edema occurs commonly due to endothelial dysfunction of the brain in preeclampsia and eclampsia. Failure of autoregulation with reduced global cerebral blood flow and hyperperfusion commonly occurs in posterior circulation, such that the changes in the brain of patients with preeclampsia/eclampsia result in posterior reversible leukoencephalopathy syndrome (PRES) [37].

Intense ocular arteriolar constriction may cause visual disturbances, and may include blurred vision, scotoma, amaurosis [38], and retinal detachment (Figure 7).

Airway: In normal healthy pregnancy, the internal diameter of the trachea is reduced because of mucosal capillary engorgement, which can be exaggerated with narrowing of upper airway, resulting in pharyngolaryngeal edema, and subglottic edema with signs of airway obstructions such as dysphonia, hoarseness, snoring, stridor, and hypoxemia; these changes may compromise visualization of airway landmarks during direct laryngoscopy making intubation difficult [39].

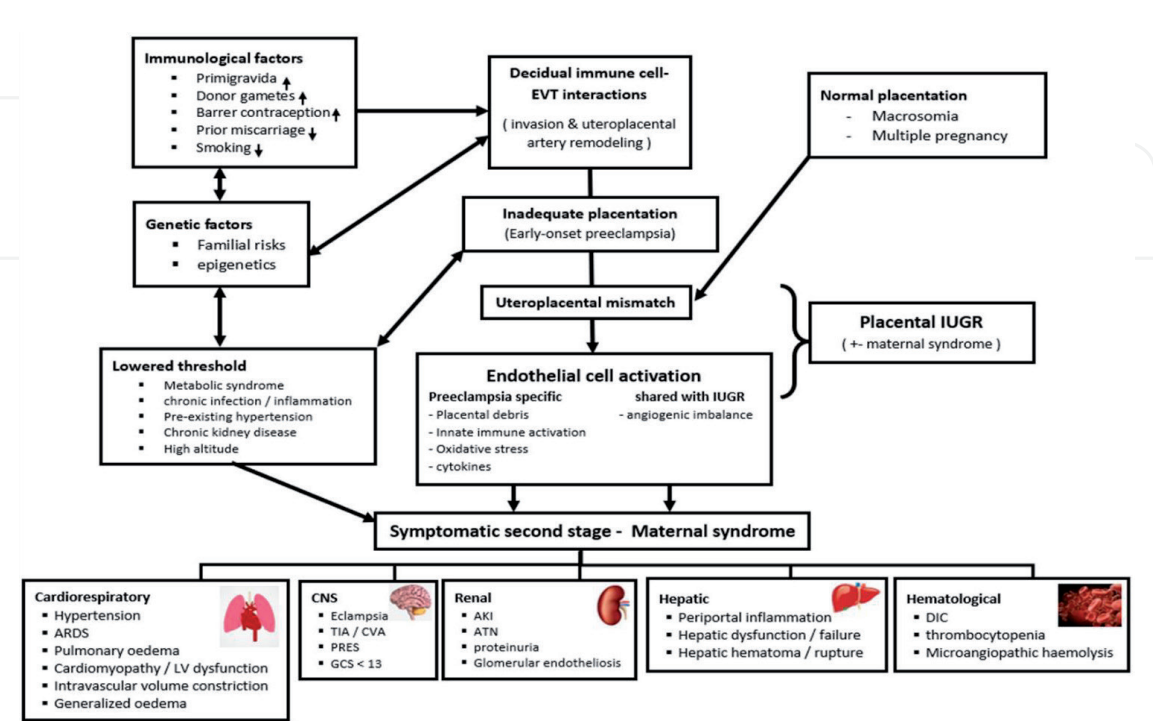


Figure 6.
Etiopathogenesis of preeclampsia.

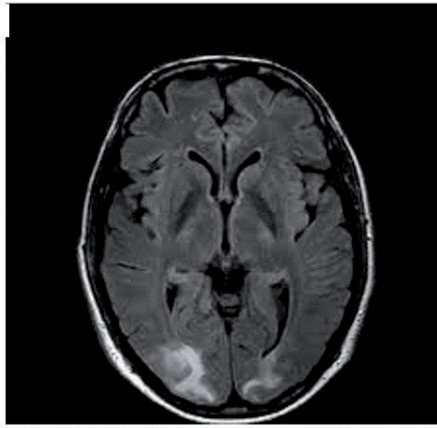


Figure 7.
PRES syndrome.

7.2 Respiratory system dysfunction

Pulmonary edema occurs in approximately 3% of preeclamptic women [40]. It is relatively infrequent in young healthy women than multiparous women. Decreased colloid osmotic pressure, in combination with increased permeability and the loss of intravascular fluid and protein into the interstitium, increases the risk for pulmonary edema [41]. Endothelial activations lead to extravasation of intravascular fluid into the extracellular space and, importantly, into the lungs. Excess intravenous fluid administration is an important risk factor for pulmonary edema in preeclampsia patients [42].

7.3 Cardiovascular system dysfunction

Common cardiovascular disturbances in preeclampsia syndrome are increased afterload caused by hypertension and reduced preload by pathologically diminished volume expansion during pregnancy.

Preeclampsia is a hyperdynamic state with increased vascular tone and increased sensitivity to vasoconstrictor, resulting in clinical manifestation of hypertension, vasospasm, and end-organ ischemia [43]. Hemodynamic response to circulatory catecholamine is exaggerated and characterized by severe vasospasm. Typically, blood pressure and systemic vascular resistance are elevated.

The majority of preeclamptic women show increased cardiac output [44], mild-to-moderate increased systemic vascular resistance [45], and hyperdynamic left ventricular function.

In summary, aggressive fluid administration in severe preeclampsia substantially elevates left-sided filling pressures and cardiac output to hyperdynamic levels. This elevates pulmonary capillary wedge pressure, causing pulmonary edema despite normal ventricular function.

7.4 Hematologic system dysfunction

Increase in blood volume is not evident in severe preeclampsia due to vasospastic state that follows endothelial activation and worsens with increased vascular permeability, and leakage of plasma into the interstitial space, resulting in increased hemoconcentration and hematocrit values that signify preeclampsia. These women with severe hemoconcentration are unduly sensitive to blood loss at delivery than normal [45].

7.5 Maternal thrombocytopenia

Thrombocytopenia is the most common hematologic disorder with platelet count of less than $100,000/\text{mm}^3$ in severe preeclampsia disease or HELLP (hemolysis elevated liver function low platelets) syndrome [46] that creates a hypocoagulable state correlating with the severity of the disease process.

In preeclampsia [47], platelets are activated, subsequent degranulation accounting for decrease in platelet function, and aggregation appears to account for the decrease in platelet count.

HELLP syndrome: It is characterized by hemolysis, elevated levels of liver enzymes, and low platelet count. It is associated with increased rates of maternal and perinatal morbidity. Weinstein coined the acronym HELLP. Women who do not reveal one or more of the clinical features is called partial HELLP syndrome [48].

Clinical presentation of maternal signs and symptoms vary from right upper quadrant or epigastric pain, nausea and vomiting, headache, hypertension, and proteinuria, and 12–18% of women may be normotensive and 13% may be without proteinuria. Clinical management has to prioritize maternal stability, particularly, hypertension and Coagulation abnormalities, and assess the fetal condition *via* FHR monitoring. Risk of postpartum hemorrhage is significantly increased in HELLP patients [48].

7.6 Hemolysis

Severe preeclampsia is frequently accompanied by microangiopathic hemolysis that manifests as elevated lactate dehydrogenase, reduced haptoglobin levels, hemolytic anemia, and abnormal peripheral blood smear with schistocytes, spherocytes, and reticulocytosis [49].

7.7 Coagulation changes

Disseminated intravascular coagulation is a syndrome secondary to microthrombi formation in severe preeclampsia with liver derangement [50]. Activation of coagulation system is marked by consumptions of procoagulants, increased levels of fibrin degradation products, and end-organ dysfunction. In advanced stages of DIC (disseminated intravascular coagulation), it may cause spontaneous hemorrhage, intrauterine fetal demise, placental abruption, or postpartum hemorrhage.

7.8 Endocrine and hormonal alternations

Plasma levels of renin, angiotensin I & II, aldosterone, deoxycorticosterone, and atrial natriuretic peptide (ANP) are substantially increased during normal pregnancy, which is further enhanced in preeclampsia women.

7.9 Fluid and electrolyte alterations

Extracellular fluid manifests as edema with pathological fluid retention in women with severe preeclampsia due to endothelial injury. In addition to generalized edema and proteinuria, these women have reduced plasma oncotic pressure, which creates a filtration imbalance and further displaces intravascular fluid into the surrounding interstitium, creating intravascular dehydration and extravascular overhydration. Electrolyte concentration does not differ grossly in preeclampsia patients.

7.10 Renal dysfunction

Defining component of preeclampsia is proteinuria, with its renal manifestations of persistent proteinuria, changes in glomerular filtration rate, renal blood flow, and hyperuricemia. In preeclampsia serum markers, blood urea nitrogen (BUN), creatinine, and uric acid reflect a decrease in renal functions. Hyperuricemia (elevated uric acid levels) is one of the recognized early predictors of preeclampsia, with the primary mechanism of decreased renal clearance [51]. High level of serum uric acid correlates with the severity of the disease. Glomerular endotheliosis is the main feature of the preeclamptic kidney defined by endothelial swelling and glomerular capillary narrowing.

Oliguria is a probable late manifestation and parallels the severity of preeclampsia. Persistent oliguria (< 500-mL urine output in 24 hours) requires immediate attention for evaluation of intravascular volume status.

Major pathological process of acute renal failure in preeclampsia (83–90%) is from prerenal and intrarenal pathology (most commonly acute tubular necrosis), which resolves completely after delivery.

7.11 Hepatic dysfunction

Reduced blood flow to the liver may lead to periportal necrosis and are at risk of periportal hemorrhage, fibrin deposit, subcapsular bleeding, and hepatic rupture.

Hepatic involvement frequently presents as right upper quadrant or epigastric pain and accounts for 32% maternal mortality rate [50].

Rupture of a subcapsular hematoma of the liver is a life-threatening complication that can manifest as abdominal pain, which worsens over time and becomes localized to the epigastric area or right upper quadrant associated with nausea, vomiting, and headache. Alarming hypotension and shock develop with enlarged and tender liver. Diagnosis of liver subcapsular hematoma is confirmed by ultrasonography, computerized tomography (CT), or magnetic resonant imaging (MRI). The most common cause of death is coagulopathy. Conservative management is recommended for subcapsular hematoma or intraparenchymal hemorrhage without capsular rupture in stable women with an important component to avoid all potential trauma to the liver.

7.12 Uteroplacental malperfusion

Uteroplacental perfusion can be impaired in pregnancies complicated by preeclampsia with increased downstream resistance in the uteroplacental bed, decreased diastolic flow velocity, and increased systolic-diastolic flow velocity ratio [51]. Reduced uteroplacental malperfusion is considered one of the major causes of fetal compromise (IUGR, premature birth, and perinatal death). Risk of placental abruption is increased threefold with increased perinatal morbidity and mortality in preeclampsia women [51].

8. General principles and management

- Definite treatment of preeclampsia is termination of pregnancy to prevent disease progression and reduce maternal complications and neonatal morbidity. Time of delivery is based on gestational age, severity of preeclampsia, and maternal and fetal condition.

- Birth of infant who can then thrive subsequently.
- Most patients with preeclampsia with or without severe features can be delivered vaginally. Cesarean delivery is indicated for obstetric indications.
- Fluid balance must be titrated closely to avoid excessive administration and avoid pulmonary edema.
- Expectant management of women with preeclampsia without severe features of disease process may be considered in tertiary care center setting with maternal-fetal medicine specialist (frequent laboratory monitoring, and clinical assessment of mother and fetus).
- Complete restoration of mother’s health.

9. Long-term consequences

Table 1 describes long-term complications of preeclampsia syndrome.

Cardiovascular	Neurovascular	Metabolic	Renal	Central nervous system
Chronic hypertension	Stroke	Type 2 diabetes	Glomerular dysfunction	Cognitive dysfunction
Ischemic heart disease	Retinal detachment	Metabolic syndrome	Proteinuria	Retinopathy
Atherosclerosis	Diabetic retinopathy	Obesity		White-matter lesions
Cardiomyopathy		Dyslipidemia		
Thromboembolism				

Table 1.
Long-term impact of preeclampsia.

10. Conclusion

Preeclampsia is one of the hypertensive disorders of pregnancy with increased morbidity and mortality. It occurs in up to 12% of pregnancies. Advanced maternal age, genetic factors, obesity, and chronic renal impairment increase the risk of preeclampsia in pregnant patients. Abnormal placentation, immunological changes, endothelial injury and activation, and increased pressor response are the pathogenesis of preeclampsia.

Due to these generalized endothelial changes, the preeclampsia patients develop multiple organ dysfunction, including PRES (posterior reversible encephalopathy) syndrome, pulmonary edema, HELLP syndrome, acute kidney injury, and uteroplacental insufficiencies.

Management of preeclampsia is supportive therapy, blood pressure control, and seizures prevention and delivery of the fetus. Long-term effects of preeclampsia are chronic hypertension, stroke, and chronic kidney disease.

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