Section: Anatomy

Review Article

A REVIEW ON ETIOPATHOLOGY AND OUTCOME IN PRE-ECLAMPSIA

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Abstract

Preeclampsia is major cause of premature birth, IUGR, morbidity, perinatal fatalities and 15–20% maternal mortality. It is classified as mild, moderate and severe. Risk factors include obesity, primigravida, placental abnormalities, multiple gestation, chronic renal disease, family history along with several other factors. Endothelial dysfunction and vasospasm continue to be the underlying pathologies that affect all vessels. According to current molecular investigations dysfunction of vascular endothelium is due to loss of VEGF. The mechanism of inhibition of VEGF production in preeclampsia is due to elevated levels of sFlt1 which inhibits VEGF. Ischemia and hypoxia of placenta are the last stages in the pathophysiology of preeclampsia, with vasoactive substances released into the maternal circulation and endothelial cell malfunction resulting in signs and symptoms.

INTRODUCTION

Preeclampsia (PE) is characterized by elevated blood pressure and excessive levels of proteins in urine that begins at 20 weeks of gestation. Its overall prevalence rate is 5-8% which is a major cause of IUGR, preterm birth, morbidity, perinatal fatalities and 15–20% maternal mortality.[1,2] PE predicts a greater risk of cardiovascular and also metabolic disorders as the age advances, which may necessitate lifestyle counselling and intervention. Pre-eclampsia is still the utmost mutual cause of maternal and perinatal death and morbidity.[3,4] If blood pressure and proteinuria rise significantly, or indications of end-organ damage appear, it is termed severe. There are no well-established primary preventative strategies. Despite evidence-based management, prevention measures or screening tools are limited with symptomatic treatment, and delivery remains the only cure.[5] Despite vigorous research, the etiology remains a mystery. No significant change in preeclampsia treatment in over 50 years.[6]

Classification of PE: For management purposes, PE is categorized based on blood pressure (BP) levels. Proteinuria, on the other hand, is more important than blood pressure in predicting fetal outcome. Classification by Yorkshire series based on severity forms basis for PE classification.

- **Mild:** A prolonged rise in BP greater than 140/90 mm Hg but below 160- or 110-mm Hg diastolic along with proteinuria of 0.3 g /24 hrs.
- **Moderate:** BP of 150/100 mm Hg with proteinuria of 0.3 g /24 hrs.
- **Severe:** BP of 160/110 mm Hg or more with proteinuria of 1 g/ litre.[7-9]

Causes of PE: Risk factors are basically classified into immunological and genetic [9,10] shown in table -1.

Table 1 Preeclampsia -risk factors

- Family history
- Obesity
- Primigravida
- Thrombophilia
- Placental abnormalities
- Pre -existing vascular disease
- New parity
- Prolonged pregnancy interval
- Multiple gestation
- Chronic renal disease

Other risk factors also include vision abnormalities, shortness of breath, renal dysfunction, decreased liver function, edema and low platelet count.

Etiopathogenesis of PE: Under normal circumstances, endovascular trophoblasts penetrate the spiral arterioles of the uteroplacental bed and remodel them into large diameter arteries with high

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capacitance and free blood flow.[11] Aberrant spiral arterial remodeling in pregnant women with hypertensive disorder was first noticed and studied more than five decades ago.[12] It has now been discovered to be the main cause of gestational hypertension, intrauterine growth restriction and preeclampsia in pregnancies.[13] Atypical placentation has placental hypoperfusion as a cause as well as an outcome.[14,15] In placental tissue atherosclerosis, thrombosis, arteriosclerosis, fibrinoid necrosis and infarction are the late pathologic changes observed which correlate with ischemia.[16] Endothelial dysfunction and vasospasm continue to be the underlying pathologies that affect all vessels. Development of eclampsia / preeclampsia are independent of BP level.[17]

Pathophysiology: In spite of the fact that the essential pathology driving to preeclampsia is unknown, pathological changes are well documented. Since the placenta evacuation is necessary to regress the symptoms, it always plays a significant role in etiology of PE.[18,19] Placental growth factor (PlGF) and soluble fms-like tyrosine kinase-1 (sFlt-1) are two angiogenic factors that may play a role, according to growing research. According to current molecular investigations, the decrease of VEGF causes dysfunction of vascular endothelium in PE. The mechanism of inhibition of VEGF production in PE is due to elevated levels of sFlt-1, a powerful inhibitor of VEGF production.[20-22]

In PE, endothelial dysfunction is due to antiangiogenic state mediated by soluble endoglin in relation to lower levels of PlGF, VEGF and high levels of sFlt-1. Placenta produces large amounts of sFlt-1, but in preeclampsia extra source of production is circulating mononuclear cells.[23,24] In women with PE, higher levels of circulating sFlt-1 have been reported which may antecede the onset of PE, and levels of sFlt-1 might correlate with the severity of PE.[25,26]

Key mediator in the growth of PE is sFlt-1.[27] Link between PE occurrence and adaptive immune response is inflammation.[28] Placental DNA released into fetal and maternal circulation plays major role in the characteristic inflammation linked with PE.[29] Link between PE and maternal infection revealed that women with periodontal disease and urinary tract infections are at risk of PE.[30-32] Most of the data suggest that maternal and paternal genes are responsible in the development of placental abnormalities and consequent PE.[33] The onset of the disease is likely to be influenced by genetic factors.[34,35] Final pathogenesis pathways of PE include ischemia and placental hypoxia which release vasoactive substances into maternal circulation and cause endothelial cell malfunction leading to signs and symptoms of PE.[36,37]

Maternal outcome: The rates of adverse perinatal and maternal outcomes between primigravida and multigravida pregnancies showed no significant difference.[38] The most common causes of maternal death are permanent neurological sequelae due to ischemia or cerebral hemorrhage, with 0-14% of maternal mortality rates.[39] 2 -3 % woman with preeclampsia is complicated by eclampsia which may lead to maternal morbidity and mortality.[40]

Fetal outcome: Intrauterine growth restriction, intrauterine death, asphyxia and prematurity are consequences based on the duration and severity of disease and degree of proteinuria. Belay Tolu L et al observed 1.7% stillbirth, 2.27% neonatal death, 12% IUGR and 18.2% preterm birth in their study.[38] Oligohydramnios and IUGR are the primary consequences in preeclampsia due to decreased placental perfusion.[41] Adverse perinatal events are due to underlying pathology of placenta. In preeclamptic mothers who deliver preterm, aberrant placental weight indicates adverse neonatal outcome.[42] Preterm delivery owing to HELLP syndrome or preeclampsia was related with necrotizing enterocolitis requiring surgery, a lower incidence of intracerebral hemorrhage, periventricular leukomalacia, and death when related to the other causes of preterm birth after adjustment for confounding variables.[43] Neonatal death and morbidity in severe preeclampsia are linked to gestational age rather than the absence or presence of the HELLP syndrome.[44] A variety of neurocognitive problems have been reported in children born during preeclamptic pregnancies. Compared to children born to women with normotension, Tuovinen et al. discovered that the children in question presented more reports of cognitive impairments and susceptibility to distraction The severity of eclampsia implies that similar, if not more severe, neurodevelopmental problems may arise, even if particular research on eclampsia-related neurocognitive outcomes in offspring is less thorough. Although there is no concrete proof, the severe form of eclampsia may increase the risk of cognitive deficits and developmental problems; however, more research is necessary. [45]

Management: Preeclampsia cannot be spotted with a single, reasonable, and accurate screening test, since there are no proven primary prevention strategies. Close observation of the mother's and the fetus's health is part of the management prior to the start of labor. Limiting seizures with magnesium sulfate and, if required, treating hypertension medically are part of the treatment during delivery. [46] In order to treat severe preeclampsia and deliver a live baby without the need for extensive neonatal care, the mother's wellbeing must come first. [47] Probable, randomized controlled trials revealed that magnesium therapy is connected with a diminished occurrence of cerebral palsy amongst survivors exposed to the medication between 24 to 31 weeks of gestation. [48]

CONCLUSION

In spite of several theories and mechanism documented etiology of preeclampsia remain still

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unclear. Principal basis of maternal mortality and morbidity is PE that affect mother and fetus. Its etiology throws a challenge that requires a thorough research to understand its complexity. Translational research is now required to demonstrate how these developing concepts might be used to aid early diagnosis and treatment.

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