

# Risk of Pre-Eclampsia in Pregnant Women: A Scoping Review

Madhu Sudhan Yalam<sup>1</sup>, Neelima Ganta<sup>1</sup>, Nandan Peri<sup>1</sup>, Raj Kiran Kolakota<sup>2</sup>,  
Vinodkumar Mugada<sup>3</sup>

<sup>1</sup>V Year Pharm. D, <sup>2</sup>Professor and HOD, <sup>3</sup>Assistant Professor,  
Department of Pharmacy Practice, Vignan Institute of Pharmaceutical Technology,  
Duvvada, Visakhapatnam, AP, India

Corresponding Author: Madhu Sudhan Yalam

## ABSTRACT

Preeclampsia/eclampsia is a potentially fatal disorder in pregnant women and remains one of the leading causes of maternal mortality and morbidity maternal and fetal mortality. Pre-eclampsia is 2–10% of all pregnancies and this may be higher in low resource settings. The databases searched included Pub Med, Science direct, and Trip database. To conduct this study the inclusive criteria we considered the population all over the world, pregnant women since 2011, research articles, association of certain factors with risk of preeclampsia, influence of certain drugs for those who are already at risk, pregnant women who are giving birth for the first time & second, obese patients. Exclusion criteria include patients who are previously diagnosed with Hypertension, Postpartum women, Diabetic women, Women having any habits (Smoking, alcohol), Postmenopausal women, and Healthy pregnant women. Data extraction included information about demographic details, Intervention, Participants, Search strategy & Type of study. The extraction was carried out from the studies that were identified for inclusion. Prevalence of pre-eclampsia was reported to be 2- 10% of all pregnancies. Women who have a previous history of hypertension and LV diastolic dysfunction and those who are in treatment with various types of antidepressants are more likely to develop pre-eclampsia.

**Keywords:** Risk, pre-eclampsia, pregnant women, LV diastolic dysfunction, hypertension.

## INTRODUCTION

Pre-eclampsia is a pregnancy-specific malady often accompanied by hypertension (high blood pressure of 140/90 mmHg or more), proteinuria occurring after 20 weeks of gestation<sup>(1-3)</sup> and characterized by widespread dysfunction of the endothelium in the mother.<sup>(4)</sup> Preeclampsia/eclampsia is thus a potentially fatal disorder in pregnant women and remains one of the leading causes of maternal mortality and morbidity maternal

and fetal mortality,<sup>(5,6)</sup> intrauterine growth restriction, and preterm birth.<sup>(7-9)</sup>

Prevalence of Pre-eclampsia is 2-10% of all pregnancies and this may be higher in low resource settings.<sup>(10)</sup> Approximately 36% of women with pregnancy-associated strokes (PASs) have co-morbid preeclampsia.<sup>(11)</sup> Overall, 10 % of women have high blood pressure during pregnancy and 2-5% will develop pre-eclampsia.<sup>(12)</sup> Worldwide, HDP is more common and may complicate 5-10% of all

pregnancies. HDP is responsible for 12-25% of cases of maternal mortality during pregnancy and the puerperium. <sup>(13)</sup> Preeclampsia has shown an increasing trend in Ethiopia with an estimated prevalence of 8.4 %, and ranks third among the top four causes of maternal mortality in the country. <sup>(14)</sup> Together, pre-eclampsia and eclampsia account for approximately 50000 deaths each year, which is 12% of all maternal death. <sup>(15)</sup> Although relatively rare (3-6 per 10,000 births), eclampsia carries a major burden on maternal and perinatal morbidity and mortality worldwide. <sup>(16)</sup>

### **Risk factors**

In women receiving prophylactic aspirin, higher blood pressure measured at a single occasion between 11-14 weeks was associated with increased pre-eclampsia risk. <sup>(17)</sup> The known risk factors for pre-eclampsia include primiparity, multigravidity, obesity, renal disease, uterine malformation, fetal hydrops, elevated serum lipid ratio, non-smoking, no prenatal care, and diabetes. <sup>(18)</sup> Exposure to noise can result in increased blood pressure, and that noise evokes secretion of adrenalin, noradrenalin, and cortisol, endocrine hormones that cause vasoconstriction and have a cardiovascular impact. <sup>(19)</sup> Although preeclampsia resolves following delivery, women with prior preeclampsia have increased the long-term risk for hypertension (4-fold increased risk) and cardiovascular disease (CVD) (2-fold increased risk). <sup>(20)</sup> It has been demonstrated that lack of anti-oxidants may be related with the onset of preeclampsia. <sup>(21,22)</sup> Evidence suggests that several factors, including but not limited to, age, body size & maternal diet play a role in the etiology of preeclampsia <sup>(23)</sup> Plasma fibronectin (FN) levels in obese/overweight and non-obese pregnant women were evaluated as a possible risk factor for preeclampsia. A deficiency of maternal NO might be important in the development of pre-eclampsia. <sup>(24)</sup> Lack of adequate transformation of spiral arteries is an important event on the road to pre-

eclampsia. <sup>(25)</sup> Due to changes in people lifestyle and also due to regional and racial differences, there are significant differences in high-risk factors and low-risk factors for pre-eclampsia. <sup>(26)</sup>

## **METHODOLOGY**

**Search Strategy & Databases:** The databases searched included PubMed, Science direct, and Trip database. A broad search included the following keywords: Risk, Pre Eclampsia, Pregnant women.

### **Eligibility criteria:**

#### **a) Inclusive Criteria:**

To conduct this study the inclusive criteria we considered are Population all over the world were considered, pregnant women since 2011, research articles, association of certain factors with risk of pre-eclampsia, influence of certain drugs for those who are already at risk, pregnant women who are giving birth for the first time & second, obese patients

#### **b) Exclusive criteria:**

Exclusion criteria include Patients who are previously diagnosed with Hypertension, Postpartum women, Diabetic women, Women having any habits (Smoking, alcohol), Postmenopausal women, and Healthy pregnant women

**Data extraction:** Author and year of publication, type of study, study population, sample size of the study, type of study, risk factor assessed, and the outcome were included in the table.

## **DISCUSSION**

A significant risk reduction for the development of preeclampsia is achieved when low-dose aspirin prophylaxis is initiated before 16 weeks of gestation in high-risk women. <sup>(27-29)</sup> In women receiving first-trimester aspirin, maternal characteristics such as higher blood pressure or BMI at a single occasion in the first trimester leads to failure of aspirin prophylaxis.

<sup>(30)</sup> Selective serotonin reuptake inhibitor (SSRI) antidepressants inhibit serotonin reuptake, and serotonin-

norepinephrine reuptake inhibitor (SNRI) antidepressants and tricyclic antidepressants (TCAs) inhibit serotonin and norepinephrine reuptake to varying degrees. (31,32) Increased serotonin and norepinephrine levels may contribute to the development of preeclampsia. (33, 34) Magnesium sulfate is the drug of choice for preventing both the initial episode of eclampsia and the recurrence of seizures. For women with preeclampsia, magnesium sulfate reduces the risk of developing eclampsia by 60% compared with placebo. (35,36)

It is generally agreed that the placenta plays a critical role in the pathophysiology of PE. Redman et al (37) described a two-stage model explaining the pathophysiology: in the first stage, which takes place in the first half of the pregnancy, placental development is disturbed. Remodeling of the maternal spiral arteries is impaired leading to a decreased maternal blood supply to the placenta. This is called poor placentation. Pre-eclampsia is found to be associated with left ventricular (LV) diastolic dysfunction and increased LV mass when compared to normotensive pregnant women. (38, 39) The utero placental insufficiency, which is the failure of the placenta to deliver adequate nutrients and oxygen, triggers events that lead to endothelial and vascular smooth muscle cell dysfunction, increasing vascular resistance and high blood pressure. (40-42) Although preeclampsia resolves following delivery, women with prior preeclampsia have increased the long-term risk for hypertension (4-fold increased risk) and cardiovascular disease (CVD) (2-fold increased risk) (43,44) Women with a history of a hypertensive pregnancy disorder, including pre-eclampsia, have an elevated cardiovascular risk. (45, 46)

Indoor air pollution, from traditional fuels (such as biomass and coal) and cooking stoves, is associated with an increase in the incidence of respiratory infections, including pneumonia, tuberculosis and chronic obstructive pulmonary disease, low birth weight,

cataracts, cardiovascular events, and all-cause mortality both in adults and children and even to noise can result in increased blood pressure and have a cardiovascular impact. (47)

Consumption of multi-mineral Vitamin D3 supplements for nine weeks among pregnant women at risk for preeclampsia resulted in a significant increase in newborn's length, maternal serum calcium, magnesium, zinc and Vitamin D levels, and also a significant reduction in maternal SBP and DBP. (48) Women with depression diagnoses who had antidepressant dispensing between gestational weeks 10 and 20 had a higher risk of pre-eclampsia than did women with depression but no dispensing. Use of SNRIs or TCAs was associated with a 2- and 3-fold increased risk of preeclampsia, respectively. (49)

The study revealed that a history of preeclampsia in a first pregnancy was a risk factor for the development of GDM in the subsequent pregnancy. The researchers have studied the potential impact of GDM on the development of hypertension, type 2 DM, and other cardiovascular diseases after delivery. (50, 51) GDM and gestational hypertension have been long associated with each other as they share several common risk factors. (52, 53) The risk of preeclampsia was significantly higher for pregnant women with gestational diabetes than for pregnant women without gestational diabetes. (54)

Poston et al (55) and Rumbold et al, (56) the risk of severe pre-eclampsia/eclampsia/HELLP may decrease with increasing intake of vitamin C. Hypertensive disorders of pregnancy, including preeclampsia, are a leading cause of maternal morbidity and mortality. (57,58) The effects of preeclampsia are not limited to the duration of pregnancy: women with preeclampsia are at increased risk for future cardiovascular disease and their offspring, if born premature or at the low birth weight, are at increased risk for chronic disease in adulthood. (59)

**Table 1: Studies and outcomes on the risk of pre-eclampsia in pregnant women**

S. No.	Author & year of publication	Study population	Sample size	Type of research	Risk factor measured	Outcome
1.	Asemi et al., 2015 <sup>(60)</sup>	Women with 27 weeks of gestation	46	Randomized double-blind controlled clinical trial	Multivitamin D supplementation	Increase risk of Pre-eclampsia
2.	Samimi et al., 2015 <sup>(61)</sup>	Women at risk of pre-eclampsia	60	Double blind placebo-controlled trial	Vitamin D+ calcium supplementation	Beneficial outcome
3.	Varol et al., 2007 <sup>(62)</sup>	Mild pre-eclamptic, severe pre-eclamptic, healthy pregnant women	59	Cross Sectional study	Periodontal disease	Increased risk of pre-eclampsia
4.	Kristin et al., 2011 <sup>(63)</sup>	Women with depression.	69,448	Comprehensive study	Risk of pre-eclampsia in depressed women	gestational weeks 10 and 20 had a higher risk for preeclampsia
5.	Duvekot et al., 2002 <sup>(64)</sup>	Women with pre-eclampsia from 1991-1996	163	Case control study	Low milk intake	Increased risk
6.	Fieg et al., 2013 <sup>(65)</sup>	pregnant women who delivered in Ontario, Canada between April 1994 and March 2008.	1,010,068	Retrospective cohort study	Risk of Diabetes	Women with PEC/GH have a 2-fold increased risk of developing diabetes
7.	Rayman et al., 2014 <sup>(66)</sup>	primiparous pregnant women	230	double-blind, placebo-controlled, pilot trial,	Effect of selenium	Selenium supplementation has the potential to reduce the risk of pre-eclampsia
8.	Auger et al., 2018 <sup>(67)</sup>	deliveries on the island of Montreal, Canada between 2000 and 2013.	269,263	cohort study	Environmental noise pollution	Prevalence of preeclampsia was higher for women exposed to elevated environmental noise Pollution
9.	Ghossein-doha et al., 2017 <sup>(68)</sup>	formerly pre-eclamptic women and women with uneventful previous pregnancy (controls)	148	cross-sectional cohort study	The risk of asymptomatic heart failure	asymptomatic HF-B was approximately 3.5-fold higher in pre- eclampsia
10.	Vieira et al., 2016 <sup>(69)</sup>	Eligible nulliparous women.	3,940	Cohort study	family history of thrombotic disease, low plasma placental growth factor, and higher uterine artery resistance index at 20 weeks.	Women with obesity and a normal BMI have different early pregnancy clinical and bio-marker risk factors for preeclampsia.

## CONCLUSION

Pre-eclampsia is a pregnancy-specific disorder often accompanied by hypertension, proteinuria usually after 20 weeks of gestation which is associated with endothelial dysfunction and increased risk of various cardiovascular abnormalities that are prone to increase the risk of morbidity and mortality. Among drugs, aspirin was found to either delay or prevent the onset of pre-eclampsia but however, it's not much effective in the first trimester. Drugs like SSRIs, SNRIs, and TCAs are likely to increase the risk of pre-eclampsia by increasing either serotonin or norepinephrine levels. Drugs like

magnesium sulfate lower the initial episode of pre-eclampsia and also reduce the risk of developing seizures. Among cardiovascular events, LV diastolic dysfunction was found to play a role. Increase in the LV mass contributes to developing pre-eclampsia. It was found that a history of pre-eclampsia during the first pregnancy was a risk factor for developing GDM during a subsequent pregnancy. Moreover, it may also contribute to AKI during the first trimester which is called pregnancy-related AKI (PRAKI) due to increased levels of catecholamines. So, it can be concluded that pre-eclampsia if neglected, can progress to eclampsia that can cause many serious life-threatening

complications. Hence it should be treated as early as possible to protect both mother and the fetus.

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