Preeclampsia is a syndrome that is characterized by heterogeneous clinical and laboratory findings. The clinical features and manifestations are generally in the mother. However, sometimes the fetal syndrome may dominate the clinical picture. The current understanding of preeclampsia has not given us an exact etiological factor or a precise pathophysiologic mechanism. However, it is becoming clear that it is much more than hypertension, proteinuria and edema in pregnancy. Despite extensive research in the pathogenesis of preeclampsia, the etiology remains a mystery. A number of mechanisms postulating the development of preeclampsia have been put forward. Some of these mechanisms have included impaired trophoblast differentiation and invasion, placental and endothelial dysfunction, immune maladaptation to paternal antigens, and exaggerated systemic inflammatory response. Because the disorder is heterogeneous, the pathogenesis can differ in women with various risk factors. The mechanisms underlying preeclampsia in a healthy primigravida may be quite different from those through which occur in a 40-year old chronic hypertensive woman or a woman with a previous pregnancy affected by preeclampsia.

From the public health perspective, the condition complicates 2–8% of pregnancies. Worldwide, 10–15% of the half million maternal deaths that occur every year are associated with hypertensive disorders of pregnancy. 99% of these occur in low-resource countries. Preeclampsia also takes a massive toll on perinatal health and is responsible for a significant proportion of preterm births (iatrogenic and spontaneous), growth restriction and mortality. Preventing preeclampsia would therefore be a highly desirable goal.

**Who is at risk?**

Preventing preeclampsia would be possible if we can identify the underlying pathophysiological mechanisms. This would also allow us to predict preeclampsia more successfully and target the high risk population. As things stand today, strategies to predict preeclampsia are based on epidemiological data, biochemical and sonographic markers. These seem to be either the consequence of the disease or its epiphenomena. When the biological markers become apparent, it is likely that the disease process is already underway in the body and measures taken at this stage would be more to do with preventing the consequence rather than the occurrence of the disease. Table 1 gives a comprehensive list of risk factors that are associated with a higher risk of preeclampsia. In clinical practice, the following are encountered most commonly:

- Age over 40 years
- Chronic hypertension, obesity and diabetes
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- Previous pregnancy complicated by severe preeclampsia (especially early onset), IUGR or abruption
- Multiple pregnancy
- False positive results for trisomy screening
- Abnormal uterine artery Doppler waveform (high S/D ratio or notching).

Some of these factors are known before the index pregnancy begins and are amenable to correction. Women should attempt to bear children in their best possible condition. Potential measures to ensure an optimal health status would include achieving a normal body weight and BMI, control of preexisting medical disorders and achieving optimal organ function for renal disease patients. The drugs used for control of hypertension and diabetes should be suitable for pregnancy and doses and class of agents may have to be changed keeping this in mind. It would be ideal if this control could be achieved for a few months before conception occurs. Though there are no randomized trials to prove these benefits, these measures are supported by widely available epidemiological data.6, 7

Preexisting or Preconceptional risk factors

- Chronic hypertension
- Renal disease
- Pregestational diabetes mellitus
- Autoimmune disease (SLE, rheumatoid arthritis)
- Primary antiphospholipid antibody syndrome and other thrombophilias
- Obesity, insulin resistance
- Age > 40 years
- Previous pregnancy with severe preeclampsia especially of early onset, IUGR, abruption or fetal death
- Family history of preeclampsia in mother
- Partner who has a fathered a pregnancy affected by preeclampsia in another woman
- Limited sperm exposure (donor insemination)

Pregnancy-related risk factors

- Hydrops/hydrops degeneration of placenta (triploidy, trisomy 13)
- Multifetal gestation (depends on number of fetuses and maternal age)
- Unexplained fetal growth restriction
- Gestational hypertension
- Urinary tract and periodontal infections

Biochemical and Biophysical markers

- Unexplained second-trimester elevations of serum alpha-fetoprotein, human chorionic gonadotropin, inhibin A, activin A
- Abnormal uterine artery Doppler velocimetry in first and second trimesters
- Decreased placental growth factor in the second trimester
- Elevated soluble fms-like tyrosine kinase-1 in second trimester
- Elevated soluble endoglin in second trimester
- Elevated asymmetric dimethylarginine in second trimester
- Reduced serum placental protein-13 in the first trimester
- Reduced pregnancy associated plasma protein A in first trimester

Table 1. Prediction of Preeclampsia.