REVIEW ARTICLE

Preeclampsia–Eclampsia

Gupte Sanjay · Wagh Girija

Abstract Preeclampsia and eclampsia are grave complications of pregnancy responsible for morbidity and mortality. National Eclampsia Registry of the FOGSI has helped in quantifying the magnanimity and also the clinical relevant pointers which can help in improving the health care delivery. Many complex pathogenic mechanisms are now implicated to be responsible for this disease rightfully called the GESTOSIS which means pregnancy going abnormal. Many preventive strategies have been suggested but only a few are scientifically proved to be useful. Early antenatal care, clinical risk assessment, biomarkers, close vigilance, calcium and nutritional supplementation are useful.

Keywords Preeclampsia · Eclampsia · GESTOSIS · Hypertension in pregnancy · Registry

Introduction

Hypertensive disorders of pregnancy constitute a perplexing and clinically challenging group of pregnancy complications that are responsible for a substantial burden of illness in developed as well as underdeveloped countries of the world. They are a leading cause of maternal and perinatal mortality and morbidity worldwide.

Approximately 72,000 pregnant women die every year because of eclampsia and severe preeclampsia. That amounts to nearly 200 women every day. Preeclampsia–eclampsia ranks second only to hemorrhage as a specific, direct cause of maternal death. The risk that a woman in a developing country will die of preeclampsia or eclampsia is about 300 times that of a woman in a developed country [1].

Definition

Preeclampsia is defined as a systemic syndrome that is typically characterized by new-onset hypertension and proteinuria in pregnancy. Urinary excretion of 300 mg of protein in 24 h is defined as significant proteinuria. The syndrome is characterized by poor placental perfusion and a general disease process which may affect multiple organ systems.

Eclampsia is a complex phenomenon as a result of cerebral dysrhythmia due to the multifarious pathogenesis started by abnormal trophoblastic invasion initiating vasospasm, endothelial dysfunction, and platelet aggregation.

Epidemiology of Preeclampsia

Globally hypertensive disorders of pregnancy complicate approximately 5–10 % of pregnancies [2]. In Africa and

Gupte S. (✉), Director
Gupte Hospital, Postgraduate Institution and Centre of Research in Reproduction, 904 Bhandarkar Road, Pune 411 004, India
e-mail: guptehospital@gmail.com

Wagh G., Professor
Department of Obstetrics and Gynecology, Bharati Vidyapeeth University Medical College, Pune, India

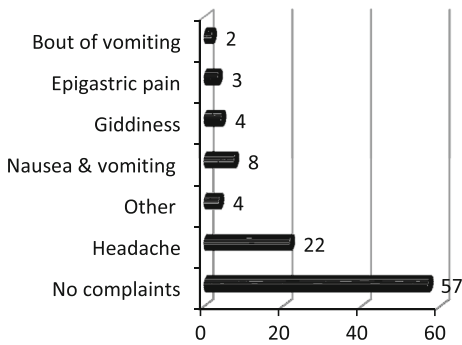**Table 1** NER: Presenting complaints of eclampsia mothers

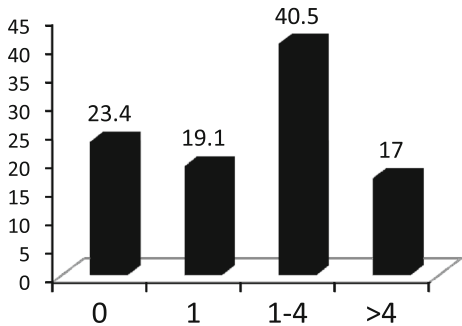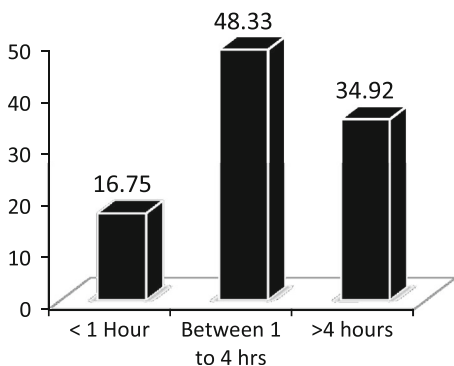**Table 2** Number of convulsions before admission

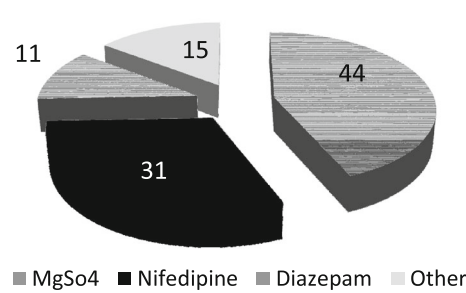**Table 3** Duration between convulsion and admission

Asia, hypertensive diseases accounted for 9 % maternal deaths, whereas, in Latin America and the Carribean, the figure is over 25 % [3].

Context India

Incidence of hypertensive disorders in India is found to be 10.08 % as observed through the data collected by the National Eclampsia Registry (NER) (11,266 out of 1,11,725 deliveries) over the past 3 years with 2,554 patients out of this presenting with eclampsia.

Table 4 Drugs administered in critical cases

The FOGSI-ICOG NER has brought forth some revealing trends. Eclampsia prevalence among registry patients is 1.9 %. National sample surveys in the past have shown prevalence to be 1–5 %. This is out of the 11,725 deliveries analyzed from the cases reported by 175 reporting centers. Number of cases of eclampsia is more than cases of imminent eclampsia. This points to the lost opportunities of prevention. 17 % of preeclampsia patients are actually in the adolescent age group reflecting the very early age at marriage in spite of several awareness pro- grams and legal guidelines. 76.34 % of the patients were between 21 and 30 years of age thus rendering a very young population morbid and at risk of mortality. It also is a disease of the first-time pregnant woman as 81 % of the patients with preeclampsia were primigravid.

Antenatal care has been identified as the single inter- vention which could influence the maternal mortality of our country. Many women still seem to be unreached with this basic pregnancy evaluation. Most of the patients reported by the registry were registered for antenatal care either in the second (40.98 %) or the third trimester (46.28 %). Very few (12.54 %) booked in the first trimester.

As per the NER data most of the times preeclampsia was found not to be associated with any symptoms (57 %); 22 % had headache and very few had vomiting, epigastric pain, giddiness, etc. (Table 1). Antenatal eclampsia is noted to be common (76.78 %); however, post-partum convulsions (13.72 %) are also significant. 40.5 % mothers had 1–4 convulsions before admission, while 23 % had just one. Greater numbers of convulsions prior to care may be due to lack of reachable facilities (Table 2). Time spent in access to care is crucial and may alter maternal and fetal outcome. Convulsions post admission (76.6 %) indicate lack of standardized care protocol for eclampsia which is mandatory. Time spent between the first episode of con- vulsion and access to care is between 1 and 4 h in majority (48.33 %) of patients. This indicates the severe need to train medical officers, birth attendants, and paramedical personnel in remote interiors as well as better transport facilities to handle obstetric emergencies (Table 3).
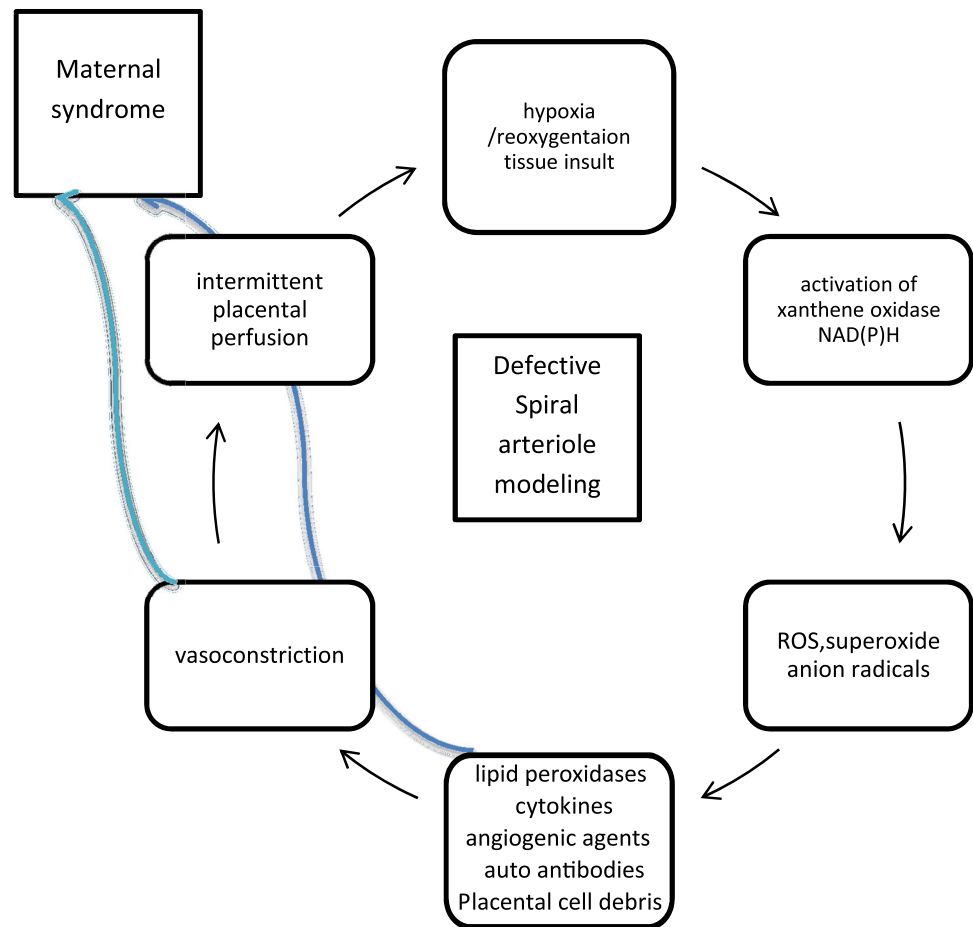
Magnesium sulfate was used only in 44 % cases of patients before admission (Table 4).

Etiopathology of Preeclampsia

Preeclampsia is a multisystemic disorder with profound implications for both the mother and the fetus. Abnormal interactions between fetal trophoblast and maternal decidua, including the cells of the maternal immune system, lead to inadequate placental invasion and maternal vascular remodeling. Thus, the origins of preeclampsia lie in the earliest stages of pregnancy. Preeclampsia generally manifests during late pregnancy and remits after delivery attributing the critical role of its appearance to placenta. Generally, preeclampsia is considered a disorder with two components: 1. An unidentified signal from the placenta associated either with defective implantation or greater placental mass as in multifetal pregnancies or vesicular mole. 2. The aberrant maternal response to this signal is determined by her genotype and phenotype and influenced by physiological and metabolic changes in pregnancy and also causes endothelial dysfunction with multisystemic affliction.

The pathogenesis is result of multifactorial origin which can grossly be understood under following components:

1. *Uteroplacental pathology*: there is a failure of the maternal uterine spiral arterioles arteries to convert into wide sinusoids. In normal pregnancy, the trophoblastic invasion into the myometrium and the decidua converts the muscular arterioles into low-resistance sinusoids transforming the vascular supply from a high-pressure low-flow system to a low-pressure high-flow system to nourish the developing placenta and the fetus. Also, the loss of the muscle layer and the endothelium within these vessels make them insensitive to vasomotor stimuli. In preeclampsia, this trophoblastic invasion of the uterine vessel is incomplete giving rise to restricted blood supply leading to fetoplacental hypoxia. Variable oxygenation in the placenta leads to oxidative stress and release of free radicals. The aberrations in the perfusion and hemodynamics may result in the formation of the acute atherosis and atherosclerotic plaques in these unmodified spiral arterioles. Placental factors are liberated to compensate for the compromised blood flow. These factors initiate the systemic alterations that result in the maternal syndrome. The placental factors identified are the angiogenic agents, cytokines, products of lipid peroxidation, autoantibodies, and (Fig. 1) placental cell debris.

2. *Angiogenic factors*: ischemic placenta is believed to contribute to the endothelial cell dysfunction by altering the balance between the circulating levels of the angiogenic and the anti-angiogenic growth factors. These are vascular endothelial growth factor (VEGF), placental growth factor (PIGF), and soluble fms-like tyrosine kinase-1 (sFlt-1). SFlt-1 is known to bind to and inhibit the VEGF and PIGF activity. Similarly, endoglin is another antiangiogenic protein implicated in the pathogenesis of preeclampsia. Both sFlt-1 and endoglin are found to be raised in the maternal circulation before the onset of preeclampsia.

3. *Lipid peroxides*: lipoprotein oxidation (oxidative stress) is present in normal pregnancy but is greatly enhanced in preeclampsia. Lipid peroxidation of the synciotrophoblast is responsible for the release of stable oxidative metabolites such as malondialdehyde and 4-hydroxynonenal which cause wide-spread endothelial damage.

4. *Inflammation and cytokines*: the role of placenta in direct dissemination of inflammatory cytokines is not proved. But, poor placentation leading to hypoxia can amplify the release of inflammatory stimuli in the maternal circulation. Leukocytes in the placental bed and the uterine veins are activated to release cytokines and reactive oxygen species. Elastase-positive cells which are markers of neutrophil activation are found to be increased in numbers in the decidua and the placental bed.

5. *Placental fragments and micro particles*: a lot of cellular debris from the placental surface and the syncytiotrophoblast is shed in the maternal circulation in preeclampsia as a result of cell death due to hypoxia. The inadequate clearance of this exaggerates the maternal inflammatory response to pregnancy. Placental-derived material such as the circulating cytokeratin and soluble fetal DNA are directly damaging to the vascular endothelial cells. They also interact with the phagocytes and contribute to the inflammatory response.

6. *Autoantiobodies*: recent studies have shown that women with preeclampsia have autoantibodies termed ATI-AAs. These antibodies activate the angiotensin II receptors. These are known to be present in the maternal circulation 2 years after child birth and imply that preeclampsia may be a pregnancy-induced auto-immune disease.

7. *Genetics*: preeclampsia is a genetic disorder and is influenced by environmental factors. It is found with increased frequency in mothers, daughters, sisters, and granddaughters of women having preeclampsia studied. The tendency for preeclampsia and eclampsia in the family members has been studied with the possibility that it is inherited [4]. A multifactorial inheritance was also considered possible. An association between the histocompatibility antigen HLA-DR4 and proteinuric hypertension is also a possibility.

Fig. 1 Overview of the pathogenesis

Certain HLA types are more common in the mother and the fetus from preeclamptic pregnancies.

8. *Immunological factors*: the immunization concept is supported by the observation that preeclampsia develops more frequently in multiparous women impregnated by a new consort. Dekker and Sibai [5] have reviewed the possible role of immune maladaptation in the pathophysiology of preeclampsia. Beginning in the early second trimester, women destined to develop preeclampsia have a significantly lower proportion of T-helper cells compared with women who remain normotensive. Antibodies against endothelial cells have been found in 50 % of women with preeclampsia versus 15 % of normotensive controls.

Many possibilities have been speculated to give rise to preeclampsia. But, the novel and unifying theory about the pathophysiology of preeclampsia which is more convincing is the one originally proposed by Feinberg et al. from USA in 2005. It is the GESTOSIS theory which states that there is excess of immune complexes produced because of placental antigenicity which are not cleared by maternal immune system. Hence, they are deposited in the various

endothelial layers causing pro-inflammatory cytokines and oxidative stress. This results in clinical preeclampsia which is inflammatory response of pregnancy. Support for this theory comes from the fact that this disorder is more frequent in primigravidas, adaptive protection is acquired in subsequent pregnancies of the same paternity, and baseline risk returns with first pregnancies of a new partner. Higher incidence is seen in oocyte donation pregnancy, is common in pregnancy with hyper placentation, and is cured after placenta is removed. The natural mechanisms in the body cannot curb the inflammatory response, and the overwhelming inflammatory response is a clinical turning point in the disease process. This maternal oxidative stress in turn stimulates further placental apoptosis and necrosis generating, an auto-amplification process. This leads to varying severity of clinical preeclampsia. Neutrophils accumulated in the inflammatory site are activated by the immune complexes. They release proteases and toxic oxygen radicals which cause further damage to the so called ''oxidative stress'' seen in preeclampsia. The main immune complex clearance mechanism in the humans is via the erythrocyte complement receptor type1 (CR1).

Erythrocytes express approximately 500 CR1 receptors per cell. A decreased expression of erythrocyte CRI in preeclamptic patients correlates with severity of disease—as happens in anemia. If low CR1 is matched with low immune complex production, no adverse sequel would be anticipated. Hence, all anemic patients don't get preeclampsia. This is where other factors such genetic, lifestyle, nutrition, etc., could be implicated.

The degree of complement activation reflects the severity of the disease. Pregnancies complicated by HELLP syndrome have increased plasma levels of C3a and C5a as compared to women with preeclampsia without HELLP syndrome.

Pathophysiology and Multisystemic Affliction in Preeclampsia

The common pathophysiology of preeclampsia results from: 1. Vasoconstriction with exaggerated response to vasoactive substances. 2. Plasma volume reduction due to capillary leakage and redistribution and shift of the extracellular volume from the intravascular to the interstitial compartments 3. Platelet aggregation triggered by endothelial dysfunction which leads to intravascular thrombosis. These three factors cause reduced perfusion of the brain, liver, kidneys, and the utero-placental complex reflected in the clinical syndrome.

Renal Dysfunction

The renal lesion typical of preeclampsia is ''glomerular endotheliosis''. This is a variant of thrombotic micorangiopathy and is characterized by endothelial cell swelling, obliteration of the endothelial cell fenestrae, and occlusion of the capillary lumens. Excess amounts of sFlt-1 and decreased VEGF production by the podocytes cause proteinuria. VEGF deficiency causes disruption of the glomerular endothelium leading to proteinuria, oliguria, and increased creatinine which imply severe disease. Increased uric acid is a marker of sodium reabsorption which occurs due to reduced renal blood flow and Angiotensin II. Uric acid also is produced by placental trophoblasts and is a marker of apoptosis and senescence of these cells. Uric acid, therefore, is a marker of severity of the disease at both renal and placental levels.

Hepatic Dysfunction

Intravascular fibrin deposits block the hepatic sinusoids, leading to hepatic dysfunction which is a component of the HELLP syndrome. Clinically epigastric or upper quadrant pain is sign of hepatic affliction. Biochemically elevated liver enzymes and coagulopathy are associated extreme consequences of subcapsular hematoma and hepatic rupture.

Hematological Abnormalities

Microangiopathic hemolysis and thrombocytopenia are the main hematological components. Hemolysis is the result of microvascular endothelial injury and activation. Initial platelet activation is followed by increased consumption leading to thrombocytopenia with increased risk of hemorrhage and further reduction in the organ perfusion [6].

Effects on the Brain

Eclampsia and other neurological abnormalities are associated with preeclampsia, and their pathogenesis is poorly understood. There are two theories postulated: 1. Hypertension and vasospasm result in vascular disregulation which leads to reduced cerebral perfusion, cytotoxic edema, ischemia, and infarction. 2. Autoregulatory mechanism of the cerebral vasculature is overcome by sudden increases in the blood pressure. This results in the development of areas of vasoconstriction and forced vasodilatation. Vasogenic edema and hyperperfusion and extravasation of erythrocytes and plasma ensue in patches. The latter entity is also called the posterior reversible leucoencephalopathy syndrome (PRES). Transient cortical blindness and intracranial hemorrhages are also associated with preeclampsia.

Cardiopulmonary Effects

Exaggerated capillary permeability and decreased plasma colloid osmotic pressure predispose the woman to pulmonary edema. It can occur spontaneously or secondary to fluid overload. Also, the left ventricular dysfunction leading to cardiac under filling is commonly associated with preeclampsia.

Prediction of Preeclampsia

None of the tests proposed to predict the at-risk population for preeclampsia have risen to the level that they can be recommended for general population screening. Uterine artery Doppler (UAD) can be of help in predicting preeclampsia in the at-risk population. Doppler ultrasonography of the uterine arteries at 20–24 weeks' gestation, to detect abnormal trophoblast invasion, predicts about 40 % of subsequent preeclampsia, however, its success in predicting severe early onset preeclampsia approaches 80 % [7]. Recently, several predictive biochemical markers—including placental growth factor, soluble fms-like tyrosine

kinase-1 (sFlt-1), plasma protein 13, and pregnancy-associated plasma protein-A (PAPP-A)—have been evaluated, but none is as yet in routine clinical use [8].

Risk Factors: To Assess at the First Antenatal Visit of all Patients

In the absence of effective screening modalities, *clinical* risk factors can help us to be more vigilant. These factors are chronic hypertension/renal disease (15–40 %), Pregestational diabetes (10–35 %), connective tissue disease (lupus, rheumatoid arthritis) (10–20 %), thrombophilia (acquired or congenital) (10–40 %), obesity/insulin resistance (10–15 %), age older than 40 years (10–20 %), limited sperm exposure (10–35 %), family history of preeclampsia/cardiovascular disease (10–15 %), woman born as SFGA (1.5 fold), adverse outcome in a previous pregnancy: IUGR, abruptio placentae, and IUFD (2–3 fold).

Early Diagnosis of Preeclampsia

Specific inquiry of signs and symptoms mentioned below can help early diagnosis and reduce the adverse outcomes of preeclampsia. Weight gain (more than 600 g/week), increasing edema (especially sudden onset), persistent headache (needs attention), blurred vision (Immediate attention needed as can be a sign of cerebral edema), malaise, nausea (prolonged or severe first-trimester emesis), epigastric discomfort (may be mistaken as dyspepsia), and right upper quadrant discomfort (can be due to Glisson's subcapsular bleed and hepatic hemorrhage) are these clinical clues. Several measurements of blood pressure including systolic blood pressure, diastolic blood pressure, pulse, mean arterial pressure, and 24-h ambulatory pressure have been studied in early pregnancy as predictors of preeclampsia [9]. The mid-trimester mean arterial pressure has been found to be the best predictor of preeclampsia in low-risk women, but the authors admit that the low positive likelihood ratio makes it unlikely that this measure would have a clinical effect in isolation [10].

In the light of abnormal blood pressure reading existence of severe preeclampsia should be assessed. Persistent blood pressure above 160/110 mmHg, proteinuria, refractory oliguria (<500 cc over 24 h), renal function compromise (minimal criterion would be a rise in serum creatinine of 1 mg/dl above baseline), persistent right upper quadrant or epigastric pain or both, persistent headache, scotomata or blurred vision, shortness of breath with reduced oxygen saturation or pulmonary edema, thrombocytopenia (platelets <100,000/cu.mm), hemolysis (based on peripheral smear analysis or increased bilirubin), impaired liver function of unclear etiology, and estimated fetal weight below 5th percentile for gestational age are important parameters to be noted.

Classification

The correct diagnosis and classification of hypertension in pregnancy are essential for proper management of the mother and the baby. The classification proposed by the International Society for the Study of Hypertension in Pregnancy (ISSHP) is easy to use in clinical settings (Table 5). It also is self-explanatory and practical.

Atypical Preeclampsia

Hypertension and proteinuria before 20 weeks (e.g., in gestational trophoblastic disease), preeclampsia with hypertension but without proteinuria, or preeclampsia with proteinuria without hypertension when associated with above-mentioned systemic involvement is designated at atypical preeclampsia. Preeclampsia arising first time after 48 h of delivery can also be included in this definition. This is an important entity for diagnosis and management of unusual cases.

Table 5 Classification of hypertensive disorders in pregnancy [11]

Gestational hypertension	Hypertension that	6–7 % of pregnancies
	(1) develops beyond 20 weeks of gestation	
	(2) returns to normal within 42nd postpartum day and is not associated with any other features of preeclampsia	
Preeclampsia/eclampsia	Hypertension presenting beyond 20 weeks of gestation with >300 mg protein in a 24-h urine collection or 1 + (0.3 g/l) on urine dipstick	5–7 % of pregnancies
	Eclampsia is the occurrence of seizures in a pregnant woman with preeclampsia	
Chronic hypertension	Blood pressure 140/90 mmHg present before pregnancy, before the 20th week of gestation, or persisting beyond the 42nd postpartum day	1–5 % of pregnancies
Preeclampsia superimposed on chronic hypertension	The onset of features diagnostic of preeclampsia in a woman with chronic hypertension beyond 20 weeks of gestation	20–25 % of chronic hypertension pregnancies

Table 6 Clinical classification of preeclampsia

Early onset preeclampsia	Late onset preeclampsia
A fetal disorder that is typically associated with placental dysfunction	Maternal disorder, due to underlying maternal constitutional factors
Reduction in placental volume	Normal or larger placental volume
Intrauterine growth restriction	Normal fetal growth
Abnormal uterine and umbilical artery Doppler evaluation	Normal uterine and umbilical artery Doppler evaluation
Low birth weight	Normal birth weight
Adverse maternal and neonatal outcomes	More favorable maternal and neonatal outcomes

Clinical Classification of Preeclampsia

Classification as early onset preeclampsia and late onset preeclampsia is clinically useful. Appearance of preeclampsia before 34 weeks is called as early onset preeclampsia (EOPET). EOPET is associated with greater morbidity and fourfold increased risk of stillbirth in a subsequent pregnancy, and higher recurrence risk in subsequent pregnancy than when the disorder presents later. It is suggested to subdivide preeclampsia into two groups by time (gestation) of onset because of differences in prognosis and management. This distinction is held important as there is a suspicion that these two are separate entities with distinct predisposing factors. The early onset disease may be associated with the underlying genetic or environmental factors leading to abnormal placentation. The late onset disease called the late onset preeclampsia (LO-PET) may be the result of obesity, diabetes, cardiovascular abnormalities (Table 6), or multifetal pregnancy.

Management

Mild preeclampsia can be managed expectantly until fetal maturity of 37 weeks of gestation and also till spontaneous onset of labor if well controlled. A day's hospitalization may be undertaken for blood pressure monitoring, fetal evaluation, assessing 24-h proteinuria, and assessing any other systemic involvement. Also, the patient can be offered dietary advice and the correct categorization after her blood pressure has been monitored round the clock. Any serious presentations such as severe edema, ascites, high blood pressure, severe proteinuria, headache, pain, severe growth restriction, convulsions, etc., demand a hospital care.

The primary evaluation in the presence of abnormal blood pressure should include non-stress testing (if gestational age more than 32 weeks), amniotic fluid index, serial blood pressure (4 h.) determination, and 24-h urine collection (if dipstick proteinuria is negative). Initial laboratory evaluation comprising a complete blood count with platelets (<100,000/μl: severe disease repeat after 6–12 h) (coagulation profile essential if platelets less), liver enzymes such as AST, ALT, serum creatinine levels (0.9 mg/dl >1.2 denotes renal impairment), and LDH levels (600 IU is the cutoff) should be undertaken.
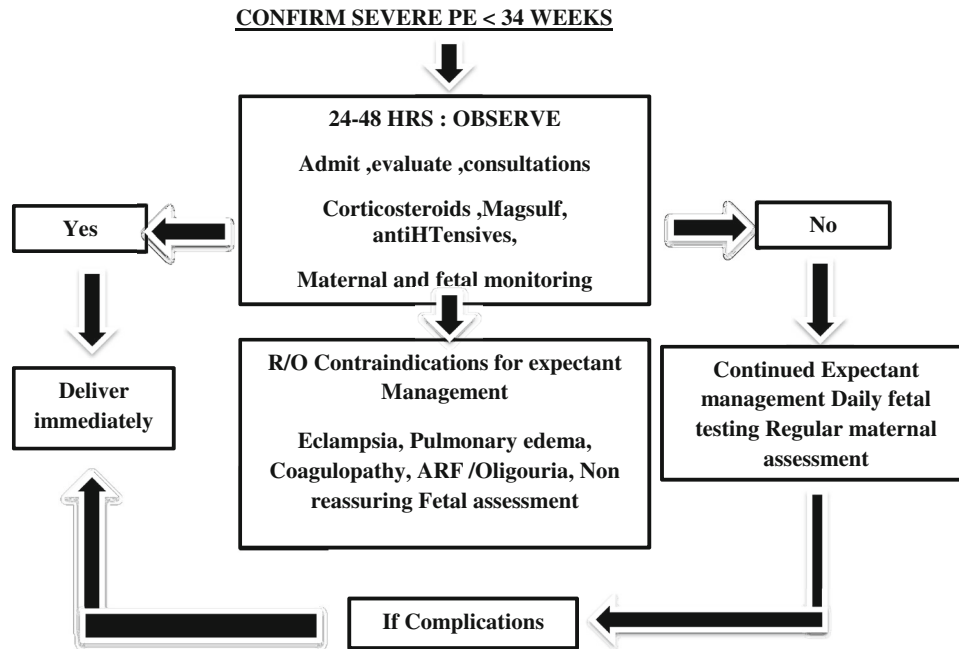
WHO and FOGSI guidelines are now formulated and should be followed to manage these patients. In short, the principles of management as per WHO guidelines are [12]:

Interventions that are recommended for prevention or treatment of preeclampsia & eclampsia

- Women with severe hypertension during pregnancy should receive treatment with antihypertensive drugs.
- The choice and route of administration should be based primarily on the clinician's experience with that particular drug, its cost, and local availability.

WHO Recommendations

- Magnesium sulfate is recommended for the prevention of eclampsia in women with severe preeclampsia
- Magnesium sulfate is recommended for the treatment of women with eclampsia
- The full intravenous or intramuscular magnesium sulfate regimens are recommended for the prevention and treatment of eclampsia.
- For settings where it is not possible to administer the full magnesium sulfate regimen, the use of magnesium sulfate loading dose followed by immediate transfer to a higher level health-care facility is recommended for women with severe preeclampsia and eclampsia.
- Induction of labor is recommended for women with severe preeclampsia at a gestational age when the fetus is not viable (usually before 25 weeks)
- In women with severe preeclampsia, with viable fetus (25–34 weeks), a policy of expectant management is recommended, provided that uncontrolled maternal hypertension, increasing maternal organ dysfunction, or fetal distress is absent and can be monitored.
- In women with severe preeclampsia, a viable fetus and between 34 and 36 weeks of gestation, a policy of expectant management may be recommended, provided

Table 7 Severe preeclampsia-management algorithm

CONFIRM SEVERE PE < 34 WEEKS

```
                    24-48 HRS : OBSERVE
                Admit ,evaluate ,consultations
  Yes           Corticosteroids ,Magsulf,              No
                    antiHTensives,
                Maternal and fetal monitoring


  Deliver        R/O Contraindications for expectant    Continued Expectant
  immediately            Management                      management Daily fetal
                                                          testing Regular maternal
                 Eclampsia, Pulmonary edema,              assessment
                 Coagulopathy, ARF /Oligouria, Non
                 reassuring Fetal assessment


                         If Complications
```

that uncontrolled maternal hypertension, increasing maternal organ dysfunction, or fetal distress is absent and can be monitored.

- In women with severe preeclampsia at term, early delivery is recommended
- In women with mild preeclampsia or mild gestational hypertension at term, induction of labor is recommended.
- In women treated with antihypertensive drugs antenatally, continued treatment postpartum is recommended.
- Treatment with antihypertensive drugs is recommended for severe postpartum hypertension.

Simple algorithm which is recommended for management is as follows (Table 7).

Labor Management

Vaginal delivery is less hemodynamically stressful than cesarean delivery for the mother. To accomplish vaginal delivery, it is necessary to provide optimal anesthesia and analgesia. Also, caution must be observed while using intravenous infusions. The system of fluid restriction should be maintained until there is a postpartum diuresis, as oliguria is common with severe preeclampsia. Women who have preeclampsia are volume depleted. As such, they are prone to hypotension after administration of regional anesthesia if the block sets up too rapidly. For this reason,

epidural anesthesia or some of the newer combined techniques offer optimal analgesia by allowing for slower implementation of the regional block.

Fluid overload can pose a serious threat to the mother in the form of pulmonary edema, and close vigilance is essential. Epidural anesthesia is a preferred choice of anesthesia, and spinal anesthesia is not entirely contraindicated. General anesthesia poses a challenge, and its actions with anticonvulsants need to be considered

Whether a vaginal delivery or a CS, active management with oxytocics should be practiced to prevent PPH. It is safe to use Oxytocin 5 U bolus equally diluted over 2–3 min or prostaglandin injections. Prostaglandins can be used also as misoprostol sublingually or transvaginally. Due to hemoconcentration, even average loss may not be well tolerated by these patients. All attempts to reduce blood loss should be undertaken. The fluids used should be liberal but judicious. Recommendation is 80 ml/kg/h as over infusion can cause pulmonary edema in these women.

Post-delivery Management and Postpartum Care

It involves close vigilance for eclampsia, PPH, HELLP, Pulmonary edema, and thromboembolic complications. 72 h post-delivery are an important period when hemodynamic transition is occurring in the mother, which need

close observation and early detection of eclampsia. The NER data have shown a high index of postpartum eclampsia (13 %), and it has to be remembered that such an occurrence leading to morbidity has to be avoided by all means.

Post-partum every patient of preeclampsia should be monitored closely for 6 weeks with proper advice regarding the use of antihypertensive medication and should report at regular intervals. They should be guided and encouraged to use contraception at least for a period of 2–3 years. The preferred method would be an IUCD. They should be counseled regarding the importance of preconceptional checkup counseling and the necessary care periconceptionally in the subsequent pregnancy.

Long Term Sequel

Long term sequelae such as cardiovascular and metabolic diseases are observed. Women with preeclampsia have a three–four fold increased risk of developing chronic hypertension and an approximately two-fold increased risk of ischemic heart disease, stroke, and venous thromboembolism [8].

Fetal Effects

There is an increased risk of still births and neonatal death associated with preeclampsia. Preterm delivery incidence is high with iatrogenic preterm delivery before 33 weeks being 80 fold more and between 33 and 36 weeks being about 40 fold. There is a twofold increased risk of neonatal mortality associated with preeclampsia.

Recurrence in Succeeding Pregnancies

Preeclampsia in previous pregnancy is an important risk factor for recurrence in the subsequent pregnancy with 7–15 % 9 chance, while it is 1 % for women with no preeclampsia in their antecedent pregnancy.

Prevention

Unfortunately, very few measures can be taken to prevent preeclampsia, which are as follows. (1) Non pharmacological: daily bed rest, life-style changes, smoking, and regular prenatal exercise. (2) Nutritional: higher total dietary fiber intake, dietary protein and energy, garlic, dietary sodium restriction, weight reduction, and fish oil supplementation. (3) Pharmacological: vitamin D, magnesium,

folic acid and other B-vitamins, zinc supplementation, nitric oxide, progesterone, low-dose aspirin, low-dose aspirin/heparin, calcium supplementation, antihypertensive drugs, diuretics, antioxidant supplementation, and concomitant vitamin C and E supplementation.

All these above have been recommended, but none of them are proved to be useful.

Low-dose aspirin is associated with a 10–19 % reduction in preeclampsia risk and a 10–16 % decrease in perinatal morbidity and mortality. This risk reduction was seen in women who were in the ''moderate to high risk category'' [13]. Antiplatelet agents for preventing PE and its complications [14] and calcium supplementation reduce the risk of preeclampsia, particularly in populations that have diets deficient in calcium (level 1 evidence) [15]. Good quality studies have shown that calcium supplementation of at least 1 g daily started around mid-pregnancy is associated with a modest reduction in PE and a more notable reduction in its severe manifestations among women with low dietary calcium intake [15]. If prevention is not possible, then at least early detection and better management should be the aim. Presently unfortunately when we so called "TREAT" preeclampsia, we are only treating the symptoms and not the cause and that must be clearly borne in mind.

What We Need To Do?

Things that can be done at a grass-roots level include early referral from medical officer to specialist especially in the circumstances like multiple pregnancy, preeclampsia in any previous pregnancy, underlying medical conditions, preexisting hypertension or booking diastolic BP ≥90 mm of Hg, preexisting renal disease or booking proteinuria (≥ 1+ on more than one occasion or quantified at ≥0.3 g/24 h), preexisting diabetes, presence of antiphospholipid antibodies, first pregnancy, age of 40 years or more, BMI of 35 kg/m^2 or more, family history of preeclampsia, and booking diastolic BP ≥80 mm of Hg <90 mm of Hg. Immediate admission should be arranged for a woman whose diastolic BP ≥110 mm of Hg and new proteinuria ≥1+ on dipstick, systolic BP ≥170 mm of Hg and new proteinuria ≥1+ on dipstick, diastolic BP ≥90 mm of Hg and new proteinuria ≥1+ on dipstick and significant symptoms.

Conclusion

Preeclampsia has always played a major role in maternal mortality and morbidity. The least we can do is to create awareness among the patients, expect alertness from our

fellow obstetricians, and continue research to find the causes and new treatment modalities. It seems that we have come a full circle calling it toxemia of pregnancy 100 years back because it was thought that there were toxins in the blood and now again finding that there are subcellular soluble factors in the blood which may be the reason for this scourge. We may not have solved the enigma as yet, but if we remember simple messages like,

- Think of the clinical preconceptional risk factors
- Advice good nutrition
- Insist on correct BP measurement and look for proteinuria
- Think of aspirin and iron and calcium supplements
- Use anti-hypertensive and magnesium sulfate correctly
- Take help of color Doppler when feasible
- Deliver patient at a proper time and a proper facility, we will be able to truly achieve a healthier outcome in these settings.

References

1. Balancing the scales: expanding treatment for pregnant women with life-threatening hypertensive conditions in developing countries. A report on barriers and solutions to treat preeclampsia and eclampsia. EngenderHealth. 2007.
2. Zenebe W, Hailemariam S, Mirkuzie W. Hypertensive disorders of pregnancy in Jimma University specialized hospital. Ethiop J Health Sci. 2011;21(3):147–54.
3. Khan KS, Wojdyla D, Say L, et al. WHO analysis of causes of maternal death: a systematic review. Lancet. 2006;367(9516):1066–74.
4. Chesley LC, Cooper DW. Genetics of hypertension in pregnancy: possible single gene control in eclampsia and preclampsia in the descendants of eclamptic women. Br J Obstet Gynaecol. 1986;93:898–908.
5. Dekker GA, Sibai BM. Etiology and pathogenesis of preclampsia: current concepts. Am J Obstet Gynecol. 1998;179(5):1359–75.
6. Brown MA. The physiology of preeclampsia. Clin Exp Pharmacol Physiol. 1995;22:781–91.
7. Chandiramani M, Shennan A. Hypertensive disorders of pregnancy: a UK-based perspective. Curr Opin Obstet Gynecol. 2008;20:96–101.
8. Bellamy L, Casas JP, Hingorani AD, et al. Preclampsia and risk of cardiovascular disease and cancer in later life; systematic review and metaanalysis. BMJ. 2007;335:974.
9. Farag K, Hassan I, Ledger WL. Prediction of pre-eclampsia: can it be achieved? Obstet Gynecol Sur. 2004;59:464–82.
10. Cnossen JS, Vollebregt KC, de Vrieze N, et al. Accuracy of mean arterial pressure and blood pressure measurements in predicting pre-eclampsia: systematic review and meta-analysis. BMJ. 2008; 336:1117.
11. Anonymous. Report of the national high blood pressure education program working group on high blood pressure in pregnancy. Am J Obstet Gynecol. 2000;183(1):S1–22.
12. WHO Guidelines Approved by the Guidelines Review Committee. WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia. Geneva: World Health Organization; 2011.
13. Duley L, Henderson-Smart D, Knight M, et al. Anitplatelet drugs for prevention of pre-eclampsia and its consequences: systematic review. BMJ. 2001;322:329–33.
14. Askie LM, Henderson-Smart DJ, Stewart LA. Antiplatelet agents for the prevention of preclampsia: a meta-analysis of individual patient data. Lancet. 2007;369:179.
15. Hofmeyr GJ, Lawrey TA, Atallah AN, et al. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev. 2010; 8:CD001059.