REVIEW ARTICLE

Hypertensive disorders in pregnancy

Prabinendra Nath Nobis

Correspondence: Dr Prabinendra Nath Nobis, 15- Baikuntha path, South Sarania, Guwahati, Pin-781007, Assam. Email- pknabis@rediffmail.com

ABSTRACT

Hypertensive disorders in pregnancy are common medical complication of pregnancy. Maternal and perinatal mortality and morbidity associated with these conditions are very high. Pre- eclampsia and eclampsia are variant of these disorders. Aetiology of these disorders is not known. Several theories are postulated. Now it is believed to be an exaggerated response to inflammatory reaction of pregnancy. No single test has so far been identified for prediction. Depending on clinical factors like family history of hypertension, past history of hypertension aspirin in low dose is used to minimize the incidence. In eclampsia magnesium sulphate is the anticonvulsant of choice worldwide. Antihypertensive drugs like methyl dopa, labetalol, and hydralazine are used to lower blood pressure to a safe level. Delivery should be planned at the oportunate time. Factors to be considered for timing of delivery are gestational age, maternal, and fetal conditions. HELLP syndrome is another complication of preeclampsia. Diagnosis and management of HELLP syndrome are reviewed.

Keywords: Hypertension, preeclampsia, eclampsia prevention.

Hypertensive disorders in pregnancy are common medical complication encountered during pregnancy. Incidence various, but on an average it effects about 5% to 10% of all pregnancies [1]. Hypertensive disorders in its different types and severity affects the course and outcome of pregnancy. These disorders are associated with a high maternal and perinatal mortality and morbidity worldwide. In India these disorders account for about 5% of all maternal death [2].

Blood pressure should be measured accurately and preferably by the same observer to avoid inter observer variation, in sitting position or in left lateral recumbent position. Blood pressure cuff should be of appropriate size and it should be placed at the level of the woman's heart. The observer should keep his/ her eyes at the level of the mercury column. Following initial measurement second measurement should the taken after at least 6 hour of rest. Hypertension is defined as systolic blood pressure (SBP) of 140 mm of Hg or more or diastolic blood pressure (DBP) of 90 mm of Hg or more. Edema in lower extremities is found in many conditions during pregnancy and hence has no significance in hypertensive disorders. But pathological edema seen in non dependent areas like face, hands and rapid weight gain during later part of pregnancy heralds, excessive fluid retention and is taken seriously.

Proteinuria is defined as concentration of protein > 300mg/ 24 hours urine collection or a concentration of 30mg/dl (1+ an dipstick) or more, in at least two random urine samples collected 4 hours apart. The

Received: 28th June 2015. **Accepted:** 10th August 2015.
Nobis PN. Hypertensive disorders in pregnancy. The New Indian Journal of OBGYN. 2016; 2(2): 65-72

concentration of urinary protein in random urine sample correlates poorly with proteinuria found in 24 hours urine. So, it is preferable to examine 24 hours urine collection for proteinuria.

Classifications of Hypertensive Disorders in Pregnancy

Different classifications have been proposed by different authors in different times. The American College of obstetricians and Gynaecologists Committee on Terminology proposed a classification in 1972, which has been modified by the National High Blood Pressure Education programme working group in 2000. It is of simple, concise and clinically relevant [3].

Classification of Hypertensive Disorders of Pregnancy

a) Gestational hypertension: Hypertension developing after 20 weeks of gestation or during the first 24 hours postpartum without proteinuria.

b) Transient hypertension: Hypertension resolves by 12 weeks post partum.

c) Chronic hypertension: Hypertension diagnosed prior to pregnancy or before 20 weeks gestation or after 12 weeks post partum.

d) Preeclampsia/Eclampsia: Hypertension develops after 20 weeks of gestation with proteinuria, eclampsia is occurrence of seizure activity without other identifiable causes.

e) Chronic hypertension superimposed pre eclampsia: Development of Pre eclampsia or eclampsia in a women with chronic hypertension.

Gestational hypertension

Gestational hypertension is rise of blood pressure after 20 weeks of gestation or within 24 hours of delivery. This is the common cause of hypertension in pregnancy. The incidence ranges between 6% to 17% in nulliparous women [1]. Blood pressure is usually mild, but sometimes may be elevated to 160 mg Hg systolic and 110 mgHg. diastolic pressure without proteinuria. In about 46% of women preterm gestational hypertension may progress to preeclampsia with proteinurea [4]. Pregnancy outcome in mild variety is usually favourable. The mother needs no antihypertensive drug, except in severe hypertension. Blood pressure usually resolves within 12 weeks post partum.

Chronic hypertension in pregnancy

Chronic hypertension in pregnancy is diagnosed when pregnancy occurs in an already hypertensive women or when hypertension develops before 20 weeks of pregnancy or when hypertension persists even after 12 weeks of delivery. Chronic hypertension is a risk factor for development of superimposed preeclampsia at a later stage of pregnancy. The reported incidence of superimposed preeclampsia is about 10% -25%. Chronic hypertension in pregnancy is usually primary or essential hypertension. Secondary hypertension is mostly due to chronic kidney disease, adrenal disease, or collagen disease etc.

It is important to remember that many hypertensive women have greater decrease in blood pressure during early pregnancy than normotensive women [5]. Mid pregnancy fall in blood pressure is observed in about 30-40% of women, even in women with chronic pregnancy hypertension. In our observation in 43.43% of women fall in blood pressure started from early pregnancy and maximum fall was around 20 weeks of pregnancy, then gradually elevated in third trimester [6]. Diagnosis of chronic hypertension is likely to miss unless proper history of pre-pregnancy blood pressure is known. It is a complex disorder involving genetic, immunological and environmental factors [7].

Pre eclampsia

Preeclampsia is a multisystem disorder. Pre-eclampsia is gestational hypertension with proteinurea. Incidence varies from 3-7% of all pregnancies. Preeclampsia may superimpose with essential hypertension. The pathogenesis of Preeclampsia is still not fully understood and hence management is early detection, symptomatic treatment and delivery.

Etiopathology

Etiology of preeclampsia is still not fully under-

stood. Different etiological factors have been suggested, but no one could satisfy the scientific world. Removal of the placenta is the key to the recovery from preeclampsia, hence it stands to reason that placenta plays an important role in the development of the disorder [7]. Failure of effective trophoblastic invasion leads to inadequate spiral artery remodeling in the placental bed. Wide spread maternal endothelial dysfunction is observed in preeclampsia. Hypoxia likely to induce expression of a number of factors, that activate the maternal endothelium which leads to endothelial dysfunction [8]. Oxidative stress is thought to be a factor responsible for endothelial dysfunction. Oxidative stress activates leukocytes, platelets and neutrophils in intervillus space. These inflammatory factors reflect endothelial dysfunctions. Circulating angiogenic factors also play an important role in the pathogenesis of preeclampsia. Angiogenic factors are vascular endothelial growth factor (VEGF), placental growth factor (PIGF), endoglobin, Flt-1(f ms-like tyrosin kinase 1). VEGF and PIGF are angiogenic while sFlt-1 is antiangiogenic. In preeclampsia concentration of sFlt-1 is increased whereas that of VEGF and PIGF is decreased [9]. Recently immunological theory of preeclampsia has got momentum. It has been postulated that pathophysiology of preeclampsia is an excessive maternal inflammatory response to pregnancy. The pathophysiologic basis for preeclampsia is the exaggeration of the normal process of circulating immune complex processing leading to vascular injury and inflammation [10].

Prediction and Prevention

Obstetricians throughout the globe are trying to find out some test to predict preeclampsia. Several test both clinical and biochemical has been proposed but none of these is reliable as a single test. As of today the various high risk factors present in women are the more practical guide for a clinician.

Clinical risk factors – "But after exploring lot of high end technological tests and predictors, we have again come back to recognize the importance of these clinical risk factors [11].

Risk factors for development of Pre-eclampsia-

Maternal age <20 or >35 years of age, Family history of hypertension, Primigravida, Hydotidiform mode, Multiple pregnancy, Pre-existing hypertension, Diabetes mellitus, Pre-existing kidney disease, Obesity, Previous history of pre eclampsia/eclampsia, Preexisting vascular disease, Fetal hydrops, Fetal Trisomy.

Doppler ultrasonography of uterine artery blood flow in second trimester is suggested for prediction of preeclampsia. Abnormal velocity waveform is characterized by a high resistance index or an early diastolic notch. Recent addition in the list of biochemical markers are soluble FMS like tyrosine kinase -1 receptor (sFlt-1) and placental growth factor (PIGF.)

Prevention

Obstetrician throughout the world are trying to minimize the incidence and associated high maternal and prenatal mortality and morbidity from hypertensive disorder in pregnancy with conflicting results. Methods tried include life style modification, non-pharmaceutical, dietary and pharmacological agents. Reports of several randomised trials are published during the last decade. Usually practised methods are bed rest, to stop or restrict smoking, regular prenatal exercise, high protein diet, salt restriction, supplementation of zinc, fish oil, vit C, vit-E etc. Among the pharmaceutical agents aspirin, calcium, antioxidants are important. World Health Organization conducted trial on calcium supplementation and reported that calcium supplementation does not prevent preeclampsia but can reduce the severity and hence may improve maternal and perinatal outcome.

Most of the obstetricians use aspirin in low dose in women with high risk for development of preeclampsia, but efficacy is still doubtful. Collaborative low dose aspirin study in pregnancy (CLASP) failed to find reduction in incidence [12]. In another meta-analysis using low dose aspirin in women

with mean gestational age at randomization was less than 20 weeks, no significant different was observed in the incidence of preeclampsia [13]. On the other hand low dose aspirin initiated in women, to be at risk, for preeclampsia before 16 weeks of gestation was associated with a 20% decrease in the incidence of preeclampsia [14].

Management

Delivery is the definitive step to cure from preeclampsia. But the aim of management should be to ensure safety of the mother and delivery of a mature healthy baby. Decision for delivery depends maternal fetal condition.

Mild preeclampsia

Mild preeclampsia can be managed as out patient following satisfactory maternal and fetal evaluation reports. They should be asked to report twice a week. They may have average diet and no sedative or antihypertensive drug. Maternal evaluation include measurement of blood pressure, weight gain, 24 hours urinary protein estimation, haematocrit, platelet count, liver function tests, serum creatinine and uric acid level. For evaluation of fetal condition- daily fetal movement count, serial ultrasonography to ensure fetal growth every 3 weeks, non- stress test and fetal biophysical profiles are important.

In women with favourable cervix at or near term labour should be induced with prostaglandin or oxytocin drip. In preeclampsia remote from term pregnancy is allowed to continue till 37 weeks under strict monitoring for better fetal survived. Between 34 to 37 weeks of pregnancy induction of labour is indicated in patients with IUGR, rupture membrane or worsening maternal or fetal condition, evident from monitoring procedure.

Severe preeclampsia

Diagnostic criteria for severe preeclampsia: 1) Blood pressure 160mmHg or more systolic or 110 mmHg or more diastolic pressure, 2) Proteinuria of >5gm in 24 hours urine, 3) 24 hours Urinary output 400ml or less, 4) Nausea, vomiting , epigastric pain, 5) Headache, blurred vision, 6) Pulmonary edema, 7) Impaired liver function tests, 8) Thrombocytopenia, 9) Oligohydromnios and / or IUGR

The aim of management of severe preeclampsia are to prevent maternal complications like eclampsia, pulmonary edema, intracranial haemorrhage etc.and to deliver a healthy baby. Following initial evaluation patients are managed with administration of magnesium sulphate to prevent seizure. And antihypertensive are used to lower blood pressure to about 144-150 mmHg systolic and 90-105 mmHg of diastolic pressure. Decision is taken regarding timing of delivery of the baby. If duration of gestation is <34 weeks to achieve adequate lung maturity of the baby betamethaxone 12 mg intramuscularly is administered, two doses 24 hours apart. The dose schedule of magnesium sulphate for prophylaxis is same as that for treatment of eclampsia. The prophylaxis should be continued for further 12-24 hours postpartum. Higher rate of eclampsia in women with severe preeclampsia justifies use of magnesium sulphate prophylaxis [15].

Clinical course of severe preeclampsia may deteriorate jeopardizing both the mother and fetal condition. These women should be delivered at 34 weeks of pregnancy. Delivery is also indicated in reupture of membranes and severe IUGR. In severe preeclampsia before 24 weeks of pregnancy fetal survival rate is very low. Pregnancy should be terminated. Labour should be induced and maternal condition during labour should be closely monitored. Opinion differs as to management of patient with severe preeclampsia between 24 and 34 weeks of pregnancy. Some favour termination of pregnancy and other group favour conservative management till fetal maturity. With expectant management fetal survival rate is found to be better. For conservative management patient should be admitted in tertiary level hospital and managed with magnesium sulphate, antihypertensive drugs and frequent maternal and fetal monitoring. Time of delivery depends on period of gestation, fetal condition, presence of labour. Vaginal delivery should be attempted in all women. Elective caesarean section should be considered for women with severe

preeclampsia below 30 weeks of gestation, not in labour, severe IUGR and with unfavourable cervix.

Severe preeclampsia is associated with maternal mortality rate of 0.2 percent and morbidity rate of 5 percent [16]. Increased mortality and morbidity are due to cardiovascular accident, pulmonary edema, HELLP syndrome, acute renal failure, disseminated intravascular coagulation etc. Perinatal mortality and morbidity in severe preeclampsia is very high , causes are mainly IUGR, prematurity, abruptio placenta and even IUFD.

Among different antihypertensive drugs methyldopa, labetalol, nifedepine and hydralazine are accepted as drug of choice for hypertensive pregnant women.

Methyl dopa is effective and has best maternal safety. It is a centrally acting drug. Usual dose is 250mg orally three times a day, maximum daily dose should not exceed 3gm/day.

Labetalol is a combination of alpha and beta-adrenoreceptor. The usual oral dose is 100mg thrice a day upto 800mg/day. In emergency it can be used intravenously; initially 20 mg, increasing the dose to 40 mg or even 80 mg every 30 minutes, if required. Maximum dose should not exceed 200 mg/day.

Nifedepin is a calcium channel blocker. It exerts its antihypertensive effect by vasodilatation. The dose of slow release tablet in 10-30mg orally four times a day, not to exeed 120 mg a day. Capsule of 10-30 mg orally can be given for fast action, if needed another dose of 10 mg can be given every 30 minutes.

To treat severe hypertension in preeclampsia hydralazine is used intravenously. The dose in 5 mg given slowly intravenously, can be repeated after 20 minutes with 10mg, if required, total dose being 20mg.

Eclampsia

Eclampsia is defined as the development of convulsion and/ or unexplained coma during pregnancy or postpartum in patients with signs and symptoms of preeclampsia [17]. Reported incidence of eclampsia in Western World is 1 in 2000-3448 pregnancies [18,19]. In India incidence varies from 0.5 to 3.7 percent. in different hospitals [20-22]. Imaging studies of brain shows vasogenic edema of brain. This suggests that hypertensive encephalopathy plays central role in causation of convulsion in eclampsia [17]. Antepartum eclampsia is reported to ranges from 38 to 53 percent and post partum eclampsia ranges from 11 to 44 percent [19, 23]. Patients with late post partum eclampsia or eclampsia developing at or before 20 weeks of gestation are likely to create confusion. In these two atypical eclampsia cerebral imaging like CT scan or MRI is helpful to excludes any cerebral pathology.

A women with eclampsia should be managed in a tertiary level hospital. The objectives for management of eclampsia include – control of convulsion, prevent further convulsion, control of blood pressure and delivery after adequate stabilization of the patient.

During or immediately after a convulsive episode care should be taken to prevent maternal injury, maintenance of airway, to prevent aspiration of vomitus or secretion. The patient should be put in left lateral position, airway is secured, administer oxygen with a face mask, padded tongue blade should be introduced to prevent maternal injury. Pulse oxymetry should be used to monitor oxygenation, wide bore intravenous line should be started to administer anticonvulsant.

Magnesium sulphate is accept-ed world wide as the anticonvulsant of choice. Findings of the Collaborative Eclamp-sia Trial confirmed the

Table -1: Different dosage schedule have been suggested by different workers

Pritchard et al [25]	Loading dose -- Maintenance --	4 gm as 10% solution I.V. 1gm/min 5gm I.M. 4 hourly
Zuspan et al [26]	Loading dose -- Maintenance --	4gm I.V. over 3-5 minutes 1-2gm/ hour, I.V.
Sibai [27]	Loading dose -- Maintenance --	6gm I.V. over 20 minutes 2gm/ hour I.V.

superiority of magnesi-um sulphate over phenytoin and diazepam in the management of eclampsia [24]. A loading dose of Magnesium sulphate 4 gm (20ml of 20% solution) is administered intravenously slowly over 15 to 20 minutes, then 5 gm in each buttock (10ml of 50% solution) is administered deep intramuscularly. This is followed by 5gm intramuscularly every 4 hours. Addition of lignocaine at the site of injected reduces pain. Alternatively after the loading dose of intravenous 4 gm of magnesium sulphate, intravenous infusion can be started at the rate of 1-2gm/hour. In recurrence of convulsion 2gm magnesium sulphate is administered IV over 3-5 minutes. In rare case, if convulsion continues sodium amobarbital 250 mg may be given intravenously. Arrangement for intubation and positive pressure ventilation by an expert anaesthetist is required. Patient should be treated in an intensive care unit.

In low dose regime a loading dose of 4gm intravenously is followed by 3gm intramuscularly in each buttock, followed by a maintenance dose of 2.5gm every 4 hourly. Magnesium sulphate is continued for at least 24 hours post partum or after the last convulsion.

Magnesium sulphate is excreted in urine, so urinary output should be measured accurately. In therapeutic dose it slows neuromascular conduction and thereby, depresses central nervous system irritability. Maternal respiration rate, deep tendon reflex and state of consciousness must be monitored frequently. The following to be monitored before each injection of magnesium sulphate.

- Petellar reflex – Present
- Respiration rate – 16 or more/ minute
- Urinary output during the previous 4 hours is 100ml of more

Antidote of Magnesium sulpahte is calcium gluconate, 10ml of 10% calcium gluconate is administered intravenously very slowly over a period of 3 minutes. Other anticonvulsant used were lytic cocktail, phenytoin sodium and diazepam. Blood pressure should be lowered to a desired level. Systolic blood pressure should be brought down to 140-150 mmHg and diastolic pressure to 90-100mmHg. To bring the blood pressure down hydralazine 5-10mg intravenously or labetalol 20-24 mg is administered intravenously. Hydralazine can be repeated every 15 minutes and labetalol every 20-30 minutes. Alternatively nifedepin can be given orally in the dose of 10-30mg capsule, can be repeated after 30 minutes.

Careful monitoring of intravenous fluid used in preeclampsia and eclampsia is needed. Ringer lactate solution is used routinely at a rate of 100ml per hour. Intake and output chart should be maintained. Amount of fluid infused depends on urinary output. Care should be taken to avoid circulatory overload.

Delivery should be planned following stabilization of the patient. Factors to be considered before deciding the mode of delivery are duration of gestation, fetal condition, Bishop score and whether the patient is in labour or not. Patient in labour or with ruptured membranes and when gestation period is more than 30 weeks vaginal delivery should be planned. Labour should be induced with prostaglandin or oxytocin drip. Patients with gestational age less than 30 weeks but with favourable Bishop score, labour should be induced. Caesarean section is considered in other obstetric conditions and when vaginal delivery is unlikely within 6-8 hours of first convulsion and in fetal distress. Patients with IUGR, abruptio placentae are better managed with caesarean section. Regional anaesthesia like spinal or epidural anaesthesia is favoured by many. Regional anaesthesia is contraindicated in presence of coagulopathy or severe thrombocytopenia.

Eclampsia is associated with high maternal and perinatal mortality and morbidity. In developed countries maternal mortality ranges from 0-1.8 percent [19,23,25], while in India it ranges from 2.63 to 14 percent[20,24,28]. The main causes of death are cardiovascular accident, pulmonary edema, abruptio placentae and HELLP syndrome. Perinatal mortality and morbidity are also high in eclampsia. In India reported mortality ranges from 18 to 40 percent [24,28,29] and mainly related to prematurity, birth asphyxia, IUGR and abruptio placentae.

After delivery an eclamptic patient should be

monitored carefully. During this period vital signs, fluid intake and output and other symptoms should be carefully observed for at least 24 hours. Magnesium sulphate should be continued for at least 24 hours after delivery.

HELLP Syndrome

HELLP Syndrome is a variant of preeclampsia. The syndrome is characterized by hemolysis, elevated liver enzymes and low platelet count. Platelet count of >100,000/cubic mm is the most consistant finding in HELLP syndrome [30]. The syndrome occurs in about 2-12 percent of preeclamptic and 30 percent of eclamptic patients.

Criteria for diagnosis of HELLP syndrome [16]- 1) Hemolysis (at least two of these findings): peripheral smear (schistocytes, burr cell), serum bilirubin (>12 mg/dl), low serum heptoglobin, severe anaemia, unrelated to blood loss, 2) Elevated liver enzymes: AST or ALT > twice upper limit of normal, LDH > twice upper limit of normal, 3)Low platelet count.

Presence of HELLP syndrome further deteriorates the maternal and perinatal outcome. Reported maternal mortality is about 1 percent and perinatal death rate ranges from 7.4 to 20.4 percent [16].

Management of woman with HELLP syndrome is same as with severe preeclampsia. Patients should be delivered at any gestational period. After initial assessment patients should be stabilized, coagulopathy, if any, should be corrected. Platelet count should be maintained greater than 20,000/cubic mm for vaginal delivery and greater than 40,000/cubic mm. for ceasarean section [16, 30]. To increase platelet count platelet transfusion may be required. Post delivery monitoring is same as in severe preeclampsia.

Conflict of interest: None. **Disclaimer:** Nil.

References

1. Habli M, Sibai BM. Hypertensive disorders in pregnancy, Danforths Obstetrics & Gynaecology. 10th ed. New Delhi: Lippincott Williams & Wilkins (India) Pvt. Ltd; 2010. p 257-75.

2. Registrar General. Maternal Mortality in India: 1997-2003 Trends, causes and Risk Factor. New Delhi; 2006.

3. Habli M, Sibai BM. Hypertensive disorders of Pregnancy, Danforths Obstetrics & Gynaecology. 10th ed. New Delhi: Lippincott Williams & Wilkins (India) Pvt. Ltd; 2010. p257-73.

4. Barton JR, O'Brien JN, Berganer NK, Jacques Dl, Sibai BM. Mild Gestational hypertension remote from term: progression and outcome. Am J Obstat Gynecol. 2001 (Apr); 184: 933-79.

5. Chesley LC. Hypertensive Disorders in Pregnancy. New York: Appleton-Century- Croft; 1988. p 479.

6. Nobis PN. Blood Pressure in Pregnancy. The Obstat & Gynec of India. 1986; 36(4): 625-29.

7. Tjoa ML, Khankin EV, Rana S, Karumanchi A. Angiogenic factors and preeclampsia. Placental Bed Disorders. New Delhi: Cambridge University Press; 2010. p229-91.

8. Many A, Hubel CA, Fisher SJ, Roberts JM, Zhou Y. Invasive Cytotrophoblasts menifest evidence of Oxidative Stress in preeclampsia. Am J Pathol. 2000 (Jan); 156(1): 321-31.

9. Maynard S, Epstein FH, Karumanchi SA. Preeclampsia and angiogenic factors. Ann Rev Med. 2008; 59: 61-78.

10. Feinberg BB. Preeclampsia: The Death of Goliath. Amer J Reproductive Immunology. 2006; 55: 85-98.

11. Gupta S, Wagh G. Preeclampsia and Eclampsia: A challenges in its truest sense: Busting the challenge, ICOG Evidence News letter of the Indian College of Obstetrician & Gynaecologist. 2012(Apr); 8-10.

12. CLASP Collaborative Group. A randomized trial of low dose aspirin for the prevention and treatment of Preeclampsia among 9364 women. Lancet. 1994; 343: 619-29.

13. Duley L, Henderson-Smart DJ, Mecher S, King JF. Antiplatelet agents for preventing preeclampsia and its complications. The Cochrance Database of Systemic Reviews. 2007; 2. No. CD004659 DOI 10. 1002.

14. Bujold E, Roberge S, Lacasse Y, Bureau M, Andibert F, Marcoux S, Forest JC , Giquere Y. Prevention of preeclampsia and Intrauterine Growth Restriction with Aspirin started in Early Pregnancy: A meta analysis. Obstet Gynecol. 2010; 116: 402-14.

15. Lucus MJ, Leveno KJ, Cunninghum FG. A comparison of Magnesium Sulphate with phenytoin for

prevention of eclampsia. N Eng J. Med. 1995; 333: 201.

16. Lakib M, Sibai BM. Gestational hypertension-preeclampsia and eclampsia, Management of high risk pregnancy. 5th ed. Machachusetts: Blackwell Publishing Ltd; 2007. p 271 - 79.

17. Sibai BM. Diagnosis, Prevention and Management of Eclampsia. Obstet Gynecol. 2005; 105(2): 402-10.

18. Saftlas AF, Olson DR, Franks AC, et al. Epidemiology of preeclampsia and eclampsia in the United States, 1979-86. Amer J Obstet Gynecol. 1990; 163: 460-65.

19. Douglas AK, Redman CW. Eclampsia in the United Kingdom. BMJ. 1994; 309: 1395-400.

20. Nobis PN. Maternal outcome in Eclampsia. Asian J Obstet Gynec Practice. 2002; 1(6): 25-28.

21. Suman G, Somegowda S. Maternal and perinatal outcome in eclampsia in a district hospital. J Obstet Gynecol India. 2007; 57: 324-6.

22. Samel S, Gupta U, Agarwal P. Management of Eclampsia with magnesium sulphate and Nifedepin. J Obstet Gynecol India. 2001; 51(3): 71-74.

23. Mattar F, Sibai BM. Eclampsia VIII; risk factors for maternal mortality. Am J Obset Gynecol. 2000; 182: 307- 12.

24. Doley L, Carroli G, Belijan J, et al. Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial. Lancet. 1995; 345: 1455-69.

25. Pritchard JA, Pritchard SA, Cunningham FG. The Parkland Memorial Hospital Protocol for treatment of eclampsia: Evaluation of 245 cases. Am J Obstet Gynecol. 1984; 148: 951.

26. Zuspan FP. Problems encountered in the treatment of pregnancy induced hypertension. Am J Obstet Gynecol. 1978; 131: 591-96.

27. Witlin AG, Sibai BM. Magnesium Sulphate therapy in preeclampsia and eclampsia. Obstet Gynecol. 1998: 92: 883-9.

28. Sardesai S, Maira S, Patil A. Low dose magnesium therapy for eclampsia and imminent eclampsia: Regime tailored for Indian women. J Obstet Gynecol India. 2003; 53 (6): 546-50.

29. Nobis PN. Perinatal mortality in eclampsia. J Obstet Gynecol India. 1988; 38(1): 38-42.

30. Sibai BM. Diagnosis and management of Gestational hypertension and preeclampsia. Obstet Gynecol. 2003; 102: 81-192.

Prabinendra Nath Nobis

Consultant, International Hospital, Christianbasti, Guwahati, Assam, India.