# ECLAMPSIA : AN OBSTETRIC DISASTER

**Pradhan P**


## ABSTRACT

**Eclampsia has been graded as fatal and dreadful disease even before Christ and is the important cause of maternal and perinatal mortality in developed and developing countries. Severe morbidity associated with eclampsia include placental abruptio, cerebral haemorrhage, cortical blindness, renal failure, disseminated intravascular coagulopathy, pulmonary oedema, psychosis and growth retardation and preterm or both. Present management of eclampsia aims to stop the convulsions, its recurrences, control of blood pressure and correct fluid and electrolyte balance and delivery of the baby. There have been great controversies about the best anticonvulsants to use. The randomised trials comparing magnesium sulphate with diazepam or phenytoin showed greater efficacy of magnesium sulphate in the control and prevention of recurrence of fits. Perinatal mortality is also better with magnesium sulphate. Intramuscular injection is painful and local abscess formation at the site of injection is possible. Control of dose is better with intravenous route therefore preferred. Magnesium sulphate should be continued for 24 hours after the delivery or after the last fit. Antihypertensive drug therapy is now a routine practice in the management of pre-eclampsia and eclampsia. Methyl dopa, Lobetelol, Nefedipine are well tried in pregnancy and safe in pregnancy. However, hydralazine intravenous is good for quick and smooth control of blood pressure. Termination of pregnancy has been an important part of the management of eclampsia. Studies have shown that maternal outcomes seems better with caesarean delivery compared to vaginal delivery. The caesarean section rate is high at 26.3-80.4% in different studies. Recently maternal mortality and morbidity has been greatly improved even in developing countries by better control of fits by magnesium sulphate and caring them in intensive care unit.**


***Key Words: Eclampsia, Anticonvulsants, Antihypertensives, Delivery.***

## INTRODUCTION

Eclampsia is defined as the occurrence of one or more convulsions in association with the syndrome of pre-eclampsia. Pre-eclampsia is a multi system disorder associated with hypertension and proteinuria and is a fairly common complication of pregnancy at around 10%.[1] The incidence of eclampsia is reducing and it complicates 1 in 2000 deliveries in developed countries while in developing countries estimates vary widely from 1 in 100 to 1 in 700 deliveries.[2-4] The word eclampsia was first described in 1691 as a Greek word 'Ekampecin' mean 'Flash-out' because of visual phenomenon accompanying convulsions.[5] Despite the rarity of this severe disease, it is still a major cause of maternal mortality and is a factor in 2-10% of direct maternal death in developed countries.[6,7,8] In the developing countries, where maternal mortality rate is 100-200 times higher than Europe and North America, it has been estimated that 10-22% of all maternal deaths are attributed to eclampsia.[8,9,10] Despite the higher prevalence of eclampsia in developing countries and the wealth

**Address for correspondence :** Prof. P. Pradhan
Nepal Medical College and Teaching Hospital
Atterkhel, Jorpati
P.O. Box: 13344, Kathmandu, Nepal.
Email: nmc@nmcth.edu

of experience gained in its management, maternal mortality rates remain high. This may be partly due to the fact that pre-eclampsia is a multi system disease and the extent of involvement of the various organs is unpredictable. Treatment of pre-eclampsia and eclampsia is also empirical because the pathology of this condition remains unknown. Maternal mortality in eclampsia results from combination of several factors. Most important issue is whether the patient has recurrence of fits, reaches the hospital in reversible stage or her condition is already in bad shape. Mortality is very high (37.7-46%) in patients who are deeply comatosed on admission.[11,12] Lack of prenatal care is associated with increased risk of comlicated eclampsia and maternal mortality of 33.3% reported in complicated eclampisa and none in uncomplicated eclampsia.[12-14] Ozumbic BC et al[15] reported the incidence of eclampsia among unbooked cases was 4.3/1000 birth compared to 1.1/1000 birth among booked cases. In Nepal 13% of ostetrics population have antenatal care provided by doctors and 11% by midwives and nurses.[9] On the other hand Douglas and Redman[2] reported that eclampsia was seen despite antenatal care and within a week of women last visit to a midwife or doctor. Probably routine screening methods during antenatal check up may not detect all potential eclamptic women and eclampsia is often unpredictable and therefore not completely preventable. The problem is not limited to that of maternal mortality. Severe morbidity associated with eclampsia include placental abruption, cerebral haemorrhage, cortical blindness, renal failure, disseminated intravascular coagulopathy, pulmonary oedema and psychosis are very important.[7] In Sweden during 1976-80 nearly 15% of affected women had serious maternal complication in addition to eclamptic convulsion[16]. Douglas and Redman2 demonstrated that 35% of the eclamptic patients had at least one or other complication whereas the collaborative eclampsia trial[17] found the incidence of morbidity ranging from 12.4% to 25.3%. Eclampsia is also a major cause of perinatal death worldwide. The collaborative eclampsia trial found the incidence of perinatal mortality range from 177-307/1000 total birth.[17] Douglas and Redman[2] from UK found a rate of 56/1000 total birth. In Nepal, the rate of 200-300/1000 birth reported1[8,19] late arrival of patients after the onset of fits results in intrauterine hypoxia and intrauterine death. The perinatal mortality is more related to gestational age at delivery than to the severity of disease. A further improvement in neonatal survival for infants born to eclamptic mothers will depend on therapy that will allow prolongation of pregnancy or on future advances in neonatal care. The great risk for the fetus is when eclamptic fits with their attendant period of acute maternal and therefore fetal anoxia occurs before delivery and the fetus is already compromised by placental insufficiency.[20,21] Detecting pre-eclampsia and implementing treatment earlier might have been more effective. Treatment should be simple, avoiding large doses of drugs such as diazepam, which adversely affect the baby.[19] Because of the perinatal problems resulting from anoxia more liberal recourse to caesarean section should be considered especially when there is evidence of impaired placental function and preterm delivery is required.[1] Effectiveness of available beonatal care also determines the perinatal outcome.

## AETIOLOGY

Genetic influence has long been regarded as aetiologically important in pre-eclampsia and eclampsia.[22] A family history of pre-eclampsia and eclampsia is associated with 4 fold increase in the relative risk of severe pre-eclampsia in primigravida women. Inheritance was followed both through sons and daughters. The prevalence of pre-eclampsia and eclampsia in daughter was significantly higher 23% than that in daughters-in-laws 10% and appears to involve a genetically determined susceptibility possibly bases on single gene inheritance.[23]

## TREATMENT OF ECLAMPSIA

Eclampsia remains one of the leading causes of maternal and perinatal mortality in many parts of the world.[17,24,25] Present management of eclampsia aims to stop the convulsions and prevent recurrence, control of blood pressure, correct fluid and electrolyte imbalance and deliver the patient promptly. Standard practice is to use anti-convulsants to control fit immediately and prevent further seizures but the choice of an ideal anticonvulsant is controversial. Currently the most widely used anticonvulsants are diazepam, phenytoin and magnesium sulphate.[26,27] Excellent reports have been reported from all these anticonvulsant drugs with respect to maternal and perinatal mortality. In UK and many other countries diazepam and phenytoin are favoured[28,29] whereas magnesium sulphate is the drug of choice in USA.

In UK diazepam has been popular since 1970 and most clinicians agree that diazepam should be used for immediate control of convulsions rapidly. Diazepam is to be given according to the regime described by Lean and co-workers.[29] A loading dose of 10mg intravenously over 2 minutes by an intravenous infusion of 40mg diazepam in 500ml of normal saline for 24 hour. The rate of infusionis titrated against the level of consciousness with the aim of overcoming restlessness and keeping the women sedated but rousable easily. During the next 24 hour, an infusion of 20 mg of diazepam is 500ml normal saline is to be given and slowly reduced. Lean et al demonstrated a mortality rate of only 3.3% in a population of eclamptic patients who are moribound at the time of admission and were treated with diazepam and the hypertensive agent

hydralazine.[29] Diazepam is an inexpensive, readily available, easily administered and therefore suitable for use by staffs in outlying clinic and hospital before the eclamptic women can be transferred to the referral hospital. Concern over the respiratory and cortical depressant effects of large doses of diazepam on both fetus and mother have been expressed. Heavy prolong sedation of the women increases the risk of aspiration pneumonia and other respiratory problem requiring ventilation in Intensive Care Unit which contribute to maternal mortality and morbidity.[25] Large doses of diazepam is often required and these can lead to neonatal respiratory depression, hypothermia, hypotonia and poor suckling.[19,28] Retrospective study of eclampsia in Harare Maternity Hospital revealed high rate of maternal 9% and perinatal 29% mortality when diazepam was used to manage eclampsia.[28] The risk of maternal and perinatal death increases as the number of fit increases and effective treatment should prevent further convulsions. The recurrence rate of convulsions of 27.9%[17,28] is considerably higher than the rate of 10% reported by Lean et al.[29] This may mean that diazepam serum level may be inadequate in studies with higher recurrence rate.[28] Too little diazepam results in recurrence of convulsions and too much diazepam results in over sedation and respiratory depression.

## PHENYTOIN

More recently phenytoin has been advocated for eclampsia on the basis of proven efficacy for otehr types of convulsions and the lack of sedative effects.[31,32] Phenytoin sodium was first used as a specific drug for prevention and control of epileptic seizure in 1938 and its pharmacological action is well described.[33] Slater et al in 1987[31] have reported good results with this drug in patients with severe pre-eclampsia but in cases of eclampsia the response is highly variable. The properties of this drug are rapid crossing of blood brain barrier and stabilising effect on all neuronal membranes and episodes of repetitive firing are specially supressed.[33] Phenytoin enters the brain rapidly and antiwomen's weight (not practical for emergency situation) Slater et al[31] recommended an initial loading dose of one gram intravenously by slow infusion in 200ml normal saline over 20 minutes with continuous cardiac monitoring. Maintenance dose of 500 mg diluted in 200ml every 4 hour for the next 24 hour. Phenytoin serum levels were measured (Abbott TD X 1R) flourescence polarization immunoassay 30min after loading dose and every 6 hr thereafter. The therapeutic serum level should be maintained at 40-100ug/L. The occurrence of side effects such as nausea, vomiting, nystagmus, ataxia and incoordination and arrhythmias were noted.[34] A small increase in dosage can cause a disproportionately large increase in phenytoin level and rapid administration may produce cardiac arrythmias. The rate of direct intravenous injection should not exceed effective as magnesium sulphate in the control of eclamptic convulsion. The recurrent convulsion rate of 17.1% and maternal death rate 5.2% and perinatal mortality of 30.7% is reported. More 1-35 babies with phenytoin treatment have low APGAR socer at one min and admitted to special care baby unit for more than 7 days. Phenytoin appeared particularly ineffective in comparision with magnesium sulphate with the possibility even of increases in maternal ventilation, pneumonia and admission to intensive care unit so would not seem justified for the routine use in the management of eclampsia[17]. Similar results are reported by other studies.[36,37]

## MAGNESIUM SULPHATE

Magnesium sulphate is the anticonvulsant agent of choice for the treatment of eclampsia in USA.[2530,38] As early as 1906 magnesium sulphate was injected intrathecally to control eclamptic seizures.[17,37] Because of reports that intramuscular magnesium sulphate controlled convulsions associated with tetanus, a similar regime was used in 1926 to prevent recurrent seizures in women with eclampsia.[39] In 1933 the drug was given intravenously to hundred of women with pre-eclampsia and eclampsia at the Los Angeles General Hospital.[37] Later Pritchard[32] and Zuspan[40] advised intramuscular and intravenous treatment with magnesium sulphate. According to the National high blood pressure education working group on high blood pressure in pregnancy, most authorities in North America recommend the use of magnesium sulphate for women with pregnancy induced hypertension to prevent eclamptic seizures during labour and the immediate puerperium.[41] There is little properly controlled evidence about the differential effects of anticonvulsants in eclampsia. The first two randomised trials of anticonvulsant treatment in eclampsia was published in 1990. The first trial compared magnesium sulphate with diazepam.[28] Fifty one women were randomised and the results tended to favour magnesium sulphate although none of the differences were statistically significant. The second trial compared magnesium sulphate with phenytoin was stopped early when 4 of 11 women allocated phenytoin had further convulsions while none of 11 women allocated magnesium sulphate did.[17,35] The collaborative eclampsia trial report was designed to estimate more reliably the differential effects of anticonvulsants commonly used for the care of women with eclampsia. This trial was a large scale study involving 1987 women in nine developing countries and provides compelling evidence in favour of magnesium sulphate rather than diazepam or phenytoin for the treatment of eclampsia. This trial has two arms: one comparing magnesium sulphate with diazepam arm and other comparing magnesium sulphate with phenytoin. There were fewer convulsions (13.2 Vs 27.9) and slightly lowering of maternal mortality (3.8 Vs 5.1) in

women given magnesium sulphate. In the magnesium sulphate phenytoin arm: recurrent fits were 5.7% versus 17.1% and lowering of maternal mortality (2.6% versus 6.2). Other serious maternal morbidities were that fewer women allocated magnesium were ventilated 14.9% versus 22.5% fewer had pneumonia, fewer needed intensive care facilities, fewer had blood transfusion. Two women allocated magnesium sulphate had an abscess at the injection site. Non significantly more perinatal death occurred among those allocated phenytoin than those allocated magnesium sulphate compared to diazepam or phenytoin in the treatment of eclampsia in now generally accepted.[17,18,28,30,34-42] Since magnesium sulphate is cheap and easy to produce, its ready availability should be a priority for all those concerned with maternal health and the essential drugs list of the world health organization and other bodies need to be amended accordingly. The mechanism of action of magnesium sulphate on central nervous system is unclear. It is potent vasodilator especially in cerebral vasculature and reduces intracerebral arterial spasm.[43] Cortical irritability and agitation are reduced. It is suggested that magnesium sulphate acts as an anticonvulsant by means of neuronal calcium-channel blockers through excitatory amino acid receptors on the cell surface. The N-methyl-D-aspartate (NMDA) receptor is the best characterised excitatory amino acid receptor subtype. It has been shown that the anticonvulsant activity of magnesium sulphate may be partially mediated by blockage or supression of the NMDA receptor activity.[44] The transient hypotensive effects may be mediated by a variety of mechanism such as increased prostacyclin release from vascular endothelium, decrease angiotensin converting enzyme activity and inhibition of catecholamines release. It also inhibit platelets aggregation. These observations fit well with the more recent recognition that pre-eclampsia is associated with widespread endothelial injury. Although the mode of action of magnesium sulphate is incompletely understood benefecial increase in renal and uterine blood flow may occur[45]. Despite its generalised action, magnesium sulphate does not cross the blood-brain barrier and has no effect on EEG abnormalities present with eclampsia.[25] Although magnesium readily crosses the placenta and fetal magnesium level correlates well with the maternal level no untoward effects has been reported with fetus, labour process or off springs.[46]

## TREATMENT REGIME FOR MAGNESIUM SULPHATE

There was no evidence from collaborative trial of any difference between the intramuscular and intravenous regime in their effect on recurrent convulsions. However intramuscular injections are painful and are complicated by local abscess formation in 0.5% of the cases.[17] The intravenous route is therefore preferred.

## INTRAVENOUS REGIME : BY ZUSPAN[40]

An intravenouss loading dose of 4gm in 20% solution over 5-10 minutes given slowly. This is followed by an infusion of 1gm/hr continued for 24 hour after the last fit or delivery. The rate of infusion could be controlled manually.

## INTRAMUSCULAR ROUTE : PRITCHARD METHOD[30]

A loading dose of 4gm intravenously in 20% solution over 5-10 mins followed by 5gm in 50% solution as a deep IM injection into the upper outer quadrant of each buttock. Maintenance therapy is a further 5gm. IM every 4 hr in alternate buttock continued for 24 hr after the last fit.

## RECURRENT CONVULSION

In both the intramuscular and intravenous regime if convulsion recurred, a further 2-4gm depending upon woman's weight (2gm if <70kg) is to be given intravenously over 5-10 minutes.

## MONITORING DURING THERAPY

Magnesium sulphate has no sedative effect, so on recovery from the post-ictal phase, the woman should be alert or oriented. However, magnesium can depress neuromuscular transmission at the myometrial junction causing muscular paralysis as serum level increases. The therapeutic serum level needed to prevent convulsions is generally believed to be between 2-4mmol / L The clinical monitoring during magnesium therapy is as follows:

| | |
|---|---|
| Respiratory rate | >12/min |
| Urine output | >25ml/hr |
| Knee / Patellar reflexes | are present |

The maintenance dose given only if above monitoring are normal. Frequent monitoring every 1 hour is necessary if complications of therapy is to be minimised. Monitoring by serum level of magnesium may not be available in many places and was not done in collaborative trial but clinical monitoring was strictly undertaken to ensure that respiration was not depressed, the knee reflex is present and the renal function is adequate. Magnesium is cleared by the kidneys so if renal function is impaired, less magnesium is required.

## MAGNESIUM TOXICITY

Guidelines for the management of potential complications of magnesium sulphate.

1. Respiratory depression
   Give oxygen by mask. 1 gm calcium gluconate IV slowly

and stop magnesium therapy. Maintain the airway and nurse in recovery position.

2. Respiratory arrest
   Intubate and ventilate immediately and stop magnesium sulphate therapy. Give 1 gm calcium gluconate intravenously as 10% solution. Ventilation should be continued until the resumption of normal spontaneous respiration.
3. Absent knee reflexes
   If respiration is normal, withhold further doses of magnesium sulphate until the reflexes return. If respiration is depressed manage as in no 1 above. Magnesium sulphate can be restarted if considered necessary, at a reduced rate (unless there have been further convulsions) once the reflexes have returned.
4. Urine output less than 100ml in 4 hour
   If there are no other signs of magnesium toxicity, reduce the next magnesium dose to half the dose (2.5gm IM or 0.5gm/hr IV). When there are other signs of magnesium toxicity manage as for the appropriate section above. Review the overall management with particular attention to fluid balance and blood loss.

## FURTHER MANAGEMENT

The following investigations should be done in all the women with eclampsia. Full blood count, platelets count, urea and electrolytes, serum creatinine, uric acid, fibrinogen and fibrin degradation products. Frequent pulse, blood pressure, respiratory rate and conscious level are monitored one hourly. Foley's catheter is inserted for continuous urine drainage. A central venous pressure line is inserted when appropriate. Intravenous fluid to maintain an adequate urine output.

## CONTROL OF HYPERTENSION

Antihypertensive drug therapy is now routine practice in the management of women with pre-eclampsia and eclampsia. Oral therapy is started at a diastolic pressure of 100mm Hg. Lobetelol, methyl dopa have been well studied and preferred. Hydralazine is the preferred antihypertensive drug in the management of eclampsia. In eclampsia, the blood pressure is assessed after completion of the loading dose of anticonvulsants. If the diastolic blood pressure is 115 mm Hg dihydralazine 25mg in 200ml of normal saline is administered by controlled continuous intravenous infusion to achieve a gradual reduction of diastolic blood pressure to 100-90mmHg. Another new antihypertensive agent Nifedipine is commonly used in pre-eclampsia, fulminating pre-eclampsia or eclampsia. In addition to greater antihypertensive action, better neonatal outcome is noted compared with hydralazine.[47] It also has a beneficial effect on urinary output by increasing renal perfusion.[48] There is a risk of potentiation of hypontension action and neuromuscular blockage when combined with magnesium sulphate.[49]

## OBSTETRIC MANAGEMENT

The termination of pregnancy has classically been an important part of the management of eclampsia. In all cases the pregnancy should be terminated by induction of labour or caesarean section once the convulsions and hypertension are under control. Caesarean section is very high in eclampsia varying from 26.3% to 80.4% in different studies.[50-52] It has been observed that maternal outcome was better with caesarean delivery compared to vaginal delivery in eclamptic patients. Maternal and perinatal mortality also shows favourable results 8.06% and 12.9% in caesarean delivery group whereas corresponding figures were 15.48% and 33.7% respectively in vaginal delivery.[53,54] Caesarean section may be beneficial to control eclampsia process as it involves complete muscle relaxation and anaesthesia. On the other hand majority of patients are in low socio-economic class, caesarean section definitely adds to morbidity because of poor patient compliance for follow-up and contraceptive use leading to the problems and complications of post caesarean pregnancy and delivery. Therefore if fits can be effectively controlled by a good anticonvulsant, it is preferrable that induction or augmentation of labour should be done with amniotomy and syntocinon infusion with the aim of vaginal delivery. However, unfavourable Bishop score is definitely an indication for caesarean section.

## CONCLUSION

Eclampsia is often regarded as largely a problem for developing countries but it is still associated with a substantial mortality in the developed world. A problem for prevention and treating eclampsia is that the pathogenesis of this condition is not clearly known. The collaborative eclampsia trial now provides strong support for routine use of magnesium sulphate rather than either diazepam or phenytoin. But despite better control of convulsions than with either diazepam or phenytoin other morbidity closely related to eclampsia was not significantly influenced by magnesium sulphate. This suggests that the mechanism by which magnesium sulphate exerts its effect is largely related to the cerebral complication of eclampsia. Further studies are needed to assess the usefulness of treatment to prevent eclampsia in women with pre-eclampsia comparing routine use of anticonvulsant with none.

## REFERENCE


1. Leitch Cr. Cameron AD. Walker JJ. The changing pattern of eclampsia over a 60 year period. *Br. J. Obstet Gynecol* 1997: 104: 917-22

2. Douglas KA. Redman CWG. Eclampsia in the united Kingdom. *BMJ* 1994: 309: 1395-1400

3. World Health Organization International Collaborative Study of hypertensive disorder of pregnancy. Geographic variation in the incidence of hypertension in pregnancy. *AM J Obstet Gynecol* 1988: 158: 80-83

4. Whitefield CR. Dewhurst's textbook of obstetrics and gynaecology for Post graduates 5th Edition. *Blackwell Science Cted*. 1995: 81,83,90,92,177, 182, 186, 187, 209

5. Dickman WJ. The toxaemia of pregnancy. St. Lions C. V. Mosby 2nd edition. 1952: 17: 507-17

6. Department of health, welsh office, scottish home and health department. DHSS Northern Ireland, Report on Confidence inquiries into maternal death in the united kingdom 1988-1990 London HMSO 1994.

7. Douglas KA. Redman CWG. Eclampsia in the united kingdom. The BEST way forward. *Br J Obstet Gynecol*. 1992: 99: 355-5 9

8. Duley L. Maternal mortality associated with hypertension disorder of pregnancy in Africa, Asia, Latin America ad Caribean. *Br. J. Obstet. Gynecol* 1992: 99: 547-53

9. Family Health Division. Ministry of Health 1996. Making safe motherhood work in Nepal: Programmatic and elements of challenges. *JNMA* 1996: 34: 118: 180-84

10. Eclampsia working group eclampsia in Bangladesh: a review and guideline. *Bangladesh J Obstet Gynecol*. 1996: 12: 1-25

11. Sawhney H, Aggarwal N, Biswas R, Vasistita K. Gopalan S. Maternal Mortality associated with eclampsia and severe pre-eclampsia of pregnancy. *Jr. Obstet. Gynecol*. Research. 2000: 26: 5: 351-56

12. Arora P, Ganguly RP, Swains, Oumachigui A, Payram P, Determinants of maternal mortality in eclampsia in India. *Aust. N. J. Obstet. Gynecol* 1994; 34:537-539

13. Agudelo AC, Katary-goeta AC. Case control study of risk factors for complicated eclampsia. *Obstet. Gynecol*. 1997; 90: 172-7 5

14. Swain S, Ojha KN, Prakash A, Bhaha BD. Maternal and perinatal mortality due to eclampsia. *India Paediatric Jr*. 1993; 30(6): 771-73

15. Ozymbia BC, Ibe-AL, Eclampsia in Enugu Eastern Nigeria Acta: *Obstet Gynecol Scand* 1993; 72(3): 189-92

16. Douglas KA, Redman CWG. Eclampsia in the united kingdom. The BEST way forward. *Br. J. Obstet. Gynecol*. 1992; 99: 355-5 9

17. Duley L, Carroli G, Belizan J et. al. What anticonvulsants for women with eclampsia-evidence from the collaborative eclampsia trial. *Lancet* 1995; 345: 1455-63

18. Al-Mulhim S, At Najash, Rehman J, Rehma MS. Management of Eclampsia, a reveiw of 50 cases. *Jr. of Obstet. Gynecol*. 1994; 14:40-49

19. Wrighman H, Hibbard Bin, Rosen M. Perinatal mortality and morbidity association with eclampsia. *BMJ* 1978; 2:235-37

20. Chaudhary P, Eclampsia in maternity hospital: impact of changing in the intervention strategy. Souvenir 6th National conference of NESOG.

21. Acharya G, Scholtz S. Eclampsia in Patan Hospital: A two year retrospective study. *JNMA*, 1991; 29: 254-58

22. Trelour SA, Cooper DW, Brennecke SP, Greham MM, Martin NG. An Australian study of the genetic basis of pre-eclampsia and eclampsia. *AmJ Obstet. Gynecol*. 2001; 184:374-81

23. Arngrimsson R, Bjornsson S, Geirsson RJ, Bjornsson H, Walker JJ, Sanedal G. Genetic and familial predisposition to eclampsia and pre-eclampsia in a defined population. *Br. J. Obstet. Gynecol*. 1990; 97:762-69

24. Redman C, Eclampsia Still Kills. *BMJ* 1988; 296:1209-1210

25. Moodley J. Treatment of Eclampsia. *Br. J. Obstet. Gynecol*. 1990; 97: 99-101

26. Hutton JD, James DK, Stirrat GM, Douglas KA, Redman CWG. Management of severe pre-eclampsia and eclampsia by U. K.consultants. *Br J. Obstet. Gynecol*. 1992; 99: 534-56

27. Redman CW, Roberts JM. Management of pre-eclampsia. *Lancet* 1993; 341: 1451-59

28. Crowther C. Magnesium versus diazepam in the management of eclampsia, a randomised controlled trial. *Br. J. Obstet. Gynecol*. 1990; 97:110-117

29. Lean TH, Ratnum SS, Sivasanbo R. Use of Benzodiazepines in the management of eclampsia. *J. Obstet. Gynecol. Br. Comnon W* 1968; 75: 856-62

30. Pritchard JA, Cunningham FG, Pritchard SA. The parkland memorial hospital protocal for treatment of eclampsia. Evaluation of 245 cases. *Am J. Obstet. Gynecol*. 1984; 148: 951-60

31. Slater RM, Wilmox H, Smith WD et. al. Phenytoin infusion in severe pre-eclampsia. *Lancet* 1987; 1: 1417-21

32. Coyagi KT, Otiv SR. Single high dose of intravenous phenytoin sodium for the treatment of eclampsia. *Acta Obstet. Gynecol. Scand* 1990; 69: 115-18

33. Gilman AG, Goodman LS, Rall TW, Murad E (eds) 1985. Goodman and Gilman's the Pharmacological basis of Therapeutics, 7th edi. Mac Milan New York.

34. Appleten MP, Kuchl TJ, Racbel et. al. Magnesium Sulphate versus Phenytoin for Seizure prophylaxis in Pregnancy induced hypertension. *Am. J. Obstet. Gynecol*. 1991; 165: 907-13

35. Dommisse J. Phenytoin Sodium and magnesium sulphate in the management of eclampsia. *Br. J. Obstet. Gynecol.* 1990; 97: 104-9

36. Robson SC, Redforn N, Seviour J et. al. Phenytoin Prophylaxis in severe pre-eclampsia and eclampsia. *Br. J. Obstet. Gynecol.* 1793; 100: 623:8

37. Lueas JM, Leveno KT, Cunningham GA. A comparision of magnesium sulphate with phenytoin for the prevention of eclampsia. *N. Eng. J. Med*. 1995; 333: 201-15

38. Sibai BM, Mc Cubbin JH, Anderson GD, Lipshitz J, Ditts PV: Eclampsia observation for 67 recent cases. *Obstet. Gynecol* 1981; 58: 608-13

39. Pritchard JA. The use of Magnesium ion in the management of eclamprogenic toxaemia. *Surg. gynecol. obstet*. 1955; 100: 131-140

40. Zuspan FP. Treatment of severe pre-eclampsia and eclampsia. *Clin. Obst. Gynecol*. 1996; 9: 954-72

41. National high blood pressure education program working group report on high blood pressure in pregnancy. *Am. J. Obstet. Gynecol*. 1990; 163: 1689-712

42. Bhalla A. Dhak GI, Dhall K. A safer and more effective treatment regime for eclampsia. *Aust. NZJ obst. gynecol*. 1994; 34: 144-48

43. Magnesium sulphate: review of clinical pharmacology applied to obstetrics. *Br. J. obstet. gynecol*. 1998; 105: 260-68

44. Cotton DB, Hallakh, Janusz C, Irtenkan LSN, Borman RF, Central anticonvulsant effect of magnesium sulphate on N-methyl-D-aspartate induced seizures. *Am. J. Obstet. Gynecol*. 1993; 168: 974-78

45. Nelson SH, Suresh MS. Magnesium sulphate induces relaxation of uterine arteries from pregnancy and non-pregnant patients. *Am. J. Obstet. Gynecol*. 1991; 164: 1345-50

46. Leveno KJ, Alexander JM, Mc Intire DD, Lucas MJ. Does magnesium sulphate given for prevention of eclampsia affect the outcome of labour. *Am. J. Obstet. Gynecol*. 1998; 178: 707-12

47. James A, Scardo MD, Vermillion St, Hogg BB, Newman RB, Haemodynamic in pre-eclamptic hypertensive emergencies. *Am. J. Obstet. Gynecol*. 1996; 175: 336-46

48. John RB, Heitt DK, Cononer WB. The use of Nifedipine during the postpartum period in patient with severe pre-eclampsia. *Am. J. Obstet. Gynecol*. 1990; 162: 788-92

49. Ami MB, Giladiy, Shalev E. The combination of magnesium sulphate and nifedipine: a cause of Neuromuscular blockage. *Br. J. Obstet. Gynecol*. 1994; 101: 263-63

50. Kuruvilla A, Bassaw B, Singh RS. A retrospective study of eclampsia in the trinidal. *Jr. Obstet. Gynecol*. 1992; 12: 169-172

51. Varawalla NY, Ghamande S, Ingle KM. A Five year analysis of eclampsia. *J. Obst. Gynecol*. India 1989; 39: 512-515

52. Mwingoglee JA, Matrivate SN. Eclampsia at Ga Runkuwa Hospital. *South African Medical Journal*. 1996; 86(12): 1536-9

53. Bhattacharya PK, Purkayastha S, Basu M, Mandal R. Caesarean Section in Eclampsia: Still a dilemma analysis of 314 cases. *Jr. Obstet. Gynecol*. India 1992; 42(1): 51-5

54. Arora R, Swain S, Agrawal A, Habeebullan S. Impact of mode of delivery on maternal mortality in eclampsia. *J India Med Assoc*. 1997; 95(4): 103-6