EARLY ONSET PREECLAMPSIA: MATERNAL AND PERINATAL OUTCOME

Gynecology

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ABSTRACT

Preeclampsia is a heterogeneous clinical syndrome which is a leading cause of maternal, fetal, and neonatal morbidity and mortality. The aim of the study evaluate the maternal and fetal outcome in women with diagnosis of early onset preeclampsia.

The present study was conducted with the primary objective to study the maternal, fetal and neonatal outcome among women diagnosed with early onset of preeclampsia without severe feature and with severe features. The overall outcome in women where pregnancies were continued after giving Mgso4 therapy were also studied. This was a prospective hospital based study in which 119 pregnant women were enrolled from emergency ward (labour room) who were diagnosed to have early onset preeclampsia at less than 32 weeks of gestation.

Women with early onset preeclampsia were given expectant management and the maternal and perinatal outcome in women were reviewed as per severity that is whether PE occurred with or without severe features. The maternal complications did not increase in women who received expectant management in women with PE with severe features, as well as the group which had received prophylactic Mgso4 therapy and in whom subsequently pregnancy continued for few days to weeks. The perinatal outcome was compromised because of early presentation of PE which probably causes the placental insufficiency even in women without severe features.

Significant number of days gained during expectant management has an impact on the perinatal outcome which was from few days to weeks in this study.

KEYWORDS

Early Onset, Preeclampsia, Maternal And Perinatal Outcome.

INTRODUCTION

Preeclampsia is a heterogeneous clinical syndrome which is a leading cause of maternal, fetal, and neonatal morbidity and mortality. It is characterised by de novo hypertension after 20 week of gestation. Preeclampsia is the leading cause of morbidity and mortality in women during child bearing age, incidence being 2-7%. Preeclampsia increases the risk of maternal mortality by 14% in developing and 1.8% in developed countries. The incidences of severe preeclampsia prior to the 34th week of gestation is 0.3%, and in many countries preeclampsia is still the most frequent cause of maternal and perinatal mortality.¹ The high incidence of preeclampsia in developing countries are due to malnutrition, hypoproteinemia and poor obstetric facilities. Incidence of preeclampsia in India is reported to be 8 to 10%.²

In most of the studies early onset preeclampsia has taken when preeclampsia developed before 34 week of gestation, however few studies have included women with preeclampsia who developed it before 32 weeks of period of gestation.³

Preeclampsia most often occurs at or close term and prompt delivery is recommended, as any benefits of deferring delivery are not justified likewise may lead to increase maternal and fetal risks. The onset of preeclampsia in the 2nd trimester or early 3rd trimester is less common, however, it accounts for substantial perinatal morbidity and mortality, in large part due to prematurity.

This preterm delivery has strong impact on increasing the maternal morbidity and mortality. Long-term, the burden of preterm birth is immense, particularly in terms of neurodevelopmental impairment, impaired learning, cerebral palsy, and need for special care resources. With aggressive treatment and immediate delivery most surviving neonates experience significant neonatal complications requiring prolonged hospitalisation in neonatal intensive care unit and various interventions. Research suggests that fetal lung maturity is not accelerated in preeclamptic pregnancies.⁴

Magnesium sulphate plays an important role in management of severe preeclampsia by preventing eclampsia⁵. Magnesium sulphate administration has the additional benefit of fetal neuroprotection for those undergoing delivery at extremely premature gestational ages¹. The outcome of severe PE remote from term in a developing country would not be the same as that in developed countries where the expertise and resources are far better. In this study, we tried to evaluate the maternal and perinatal outcome of early onset PE in a tertiary hospital in North India. We also tried to find out if expectant

management provided in our setup succeeds in reducing perinatal mortality, or significantly increases maternal morbidity in women received expectant management of severe preeclampsia occurring below 32 weeks gestation. Our aim was to achieve a higher gestational age at delivery and birth weight, and decreasing neonatal complications in selected cases, under careful in-hospital maternal and fetal surveillance. We specially focused on outcome of cases those received Mgso4 but pregnancies were allowed to continue after Mgso4 therapy and termination of pregnancy were done until maternal or fetal parameters deteriorate further.

The aim of the study evaluate the maternal and fetal outcome in women with diagnosis of early onset preeclampsia.

MATERIAL AND METHODS

Prospective observational study design was used to address the objectives of this study. The study was conducted in 18 months from January 2016 to June 2017. This study was conducted in Department of Obstetrics and Gynaecology Post Graduate Institute of Medical Education and Research, Chandigarh, which is a tertiary care referral hospital of North India.

Study Population:

Women admitted with diagnosis of early onset of preeclampsia at less than 32 weeks of gestational age were included.

The operational definition of preeclampsia considered was as per American Congress of Obstetricians and Gynecologists (ACOG).

"Hypertension (Blood pressure greater than or equal to 140 mm of Hg systolic or greater than or equal to 90 mm of Hg diastolic on two occasions at least 4 hours apart after 20 weeks of gestation in a women with a previously normal blood pressure) and Proteinuria (greater than or equal to 300 mg per 24 hours urine collection (or this amount extrapolated from a timed collection), or protein and creatinine ratio greater than or equal to 0.3, dipstick reading of 1+ (used only when quantitative method not available) or in the absence of proteinuria, new onset hypertension with the new onset any of the following.

RESULT & DISCUSSION

Mean maternal age of the present study population was 27.89 +4.7 years. The mean gestational age at which preeclampsia was diagnosed was 28.64+2.66 weeks of gestation. Out of 119 women with early onset preeclampsia in our study, 45.3% were primigravida. Among Group 1 which include women having PE without severe feature,

33.3% women were primigravida; and among Group 2 where women had PE with severe feature, 50.6% women were primigravida. As in previous literature it was found that the preeclampsia occurs more commonly in first pregnancy probably due to first time exposure of paternal antigen leading to exaggerated presentation of the disease. Mean BMI of women included in the study group was 26.69±2.1 kg/m².

In a study by Saadati et al⁶ he found that the mean age, BMI, and period of gestation (POG) of women with early onset PE was 26.77± 6.26 years, 25.76±4.73, and 28±2 weeks respectively, which was similar to the findings of present study. In his study 51.1% women were primigravida among those having early onset preeclampsia.

Van Esch et al⁷ studied 109 women with early onset preeclampsia diagnosed from 24 to 32 week POG and found that 78 % of this study population were primigravida. The mean gestational age and maternal age was 29±2 weeks and 30±5 years respectively. Similar findings were seen in study conducted by Kumar et al⁸ Recurrence of preeclampsia: Among multigravida women, recurrence of preeclampsia was reported in 44.61% women in present study. Among these women, 58.62% required MgSO₄ therapy in previous pregnancy and 65.5% required Mgso₄ therapy in index pregnancy. There were 64.7 % risk to developed early onset severe PE with severe feature who had severe features in her previous pregnancy also. About 65% chances to develop severe feature in next pregnancy in women who had developed PE in her previous pregnancy, irrespective of whether associated with severe features or not.

Hnat and Sibai⁹ studied women who had PE in their previous pregnancy and they found that rates of recurrence of preeclampsia was 17.9% and risk of recurrence of PE with severe feature 5.3%.

In analysis by Takahas et al¹⁰ they found that PE recurred in almost one-seventh of women with a past history of PE. The occurrence risk of PE and early onset PE in women with a past history of severe hypertensive disorder was almost twice as high as in those with a past history of PE.

Van Oostwaard et al¹¹ studied 133 women with early onset preeclampsia before 26 week. Among them 48 (36%) women were multigravida and among them 44% had history of preeclampsia in former pregnancy. Similarly studied women with early onset preeclampsia and received expectant management and concluded that women who had pregnancy after a pregnancy with early onset preeclampsia, there was increased likelihood of recurrence.

Amongst of 119 women in this study, 29.4% had chronic hypertension with superimposed preeclampsia. Among women of PE without severe feature 47.1% and in women with PE with severe feature 24.1% women had chronic hypertension. It was found that more percentage (41.6%) of women without severe features had history of chronic hypertension as compared to women with severe features (24%) and this finding was statistically significant as well. This finding indicated that due to long standing history of hypertension, the body of mother had physiologically adapted itself to high blood pressure thus reducing the number of maternal complications but after conception, it lead to fetal complications. In present study there was a high risk of recurrence of PE with severe features (60%) in women who had chronic hypertension. There was 73.3% risk to develop severe features in subsequent pregnancy in women with chronic hypertension, who had history of development of PE in her previous pregnancy irrespective of whether previous pregnancy was associated with severe features or not. 26% had chronic hypertension with superimposed preeclampsia with severe feature. Studied 51 women with early onset PE with severe feature at less than 26 week POG and 14% women had chronic hypertension. 32% of study cohort had history of chronic hypertension. In study high recurrence of PE in women who had chronic hypertension.

Burwick et al¹² found in their study that chronic HTN remained a strong independent risk factor for PE both for with or without severe features and also for early-onset severe PE. They concluded that women with chronic hypertension were less likely to develop severe feature; however, when they developed PE with severe feature, it was more likely to be early-onset disease.

In present study, period of gestation for diagnosis of PE was 28.64 ± 2.6 week in total study population and 28.44 ±2.7 week in PE with severe feature women. POG of admission was 30.06±1.69 week in

total studied women and 29.9±1.7 week in women with PE with severe feature.

Saadati et al⁶ studied total 120 women with PE of which 50% were early onset preeclampsia. Mean gestation of diagnosis of early onset preeclampsia was 28±2 week and delivery was 32±2 week. a retrospective study of 106 women with early onset severe PE in India to find out whether expectant management improves perinatal outcome, and in his study the mean POG of admission was 31.51 weeks and POG of delivery was 32.49 weeks.

Ganzevoort et al¹³ carried out PETRA trial (Preeclampsia Eclampsia Trial Amsterdam), a 2-center, randomized, open-label trial between 2000 and 2003 in Amsterdam and Netherlands. A total of 216 women with early onset severe preeclampsia who received expectant management were included in this trial and the association between clinical parameters at admission and the subsequent development of major maternal complications or adverse infant outcome were evaluated. Median prolongation of pregnancy in the total group was 8.7 days.

Another study by Viswanathan et al¹⁴, mean days of pregnancy prolongation in women with early onset preeclampsia was 16.7 days with a median 14.2 days.

In a study of 65.1% women with preeclampsia between 27 to 33 of gestation, needed termination for maternal reason and 27.7% for fetal indication. Fetal indication of delivery were IUGR fetus with abnormal testing, non reassuring fetal NST.

In present study 35 women (29.4%) had vaginal delivery; among them 30 (85.7%) women had induction of labour and 5 went in spontaneous labour. Total operative delivery (LSCS) was in 70.5% (84 women) out of which, emergency LSCS was required in 67.2% (80 women) and 4(3.36%) had elective LSCS.

A total of 21 women (17.6%) required emergency LSCS after induction of labour due to non reassuring CTG. Vaginal delivery following induction of labour was in 56.6%. In current study 65.1% women with severe feature needed emergency LSCS. A total of 44.5% had induction of labour. In study 36% required emergency LSCS.

A prospective study by Viswanathan et al¹⁴ over 1 year, 5% had spontaneous onset of labour. Ninety-five (95%) were induced with dinoprostone gel. Of these 85.5% had vaginal delivery and rest 14.5% had LSCS.

In present study there were no major complication both in women with or without severe feature of preeclampsia. About 42.5% women developed some derangement in their biochemical and clinical parameter but no women developed serious maternal complication, such as eclampsia, pulmonary oedema, DIC, CVA, left ventricular failure. There was no maternal death or ICU admission in the present study. Among women with severe feature 39.39% women developed complications, but none of these led to any serious morbidity in mothers. In present study majority of women developed HELLP (26.7%) followed by abruptio placentae (10.0%). One woman developed increased serum creatinine level in postpartum period following abruptio placentae which was resolved with conservative management.

In study of 54% women developed complications. HELLP syndrome occurred in 62%. Other complications were Eclampsia in 3%, lung oedema 7.5%, hepatic capsular rupture 0.8%, renal failure 0.8%. No maternal death occurred in their study.

The maternal complications in Viswanathan et al¹⁴ study were abruptio placentae placentae (1%), eclampsia (1%), HELLP (2.8%), uncontrolled BP (4.7%), renal impairment (1.9%). No maternal death occurred.

Saadati et al⁶ in his retrospective analysis found hepatic functional derangement in 75% women, 25% had hematological involvement, 13.3% had pulmonary involvement, 11.7% had abruptio placentae. There were 4 (6.6%) maternal death in their study.

In this study, vigorous feto-maternal monitoring and intervention where indicated helped prevent high rates of serious complications in the mothers.

In current study, total 37.8% women were detected to have IUGR in antenatal period during USG monitoring. In women with PE without severe feature 41.7% women had IUGR where as 36.1 % of fetus of women with PE with severe feature were detected to have IUGR. In study 34.9% fetal scan were reported to suggest IUGR.

Van Esch et al ⁷ stated that pregnancies complicated by early- onset of PE are associated with the highest rate of small fo gestational age(SGA) neonates comparing to PIH(pregnancy induced hypertension), suggesting the influence of the patho- physiology of early-onset PE on fetal outcome in hypertensive women.

In study of Viswanathan et al ¹⁴, 47% fetus had IUGR of which 58% had mild IUGR and 42% had severe IUGR. The major cause of intra uterine death was placental insufficiency producing severe intra uterine growth retardation. The major cause of still birth also was placental insufficiency. Women with severe IUGR had poor neonatal outcome.

In study of neonates born to mother with early onset severe PE at 22 to 26 week, 57% were SGA.

In study of Viswanathan et al ¹⁴, they found that out of the 23 patients with severe IUGR only 7 babies survived.

A total of 70.19% babies in our study required respiratory support in the form of oxygen supplementation by head box or bag mask ventilation, or CPAP mechanical ventilatory support. A total 15.3% babies needed mechanical ventilator support. Very few babies had uneventful neonatal period and majority of babies developed complications of prematurity in the form of apnoea (38.4%), TTNB (31.7%), HMD (19.2%), NEC (4.8%), septicemia (29.8%), feeding intolerance (31.8%), hypoglycaemia (19.2%), pulmonary hemorrhage (1.9%), HIE (1.9%), IVH (4.8%). Although there was no difference according to severity of preeclampsia or according to whether mothers received expectant management or not. Majority of babies did not come for follow up for after discharge, so long term survival could not be ascertained.

Perinatal death was significantly high in women who had PE with severe feature mainly because of manifestation at a very early gestational age and interventions for fetus were not considered due to non- availability of resources and financial constraints of the couple or due to expected very poor fetal survival both intrauterine and after birth.

Although perinatal mortality was more in women with PE with severe feature, there was more duration of NICU stay and more duration of hospital stay in babies born in mother with PE without severe feature. In present study 23.5% babies had Apgar score less than 7 at one minute of life and 29.4% had less than 9 Apgar at 5 minute of life with no difference in mother with immediate termination of pregnancy group and expectant management group. HIE developed in 1.6% babies. In study cohort 72.1 % babies were SGA. In study of he recommended expectant management in all patients with gestational age below 30 weeks irrespective of presence of severe IUGR.

Van Esch et al ⁷ analysed neonates born to mothers with early onset PE (24 - 32 weeks) and compared with gestational age matched neonates born to mother without PE. There was 13% perinatal mortality in PE group with 22% had small for gestational age (SGA). Mean birth weight in PE group was lower.

In study average APGAR score of neonates ranged from 4 to 6 at 1 minute and 5 minutes, with no significant difference in group where immediate termination of pregnancy was done and the expectant management group. They found 31.13% perinatal mortality rates. Perinatal outcome of the expectant and aggressive management groups did not differ ($p=0.141$); there was no increase in maternal complications on expectant management.

In the retrospective study of Simsek et al ¹⁵, there was 22.1% still birth with 31.9% perinatal mortality in women with early onset preeclampsia. They found that there was no significant difference between the incidences of stillbirth, early neonatal death and neonatal death rates of early onset PE with or without severe symptoms. The study of Bucbinder et al ¹⁶ showed the differences in the incidence of intrauterine death due to the severity of preeclampsia, where the severe forms had a higher incidence of intrauterine death.

A total 56 newborn (53.84%) required NICU admission in the present study. Mean duration of NICU stay was 15.67 +9.848 days. In index study mean duration of NICU stay in babies born to PE without severe feature were more than in babies born to mother with PE with m severe feature (18.18 +10.8 days vs 12.15+9.0 days). Mean duration of hospital stay was also more in babies born to PE without severe feature than babies born to mother with PE with severe feature (26.72+12.7 days vs 19.20+9.0 days). In present study mean duration of NICU stay and hospital stay were more in babies born to mother who received expectant management Group than to immediate termination group (9.73+7.6 days vs 15.02+10.2 days and 20.46+11.6 days vs 22.15+13.6 days respectively). This may be due to the fact that where baby survival was good decisions were in favour of termination of pregnancy and most women considered for expectant management were those where fetal weight or gestation was less. Most women with early onset PE without severe features were referred to our institute for fetal indications therefore we received more women with fetal compromise in this group.

In study of Viswanathan et al ¹⁴, 58% of live born were admitted in NICU and mean duration was 8.2 days with range of 1 to 21 days. They concluded that gestational age at delivery was the key factor that decides the neonatal outcome. In study cohort of Saadati et al ⁶ 63.3% neonates born to mother with early onset preeclampsia required NICU admission.

In present study 26.8% women received prophylactic Mgso4. These women received Mgso4 therapy and their pregnancies were allowed to continue after initial stabilisation with Mgso4 therapy until maternal or fetal parameters deteriorated or adequate maturity attained.

The neonatal outcome in prophylactic Mgso4 group was comparable with babies born to mother with severe feature. There was 41% fetus developed apnea of prematurity, 32.2% developed septicaemia 29% developed HMD, 18.5% thrombocytopenia, 3.2% HIE which were similar with neonatal outcome in rest of babies born in mother with PE with severe features (33.3%, 31.3%, 11.7%, 2% respectively in women with PE with severe feature who did not received prophylactic Mgso4).

CONCLUSION

In pregnancy with chronic hypertension gestational age can be gained after giving prophylactic Mgso4 therapy without increase maternal risk however this demands vigilant monitoring for worsening of disease.

Early onset preeclampsia is a progressive disease unlike late onset preeclampsia, and it increases in severity in successive pregnancy and this was also seen in women with chronic hypertension where women are more likely to have recurrence with increases severity in subsequent pregnancy.

REFERENCE

- Marret S, Ancel PY. Neuroprotection for preterm infants with antenatal magnesium sulphate. *J Gynecol Obstet Biol Reprod*. 2016 Dec;45(10):1418-1433.
- American College of Obstetricians and Gynaecologist. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologist Task Force on Hypertension in pregnancy. *Obstet Gynecol* 2013;122:5.
- Blackwell SC, Redman ME, Tomlinson M, Berry SM, Sorokin Y, Cotton DB et al. Severe pre-eclampsia remote from term: what to expect of expectant management. *J Matern Fetal Neonatal Med* 2002; 11: 321-24.
- Sibai BM, Akl S, Fairlie F, Moretti M. A protocol for managing severe preeclampsia in the second trimester. *Am J Obstet Gynecol* 1990;163:733-8.
- Royal College of Obstetricians and Gynaecologist. Guideline No.10(A). The management of severe preeclampsia /Eclampsia. In London: Royal college of obstetricians and Gynaecologist. RCOG. 2010.
- Saadati N, Zargar M, Barati M, Dodangeh E. A comparative Assessment of Pregnancy Outcomes in Patients with Early and Late Pregnancy Hypertension Disorders. *Int. J. Pharm. Res. Allied Sci* 2016; 5(3):365-370.
- Van Esch JJA, Van Heijst AF, Haan AFJ, Oliver WH, Van Der Heijden. Early onset preeclampsia is associated with perinatal mortality and severe neonatal morbidity. *J of maternal-fetal and neonatal medicine*. 2017 Feb;30(16):1-6.
- Kumar M, Meena J, Gupta U, Singh A, Jain N. Management of early onset severe preeclampsia in a tertiary hospital in India: does expectant management alter perinatal outcome?. *Indian J Med Sci* 2011;65:535-42.
- Hnat MD, Sibai BM, Caritis S, Haut J, Lindheimer MD, MacPherson C et al; Perinatal Outcome in women with recurrent preeclampsia compared with women who develop preeclampsia as nulliparas. *Am J Obstet Gynecol*. 2002 Mar;186(3):422-6.
- Takahashi K, Ohkuchi A, Kobayashi M, Matsubara S, Suzuki M. Recurrence Risk of Hypertensive Disease in Pregnancy. *Med J Obstet Gynecol*. 2014;2(2): 1023.
- Van Oostwaard MF, van Eerden L, de Laat MW, Duvekot JJ, Erwich JJHM, Bloemenkamp KWM, et al. Maternal and neonatal outcomes in women with severe early onset pre-eclampsia before 26 weeks of gestation, a case series. *BJOG*. 2017 Jan;10: 1-9.
- Burwick R, Pilliod R, Caughey A. Chronic hypertension increases risk for all preeclampsia phenotypes. 2015 Jan; 212(1):S198-S199.
- Ganzevoort W, Annelies R, Johanna I, Bonsel VGJ, Wolf H. Prediction of maternal complications and adverse infant outcome at admission for temporizing management of

- early-onset severe hypertensive disorders of pregnancy. *Am J of Obstet and Gynecol* .2006; 195:495-503.
14. Viswanathan M, Viswanathan KV, Daniel S. Perinatal Outcome during Expectant Management of Early Onset Severe Preeclampsia. *Sch. J. App. Med. Sci.* 2015; 3(2C):751-755.
 15. Simsek A, Uludag S, Tuten A, Oncul M, Acikgoz AS, Uludag S et al. Maternal and perinatal outcomes in early onset and late onset preeclampsia. Paper presented at: 15th World Congress in Fetal Medicine;2016 Jun; 26-30.
 16. Buchbinder A, Sibai BM, Caritis S. Adverse perinatal outcome are significantly higher in severe gestational hypertension than in mild preeclampsia. *Am J Obstet Gynecol* 2002;186:66-67.