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Original Research Article

Fetal and maternal outcome of severe pre-eclampsia remote from term: expectant versus interventional management

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ABSTRACT

Background: This study was conducted to compare the safety and effect on maternal and perinatal outcome of expectant versus interventional management in women with preterm severe preeclampsia with gestational age between 28 to 34 weeks.
Methods: This was a non-blinded prospective analytical study carried out in the department of obstetrics and gynaecology, SSG hospital, Vadodara from January 2021-December 2021. 40 women diagnosed with severe pre-eclampsia remote from term meeting the inclusion criteria were divided in two groups (20 in each). First group comprised of women undergoing interventional management i.e. prompt delivery and the second group comprised of women undergoing expectant management till 34 completed weeks. The women in the expectant management underwent pregnancy termination before 34 weeks if any complication arises (e.g. anhydramnios, abruption, eclampsia etc).
Results: The mean prolongation of pregnancy in the expectant management group was 11.45 days (range: 4-35 days). There was no increase in incidence of maternal complications (p value: 0.003). The fetal outcome was favourable in the expectant management group in terms of higher gestational age at delivery (33 versus 31 weeks; p value: 0.001), higher birth weight (1.7 versus 1.5 kg; p value: 0.05), higher APGAR score at 1 minute (7.5 versus 7; p value :0.05), lesser incidence of neonatal complications (55% versus 95%; p value 0.003).
Conclusions: Considering the results of this study, it can be concluded that expectant management is recommended in patients with severe preeclampsia remote from term with intensive monitoring.

Keywords: Early onset severe pre-eclampsia, Expectant management, Fetal outcome, Maternal outcome

INTRODUCTION

Hypertensive disorders of pregnancy constitute one of the leading causes of maternal and perinatal mortality and morbidity worldwide. It is responsible for 14% of maternal mortality in the world including India (WHO 2015). Although progressive by nature, it is one of the disorders in pregnancy which can be controlled to some extent if detected early with more frequent monitoring.

Pre-eclampsia is a multisystem and multifactorial disorder involving the placenta, kidney, liver, blood, cardiovascular and neurovascular system, occurring exclusively during pregnancy. Pre-eclampsia is described as a new onset rise in blood pressure and proteinuria occurring after 20 weeks of gestation. It is described as severe pre-eclampsia if there is substantial increase of blood pressure (systolic BP>160 mm hg and/or diastolic BP>110 mm hg) and proteinuria or the occurrence of symptoms due to end organ damage.[1] Early onset severe pre-eclampsia is when elevation of blood pressure and proteinuria occur before 34 weeks of gestation.

In case of early onset severe pre-eclampsia, there is progressive worsening in the health condition of mother and also high mortality in the fetus during the perinatal

period. There is increased risk of abruptio placenta, acute renal failure, cardiovascular and cerebrovascular complications, disseminated intravascular coagulation and even maternal death.[2] Termination of pregnancy is considered the only way to prevent as well as revert most of these complications. But, prematurity due to early termination leads to high perinatal morbidity and mortality.

As seen in many studies, timely use of antenatal corticosteroids in a threatened preterm labour before 34 weeks of gestation has the following clinical impacts in newborns who receive good supportive care: 34% reduction in respiratory distress syndrome (RDS), 46% reduction in intra ventricular haemorrhage (IVH), 54% reduction in necrotising enterocolitis (NEC) and 31% reduction in mortality.[3] Also, it has been reported that use of antenatal corticosteroids leads to other benefits too like reduction in the incidence of PDA, reduction in systemic infections, respiratory support requirement and therefore, reduced length of hospital stay, low rate of neonatal intensive care admissions and finally reduced expenditure.

Similarly, use of magnesium sulphate in women with preterm severe pre-eclampsia serves dual purpose of maternal neuroprotection and prevention of eclampsia as well as fetal neurostability and decreases the incidence of cerebral palsy in preterm newborns.[4]

Due to advancement of medical care in India and intensive care facilities in tertiary health care centres some selected women diagnosed with preterm pre-eclampsia with severe features can be kept under strict monitoring and gestation can be prolonged to improve fetal maturity and perinatal outcome instead of the traditional norm of immediate termination of pregnancy.

Hence, the present study was carried out in order to compare the potential benefits and risks of interventional and expectant management in women with preterm severe pre-eclampsia of gestational age 28 to 34 weeks.

METHODS

This was a prospective analytical study conducted in the department of obstetrics and gynaecology, Medical College, Baroda for a period of one year from January 2021 to December 2021.

Sample size

It was a time bound study. We were expecting 4 patients per month as per inclusion and exclusion criteria. Hence for 10-month data collection period around 40 patients were included.

Inclusion criteria

Singleton live intrauterine pregnancy diagnosed with severe pre-eclampsia (pre-eclampsia with severe features) according to ACOG guidelines with no other significant comorbidity between gestational age >28 and <34 weeks and not in labour.

Exclusion criteria

Multiple gestation,u ncontrolled severe hypertension, eclampsia or HELLP syndrome, pulmonary edema, placental abruption, disseminated intravascular coagulation, non-reassuring fetal status, fetal demise or congenital anomaly, evidence of end organ damage (hepatic transaminase levels twice normal, thrombocytopenia <1 lac/microliter, creatinine >1.1 mg/dl, or cerebral symptoms like headache, visual disturbances, convulsions.), fetal growth restriction, oligohydramnios, reversed end diastolic flow in umbilical artery doppler.

All eligible women coming to the SSG hospital labour room were enrolled in the study taking inclusion and exclusion criteria in consideration. Participants were briefed about the nature of the study, details of the treatment and a written informed consent was obtained after being explained about the risks and benefits of the study. It was a non-blinded study.

After initial evaluation and stabilization, magnesium sulphate and corticosteroid was administered to all patients. Magnesium sulphate was given by intravenous Zuspan regime (4 gm loading followed by 1 gm/hour infusion). Immediate blood pressure control was achieved using intravenous labetalol. After achieving the target blood pressure oral anti-hypertensives (labetalol or nifedipine) were started. Corticosteroid was given as injection dexamethasone 6 mg: total 4 doses 12 hourly via intramuscular route.

In the interventional management, this was followed by termination of pregnancy. Patients who delivered between 24 to 48 hours of admission and steroid administration were included in the interventional management group.

In the expectant management, this was followed by intensive maternal and fetal monitoring and pregnancy was terminated only for a specific indication or at 34 weeks.

Maternal monitoring was done by 4-hourly vitals, urine albumin, input output chart, biweekly platelet count and liver function test.

Fetal monitoring was done by non-stress test, biweekly fetal doppler and weekly ultrasound scan for fetal growth. At any time during the concerned period of prolongation of pregnancy, if any contraindication to continue pregnancy appeared expectant management was terminated. Patients who delivered after 48 hours of admission were included in the expectant management group.

In both groups, the mode of delivery was dictated by the maternal and fetal condition, cervical assessment, with intensive intrapartum and postpartum care.

Maternal outcome was assessed by comparing incidence of complications like abruption, HELLP/DIC, eclampsia, renal impairment, pulmonary edema, cerebral edema and maternal death. Perinatal outcome was assessed using gestational age at delivery, birth weight, APGAR score, requirement of neonatal resuscitation, NICU admission, neonatal complications and perinatal mortality.

Statistical analysis

The categorical variables were presented in the form of number and percentage (%). The presentation of quantitative data was done as the mean ±SD and as median with 25th and 75th percentiles (interquartile range). The comparison of the quantitative variables which were not normally distributed in nature were analysed using Mann-Whitney test (for two groups) and for comparison of normally distributed data between two groups independent t test was used. The comparison of the qualitative variables was analysed using Chi-Square test. Fisher's exact test was used if any cell had an expected value of less than 5. P value of less than 0.05 was considered to be statistically significant.

RESULTS

A total of 40 women with preterm severe pre-eclampsia satisfying the inclusion and exclusion criteria were enrolled and randomised into two groups A and B comprised of 20 women each. In the interventional management group, after initial stabilization the women underwent termination of pregnancy. While in the expectant management group, after initial stabilization of the patient, if the maternal and fetal status was reassuring, prolongation of pregnancy was carried out under intensive feto-maternal monitoring.

Both groups were similar with respect to their age group. The mean age group was 25 years. Similarly the socio-economic status and areas of residence (rural versus urban) were similarly distributed in both groups.

Gestational age on admission

Table 1 includes gestational age at which the patient first fulfilled the inclusion criteria for severe preeclampsia. The mean gestational age was found to be 31 weeks with range from 29-33 weeks. Both groups were matched in terms of gestational age on admission.

Parity

Table 2 compares the parity in the 2 groups. There were larger number of primigravida patients (55%) as compared to multigravida patients (45%). However, the difference in both groups was not found to be statistically significant i.e. they were matched in terms of parity.

Brown et al said preeclampsia is predominant in nulliparous women.[5]

Table 1: Comparison of gestational age on admission (weeks) between expectant and interventional group.

Gestational age on admission (weeks)	Expectant group (n=20)	Interventional group (n=20)	Total	P value
28 weeks to 31 weeks+ 6 days	10 (50%)	10 (50%)	20 (50%)	1§
32 weeks to 33 weeks + 6 days	10 (50%)	10 (50%)	20 (50%)	
Mean±SD	31.6±1.34	31.69±1.37	31.65±1.34	0.83*

*Independent t test, § Chi square test

Table 2: Comparison of parity between expectant and interventional group.

Parity	Expectant group (n=20)	Interventional group (n=20)	Total	P value
Primi	13 (65%)	9 (45%)	22 (55%)	0.204§
Multi	7 (35%)	11 (55%)	18 (45%)	
Total	20 (100%)	20 (100%)	40 (100%)	

§Chi square test

Table 3: Comparison of mode of delivery between expectant and interventional group.

Mode of delivery	Expectant group (n=20)	Interventional group (n=20)	Total	P value
Cesarean section	8 (40%)	7 (35%)	15 (37.50%)	0.744§
Vaginal delivery	12 (60%)	13 (65%)	25 (62.50%)	
Total	20 (100%)	20 (100%)	40 (100%)	

§Chi square test

Mode of delivery

Delivery is the ultimate treatment for pre-eclampsia. Table 3 compares the mode of delivery in the two groups. There was no statistically significant difference found in the mode of delivery between the 2 groups.

In the interventional group, 43% of women underwent caesarean section for fetal distress and 43% of women underwent caesarean section for previous caesarean section. In the expectant management group, 25% women underwent caesarean section for Doppler changes (absent end diastolic flow), 25% of women underwent caesarean section for anhydramnios and 25% women underwent caesarean section due to previous caesarean section. Fetal distress and non-progression of labour were the other indications of caesarean delivery.

In the expectant group- maternal indications attributed to 70% of the reason for termination of pregnancy in the expectant group as compared to fetal indication 30%. Among the maternal indications the most common indication was completed 34 weeks (35%) followed by spontaneous preterm labour (28%) and HELLP/partial HELLP syndrome (14%). Among the fetal indications, the termination of pregnancy was carried out in view of worsening fetal Doppler (66%) followed by severe oligohydramnios (33%). In the study by Blackwell et al in 2002, termination was done for maternal indication in 80% and for fetal indication in 20% of the patients.[10]

Maternal complications

Ultimate goal in the management of severe preeclampsia must first be the safety of the mother and second the delivery of a live infant who will not require prolonged neonatal care.

Table 4 compares the incidence of various maternal complications in both groups. The incidence of HELLP/partial HELLP syndrome was higher in the expectant management group (20%) as compared to interventional group (10%). Similarly, the incidence of renal impairment was higher in the expectant group (10%) as compared to interventional group (5%). Whereas, incidence of abruption and eclampsia was found to be higher in the expectant management group. Though the difference in the maternal complications was not found to be statistically significant (p value: 0.487). There was no maternal death reported during the study.

Table 4: Comparison of maternal complications between expectant and interventional group.

Maternal complications	Expectant group (n=20)	Interventional group (n=20)	Total	P value
Abruption	0 (0%)	2 (10%)	2 (5%)	
HELLP/partial HELLP	4 (20%)	2 (10%)	6 (15%)	
Eclampsia	3 (15%)	4 (20%)	7 (17.50%)	0.487‡
Renal impairment	2 (10%)	1 (5%)	3 (7.50%)	
Maternal death	0 (0%)	0 (0%)	0 (0%)	

‡ Fisher's exact test

Table 5: Comparison of gestational age at delivery (weeks) between expectant and interventional group.

Gestational age at delivery (weeks)	Expectant group (n=20)	Interventional group (n=20)	Total	P value
28 weeks to 31 weeks+ 6 days	2 (10%)	10 (50%)	12 (30%)	
32 weeks to 33 weeks + 6 days	11 (55%)	10 (50%)	21 (52.50%)	0.001‡
34 weeks to 34 weeks + 6 days	7 (35%)	0 (0%)	7 (17.50%)	
Mean±SD	33.21±1.03	31.69±1.4	32.45±1.44	0.0004*
Range	30.71-34.29	29.86-33.86	29.86-34.29	

* Independent t test, ‡ Fisher's exact test

Gestational age at delivery

Table 5 compares the gestational age at delivery in both the groups. The mean gestational age at delivery was 33 weeks in expectant management group and 31 weeks in the interventional group. Thus, gestational age at delivery was higher in the expectant management group and was found to be statistically significant with p value of 0.001. The mean prolongation of gestation in the expectant management group was 11.45 days with range from 4-35 days. The maximum number of days gained in this study was 35 days.

Fetal outcome

Table 6 compares the fetal outcome in both the groups. The neonatal outcome depends on the intensive care facilities and the gestational age at birth. In our study all the women underwent live birth. The mean birth weight in the expectant management group was 1.7 kg while the mean birth weight in the interventional group was 1.5 kg (p value of 0.05).

Table 6: Comparison of fetal outcome between expectant and interventional group.

Fetal outcome	Expectant group (n=20)	Interventional group (n=20)	Total	P value
Birthweight (gm)				
1000 to <1500 gm	6 (30%)	9 (45%)	15 (37.50%)	0.313‡
1500 to <2000 gm	8 (40%)	9 (45%)	17 (42.50%)	
2000 to <2500gm	6 (30%)	2 (10%)	8 (20%)	
Mean±SD	1743.85±343.3	1540.9±292.63	1642.38±331.2	0.051*
APGAR score				
<7	1 (5%)	5 (25%)	6 (15%)	0.182‡
≥7	19 (95%)	15 (75%)	34 (85%)	
Mean±SD	7.55 ± 0.6	7 ± 0.97	7.28 ± 0.85	0.057†
NICU admission				
No	4 (20%)	1 (5%)	5 (12.50%)	0.342‡
Yes	16 (80%)	19 (95%)	35 (87.50%)	
Total	20 (100%)	20 (100%)	40 (100%)	

* Independent t test, ‡ Fisher's exact test

The mean APGAR score in the expectant group was 7.5 while the mean APGAR score in the interventional group was 7. This difference in the neonatal APGAR score at 1 minute was found to be statistically significant with p value of 0.05. There was no significant difference found in the APGAR score of the neonates at 5 minutes of life. Most of the neonates were born pre-term, hence about 80% neonates in the expectant group and 95% neonates in interventional group required neonatal intensive care unit (NICU) admission. There was 1 case (5%) of early neonatal death in the expectant management group while there were 2 neonatal deaths (10%) reported in the interventional management group.

The most common neonatal complication was respiratory distress (47%). Other common neonatal complications were neonatal seizures (10%), necrotizing enterocolitis (7.5%) and early neonatal sepsis (7.5%). The incidence of respiratory distress was 60% in the interventional group and 35% in the expectant management group. Total 11 neonates (55%) suffered from neonatal complications in the expectant management group while around 19 (95%) neonates suffered from one or another neonatal complication in the interventional group. The difference in the incidence of neonatal complications was statistically significant with p value 0.003.

DISCUSSION

Pre-eclampsia is a complex disease with various associated theories. Eclamptic convulsions have been recognized in ancient Indian, Chinese and Greek literature dating back 4000 years.

For severe pre-eclampsia in women with gestational age between 28 to 34 weeks expectant management can be offered in a tertiary care center with ICU backup and round the clock emergency services. As observed in our study the mean prolongation of gestation was 11 days which is comparable to other studies as seen in Table 7.

Table 7: mean prolongation of gestation in the expectant management group.

Study	Prolongation of gestation (mean)
Odendall et al (1990)[11]	7.1 days
Olah KS (1993)[12]	9.5 days
Vissur W, Wallberg (1995)[13]	14 days
Murphy DJ(2000)[14]	14 days
Raida al-Wazzan (2008)[15]	9.2 days
Anitha et al (2011)[7]	7.5 days
Our study	11.45 days

Table 8: maternal complications in the expectant management group.

Study	Complications
Railton et al (1987)[16]	23.2% had increase in major complications
Odendaal et al (1990)[11]	No increase in complication
Sibai et al (1994)[8]	No increase in complication
Hall et al (2000)[6]	No maternal death, 3 needed ICU.1 needed dialysis
Haddad et al (2004)[17]	No maternal death or eclampsia. Morbidity similar in both groups
Anitha et al (2011)[7]	11.0% in aggressive 18.0% in expectant group. Statistically insignificant
Our study	Statistically insignificant difference in maternal outcome

Similarly in terms of maternal complications there was no significant increase in maternal complications in the expectant management group as compared to immediate delivery (interventional) group as seen in Table 8.

Witlin et al reported that neonatal outcome in early onset severe pre-eclampsia directly correlated with increasing birth weight and respiratory distress syndrome reduced with increasing gestational age.[9]

In the study by Al-Wazzan et al the APGAR score at 1 minute was 3.56±1.72 in the aggressively managed group while it was 5.05±1.77 in the expectantly managed group (p value <0.001).[15] In their study, respiratory distress developed in 59% of aggressively managed group while it was only 23% in the expectantly managed group. The difference was statistically significant with p- 0.003. Similarly, our study had lower incidence of neonatal complications in the expectant group as compared to the interventional group (55% versus 95%) (p-0.003).

CONCLUSION

Severe pre-eclampsia is associated with significant maternal and fetal complications. Decision regarding pregnancy termination is to be taken on the grounds of both maternal and fetal factors. In case of severe uncontrolled blood pressure with complications, termination should be done irrespective of fetal maturity. In selected cases the expectant management of severe pre-eclampsia results in a good fetal outcome in terms of :1) Higher birth weight (1.7 kg versus 1.5 kg) (p value of 0.05), 2) better fetal maturity in terms of higher gestational age at delivery (33 versus 31 weeks) (p value of 0.001) and completed corticosteroid coverage, 3) lesser neonatal complications (55% versus 95%) (p value 0.003); lesser NICU admissions and higher APGAR score. But this must be weighed against the risk of maternal morbidity. In our study there was no significant increase in maternal morbidity in the expectant management group. Hence the expectant management should be carried out only in tertiary care centres where the experienced obstetrician and multidisciplinary care in terms of physician, anaesthetist, radiologist and neonatologist are available. Intensive care facilities for the mother and technologically advanced NICU facilities are necessary for management of severe pre-eclampsia remote from term.

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