EXPECTANT MANAGEMENT OF EARLY ONSET SEVERE PRE ECLAMPSIA: FETOMATERNAL OUTCOME: A STUDY IN A TERTIARY INSTITUTION IN NORTH KERALA

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ABSTRACT: BACKGROUND: Preeclampsia is a major cause of maternal and perinatal mortality and morbidity worldwide and it is responsible for 14% of maternal deaths per year. The clinical course of preeclampsia is associated with progressive deterioration of foetal and maternal conditions and hence delivery is the only way of curing the disease. But delivery at an early gestation is associated with high perinatal mortality and morbidity from prematurity. Several randomized controlled studies have shown that expectant management of women with severe preeclampsia improves neonatal outcome of the babies without compromising the maternal health much. Ours is a tertiary institution where antenatal patients with preeclampsia is referred from five northern districts of Kerala. Hence an attempt is made to study the fetomaternal outcome of severe preeclampsia between 24 to 34 weeks when they are kept for expectant management. AIM: To evaluate the feto maternal outcome of expectant management of early onset severe pre eclampsia between 24 and 34 weeks. SETTINGS AND DESIGN: Prospective observational study for one year from January 1st 2014to December 31st 2014, with permission from Ethics committee. METHODS AND MATERIALS: The study was conducted at a tertiary referral centre, The Institute of Maternal and Child Health, Government Medical College, Kozhikode. All women with singleton pregnancy presented with early onset preeclampsia (Between 24 and 34 weeks) where mother and fetus were otherwise stable were included in the study. Fetomaternal outcome was analyzed using appropriate statistical methods. **RESULTS:** A total of 209 patients with severe preeclampsia with gestational age between 24 and 34 weeks of gestation who were fit for expectant management were studied prospectively. Mean number of days the pregnancy was prolonged was 12 days. There was no maternal mortality. Overall perinatal survival was 45.5% and perinatal mortality rate was 52.1%. CONCLUSIONS: Perinatal mortality in severe preeclampsia is high. Expectant management in selected patients remote from term improves perinatal outcome without compromising maternal health much.

KEYWORDS: Severe preeclampsia, expectant management, perinatal outcome.

INTRODUCTION: Preeclampsia is a pregnancy specific syndrome characterized by new onset hypertension and proteinuria occurring usually after 20 weeks of gestation. Although aetiology remains unknown placental hypo perfusion and diffuse endothelial cell injury are considered to be central pathologic events. Pre eclampsia is classified into mild and severe types and in severe forms it may lead to liver and renal failure, DIC and seizures and growth retardation of the foetus. It is associated with high maternal and neonatal morbidity and mortality. Worldwide it is responsible for 14% of deaths per year (50000-75000).¹

The optimal management of a woman with preeclampsia depends upon the gestational age and severity of the disease. Since delivery is the only cure for preeclampsia, clinicians must try to

minimize the maternal risk while maximizing foetal maturity. The primary objective is the safety of the mother and then the delivery of a healthy new-born.

Many authors have emphasized the lack of uniformity in the management approaches to severe pre eclampsia.^{2,3,4} The clinical course of preeclampsia is associated with progressive deterioration of maternal and foetal conditions. Since delivery is the only way of arresting the disease, there is broad agreement on delivery in the presence of multi organ dysfunction, foetal distress or once a gestational age of 34 weeks have been reached. However hypertensive disease is an important cause for delivery of very low birth weight babies,⁵ and delivery at an early gestation is associated with high perinatal mortality and morbidity resulting from prematurity.^{6,7,8} In addition, recent research work suggests that fetal lung maturity,⁹ as well as foetal neurologic and physical development are not accelerated in pregnancies complicated by preeclampsia.

In 1989, Dehran et al,¹⁰ demonstrated that the most important factor for survival of a healthy baby was gestational age, which strongly correlated to birth weight. In a case control study Olah' etal¹¹ showed fewer neonatal complications when women with early onset severe preeclampsia were managed expectantly. Two randomized controlled trials have also shown that expectant management of women with severe preeclampsia improves neonatal outcome of their babies.^{12,13}

Expectant management of severe preeclampsia before 25 weeks is associated with high maternal mortality and ranging from $31-67\%^{14}$ and perinatal survival only 0-20%. Hence expectant management is not offered to patients with severe preeclampsia below 24 weeks. Patients with severe preeclampsia between 24 and 33 weeks should be given a course of steroids to accelerate lung maturity.

Visser et al,¹⁵ and Sibai et al,¹⁶ has cautioned that the number of reported women whose early onset severe preeclampsia were managed expectantly is limited. This study is planned to investigate the feto maternal outcome of the expectant management approach in women with gestational age between 24 and 34 weeks. The ultimate goal remains the safety of the mother and the delivery of a live infant who will not have prolonged and intensive neonatal care.

MATERIALS AND METHODS: All pregnant women with singleton pregnancies presenting with early onset severe pre eclampsia (\geq 24 &<34 weeks) when foetuses and mother were otherwise stable were studied. The definition of hypertension and proteinuria used were those put forward by Davy and Mac Gillvary and accepted by ISSHP. Severe hypertension was accepted as diastolic BP of \geq 120mm of Hg on one occasion or \geq 120 mmHg on two occasions 4 hours apart. Proteinuria on admission was tested with dipstick test and later on 24 hour urine protein was checked. All these women were admitted to high risk obstetric care unit attached to our labour room for intensive monitoring of the mother and the foetus. After admission a detailed evaluation of the mother and the foetus is done. Maternal monitoring included 4th hourly BP monitoring, clinical examination for fundal height, FHR monitoring, CTG, and ultrasound evaluation of the foetus and daily albumin and sugar.

Anti hypertensives are given for these patients to keep the systolic BP 140 and 155 and diastolic BP between 90 and 105 mm of Hg and for those with impending symptoms, Magnesium sulphate regime was given. After 24 hours observation after the BP has come down and impending symptoms have disappeared, decision is taken for expectant management. Failure to control BP or major maternal or foetal complications were indications for delivery. Women with>34 weeks gestational age, eclampsia and hellp syndrome were terminated and foetal complications like IUD, nonreactive CTG, foetal distress, abnormal doppler were indications for delivery. All women who

were stable and fit for expectant management were transferred to a high risk obstetric ward near labour room for close monitoring.

The aim was to prolong the gestational age so that foetal viability is reached without compromising the maternal health. Maternal monitoring included 4th hourly BP monitoring and daily fundal height, foetal heart rate, CTG, Daily urine albumin and sugar. A full blood count, RFT, LFT, blood sugar, LDH and 24 hour urine protein are done and repeated twice weekly. Foetus is monitored by DFMC, FHR recording, daily CTG, two weekly Ultrasound for BPP and weekly doppler. Injection Beta methasone is given from 28th week of gestation. Failure to control the blood pressure or the development of major maternal or foetal complications were indications for delivery. Women reaching 34 weeks were delivered electively.

Analysis of data included major maternal complications abruptio placenta, HELLP syndrome, renal failure, eclampsia and uncontrolled BP and recurrence of impending symptoms and maternal mortality. Major foetal complications included were IUD, FSB and neonatal complications included were death, hyaline membrane disease, septicaemia, pneumonia, convulsions, HIE, pulmonary haemorrhage and intraventricular haemorrhage.

These complications were identified retrospectively from detailed case notes after death or discharge.

RESULTS: A total of 209 patients with severe preeclampsia with gestational age between 24 and 34 weeks of gestation were studied prospectively after which they were found to be fit for expectant management. During the study period there were 15, 604 deliveries in this hospital. There were 1673(10.7%) cases of hypertension during the study period. There were 250(1.6%) cases of severe pre eclampsia with singleton pregnancies with gestational age <34 weeks. All of them were admitted, stabilized and evaluated in eclampsia room attached to our labour room for 24 hours. 209(83.6%) of them were stable enough to receive the expectant management. Remaining patients were terminated due to eclampsia, HELLP syndrome, IUD, foetal distress and renal failure.

Mean age of the patients with severe preeclampsia was 26.16 years with a range of 17-42 years. 41.6% of them were primigravidas, 45.9% multi gravidas and 12.45% were grandmulti (Table 1). 51.65% of them presented at a gestational age between 28-32 weeks, 46.55% between 33-34 weeks and only 1.9% of them were between 24-27 weeks (Table 2). Mean number of days the pregnancy was prolonged was 12 days with a range of 2- 20 days. 77.7% of them had prolongation of pregnancy for <7 days, 13.35% had prolongation between 7 and 14 days, 6.6% between 14-21 days and only 2.35% more than 21 days (Table 4).

There were no maternal deaths in the study group. Maternal complications while on expectant management included, HELLP syndrome (6.6%), abruptioplacenta (2.3%), eclampsia (1.6%) and acute kidney injury (0.95%) (Table11). Most common reason for termination of pregnancy was Intrauterinefetal demise (18.3%) followed by gestational age of 34 weeks (16.04%) (Table5). 97.1% of them had cephalic presentation 2.87% presented with breech. 89.4% of them had labour induction, 6.69% had elective Caesarean section and 1.95% had spontaneous onset of labour while on expectant management (Table 3).

Majority had induction with PGE2 (50.8%). 55.02% of the babies were having birth weight between 1 & 1.5 kg. and 23.45% had birth weight <1 kg and 21.5% had weight between 1.6 & 2 kg.

There were no babies with >2 kg (Table 6). Out of the 145 live born babies, 55.1% had low APGAR at 1' after birth and 44.8% had normal APGAR (Table 7). During the expectant management

period 30.6% had gone for IUD and only 69.5% were alive at birth of which 34.4% had ended in NND (Table 8). Out of the total live born, 34.4% ended in NND (Table 9). Major causes for NND includes HMD (30%), sepsis (20%), and seizures 10% (Table 10). Over all perinatal survival was 45.5%. Perinatal mortality rate in this study was 52.1%. All the cases delivered before 28 weeks had ended in IUD. Between 28- 32 weeks perinatal survival was 62.03% and perinatal mortality rate was 59.7%. Between 33 and 34 weeks perinatal survival was 80.4% and perinatal mortality was 12.8%. (Table 12).

DISCUSSION: Severe pre eclampsia between 24 and 34 weeks is a rare complication of pregnancy. Hence many of the doctors have limited experience. There were 1673(10.7%) cases of hypertension during the study period. There were 250(1.6%) cases of severe pre eclampsia with singleton pregnancies with gestational age between 24 -34 weeks. Our incidence is very high when compared to the western. (3% of pregnancies),⁽¹⁷⁾ 209(83.6%) of them were stable enough to receive the expectant management. Remaining patients were terminated due to eclampsia, HELLP syndrome, IUD, foetal distress and renal failure.

Mean age of the patients with severe preeclampsia was 26.16 years with a range of 17- 42 years. 41.6% of them were primigravidas. Al-Mulhim et al estimated that 42% of the women in their study were nullipara which is similar to our finding, (18) Mean number of days the pregnancy was prolonged was 12days with a minimum of 2 days and a maximum of 20 days. 15 non randomized non controlled trials in English and 4 in Latin American literature highlight 10-14 days pregnancy prolongation without increased maternal morbidity with conservative management. (19) There were no maternal deaths in the study group.

This is similar to a study in Lady Hardinge medical college, New Delhi, India. (20) Since 1990 there was one maternal death reported among 1790 women who underwent treatment for severe preeclampsia at >24 weeks gestation, (21) In contrast maternal morbidity such as HELLP syndrome (4-25%), placental abruption (1-9%) and pulmonary oedema (1-9%) remain high. (20) Maternal complications while on expectant management in our study were, HELLP syndrome (6.6%), abruptio placenta (2.3%), eclampsia (1.6%) and acute kidney injury (0.95%). Most common reason for termination of pregnancy was intra uterine fetal demise (18.3%) followed by gestational age of 34 weeks (16.04%). During the expectant management period 30.6% had gone for IUD and only 69.5% were alive at birth of which 34.4 % had ended in NND.

This also similar to the study by Manish Kumar.⁽¹⁸⁾ Out of the total live born, 34.4% ended in NND. Over all perinatal survival was 45.5%. Perinatal mortality rate in this study was 52.1%. All the cases delivered before 28 weeks had ended in IUD. Between 28- 32 weeks perinatal survival was 62.035 and perinatal mortality rate was 59.7%. Between 33 and 34 weeks perinatal survival was 80.4% and perinatal mortality was 12.8%. This study has shown improvement in perinatal survival when the pregnancy is >28 weeks gestation. Expectant management in selected patients remote from term may be appropriate with a view to get a foetus to a more favourable gestational age before delivery and thereby can improve perinatal outcome. But it should be undertaken only in a tertiary institution with the capacity to handle potential complications and to effect immediate delivery if indicated.

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Age	No.	Percentage		
<20	2	0.95		
20-34	92	91.8		
≥35	15	7.17		
Gravidity	No	Percentage		
PRIMI	87	41.62		
G2-G3	96	45.9		
G4	26	12.44		
Table 1				

Gestational age	No.	Percentage		
24-27 weeks	4	1.91%		
28-32 weeks	108	51.6%		
33- 34 weeks	97	46.45		
Table 2				

Route of delivery	No.	Percentage		
Vaginal	183	87.5%		
LSCS	17	8.1%		
VBAC	5	2.3%		
Hysterotomy	4	1.9%		
Table 3				

Admission to delivery interval	Alive	IUD	NND
<7days	70	50	42
7-13	13	12	3
14-20	10	1	3
≥21	2	1	2

Table 4

Reasons for induction		Percentage
IUD	35	18.7%
Uncontrolled hypertension	2	1.06
HELLP syndrome	26	13.9
abruption	8	4.27
Abnormal RFT	2	1.06
Eclampsia		1.6
Persistant impending symptoms		9.09
Thrombocytopenia		0.53
33weeks+ steroids		10.6
34weeks		16.04
Severe IUGR		9.6
Abnormal doppler		13.36
PPROM	3	1.60

Table 5

Birth weight	No.	Percentage
<1 kg	49	23.44%
1-1.5	115	55.02%
1.6-2	45	21.53
>2kg	0	0

Table 6

1' APGAR	No.	%
0	64	
Low	80	55.1
Normal	65	44.8

Table 7

Condition of the baby at delivery	No.	%
IUD	64 (FSB-25& MSB 39)	30.6
LIVE	145	69.3
Neonatal outcome	No	%
Live	95	65.5
NND	50	34.4

Table 8

Neonatal outcome	No	%
Live	95	65.5
NND	50	34.4
NND	No	%
<7days	45	90
>7days	5	10
Table 9		

Causes of NND	No.	%
sepsis	10	20
Intra cerebral haemorrhage	3	6
HMD	15	30
Pneumonia	2	4
Seizures	5	10
HIE	3	6
Pulmonary haemorrhage	1	1
VLBW	4	8
Birth asphyxia	1	1
Necrotizing enterocolitis	1	1
Severe anaemia	2	4
Extreme prematurity	3	6
Table 10		

Maternal complications	No.	%
Hellp	14	6.6
Abruptio placenta	5	2.39
eclampsia	3	1.43
Acute kidney injury	2	0.9

Table 11

Gestational age	Outcome	<7 days	7-13 days	14-21	>21	Total
24-27 weeks (n=3)	Live	0	0			0
	FSB	2	1			3 (100%)
	MSB	0	0			0
	NND	0	0			0
28-32 (n=114)	Live	7	9	7	4	27 (23.6%)
	FSB	20	5	0	1	27 (23.6%)
	MSB	12	6	2	0	20 (17.5%)
	NND	28	9	1	2	40 (35.08%)
33-34 (n= 92)	Live	55	12	1		68 (73.9%)
	FSB	5	0			5 (5.4%)
	MSB	5	4			9 (9.7%)
	NND	8	1	1		10 (13%)
Table 12						

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