Expectant versus aggressive management in severe preeclampsia remote from term

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ABSTRACT

Introduction: Our study aims to compare neonatal and maternal outcomes between expectant (or conservative) and aggressive (or immediate) management in cases with severe preeclampsia remote from term.

Methods: This is a comparative study conducted at Al-Batool Teaching Hospital in Mosul City, Iraq, from April 2003 to August 2004. A total of 74 singleton pregnancies complicated by severe pre-eclampsia with gestational age of 24–34 weeks were studied during this period. The criteria used for the diagnosis of severe preeclampsia were in accordance with the guidelines of the American College of Obstetricians and Gynaecologists. All the patients were counselled for expectant management. 39 patients were delivered immediately due to refusal of expectant management either by the patient or the attending physician. The other 35 patients were managed expectantly; this group was followed-up and carefully monitored for a period ranging from 72 hours to 18 days. Neonatal parameters, neonatal outcome and maternal outcome were compared between the two groups.

Results: The mean value of pregnancy prolongation was 9.2 days. Median gestational age for the first group was 29 weeks, and for the second group, it was 30 weeks. Regarding neonatal parameters, the expectantly-managed group had a higher Apgar score at one minute (3.56 +/- 1.72 vs. 5.05 +/- 1.77, p-value equals 0.001), lower mean days of hospitalisation in the neonatal intensive care unit (6.83 +/- 5.38 vs. 4.50 +/- 3.46, p-value equals 0.03), with a lower incidence of neonatal and maternal complications.

Conclusion: Expectant management is recommended in patients with severe pre-eclampsia remote from term, after proper selection of patients and careful monitoring.

Keywords: expectant management of pregnancy, maternal complications, neonatal complications, pregnancy complications, severe preeclampsia

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INTRODUCTION

Preeclampsia is an idiopathic, unpredictable, multiorgan disorder unique to human pregnancy and the puerperium.[1] It is the second most common cause of maternal mortality in the United States (after thromboembolic diseases), accounting for 12%–18% of all pregnancy-related maternal deaths.[2-5] It is also associated with high perinatal mortality and morbidity, due primarily to iatrogenic prematurity.[6] Preeclampsia complicates 6%–8% of all pregnancies,[1] with 5%–10% being severe.[7] In a study done at Al-Batool Teaching Hospital, Mosul, Iraq in the year 2003, 1.9% of pregnancies were complicated by severe preeclampsia.[8] Although the pathogenesis of pre-eclampsia is poorly understood, it is clear that the blueprint for its development is laid down early in pregnancy.[9]

The signs and symptoms of pregnancy-induced hypertension (PIH) become apparent relatively late in the course of the disease, usually during the third trimester of pregnancy. The healthcare provider must be aware of subtle changes that may be indicative of impending disease. It is important to emphasise that preeclampsia is a multisystem disorder, but the organ system predominantly affected cannot be predicted. There is disagreement on the mode of treatment of patients with severe preeclampsia before 34 weeks' gestation, after which maternal condition is stable and the foetal condition is reassuring. In such patients, some authors consider delivery as the definitive treatment regardless of gestational age, whereas others recommend prolonging pregnancy until development of maternal or foetal indications for delivery, or until achievement of foetal lung maturity, or 34 weeks gestation.[10]

Although delivery is always appropriate for the mother, it may not be optimal for the premature foetus. In the past, it was believed that infants born prematurely to severely preeclamptic women had lower rates of neonatal mortality and morbidity than infants of similar gestational age born to non-preeclamptic women. In contrast, several recent case-control studies have demonstrated that

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premature infants born after severe preeclampsia have neonatal complications and mortality similar to those of other premature infants of similar gestational age and have higher rates of admission to neonatal intensive care units.[10] In addition, case-control studies have revealed that foetuses of preeclamptic women do not exhibit accelerated lung or neurological maturation.[10] Most maternal deaths occur postpartum. The main cause of maternal mortality in severe preeclampsia is now pulmonary oedema.[11] A rushed delivery in an unstable patient probably adds to her risk rather than reduces it. On the other hand, a delay in a sick patient may be dangerous.[12] However, the mother's condition must be stable so that prolongation of pregnancy does not jeopardise her life. The situation should be constantly reassessed and the management plan regularly reviewed by a senior doctor.

METHODS

This study was done at Al-Batool Teaching Hospital, a tertiary centre in Mosul, Iraq, in the period between April 2003 and August 2004. 74 eligible singleton pregnancies at 24 and 34 weeks, complicated with severe preeclampsia, qualified for this comparative study. All the patients had been admitted to the hospital and were fully assessed based on their history, physical and obstetrical examinations. Laboratory studies included complete blood count with platelet count, determination of haematocrit, serum concentration of electrolytes, urea nitrogen, creatinine, uric acid, transaminases, lactate dehydrogenase, albumin and clotting profile. Urine was also analysed for protein urea on admission, and 24-hour urine collection was performed to determine total protein. Central nervous system evaluation was performed as indicated, by means of computed tomography or magnetic resonance imaging. Indications included focal neurological signs, recurrent seizures after delivery, coma and unusual behavioural changes. The criteria used for the diagnosis of severe preeclampsia were in accordance with the guidelines of the American College of Obstetricians and Gynaecologists.[1]

Failure to control blood pressure, defined by a diastolic blood pressure ≥ 110 mmHg despite combined intravenous antihypertensive treatment on maximal dose, or the development of major maternal complications (cerebral or hepatic haematoma, severe oedema/ascites) at any gestation at age were indications for delivery by the attending obstetrician. A non-reassuring cardiotocography (CTG) was the foetal indication for delivery. All the patients were counselled for expectant management. 39 patients were delivered immediately because of refusal of expectant management either by the patient or the attending physician. The other 35 patients were managed expectantly; this group was followed-up and carefully monitored for a period ranging from 72 hours to 18 days. Expectant (or conservative) management consisted of monitoring the patients by checking blood pressure, pulse rate, respiratory rate, abdominal examination, foetal heart, CTG and protein urea daily. Intravenous fluids and urinary output were monitored daily and a full blood count was performed at least twice weekly, renal function, liver function and ultrasonography (US) twice-weekly.

Bed rest and correction of the maternal circulation by means of pharmacological vasodilatation (dihydralazine and/or oral medication: methyldopa, nifidipine or a combination). Magnesium sulphate prophylaxis was not considered unless the women developed imminent eclampsia. Betamethazone (12 mg) was given, and repeated after 24 hours. The foetus was then monitored daily by CTG, and US evaluation of growth and amniotic fluid index every second week. Pregnancy was continued until a maternal or foetal indication for delivery arose. Indications for termination of pregnancy in both groups were: severe uncontrolled hypertension, haemolysis with thrombocytopenia and elevated ALT, progressive symptoms (headache, visual disturbance and epigastric pain), pulmonary oedema, and renal compromise with oliguria, eclampsia and foetal distress. The situation was constantly reassessed and the management plan regularly reviewed by a senior doctor. The mode of delivery was chosen according to the maternal condition, gestational age and the condition of the cervix. A senior anaesthetist was involved in our management in case we needed anaesthesia. A member of the neonatology staff evaluated live-born infants at birth. The decision to resuscitate or to render hospice care was based on birth weight and gestational age at delivery.

The main outcome of the study was pregnancy prolongation, defined as full days gained since the admission, and perinatal mortality and morbidity, Apgar score (A/S) at one minute, days hospitalised in neonatal intensive care unit (NICU), foetal outcome and life-threatening maternal morbidity. Major perinatal complications included: foetal and neonatal death, respiratory distress syndrome (RDS), intraventricular haemorrhage and sepsis. RDS was defined by the presence of characteristic radiographical findings and an oxygen requirement at 24 hours. Gestational age was calculated from the last menstrual period and confirmed at the first trimester ultrasonography. Intrauterine growth restriction (IUGR) was defined as birth weight less than the fifth percentile.[13] Major maternal complications included: maternal death, eclampsia, HELLP syndrome, abruptio

placentae, disseminated intravascular coagulopathy (DIC), pulmonary oedema and acute renal failure. Eclampsia was defined as the occurrence of generalised convulsions associated with signs of preeclampsia during pregnancy, labour, or within seven days of delivery and not caused by epilepsy or other convulsive disorders.[14] HELLP syndrome was defined by the presence of all three of the following criteria: haemolysis (characteristic peripheral blood smear and serum lactate dehydrogenase ≥ 600 U/L or serum total bilirubin ≥ 1.2 mg/dL), elevated liver enzymes (serum aspartate aminotransferase ≥ 70 u/L), and low platelet count (< 100,000 cells/uL).[15]

DIC was defined as the presence of three or more of the following criteria: low platelet (< 100,000 cells/uL), low fibrinogen (< 300 mg/dL), positive D-dimers (≥ 50 mg/dL), or prolonged prothrombin (≥ 14 seconds) and partial thromboplastin (≥ 40 seconds) times. Pulmonary oedema was diagnosed on the basis of clinical findings and chest radiograph. Acute renal failure was diagnosed in the presence of oliguria in association with elevated serum creatinine > 120 umol/L. The need for dialysis was considered as severe acute renal failure. Data was analysed using Minitab software version 13.20. (Minitab Inc, State College, PA, USA). Statistical analysis was performed via Student's *t*-test and chi-square tests. A probability value of 0.05 was considered statistically significant.

Table I. Mode of delivery in the aggressively-managed and expectantly-managed groups.

Mode of delivery	No. vaginal delivery (%)	No. caesarean section (%)
Aggressively-managed group	12 (30.76)	27 (69.23)
Expectantly-managed group	12 (34.29)	23 (65.71)

Table II. Neonatal parameters of aggressively-managed and expectantly-managed groups.

Neonatal parameters	Aggressively-managed group (n = 39)	Expectantly-managed group (n = 35)	p-value
Foetal birth weight (g)	1.3 ± 0.357	1.416 ± 0.359	0.172
A/S at one minute	3.56 ± 1.72	5.05 ± 1.77	0.001
NICU (days)	6.83 ± 5.38	4.50 ± 3.46	0.03

Data is expressed as mean and standard deviation

Table III. Neonatal outcomes in the aggressively-managed and expectantly-managed groups.

Neonatal outcome	No. aggressively-managed group (%) (n = 39)	No. expectantly-managed group (%) (n = 35)	p-value
IUGR	6 (15.38)	11 (31.42)	NS
RDS	23 (58.97)	8 (22.86)	0.003
Intraventricular haemorrhage	1 (2.56)	0	NS
Abnormal foetus	1 (2.56)	1 (2.86)	NS
Sepsis	5 (12.82)	2 (5.71)	NS
Mortality	10 (25.64)	4 (11.43)	NS

NS: not significant

RESULTS

74 singleton pregnancies complicated with severe pre-eclampsia and with gestational age between 24 and 34 weeks were included in this study. 39 of the cases were delivered immediately, while expectant management was decided for the remaining 35 patients. Median gestational age was 29 weeks for the first group, and 30 weeks for the second group. Pregnancy of patients in the first group was terminated immediately within hours. The indications of termination of pregnancy in this group were: imminent eclampsia (n = 10), HELLP syndrome (n = 5), eclampsia (n = 15), renal cause (n = 2), antepartum haemorrhage (n = 4), and foetal cause (n = 3). The mode of delivery was by caesarean section or vaginal delivery for obstetrical causes and foetal indications. 27 (69.23%) women delivered by caesarean section and 12 (30.76%) women delivered vaginally.

The second group was fully assessed, after which we chose to manage them expectantly. They were followed-up and carefully monitored, and had an average prolongation of gestational age between 3 and 18 (mean 9.2) days. The indications for termination in the second group were uncontrolled hypertension (n = 6), headache and blurred vision (n = 7), eclampsia (n = 2), HELLP syndrome (n = 4), renal causes (n = 3), vaginal bleeding (n = 2), and foetal cause (n = 7). Three patients reached 34 weeks, and one case with intrauterine death ended with vaginal delivery. 23 (65.71%) patients delivered by caesarean section, and 12 (34.28%) patients delivered vaginally after expectant management (Table I).

The results were compared between the two groups with regard to perinatal mortality, morbidity and maternal morbidity. Neonatal parameters included here are foetal birth weight, A/S at one minute and neonatal stay in the NICU. The comparison between these parameters is seen in Table II.

The neonatal outcome in both groups is shown in Table III. There is significant difference between the two groups, with regard to RDS. In the aggressively-managed group, ten (25.64%) neonates died—eight (20.5%) due to RDS, one (2.56%) was an abnormal baby and one (2.56%) due to intracranial haemorrhage. The survival rate was 74.36%. In the expectantly-managed group, four (11.43%) neonates died; of the four mortalities, there was one intrauterine death two days after admission of the mother with severe preeclampsia at 27 weeks gestation, one abnormal (2.86%) baby and two died due to respiratory distress syndrome. The survival rate was 88.57%.

Regarding maternal outcome, there was no maternal

Table IV. Maternal morbidities in both groups.

Maternal morbidities	No. aggressively-managed group (%) (n = 39)	No. expectantly-managed group (%) (n = 35)	p-value
Pulmonary oedema	3 (7.69)	1 (2.86)	NS
Renal failure	1 (2.56)	1 (2.86)	NS
Neurological problems	1 (2.56)	0	NS
Cardiac problems	2 (5.13)	0	NS
Repeated convulsions	7 (17.95)	1 (2.86)	0.033*
Liver problems	4 (10.26)	1 (2.86)	NS
Hypertensive crisis	3 (7.69)	1 (2.86)	NS
DIC	2 (5.13)	0	NS
PPH	6 (15.38)	2 (5.71)	NS

* p-value is significant; NS: not significant

mortality in both groups. In the aggressively-managed group: after delivery, three (7.69%) patients developed pulmonary oedema, one (2.56%) patient had renal failure, two (5.13%) developed cardiac problems, one (2.56%) had brain infarction, seven (17.95%) continued to have repeated fits after delivery, four (10.26%) had liver problems, three (7.65%) developed hypertensive crisis, two (5.13%) had DIC and six (15.38%) cases developed postpartum haemorrhage (PPH).

In the group with expectant management: a primigravid woman who was in her 27th week was discovered to have intrauterine foetal death two days after admission, and ended with spontaneous vaginal delivery of a severely IUGR foetus. Two (5.71%) patients developed vaginal bleeding and their pregnancies had to be terminated. Other complications that occurred after delivery included one (2.86%) patient who developed pulmonary edema, one (2.86%) had deterioration in the liver function, one (2.86%) had renal failure, one (2.86%) continued to have repeated convulsions, one (2.86%) had hypertensive crisis and two (5.71%) cases developed PPH. These results are shown in Table IV.

DISCUSSION

Once severe preeclampsia is diagnosed, the obstetrical propensity is for prompt delivery. The timing of delivery affects the outcome of both mother and baby. A woman who is stable may not remain so. The plan of management is more among the lines of "not needing delivery now" rather than "let's deliver her tomorrow". However, most maternal deaths occur postpartum.[12] Treatment of this disorder remains a challenge to even the most experienced obstetricians. Most clinical centres have limited experience in managing such patients. As a result, all recommended protocols have been based on retrospective observation and empirical clinical experience. The goal of any recommended protocol of management must always be safety of the mother first, and then delivery of a live mature newborn in optimal conditions.

In recent years, a different approach in the treatment of women with severe preeclampsia remote from term has been advocated by several investigators worldwide.[16] Aggressive management with delivery may result in a high neonatal mortality, while expectant management may be associated with an increase in maternal complications. It is clearly evident from the literature that expectant management of patients in highly specialised units, with the necessary maternal and foetal surveillance facilities, can result in improvement of foetal survival without an increase in maternal complications.[17] The decision between delivery and expectant management depends on foetal gestational age, foetal status, and severity of maternal condition at time of evaluation. Neonatal morbidity is closely dependent on gestational age at delivery,[18] and on the use of corticosteroid treatment to enhance foetal lung maturity.[19]

In our department, we were accustomed to terminate pregnancy with severe preeclampsia within hours from the diagnosis regardless of the gestational age, but we were left with complications, especially in the postpartum period. 74 singleton pregnant women were included in this study. All the patients were admitted and carefully evaluated and monitored. 39 cases had their pregnancy terminated within hours, and 35 were scheduled for expectant management with an average prolongation of gestational age between three and 18 (mean 9.2) days. Two randomised trials by Odendaal et al[20] and Sibai et al[21] showed a satisfactory significant prolongation of gestational age of a mean of 7.1 days and two weeks, respectively, in expectant management, when compared to aggressive management. Walker reported that in the absence of convulsion, prolongation of pregnancy is possible in most cases, with an average of 15 days.[22] Other studies showed that average pregnancy prolongation in women managed expectantly appears to be 10–14 days.[7]

The results were compared between the two groups, in terms of neonatal parameters, outcome and maternal outcome. As shown in the Tables II and III, there was no significant difference between the birth weight of the neonates in both groups, but there was a significant difference regarding the A/S at one minute and the days of hospitalisation in the NICU. Also, more neonates had respiratory distress syndrome in the aggressively-managed

group, and this difference was significant. In our study, the neonatal survival rate in the aggressively-managed group, was 74.36%, while in the expectantly-managed group, it was 88.57%; this is comparable to Hall et al's study, which showed a neonatal survival rate of 94% in expectant management.[23] Sibai et al, in a study on severe preeclampsia, reported that expectant management, with close monitoring of mother and foetus at a perinatal centre, reduces neonatal complications and neonatal stay in the NICU.[21] Odendaal et al also showed a reduction in total neonatal complications (33% vs. 75%) and no increase in maternal mortality.[20]

Our results agrees well with the results of Haddad et al[24] and Olah et al.[25] Odendaal et al[20] and Sibai et al[26] also reported that in pregnancies between 28 and 32 weeks, expectant management together with antenatal steroid administration, and appropriate maternal and foetal surveillance, should be recommended. Regarding maternal outcome, we had no maternal mortality in both groups; this may be due to close supervision. One patient from the second group had intrauterine death two days after admission, her pregnancy ended with spontaneous delivery of a dead foetus with severe IUGR. Two patients had vaginal bleeding during the follow-up period for which we terminated their pregnancies, and no patient developed eclampsia. The maternal morbidities were higher in the aggressively-managed group, especially in patients with eclampsia. Seven (17.95%) cases developed repeated fits after delivery in the aggressively-managed group, compared with one (2.86%) case in the expectantly-managed group. The difference was significant, and there was no increase in maternal morbidity in the expectantly-managed group (Table IV).

Our results agree with the Bangladeshi study conducted by Begum et al, who reported that in carefully-selected cases and with close supervision, pregnancy may be continued in women with eclampsia and severe preeclampsia to increase foetal maturity without increasing the risk to the mother.[27] Haddad et al reported that expectant management in patients with severe preeclampsia between 24 and 32 weeks in a tertiary care facility is associated with minimal risk to the mother.[24] Sibai et al[21] and Odendaal et al[20] also agreed with this. Visser and Wallenburg studied 256 women and they were able to prolong pregnancy for another 10–14 days; 5% developed abruption and three developed eclampsia.[28] Hall et al gained a mean duration of 11 days, 20% had abruption, 2% had pulmonary oedema, and 1.2% had eclampsia.[29] Yang et al recommended that expectant management should be carried out in well-selected patients with severe preeclampsia remote from term individually.[30] Pregnancy is continued until a maternal or foetal indication for delivery arises. It should be noted that appropriate patient selection for expectant management is of paramount importance in severe preeclamptic patients. This approach advocates conservative or "expectant" management in a selected group of women, with the aim of improving infant outcome without compromising the safety of the mother. Expectant management is recommended in patients with severe preeclampsia remote from term, after proper selection of patients and careful monitoring.

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