Expectant management of early onset of severe pre-eclampsia in Durban

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Abstract **Fifty patients with severe pre-eclampsia who presented before 32 weeks' gestation were managed conservatively (sedation, bed rest, antihypertensive therapy and intensive fetal and maternal monitoring) until intervention was indicated. Twelve patients presented before 26 weeks of pregnancy and there were no fetal survivors in this group; 23 presented between 26 and 29 weeks and 8(34,8%) of the babies in this group survived. The rate of perinatal loss in those presenting between 30 and 32 weeks was 26,6% (N = 4). Patients who had a history of a hypertensive disorder in their previous pregnancy(ies) had a higher perinatal mortality rate; 23 such mothers experienced 16 perinatal losses compared with 27 mothers who had no such history and who had only 8 perinatal losses.**

There was 1 maternal death, there were 2 cases of eclampsia, 3 of pulmonary oedema, 4 of abruptio placentae and 1 case of renal failure; 2 patients had disseminated intravascular coagulation. The local indigent and underprivileged black population have a more aggressive form of early onset of severe pre-eclampsia than that reported for other population groups. The high maternal complication rate of 30,8% and the low fetal survival rate before 26 weeks indicate that there is no place in our setting for expectant management of severe pre-eclampsia in patients presenting before 26 weeks. This applies particularly to those with a previous history of hypertension in pregnancy.

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Severe pre-eclampsia that complicates chronic hypertension or renal disease occurring in mid-trimester is a decision-making dilemma for the obstetrician. On the one hand is the knowledge that the ultimate cure is delivery of the fetus and placenta, and on the other is knowledge of the high perinatal mortality rate among babies delivered too early. Most obstetricians choose to manage these patients conservatively, hoping to achieve fetal lung maturity before delivery.[1,2] Sibai *et al.*,[3] however, highlighted the high maternal risks and the high number of perinatal losses associated with conservative management and concluded that there was no place for such an approach. Pattinson *et al.*[1] have more recently advocated conservative management in patients presenting later than 24 weeks based on a 38% salvage rate in their study. The present study was undertaken to assess the outcome of severe pre-eclampsia before 32 weeks' gestation in members of an indigent and underprivileged black community attending a large tertiary urban hospital, viz. King Edward VIII Hospital, and to assess the value of expectant management.

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Patients and methods

All patients with severe pre-eclampsia (defined as two recordings of diastolic blood pressure greater than 110 mmHg at least 6 hours apart with proteinuria) admitted to hospital between May and August 1991 were included in the study. Gestational age was determined by the date of the last menstrual period and confirmed by ultrasonography. Only patients with a live fetus of less than 32 weeks' gestational age were included in the study.

Patients were managed according to standard methods.[4] Briefly these comprised an initial intramuscular injection of 200 mg sodium phenobarbitone and a loading dose of 1 g α-methyldopa followed by 2 g every 24 hours in divided doses. Intravenous crystalloid infusion was administered to raise the intravascular volume to 6 cm H_2O in those patients with a low central venous pressure (CVP) reading. Intravenous fluids were not infused if the CVP reading was 6 cm H_2O or greater. Intravenous dihydralazine 6,25 mg was given if the blood pressure remained elevated at a diastolic level of 110 mmHg or more, 2 hours after sedation and the loading dose of α-methyldopa. Where the gestational age was 28 weeks or more, dihydralazine was administered while the fetal heart rate was continuously monitored by external cardiotocography in order to detect acute fetal distress due to any inadvertent rapid lowering of the high blood pressure and subsequent decrease in uteroplacental circulation.[5]

A second drug, monohydralazine, 75 - 200 mg in 24 hours, was added to the treatment if the high blood pressure was not lowered within 24 - 48 hours of α-methyldopa therapy and bed rest. It a third antihypertensive agent had to be added to the drug regimen, the patient was considered to have resistant hypertension, and serious consideration was given to termination of pregnancy.

Initial laboratory screening included urine protein detection by means of a dipstick technique, assessment of urea and electrolyte levels, blood uric acid and serum creatinine, full blood count including platelet count and measurement of haematocrit levels, liver function tests, a coagulation profile, a full 24-hour urine protein and creatinine clearance estimation and urine microscopy to detect underlying renal disease. All patients who were more than 28 weeks pregnant were given dexamethazone 8 mg 8-hourly for 48 hours; this was repeated weekly with the aim of achieving fetal lung maturity.

Indications for delivery were divided into maternal factors and fetal factors. Maternal indications were uncontrollable hypertension, imminent eclampsia, eclampsia, pulmonary oedema, renal failure, an impaired liver function test, coagulopathy and abruptio placentae. Fetal indications for delivery were abnormal fetal heart rate patterns, intra-uterine growth retardation and severe oligohydramnios.

The mode of delivery was individualised. Caesarean section was decided upon if there was an obstetric indication and not for prematurity *per se*.[6] In the post-delivery period, the patients were kept in a high-care ward for 24 hours and subsequently transferred to the post-natal ward if their condition had stabilised. All infants discharged were considered to have survived. Patients who presented with impending eclampsia and eclampsia

were not included in the study because the standard management of these patients was immediate delivery.

All results are presented as means and ranges. Where applicable, Student's *t*-test was applied and a *P*-value of < 0,05 taken as significant.

Results

Fifty patients who fulfilled the criteria for admission to the study were seen during a 4-month period. Their clinical data are shown in Table I. None of the patients was under 17 years old; 19 were aged between 21 and 29 years and 8 were more than 35 years of age. There were 12 primigravidas; 8 patients had 4 or more children, 20 patients had 2 or 3 children, and 10 were secundigravidas.

TABLE I.
Clinical data on all patients

N = 50	Mean (SD)	Range
Age (yrs)	29 (6,39)	17 - 40
Parity	2,3 (2,06)	0 - 7
Blood presure (mmHg)		
Systolic	175 (22,77)	140 - 250
Diastolic	122 (13,99)	110 - 160
Proteinuria (g/24 h)	3,6 (2,88)	0,63 - 8,7

The perinatal survival rate at varying gestational ages is shown in Table II. All pregnancies of 26 weeks' gestational age and less resulted in intra-uterine deaths (Table III). Of the 2 neonatal deaths in pregnancies between 28 and 29 weeks' gestation, 1 had multiple congenital abnormalities and the other died of severe sepsis. There were 3 macerated stillbirths between 30 and 32 weeks' gestation.

In the gestational age group 27 - 32 weeks, there were 15 stillbirths (30%); 3 of these weighed less than 500 g; 7 weighed between 500 g and 1 000 g and 5 between 1 000 g and 1 500 g. Four patients with abruptio placentae delivered babies less than 1 000 g in weight.

Apart from a previous history of pre-eclampsia no other factors, viz. age, parity or proteinuria, predicted the outcome of any of the pregnancies. Twenty-three (46%) of the 50 patients had a history of pre-eclampsia in their previous pregnancies. The fetal loss in these 23 patients was 16 (69,6%) compared with a fetal loss of 8 (29,6%) in those patients without a history of pre-eclampsia ($P < 0,01$). The average number of days gained by conservative management was 12,3 days. The mean weight of all surviving babies was 1 300 g and that of non-surviving babies 817 g. Table III shows that those patients admitted before they reached 26 weeks' gestation gained more days by expectant medical management than those admitted later.

Maternal complications are shown in Table IV. Two patients developed eclampsia during the study period. One was a 21-year-old primigravida admitted at 26 weeks, with a blood pressure of 150/120 mmHg. She had her blood pressure controlled with α-methyldopa but absconded after a 30-day stay in hospital. She returned a week later, having had a convulsion at home. A diagnosis of eclampsia was made on readmission (blood pressure = 160/110 mmHg; proteinuria ++) and a live baby weighing 1 500 g was delivered by caesarean section. The second patient had requested a weekend's leave to attend to her domestic problems following a 3-week stay in hospital. She did not return after the weekend but was readmitted a week later with eclampsia. Following caesarean section, she went into pulmonary oedema. Four patients developed abruptio placentae during expectant management. Their ages

TABLE II.
Survival rate of babies at different gestational ages

Gestational age (wks)	No. of patients	Babies dead at birth*		Early neonatal death		Fetal salvage	
		No.	%	No.	%	No.	%
< 26	12	12	–	–	–	–	–
26 - 27	9	5	55,6	1	11,1	3	33,3
28 - 29	14	7	50	2	12,3	5	35,7
30 - 32	15	3	20,0	1	6,7	11	73,3
Total	50	27	52	4	8	19	40

* Stillbirths and abortions.

TABLE III.
Pregnancies below 26 weeks' gestation

Age (yrs)	Parity	Gestational age (wks)	Blood pressure (mmHg)	Proteinuria	Complication	Outcome	Interval (d)	Gestational age at delivery*	Fetal weight (g)
24	1	24	210/160	3+	↑ BP, ascites	IUD	8	25	500
21	0	23	160/120	3+	Oligohydramnios	IUD	12	25	400
35	2	22	210/160	2+	↑ BP	IUD	2	22	400
22	0	24	200/140	3+	Imminent eclampsia	Abortion	2	24	400
22	0[-1]	22	190/140	2+	DIC, ↑ BP, ↑ urates	IUD	23	25	650
40	7	24	210/110	2+	↑ BP	FSB	4	25	600
30	3	11	230/120	4+	Maternal death	Abortion	81	23	300
31	3	16	180/130	3+	Renal failure	IOL	45	22	250
20	1	20	250/160	3+	↑ BP	IOL	1	20	250
25	3	25	150/120	3+	↑ Urates	IOL,MSB	25	29	1 000
33	6	22	150/110	3+	Abruptio	Abortion	8	23	300
29	1	20	150/120	3+	↑ BP	IOL	21	23	500

↑ BP — rising blood pressure values; DIC — disseminated intravascular coagulation; IUD — intra-uterine death; FSB — fresh stillbirth; IOL — induction of labour; MSB — macerated stillbirth.
* Days gained: mean ± SD = 32,7 ± 22,9; median = 10.

ranged from 29 to 35 years and parity from 3 to 8; 3 had proteinuria with diastolic blood pressures ranging from 110 to 120 mmHg and 3 had had hypertension in a previous pregnancy. All 4 were less than 29 weeks pregnant and did not have non-stress tests.

TABLE IV.
Maternal complications

Uncontrollable hypertension	19
Abruptio placentae	4
Pulmonary oedema	3
Coagulopathy (low platelet counts)	3
Imminent eclampsia	9
Renal failure (decreased UO; ↑ urea)	1
Eclampsia	2
Maternal death	1

UO = urine output.

There was one maternal death in a known hypertensive, aged 30 years. Her hypertension had required 5 different medications. This patient was lost to follow-up and then presented at 11 weeks' gestation with a blood pressure of 230/120 mmHg and 4 + albuminuria. She had had 3 previous pregnancies which had resulted in non-obstetric deaths and therefore refused termination of pregnancy despite intensive counselling. She collapsed suddenly at 21 weeks' gestation. Post-mortem findings included nephrosclerosis, hypertensive cardiac disease, old dissection of abdominal aorta and right-sided cardiac failure, but the exact cause of death was not established. Sections of the brain did not reveal any intracerebral haemorrhage nor was there any evidence of subendocardial ischaemia.

Three patients developed pulmonary oedema. One case of pulmonary oedema occurred in an eclamptic described above, the other in a 29-year-old patient with a previous history of eclampsia and stillbirth. She was admitted at 23 weeks with a blood pressure of 150/120 mmHg and 3 + proteinuria, and developed pulmonary oedema 2 hours after admission. She had had only 200 ml Ringer's lactate in this 2-hour period. The central venous line was only inserted after the onset of pulmonary oedema. She refused termination of pregnancy after she was resuscitated and subsequently suffered an intra-uterine death. She delivered a macerated stillborn baby 3 weeks later.

The third patient was admitted at 29 weeks with a blood pressure of 200/130 mmHg and a previous history of pre-eclampsia. She was given a rapid-acting antihypertensive agent on admission with concomitant central venous pressure recordings and electronic fetal heart rate monitoring. The blood pressure was well controlled and she was transferred to the lying-in ward. She developed pulmonary oedema on the third day post-admission, had an intra-uterine fetal death and delivered a 1 200 g macerated stillborn baby. This patient did not have an intravenous line in the lying-in ward. Renal failure occurred in a 31-year-old patient admitted at 31 weeks' gestation with a blood pressure of 230/120 mmHg. Antihypertensive therapy initially included intravenous dihydralazine. This was followed by a α-methyldopa and monohydralazine. She was given dexamethazone 8 mg every 8 hours for 48 hours to achieve fetal lung maturity. Her blood urea and electrolyte values however started rising and creatinine clearance fell to less than 50 ml/min during expectant management. She was therefore delivered of a live 1 700 g baby by emergency caesarean section on the 8th day. She had to have renal dialysis when her urine output failed to improve and her serum potassium levels began rising postoperatively.

Nine patients who developed signs of imminent eclampsia while in hospital were delivered after stabilisation of high blood pressure.

Discussion

Pregnant women presenting at or before 28 weeks' gestation with severe pre-eclampsia are associated with high maternal and perinatal mortality rates.[1,2] This study confirms the findings of previous workers[1,2] that fetal salvage rates before 26 weeks' gestation in severe pre-eclampsia are poor. There were no fetal survivors among the 12 patients presenting before 26 weeks' gestation.

The overall perinatal mortality rate in the present study was extremely high (620/1 000 deliveries). This is much higher than the figure quoted by Moodley[4] — 215/1 000 deliveries for all cases of hypertension and proteinuria for the same population group. However, the present study was performed in a very high-risk group from an indigent population in a developing community with limited neonatal facilities. If only pregnancies of 30 weeks' gestation and more are included, then the perinatal mortality rate in this study falls to 80/1 000 deliveries. This is similar to that reported by Odendaal *et al.*[2] and Davey[7] for gestational ages of 30 weeks and more.

Sibai *et al.*[3] also reported a high perinatal mortality rate of 250/1 000 deliveries (despite intensive treatment of severe hypertension in the mid-trimester). They reviewed pregnancy outcome over a 7-year period in 60 patients with severe pre-eclampsia between 18 and 27 weeks' gestation. The perinatal outcome for these pregnancies was extremely poor, 31 of the 60 pregnancies ended in fetal demise and 21 in neonatal deaths, giving a total perinatal mortality rate of 87%. In addition, the perinatal survival rate was 3% for those developing severe disease before 25 weeks' gestation compared with 24% for those developing disease at or after 25 weeks' gestation. The majority of patients (70%) in this study were black and indigent.

Odendaal *et al.*[2] described favourable results with expectant management in 45 patients developing severe hypertension before 28 weeks. Eleven were less than 24 weeks pregnant and all 11 suffered perinatal deaths. The remaining 34 patients were between 24 and 28 weeks' gestation and 14 of these (41%) produced an infant that survived. Thus all these studies[1-3] and the present one confirm the poor perinatal outcome in pregnancies of 24 weeks' gestation or below.

There were only 12 (24%) primigravidas in this study. This figure is lower than those reported in other series of severe early pre-eclampsia where the proportion of primigravidas varied between 31% and 67%.[8-10] This might therefore explain the poor outcome in this study compared with other studies which had a larger number of primigravidas. Moodley[4] reported that the perinatal mortality rate in primigravidas with proteinuric hypertension was 117/1 000 deliveries while that of multigravidas with proteinuric hypertension in late pregnancy was 215/1 000 in a population similar to that of the present study. Explanation of the high incidence of multigravidas is difficult as follow-up of patients in a large hospital is poor; consequently the role of essential hypertension and renal disease is difficult to assess. Feeny[11] has reported that change of partners may play a role in multiparous women presenting with pre-eclampsia for the first time and as this is not an uncommon feature in the local population, it may be a factor.

A history of hypertension in a previous pregnancy was present in 23 (46%) patients in this study and these patients had a greater fetal loss rate than those without a

history of previous hypertension — 16 (69,6%) compared with 8 (29,6%). In a case control study of severe pre-eclampsia of early onset Moore and Redman[10] found that a history of chronic hypertension or renal disease was not significantly associated with pre-eclampsia but that significantly more patients had had previous pre-eclampsia.

The policy at King Edward VIII Hospital at the time of the study was not to deliver fetuses before 28 weeks or if they weighed less than 1 000 g (unless specific maternal indications necessitated delivery) because the perinatal mortality rate in this group at the hospital is 100%. Ten of the 15 stillbirths weighed less than 1 000 g. It is very likely that expectant management may have converted these stillbirths to early neonatal deaths.

The maternal complication rate of 30% in the present study is similar to that reported by Sibai *et al.*[3] It is difficult to explain the differing maternal complication rates between the population groups studied in Cape Town by Odendaal *et al.*[1,2] and that of the present study. Odendaal[1,2] studied a stable urban population and reported a low maternal complication rate, while the population studied in Durban was black and indigent. Many patients come from rural areas for maternity care or were transferred to King Edward VIII Hospital from regional hospitals and community clincs. There is some evidence from epidemiological studies of non-pregnant patients in South Africa[12,13] that the urban black population has a higher incidence of hypertension than other racial groups and that the highest incidence of hypertension occurs in urban black women. The high incidence may be due to stress caused by urban living on a population in transition from a rural to an urban setting.

Three patients developed pulmonary oedema in this study. In only 2 patients, however, could this be ascribed to iatrogenic fluid overload. No patient had the CVP rise to greater than 6 cm H_2O. It is possible that in the 2 patients who developed pulmonary oedema, pulmonary capillary wedge pressure monitoring would have demonstrated a higher value than CVP. However this facility is not available to us at present.

Intensive maternal monitoring might have prevented some of the complications found by Odendaal *et al.*[2] who recommend frequent antenatal fetal heart rate monitoring to detect abruptio placentae. This is certainly of value in institutions with the appropriate neonatal facilities to care for these very small babies. Sibai *et al.*[3,14] reported conflicting results on the outcome of severe pre-eclampsia in mid-trimester. In their second study,[14] they noted an improved outcome because of frequent fetal monitoring (non-stress tests and biophysical profile). Their previous protocol[3] did not institute fetal monitoring until 27 weeks. They also note that the high maternal complication rate of their earlier study[3] was probably related to management of these cases at regional hospitals with referral to the tertiary centre only after the onset of maternal complications. The reduced maternal complication rate is attributed to early and intensive maternal and fetal monitoring and suggests the need for conservative management beyond 24 weeks' gestation. Nevertheless only 2 weeks were gained by conservative management in patients between 24 weeks' and 28 weeks' gestation. Perinatal and maternal outcome is dependent on the availability of sophisticated neonatal facilities and an improved neonatal outcome is normally to be expected once gestation of more than 26 weeks has been achieved. Only 1 of our patients however reached a gestation beyond 26 weeks (IUD at 29 weeks). It is therefore totally inappropriate in our setting to attempt prolongation of pregnancy in patients for more than 26 weeks, particularly in view of the unacceptable incidence of maternal morbidity and mortality. Unless such neonatal facilities are available for the management of very small babies and their long-term outcome established in developing communities, a more aggressive approach to the management of severe hypertension in patients below 26 weeks' gestation (particularly multigravidas with a history of hypertension in a previous pregnancy) is recommended. Such patients should be advised to terminate their pregnancies. In pregnancies of more than 28 weeks' duration a conservative approach with the use of dexamethazone to promote lung maturity is suggested. Intensive maternal and fetal monitoring (frequent non-stress tests, biophysical profiles, continuous blood pressure monitoring, correction of hypovolaemia and testing for coagulopathies) should be performed in such circumstances. Patients with severe hypertension should be referred to a tertiary hospital at an early stage rather than at the onset of fetal or maternal complications.

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