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Re-evaluation of abruptio placentae and other maternal complications during expectant management of early onset pre-eclampsia

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ABSTRACT

Objective: Expectant management of appropriately selected cases of early pre-eclampsia in a dedicated, tertiary in-patient setting with frequent non-invasive maternal and fetal surveillance, prolongs pregnancy, improves perinatal outcome and mitigates the impact of maternal complications. As the rate of abruptio placentae in a large descriptive study performed nearly 20 years ago was 20%, a study to re-evaluate the rate of abruptio placentae and other maternal complications was performed.

Study design: A retrospective study that included all women admitted for expectant management with stable early pre-eclampsia (≥ 24 and < 34 weeks' gestation) was performed at Tygerberg Hospital, a secondary and tertiary referral centre in South Africa over a period of 12 months.

Main outcome measures: Abruptio placentae and other maternal complications.

Results: During the study period, 9137 women were delivered at the study institution. The data of 102 of 106 women admitted for expectant management of early pre-eclampsia were available. Thirty-four (33%) reached the elective delivery threshold of 34 weeks. Seventeen women (17%) experienced ≥ 1 complication. There were four cases (4%) each with abruptio placentae, HELLP syndrome and renal insufficiency. Three of the cases with abruptio placentae were asymptomatic, only being diagnosed at caesarean section for fetal distress. Nine women developed mild/moderate ascites. There were no admissions to the critical care unit and no deaths.

Conclusions: Abruptio placentae occurred in 4% of women managed expectantly with early pre-eclampsia and was most often asymptomatic before delivery.

1. Introduction

Pre-eclampsia is a dangerous condition that is unique to human pregnancy. Although it represents a global scourge, occurring in approximately 5–15% of pregnancies [1,2], it is particularly common in Low and Middle Income countries (LMICs) where it is a major cause of maternal and perinatal mortality and morbidity. Pre-eclampsia is often super-imposed on other pre-existing conditions such as obesity, chronic diseases such as diabetes, infections such as HIV [3,4] and may even show seasonal variation [5].

At present, there is no definitive treatment for established pre-eclampsia, thus delivery is the only definitive cure for this dangerous pregnancy-associated disease. However, delivery is not always in the best interests of the fetus, as when delivery occurs at an extremely preterm gestation, the baby may not survive, or if it does, survival is associated with a high risk of severe complications. The high level, neonatal ICU support that must be provided for such babies born remote from term is an extremely limited and expensive resource. This context informed the sentinel studies performed in South Africa that assessed the risks and benefits of expectant management and provided recommendations for evaluation, management and delivery [6–9]. Data from the Tygerberg/Stellenbosch unit has also featured prominently in North American Clinical Opinion papers that address these matters [10,11]. Expectant management of appropriately selected cases of early pre-eclampsia in a dedicated, tertiary in-patient setting with frequent non-invasive maternal and fetal surveillance, prolongs pregnancy, improves the perinatal outcome and mitigates the impact of maternal complications [9,12,13].

One of the important complications of pre-eclampsia is abruptio placentae. When frequent fetal heart rate monitoring is performed as part of inpatient expectant management of early pre-eclampsia, abruptio placentae can usually be detected very early and the clinical impact mitigated by urgent delivery by caesarean section [7]. It is interesting to note that the two largest reported series on expectant management of early pre-eclampsia documented widely different rates of abruptio placentae, namely 20% in South Africa [7] and 6% in

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France [14]. Since that time, expectant management of early pre-eclampsia has continued to be refined. The aim of this study was to determine the current rate of abruptio placentae, as well as other maternal complications in patients undergoing expectant management of early onset pre-eclampsia at the Stellenbosch University/Tygerberg Hospital unit in South Africa.

2. Methods

This study was performed as a retrospective audit over 12 months in the Obstetric Special Care Unit (OSCU) at Tygerberg hospital, a secondary and a tertiary referral centre. This is the same unit where the largest published observational study on expectant management of early pre-eclampsia, was performed 18 years earlier [7,12]. The drainage area comprises half of the Cape Town Metro (East), Boland and the West Coast districts, with most women having low socio-economic status. Pre-eclampsia was defined as the new onset of hypertension (≥140 mmHg systolic or ≥90 mmHg diastolic) after 20 weeks of gestation and the coexistence of the one or more of the following new onset conditions: proteinuria (a 24-hour urinary protein loss of ≥300 mg/day or urine protein/creatinine ratio ≥30 mg/mmol, or persistent values ≥1+ on dipstick); other maternal organ dysfunction including renal insufficiency, liver involvement, neurological and haematological complications; and uteroplacental dysfunction. These specifications are in accordance with the previous and current guidelines of the International Society for the Study of Hypertension in Pregnancy (ISSHP) [15].

All women with the diagnosis of early pre-eclampsia (< 34 weeks' gestation), within the drainage area were referred to Tygerberg Hospital for stabilisation and evaluation. When the mother and the fetus were otherwise stable and the gestational age was ≥24 and < 34 weeks, expectant management was commenced by the OSCU, after counselling and consent. This practice has been described in greater detail in previous publications from the unit [8]. All women who underwent expectant management for early pre-eclampsia were included into the study. Abruptio placentae was defined as a retroplacental clot covering > 15% of placental surface or clear evidence on histopathology. Other major maternal complications included eclampsia, pulmonary oedema (clinical and radiographic diagnosis), HELLP syndrome (platelets < 100×10^9/l, AST > 70 μ/l, haemolysis as demonstrated by LDH > 600 μ/l, [16], admission to the adult intensive care unit, moderate or severe ascites (clinically detectable or on ultrasound evaluation) or severe renal impairment (serum creatinine > 120 μmol/l) or failure to control blood pressure with up to three antihypertensive agents. Perinatal outcomes did not form part of this study.

Data was collected by the principal investigator from the electronic records of the study population and transferred onto an anonymized data sheet with case numbers only. Thereafter it was captured into an Excel© spread sheet. The statistical analysis was conducted by the in Biostatistics Unit of Stellenbosch University using the STATA 14 programme. Normality was determined both qualitatively and quantitatively while simple descriptive statistics applied most often.

The primary aim of the study was to ascertain the current rate of placental abruption in patients undergoing expectant management of early onset pre-eclampsia at Tygerberg Hospital. The secondary outcomes were to evaluate other maternal complications of the same group.

The study was approved and registered with the Human Research and Ethics Committee of Stellenbosch University (S16/10/195) which granted a waiver of consent due to the retrospective, audit design.

3. Results

This study was conducted from 01 July 2016 to 30 June 2017, during which period 9137 women were delivered at the study institution and 106 women qualified for and were admitted to the OSCU for expectant management of early pre-eclampsia. Of these four were excluded from analysis due to insufficient information. The descriptive data of the included women are given in Table 1. Of the 102 cases, 82 (80.4%) were diagnosed with pre-eclampsia and 20 (19.6) with chronic hypertension and superimposed pre-eclampsia, while 16 (15.7%) were HIV positive on treatment. One patient declined offered termination of pregnancy at 21 weeks' gestation and was later admitted for expectant management. There were nine (8.8%) self-reported cigarette smokers, five (4.9%) who drank alcohol and three (2.9%) who used both. Regarding medical conditions, in addition to those with chronic hypertension, there were five cases with Systemic Lupus Erythematosis, two with diabetes mellitus, and three with asthma.

Table 1
Characteristics of patients on admission (n = 102).

Description	Mean (sd) or % (n)
Age (years)	28 (7.2)
Primigravid	42.2% (43)
Multigravid	57.8% (59)
Gestation all (weeks)	29.1 (2.4)
< 27 weeks	17.6% (18)
27w0d − 31w6d	53.9% (55)
32w0d- 33w6d	25.5% (26)
Gestation uncertain	2.9% (3)
Systolic blood pressure (mmHg)#	159 (16.9)
Diastolic blood pressure(mmHg)#	97 (11.7)
Urinary protein (grams/24 h)	2.6 (3.1)
Dipstick proteinuria (n = 99)[&]	
Negative	17.2% (17)
1+	24.2% (24)
2+	26.3% (26)
3+	32.3% (32)
BMI[$] ($kg/m^2$)	29.5 (7.22)
< 19	3% (3)
19–24.9	35%(35)
25–29.9	20%(20)
30–39.9	31%(31)
40–49.9	10%(10)
≥50	1%(1)

Results are expressed as mean with standard deviation or % (n). Not all denominators n = 102; w = weeks; d = days; # = highest value in first 48 h; & = first hospital test; [$]n = 100.

Previous obstetric history revealed that, nine (8.8%) women had previous early- and seven (6.7%) late-onset pre-eclampsia, while two (2%) had previous eclampsia. Nine women (8.8%) had experienced a previous intra-uterine death (IUD) and one a previous placental abruption.

Following admission, the median duration of expectant management was 15 (range 3–80) days. All mothers received antenatal corticosteroids to enhance fetal organ maturity. Immediately before delivery 56 (54.9%) patients were on a single oral agent (either methyldopa or long-acting nifedipine) to control blood pressure and 46 (45.1%) on two antihypertensive agents. The details of patients at delivery, including broad indications for, and the route of delivery are shown in Table 2. Induction of labour was attempted in 31 women but only 14 achieved a vaginal delivery. Seventeen (16.7%) of patients experienced at least one major maternal complication.

Abruptio placentae, as well as other major maternal complications occurring before delivery, that constituted the main outcomes of this study are shown in Table 3. Of the four (3.9%) cases with abruptio placentae, only one patient experienced maternal symptoms and an abnormal cardiotocogram (CTG). The other three had only abnormal CTGs requiring urgent delivery, but at caesarean section, significant retroplacental clots were noted when the placentas were examined. These four cases were delivered at 30, 31, 29 and 32 weeks respectively, with none of the babies having an Apgar score < 7 at five minutes. The fourth baby required ventilation after birth. These babies were discharged in stable conditions into the care of step-down institutions at

Table 2
Characteristics of patients at delivery.

	Mean (sd) or % (n)
Gestation at delivery (weeks)	31.8 (2.1)
Prolongation of pregnancy (days)	18 (12.3)
Systolic blood pressure (mmHg)^	137 (11)
Diastolic blood pressure (mmHg)^	82 (11)
Serum Creatinine	66 (27)
Platelets $\times 10^9/\ell$	189 (78)
Indication for delivery	
Maternal complication	16.7% (17)
Fetal distress (CTG +/− Doppler)#	45.1% (46)
Maternal and fetal combined	3.9% (4)
Elective (34 weeks)	33.3% (34)
Preterm labour	1% (1)
Route of delivery	
Caesarean section – emergency	75.5% (77)
Caesarean section – elective	10.8% (11)
Vaginal delivery	13.7% (14)

Data as mean (standard deviation) or % (n)*; # abnormal CTG and or severely abnormal Doppler indices; ^ = highest value in last 48 h.

Table 3
Abruptio placentae and major antepartum maternal complications.

Complication	% (n)
Abruptio placentae	3.9 (4)
Ascites*	8.8 (9)
HELLP syndrome	3.9 (4)
Severe renal impairment#	3.9 (4)
Loss of blood pressure control	2 (2)
Pulmonary oedema	1 (1)
Eclampsia	1 (1)
Intensive Care Unit Admission	0
Death	0
Patients with major complication	16.7 (17)

Patients may experience > 1 complication; HELLP = Haemolysis, Elevated Liver enzymes and Low Platelets; # = serum creatinine creatinine > 120 μmol/l; * = clinically detected or moderate/severe degree on ultrasound.

14, 14, 33 and 12 days respectively.

After delivery 11 cases with new complications were recorded of which only three were directly linked to pre-eclampsia namely, a single case with acute kidney injury and two with difficult blood pressure control. The other eight cases included six with post-operative wound sepsis, one with a wound haematoma and one with postpartum haemorrhage. The mean (sd) duration of postpartum hospitalization was 3.5 (2.9) days.

Only limited data were collected on the babies. The mean (sd) birthweight was 1472 (490) grams, with 62 (60.8%) < 10th and 30 (29.4%) < 3rd centiles (using locally customised centiles). Fifty (49%) of the babies were female and only two babies (2%) had an Apgar score of less than seven at five minutes. There were no stillbirths. Neonatal outcomes were not followed beyond delivery.

4. Discussion

The results from this retrospective audit over one year from a unit well experienced with expectant management of early pre-eclampsia demonstrated that most cases (83%) did not experience maternal complications. The rates of abruptio placentae, HELLP syndrome and renal insufficiency were four percent each, while nine women developed moderate/severe ascites necessitating delivery. There were no admissions to the critical care unit and no deaths.

While prompt delivery is always in the best interest of the woman who develops pre-eclampsia, the rationale and chronological development of the concept of expectant management of early pre-eclampsia have been described previously [9]. Two small, initial randomised trials investigated and demonstrated the perinatal benefits of this approach [6,17], while larger descriptive trials that followed were better suited to describe maternal safety aspects [7,14]. In the largest descriptive series of expectant management of early pre-eclampsia, conducted in a LMIC, 27% of women experienced a pre-defined major complication [7], while in the index study conducted in the same institution, nearly 20 years later, this figure had dropped to 17%. A key message from the studies by Hall et al. and Haddad et al, was that with careful safeguards the clinical impact of these complications was limited [7,14]. In the index study, as well as in previous descriptive trials on early pre-eclampsia from the Tygerberg/Stellenbosch unit in South Africa, fetal indications for delivery were more common than maternal ones with both expectant and aggressive management approaches [8,12]. This contrasts with a recently published series with early pre-eclampsia in India that described improved perinatal outcomes with expectant management, but where maternal indications (complications) for delivery were almost double fetal ones [13].

Abruptio placentae is a prominent complication of pre-eclampsia that is well described [8,10,18] as it may endanger both the mother and her baby, before and after delivery. Although small episodes may escape detection, severe forms of abruptio placentae can lead to fetal death, perinatal asphyxia, preterm birth and on the mother's side shock, disseminated intravascular coagulopathy, renal failure and even death may occur. The classic maternal clinical picture is however preceded by fetal clues. During the early stages of abruption, catecholamine-induced vasoconstriction may selectively maintain perfusion of the maternal heart and brain at the expense of uteroplacental blood flow. Thus, fetal distress is an important early sign of impending haemodynamic compromise. In a case-control series with 69 consecutive cases of abruptio placentae amongst women undergoing expectant management of early pre-eclampsia, Odendaal et al., [19] showed that fetal heart rate decelerations detected by cardiotocograph (CTG) served as an early warning of abruptio placentae, with the "incidental" finding of a significant area/size of fresh retroplacental haematoma described at caesarean section. Such rapid intervention in tertiary units by dedicated teams limits the impact of complications for the mother and baby. In the index study, three of the four cases with abruptio placentae were asymptomatic, only being diagnosed at caesarean section for fetal distress. However, despite six-hourly CTGs, sudden intra-uterine deaths can still occur [12]. Although expectant management of early, severe pre-eclampsia is now more widely advocated [13,20] placental abruption remains a concern. The rates range from 4.1% to 22.9% [21] and were 20% and 6% in the two largest reported studies [7,14]. It is therefore encouraging to note that as expectant management of early pre-eclampsia has been refined at the Tygerberg/Stellenbosch unit over 20 years, the rate of maternal complications and abruptio placentae have declined the latter from 20% to 4%.

Ascites detected clinically or of a moderate/severe degree on ultrasound, was the most frequent complication at nine percent, down from 11% in the previous large descriptive study [7]. Ascites was also noted to be the most frequent maternal complication (18%) preventing the initiation of expectant management of early pre-eclampsia in an earlier study from the same unit [8]. This complication has received scant attention in recent pre-eclampsia literature but when capillary leak is exaggerated in the presence of hypertension, ascites and pleural effusions together with the dangerous conditions of pulmonary and cerebral oedema may develop. In a moderately sized, matched cohort study in India, Suriya et al., compared the maternal outcomes of pre-eclampsia cases with and without ascites. They defined ascites as the presence of fluid in the peritoneal cavity detected clinically and confirmed by ultrasound, which correlates with the criteria used in the index study. Ascites was found to be an independent risk factor for adverse outcome and was also associated more frequently with abruptio placentae ($p = 0.04$) [22].

This descriptive study has some limitations. More extensive

biochemical parameters were not captured on admission for expectant management and the neonatal outcomes of all babies were not followed beyond delivery, the latter omission was due to the focus on maternal outcomes. The index study involved admissions over a one-year period, whereas the previous study from the same institution to which it is largely compared was conducted over five years, although admissions per year have increased substantially.

In summary, 17% of women undergoing expectant management of early pre-eclampsia experienced at least one complication. Abruptio placentae occurred in 4% of women managed expectantly with early pre-eclampsia and was most often asymptomatic before delivery. The rate of abruptio placentae has declined substantially from the figure of 20% reported from the same unit some 20 years earlier but the decline in ascites from 11% to 9% is less dramatic.

5. Declarations of interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.preghy.2019.02.008.

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