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CLINICAL ARTICLE

Clinical characteristics of early-onset pre-eclampsia in singleton versus multiple pregnancies

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ABSTRACT

Objective: To analyze the clinical differences between multiple and singleton pregnancies with early-onset pre-eclampsia. *Methods:* The present retrospective cohort study included patients with early-onset pre-eclampsia diagnosed at a tertiary hospital in China between January 2012 and June 2014. The patients were divided into a multiple pregnancy group (MP group) and a singleton pregnancy group (SP group). Differences in maternal and fetal outcomes before and after birth were compared between the two groups. *Results:* Overall, 100 patients were included (21 MP group; 79 SP group). The systolic and diastolic blood pressure values at admission were significantly lower in the MP group than in the SP group ($P = 0.032$ and $P = 0.015$, respectively), and the incidence of pregnancy edema was significantly higher ($P = 0.015$). Moreover, the mean neonatal birth weight in the MP group was significantly higher than that in the SP group ($P < 0.001$). The frequencies of abnormal umbilical arterial resistance score, abnormal fetal heart rate, low birth weight, low Apgar score, neonatal cardiovascular abnormalities, and neonatal infections were significantly lower in multiple pregnancies ($P < 0.05$ for all). *Conclusion:* Early-onset pre-eclampsia in multiple pregnancies seems to have a protective effect on neonatal survival and improves maternal and fetal outcomes. Disease progression might be delayed when compared with early-onset pre-eclampsia in singleton pregnancies.

1. Introduction

Women with twin pregnancies are more likely to acquire a hypertensive disorder during pregnancy, and to do so much earlier, than are women with singleton pregnancies [1–6]. The plasma volume increases because of sodium and water retention in the interstitial tissue during pregnancy. However, plasma volume expansion and sodium and water retention in twin pregnancies could be more pronounced than in singleton pregnancies, and twin pregnancies are therefore more likely—even two to three times more likely—to lead to a hypertensive disorder [7]. The rate of hypertensive disorders in twin pregnancies is 13%–26% [2].

However, hypertension in twin pregnancies might not be associated with adverse birth outcomes [8]—it might in fact be beneficial to fetal survival because the demand for blood and nutrients is much greater than in singleton pregnancies [9]. In line with this hypothesis, the risk of fetal and infant mortality in twin pregnancies ending in preterm birth is reduced if the mother has pregnancy-induced hypertension [10]. By contrast, pregnancy-induced hypertension in singleton pregnancies is associated with adverse birth outcomes [8]. On the basis of a retrospective analysis of 278 821 twin pregnancies from the US 1995–2000 Matched Multiple Birth Data Set, Luo et al. [11] concluded that pregnancy-induced hypertension seems to be beneficial for fetal survival in twin pregnancies, especially those ending prematurely, with the strongest protective effect seen for deaths related to infections or immaturity-related conditions.

Like pregnancy-induced hypertension, early-onset pre-eclampsia is a hypertensive disorder complicating pregnancy. Because pregnancy-induced hypertension seems to be beneficial to fetal survival in multiple pregnancies, the question arises whether early-onset pre-eclampsia is also protective against perinatal mortality in multiple pregnancies. The present study was conducted to compare the clinical differences in early-onset pre-eclampsia between multiple and singleton pregnancies and to evaluate whether early-onset pre-eclampsia might have a protective effect on the perinatal survival of infants in multiple pregnancies.

2. Materials and methods

The present study was a retrospective analysis of all patients diagnosed with early-onset pre-eclampsia between January 1, 2012, and June 30, 2014, at the International Peace Maternity and Child Health Hospital, Shanghai Jiao-Tong University School of Medicine in Shanghai, China. Early-onset pre-eclampsia was defined as a blood pressure of 140/90 mm Hg or more (taken twice 6 hours apart) combined with proteinuria (protein level of 0.3 g or more in a 24-hour urine collection),

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both occurring at 20–34 weeks of pregnancy in a previously normotensive woman [12,13]. Alternatively, confirmation of proteinuria by semiquantitative urine dipstick analysis with a result of at least 1 + was allowed [14]. The use of data from the hospital database was approved by the Institutional Review Board of Shanghai Jiao-Tong University School of Medicine.

The patients had been hospitalized on the day they were diagnosed with early-onset pre-eclampsia. Antihypertensive drugs, magnesium sulfate, and sedative drugs were administered as appropriate. The blood pressure was measured three times a day; fetal heart rate tracing was performed every day; proteinuria was evaluated every 2–3 days on the basis of 24-hour urine collections; maternal laboratory values were measured once or twice per week; and ultrasonography, including fetal biometry, umbilical artery blood flow, and estimation of the amniotic fluid volume, was performed weekly. Delivery was considered when severe maternal or fetal complications occurred. All clinical data were recorded in the medical history in real time.

The following maternal characteristics were obtained: maternal age, length of pregnancy at pre-eclampsia onset and delivery, time between onset and delivery, systolic and diastolic blood pressure on admission, and peak 24-hour urine protein level. The pregnancy duration was confirmed on the basis of the first day of the last menstrual period and corrected by ultrasonography if the crown–rump length measurement taken during the first trimester revealed a difference of more than 7 days [15]. In addition, the frequencies of the following clinical findings for the mothers were evaluated: fundus lesion (abnormal ratio of eyeground arteries to veins); prodromal symptoms (headache, nausea, vomiting, visual disturbance); edema; abnormal cardiac function (palpitation, chest congestion, anhelation); placental abruption; hydrothorax and ascites; hemolysis, elevated liver enzymes, and low platelets syndrome (HELLP syndrome, defined by a lactate dehydrogenase concentration of 600 U/L or more or a serum total bilirubin level of more than 1.2 mg/dL, a serum alanine aminotransferase concentration of 40 U/L or more, and a platelet count of less than 100×10^9 cells per L [16]); premature rupture of membranes; and eclampsia.

Moreover, the number of pregnant women with the following laboratory findings was determined: platelet count less than 100×10^9 cells/L, alanine aminotransferase value more than 42 U/L, lactate dehydrogenase value 229 U/L or more, hemoglobin value less than 110 g/L, uric acid concentration more than 357 μmol/L, blood urea nitrogen concentration more than 8.2 mmol/L, blood creatinine value more than 84 μmol/L, and total bile acid value more than 10 μmol/L.

The frequency of the following fetal clinical findings was evaluated: abnormal systolic-to-diastolic (S/D) ratio of the umbilical artery waveform (S/D ratio ≥3), abnormal fetal heart rate, intrauterine death, and oligohydramnios (defined as an amniotic fluid index of 8 cm or less [17]).

Postpartum maternal outcome measures included disseminated intravascular coagulation, postpartum hemorrhage, postpartum hypertension, postpartum oliguria, and postpartum retinopathy. Postpartum neonatal outcome measures comprised the neonatal birth weight and the incidence rates of low birth weight (small for gestational age, defined as a birth weight below the 10th percentile for the gestational age [11]), a low Apgar score (score of 7 or less at 1 minute), neonatal cardiovascular abnormalities, neonatal infections, neonatal death, neonatal respiratory distress syndrome, neonatal wet lung, neonatal respiratory acidosis, neonatal electrolyte disturbances, neonatal hypoglycemia or hyperglycemia, neonatal cholestasis, neonatal necrotizing enterocolitis, neonatal hypoproteinemia, neonatal anemia, neonatal disseminated intravascular coagulation, neonatal intracranial hemorrhage, neonatal metabolic acidosis, and neonatal bilirubin metabolism disorder.

The participants were divided into a multiple pregnancy group (MP group) and a singleton pregnancy group (SP group). The statistical analyses were carried out with SPSS version 19.0 (IBM, Amonk, NY, USA). The Kolmogorov–Smirnov test was used to evaluate the normality of the distribution of a variable. Differences between continuous variables in the MP and SP groups were tested with the two-sample *t* test for independent samples, whereas differences between categorical variables were tested with the χ^2 test. $P < 0.05$ was considered statistically significant.

3. Results

A total of 100 patients were included. The MP group contained 19 twin pregnancies and two triple pregnancies, with three fetuses dying in utero. Thirteen women had a pregnancy with polyzygotic fetuses achieved by artificial reproductive technology and eight had a spontaneous pregnancy with monozygotic twins. The SP group contained 79 singleton pregnancies, with four fetuses dying in utero. Therefore, 44 fetuses and 41 neonates were evaluated in the MP group, whereas 79 fetuses and 75 neonates were evaluated in the SP group.

There were no statistically significant differences between the two groups in maternal age, length of pregnancy at pre-eclampsia onset and at delivery, and time between onset and delivery (Table 1). All women received regular treatment when they were diagnosed with early-onset pre-eclampsia. The systolic and diastolic blood pressure values on admission were significantly lower in the MP group than in the SP group ($P < 0.05$ for both) (Table 1).

No statistically significant differences between the women in the two groups were seen in terms of prenatal and postpartum clinical findings, with the exception of a significantly higher incidence of pregnancy edema in the MP group than in the SP group ($P = 0.015$) (Table 2). The laboratory findings for women in the two groups were also similar (Table 3).

Table 4 shows the prenatal clinical findings of 44 fetuses in the MP group and 79 fetuses in the SP group. An abnormal S/D ratio and an abnormal fetal heart rate were significantly more common in the SP group than in the MP group ($P < 0.05$ for both). No statistically significant differences were found in the frequency of intrauterine death or oligohydramnios.

The mean neonatal birth weight was significantly higher in the MP group than in the SP group (2043.88 ± 424.88 g vs 1676.33 ± 568.49 g; $P < 0.001$). The frequency of low birth weight, low Apgar score, neonatal cardiovascular abnormalities, and neonatal infections were significantly higher in the SP group than in the MP group ($P < 0.05$ for all) (Table 5). No significant differences between the two groups were found with respect to the other neonatal outcomes investigated.

4. Discussion

The present study explored whether a multiple pregnancy status has beneficial effects on maternal and neonatal outcomes in early-onset pre-eclampsia. The results showed that most of the investigated clinical

Table 1
Characteristics of pregnant women with early-onset pre-eclampsia.[a]

Characteristic	Multiple pregnancies (n = 21)	Single pregnancies (n = 79)	*P* value
Age, y	30.95 ± 4.92	30.73 ± 4.40	0.849
Length of pregnancy at pre-eclampsia onset, wk	31.64 ± 2.79	31.29 ± 2.51	0.584
Time between onset of pre-eclampsia and delivery, d	13.48 ± 15.48	10.59 ± 10.14	0.307
Length of pregnancy at delivery, wk	33.38 ± 1.60	32.65 ± 2.30	0.174
Systolic pressure on admission, mm Hg	135.57 ± 11.99	143.23 ± 14.87	0.032
Diastolic pressure on admission, mm Hg	87.24 ± 5.97	93.61 ± 11.31	0.015

[a] Values are given as mean ± SD unless indicated otherwise.

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