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CLINICAL ARTICLE

Risk factors for cardiopulmonary dysfunction in early-onset severe pre-eclampsia

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ABSTRACT

Objective: To explore associations between patient characteristics and cardiopulmonary function among patients with early-onset severe pre-eclampsia being treated with expectant management. *Method:* The present retrospective study included patients who received expectant management for early-onset pre-eclampsia between January 1 and December 31, 2014 at Shanghai Jiao Tong University School of Medicine, China. Patients were divided into two groups based on cardiopulmonary function, a decompensatory group and a normal group. The clinical characteristics of patients in the two groups were compared by binary logistic regression analysis and using the Student *t* test. *Results:* Data from 93 patients were included in the analysis. Serum creatinine levels ($P = 0.017$), ascites ($P = 0.001$), and increased proteinuria ($P = 0.015$) were associated with decompensation of cardiopulmonary function during early-onset severe pre-eclampsia. Hypoproteinemia was associated with significantly increased odds of ascites occurring (odds ratio 3.16; 95% confidence interval 1.34–7.44) and the mean serum albumin level was higher in patients without ascites ($P < 0.001$). *Conclusions:* Renal insufficiency and ascites were associated with cardiopulmonary dysfunction. Ascites should receive greater medical attention during the expectant management of early-onset severe pre-eclampsia.

1. Introduction

Pre-eclampsia is a multisystem disorder that can be defined as hypertension accompanied by either proteinuria or end-organ dysfunction during pregnancy in previously normotensive women [1]. While expectant management has been proposed to improve neonatal outcomes in early-onset severe pre-eclampsia, delivery of the placenta remains the only definitive treatment [2].

Pre-eclampsia shares many of the same proposed etiologies as cardiovascular disease, including diseased arteries, inflammation, and hyper-coagulability [3,4]. Cardiovascular and pulmonary complications increase the probability of adverse maternal and perinatal outcomes, and tend to be significantly more severe in early-onset pre-eclampsia compared with late-onset pre-eclampsia [5]. Furthermore, pre-eclampsia is correlated with stage B heart failure (asymptomatic left ventricular dysfunction/hypertrophy) [6]. Clinical studies have reported consistent findings regarding the short-term cardiovascular risks associated with pre-eclampsia [7,8]. These risks can manifest several years after delivery, especially following early-onset pre-eclampsia [7,8]. It is important that clinicians ensure that pregnant women do not develop these complications during expectant management.

Some previous studies have also described the characteristics of heart failure or linked cardiovascular impairment to the long-term cardiovascular health of women with pre-eclampsia [9,10]. However, only sporadic case reports have described cardiac or pulmonary dysfunction in pre-eclampsia [11], and even fewer studies have explored how to prevent women from developing pre-eclampsia-associated acute cardiac or respiratory complications.

The aim of the present study was to examine associations between the characteristics of patients with early-onset pre-eclampsia and cardiopulmonary function during expectant management.

2. Materials and methods

The present retrospective study reviewed the medical records of patients with severe pre-eclampsia diagnosed at less than 34 weeks of pregnancy, who received expectant management to prolong their pregnancy. All patients included in the study had been admitted to the Renji Hospital, Shanghai Jiao Tong University School of Medicine, China, between January 1 and December 31, 2014, and severe pre-eclampsia was diagnosed according to the American College of Obstetricians and Gynecologists (ACOG) criteria [1]. Any patients who experienced multiple pregnancies; maternal death; eclampsia; renal failure; hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome; or autoimmune diseases were excluded from

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the analysis to eliminate direct or obvious factors that could cause cardiopulmonary dysfunction. Acute renal failure is correlated with hypoxemia, respiratory distress or increased burden on the heart [12] but no studies have found renal insufficiency to be a cause of cardiopulmonary dysfunction. If any unstable conditions according to ACOG criteria were recorded affecting the mother or fetus during the 48 hours following admission to the study institution, these patients were also excluded from the analysis. The study protocol was approved by the ethics review board of Ren Ji Hospital and each patient provided signed informed consent at admission for their data to be included in studies at a later time.

All patients included in the study received expectant management according to the same protocol. Prophylactic magnesium sulfate was administered during the first 5 days of expectant management, intrapartum, and for 3 days postpartum. All patients received dexamethasone upon hospital admission. Maternal monitoring included blood pressure measurements every 4 hours, a clinical evaluation of symptoms at least twice daily, and a 24-hour urine analysis twice weekly. Antihypertensive drugs including labetalol (Desano, Shanghai, China) and nifedipine (Bayer, Leverkusen, Germany) were used to maintain systolic blood pressure at no higher than 160 mm Hg and diastolic blood pressure below 100 mm Hg. Intravenous nicardipine (Astellas, Liaoning, China) was used as first-line treatment following the failure of oral hypertensive agents for patients with severe hypertension. When necessary, labetalol, nifedipine, and nicardipine were administered together.

Fetal indications for delivery during expectant management were category-III tracings on fetal heart rate monitoring, severe intrauterine growth retardation, intrauterine fetal death, absent or reversed end-diastolic flow on umbilical artery Doppler examination, and oligohydramnios.

Maternal indications for delivery during expectant management were major maternal complications including abruptio placentae, disseminated intravascular coagulopathy, pulmonary edema, severe uncontrolled hypertension despite receiving maximum doses of combined antihypertensive agents (labetalol, nifedipine, and nicardipine), thrombocytopenia (<100 000 cells/μL), and renal insufficiency. Disseminated intravascular coagulopathy was defined as the presence of three or more of the following criteria: low platelet count (<100 000 cells/μL), low fibrinogen (<3 g/L), positive for D-dimers (≥0.5 g/L), or prolonged prothrombin (≥14 seconds) and partial thromboplastin (≥40 seconds) times. Pulmonary edema was diagnosed based on clinical findings and chest radiograph images. Renal insufficiency was diagnosed as the presence of oliguria or anuria associated with an elevated serum creatinine level (>120 μmol/L or >14 mg/L).

Patients were divided into two groups based on cardiopulmonary function (either decompensatory or normal/control) and the clinical characteristics of the two groups were compared. Patients in the compensatory group had stage B or C heart failure, hypoxemia, or respiratory distress. Stage B heart failure is defined as a structural heart disorder without symptoms of end stage disease. Stage C heart failure is defined as previous or current symptoms of heart failure that are being managed medically in the context of structural heart problems [12]. Patients were assigned to the control group if they had pre-eclampsia but were not experiencing any other cardiopulmonary problems.

Data were extracted from the medical records of all patients included in the analysis, and a pre-constructed customized chart was used to collect information regarding each patient's age, any signs indicating intrauterine growth retardation, platelet counts, levels of alanine aminotransferase, plasma albumin, and creatinine, 24-hour urine protein levels, doses of antihypertensive drugs, and signs of pleural effusion and ascites. Blood-test cut-off points for low platelet counts, high alanine aminotransferase, low plasma albumin, and high creatinine levels were set at less than 100 000 cells/μL, a greater than two-fold increase compared with normal concentration, under 28 g/L, and above 11 mg/L, respectively. Ascites were diagnosed using ultrasonography, physical examination, or operation.

A binary logistic analysis and the Student *t* test were used to compare characteristics between the two groups of patients. All data were analyzed using SPSS version 16.0 (SPSS Inc, Chicago, IL, USA) and $P < 0.05$ was considered statistically significant.

3. Results

During the study period, a total of 152 pregnancies were admitted owing to pre-eclampsia and 106 (69.7%) patients were expectantly managed between 17^{+0} weeks and 33^{+5} weeks of pregnancy. All the 106 women received antihypertensive therapy to prevent blood-pressure instability. Multiple pregnancy, maternal death, eclampsia, renal failure, HELLP syndrome, and autoimmune diseases resulted in 13 patients being excluded from the analysis, resulting in a final study

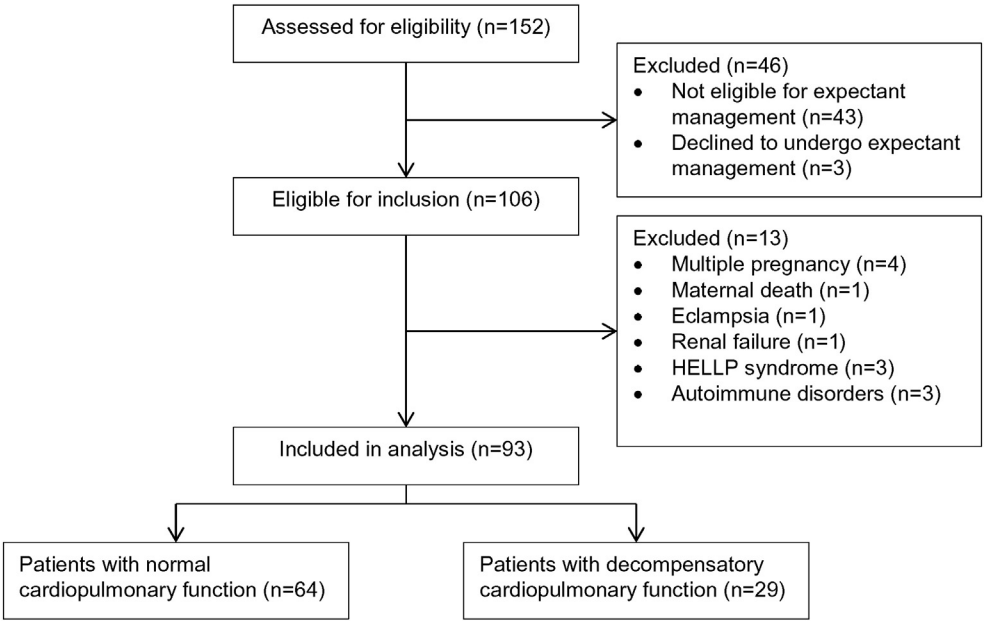

Fig. 1. Flow of patients through the study. Abbreviation: HELLP, hemolysis, elevated liver enzymes, and low platelet count.

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