Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health 7 (2017) 39–43

Contents lists available at ScienceDirect

Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health

journal homepage: www.elsevier.com/locate/preghy

Incidence and pregnancy outcomes of superimposed preeclampsia with or without proteinuria among women with chronic hypertension

Sayuri Nakanishi, Shigeru Aoki *, Ami Nagashima, Kazuo Seki

Perinatal Center for Maternity and Neonate, Yokohama City University Medical Center, Yokohama, Japan

ARTICLE INFO

Article history:
Received 3 October 2016
Received in revised form 13 December 2016
Accepted 9 January 2017
Available online 10 January 2017

Keywords:
Chronic hypertension
Superimposed preeclampsia
Proteinuria
Diagnostic criteria

ABSTRACT

Objective: To investigate the incidence and pregnancy outcomes of superimposed preeclampsia (PE) with or without proteinuria among women with chronic hypertension.
Methods: This retrospective study included 142 women with essential hypertension diagnosed at ⩽20 weeks of gestation, managed at a tertiary center. They were divided into three groups (non-PE, PE with proteinuria, and PE without proteinuria) to compare pregnancy outcomes. The non-PE group was further divided into two subgroups (controlled and uncontrolled hypertension).
Results: There were 87 women in the non-PE group, 47 in the PE with proteinuria group, and 8 in the PE without proteinuria group. Median gestational age at delivery was 38.7 weeks in the non-PE group, 30.4 in the PE with proteinuria group, and 28.4 in the PE without proteinuria group. In three of the women in the PE without proteinuria group, the diagnostic criteria were fulfilled by liver involvement (complicated by thrombocytopenia in one woman). The remaining five women had uteroplacental dysfunction. The 87 women in the non-PE group were divided into a controlled hypertension subgroup of 75 women and uncontrolled hypertension subgroup of 12. The median gestational age at delivery was 39.1 weeks in the controlled HT subgroup and 34.1 weeks in the uncontrolled hypertension subgroup. The pregnancy outcomes were significantly poorer in the latter group.
Conclusion: Pregnancy outcomes were unfavorable in both the PE without proteinuria and PE with proteinuria groups. Women with non-PE uncontrolled hypertension also had poor pregnancy outcomes, although their outcomes were better than those of women with PE.

1. Introduction

Hypertensive disorders in pregnancy are potentially serious complications, associated with maternal and perinatal mortality. They occur in 5%–10% of all pregnancies [1–3]. Nevertheless, no uniform classification or diagnostic criteria for hypertensive disorders in pregnancy have been established [4,5].

Traditionally, proteinuria was considered the hallmark for the diagnosis of preeclampsia (PE), because it usually develops after the onset of hypertension and/or onset of symptoms. However, its onset in clinical practice may be variable in relation to hypertension and/or other end-organ effects. Therefore, its presence should not be considered mandatory to establish the clinical diagnosis of PE [6].

For these reasons, the American College of Obstetricians and Gynecologists (ACOG) changed its diagnostic criteria for PE in 2013 on the basis of alternative systemic findings revealing that new-onset hypertension can fulfill the diagnosis of PE even in the absence of proteinuria as follows: PE is diagnosed even in pregnant women without proteinuria if they present with any of thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, or cerebral or visual symptoms [7].

In 2014, the International Society for the Study of Hypertension in Pregnancy (ISSHP) revised the definition of PE as a combination of hypertension developing at or after the 20th week of gestation and one or more of the following conditions: 1) proteinuria, 2–1) renal insufficiency, 2–2) liver involvement, 2–3) neurological complications, 2–4) hematological complications, and 3) uteroplacental dysfunction [5].

According to these changes, pregnant women with chronic hypertension will be diagnosed as having PE superimposed on chronic hypertension if they present with one or more of the following conditions: proteinuria, renal insufficiency, liver involve-

* Corresponding author at: Perinatal Center for Maternity and Neonate, Yokohama City University Medical Center, 4-57 Urafunecyou, Minami-ku, Yokohama City, Kanagawa 232-0024, Japan.
E-mail address: smyyaoki@yahoo.co.jp (S. Aoki).

http://dx.doi.org/10.1016/j.preghy.2017.01.001
2210-7789/

ment, neurological complications, hematological complications, or uteroplacental dysfunction [5]. However, we have not found any reports on the incidence of PE superimposed on chronic hypertension without proteinuria, which is not mentioned in the conventional diagnostic criteria, as well as pregnancy outcomes.

This study aimed to compare the incidence rates and pregnancy outcomes among the three groups, the non-PE group, PE with proteinuria group, and PE without proteinuria group, and to evaluate the validity of the diagnostic criteria for PE superimposed on chronic hypertension without the requirement for proteinuria.

2. Methods

This study included 142 women who delivered neonates at the Perinatal Center for Maternity and Neonate of Yokohama City University Medical Center between April 2000 and March 2015, and who had been diagnosed as having hypertension before conception or developed essential hypertension with a blood pressure of ⩾140/90 mmHg before the 20th week of gestation. Those with multiple pregnancy or fetal abnormalities were excluded. Using the institutional perinatal database, their medical charts were retrospectively reviewed. This study has been approved by the ethics committee of the Yokohama City University Medical Center (B160600003)

The 142 women with chronic hypertension were divided into three groups: the non-PE, PE with proteinuria, and PE without proteinuria groups. The PE with proteinuria group included women with hypertension diagnosed before the 20th week of gestation and proteinuria of ⩾300 mg/day first detected after 20 gestational weeks. The PE without proteinuria group included women negative for proteinuria who had been diagnosed as having hypertension before the 20th week of gestation and concurrently had renal insufficiency, liver involvement, neurological complications, hematological complications, or uteroplacental dysfunction. Renal insufficiency was defined as a serum creatine concentration of >1.1 mg/dL; liver involvement as elevated transaminases and/or severe right upper quadrant or epigastric pain; neurological complications as eclampsia, altered mental status, blindness, stroke, hyperreflexia accompanied by clonus, severe headaches accompanied by hyperreflexia, or persistent scotoma; hematological complications as thrombocytopenia (<100,000/μL), disseminated intravascular coagulation, or hemolysis; and uteroplacental dysfunction as fetal growth restriction (FGR) due to placental insufficiency that resulted in termination of the pregnancy. The non-PE group included women who did not fulfill the diagnostic criteria for PE. Because some women developed hematological complications after delivery, diagnoses were made with data available at the time of delivery.

Women with the following conditions were hospitalized for treatment of chronic hypertension: novel onset of proteinuria during outpatient care, poorly controlled blood pressure, or FGR due to suspected uteroplacental dysfunction. After admission, the patients were monitored for blood pressure and urine excretion every 4–6 h at the maternal fetal intensive care unit. Full blood counts, coagulation profiles, liver functions, creatinine clearance, and urinary protein levels were measured 2–3 times per week. For fetal monitoring, non-stress tests (NSTs) were performed twice daily. When the attending physician determined NST assessment to be insufficient, biophysical profile scores were determined daily. Moreover, ultrasound assessment of fetal growth and amniotic fluid index measurement were performed 2–3 times per week. In order to achieve a target blood pressure of 140/90 mmHg, oral hydralazine or oral methyldopa was used as the first-line antihypertensive drug while intravenous hydralazine or continuous intravenous nicardipine was used as the second-line drug if the first-line drugs provided an insufficient effect. In patients requiring urgent blood pressure reduction, antihypertensive therapy was initiated with the second-line drugs. When women were expected to go into labor within one week before 34 gestational weeks, betamethasone was administered to accelerate fetal lung maturation [8]. Delivery was performed when the following symptoms were detected during expectant management or at 34 gestational weeks. Maternal indications for termination of pregnancy included: 1) failure of blood pressure control despite administration of antihypertensive medications at adequate doses, 2) eclampsia and hypertensive encephalopathy manifesting as visual disturbance, cortical blindness, and persistent severe headache 3) HELLP syndrome, 4) pulmonary edema, 5) acute renal failure (serum creatinine: baseline value +1), and 6) placental abruption. Fetal indications for termination of pregnancy included: 1) abnormal fetal heart rate showing repeated late decelerations or severe variable decelerations in the form of traditional NST, 2) biophysical profile score ⩽4 and 3) reversed end-diastolic flow in the umbilical artery at or after 32 gestational weeks. In all women diagnosed as having severe superimposed PE at or after 34 gestational weeks, their pregnancies were terminated at the time of diagnosis regardless of the presence or absence of proteinuria.

Maternal characteristics and pregnancy outcomes were compared among the non-PE, PE with proteinuria, and PE without proteinuria groups. In addition, the non-PE group was further divided into the following subgroups for the comparison of pregnancy outcomes: the controlled HT subgroup that included women with well-controlled blood pressure during pregnancy, and the uncontrolled HT subgroup that included women with poorly controlled blood pressure resulting in induced preterm delivery.

The data are presented as medians (range) or frequencies (percentage). IBM SPSS Statistics 24 was used for statistical analyses. We applied the Mann-Whitney *U* test and Kruskal-Wallis test for determining coefficients of variation. Fisher's exact tests were used to detect differences in categorical data by group. The level of statistical significance was set at $P < 0.05$.

3. Results

Table 1 shows the maternal characteristics for the three groups. There were 87 women (61.3%) in the non-PE group, 47 (33.1%) in the PE with proteinuria group, and eight (5.6%) in the PE without proteinuria group. Of the 142 women, 55 (38.7%) were diagnosed as having PE superimposed on chronic hypertension. Of the eight women in the PE without proteinuria group, three had liver involvement, with one of the three having concomitant thrombocytopenia. In the remaining five women, whose blood pressure had been well controlled, their pregnancies were terminated because of FGR caused by uteroplacental dysfunction. No women in the PE without proteinuria had either renal insufficiency or neurological complications. In the PE with proteinuria group, renal insufficiency, liver involvement, neurological complications, and hematological complications all occurred at the onset of proteinuria or during expectant management, whereas no women developed any of these symptoms before the onset of proteinuria. Although systolic blood pressure during the early gestational period was higher in the PE with and without proteinuria groups than in the non-PE group ($P = 0.024$), no significant differences were observed in any other maternal characteristics between the three groups.

Table 2 shows the pregnancy outcomes for the three groups. The gestational age at delivery was 38.7 weeks in the non-PE group, 30.4 weeks in the PE with proteinuria group, and 28.4 weeks in the PE without proteinuria group. The PE without proteinuria group showed the smallest gestational age, which contributed to the high frequency of delivery before 28 and 34 weeks of gestation. However, no statistically significant difference was observed between the PE with and without proteinuria groups