Contents lists available at ScienceDirect

International Journal of Cardiology

Metabolic syndrome in the non-pregnant state is associated with the development of preeclampsia☆

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ARTICLE INFO

ABSTRACT

Background: The aim of this study was to investigate the association between metabolic syndrome in the non-pregnant state and the development of preeclampsia.
Methods: We enrolled 212,463 Korean women who had their first delivery between January, 2011 and December, 2012 and had undergone a national health screening examination through the National Health Insurance during the 1–2 years before their first delivery. Women who had hypertension in the non-pregnant state were excluded. The presence of metabolic syndrome was defined using the modified criteria published in National Cholesterol Education Program Adult Treatment Panel III criteria.
Results: The prevalence of metabolic syndrome in non-pregnant state was 1.2%. Preeclampsia developed in 3.1% and its prevalence among women with and without metabolic syndrome was 7.3% and 3.0%, respectively.
The pre-pregnancy prevalence of metabolic syndrome was higher in women who developed preeclampsia compared to that in those who had a normal pregnancy (1.1% vs. 2.8%; p < 0.001). On multivariate regression analysis, women with metabolic syndrome had an increased risk of developing preeclampsia (odds ratio: 1.48; 95% CI: 1.26 to 1.74) compared to that in those without metabolic syndrome, after adjusting for age, family history of hypertension, smoking status, and pre-pregnancy body mass index. The risk of preeclampsia increased with a rise in the number of components of metabolic syndrome.
Conclusion: Metabolic syndrome in the non-pregnant state was associated with the development of preeclampsia. Further studies are needed to evaluate whether early intervention for metabolic syndrome before pregnancy can decrease the risk of developing preeclampsia.

1. Introduction

Preeclampsia, a disorder of pregnancy characterized by hypertension (HTN) after 20 weeks' gestation combined with proteinuria, affects 5–8% of pregnancies and is associated with increased risk for adverse pregnancy outcomes, including placental abruption, prematurity, and intrauterine growth restriction (IUGR) [1,2,3]. Although HTN typically resolves in the postpartum period, women with preeclampsia have a higher risk of ultimately developing HTN [4,5]. Women with a history of preeclampsia are also at risk for future diabetes mellitus (DM), cardiovascular disease (CVD), stroke, and overall increased mortality [4,5,6,7].

Metabolic syndrome is a clustering of metabolic abnormalities that increase the risk for the above conditions [8,9,10]. Most studies reported that women affected by preeclampsia had an increased risk of developing metabolic syndrome after delivery, [11,12] suggesting a role in the pathophysiology linking preeclampsia to long-term CVD [12]. However, these studies did not evaluate whether metabolic syndrome exists before index pregnancy due to lack of data on pre-pregnancy metabolic health.

A growing body of literature reports that pre-pregnancy factors are associated with the development of preeclampsia. These include obesity, HTN, dyslipidemia, insulin resistance, and hyperglycemia, which are components of metabolic syndrome [13,14,15,16,17,18]. Ray et al. also reported that women who exhibit features of metabolic syndrome before pregnancy have a higher graded risk for placental disorders,

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including hypertensive pregnancy disorders, placental abruption, and placental infarction [19]. However, little is known about the association between metabolic syndrome in the non-pregnant state and the development of preeclampsia in a future pregnancy. Therefore, in this study, we investigated the association between metabolic syndrome in the non-pregnant state and the development of preeclampsia.

2. Methods

2.1. Health care delivery system in Korea

Year 2000, the health insurance systems in South Korea was merged into a single system run by the National Health Insurance(KNHI). Consequently, nearly all people living in South Korea are insured by the KNHI.

Study data were collected from the Korea National Health Insurance Service(KNIS) Claims Database for 2006–2010. In Korea, 97% of the population is required to enroll in the KNHI program. The remaining 3% of the population is under the Medical Aid Program. Thus, the Health Insurance Review and Assessment(HIRA) database contains information on all claims for approximately 50 million Koreans, and nearly all information about the extent of disease can be obtained from this centralized database, with the exception of procedures not covered by insurance, such as cosmetic surgery.

As part of the NHIS health-care system, all insurance subscribers and dependents are invited to participate in national health screening examination (NHSE) once every two years free of charge. The data was provided for the study after it had been de-identified. This study was approved by the Institutional Review Boards of Korea University Medical Center (KUGH15066).

2.2. Study population

Fig. 1 illustrates the inclusion and exclusion of study participants. Using the NHIC database, we identified all women who had their first delivery between January 1, 2011 and December 31, 2012. Among these, women were included in the analysis if they had an NHSE during the 1–2 years before their first delivery, to evaluate pre-pregnancy characteristics.

Preeclampsia during the first pregnancy was identified as a principal or secondary diagnosis using the International Classification of Diseases—10th Revision (ICD-10 codes O12.0, O12.1, O12.2, O13, O14, O14.0, O14.1, O14.2, O14.9, O15, O15.0, O15.1, O15.2, O15.9).

2.3. Measurement of pre-pregnancy characteristics

Pre-pregnancy factors were evaluated using the NHSE data. The NHSE consists of 2 components: a health interview and health examination.

The health interview included questions regarding demographic, socioeconomic, and lifestyle status. Data for the following covariates were obtained: age, smoking status, and exercise level. Smoking status was divided into 3 categories: current smoker, past smoker, and never a smoker, based on the answers to "Have you ever been a smoker?", and "If yes, do you smoke currently?" Exercise was categorized by the frequency of full-body, sweaty exercise in a week: no exercise, 1–2 exercise sessions, 3–4 exercise sessions, or ≥5 exercise sessions.

Health examination included the body mass index ([BMI] in kilograms per square meter). Obesity was defined as BMI ≥25 kg/m^2, which was adopted from the cutoffs established for Korean adults as proposed by the Korean Society for the Study of Obesity [20]. Waist circumference (WC) was measured at the narrowest point between the lower border of the rib cage and the iliac crest during minimal respiration. Blood pressure (BP) was measured using a standard mercury sphygmomanometer.

All blood samples were obtained after a minimum fast of 8 h. The levels of fasting glucose, total cholesterol, triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were measured with a Hitachi 747 Autoanalyzer (Hitachi Instruments Inc., Tokyo, Japan) by using enzymatic methods.

Women with a diagnosis of unrecognized HTN, defined as BP ≥140/90 mm Hg at NHSE (n = 2376), were excluded, after the exclusion of patients with previously known HTN (n = 321).

2.4. The definition of metabolic syndrome

The presence of metabolic syndrome was defined using the National Cholesterol Education Program Adult Treatment Panel III criteria [10].
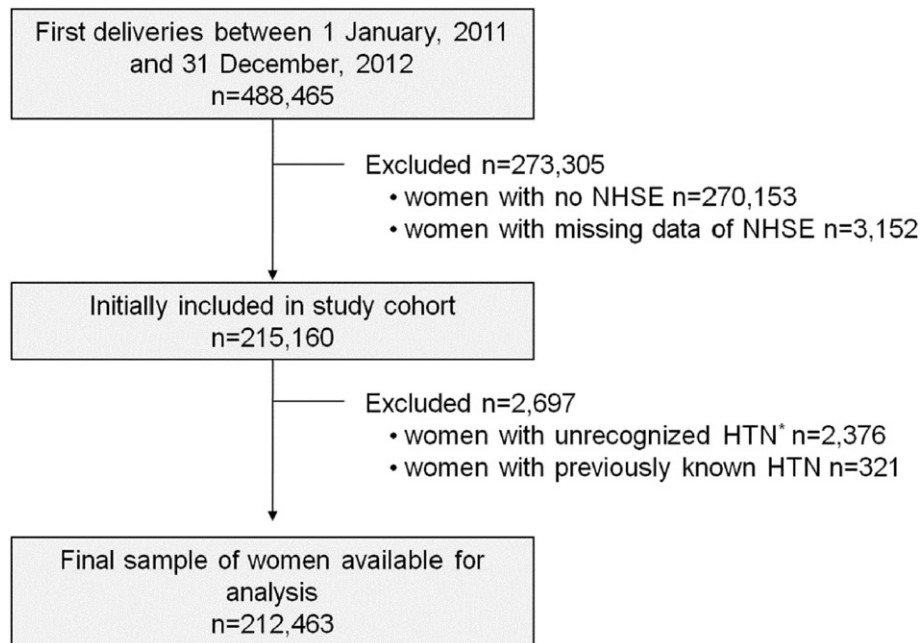

Fig. 1. Cohort flow chart illustrating the inclusion and exclusion of participants. NHSE, National Health Screening Examination. *Newly diagnosed hypertension when BP ≥140/90 mm Hg at NHSE, after the exclusion of patients with previously known hypertension.