OBSTETRICS

Prepregnancy body mass index, hypertensive disorders of pregnancy, and long-term maternal mortality

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OBJECTIVE: Recent studies have shown increased maternal mortality rates after hypertensive disorders of pregnancy (HDP), but the reasons for this increase remain unclear. This study examines the relationship between elevated prepregnancy body mass index (BMI), HDP, and postpregnancy mortality.

STUDY DESIGN: Data came from a 1975-1976 subset (n = 13,722 women) of a population-based cohort. Multiple logistic regression was used to examine the risk of HDP by BMI; age-adjusted Cox proportional hazards models were used to examine survival rates.

RESULTS: Overweight (BMI, 25-29.9 kg/m²) and obesity (BMI, \geq 30 kg/m²) were associated with increased HDP (odds ratio [OR], 2.82; 95% confidence interval [CI], 2.40-3.31 and OR, 5.51; 95% CI, 4.15-7.31]) and decreased survival (hazard ratio [HR], 1.42; 95% CI, 1.10-1.83 and HR, 2.43; 95% CI, 1.61-3.68), compared with normal weight

(BMI, 18.5-24.9 kg/m²). HDP was significantly associated with increased mortality rates for women who survived >15 years (HR, 1.94; 95% CI, 1.42-2.67]; HR adjusted for BMI, 1.65; 95% CI, 1.19-2.79]). A greater increase in risk of death after HDP was seen in the overweight women (HR, 1.86; 95% CI, 1.07-3.20) and obese women (HR, 2.90; 95% CI, 1.28-6.58), compared with normal weight women (HR, 1.26; 95% CI, 0.74-2.14).

CONCLUSION: Elevated prepregnancy BMI is associated with increased risk of HDP, which are in turn is associated with increased long-term maternal mortality rates. This association between HDP and mortality rates increases with elevated prepregnancy BMI.

Key words: body mass index, hypertensive disorders of pregnancy, maternal mortality

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Hypertensive disorders of pregnancy complicate between 6-8% of all pregnancies and are the second leading cause of maternal death.¹ Although early reports argued that there were no adverse maternal health consequences after delivery of a pregnancy that was complicated by hypertensive disease, more recent studies have shown elevated mortality and morbidity rates,

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0002-9378/\$32.00 © 2007 Mosby, Inc. All rights reserved. doi: 10.1016/j.ajog.2007.04.043 particularly from cardiovascular causes.²⁻⁴ For example, in this cohort, long-term mortality rates have been shown to be significantly elevated after delivery of a pregnancy that is complicated by preeclampsia (relative risk, 2.1; 95% confidence interval [CI], 1.8-2.5), with deaths from cardiovascular disease as the strongest contributor.² Similar findings have been reported in other studies,³ and additional associations have been reported between preeclampsia and subsequent maternal cardiovascular disease.4-8

Hypertensive disorders of pregnancy have been associated with a variety of metabolic abnormalities that are also known risk factors for cardiovascular disease including higher waist circumference, waist/hip ratio, body mass index (BMI), serum insulin level, and lower glucose/insulin ratio.⁹ Without information on the prepregnancy metabolic status, however, it is difficult to tell whether the subsequent development of cardiovascular disease in women who previously have had a hypertensive pregnancy is a result of pathologic events that occurred during the pregnancy or a result of preexisting risk factors. To further explore this issue, we chose to focus on a single risk factor that can be measured easily before pregnancy, namely BMI.

Elevated prepregnancy BMI has been linked to a variety of pregnancy complications^{10,11} that include preeclampsia.¹²⁻¹⁷ A systematic review calculated that an increase in BMI of between 5-7 kg/m² was associated with a doubled risk of preeclampsia.¹⁸ Elevated BMI has also been linked to increased morbidity and death from cardiovascular disease.^{19,20} However, the relationship between BMI, hypertensive disorders of pregnancy, and death has not been well-characterized. We examined the association between prepregnancy BMI, hypertensive disorders of pregnancy, and subsequent maternal death.

MATERIALS AND METHODS Cohort

The Jerusalem Perinatal Study is a population-based cohort of consecutive births to Israeli residents of urban Jerusalem and the surrounding rural county from 1964-1976. This dataset has been described in detail previously.^{2,21} This analysis used data on a subset of Jewish women who delivered between 1975-1976 who were interviewed about their prepregnancy weight and height. Hypertensive disorders of pregnancy were defined as gestational hypertension or preeclampsia. Gestational hypertension was defined as a systolic blood pressure of ≥ 140 mm Hg or a diastolic blood pressure of \geq 90 mm Hg. On the basis of well-recognized clinical criteria, preeclampsia was defined as gestational hypertension with $\geq 1 +$ proteinuria and edema. Preexisting chronic hypertension was coded under a separate rubric.

Long-term follow-up evaluation of the women was conducted by linking the personal identification numbers of the subjects to national registries. In the original follow-up evaluation, 92% of the women were traced successfully.² The numbers were validated with the use of the Population Registry of Israel, with the approval of the institutional review boards in New York and Jerusalem and the authorities at Israel's Ministry of Health and Ministry of the Interior. The study was exempted from the requirement for written informed consent.² The current analysis examines a subgroup of these women and was approved by the Human Investigation Committee at Yale University.

Data analysis

The final analysis was restricted to women who had survived to 1978 and for whom data on prepregnancy BMI had been recorded (n = 13,722). Multiple logistic regression was used to examine the association between hypertensive disorders of pregnancy (HDP) and BMI and to compute the odds ratio and 95% CI. A BMI of $<18.5 \text{ kg/m}^2$ was considered to be underweight, 18.5-24.9 kg/m² was considered to be normal weight, 25-29.9 kg/m² was considered to be overweight, and $\geq 30 \text{ kg/m}^2$ was considered to be obese.²² HDP were defined as a history of preeclampsia or gestational hypertension in the index pregnancy and/or past pregnancies. The results were unchanged by restriction of the analysis to women who had preeclampsia or gestational hypertension only in the index pregnancy.

Survival was examined with multivariate Cox proportional hazards models and the computation of the hazard ratio (HR) and the 95% CI. Survivors were censored on January 1, 2005. Because of a change in the hazard function over time, we constructed 2 models: 1 model for women who survived <15 years and 1 model for women who survived ≥ 15 years. Schoenfeld residuals were used to ensure the validity of the proportional hazards assumption. Age was modeled as a continuous variable, based on the mother's age at the index pregnancy. Adjustment for parity did not change the results significantly.

Survival analysis was used to examine the risk of death by BMI category, the risk of death after HDP, and how the risk of death after HDP changed after adjustment for prepregnancy BMI. In addition, we modeled the HR for death after HDP for women in each BMI category separately.

RESULTS **Characteristics of the cohort**

Demographic characteristics of the population are summarized in Table 1. Of the 13,722 women in the cohort, 30.5% were having their first birth; 45.3% were having their second to third birth; 19.6% were having their fourth to fifth birth, and 4.6% were having their seventh birth or more. The following statistics were calculated for the cohort: 1.2% of the mothers had no formal education; 61.1% had 1-12 years of education; 37.7% had \geq 13 years of education; 99.5% were married at the time of the interview; 46.2% were immigrants: of these, 12% were from Western Asia, 15.9% were from North Africa, and 18.3% were from Western Europe.

BMI and HDP

Figure 1 shows the association between prepregnancy BMI and HDP. As expected, there was an increasing prevalence of HDP with increasing BMI. Compared with the reference category of normal weight, overweight women showed nearly a 3-fold excess; those women who were obese showed more than a 5-fold excess of HDP. The crude prevalence rates of HDP were 3.3% and 5.3% for underweight and normal weight, compared with 14.8% and 26.9% for women who were overweight and obese, respectively. After adjustment for age, the odds ratios were 0.67 (95% CI, 0.48-0.92) for underweight, 1 for normal weight (reference category), 2.82 (95% CI, 2.40-3.31) for overweight, and 5.51 (95% CI, 4.15-7.31) for obese women.

BMI and mortality risk

Figure 2 shows the HRs for subsequent maternal death by categories of prepregnancy BMI. Compared with women who were of normal weight before pregnancy, those women who were overweight showed a 42% increase in subsequent death and those women who were obese Download English Version:

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