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Interpregnancy Body Mass Index Changes and Risk of Stillbirth

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Key Words
Body mass index · Obesity · Pregnancy · Stillbirth

Abstract
Background/Aims: To examine the association between interpregnancy body mass index (BMI) change and stillbirth. ***Methods:*** Retrospective study using Missouri maternally linked cohort files (1978–2005). A total of 218,389 women were used in the analysis. BMI was classified as: underweight (<18.5), normal (18.5–24.9), overweight (25–29.9), or obese (≥30.0). Weight change was defined based on BMI category (i.e. normal-normal, normal-obese, etc.). Cox proportional hazard regression models were used to generate adjusted hazard ratios (HR) and 95% CI for the risk of stillbirth in the second pregnancy. ***Results:*** Significant findings were associated with interpregnancy BMI changes involving overweight mothers becoming obese (HR = 1.4, 95% CI 1.1–1.7), normal-weight mothers becoming overweight (HR = 1.2, 95% CI 1.0–1.4) or obese (HR = 1.5, 95% CI 1.1–2.1), or obese mothers maintaining their obesity status across the two pregnancies (HR = 1.4, 95% CI 1.2–1.7). Other weight change categories did not show significant risk elevation for stillbirth. ***Conclusions:*** BMI change appears to play an important role in subsequent stillbirth risk.

Introduction

An increasing number of studies are reporting links between prepregnancy body mass index (BMI) and pregnancy outcomes, including stillbirth and neonatal death [1, 2]. Most notably, previous authors have reported an association between maternal obesity and an increased risk of both immediate and long term adverse outcomes for the developing fetus and mother [3–7]. The risk of stillbirth follows a similar pattern whereby overweight and obese women are more likely to have a stillbirth than their normal weight counterparts [1, 8]. Previous studies also suggest that attaining a normal BMI before pregnancy may considerably decrease the risk of stillbirth [1, 8, 9]. However, to our knowledge few studies have examined interpregnancy BMI changes in relation to stillbirth. Villamor and Cnattingius [10] found that women whose interpregnancy BMI increased by 3 or more points were 63% more likely to have a stillbirth than those whose BMI remained relatively stable. Nonetheless, it is unclear whether the reported increases in BMI actually caused a woman to have an unhealthy weight.

A better understanding of the role of suboptimal BMI in adverse pregnancy outcomes is critical to planning tar-

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geted interventions, especially in light of the recent obesity epidemic [11]. Consequently, we seek to examine the risk of stillbirth in relation to interpregnancy BMI changes using a large-population-based data file.

Materials and Methods

The Missouri maternally linked cohort data file from 1978 to 2005 was used for this investigation. Previous detailed reports have expounded on the methods and algorithm used to link infant data to maternal sibling records and the validation of the linkage [12]. The Missouri vital record system is considered a gold standard in the validation of national datasets that involve matching and linking, as it has been proven to be both reliable and valid [13].

A total of 218,389 women with their first two successive singleton pregnancies in the database were used in this retrospective cohort analysis. Only births that occurred between 20 and 44 weeks of gestation were eligible for inclusion. Change in maternal body mass index (BMI) was the main exposure of interest. BMI was defined as weight in kilograms (kg) divided by height in square meters (kg/m^2). Maternal height was derived from that recorded at the first prenatal visit and prepregnancy weight as reported by the mother at the first prenatal visit of each pregnancy [14]. BMI categories were assigned based on the following Institute of Medicine (IOM) guidelines: <18.5 (underweight), 18.5–24.9 (normal weight), 25–29.9 (overweight), and ≥30.0 (obese) [15]. Maternal interpregnancy weight change categories were created using the 1st and 2nd prepregnancy BMI groups. For example, a woman who was overweight before her first pregnancy and normal weight in her second was categorized as overweight-normal.

A stillbirth, in the second pregnancy was the main outcome of interest. First pregnancies that resulted in stillbirth were excluded from the study. Stillbirth was defined as intrauterine fetal demise at ≥20 gestational weeks.

Common maternal sociodemographic variables were assessed and compared at baseline of the second pregnancy for each BMI category. These included the following: maternal age, race, education, marital status, prenatal smoking, alcohol use during pregnancy, adequacy of prenatal care, second pregnancy BMI and the interval between both pregnancies lasting at least 20 weeks. Interpregnancy interval was calculated as the interval between birth of the first and second child minus the gestational age of the second child. It was grouped as 1st (<1.1 years), 2nd (1.1–1.9 years), 3rd (1.9–3.1 years), and 4th (>3.1 years) quartiles [16].

The revised graduated index algorithm is a means of describing the level of prenatal care utilization among pregnant women, especially in high-risk populations [17, 18]. The index assesses the adequacy of care based on the trimester of prenatal care initiation, the number of visits and the gestational age of the infant at birth. Inadequate prenatal care was defined as: missing prenatal care information, suboptimal prenatal care, or no prenatal care.

Differences in maternal socio-demographic characteristics across BMI categories were analyzed using the χ^2 test. We applied Cox proportional hazard regression models to estimate risks for stillbirth. Adjusted hazard ratios (HR) and 95% CI were generated. Hazards ratios were obtained after confirming the nonviolation of the proportionality assumption. We confirmed this by plotting the log-negative-log of the Kaplan-Meier estimates of the survival function versus the log of time [19]. The results were parallel. Adjusted hazards ratios were derived by including all of the following covariates in the model: maternal age, race, education, marital status, prenatal smoking, alcohol use, prenatal care, interpregnancy interval, obstetric complications (pre-eclampsia and diabetes) year of birth and gender of the infant. Maintenance of normal BMI between the first and second pregnancies (normal-normal) was set as the referent category.

All tests of hypothesis were two-tailed with a type 1 error rate set at 5%. Statistical analysis was performed using SAS version 9.2 (SAS Institute, Cary, N.C., USA). The study was approved by the Institutional Review Board at the University of South Florida.

Results

From 1978 to 2005, 1,291,444 records of singleton live births were available for analysis. We excluded 244,585 (18.9%) records that were not the first two successive singleton births for each mother. An additional 59,016 (4.6%) pregnancies were outside the range of 20–44 weeks of gestation and were thus excluded from analysis. Of the remaining, 80,199 (6.2%) records were excluded because sib-ships could not be identified and 34,088 (2.6%) were missing BMI values. This left a total of 436,778 sibling-pairs for the analysis.

Crude frequency comparisons for common maternal socio-demographic characteristics in the second pregnancy were calculated. Compared to mothers in higher BMI categories, normal BMI mothers tended to be white, younger, married and were more educated ($p < 0.001$). Conversely, mothers with a high BMI were more likely to use alcohol during pregnancy and also to have a longer duration between pregnancies when compared to mothers of lower BMI categories ($p < 0.001$).

We assessed the association between maternal second prepregnancy BMI and stillbirth. When compared to mothers with a normal BMI, mothers of all other BMI categories were more likely to experience a stillbirth in the second pregnancy ($p < 0.0001$). With a 40% increased risk, obese mothers had the greatest threat for stillbirth (adjusted HR = 1.4, 95% CI 1.2–1.6).

The association between maternal interpregnancy BMI changes and stillbirth is shown in table 1. Significant findings were associated with, interpregnancy BMI changes involving overweight mothers becoming obese (HR = 1.4, 95% CI 1.1–1.7), normal-weight mothers becoming overweight (HR = 1.2, 95% CI 1.0–1.4), or obese (HR = 1.5, 95% CI 1.1–2.1), or obese mothers maintaining

Table 1. Association between maternal prepregnancy BMI changes and stillbirth in the second pregnancy, Missouri, USA, 1978–2005

First pregnancy BMI	Second pregnancy BMI	Number of nonstillbirths n = 430,225 (%)	Number of stillbirths n = 1,513 (%)	Stillbirth adjusted HR (95% CI)
Obese	obese	29,144 (6.77)	137 (9.05)	1.4 (1.2–1.7)
Overweight	obese	20,220 (4.70)	90 (5.95)	1.4 (1.1–1.7)
Normal weight	obese	9,074 (2.11)	47 (3.11)	1.5 (1.1–2.1)
Underweight	obese	214 (0.05)	2 (0.13)	2.6 (0.7–10.6)
Obese	overweight	3,419 (0.79)	13 (0.86)	1.2 (0.7–2.0)
Overweight	overweight	30,414 (7.07)	106 (7.01)	1.1 (0.9–1.3)
Normal weight	overweight	43,130 (10.02)	168 (11.10)	1.2 (1.0–1.4)
Underweight	overweight	910 (0.21)	6 (0.40)	1.9 (0.9–4.3)
Obese	normal weight	901 (0.21)	4 (0.26)	1.4 (0.5–3.7)
Overweight	normal weight	8,783 (2.04)	39 (2.58)	1.4 (1.0–1.9)
Normal weight	normal weight	223,654 (51.99)	694 (45.87)	referent
Underweight	normal weight	23,640 (5.49)	72 (4.76)	1.0 (0.8–1.2)
Obese	underweight	62 (0.01)	0	–
Overweight	underweight	150 (0.03)	1 (0.07)	2.0 (0.3–13.9)
Normal weight	underweight	10,676 (2.48)	43 (2.84)	1.3 (0.9–1.7)
Underweight	underweight	25,864 (6.01)	91 (6.01)	1.1 (0.9–1.4)

their obesity status across the two pregnancies (HR = 1.4, 95% CI 1.2–1.7). Other weight change categories did not show significant risk elevation for stillbirth.

Comment

Our study confirmed earlier reports that a prepregnancy BMI indicative of being overweight or obese increased the risk of stillbirth [1, 8]. With the exception of women who were underweight prior to their first pregnancy, increases in prepregnancy BMI between two successive pregnancies resulted in an overall elevated risk of stillbirth, with the highest risk of stillbirth occurring among women with a BMI that changed from normal to obese between two consecutive pregnancies. Obese women that maintained their BMI status for both pregnancies also had an elevated risk of stillbirth compared to their normal weight counterparts (HR = 1.4, 95% CI = 1.2, 1.7). Villamor and Cnattingius [10] found that an interpregnancy BMI change of 3 or more units increased the risk of stillbirth (HR = 1.63, 95% CI = 1.20, 2.21). Our study confirms these findings and adds additional strength by expanding the sample size and examining BMI changes in a different way.

Our results suggested that weight loss had little impact on risk of stillbirth. Many factors could have contributed to this lack of association including the fact that only a small percentage of women experienced stillbirth in any of the weight loss categories. Our results may have been further affected since distinction of type of weight loss (voluntary or involuntary) was not known.

The strengths of our study lie in its large sample size and ability to control for numerous potential confounders. Several limitations of this study also merit mention. Since this study was based on vital statistics data, differential reporting of maternal prepregnancy height and weight measures may have occurred. However, McAdams et al. [20] found that self-reported measures can provide accurate information for obesity related diseases. Underreporting of prepregnancy weight could have caused an underestimation of the calculated BMI, and would most likely occur among obese women [21, 22]. Additionally, differences in sample size regarding each interpregnancy BMI category may have affected our results. It is likely that these differences could have either overestimated or underestimated the true association between interpregnancy BMI change and risk of stillbirth.

Our findings suggest that a prepregnancy obese or overweight BMI increases the risk of stillbirth; however, this association does not seem to be robust due to the differences in stillbirth prevalence in each weight change category. More studies are needed to delineate the nature of the relationship between interpregnancy BMI change and adverse pregnancy outcomes. However, the findings in this study are important for counseling purposes by obstetric care providers as they increasingly encounter obese women in an era of growing obesity epidemic.

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