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Stillbirth, Inflammatory Markers, and Obesity: Results from the Stillbirth Collaborative Research Network

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Abstract

Background—Obesity is associated with increased risk of stillbirth, although the mechanisms are unknown. Obesity is also associated with inflammation. Serum ferritin, C-reactive protein, white blood cell count, and histologic chorioamnionitis are all markers of inflammation.

Objective—This article determines if inflammatory markers are associated with stillbirth and body mass index (BMI). Additionally, we determined whether inflammatory markers help to explain the known relationship between obesity and stillbirth.

Study Design—White blood cell count was assessed at admission to labor and delivery, maternal serum for assessment of various biomarkers was collected after study enrollment, and histologic chorioamnionitis was based on placental histology. These markers were compared for stillbirths and live births overall and within categories of BMI using analysis of variance on logarithmic-transformed markers and logistic regression for dichotomous variables. The impact of inflammatory markers on the association of BMI categories with stillbirth status was assessed using crude and adjusted odds ratios (COR and AOR, respectively) from logistic regression models. The interaction of inflammatory markers and BMI categories on stillbirth status was also assessed through logistic regression. Additional logistic regression models were used to determine

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Conflict of Interest

None.

Condensation

The relationship between BMI and SB is not fully explained by the inflammatory markers studied (serum ferritin, CRP, WBC count, and chorioamnionitis).

if the association of maternal serum ferritin with stillbirth is different for preterm versus term births. Analyses were weighted for the overall population from which this sample was derived.

Results—A total of 497 women with singleton stillbirths and 1,414 women with live births were studied with prepregnancy BMI (kg/m^2) categorized as normal (18.5–24.9), overweight (25.0–29.9), or obese (30.0 +). Overweight (COR, 1.48; 95% confidence interval [CI]: 1.14–1.94) and obese women (COR, 1.60; 95% CI: 1.23–2.08) were more likely than normal weight women to experience stillbirth. Serum ferritin levels were higher (geometric mean: 37.4 ng/mL vs. 23.3, $p < 0.0001$) and C-reactive protein levels lower (geometric mean: 2.9 mg/dL vs. 3.3, $p = 0.0279$), among women with stillbirth compared with live birth. Elevated white blood cell count ($15.0 \text{ uL} \times 10^3$ or greater) was associated with stillbirth (21.2% SB vs. 10.0% live birth, $p < 0.0001$). Histologic chorioamnionitis was more common (33.2% vs. 15.7%, $p < 0.0001$) among women with stillbirth compared with those with live birth. Serum ferritin, C-reactive protein, and chorioamnionitis had little impact on the ORs associating stillbirth with overweight or obesity. Adjustment for elevated white blood cell count did not meaningfully change the OR for stillbirth in overweight versus normal weight women. However, the stillbirth OR for obese versus normal BMI changed by more than 10% when adjusting for histologic chorioamnionitis (AOR, 1.38; 95% CI: 1.02–1.88), indicating confounding. BMI by inflammatory marker interaction terms were not significant. The association of serum ferritin levels with stillbirth was stronger among preterm births ($p = 0.0066$).

Conclusion—Maternal serum ferritin levels, elevated white blood cell count, and histologic chorioamnionitis were positively and C-reactive protein levels negatively associated with stillbirth. Elevated BMIs, both overweight and obese, were associated with stillbirth when compared with women with normal BMI. None of the inflammatory markers fully accounted for the relationship between obesity and stillbirth. The association of maternal serum ferritin with stillbirth was stronger in preterm than term stillbirths.

Keywords

stillbirth; obesity; body mass index; inflammation; biomarkers

Obesity has been associated with an increased risk of stillbirth (SB), although the mechanism is unknown.¹ Obesity has been described as a state of low-grade chronic inflammation marked by an increase in systemic markers of inflammation.² Deregulation of adipocytes results in adipokine and fatty acid release into the circulation and results in immune cell activation. This is believed to be the etiology of obesity-related local and systemic inflammation.² Additionally, dysregulated production or secretion of adipokines, which are pro- and anti-inflammatory markers, can contribute to the pathogenesis of obesity-related diseases.³ Further, obesity-related inflammation has been associated with other pregnancy complications, such as preterm birth, diabetes, and preeclampsia, all of which also have an association with SB.⁴

While the underlying basis for the relationship of systemic inflammation with SB is unknown, there is evidence that placental inflammation (histologic chorioamnionitis [HCA]) is increased in women with SBs.⁵ To better understand the relationship of systemic inflammation and SBs, researchers have called for greater assessment of molecular evidence

of inflammation that may contribute to SB.⁶ The goal of our analysis was to determine if certain inflammatory markers are associated with SB. Additionally, we aimed to determine whether these inflammatory markers help to explain the known relationship between body mass index (BMI) and SB. We evaluated maternal serum ferritin (MSF), serum C-reactive protein (CRP), white blood cell (WBC) count, and HCA. All four markers have been associated with systemic inflammation and inflammatory conditions.

Materials and Methods

The Stillbirth Collaborative Research Network (SCRN) of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) conducted a population-based case-control study of SB with enrollment of women from March 2006 through September 2008. Details of the study design have been published.⁷

Our analysis included 497 women with singleton SB and 1,414 with a live birth (LB). The analysis is limited to singletons and excludes underweight women, as were those who were incarcerated, and could not give informed consent. Women serving as control subjects in the trial had to be at least 13 years old, live in the catchment area, be identified for enrolment during the hospital stay, and delivered a LB at greater than or equal to 20 weeks' gestational age (GA).

All participants gave written informed consent and were enrolled at the time of delivery. Institutional review boards approved the study at all clinical sites and at the data coordinating center. A concerted effort was made in the SCRN catchment areas to enroll all cases (SBs) as well as a representative sample of contemporaneous controls (LBs). All of Rhode Island and selected counties in Massachusetts, Georgia, Texas, and Utah were included. More than 80,000 deliveries per year occur in these catchment areas. Recruitment was conducted in 59 tertiary care and community hospitals in which an estimated 90% of deliveries to the residents of those areas delivered. To ensure adequate numbers for stratified analyses, some subgroups of preterm LBs were oversampled. Further description of this oversampling can be found in the paper previously published on the SCRN methods.⁷

GA determination reflected the best clinical estimate from several sources, which was primarily the first day of the patient's last menstrual period (LMP) verified by ultrasound, dated fully by ultrasound when LMP was unknown, or documentation of the day of ovulation or embryo transfer, when available for pregnancies conceived with assisted reproductive technologies.⁷ To ensure inclusion of all possible eligible SBs, fetal deaths at 18 or 19 weeks and without good dating were included in the study.⁷ Infants with Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) scores of 0 at 1 and 5 minutes and no signs of life at greater than 20 weeks' gestation were determined to be stillborn. Detailed clinical and demographic information was obtained from medical record abstraction from hospital and clinic records during the antepartum and intrapartum courses, as well as from a standardized maternal interview during the delivery hospitalization. During these interviews, women self-identified their race. BMI was calculated as prepregnancy weight in kilograms divided by height in meters squared as gleaned from chart abstraction or, when not available, from patient interview. Patients enrolled in the study had uniform

placental pathology examination performed and a standardized postmortem autopsy was done for SBs.⁷ This included specific definitions of pathologic lesions and review of gross specimens (fetus and placenta) and histologic images as determined by pathologists involved in the study to ensure consistent results across sites.

Maternal serum was collected at enrollment and stored at -80°C for 2 to 5 years until the MSF and CRP levels were assayed at Associated Regional and University Pathologists, Inc (ARUP) Laboratories, Salt Lake City, Utah. Extreme high values skewed the distributions for these markers. Therefore, the data were analyzed on the natural logarithmic scale ($\log_e$) of the measures and means and 95% confidence intervals (CIs) were back transformed to geometric means with corresponding 95% CIs. WBC count was collected from delivery hospitalization records assessed on the same day as delivery when available; otherwise, results obtained the day prior to delivery were used. If multiple measurements were taken on the same day, the highest measurement for that day was used in the analysis. Elevated WBC count was defined as greater than or equal to $15.0 \text{ uL} \times 10^3$.⁸ HCA was determined from histologic examination for acute chorioamnionitis of either the placental-free membranes or the chorionic plate.⁹ Control women were selected from women having an all LB outcome. As such, controls were not enrolled to the study and the blood sample was not taken among consenting women until after delivery.

Analysis of variance was used to compare mean levels of MSF and CRP for SB versus LB on the natural logarithmic scale, and logistic regression was used to test for differences in proportions for elevated WBC and HCA. The markers were used in logistic regression models with BMI to study the associations with SB using crude (COR) and adjusted (AOR) odds ratios and corresponding 95% CIs pertaining to BMI. A 10% change or more between the COR and the AOR in either direction was considered important with respect to confounding of the inflammatory marker and BMI in association with SB. Interaction models were used to assess whether associations between inflammatory markers and SB differed by BMI. In addition, MSF levels were categorized using quartile cutoffs for term LBs to further explore the relationship between MSF and BMI in association with SB, and to evaluate whether the associations varied for term versus preterm births.

Analyses were weighted for the study design and differential consent based on characteristics recorded on the screened population. Further, the analysis of chorioamnionitis was weighted to account for differential losses of placental specimens for study protocol examination. Total sample size for both unweighted and weighted samples is provided. Additionally, the analysis is limited to women who had either MSF or CRP results available. Ferritin results, but not other markers, for women who received a blood transfusion were excluded from analysis ($n = 67$), as we did not collect data on the date and time of blood transfusion.

Results

In our analysis, 497 women with a singleton SB and 1,414 with a LB whose prepregnancy BMI (kg/m^2) was normal (18.5–24.9), overweight (25.0–29.9), or obese ($30.0 +$) were included. ► Table 1 describes our study population by maternal BMI and SCR case status

for variables that were previously associated with SB among the SCRn population.¹⁰ More overweight women were black, non-Hispanic and more obese women were Hispanic. More normal weight women were nulliparous compared with overweight and obese women.

►Table 2 compares inflammatory markers for SBs versus LBs overall and within the three BMI groups. Also, the table shows results by preterm and term births. Geometric mean (95% CI) MSF levels were higher (37.4 [34.7–40.3] ng/mL vs. 23.3 [22.2–24.5], $p < 0.0001$) and geometric mean (95% CI) CRP levels lower (2.9 [2.6–3.2] vs. 3.3 [3.1–3.5] mg/dL, $p = 0.0279$), among women with a SB compared with a LB. Elevated WBC counts ($15.0 \text{ uL} \times 10^3$ or greater) were also associated with SB (21.2% SB vs. 10.0% LB, $p < 0.0001$) and HCA was more common (33.2% vs. 15.7%, $p < 0.0001$) among women with a SB compared with those with a LB. None of the inflammatory markers were associated with BMI among LBs (p -values not significant, and not shown). Mean MSF levels as well as high WBC counts and HCA were higher in SBs than LBs in each BMI category, while mean CRP levels were lower in SBs overall and in the normal weight group.

MSF was further studied with BMI for association with SB, considering differences for term and preterm birth. In this logistic regression analysis, MSF levels were grouped into four categories using the quartiles for term LBs: 2 to 13, 14 to 24, 25 to 41, and 42+ ng/mL. The model included MSF categories, BMI categories, an indicator for preterm birth, and the interaction of MSF and BMI categories with preterm birth. The interaction of MSF with preterm birth was significant ($p = 0.0066$). This interaction is illustrated in ►Fig. 1. This figure visually illustrates that while BMI did not seem to affect the trend, MSF levels were higher in preterm SBs than in term SBs, where levels were similar across LBs and SBs.

Women who were overweight (COR, 1.48; 95% CI: 1.14–1.94) and obese (COR, 1.60; 95% CI: 1.23–2.08) were more likely than normal weight women to experience SB (►Table 3). When models with SB outcome by BMI were adjusted individually for MSF, CRP, or elevated WBC, these variables had little impact on the OR that associated SB with overweight or obesity. Adjustment for HCA did not substantially change the OR for SB in overweight versus normal weight women. The SB OR for obese versus normal women changed by more than 10% indicating confounding when adjusting for HCA (AOR, 1.38; 95% CI: 1.02–1.88). However, the association of obesity with SB remained significant. BMI by inflammatory marker interaction terms were not significant (did not meet the threshold of $p < 0.05$) for any of the four markers.

Comment

Obesity has been associated with an increased risk of SB, although the mechanism is unknown. A study of nearly 3,000,000 singleton births using a retrospective cohort of singleton nonanomalous LBs and SBs in Washington and Texas found a SB rate of 3.1 per 1,000 births.¹¹ In that study, overweight women had a hazard ratio of 1.36 for SB when compared with normal weight women. The hazard ratio increased to 1.71 for women with a BMI of 30.0 to 34.9 kg/m², 2.00 for women with a BMI of 35.0 to 39.9 kg/m², 2.48 for women with a BMI of 40.0 to 49.9 kg/m², and 3.16 for women with a BMI of > 50 kg/m²

compared with normal weight women.¹⁰ Nearly 25% of the women with SB between 37 and 42 weeks' gestation were obese.¹¹

We performed a MEDLINE search that yielded no studies exploring the relationship of MSF, CRP, or leukocytosis to SB. However, HCA has been studied in relationship to SB and a recent analysis of 543 SBs found that HCA was common among women with fetal demise, occurring in a quarter of cases.¹² While MSF is a marker for iron status, it is also a potent marker of systemic inflammation and high levels have been documented in obesity.¹³ CRP is a well-known inflammatory marker.¹⁴ CRP is positively associated with BMI; when BMI is higher, levels of CRP are higher, suggesting again that obesity is a state of systemic low-grade inflammation.¹⁴ Similarly, obesity can be associated with leukocytosis.¹⁵ Finally, a study of over 5,000 women found that obese pregnant women were more likely to have HCA compared with normal weight women.¹⁶ To better understand the relationship between obesity and SB, we evaluated whether these markers of inflammation are more common in obese patients who experience a SB as compared with those with a LB.

We found that MSF levels, elevated WBC count, and HCA were positively and CRP levels negatively associated with SB. Among SBs and LBs, CRP levels were elevated in overweight and obese women. CRP levels were negatively associated with SB while obesity is positively associated with SB, a finding we cannot explain. None of the markers studied fully accounted for the relationship between obesity and SB, suggesting that inflammation, as represented by these markers, may not fully explain the relationship between BMI and SB. It is possible that inflammation may play a role in the association of obesity and SB, but the relationship is not mediated by the biomarkers studied; if future studies find additional serum markers of inflammation, these should be further studied in the context of obesity and SB.

Strengths of our study include our analysis of a subset of participants from a large, population-based case-control study with an ethnically, racially, and geographically diverse population. Additionally, we had an accurate estimation of GA at death in SBs, and the ability to examine the contribution of factors affecting the risk of SB. Also, all participants were evaluated with a thorough standardized protocol that minimized variability in data and sample collection.

This study was restricted to singleton pregnancies, which may limit generalizability. Another limitation is the retrospective nature of case-control studies and data derived from maternal interview at the time of delivery.⁷ Also, while biomarkers were collected, the measurements were only for the time around delivery and may not reflect exposure at earlier vulnerable periods during gestation.⁷ Additionally, the time of data collection, such as when WBC was measured, may have impacted the results.

While there is biological plausibility for our hypothesis that the inflammatory state of obesity may explain the relationship between BMI and SB as explored above, our results did not fully explain this relationship. While other markers might help explain the relationship between obesity and SB, markers studied in this analysis suggest that the relationship

between obesity and SB is nuanced and not explained by inflammation. It is also possible that any inflammation was elaborated by the SB itself.

Current practice is to assess placental pathology in the case of SB, and this evaluation may be the most useful test in the investigation of the causes of SB.^{10,17,18} Also, we anticipate that women with SB will be tested for endomyometritis and systemic inflammation at the time of admission, which would include a WBC count. We do not recommend a change in current clinical practice or evaluation of SB to include testing of women with SB for MSF or CRP based on our results at this time.

We found the relationship between MSF and SB was stronger in preterm than term SBs, which warrants further study. Additionally, our results support the previously reported associations between obese and overweight women and SB. While MSF levels, elevated WBC count, and HCA were clearly associated with SB, our results do not fully explain the relationship between obesity and SB.

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Fig. 1.

Ferritin distribution for women with stillbirth versus live birth by maternal body mass index (BMI) category among preterm and term births. The interaction of maternal serum ferritin (MSF) with preterm birth was significant ($p = 0.0066$). The model included MSF categories, BMI categories, an indicator for preterm birth, and the interaction of MSF and BMI categories with preterm birth.

Table 1

Population description by maternal BMI and SCRn case status

Characteristics, weighted %	BMI (kg/m ²) category					
	Normal weight 18.5–24.9		Overweight 25.0–29.9		Obese 30.0+	
	SB	LB	SB	LB	SB	LB
Unweighted sample size ^a , <i>N</i>	204	702	137	346	156	366
Weighted sample size ^a , <i>N</i>	203	563	139	259	157	272
Maternal race/ethnicity						
White, non-Hispanic	38.5	52.6	33.0	42.7	34.9	40.4
Black, non-Hispanic	19.1	8.6	26.0	11.2	18.6	8.6
Hispanic	36.2	32.4	35.3	37.6	40.0	44.1
Other	6.2	6.4	5.6	8.5	6.5	7.0
Maternal education						
0–11 (none/primary/some secondary)	27.2	16.3	20.4	20.5	21.1	19.7
12 (completed secondary)	28.0	23.3	29.6	30.8	30.6	26.5
13+ (college)	44.8	60.3	50.0	48.7	48.3	53.8
Not married or cohabitating	26.1	14.0	26.7	16.9	20.1	13.8
Smoked cigarettes during 3 mo prior to pregnancy	21.0	12.9	19.7	16.1	19.1	9.8
Hypertension	4.1	3.3	13.7	4.6	20.0	13.1
Diabetes diagnosed prior to pregnancy	1.3	0.6	6.1	1.1	11.5	4.6
Nulliparous	48.4	39.0	41.7	30.4	35.5	29.5
Multiparous w/SB	6.4	1.1	6.4	1.8	8.2	2.7
Gestational age at delivery						
18–19 wk	2.1	0.0	4.4	0.0	1.3	0.0
20–23 wk	30.1	0.2	28.9	0.4	36.3	0.4
24–27 wk	13.3	0.5	14.1	0.6	14.1	0.7
28–31 wk	14.4	0.8	10.2	0.8	14.2	1.2
32–36 wk	20.9	6.8	22.8	6.4	17.7	9.3
37+ wk	19.3	91.6	19.5	91.8	16.4	88.3

Characteristics, weighted %	BMI (kg/m ²) category					
	Normal weight 18.5–24.9		Overweight 25.0–29.9		Obese 30.0+	
	SB	LB	SB	LB	SB	LB
Size for gestational age						
Small for gestational age	33.0	8.4	36.6	5.0	33.9	6.0
Appropriate for gestational age	63.7	85.8	59.9	85.6	62.1	81.3
Large for gestational age	3.4	5.8	3.6	9.4	3.9	12.7

Abbreviations: BMI, body mass index; CRP, C-reactive protein; LB, live birth; MSF, maternal serum ferritin; SB, stillbirth; SCRN, Stillbirth Collaborative Research Network.

^aPercentages are weighted for the study design and differential consent based on characteristics recorded on the screened population. Total sample size is given both unweighted and weighted. The analysis is limited to singletons and excludes underweight women and women missing BMI. Further, the analysis is limited to women who either had MSF or CRP results available.

Maternal inflammatory markers by maternal BMI and SCRNI case status, overall and for preterm and term births

Table 2

Inflammatory markers, weighted results ^a	Overall				Preterm ^c				Term ^c			
	SB	LB	SB vs. LB ^d		SB	LB	SB vs. LB ^c		SB	LB	SB vs. LB ^d	
Unweighted sample size ^a , N	497	1,414			404	321			93	1,093		
Weighted sample size ^a , N	498	1,094			406	100			92	994		
BMI category (kg/m ²)												
Normal, 18.5–24.9												
Geometric mean (95% CI) MSF (ng/mL) ^b	35.0 (31.2, 39.2)	23.8 (22.2, 25.4)	< 0.0001		36.8 (32.3, 42.0)	19.4 (14.9, 25.2)	< 0.0001		28.6 (23.2, 35.3)	24.2 (22.6, 25.9)	0.1413	
Geometric mean (95% CI) CRP (ng/mL) ^b	2.4 (2.0, 2.8)	3.0 (2.8, 3.3)	0.0115		2.3 (1.9, 2.8)	2.4 (1.7, 3.3)	0.8573		2.8 (2.1, 3.9)	3.1 (2.9, 3.4)	0.5559	
Elevated WBC, %	22.0	9.3	< 0.0001		20.7	11.3	0.1135		26.9	9.1	0.0016	
HCA, %	31.5	15.0	< 0.0001		27.8	17.1	0.1474		44.9	14.8	< 0.0001	
Overweight, 25.0–29.9												
Geometric mean (95% CI) MSF (ng/mL) ^b	40.3 (35.0, 46.3)	23.7 (21.5, 26.1)	< 0.0001		42.3 (36.1, 49.5)	21.8 (16.0, 29.5)	0.0002		32.8 (24.6, 43.7)	23.9 (21.6, 26.4)	0.0405	
Geometric mean (95% CI) CRP (ng/mL) ^b	3.2 (2.7, 3.9)	3.4 (3.0, 3.8)	0.6428		3.0 (2.4, 3.7)	3.0 (2.2, 4.1)	0.9621		4.2 (2.8, 6.3)	3.4 (3.0, 3.9)	0.3492	
Elevated WBC, %	22.4	12.8	0.0272		24.4	10.6	0.1534		13.6	12.9	0.9283	
HCA, %	35.7	14.8	< 0.0001		37.6	25.3	0.3319		29.0	13.9	0.0671	
Obese, 30.0 or more												
Geometric mean (95% CI) MSF (ng/mL) ^b	38.2 (33.3, 43.9)	22.1 (19.8, 24.6)	< 0.0001		40.5 (34.9, 46.9)	23.2 (17.2, 31.2)	0.0010		28.4 (19.8, 40.9)	21.9 (19.5, 24.7)	0.1811	
Geometric mean (95% CI) CRP (ng/mL) ^b	3.3 (2.9, 3.8)	3.7 (3.2, 4.3)	0.2689		3.2 (2.8, 3.7)	3.9 (3.0, 5.0)	0.2219		3.8 (2.4, 6.1)	3.7 (3.1, 4.4)	0.9008	
Elevated WBC, %	19.2	8.6	0.0050		20.3	11.6	0.2524		14.7	8.3	0.2887	
HCA, %	33.4	18.0	0.0069		34.4	21.2	0.1887		28.5	17.7	0.2431	
Overall												

Inflammatory markers, weighted results ^a	Overall			Preterm ^c			Term ^c		
	SB	LB	SB vs. LB ^d	SB	LB	SB vs. LB ^c	SB	LB	SB vs. LB ^d
Geometric mean (95% CI) MSF (ng/mL) ^b	37.4 (34.7, 40.3)	23.3 (22.2, 24.5)	< 0.0001	39.5 (36.3, 42.9)	21.0 (17.8, 24.9)	< 0.0001	29.7 (25.3, 34.8)	23.6 (22.4, 24.8)	0.0070
Geometric mean (95% CI) CRP (ng/mL) ^b	2.9 (2.6, 3.2)	3.3 (3.1, 3.5)	0.0279	2.8 (2.5, 3.1)	2.9 (2.4, 3.6)	0.6255	3.5 (2.8, 4.3)	3.3 (3.1, 3.6)	0.7417
Elevated WBC, %	21.2	10.0	< 0.0001	21.6	11.2	0.0143	19.8	9.8	0.0066
HCA, %	33.2	15.7	< 0.0001	32.5	20.2	0.0264	36.1	15.3	< 0.0001

Abbreviations: BMI, body mass index; CRP, C-reactive protein; HCA, histologic chorioamnionitis; LB, live birth; MSF, maternal serum ferritin; SB, stillbirth; SCRN, Stillbirth Collaborative Research Network; WBC, white blood cell count.

^aResults shown are weighted for study design and differential consent based on characteristics recorded on the screened population. Further, the analysis of HCA is weighted to account for differential losses of placental specimens for study protocol examination. Total sample size is given, unweighted and weighted. Analysis is limited to singletons and excludes underweight women and women missing BMI.

^bExtremely high values skewed the distributions for MSF and CRP. As such, comparisons were made on the natural logarithmic transformation of the measures and the geometric means with corresponding 95% confidence intervals are presented.

^cPreterm birth defined as < 37 weeks' gestation. Term defined as 37 weeks' gestation or greater.

^dFor continuous measures, *p*-values for the difference of means generated by adjusted Wald *F*-tests from weighted analysis of variance. For categorical variables, *p*-values from logistic regression.

Table 3

Crude and maternal inflammatory marker adjusted stillbirth odds ratios for maternal BMI

	Overall Odds ratio (95% CI) for SB	
Weighted results ^a	Overweight vs. normal ^c	Obese vs. normal ^c
Unweighted sample size, <i>N</i>	497	1,414
Weighted sample size, <i>N</i>	498	1,094
Crude	1.48 (1.14, 1.94)	1.60 (1.23, 2.08)
Adjusted for:		
MFS (log _e of ng/mL) ^b	1.44 (1.08, 1.91)	1.68 (1.26, 2.24)
MSF categories (quartiles for LBs 37+ wk)	1.45 (1.09, 1.92)	1.71 (1.29, 2.27)
CRP (log _e of mg/dL) ^b	1.52 (1.16, 1.98)	1.65 (1.27, 2.15)
CRP categories (quartiles for LBs 37+ wk)	1.49 (1.14, 1.94)	1.62 (1.24, 2.11)
Elevated WBC (15.0 uL × 10 ³ or greater)	1.41 (1.05, 1.90)	1.74 (1.30, 2.31)
HCA	1.40 (1.04, 1.90)	1.38 (1.02, 1.88)

Abbreviations: BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; HCA, histologic chorioamnionitis; LB, live birth, normal weight = 18.5–24.9 BMI, overweight = 25.0–29.9 BMI, obese = 30.0+ BMI; MSF, maternal serum ferritin; SB, stillbirth; WBC, white blood cell count.

^aResults shown are weighted for study design and differential consent based on characteristics recorded on the screened population. Further, the analysis of HCA is weighted to account for differential losses of placental specimens for study protocol examination. Total sample size is given, unweighted and weighted. Analysis is limited to singletons and excludes underweight women and women missing BMI.

^bExtremely high values skewed the distributions for MSF and CRP. As such, the measures are included in the adjusted models on the natural logarithmic scale.

^cUnadjusted odds ratios of SB for overweight versus normal weight women and obese versus normal weight women are provided. These are followed by the adjusted odds ratios for SB for overweight versus normal weight women and obese versus normal weight women individually controlling for the inflammatory markers.