

# Contribution of obesity to racial and ethnic disparities in the risk of fetal myelomeningocele: a population-based study



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**BACKGROUND:** Prepregnancy obesity and racial-ethnic disparities has been shown to be associated with meningomyelocele.

**OBJECTIVE:** This study aimed to investigate the association of maternal periconceptual factors, including race—ethnicity and prepregnancy body mass index, with the prevalence of isolated fetal myelomeningocele.

**METHODS:** This was a population-based cross-sectional study using Centers for Disease Control and Prevention birth data from 2016 to 2021. Major structural anomalies or chromosomal abnormalities were excluded. Race—ethnicity was classified as non-Hispanic White (reference population), non-Hispanic Black, non-Hispanic Asian, Hispanic, and others. Maternal prepregnancy body mass index was classified as underweight ( $<18.5$  kg/m<sup>2</sup>), normal (reference group; 18.5–24.9 kg/m<sup>2</sup>), overweight (25–29.9 kg/m<sup>2</sup>), and class I (30–34.9 kg/m<sup>2</sup>), class II (35–39.9 kg/m<sup>2</sup>), and class III obesity ( $\geq 40$  kg/m<sup>2</sup>). A chi-square test of independence was performed to identify factors significantly associated with myelomeningocele. These factors were then stratified into 3 adjusted clusters/levels. The prevalence was calculated per 10,000 live births. The Cochran—Armitage test for trend was used to detect any significant increasing or decreasing trends.

**RESULTS:** A total of 22,625,308 pregnancies with live birth, including 2866 pregnancies with isolated fetal myelomeningocele, were included in the analysis. The prevalence of isolated fetal myelomeningocele per 10,000 live births varied among different racial/ethnic groups, with the highest prevalence found among the non-Hispanic White (1.60 [1.52–1.67]) and lowest among the non-Hispanic Asian (0.50 [0.40–0.64]) population. The prevalence significantly increased with body mass index, with the highest prevalence found in the population with class III obesity (1.88 per 10,000 live births). Subgroup analysis of the associations between the significant variables (obesity, diabetes, hypertension, and education) and each ethnicity in cases with myelomeningocele showed significant variations in prevalence of these variables among different racial/ethnic groups. Following the model with the 3 levels of adjustment described in the Methods section, prepregnancy overweight and class I, II, and III obesity remained significantly associated with the odds of isolated fetal myelomeningocele. The adjusted odds ratios were 1.32 (95% confidence interval, 1.19–1.46;  $P<.001$ ) for overweight, 1.55 (95% confidence interval, 1.38–1.75;  $P<.001$ ) for class I obesity, 1.68 (95% confidence interval, 1.45–1.94;  $P<.001$ ) for class II obesity, and 1.73 (95% confidence interval, 1.47–2.04;  $P<.001$ ) for class III obesity. Similarly, following the 3-level adjustment model, the obesity-mediated effect of maternal race—ethnicity on the odds of myelomeningocele remained significant (non-Hispanic Black: adjusted odds ratio, 1.03; 95% confidence interval, 1.02–1.05;  $P<.001$ ; non-Hispanic Asian: adjusted odds ratio, 1.02; 95% confidence interval, 1.01–1.03;  $P<.001$ ; Hispanic: adjusted odds ratio, 1.5; 95% confidence interval, 1.03–1.6;  $P<.001$ ). The test for trend among different racial/ethnic groups did not show significant results across the past 6 years. However, the test for trend showed a significant increase in the prevalence of isolated myelomeningocele associated with class II and III obesity over the past 6 years.

**CONCLUSION:** There has been a rising trend of fetal isolated myelomeningocele in pregnancies with maternal class II and III obesity over the past 6 years after adjusting for other covariates. Prepregnancy obesity, a modifiable risk factor, is a significant driver of racial/ethnic disparities in the overall risk for isolated fetal myelomeningocele.

**Key words:** Fetus, meningomyelocele, obesity, pregnancy, race-ethnicity

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The authors report no conflict of interest.

No external funding was received for this study.

Patient consent was not required because no personal information or details are included.

**Cite this article as:** Mustafa HJ, Burns CT, Heydari MH, et al.

Contribution of obesity to racial and ethnic disparities in the risk of fetal myelomeningocele: a population-based study. *Am J Obstet Gynecol Glob Rep* 2024;4:100290.

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2666-5778/\$36.00

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<http://dx.doi.org/10.1016/j.xagr.2023.100290>

## AJOG MFM at a Glance

**Why was this study conducted?**

This study aimed to investigate the association of maternal periconceptional factors, including race–ethnicity and prepregnancy body mass index (BMI), with the occurrence of isolated fetal myelomeningocele (MMC) among the US population, and the trends in MMC prevalence over the past 6 years.

**Key findings**

After adjusting for multiple socioeconomic, demographic, and metabolic factors, variation remains in the prevalence of isolated fetal MMC among different racial/ethnic maternal populations. Obesity was found to be significantly associated with isolated fetal MMC, with the risk increasing with maternal BMI and the highest prevalence found among those with class II and III obesity. Obesity was a significant independent contributor to racial/ethnic disparities in the overall risk of isolated fetal MMC.

**What does this add to what is known?**

Prepregnancy obesity and racial/ethnic disparities have been previously reported to be associated with fetal MMC. Our study identified an independent role of maternal race–ethnicity in the risk of developing isolated fetal MMC irrespective of socioeconomic, demographic, and metabolic factors. Our study confirms the role of maternal obesity as an independent risk factor for the development of isolated fetal MMC and demonstrates the increasing risk of fetal MMC as maternal obesity becomes more severe.

**Introduction**

Spina bifida is caused by a failure in neural tube development leading to incomplete closure of the neural tube. It is classified into 4 types based on the involvement of the meninges or spinal cord. Myelomeningocele (MMC) is a form of open spina bifida (OSB) that is characterized by the protrusion of nerves or the spinal cord in a sac through the vertebral defect.<sup>1,2</sup> Previously identified maternal risk factors for spina bifida include maternal use of certain antiepileptic medications, obesity, and diabetes mellitus (DM).<sup>3</sup> Although there has been a dramatic decline in the incidence of spina bifida since the introduction of folic acid fortification, fetal MMC remains a well-known cause of childhood morbidity and can lead to hydrocephalus, paralysis, and bowel and bladder incontinence, resulting in severe effects on quality of life.<sup>1,2,4</sup> The estimated lifetime caregiving cost for an infant with spina bifida has been reported to be \$791,900.<sup>5</sup>

Folic acid plays a crucial role in the prevention of neural tube defects (NTDs), and its mandatory fortification

nearly 25 years ago led to a significant decline in the incidence of spina bifida.<sup>4,6</sup> It is also understood that maternal nutrition affects the development of NTDs in other ways given that maternal obesity and DM are both known risk factors.<sup>3</sup> The mechanism by which maternal obesity leads to increase in NTDs is not fully known, although it has been suggested that variable intake/bodily distribution of folic acid in populations with obesity and abnormalities in glucose metabolism may contribute.<sup>7,8</sup> Accounting for the presence of comorbid DM in women with obesity would help discern each condition's respective role in the development of fetal MMC.

Maternal obesity is an immense health care issue in the United States, with nearly 30% of women having obesity before pregnancy in 2019. The nationwide trends in obesity continue to worsen. Between 2016 and 2019, there was an 11% increase in the number of women with prepregnancy obesity.<sup>9</sup> Given the current prevalence and continued rise in maternal obesity, understanding its role as a solitary risk

factor for isolated fetal MMC is imperative.

MMC prevalence varies by race and ethnicity, as shown by the National Birth Defects Prevention Study from 1997 to 2005. The study demonstrated that compared with non-Hispanic (NH) White mothers, offspring of Hispanic mothers had higher prevalence of each OSB subtype and most subphenotypes, whereas offspring of NH Black mothers generally had lower prevalence.<sup>10</sup>

Given the established link between fetal maternal MMC and obesity, different incidence rates among different racial and ethnic groups may account for some of the difference in prevalence of MMC.<sup>11,12</sup> In addition, higher income and level of education appear to be protective against fetal MMC, suggesting that sociodemographic variables play an important role.<sup>13</sup> It is unclear whether the differences in the prevalence based on race–ethnicity would persist after adjusting for all the aforementioned variables.

Our objective was to elucidate the contribution of prepregnancy maternal obesity to the association between race–ethnicity and occurrence of isolated fetal MMC.

**Methods and Materials**  
**Study design**

This was a cross-sectional study using the live-birth data provided by the National Center for Health Statistics, Centers for Disease Control and Prevention (CDC) from January 2016 to December 2021. The population of interest included singleton pregnancies with live-born infants during the aforementioned period (excluding chromosomal and major unrelated structural anomalies, as explained below).

**Exposure variables**

The variables extracted from the birth data included year of birth, maternal and paternal age, nativity (born in/outside of the United States), race–ethnicity, education, marital status, interpregnancy interval, WIC (the Special Supplemental Nutrition Program for Women, Infants, and Children), prepregnancy body mass index (BMI),

prepregnancy DM, prepregnancy hypertension, and chromosomal and structural anomalies including NTDs, cyanotic congenital heart disease, congenital diaphragmatic hernia, omphalocele, gastroschisis, limb reduction defect, and cleft lip or palate.

The dependent variable of interest was fetal MMC. MMC cases were classified as isolated and nonisolated. Isolated MMC was defined as cases without any other chromosomal or major unrelated structural anomalies including cyanotic congenital heart disease, congenital diaphragmatic hernia, omphalocele, and gastroschisis.

Maternal age was classified as <20, 20 to 24, 25 to 29, 30 to 34, 35 to 39, and ≥40 years. Race–ethnicity is self-reported in CDC data and was grouped as NH White, NH Black, NH Asian, Hispanic, and NH others. NH others include those who are American Indian or Alaskan Native and those who are Native Hawaiian or Other Pacific Islander.

The maternal BMI was calculated on the basis of prepregnancy maternal weight and height. Per CDC user guide and worksheet, it is recommended that prepregnancy weight be obtained directly from the mother.<sup>14,15</sup> Maternal weight is also recorded at birth, enabling the calculation of gestational weight gain. According to BMI, mothers were classified into underweight (<18.5 kg/m<sup>2</sup>), normal (18.5–24.9 kg/m<sup>2</sup>), overweight (25–29.9 kg/m<sup>2</sup>), and obesity class I (30–34.9 kg/m<sup>2</sup>), class II (35–39.9 kg/m<sup>2</sup>), and class III (>40 kg/m<sup>2</sup>) categories. Maternal education was classified into <12 and ≥12 years, and payment source was classified into Medicaid, private insurance, self-pay, and other.

### Statistical analysis

The data was described on the basis of the MMC prevalence rate per 10,000 births. We performed an initial analysis to ascertain any differences between categories for each variable among those with and without isolated fetal MMC using chi-square tests of independence.

The significant factors associated with the prevalence of MMC were categorized into the following 3 clusters: (1) the socioeconomic cluster encompassing

maternal education and payment source for delivery, (2) the demographic cluster encompassing maternal race–ethnicity, age, and nativity, and (3) the metabolic profile cluster encompassing hypertension, DM, BMI, and infertility treatment use. At the first level, the models were unadjusted and included maternal race–ethnicity or BMI and the prevalence of isolated fetal MMC. At the second level, the models were adjusted for socioeconomic status, demographic characteristics, and metabolic profiles separately. At the final and third level, they were adjusted for all the aforementioned variables. The indirect obesity-mediated effect of maternal race–ethnicity on the risk of severe maternal morbidity was calculated from the regression coefficients obtained using adjusted logistic regression models, and was expressed as a percentage of the total effect. The significance of each variable was tested by the Wald chi-square test, and all variables except age were found to be significant (*P* value <.05). Furthermore, the goodness of fit of our final model was assessed using a Pearson chi-square test (*P*>.05 for both fully adjusted models).

We also calculated the trend of MMS prevalence per 10,000 live births from 2016 to 2021 based on maternal obesity and race–ethnicity. The Cochran–Armitage test for trend was used to detect any significant increasing or decreasing trends. Stata, version 17 (StataCorp LLC, College Station, TX), R (R Foundation for Statistical Computing, Vienna, Austria), and RStudio (RStudio, Inc., Boston, MA) were used for data cleaning, data analysis, and figure generation.

### Results Study characteristics

A total of 22,625,308 pregnancies with live birth including 2866 pregnancies with isolated fetal MMC were included in the final analysis.

### Comparative descriptive statistics of independent variables in pregnancies with and without isolated myelomeningocele

Compared with those without fetal MMC, participants with isolated fetal MMC were more likely to have

prepregnancy maternal DM (1.9% vs 0.99%; *P*<.001), be US-born (82.8% vs 77.2%; *P*<.001), and have education level <12th grade (15.6% vs 12.6%; *P*<.001), class I obesity (18.7% vs 15.5%; *P*<.001), class II obesity (9.9% vs 7.5%; *P*<.001), class III obesity (7.7% vs 5.5%; *P*<.001), prepregnancy maternal hypertension (3.9% vs 2.1%; *P*<.001), infertility (2.3% vs 1.6%; *P*=.01), and Medicaid payment source for delivery (43.3% vs 42.3%; *P*<.001).

Among the pregnancies with isolated fetal MMC, the maternal race–ethnicity distribution was as follows: NH White 60.5%, Hispanic 21.6%, NH Black 12%, and NH Asian 2.3%.

Characteristics not significantly associated with presence of MMC included parental marital status, enrollment in WIC, and maternal age. The results are shown in [Table 1](#).

### Prevalence of isolated fetal myelomeningocele—affected pregnancies per 10,000 births based on maternal obesity and race/ethnicity from 2016 to 2021

During the period from 2016 to 2021, the prevalence of isolated fetal MMC per 10,000 births increased with increasing severity of maternal obesity. The prevalence of isolated fetal MMC was 1.06 in the underweight BMI class (95% confidence interval [CI], 0.83–1.33), 1.08 in the normal BMI class (95% CI, 1.01–1.14), 1.36 in the overweight BMI class (95% CI, 1.27–1.46), 1.56 in the obesity I class (95% CI, 1.43–1.70), 1.73 in the obesity II class (95% CI, 1.54–1.95), and 1.94 in the obesity III class (95% CI, 1.70–2.21) ([Table 2](#); [Figure 1](#)). The test for trend showed significant increase in the trend of class II obesity (*P*=.04) and class III obesity (*P*=.002) among pregnancies with fetal MMC ([Supplemental Table](#)).

Variation was also observed in the prevalence of isolated fetal MMC among different maternal racial/ethnic population groups. The prevalence of isolated MMC per 10,000 births was 1.60 in the NH White population (95% CI, 1.52–1.67), 1.38 in the Hispanic population (95% CI, 1.18–1.38), 0.94 in the NH Black population (95% CI, 0.85

**TABLE 1**  
**Characteristics of pregnancies with and without isolated myelomeningocele in the US population between 2016 and 2021**

Characteristics		Isolated myelomeningocele		P value
		N (N=22,622,442)	Y (N=2866)	
Prepregnancy diabetes		179,299	51	<.001 <sup>a</sup>
		(0.99)	(1.9)	
Mother's nativity	Non-US-born	4,330,044	441	<.001 <sup>a</sup>
		(22.8)	(17.2)	
	US-born	14,600,339	2121	
		(77.2)	(82.8)	
Race—ethnicity	Hispanic	4,320,123	551	<.001 <sup>a</sup>
		(22.9)	(21.6)	
	Non-Hispanic Asian	1,183,966	58	
		(6.4)	(2.3)	
	Non-Hispanic Black	3,293,461	307	
	(17.5)	(12)		
	Non-Hispanic White	9,478,763	1546	
		(50.4)	(60.5)	
	Other	526,587	94	
		(2.8)	(3.6)	
Marital status	Unmarried	6,896,684	946	.082
		(38.3)	(38.4)	
	Married	10,277,206	1515	
		(61.7)	(61.6)	
Maternal education	<12 <sup>th</sup> grade	2,397,802	381	<.001 <sup>a</sup>
		(12.6)	(15.6)	
	≥12 <sup>th</sup> grade	15,800,008	2151	
		(87.4)	(84.4)	
WIC Supplemental Nutrition Program		6,741,857	932	.336
		(37.5)	(38.3)	
Body mass index	Underweight	591,377	69	<.001 <sup>a</sup>
		(3.2)	(2.7)	
	Normal	7,819,941	835	
		(41)	(33.6)	
	Overweight	4,925,691	681	
		(27.3)	(27.4)	
	Obesity class I	2,804,230	461	
		(15.5)	(18.7)	
	Obesity class II	1,386,773	247	
		(7.5)	(9.9)	
	Obesity class III	995,412	188	

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−1.04), and 0.50 in the NH Asian population (95% CI, 0.40–0.64) (Table 3). During the period from 2016 to 2021, there was an increase in the prevalence of isolated MMC in the Hispanic population, culminating in the highest total in 2021. However, the test for trend showed nonsignificant variations across the past 6 years (Figure 2).

### Multivariate analysis for adjusted risk of isolated fetal myelomeningocele based on maternal obesity

After adjusting for socioeconomic status, demographic factors, and metabolic factors (including hypertension, DM, and infertility), maternal overweight and class I to III obesity remained significantly associated with isolated fetal MMC across all 3 levels of adjustment described previously in the Methods section (Table 4). In the fully adjusted model, as maternal BMI class increased, there was a corresponding increase in the risk of offspring with isolated MMC relative to the reference group (normal BMI) (overweight class: adjusted odds ratio [aOR], 1.28; 95% CI, 1.16–1.41;  $P<.001$ ; class I obesity: aOR, 1.45; 95% CI, 1.30–1.62;  $P<.001$ ; class II obesity: aOR, 1.60; 95% CI, 1.40–1.83;  $P<.001$ ; class III obesity: aOR, 1.74; 95% CI, 1.50–2.01;  $P<.001$ ) (Table 4).

### Multivariate analysis of obesity-mediated effect of maternal race—ethnicity on adjusted risk of isolated fetal myelomeningocele

After adjusting for socioeconomic, demographic, and metabolic variables using the 3 levels of adjustment previously described in the Methods section, there remained a significant association between the prevalence of isolated MMC and maternal race—ethnicity among the population groups relative to the NH White population (reference group) (Hispanic: aOR, 1.75; 95% CI, 0.67–0.83;  $P<.001$ ; NH Black: aOR, 0.52; 95% CI, 0.46–0.59;  $P<.001$ ; NH Asian: aOR, 0.37; 95% CI, 0.29–0.49;  $P<.001$ ). With the NH White population as the reference group, association between maternal obesity and fetal MMC remained significant for

**TABLE 1**  
**Characteristics of pregnancies with and without isolated myelomeningocele in the US population between 2016 and 2021** (continued)

Characteristics	Isolated myelomeningocele		P value
	N (N=22,622,442)	Y (N=2866)	
	(5.5)	(7.7)	
Chronic hypertension	393,975 (2.1)	95 (3.9)	<.001 <sup>a</sup>
Infertility	364,478 (1.6)	67 (2.3)	.01 <sup>a</sup>
Maternal age (y)			
20	923,519 (4.8)	135 (5.3)	.217
20–24	3,665,428 (19.5)	518 (20.1)	
25–29	5,479,003 (28.8)	754 (29.3)	
30–34	5,458,604 (28.7)	699 (27.2)	
35–39	2,808,278 (14.7)	365 (14.3)	
≥40	633,900 (3.5)	100 (3.8)	
Payment source for delivery			
Medicaid	7,978,750 (42.3)	1108 (43.3)	<.001 <sup>a</sup>
Private insurance	9,365,151 (50.1)	1198 (46.8)	
Self-pay	802,979 (4.4)	120 (4.6)	
Other	703,133 (3.2)	129 (5.3)	

<sup>a</sup> Represents significance.

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Hispanic, NH Black, and NH Asian populations ( $P<.001$ ) (Table 5).

Figure 3 shows the variations of demographic and metabolic factors of pregnancies affected with isolated fetal MMC among different racial/ethnic populations.

### Comment Principal findings

There has been a rising trend of isolated fetal MMC in pregnancies with maternal class II and III obesity over the past

6 years after adjusting for other covariates. Prepregnancy obesity, a modifiable risk factor, is a significant driver of racial/ethnic disparities in the overall risk for isolated fetal MMC.

### Results in the context of what is known

The mechanism by which maternal obesity leads to increased risk of NTDs is not fully understood. It has been proposed that maternal metabolism, maternal hyperglycemia, and differences in

leptin signaling may all contribute, as evidenced by the identification of 3 obesity- and DM-related genes associated with varying risk of NTDs.<sup>7</sup> The results of 3 studies by Farah et al,<sup>8</sup> Bird et al,<sup>16</sup> and Masho et al<sup>17</sup> indicated that the efficacy of folic acid supplementation through prenatal vitamin use or diet was lower among those with high pre-pregnancy BMIs.<sup>8,17,18</sup> In addition, women with obesity appear to have lower serum folate levels after controlling for dietary and supplemental intake.<sup>16,18</sup> This could account for the findings of Werler et al,<sup>19</sup> who reported no risk reduction with supplementing  $\geq 400 \mu\text{g}$  of folate in women weighing  $>70 \text{ kg}$ .

Our findings are consistent with the findings of Watkins et al,<sup>20</sup> which demonstrated that spina bifida— or anencephaly-affected pregnancy had an aOR (adjusted for age, education, chronic illness, smoking, alcohol, and vitamin use) of 1.62 for maternal BMI  $>26$  to  $29 \text{ kg/m}^2$  and 1.92 for BMI  $>29 \text{ kg/m}^2$ . A recent meta-analysis (Vena et al<sup>21</sup> [2022]), also found a significant association between maternal obesity and fetal spina bifida relative to women with normal BMI (odds ratio [OR], 1.69). However, unlike the findings of our study, there was no significant association between risk of NTDs and overweight BMI relative to normal BMI. This discrepancy could be attributed to the inclusion of all NTDs in their study, whereas our study examined isolated fetal MMC alone. The dose—response analysis by Huang et al<sup>22</sup> showed an OR of NTDs in offspring of 1.027 per  $1\text{-kg/m}^2$  increase in maternal BMI, demonstrating the linear relationship between BMI and risk of offspring with fetal NTD. Although these meta-analyses only included studies published up to 2017, the association between increasing BMI and increasing risk of NTDs is consistent with our results.

Much of the literature examining the association between ethnicity and NTDs originates from the National Birth Defects Prevention Study, which analyzed CDC data from 1997 through 2011.<sup>23</sup> According to data from Agopian et al,<sup>10</sup> the prevalence of isolated

**TABLE 2****Prevalence of isolated myelomeningocele—affected pregnancies per 10,000 births based on maternal obesity from 2016 to 2021**

Body mass index	Total number of MMC/SB-affected pregnancies	Prevalence per 10,000 births (95% CI)
Underweight	73	1.06 (0.83–1.33)
Normal	995	1.08 (1.01–1.14)
Overweight	807	1.36 (1.27–1.46)
Obesity class I	530	1.56 (1.43–1.70)
Obesity class II	293	1.73 (1.54–1.95)
Obesity class III	236	1.94 (1.70–2.21)

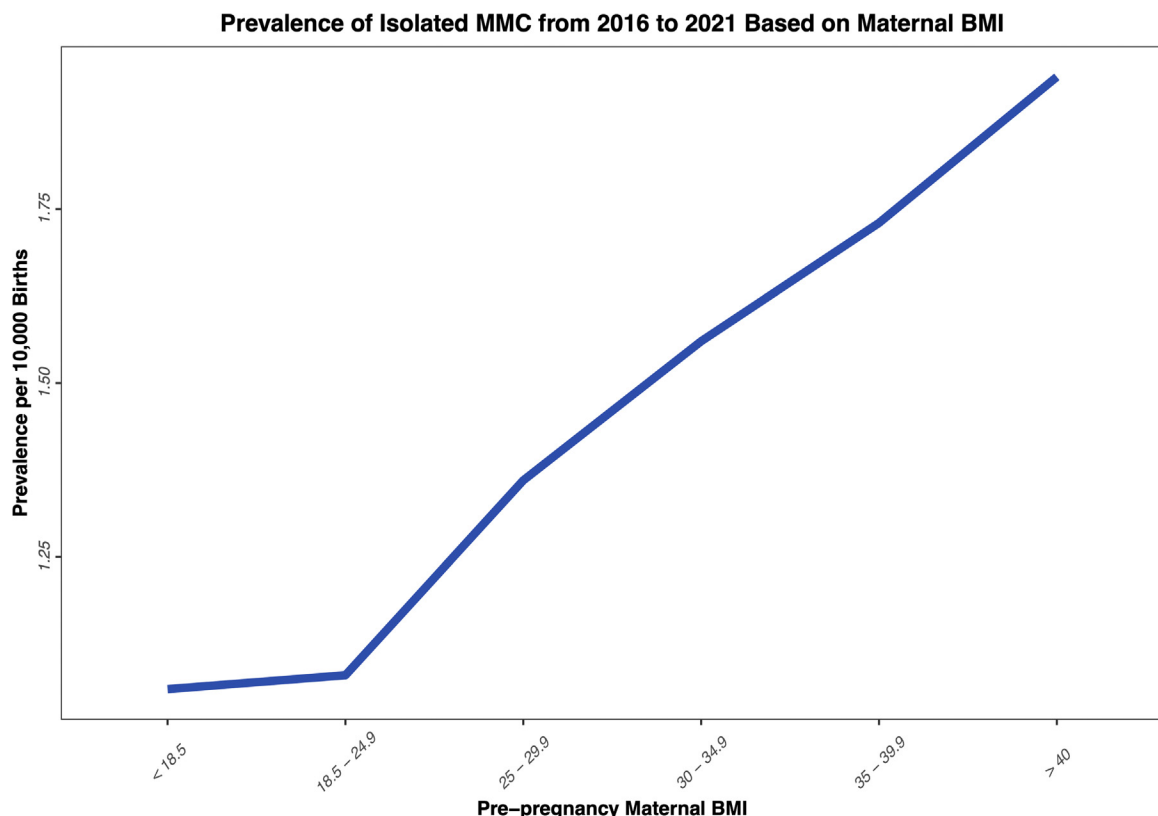
CI, confidence interval; MMC, myelomeningocele; SB, spina bifida.

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fetal MMC is 2.31 per 100,000 live births in the Hispanic/Latino US population, as opposed to 1.95 per 100,000 in the NH White population, indicating a statistically significant increased risk of isolated fetal MMC in the Hispanic population. The higher rates of isolated

MMC in the US Hispanic population relative to the NH White population can be attributed to variations in socioeconomic and demographic factors, and metabolic differences, as demonstrated in our study. In the study by Kirby et al,<sup>24</sup> the authors noted that stratifying

the rates of spina bifida without anencephaly by maternal nativity status did not result in any significant difference in spina bifida prevalence between the US-born Hispanic and the US-born NH White population. However, the non-US-born Hispanic population had

**FIGURE 1****Prevalence of isolated fetal MMC by maternal BMI (2016–2021)**

BMI, body mass index; MMC, myelomeningocele.

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**TABLE 3****Prevalence of isolated myelomeningocele-affected pregnancies per 10,000 births based on maternal race—ethnicity from 2016 to 2021**

Race—ethnicity		Total number of MMC/SB-affected pregnancies	Prevalence per 10,000 births (95% CI)
NH White		1820	1.60 (1.52–1.67)
NH Black		359	0.94 (0.85–1.04)
NH Asian		71	0.50 (0.40–0.64)
Hispanic		668	1.28 (1.18–1.38)
NH others		98	1.51 (1.23–1.18)

CI, confidence interval; MMC, myelomeningocele; NH, non-Hispanic; SB, spina bifida.

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significantly higher prevalence of spina bifida without anencephaly compared with both the US-born NH White population and the US-born Hispanic population.<sup>24</sup> This study aligns with our findings and further supports that the increased prevalence of isolated MMC

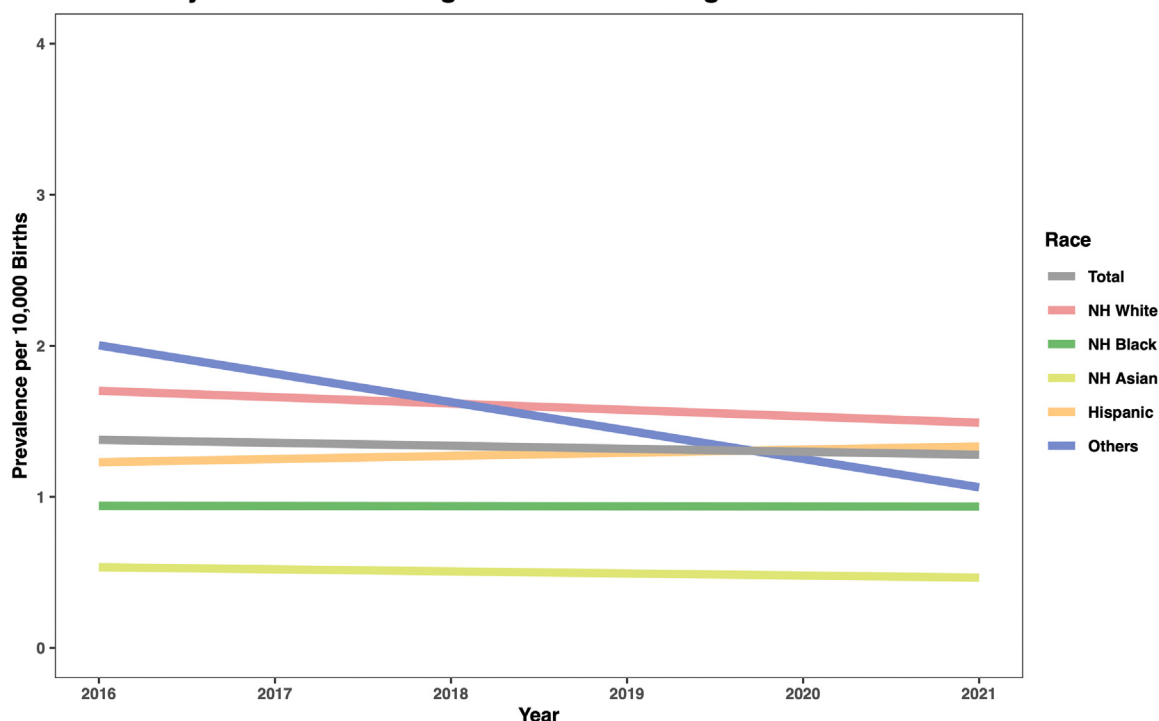
in the Hispanic population is likely secondary to other variables.

Furthermore, in a study by Canfield et al,<sup>13</sup> which also used data from the National Birth Defects Prevention Study, factors that appeared significantly protective against fetal NTDs in

the US Hispanic population included a maternal education level >12 years and a maternal income level >\$40,000 per year, suggesting that sociodemographic factors play a role in the risk of fetal NTDs. DM was also significantly associated with increased risk of spina bifida in the maternal Hispanic population in this study, although this association was not observed in the NH White controls.<sup>13</sup>

**Clinical and research implications**

Factors such as inequalities in the social and built environments, physical activity levels, and dietary behavior are likely determinants of the racial/ethnic and nativity disparities in maternal prepregnancy obesity demonstrated herein. Regular obstetrical/gynecologic encounters offer an opportunity for behavioral counseling and lifestyle interventions to improve dietary intake and physical activity from preconception through

**FIGURE 2****Trend in racial/ethnic disparities among fetal MMC-affected pregnancies (2016–2021)****Race/ethnicity Differences among MMC-affected Pregnancies from 2016 to 2021**

(1) Significant Trend from 2016 to 2021 only in Others Group ( $p < 0.05$ ).  
(2) Significant Difference Between All Groups ( $p < 0.05$ ).

MMC, myelomeningocele; NH, non-Hispanic.

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**TABLE 4**

**Association between body mass index and risk of isolated myelomeningocele–affected pregnancies, unadjusted and adjusted for socioeconomic status, demographics, and metabolic characteristics**

		Unadjusted OR			Adjusted OR (socioeconomic status <sup>a</sup> )			Adjusted OR (demographics <sup>b</sup> )		
		OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
BMI	Underweight	0.98	0.77–1.25	.896	0.97	0.76–1.24	.845	1.01	0.79–1.27	.957
	Normal	1.0 (ref)	—	—	1.0 (ref)	—	—	1.0 (ref)	—	—
	Overweight	1.26	1.15–1.38	<.001 <sup>c</sup>	1.27	1.15–1.39	<.001 <sup>c</sup>	1.32	1.17–1.41	<.001 <sup>c</sup>
	Class I obesity	1.44	1.30–1.60	<.001 <sup>c</sup>	1.46	1.31–1.62	<.001 <sup>c</sup>	1.57	1.32–1.63	<.001 <sup>c</sup>
	Class II obesity	1.61	1.41–1.83	<.001 <sup>c</sup>	1.64	1.44–1.87	<.001 <sup>c</sup>	1.69	1.43–1.86	<.001 <sup>c</sup>
	Class III obesity	1.80	1.56–2.08	<.001 <sup>c</sup>	1.83	1.59–2.12	<.001 <sup>c</sup>	1.79	1.58–2.11	<.001 <sup>c</sup>

		Adjusted OR (metabolic characteristics <sup>d</sup> )			Adjusted OR (fully adjusted <sup>e</sup> )		
		OR	95% CI	P value	OR	95% CI	P value
BMI	Underweight	0.98	0.78–1.25	.927	0.99	0.78–1.27	.985
	Normal	1.0 (ref)	—	—	1.0 (ref)	—	—
	Overweight	1.26	1.28–1.38	<.001 <sup>c</sup>	1.28	1.16–1.41	<.001 <sup>c</sup>
	Class I obesity	1.42	1.28–1.58	<.001 <sup>c</sup>	1.45	1.30–1.62	<.001 <sup>c</sup>
	Class II obesity	1.56	1.37–1.78	<.001 <sup>c</sup>	1.60	1.40–1.83	<.001 <sup>c</sup>
	Class III obesity	1.70	1.47–1.97	<.001 <sup>c</sup>	1.74	1.50–2.01	<.001 <sup>c</sup>

BMI, body mass index; CI, confidence interval; OR, odds ratio.

<sup>a</sup> Adjusted for maternal education and payment source for delivery; <sup>b</sup> Adjusted for maternal race–ethnicity, age, and nativity; <sup>c</sup> Statistically significant; <sup>d</sup> Adjusted for hypertension, diabetes mellitus, and infertility treatment use; <sup>e</sup> Adjusted for all the aforementioned variables.

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**TABLE 5**

**Obesity-mediated effect of maternal race–ethnicity on the risk of isolated myelomeningocele–affected pregnancies, unadjusted and adjusted for socioeconomic status, demographics, and metabolic characteristics**

		Unadjusted OR			Adjusted OR (socioeconomic status <sup>a</sup> )			Adjusted OR (demographics <sup>b</sup> )		
		OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Race–ethnicity	NH White	1.0 (ref)	—	—	1.0 (ref)	—	—	1.0 (ref)	—	—
	NH Black	0.59	0.52–0.66	<.001 <sup>c</sup>	0.55	0.49–0.62	<.001 <sup>c</sup>	0.55	0.49–0.62	<.001 <sup>c</sup>
	NH Asian	0.32	0.25–0.40	<.001 <sup>c</sup>	0.31	0.25–0.40	<.001 <sup>c</sup>	0.37	0.28–0.48	<.001 <sup>c</sup>
	Hispanic	1.81	1.73–1.87	<.001 <sup>c</sup>	1.72	1.65–1.79	<.001 <sup>c</sup>	1.79	1.72–1.88	<.001 <sup>c</sup>
	NH others	0.94	0.77–1.15	.569	0.89	0.72–1.09	.260	0.90	0.73–1.10	.326

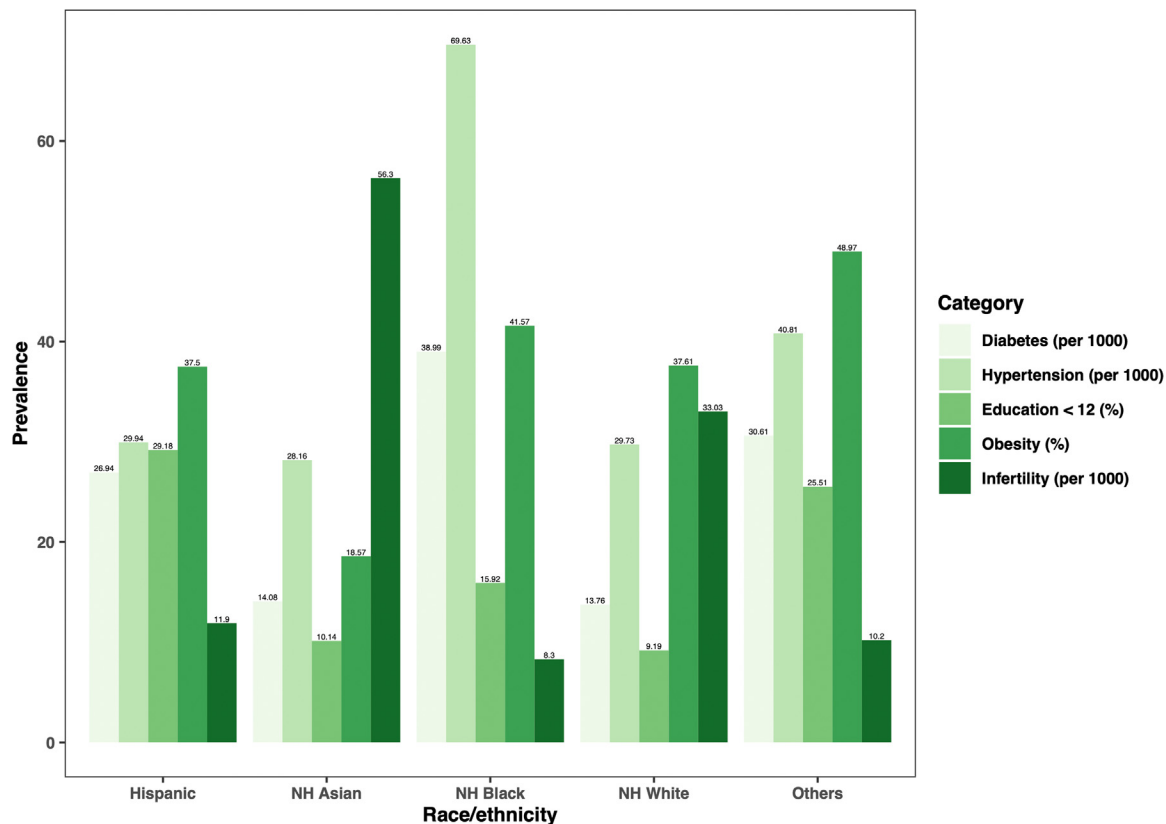
		Adjusted OR (metabolic characteristic <sup>d</sup> )			Adjusted OR (fully adjusted <sup>e</sup> )			Obesity-mediated indirect aOR (95% CI)		
		OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Race–ethnicity	NH White	1.0 (ref)	—	—	1.0 (ref)	—	—	1.0 (ref)	—	—
	NH Black	0.58	0.52–0.65	<.001 <sup>c</sup>	0.52	0.46–0.59	<.001 <sup>c</sup>	1.03	1.02–1.05	<.001 <sup>c</sup>
	NH Asian	0.32	0.25–0.40	<.001 <sup>c</sup>	0.37	0.29–0.49	<.001 <sup>c</sup>	1.02	1.01–1.03	<.001 <sup>c</sup>
	Hispanic	1.80	1.74–1.88	<.001 <sup>c</sup>	1.75	1.67–1.83	<.001 <sup>c</sup>	1.5	1.03–1.6	<.001 <sup>c</sup>
	NH others	0.93	0.76–1.15	.549	0.86	0.70–1.06	.160	1.03	1.02–1.05	.549

CI, confidence interval; NH, non-Hispanic; OR, odds ratio.

<sup>a</sup> Adjusted for maternal education and payment source for delivery; <sup>b</sup> Adjusted for age and nativity; <sup>c</sup> Statistically significant; <sup>d</sup> Adjusted for hypertension, diabetes mellitus, and infertility treatment use; <sup>e</sup> Adjusted for all the aforementioned variables.

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**FIGURE 3****Variations of demographic and metabolic factors of pregnancies affected with isolated fetal MMC among different racial/ethnic populations**

MMC, myelomeningocele; NH, non-Hispanic.

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pregnancy and well into the postpartum period.

Clinical guidelines are necessary to make improvements to the preconception, pregnancy, and postpartum visits. Interventions during these frequent medical encounters may be an effective strategy to counteract the rising rates of maternal obesity in the United States. Obesity is a leading health-risk factor for the nation and is associated with excess morbidity and mortality.

Further research is needed to understand the protective factors that may counter the increased obesity trend. There has yet to be a well-understood underlying mechanism for the increased risk of fetal NTDs in the setting of maternal obesity. More research directed at understanding the pathophysiology behind the association between maternal obesity and fetal

NTDs would assist in identifying preventative therapy.

### Strengths and limitations

Our data are based on a large sample with few missing records. We also adjusted the analysis for several potential confounders, including metabolic and sociodemographic factors. Given that our study used CDC birth data, our study sample is representative of the entire US population. Moreover, the ability to estimate the prevalence of prepregnancy obesity in a large number of racial/ethnic and immigrant groups facilitated a more nuanced understanding of ethnic and socioeconomic disparities.

We acknowledge the following limitations. Because of lack of data, important risk factors for obesity such as diet, physical activity, and the social and

built environments could not be taken into account. Moreover, the prevalence estimates of prepregnancy obesity and overweight included women who had a live birth from 2016 to 2021 and excluded women who became pregnant but experienced fetal loss, miscarriages, or abortion. Pregnancies that were diagnosed and terminated are a source of selection bias because terminated pregnancies (especially at <20 weeks) may never show up in birth certificates. In addition, as reported by Salemi et al,<sup>25</sup> the diagnosis of spina bifida depends on accurate documentation and coding of the diagnosis at the time of birth, with false-positives resulting from teratomas, lipomas, etc. Given that prepregnancy obesity in women is associated with these adverse perinatal outcomes, the reported prevalence of prepregnancy obesity is likely to be underestimated.

Although race—ethnicity should be self-reported, there is no enforcement of this in practice. We only included MMC and no other types of NTDs. In addition, given that prepregnancy weight on the birth certificate is self-reported by the mothers, prepregnancy obesity and overweight prevalence is likely to be underestimated.

## Conclusion

Our large population study of 18,999,808 US live births encompassing 2430 isolated MMC births found considerable heterogeneity in prepregnancy obesity and overweight risks across various racial/ethnic and immigrant groups. Furthermore, over the past 6 years, we observed increased trends of severe obesity significantly associated with risk of fetal MMC even after controlling for metabolic and demographic confounders. ■

## Supplementary materials

Supplementary material associated with this article can be found in the online version at [doi:10.1016/j.xagr.2023.100290](https://doi.org/10.1016/j.xagr.2023.100290).

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