Pregnancy- Associated Diabetes and Stillbirths by Race and Ethnicity Among Hospitalized Pregnant Women in the United States: A Retrospective Cross-Sectional Analysis

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Abstract

Objective: Racial disparities in pre-existing diabetes (PDM) and gestational diabetes (GDM) remain largely unexplored. We examine national PDM and GDM prevalence trends by race/ethnicity, and the association between these conditions and fetal death. **Design**: Retrospective cross-sectional analysis **Setting**: United States Nationwide Inpatient Sample Survey **Population/Sample**: A total of 69,539,875 pregnancy-related hospitalization from 2002 to 2017 including 674,040 women with PDM (1.0%) and 2,960,797 (4.3%) with GDM. **Methods**: Joinpoint regression was used to evaluate trends in prevalence. Survey logistic regression was used to evaluate the association between exposures (PDM and GDM) and outcome. **Main Outcome Measures**: National trends in PDM and GDM prevalence by race/ethnicity, and the association between these conditions and fetal death **Results**: Overall, the average annual increase in prevalence was 5.2% (95% CI [4.2, 6.2]) for GDM and 1.0% (95% CI [-0.1, 2.0]) for PDM, over the study period. Hispanic (AAPC 5.3; 95% CI [3.6, 7.1]) and NH-Black (AAPC 0.9; 95% CI [0.1, 1.7]) women had the highest average annual percent increase in prevalence of GDM and PDM, respectively. After adjustment, odds of stillbirth were highest for Hispanic (OR 2.41:95% CI [2.23, 2.60]) women with PDM and decreased for women with GDM (OR 0.51;95% CI [0.50, 0.53), irrespective of race/ethnicity. **Conclusions and Global Health Implications**: PDM and GDM prevalence is increasing in the U.S. with highest average annual percent changes seen among minority women. Further, reasons for variation in occurrence of stillbirths among mothers with PDM and GDM by race/ethnicity are not clear and warrant additional research.

Introduction

Diabetes is recognized as one of the most common metabolic disorders of pregnancy affecting 17% of pregnancies globally.[1]Gestational diabetes mellitus (GDM), a condition defined by the American College of Obstetrics and Gynecology as carbohydrate intolerance during pregnancy, comprises most cases of pregnancy-associated diabetes.[2] Data suggest that approximately 86% of pregnancy-associated diabetes is caused by GDM, while about 14% is due to diabetes diagnosed prior to pregnancy.[1] In part due to the greater prevalence of GDM compared to pre-pregnancy diabetes (PDM), the majority of research on pregnancy-associated diabetes has focused on maternal morbidity and fetal outcomes among women with GDM. We know from previously published data that women diagnosed with GDM have an increased risk for several adverse outcomes including stillbirth, fetal overgrowth, preterm birth, preeclampsia and progression to type 2 diabetes later in life.[3–5] Data also suggest that children born to mothers with GDM are at increased risk for obesity, cardiovascular disease and type 2 diabetes later in life.[3,4] Women with PDM are reported to be at a significantly increased risk for preeclampsia, congenital malformations, fetal overgrowth and fetal death.[6-16] These data raise serious concerns given that the number of women with PDM is increasing, irrespective of diabetes subtype (type 1 insulin-dependent, or type 2 non-insulin dependent).[6,9,10,17]

The risks accompanying pregnancy-associated diabetes have been reported to disproportionately impact women from different races/ethnicities. Some studies have indicated that non-Caucasian races/ethnicities have a higher prevalence of PDM and GDM than Caucasian women.[9,18–20] Consequently, women of different racial and ethnic backgrounds, such as Black and South Asian with PDM and GDM, have also been shown to be at an increased risk for adverse fetal outcomes including perinatal loss, preterm delivery, respiratory distress syndrome and fetal anomalies.[21–23] However, the majority of these studies focused solely on GDM and assessed women from a limited geographic region. As a result, these data highlight the need for further research to better characterize existing racial/ethnic disparities.

We sought to expand the depth and breadth of the current understanding of racial and ethnic differences in the prevalence of both PDM and GDM, by using hospital data to examine national trends in prevalence by race/ethnicity. We also examined the association between these conditions, race/ethnicity and stillbirth.

Methods

Data Source and Sample

We conducted a retrospective cross-sectional analysis using hospital records from January 1, 2002 through December 31, 2017 that were contained in the Nationwide Inpatient Sample (NIS). The NIS is made available by the Healthcare Cost and Utilization Project (HCUP) and is currently the largest all-payer, publicly available inpatient database in the United States. (Healthcare Cost and Utilization Project (HCUP)) The two-staged cluster sampling design ensures that hospitalizations in the NIS are representative of the population on important factors including month of admission, primary reason for hospitalization, hospital size, location, ownership, and teaching status. Hospitalization-level weights are provided with each annual database which allow national estimates to be generated. In 2017, the NIS contained approximately seven million inpatient hospitalizations each year (35 million when weighted) from 47 participating states. HCUP transitioned from ICD-9-CM to ICD-10-CM format on October 1, 2015.

Our study sample included pregnancy-related hospitalizations among women aged 15 to 49 years, identified using an HCUP-created variable "NEOMAT" which captures maternal diagnosis records with diagnosis and procedure codes for pregnancy and delivery in the ICD-9-CM era. In the ICD-10-CM period, diagnoses codes 'Oxx.x' were used to identify pregnancy and delivery related hospitalizations. To assess the study's primary exposure, we first scanned ICD-9-CM codes (the principal diagnosis and up to 29 secondary diagnoses) in each woman's discharge record for an indication of gestational diabetes mellitus (GDM) (ICD-9-CM: 648.8x, ICD-10-CM: O24.xx or O99.81) and/or pre-existing (i.e., diagnosis of type 1 or 2 diabetes prior to the pregnancy) (ICD-9-CM:249.xx, 250.xx, 648.0x; ICD-10-CM: E10.xx, E11.xx, E13.xx). The outcome of interest was stillbirth (ICD-9-CM: 656.4x, V27.1x, V27.3x, V27.4x, V27.6x, V27.7x, 768.0, 768.1, 779.9, 632; ICD-10-CM: O36.4x, P95.xx, P96.9, Z37.1, Z37.3, Z37.4, Z37.6, Z37.7).

Individual-level sociodemographic and behavioral characteristics were also extracted from the NIS databases. Maternal age in years was classified into three categories: 15-24, 25–34, and 35-49 years. Self-reported maternal race/ethnicity was first based on ethnicity (Hispanic or non-Hispanic [NH]), and the NH group, further subdivided by race (White, Black, or other). As the 'other' racial group is not clearly defined in the dataset, our analyses were limited to NH-White, NH-Black and Hispanics pregnant women. Median household income, which served as a proxy for socio-economic status, was estimated using the patient's zip code and subsequently grouped into quartiles. We classified the primary payer for hospital admission into following categories: Medicare, Medicaid, private (commercial carriers, private health maintenance organization [HMOs], and preferred provider organization [PPOs]); and self-pay. We also considered several hospital characteristics including teaching status (teaching vs. non-teaching), location (urban vs. rural), and US region (Northeast, Midwest, South, or West).

Information for this study was obtained from a retrospective secondary de-identified data source. Therefore, patient involvement and core outcome set requirements are not applicable to this analysis.

Statistical Analysis

Joinpoint regression was used to identify and describe temporal changes in the rates of PDM and GDM among pregnancy-related hospitalizations during the 15-year study period. This type of statistical regression analysis is valuable in identifying key periods that denote a statistically significant change in the rate of events over time. [24] The iterative model-building process began by fitting the annual rate data to a straight line with no joinpoints, which assumed a single trend best described the data. Then a joinpoint, reflecting a change in the trend, was added to the model and a Monte Carlo permutation test assessed the improvement in model fit. The process continued until a final model with an optimal (best-fitting) number of joinpoints was selected, with each joinpoint indicating a change in the trend, and an annual percent change (APC) estimated to characterize how the rate was changing within each distinct trend segment.

Descriptive statistics, including frequencies and percentages, were used to describe the distribution of pregnancy-related hospitalizations across patient- and hospital-level characteristics, stratified by exposure group (PDM and GDM) across racial/ethnic groups: NH-White, NH-Blacks and Hispanics. Since national estimates were desired, all statistical analyses were weighted using an HCUP-provided discharge-level weight that accounted for the sampling design and appropriately generated variance estimates. Furthermore, we calculated the stillbirth rates in women with PDM and GDM across various racial/ethnic groups.

Multivariable survey logistic regression was also used to produce adjusted odds ratios (OR) that quantified the magnitude of the association between the exposures, PDM and GDM, and the outcome stillbirth, across various racial/ethnic groups. Statistical analyses were performed with R version 3[?]5[?] 1 (University of Auckland, Auckland, New Zealand) and R Studio Version 1[?]1[?] 423 (Boston, MA). We assumed a 5% type I error rate for all hypothesis tests (two-sided). Due to the de-identified, publicly available nature of NIS data, the analyses performed for this study were considered exempt by the Baylor College of Medicine Institutional Review Board.

Results

We analyzed a total of 69,539,875 hospitalizations from 2002 to 2017 including 674,040 women diagnosed with PDM (1.0%) and 2,960,797 (4.3%) women diagnosed with GDM.

Figure 1 displays the temporal trends in the rates of PDM and GDM in hospitalized pregnant women by race and ethnicity from 2002 to 2017. Overall, the prevalence of PDM and GDM increased over the 15-year study period from 11.1 per 1,000 hospitalizations to 12.8 per 1,000 hospitalizations and from 42.7 per 1,000 hospitalizations to 91.6 per 1,000 hospitalizations, respectively. The average annual increase in prevalence was 5.2% (95% CI [4.2, 6.2]) for GDM and 1.0% (95% CI [-0.1, 2.0]) for PDM over the study period. Hispanic women had the highest average annual percent increase in prevalence of GDM (AAPC 5.3; 95% CI [3.6, 7.1]). The prevalence of GDM among Hispanic women increased from 50% in 2002 to 109.5% in 2017. NH-Black women had the highest average annual percent increase in the prevalence of PDM over the study period (AAPC 0.9; 95% CI [0.1, 1.7]). The prevalence of PDM among NH-Black women increased from 18.9% in 2002 to 21.7% in 2017. The lowest average annual percent increase in the prevalence of GDM (AAPC 5.1; 95% CI [3.9, 6.2]) and PDM (AAPC 0.3; 95% CI [-1.4, 2.0]) was observed among NH-Whites. The prevalence of GDM among NH-Whites increased from 37.7% in 2002 to 78.9% in 2017, while the prevalence of PDM increased from 9.2% to 9.5% over the same time.

Table 1 shows the relationship between socio-demographic factors and diagnosis of PDM and GDM among hospitalized pregnant women by race/ethnicity. The age distribution of PDM and GDM was similar across groups. The prevalence of PDM and GDM increased with age in each race/ethnic group. The prevalence of PDM was highest among NH-Black hospitalized women in each age group ranging from 1.1% for those less than 24 years of age to 4.3% for those 35 to 49 years of age. The prevalence of GDM was highest among Hispanic women across all age groups ranging from 2.9% for those less than 24 years of age to 15.8% for those 35 to 49 years of age.

Among hospitalized pregnant women for which discharge status was known, there were notable differences in the prevalence of pregnancy-associated diabetes by race/ethnicity (Table 1). The highest prevalence rates for pregnancy-associated diabetes were observed among NH-Black (9.8%) and Hispanic (9.9%) women who were discharged against medical advice. Additionally, the prevalence of PDM among NH-Black mothers who died in the hospital was 7.9%, notably higher than the prevalence in other racial/ethnic groups. The prevalence of GDM among mothers who died during hospitalization was highest for Hispanic women (5.5%).

The diagnosis of PDM was more common among hospitalized women who reported a residence in a low-income zip code for all race/ethnicity groups (Table 1). In contrast, the prevalence of GDM was highest among hospitalized Hispanic (8.1%) and NH-Black (6.4%) women with residences in high-income zip codes. There were also differences in primary payer for health care services by race/ethnicity. Most NH-White hospitalized pregnant women used private insurance to pay for care, while the majority of NH-Black and Hispanic women had Medicaid as their primary payor. Among hospitalized pregnant women for which payor source was known, the prevalence of PDM and GDM was highest among women who had Medicare as their primary payor in each race and ethnic group.

With respect to hospital characteristics, the diagnosis of PDM and GDM was similar across regions for race/ethnic groups with one exception (Table 1). The prevalence of PDM among mothers increased with hospital size in each race/ethnic group but was similar across racial/ethnic groups for GDM. The prevalence of PDM and GDM was highest in urban teaching hospitals in each race/ethnic group, where most women were admitted for care.

Figure 2 depicts the rates for stillbirth among women with PDM and GDM by race and ethnicity. Overall, the rate of stillbirth was low for both groups, but the occurrence of stillbirth among hospitalized women with PDM (2.40%) was about 4.4 times higher than that for hospitalized women with GDM (0.54%). The highest frequency of stillbirth among women with PDM and GDM was in the NH-Black (0.9% and 3.13%, respectively) group and the lowest in the NH-White (0.54% and 2.40%, respectively) group.

Figure 3 depicts the association between pregnancy-associated diabetes and stillbirth by race/ethnicity. Odds ratios for stillbirth adjusted for sociodemographic hospital characteristics are provided for hospitalized women diagnosed with PDM and GDM by race/ethnicity. Unadjusted odds ratios are provided in Table S1 for PDM and in Table S2 for GDM. Compared to hospitalized pregnant women who did not have diabetes, the adjusted odds of stillbirth more than doubled for women diagnosed with PDM (OR=2.14; 95% CI [2.07,2.22]). The increase in the adjusted odds of stillbirth observed among hospitalized mothers with PDM was consistent for each race/ethnic group. The adjusted odds of stillbirth among hospitalized women with PDM was highest for Hispanic women (OR=2.41; 95% CI [2.23,2.60]) and lowest for NH Black women (OR=1.81; 95% CI [1.71,1.94]).

In contrast, the adjusted odds of stillbirth for hospitalized mothers diagnosed with GDM was lower than that for hospitalized pregnant women without diabetes. Hospitalized pregnant woman diagnosed with GDM were 49% (OR=0.51; 95% CI [0.50,0.53]) less likely to have a stillbirth. The lower adjusted odds of stillbirth observed among hospitalized women with GDM was consistent across race/ethnic groups. The adjusted odds of stillbirth among hospitalized women with GDM were the same for NH-White (OR=0.52; 95% CI [0.49,0.55]), NH-Black (OR=0.52; 95% CI [0.48 -0.56]) and Hispanic OR=0.52; 95% CI [0.49,0.56]) women. The data show that GDM is protective for stillbirth among hospitalized pregnant women when compared to their respective non-diabetic counterparts regardless of race/ethnicity.

Discussion

Main Findings and Interpretation

As reported in previous studies, results of our analyses suggest that there are racial/ethnic differences in the prevalence of PDM and GDM. However, our findings expand on previous studies by reporting data on trends in pregnancy-associated diabetes by race/ethnicity. Consistent with earlier HCUP NIS studies, our results show an increasing trend in the prevalence of PDM and GDM from 2002 to 2017.[10] In addition, our data suggest the prevalence of PDM and GDM is increasing among NH-White, NH-Black and Hispanic hospitalized mothers. These findings correlate with increasing trends in risk factors for diabetes such as obesity, inactivity, and hypertension observed among specific racial/ethnic minority women.[25–30] Another possible contributing factor is an increase in advanced maternal age pregnancies.[31–33]

Note that the graphs in Figure 1 show an inflection point in trends for PDM and GDM in 2015. This is likely caused by two factors. First, the implementation of U.S. Prevent Services Task Force recommendations for routine GDM screening in asymptomatic pregnant women after 24 weeks of pregnancy in 2014.[34] Secondly, a change in disease reporting in 2015 due to the transition from the ICD-9 to ICD-10 coding set.[35] These changes likely increased screening for PDM and GDM as well as disease reporting.

The majority of associations we found between pregnancy-associated diabetes, race/ethnicity and maternal characteristics are consistent with previously reported data.[10,36,37] One exception is the increase in GDM prevalence with increasing zip code income observed among hospitalized NH-Black and Hispanic women. A previously published study conducted in California found that high-income zip codes had a lower prevalence of GDM compared to low-income zip codes.[38] These conflicting results suggest that factors such as diabetes screening, exercise, and diet could be more important than previously suspected to the prevalence of GDM in certain racial/ethnic groups.

The highest prevalence rates for PDM and GDM were observed among Hispanic and NH-Black pregnant mothers discharged against medical advice (DAMA). Previously published data suggest DAMA is more common among hospitalized pregnant women with PDM and GDM compared to those without diabetes.[39] DAMA among hospitalized pregnant women is also associated with Black race, public insurance, substance abuse, mental illness, chronic hypertension, neonatal morbidity and fetal death.[40] Additional research is needed to better characterize this vulnerable group and develop screening tools for intervention.

Another notable finding is the prevalence of PDM among NH-Black pregnant women who died during hospitalization. Among pregnant women who died during hospitalization, NH-Black had the highest prevalence of PDM when compared to the other race/ethnic groups. Our results are consistent with previously published NIS data.[41] The causal pathway between PDM and maternal mortality among hospitalized NH-Black women is not clear but studies report African American race/ethnicity is a significant independent risk-factor for pregnancy-related cardiovascular conditions including venous thromboembolism and stroke that can be fatal.[42,43] Further, type 1 diabetes has been associated with an increased risk of maternal mortality due to complications such as hypoglycemia.[44] These data suggest NH-Black pregnant women with PDM could be predisposed to glycemic and cardiovascular conditions that increase risk for maternal mortality. However, additional research is needed.

Consistent with previously published data, stillbirth rates for hospitalized pregnant women in our study were higher for women with PDM than those with GDM.[12,14] Unlike previous studies, results of our analyses show that racial/ethnic differences in stillbirth rates exist. Additionally, we are the first to report adjusted odds of stillbirth for Hispanic mothers with PDM. Hispanic mothers with PDM had the highest adjusted odds of stillbirth when compared to their non-diabetic counterparts in our study, a previously unreported finding. Reasons for differences across racial/ethnic groups are likely underlying maternal and fetal characteristics that have not been well-studied. Previously reported risks factors for stillbirth among woman with PDM include maternal age, BMI, gestational infant size, male gender, parity, tobacco use and type of delivery.[18,35,37,45] The extent to which these factors are influenced by race/ethnicity is not clear and should be taken into consideration.

Interestingly, after adjustment for maternal and hospital characteristics, we found that GDM was protective for stillbirth in each race/ethnic group, decreasing the odds of stillbirth by approximately 50%. Similar findings are reported by Lavery et al.[46]One possible explanation could be related to the large percentage (70-78%) of women in our study with private or public medical coverage. Medical coverage may result in more aggressive diabetes screening during pregnancy and better access to follow-up care decreasing the occurrence of stillbirth.

Strength and Limitations

This study has several strengths and limitations. Strengths of this study include a sample size, study design and time of data collection. The HCUP NIS is designed to produce regional and national estimates of hospitalization utilization and outcomes. The analyses are conducted using weighted estimates that represent more than 35 million annual hospitalizations nationally. The large sample size allowed for robust analysis of rare exposures like PDM and outcomes like stillbirth in specific racial/ethnic groups at a national level using a standardized dataset. Use of this data reduces selection bias and increases precision of our analyses. Further, our findings are based on data from 2002 to 2017, more recent and comprehensive than previous national studies.[7,10,47]

Limitations of this study include the data source. HCUP NIS is limited to an inpatient population and does not account for women who delivered outside of the hospital. Additionally, results of our studies are limited to the analysis of only three racial/ethnic groups despite differences in prevalence of pregnancy-associated diabetes in other race/ethnic groups including Native Americans and NH-Asians.[7,31,33]

Another limitation of this study is variation in data reporting for PDM and GDM. Despite efforts to standardized documentation, there are differences in reporting across data sources likely due to changes in diagnosis criteria over time, coding, and health care provider experience.[48] The extent to which variation in reporting is likely to influence our results is not clear. However, a study that compared birth certificate data to other government collected data found the HCUP NIS survey to be a more acceptable source.[48]

Furthermore, our study is limited by the inability to account for sociodemographic characteristics such as education level, employment, and marital status. Additionally, we could not account for factors such as physical activity, diet, hemoglobin a1c level and diabetes type which are associated with pregnancy-associated diabetes and/or stillbirth because of NIS HCUP data limitations.[49,50] Lastly, given the design of this study, a causal relationship between PDM and stillbirth could not be determined.

Conclusion and Implications for Translation

We observed that PDM and GDM is increasing in the U.S. among minority women. Additionally, our data highlight the increased prevalence of stillbirths and maternal mortality among women with PDM, especially Hispanic and NH-Black mothers, respectively.

Our results emphasize the need for the following: 1) broader implementation of standardized guidelines for reproductive age women diagnosed with diabetes with clear pre-conception treatment goals; 2) greater public health efforts to reach women at high risk for diabetes and GDM for screening and glucose monitoring; 3) additional research to better understand race/ethnicity specific risk-factors for PDM and the causal pathway for stillbirth and maternal death; and 4) allocation of resources is needed to address maternal risk factors and social determinants of health necessary to mitigate racial/ethnic differences and target effective interventions.

Disclosure of Interests

The authors have no competing interest to declare.

Contribution of Authorship

JA conceived main conceptual idea for the project. DD and HMS secured access to the dataset. DD performed computations and verified analytical methods. All authors were involved in interpretation of the data. JA, VM, AAH, AVD, GAD and DAS were involved in drafting the article. All authors were involved in critical revision of the article and contributed to the final approval of the manuscript.

Details of Ethics Approval

Due to the de-identified, publicly available nature of NIS data, the analyses performed for this study were considered exempt by the Baylor College of Medicine Institutional Review Board.

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Table/Figure Captions List

Table 1: Patient characteristics of mothers diagnosed with pre-pregnancy and gestational diabetes by race/ethnicity

Figure 1: Temporal trends in the rates of pre-pregnancy and gestational diabetes, overall and by race/ethnicity: 2002-2017

Figure 2: Rates of stillbirth among mothers with pre-pregnancy and gestational diabetes, overall and by race/ethnicity

Figure 3: Forest plot showing association between pre-pregnancy and gestational diabetes (exposure) and stillbirth (outcome), overall and by race/ethnicity

Table 1: Patient characteristics of mothers diagnosed with pre-pregnancy and gestational diabetes by race/ethnicity

	NH-White	**NH-White**
	Pre-pregnancy diabetes	
N=304710	**Pre-pregnancy diabetes**	
N=304710	**Gestational Diabetes**	
N=1586776	**Gestational Diabetes**	
N=1586776	**Pre-pregnancy diabetes**	
N=175832	**Pre-pregnancy diabetes**	
N=175832	**Gestational Diabetes**	
N=439638	**Gestational Diabetes**	
N=439638	**Pre-pregnancy diabetes**	
N=193498	**Pre-pregnancy diabetes**	
N=193498	**Gestational Diabetes**	
N=934383	**Gestational Diabetes**	
N=934383		
	%=100	**Prevalence**
Age		
<24 years	21.2%	0.8%
25-34 years	54.7%	1.0%
35-49 years	24.1%	1.5%
Discharge Status	**Discharge Status**	
Routine	94.7%	1.0%
Transfer	1.5%	2.7%
Died	0.0%	3.5%
DAMA	1.4%	6.4%
Other	2.4%	1.3%
Missing	0.0%	0.7%
Zip Income quartile	**Zip Income quartile**	
Lowest quartile	21.8%	1.3%
2nd quartile	21.8%	1.1%

	NH-White	NH-White
3rd quartile	19.9%	1.0%
Highest quartile	14.5%	0.7%
Missing	22.0%	0.9%
Primary Payer		
Medicare	4.8%	1.4%
Medicaid	31.6%	1.2%
Private Insurance	47.2%	0.9%
Self-Pay	4.3%	1.0%
Missing	12.1%	1.0%
Hospital Characteristics	**Hospital Characteristics**	
Hospital Region		
Northeast	17.6%	0.9%
Midwest	20.8%	1.0%
South	43.5%	1.2%
West	18.0%	0.9%
Hospital Bed Size	**Hospital Bed Size**	
Small	10.8%	0.8%
Medium	25.0%	0.9%
Large	63.8%	1.1%
Missing	0.4%	1.2%
Hospital Location and Teaching Status	**Hospital Location and Teaching Status**	**Hospital Location and Te**
Rural	10.8%	0.8%
Urban non-teaching	30.8%	0.8%
Urban teaching	58.0%	1.2%
Missing	0.4%	1.2%

[a]DAMA- Discharged against medical advice

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