



Associations Between Rurality, pre-pregnancy Health Status, and Macrosomia in American Indian/Alaska Native Populations

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Accepted: 9 September 2022 / Published online: 8 November 2022

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Abstract

Objectives To examine the relationships between pre-pregnancy diabetes mellitus (DM), gestational diabetes mellitus (GDM), pre-pregnancy body mass index (BMI) and county-level social determinants of health, with infant macrosomia within a sample of American Indian/Alaska Native (AI/AN) women receiving Indian Health Service (IHS) care.

Methods The sample included women-infant dyads representing 1,136 singleton births from fiscal year 2011 (10/1/2019–9/30/2011). Data stemmed from the IHS Improving Health Care Delivery Data Project. Multivariate generalized linear mixed models were fitted to assess the association of macrosomia with pre-pregnancy health status and social determinants of health.

Results Nearly half of the women in the sample were under age 25 years (48.6%), and most had Medicaid health insurance coverage (76.7%). Of those with a pre-pregnancy BMI measure, 66.2% were overweight or obese. Although few women had pre-pregnancy DM (4.0%), GDM was present in 12.8% of women. Most women had a normal term delivery (85.4%). Overweight, obesity, pre-pregnancy DM, and county-level rurality were all significantly associated with higher odds of infant macrosomia.

Keywords Maternal child health · Obesity · Diabetes · Infant weight · American Indians/Alaska Natives

Significance Statement

Birthweight is associated with the risk of metabolic syndrome, diabetes, and obesity in adulthood. Previous studies within American Indian and Alaska Native (AI/AN) populations on macrosomia have not included social determinants of health risk factors. Early life environments experienced by women, such as disadvantaged neighborhood, built environment factors and community-level socioeconomic factors are related to high birthweight and high pre-pregnancy weight. AI/AN people experience persistent health disparities across the lifespan compared to non-Hispanic whites and experience greater prevalence of poor health outcomes. Knowledge is lacking on infant outcomes as a function of maternal factors in the AI/AN population. The current study found that AI/AN women who were overweight or obese, had pre-pregnancy diabetes, or lived in a rural county had

higher odds of having an infant with a high birthweight. AI/AN women who may become pregnant should be advised on weight gain and diabetes to help decrease the risk of high birthweight and later childhood obesity.

Introduction

Early life weight is associated with the risk of metabolic syndrome, diabetes, and obesity in adulthood (Dixon et al., 2012; Marshall, 2019; Pachucki & Goodman, 2015). Systematic studies and meta-analyses have shown that birth weight, an indicator of early life development, is associated with impaired glucose tolerance, insulin resistance, and cardiovascular disease later in the life course (Knop et al., 2018; Tian et al., 2019). Childhood health outcomes result from exposures during the prenatal period, as women who are overweight, obese, or who have pre-pregnancy diabetes mellitus (DM) or gestational diabetes mellitus (GDM) are more likely to have a newborn with macrosomia (infant

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birth weight > 4000 g) (Garcia-Vargas et al., 2012; Halvorson et al., 2017; Hunt et al., 2013; Voerman et al., 2019). Infants with macrosomia are more likely to be overweight or obese in childhood and adulthood, and to have metabolic syndrome or diabetes mellitus (DM) later in life (Boney et al., 2005; Hu et al., 2020; Knop et al., 2018; Tian et al., 2019; Yu et al., 2011). Early life environments experienced by women, such as disadvantaged neighborhood and built environment factors (e.g., rurality, limited access to grocery stores) and community-level socioeconomic factors (e.g., limited education, high poverty), are related to infant macrosomia (Carter et al., 2012; Shi et al., 2013; Vaiserman, 2017).

Social determinates of health (SDOH) are occurrences that are influenced by the political, social, environmental, and economic conditions in which people are “born, grow, live, work, age,” and receive health care (Link & Phelan, 1995; Mitchell, 2012). The relationship between adverse maternal social and environmental influences and high birth weight has been an area of concern by the Indian Health Service (IHS) since the 1960’s (Rosa & Resnick, 1965; Thierry et al., 2009). American Indian/Alaska Native (AI/AN)s experience persistent health disparities across the lifespan compared to non-Hispanic whites and experience greater prevalence of poor health outcomes (e.g., diabetes, overweight/obesity, cardiovascular diseases) (Chang et al., 2016; Jones, 2006; Lanier, 2007). The drivers of health disparities are complex and persevere across generations with interactions between multiple SDOH, such as household income, educational attainment, and food insecurity, that influence poor health outcomes (Dagher & Linares, 2022; Marmot et al., 2008). The root determinates of disruptions to AI/AN health include colonization, medical pathologizing, social exclusion, racial discrimination, oppression, marginalization, and chronic inadequacy of funding of the IHS (Christensen & Damon, 2022; Jaramillo et al., 2022; Kruse et al., 2022).

AI/AN children have a higher prevalence of obesity than US children overall (Bullock et al., 2017; Ogden et al., 2015; Schell & Gallo, 2012). The prevalence of pediatric obesity has rapidly increased in the US over the last 30 years, with notable disparities in racial and ethnic minority populations (Ogden et al., 2015). AI/AN pediatric obesity is associated with obesogenic influences during gestation, which predict offspring obesity later in the life course (Dixon et al., 2012; Lynch & Smith, 2005). Women’s risk factors for AI/AN pediatric obesity include pre-pregnancy DM, pre-pregnancy overweight or obesity, smoking while pregnant, late onset of prenatal care, high gestational weight, gestational weight gain, GDM, and maternal depression (Schell & Gallo, 2012). SDOH risk factors for AI/AN pediatric obesity include high levels of poverty, unemployment, and

food insecurity, and low levels of education in the community (Schell & Gallo, 2012). Few studies have examined infant outcomes as a function of maternal factors in the AI/AN population (Anderson et al., 2016; LaVallie et al., 2003; Rockhill et al., 2015; Schell & Gallo, 2012). AI/AN children of women with pre-pregnancy DM or GDM are nearly two times more likely to be obese and 1.71 times more likely to be overweight by ages 5–8 years than are children of women without pre-pregnancy DM or GDM. Within AI/AN populations, overweight, obesity, and preexisting DM are all associated with increased odds of macrosomia (Anderson et al., 2016; Rockhill et al., 2015).

Past studies in the AI/AN population have not assessed the role of community-level SDOH risk factors in addition to maternal risk factors (e.g., diabetes, obesity). In this study, we examined the association of maternal risk factors and SDOH with macrosomia among AI/AN families accessing services through IHS. IHS clinics and programs are located on or near AI reservations and AN communities, locations that are predominantly rural and impoverished (Brenneman et al., 2006). We hypothesize that mothers’ obesity, pre-pregnancy DM, are significantly associated with higher odds of infant macrosomia; meanwhile, lower level of neighborhood socioeconomic status (i.e., lower income, education, and rurality) are also significantly associated with higher odds of infant macrosomia. The study data were extracted from a data infrastructure developed for the IHS Improving Health Care Delivery Data Project (IHS Data Project). Although the IHS Data Project was not originally created to examine AI/AN women’s risks for high birthweight infants, we were able to use data from a subset of project sites to examine macrosomia among infants of AI/AN women.

Methods

Data Source

Since 2010, the Centers for American Indian and Alaska Native Health at the Colorado School of Public Health, has collaborated with the IHS to create a longitudinal data infrastructure that houses health status, service utilization, and treatment cost data for over 640,000 AI/ANs who lived throughout the United States, representing nearly 30% of AI/ANs who use IHS services (O’Connell et al., 2014). The data infrastructure is a synthesis of existing electronic data from multiple IHS platforms and includes data for seven fiscal years (FY) 2007–2013. FY 2011, for example, is October 2010 to September 2011. The IHS Data Project provides a purposeful sample of AI/AN persons who lived in one of 15 IHS Service Units (hereafter referred to as project sites) located throughout the United States. The IHS Data Project

includes one project site in the East, four in the Northern Plains, two in the Southern Plains, five in the Southwest, two in the Pacific Coast, and one in Alaska, based on geographic areas reported elsewhere (O'Connell et al., 2014). The IHS Data Project population was identified by geographic area (i.e., Service Units), rather than by random sampling, to create important community and county measures not available elsewhere (O'Connell et al., 2014). The IHS Data Project population is comparable to the national IHS service population in terms of age and gender (Indian Health Service, 2010). More information about the data infrastructure may be found elsewhere (O'Connell et al., 2014).

Study Sample

Women were identified using obstetric admissions using the inpatient service code for 'obstetric' visits during FY2007 - FY2013. Of the fifteen project sites, four had no or almost no obstetric admissions and one site was excluded due to the large percentage of women referred to this site from other locations who may have had more complicated pregnancies. Next, we limited the obstetric admissions to individuals with a labor and delivery ICD-9 diagnostic code. If a mother had multiple admissions within 9 months, the first admission was kept as the delivery admission. We then identified infants from inpatient data using the inpatient service code for 'newborn', limiting admissions to instances where the month and year of service matched the date in the demographic information.

Mothers and their infants were linked using the delivery hospital, dates of admission, and either the household identification number or the community of residence, both from the IHS registration data. We limited this analysis to singleton births. Multiple births are excluded as they are more likely to be of a low birthweight or premature. Among the ten remaining project sites, only six sites had 75% or more of deliveries linked to newborns. Thus, we limited the study sample to those six sites.

Study Variables

Primary Outcome. Infant weight, the primary outcome, was measured in grams at birth. Macrosomia was defined as a weight ≥ 4000 g regardless of gestational age (American College of Obstetricians and Gynecologists, 2020; Duryea et al., 2014).

Women's demographic and health coverage data. Women's month and year of birth were used to calculate the women's age at the service date when the child was born and categorized into age groups. Health care insurance coverage was categorized into three categories: Medicaid,

private insurance, or no coverage in addition to access to IHS services.

Women's health status. Inpatient and outpatient data provided ICD-9 codes indicating GDM (648.80 to 648.84). Pre-pregnancy DM was determined by using data on ICD-9-CM diagnoses, procedure codes, medication use, and blood glucose control (i.e., hemoglobin A1c $\geq 6.5\%$) in the two years prior to the pregnancy. A woman's pre-pregnancy body mass index (BMI) was defined as the BMI measure that was closest to the gestation date (defined as 270 days prior to the delivery date). BMI measures that were more than one year before the gestation date, more than one month after the gestation date, or during a prior pregnancy were excluded. We excluded biologically implausible height, weight, and BMI values for adults aged 18 years and older. We used the standard definitions for obesity for individuals age 18 and older (overweight: BMI = 25.0–30.0 kg/m²; obese: BMI > 30.0 kg/m²). Relevant chronic conditions of women were identified using ICD-9 codes reported in the inpatient and outpatient service utilization records in FY2010, supplemented by medication data. Sightlines™ DxCG Risk Solutions software groups ICD-9 codes into diagnostic cost groups (Verisk Health, 2011). Diagnostic cost groups are employed by the federal government and private insurers to identify chronic conditions. We used this software to identify adults with one or more types of chronic conditions: hypertension, cardiovascular disease, mental health disorder, and substance use disorder (inclusive of drug, alcohol, and tobacco use). Pre- and post-term delivery were identified by ICD-9 diagnosis codes.

SDOH indicators. SDOH indicators were largely county-level measures drawn from Census Bureau and United States Department of Agriculture (USDA) Food Environment Atlas data sources and were added to the IHS Data Project by county of residence (Indian Health Service, 2010; US Census Bureau, 2001, 2015, 2016). From the Census, we had county-level indicators from the 2010–2014 American Community Survey (ACS) and decennial Census 2000 and 2010 (US Census Bureau, 2001, 2015). We used the Healthy People 2020 SDOH framework to organize and categorize our SDOH independent variables. For each SDOH, we calculated the median value for the 72 counties included in our data and created a binary variable of SDOH based on the median value of it (i.e., \leq median vs. $>$ median).

Education and economic stability measures were drawn from 2010 to 2014 ACS county-level data. Estimates were calculated for AI/AN persons who report accessing IHS services in the ACS response (US Census Bureau, 2016). Educational attainment was calculated as the percentage of adults aged 25 years and older who did not complete high school. We defined the percentage of households with a low income as the percentage of households with incomes below

139% of the federal poverty level (US Census Bureau, 2001, 2015, 2016). Neighborhood and built environment measures were from the USDA Food Environment Atlas, including the percent of the county population with low access to a grocery store in 2010 and the number of Supplemental Nutrition Assistance Program (SNAP) authorized stores per 1,000 population (Indian Health Service, 2010). We also coded county rurality using the National Center for Health Statistics urban-rural classification (National Center for Health Statistics, 2017).

Statistical Analysis

Descriptive statistics of the woman's individual demographic and health status characteristics and county-level SDOH were examined for the full study sample and stratified by infant macrosomia status. Multivariate generalized linear mixed models were fitted to assess the association of high birthweight with maternal health factors (i.e., DM, GDM, and obesity) and SDOH indicators, with county-level random intercepts to account for clustering of observations within counties. We subsequently introduced potential confounding covariates in steps (Fig. 1). Model 1 included maternal sociodemographic and health factors (i.e., age, health insurance, pre-pregnancy BMI category, pre-pregnancy DM, and GDM status) and pre-/post-term birth outcome. Model 2 added comorbidities (i.e., hypertension, cardiovascular disease, mental health disorder, substance use disorder) to Model (1) Model 3 added county-level neighborhood and built environment SDOH variables to Model (2) Model 4 added county-level education and economic stability variables to Model (3) Adjusted odds ratios and their p values are presented. Statistical significance was defined as $p < 0.05$ with 95% confidence intervals. We used SAS® 9.4 and Stata statistical software to conduct descriptive and multivariable analyses (SAS Institute, 2013; Stata-Corp, 2015).

Institutional and Tribal Approval

Project personnel work in a collaborative manner with IHS and the Tribal organizations that participate in the IHS Data Project. This collaboration takes place through the project's Collaborative Network, which includes three advisory committees (i.e., Steering, Project Site, and Patient) and a process to obtain approvals from the IHS Institutional Review Board (IRB), Tribal IRBs, and Tribal Councils and Authorities, in addition to the university's IRB (Colorado Multiple Institutional Review Board). Relevant IRB and community level approval of all aspects of this study were received prior to the conduct of the investigation. Patients at

study locations gave their informed consent for deidentified patient data to be used for health services research.

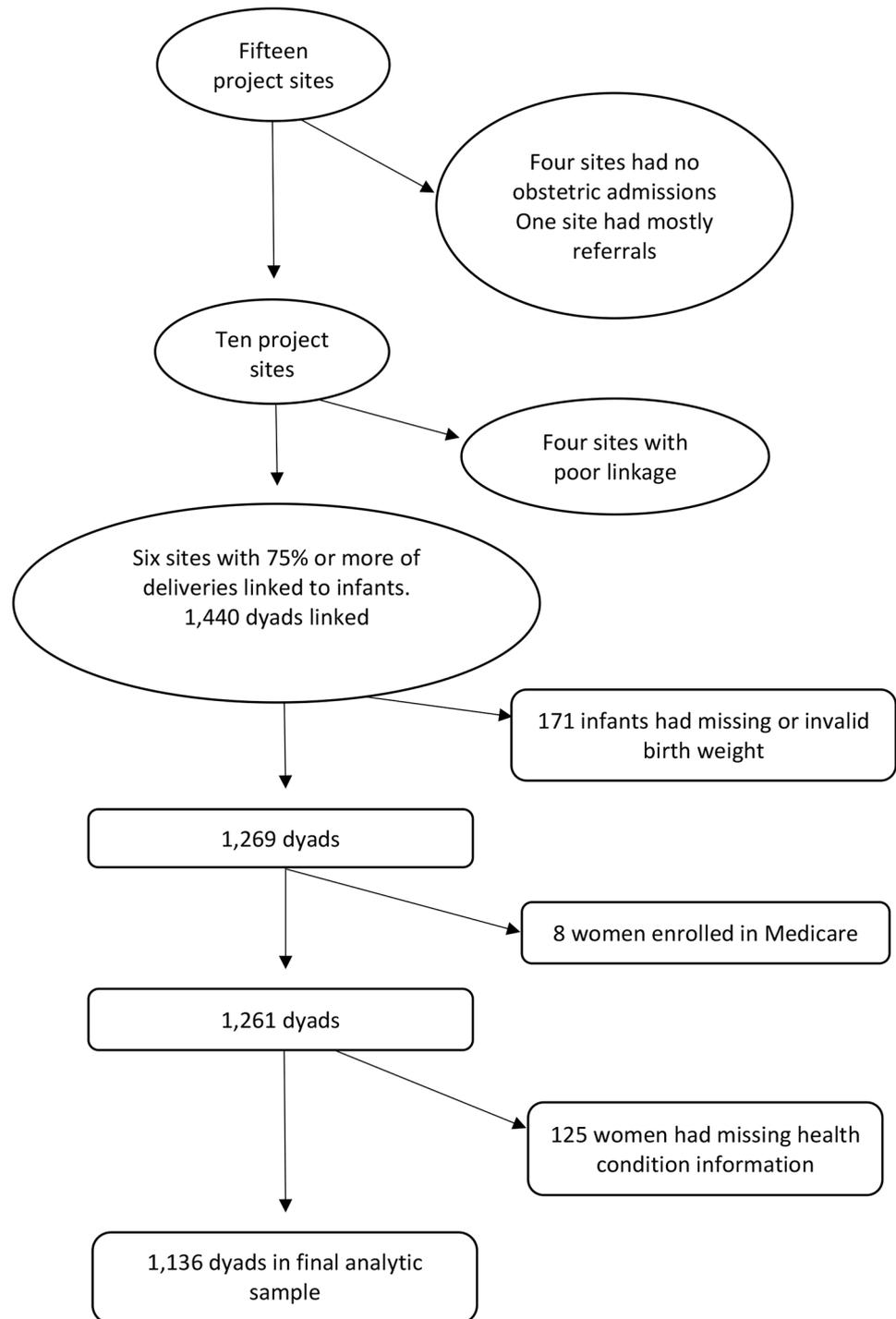
Results

Table 1 presents descriptive characteristics for women stratified by infant birth weight. Nearly half of women in the sample were under age 25 years (48.6%) and most had Medicaid health insurance coverage (76.7%). Of those with a pre-pregnancy BMI measure, 66.2% were overweight or obese. Few had a pre-pregnancy diagnosis of DM (4.0%), while 12.8% experienced GDM. Few women had a diagnosis of hypertension (2.2%), cardiovascular disease (5.0%), however, more women had a diagnosis of a mental health disorder (12.3%), or substance use disorder (9.2%) in the year prior to the birth of their child. The majority of women lived in counties that were classified as rural (54.0%), low income (59.1%), and as having a low level of education among AI/AN residents (72.5%). About half of the women resided in a county with low access to grocery stores (50.8%).

As shown in Table 1, 6.4% of infants in the study sample had macrosomia. The prevalence of macrosomia increased along with pre-pregnancy BMI category, such that macrosomia was more common for women with higher BMI. Macrosomia was also more common in post-term deliveries. No county-level differences in SDOH were noticeable between infant birth weight categories.

In Table 2, we present the adjusted odds ratios (OR) from multivariate generalized linear mixed models designed to evaluate the effects of maternal health factors and county-level SDOH characteristics on macrosomia. In Model 1, pre-pregnancy DM was significantly associated with higher odds of macrosomia (OR = 7.67; CI = 3.37, 17.43, $p < 0.0001$). Meanwhile, compared to underweight/normal pre-pregnancy BMI, the odds of having an infant with macrosomia was significantly elevated among women with pre-pregnancy BMI categorized as overweight (OR = 3.09; CI = 1.17, 8.13, $p = 0.023$) or obese (OR = 3.52; CI = 1.39, 8.93, $p = 0.008$). In Model 2, in which we adjusted for major comorbidities, the odds of having an infant with high birth weight was higher when a woman had pre-pregnancy DM (OR = 8.33; CI = 3.56, 19.47, $p < 0.0001$) or a pre-pregnancy BMI that was in the overweight (OR = 3.05; CI = 1.15, 8.04, $p = 0.025$) or obese (OR = 3.52; CI = 1.38, 8.95, $p = 0.008$) categories. In Model 3, when neighborhood and built environment measures were added, pre-pregnancy DM and pre-pregnancy overweight or obesity still increased the odds of having an infant with macrosomia. However, neighborhood and built environment factors were not associated with high infant birth weight.

Fig. 1 Flow chart defining study population and exclusions



In Model 4, in which county-level education and economic stability variables were added, we observed the largest odds ratio for having an infant with macrosomia with pre-pregnancy DM (OR = 10.31; CI = 4.19, 25.37, $p < 0.0001$). Overweight (OR = 2.81, CI = 1.05, 7.51, $p = 0.040$) and obesity (OR = 3.43; CI = 1.33, 8.87, $p = 0.011$) were also associated with having increased odds of macrosomia. Further, rurality

was associated with higher odds of macrosomia (OR = 4.01; CI = 1.02, 15.70, $p = 0.047$). Finally, when the delivery was pre-term, the odds of having a high birthweight infant was significantly lower (OR = 0.13; CI = 0.02, 0.97, $p = 0.047$).

Table 1 Maternal descriptive characteristics stratified by infant birth weight

	All	Infant low/ normal birth weight < 4,000 g	Infant high birth weight ≥ 4000 g
	N (%)	n (%)	n (%)
All	1,136 (100.0%)	1,063 (93.6%)	73 (6.4%)
Individual & healthcare			
Age group			
< 25 years	552 (48.6%)	522 (94.6%)	30 (5.4%)
25–34 years	479 (42.2%)	445 (93.5%)	34 (7.1%)
35 + years	105 (9.2%)	229 (95.0%)	9 (8.6%)
Health insurance coverage			
Had no insurance coverage	182 (16.0%)	171 (94.0%)	11 (6.0%)
Had Medicaid	871 (76.7%)	814 (93.5%)	57 (6.5%)
Had private insurance	241 (21.2%)	229 (95.0%)	12 (5.0%)
Health condition			
Non-diabetic	945 (83.2%)	895 (94.7%)	50 (5.3%)
Prepregnancy diabetes ^a	46 (4.0%)	33 (71.7%)	13 (28.3%)
Gestational diabetes	145 (12.8%)	135 (93.1%)	10 (6.9%)
Prepregnancy BMI ^a			
Underweight or normal weight	243 (21.4%)	237 (97.5%)	6 (2.5%)
Overweight	205 (18.0%)	189 (91.3%)	16 (7.8%)
Obese	271 (23.9%)	244 (87.3%)	27 (10.0%)
No BMI measure	417 (36.7%)	393 (89.3%)	24 (5.8%)
Hypertension ^a	25 (2.2%)	22 (88.0%)	3 (12.0%)
Cardiovascular disease ^a	57 (5.0%)	54 (94.7%)	3 (5.3%)
Mental health disorder ^a	140 (12.3%)	133 (95.0%)	7 (5.0%)
Substance use disorder ^a	105 (9.2%)	99 (94.3%)	6 (5.7%)
Birth outcomes			
Pre-term delivery	72 (6.3%)	71 (98.1%)	1 (1.4%)
Post-term delivery	94 (8.3%)	86 (79.5%)	8 (8.5%)
Neighborhood & built environment			
Low access to grocery stores			
Counties with less access to the grocery store (% low access > 25.3%)	577 (50.8%)	535 (92.7%)	42 (7.3%)
SNAP authorized stores per 1,000 population			
Counties above the median (0.8%)	503 (44.3%)	471 (93.6%)	32 (6.4%)
NCHS County rurality 2013	613 (54.6%)	566 (92.3%)	47 (7.7%)
Education & economic stability			
AI/AN Education: % adults < high school			
Counties with lower levels of educational attainment (% less than high school > 46.0%)	824 (72.5%)	766 (93.0%)	58 (7.0%)
AI/AN Income: % households < 139% FPL			
Counties with higher levels of poverty (% below 139% FPL > 42.5%)	671 (59.1%)	626 (93.3%)	45 (6.7%)

Abbreviations: AI/AN: American Indian/Alaska Native; BMI: Body mass index; FPL: Federal Poverty Level; g: grams; SNAP: Supplemental Nutrition Assistance Program; NCHS: National Center for Health Statistics

^a Data from FY2010

Discussion

This study examined individual- and geographic-level factors associated with macrosomia in the AI/AN population, utilizing IHS electronic medical records and county-level measures of SDOH. We found a strong association of obesogenic influences present before and during gestation with macrosomia in our sample of AI/AN infants. Macrosomia

was associated with maternal pre-pregnancy DM and pre-pregnancy overweight and obesity. GDM was not associated with increased odds of macrosomia in our study. Rural residence also increased odds of high infant birth weight.

Our results confirm findings from the few other studies examining pre-pregnancy DM, pre-pregnancy BMI, and infant birth outcomes in AI/AN populations. Dyck et al., (2019) conducted a retrospective, longitudinal, intra-inter-generational study among First Nations women and found

Table 2 Adjusted Odds Ratios (ORs) from Multivariate Generalized Linear Mixed Models Evaluating the Effects of Maternal Health Factors and County-Level Social Determinates of Health

	Model 1	Model 2	Model 3	Model 4
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age group				
<25 years	1.01 (0.59,1.73)	1.02 (0.59,1.76)	0.73 (0.49,1.08)	0.94 (0.54,1.66)
25–34 years (<i>reference</i>)				
35+ years	0.73 (0.31,1.72)	0.70 (0.29,1.69)	0.96 (0.53,1.74)	0.83 (0.33,2.09)
Health insurance coverage				
Medicaid	0.88 (0.48,1.62)	0.89 (0.48,1.63)	0.83 (0.55,1.25)	1.08 (0.57,2.04)
Private insurance	0.71 (0.37,1.36)	0.71 (0.37,1.37)	0.56 (0.32,0.95)	0.84 (0.41,1.72)
Health condition				
Prepregnancy diabetes	7.67 (3.37,17.43) ^{***}	8.33 (3.56,19.47) ^{***}	4.50 (2.14,9.45) ^{***}	10.31 (4.19,25.37) ^{***}
Gestational diabetes	1.16 (0.57,2.39)	1.18 (0.58,2.42)	0.93 (0.56,1.56)	1.28 (0.61,2.68)
Prepregnancy BMI				
Underweight or normal weight (<i>reference</i>)				
Overweight	3.09 (1.17,8.13) [*]	3.05 (1.15,8.04) [*]	2.79 (1.04,7.44) [*]	2.81 (1.05,7.51) [*]
Obese	3.52 (1.39,8.93) ^{**}	3.52 (1.38,8.95) ^{**}	3.40 (1.32,8.78) [*]	3.43 (1.33,8.87) [*]
No BMI measure	2.10 (0.84,5.27)	2.08 (0.83,5.21)	2.12 (0.82,5.46)	2.18 (0.83,4.30)
Hypertension		0.88 (0.28,2.77)	1.32 (0.32,5.41)	1.26 (0.31,5.23)
Cardiovascular disease		0.56 (0.20,1.62)	0.89 (0.26,3.13)	0.89 (0.25,3.12)
Mental health disorder		0.81 (0.48,1.37)	0.69 (0.29,1.63)	0.69 (0.29,1.65)
Substance use disorder		1.03 (0.60,1.75)	0.76 (0.29,1.98)	0.76 (0.29,1.99)
Birth outcomes				
Pre-term delivery	0.14 (0.02,1.05)	0.13 (0.02,1.02)	0.13 (0.02,0.97)	0.13 (0.02,0.97) [*]
Post-term delivery	1.57 (0.72,3.44)	1.54 (0.70,3.37)	1.91 (0.84,4.32)	1.89 (0.83,4.30)
Neighborhood & built environment				
Low access to grocery stores				
Counties with less access to the grocery store (% low access > 25.3%)			1.10 (0.76,3.36)	2.07 (0.37,11.66)
SNAP authorized stores per 1,000 pop				
Counties above the median (0.8%)			1.11 (0.38,3.25)	1.07 (0.35,3.25)
NCHS rural counties			2.55 (0.91,7.16)	4.01 (1.02,15.70) [*]
Education & economic stability				
AI/AN Education: % adults < high school				
Counties with lower levels of educational attainment (% less than high school > 46.0%)				0.62 (0.17,2.31)
AI/AN Income: % households < 139% FPL				
Counties with higher levels of poverty (% below 139% FPL > 42.5%)				0.47 (0.08,2.76)

Abbreviations: AI/AN: American Indian/Alaska Native; BMI: Body mass index; FPL: Federal Poverty Level; SNAP: Supplemental Nutrition Assistance Program; NCHS: National Center for Health Statistics

*** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$

that women with GDM and pre-GDM were more likely to have an infant with macrosomia (Dyck et al., 2019). Using national surveillance data from the Pregnancy Risk Assessment Monitoring System from AI/AN respondents with singleton births, Rockhill et al., (2015) found pre-pregnancy BMI and gestational weight gain were independent predictors of macrosomia among AI/AN women, with the prevalence of macrosomia in their sample at 14% (Rockhill et al., 2015). Anderson, Spicer, and Percy (2017) used a population-based retrospective sample of live singleton births in the United States to examine the relationship between obesity, diabetes, and birth outcomes among AI/AN and other racial/ethnic groups and found overweight, obesity, and DM were all associated with increased odds of macrosomia (Anderson et al., 2016). We too found higher than normal BMI and DM prior to pregnancy to be associated with increased odds of high birthweight. However, in our sample, the odds ratios were much higher than odds ratios reported by either Rockhill et al. (adjusted OR = 1.27; CI = 1.01, 1.59 for macrosomia with pre-pregnancy overweight; adjusted OR = 1.63; CI = 1.29, 2.07 for macrosomia with pre-pregnancy obesity) or Anderson et al. (OR = 1.47; CI = 1.35, 1.61 for macrosomia with pre-pregnancy overweight; OR = 1.99; CI = 1.83, 2.16 for macrosomia with pre-pregnancy obesity). Furthermore, unlike the studies conducted by Dyck et al. and Anderson et al., we did not find an association of macrosomia with GDM.

Many early life risk factors for childhood and adult obesity are more prevalent among United States minority populations than among non-Hispanic whites and may explain the higher prevalence of obesity among racial/ethnic minority children. Pediatric obesity currently has a prevalence of 17% in the United States and, once present, is difficult to reverse (Ogden et al., 2014). National estimates of infant obesity range from 8 to 16%, with evidence that children who are obese at six months of age are likely to remain obese at 24 months (Ogden et al., 2014). Obesity in early childhood tends to persist through childhood and across the lifespan, resulting in increased individual, social, health, and economic costs (Han et al., 2010; Wang et al., 2008) determined that obesity will account for more than 16% of all US healthcare expenditures by 2030 (Wang et al., 2008), which is particularly concerning for the chronically underfunded IHS (Sequist et al., 2011). Our findings are important for chronic disease prevention in AI/AN populations, as prevention is universally viewed as the best approach for reversing the rising global prevalence of obesity. To date, limited evidence exists regarding the most effective means of preventing obesity in AI/AN children (Bahia et al., 2019; Wang et al., 2015). Identifying crucial periods of developmental programming is important for designing effective interventions, considering that overweight, obesity, and GDM are

transgenerational health burdens in the AI/AN population (Bullock et al., 2017). Pre-pregnancy overweight and obesity and pre-pregnancy DM affected a substantial number of pregnancies in our sample and were associated with infant macrosomia. AI/AN culturally grounded interventions such as the Special Diabetes Program for Indians Diabetes Prevention (SDPI) demonstration project (Jiang et al., 2013), the Obesity Prevention and Evaluation of InterVention Effectiveness in NaTive North Americans (OPREVENT) multilevel multicomponent household intervention (Jock et al., 2022; Redmond et al., 2019), and the Tribal Health and Resilience in Vulnerable Environments (THRIVE) intervention (Love et al., 2019) have shown promising approaches to obesity prevention in AI/AN communities. Preconception counseling, or education of all women and adolescents of reproductive age, about the risks of entering pregnancy with risk factors, such as DM or obesity, and how pregnancy planning can improve both maternal and fetal outcomes is a standard of care recommended by the American Diabetes Association (American Diabetes Association, 2020). Providing preconception counseling and encouraging women to adopt a healthy lifestyle and maintain a healthy weight prior to pregnancy can reduce risk for GDM and poor pediatric outcomes (Moore et al., 2019; Nadeau et al., 2020). Postpartum interventions are also warranted to support AI/AN women (Jones et al., 2015).

Given the potential for a large impact on the population, future AI/AN overweight and obesity intervention trials aiming to reduce the prevalence of childhood and adult overweight and obesity should target pre-pregnancy weight status and diabetes prevention. Tribal nations, counties, states and the IHS need to address AI/AN overweight and obesity through multifactorial and comprehensive approaches that reckon with health inequities, colonial history, and funding inadequacies of policies and programs (Christensen & Damon, 2022; Dagher & Linares, 2022; Jaramillo et al., 2022).

In our study, most county-level SDOH variables, including AI/AN educational attainment, AI/AN household income, access to grocery stores, and SNAP authorized stores per capita, were not associated with high infant birth weight. The only county-level SDOH that was associated with macrosomia was county rurality. The associated between macrosomia and county rurality may be due in part to multiple co-occurring characteristics of the rural counties included in our analysis. The mechanism for this relationship is unclear but may be associated with SDOH and access, availability, and affordability of healthy foods in grocery stores. Jiang et al., (2018) found less BMI reduction and physical activity increase among AI/AN participants in the SDPI who lived in neighborhoods with higher concentrations of AI/ANs, when controlling for individual

level socioeconomic status. Meta-analyses have determined that environmental characteristics including rurality and low access to grocery stores were consistently associated with obesity (Leal & Chaix, 2011). Many IHS beneficiaries reside on a reservation or near a reservation, and chose to live near ancestral lands with family and cultural ties (Jiang et al., 2018), areas that tend to be rural.

We did not find an association between high birthweight and GDM, despite an increased risk for macrosomia characteristic for GDM. Although insulin is the preferred medication for treating hyperglycemia in women with GDM, some women with GDM may be placed on metformin as an alternative therapy. Our study design did not collect data on treatment for GDM (Bahia et al., 2019). However, a 2019 systemic review and meta-analysis of the impact of metformin in GDM upon the offspring growth trajectory showed that infants born to women with GDM treated with metformin weighed 108 gm lower on average than infants born to women with GDM treated with insulin (Tarry-Adkins et al., 2019). Some high-risk women in our sample with pre-existing DM or GDM may have been referred elsewhere for prenatal care and/or delivery, and thus have been excluded from our sample.

This work had strengths and limitations. A notable strength was our ability to assess both individual- and county-level variables related to infant birthweight. This study includes data on dyads who were eligible for and received health care at IHS facilities (i.e., are tribally enrolled and who elected to receive care at IHS facilities) located in six areas. Limitations included not being able to successfully link women and newborns at four of the 10 sites identified for study inclusion. Thus, the findings from our study may not be generalizable to AI/AN women and infants who receive services from other IHS Service Units or who are not eligible or access IHS services (Indian Health Service, 2010; US Census Bureau, 2015, 2016). While studies have documented future health risks associated with low birthweight (Feng et al., 2018; Knop et al., 2018), we did not investigate low birthweight, as our sample had a limited number of infants with low birthweight (N=42). Finally, individual-level education, income, family health history, and gender identity variables were not available and hence we were not able to control for individual level socioeconomic status in our models.

Conclusion

Previous studies within AI/AN populations on macrosomia have not included social determinants of health risk factors. The current study found that AI/AN women who were

overweight or obese, had pre-pregnancy diabetes, or lived in a rural county had higher odds of having an infant with a high birthweight. Our findings have implications for interventions to disrupt the cycle of obesity and adverse metabolic changes and their sequelae in subsequent generations of AI/AN people. Multigenerational interventions targeting prepregnancy weight reduction and control in a culturally appropriate manner are needed to support healthy weight. The role of rurality as a characteristic of the setting in which AI/AN people live and interventions take place should be further explored and considered in intervention planning and evaluation.

Acknowledgements Data used in this study are from the Indian Health Service (IHS) Health Care Delivery Data Project; the data include information from many American Indian and Alaska Native communities. Data Project analyses are conducted with the guidance and advice of IHS and Tribal health program colleagues, as well as members of the project's Steering, Project Site, and Patient Committees. Members of Tribal and IHS institutional review boards, Tribal Councils, and Tribal Authorities educate us about the health concerns they have for their Tribal members and how they hope this project will inform their work. This project relies on their support and approval. The authors would also like to express their gratitude to Sara Mumby for her editorial assistance.

Funding Statement The research reported in this publication was supported by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health under Award Numbers P30DK092923 (S.M. Manson) and R18DK114757 (J.M. O'Connell and S.M. Manson). Funding for the development of the data infrastructure, utilized in the reported analyses, was supported by the Agency for Healthcare Research and Quality (290-2006-00020-I, TO #11, J.M. O'Connell) and the Patient-Centered Outcomes Research Institute (AD-1304-6451, J.M. O'Connell). The content of this report is solely the responsibility of the authors and does not necessarily represent the official views of these organizations.

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