The Impact of Race-Ethnicity on the Antenatal Detection of Small for Gestational Age Infants

A Master's Thesis Presented

By

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Abstract

Objective: To examine differences in the antenatal detection rate of small for gestational age (SGA) infants among several race-ethnicity groups and determine whether perinatal outcomes differ in antenatally detected versus undetected SGA infants according to race-ethnicity.

Methods: A retrospective cohort study was conducted at a single tertiary care center that evaluated all deliveries of SGA infants >23 weeks gestation between January 2016-January 2020. Race and ethnicity were self-reported and categorized as non-Hispanic White, non-Hispanic Black, Hispanic, or Asian. The medical charts of those eligible were reviewed and the primary study outcomes were analyzed using multivariable logistic regression analyses with accompanying point estimates and 95% confidence intervals.

Results: A total of 526 childbearing persons satisfied our predefined inclusion criteria. The predominant race-ethnicity group was non-Hispanic White who comprised 50% of the study population. Antenatal detection rate of SGA was found to be 38%. The detection rate, while not statistically different, ranged from 28-40% according to race-ethnicity with Asians having the lowest detection rates. Higher rates of preterm birth, labor induction, and lower median birthweights were observed in antenatally detected versus undetected SGA pregnancies. However, no significant differences were observed with regards to perinatal outcomes when antenatally detected versus undetected SGA was compared according to race-ethnicity.

Conclusions: Antenatal detection may not be the primary solution to improving racial and ethnic disparities among SGA infants. Additional investigation to identify, address, and improve disparities in other areas of perinatal medicine is necessary to provide more equitable care. Further work to investigate the barriers to antenatal detection of SGA is warranted as an avenue for improving perinatal outcomes.

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Introduction

Birthweight is a widely accepted measure of neonatal health at both the individual and population levels.[1] Furthermore, birthweight has been recognized as a global health indicator as low birthweight is considered a multifaceted public health problem. Small for gestational age (SGA) infants, as defined by a birthweight less than the tenth percentile, are a population of particular interest given their increased risk of adverse outcomes including death, significant morbidities in the first 28 days of life, poor long-term growth/development, and several adult-onset chronic diseases.[1-4]

The clinical complications and comorbidities associated with SGA are particularly noteworthy given the disparate rates of SGA in the United States in historically marginalized racial and ethnic groups.[5] Recent investigations have observed SGA prevalence rates of 13% in Asian, 17% in non-Hispanic Black and 10% in Hispanic populations as compared to rates of 8.5% in the non-Hispanic White population.[5-7] Significant racial disparities have also been documented with regards to infant outcomes, with infants of Black, Asian, and Hispanic race-ethnicities having higher morbidity and mortality rates as compared with their White counterparts. [8-11]

While the diagnosis of SGA cannot be made until after birth, it can be suspected antenatally when ultrasound examination demonstrates fetal growth restriction, an estimated fetal weight less than the tenth percentile based on biometric measurements. Akin to the risk of adverse outcomes in SGA infants, pregnancies with fetal growth restriction are associated with adverse obstetrical outcomes including stillbirth, oligohydramnios, and cesarean delivery for non-reassuring fetal heart rate.[12-13] No antenatal therapy is currently available to reliably decrease the likelihood of delivery of an SGA infant. However, the prenatal detection, management, and surveillance of SGA infants is associated with decreased fetal and infant mortality rates.[14-16] Moreover, prenatal detection of a suspected SGA infant allows for

appropriate patient counseling, delivery planning, and establishment of a multidisciplinary approach for antenatal and postnatal care plans. Thus, high detection rates are desirable and understanding ways to improve detection hold significant clinical benefit.

The current antenatal detection of SGA infants is limited with only one-third to one-half of all possible cases being correctly identified.[14-15] There are, however, a paucity of data describing possible differences in antenatal detection rates among different racial-ethnic groups. The objectives of this retrospective cohort study were to examine possible race-ethnicity differences in the antenatal detection rate of SGA infants and to determine if perinatal outcomes differ in antenatally detected versus undetected SGA infants according to race-ethnicity.

Methods

Study Design

A retrospective cohort study was conducted in a single tertiary care center between January 2016-January 2020. The study was approved by the Human Subjects Committee/Institutional Review Board at the University of Massachusetts Chan Medical School.

The charts of all childbearing persons having delivered a liveborn or stillborn SGA infant at ≥23 weeks gestation were reviewed. An infant was classified as SGA if the birthweight was <10th percentile according to the Fenton growth curve for premature infants (born less than 37 weeks gestation) and the World Health Organization growth curve for term infants (born at 37 weeks or greater gestation).[17-18] Race and ethnicity were self-reported and then categorized as non-Hispanic White, non-Hispanic Black, Hispanic, or Asian. If an individual self-reported as Hispanic ethnicity they were placed into the Hispanic group regardless of their self-reported race. Those of other racial or ethnic groups, or for whom race-ethnicity were unknown, were excluded due to the small sample sizes. Individuals were excluded if they had a multifetal gestation, if a major congenital fetal anomaly or genetic syndrome was identified, or if they had a history of a prior pregnancy resulting in an SGA infant. Multifetal gestations or fetuses with a major congenital anomaly or genetic syndrome were excluded because specialized growth curves are

commonly used in these populations due to the underlying differences in growth potential.[19-21] Given association with increased ultrasound evaluation, those with history of prior pregnancy resulting in an SGA infant were excluded.

The electronic medical records for births that satisfied our inclusion criteria at UMass Memorial Medical Center were reviewed for the abstraction of demographic and relevant clinical data. All abstracted data were stored and managed in Research Electronic Data Capture (REDCap) tools hosted at the University of Massachusetts Medical School.[22] Maternal race and ethnicity were abstracted from patient's self-reported data. Paternal race and ethnicity are not reliably or objectively documented in the electronic medical record and were not included.

Assessment of Outcomes

The primary outcome of interest was to determine if the antenatal detection rate of SGA infants was different between the four race-ethnicity groups studied. Antenatal detection of SGA was defined as a fetus with an estimated fetal weight less than the tenth percentile as determined by ultrasound evaluation after 23 weeks gestation. In those with multiple ultrasounds, if at least one ultrasound demonstrated an estimated fetal weight less than the tenth percentile then this was considered antenatal detection. Estimated fetal weight was calculated using the Hadlock equation based on biometric measures of fetal head circumference, biparietal diameter, abdominal circumference, and femur length.[23-24] The estimated fetal weight percentiles were determined using population-based reference charts. During the years of this study, different fetal growth curves were utilized by healthcare providers as system policy changed over time and included the WHO and Hadlock reference fetal growth curves.[23-25] A subgroup analysis of the primary outcome based on type of fetal growth curve was not done due to small sample size.

The secondary outcome of interest was to investigate if the perinatal outcomes differed among prenatally detected versus undetected SGA infants according to race-ethnicity. Obstetrical and perinatal outcomes of interest were collected from review of the electronic medical record. A composite for infant morbidity was created due to the small numbers of individual morbid events and included the following

outcomes: sepsis, necrotizing enterocolitis, intraventricular hemorrhage (≥ grade III), retinopathy of prematurity, respiratory distress syndrome, and bronchopulmonary dysplasia.

Data Analysis

Patient demographic and clinical characteristics were compared across racial-ethnic groups using Chi-square or Fischer exact tests for categorical variables and Student's T-test for continuous. Unadjusted and adjusted logistic regression were used to examine the relationship of SGA with racial-ethnic groups. Confounders included in the adjusted model were those with a p-value <0.05 by racial-ethnic groups and considered clinically relevance to a diagnosis of SGA. Secondary outcomes were analyzed with a Chi-square test for each individual racial-ethnic group and unadjusted logistic regression including the interaction of SGA diagnosis with racial-ethnic group. Statistical significance was defined with a P value ≤ 0.05. All data were managed using REDCap (Research Electronic Data Capture) tools[22] and all statistical analyses were performed using Stata/MP 17.0 (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC).

Results

Study Population Characteristics

A total of 526 childbearing persons satisfied the study inclusion criteria (Figure 1). The predominant race-ethnicity group was non-Hispanic White who comprised approximately 50% of the study population. The remainder of the study population self-reported as Hispanic (26%), non-Hispanic Black (13%) and Asian (12%) (Figure 1). The average age of the population at the time of delivery was 29.3 years, with Hispanic persons being 2 years younger and Asian persons 2 years older on average. Those of Hispanic race-ethnicity had higher average pre-gravid body mass indices as compared with the other race-ethnicity groups. Asian individuals were more likely to be without any diagnosed pre-existing medical conditions at the time of pregnancy. Non-Hispanic White individuals had the highest rates of tobacco use and hypertensive diseases of pregnancy (Table 1).

Antenatal Detection by Race-ethnicity

An ultrasound for estimated fetal weight was performed in 72% of the study population. Non-Hispanic whites were the most likely and Asians were the least likely to have undergone an ultrasound for estimated fetal weight (82% versus 70%) (Table 1). Antenatal detection of SGA occurred in 38% of the study population at a mean gestational age of 33.3 weeks. Non-Hispanic Whites and non-Hispanic Blacks had the highest antenatal detection rates of approximately 40%. While the antenatal detection rates were lower in Hispanics (37%) and Asians (28%) they did not differ significantly when compared with Non-Hispanic Whites even after adjusting for potentially confounding factors (Table 2).

Perinatal Outcomes by Race-ethnicity and Detection

In the study population there was a 2.1% stillbirth rate, with only 2 of the 11 stillbirths having an antenatal diagnosis of SGA. Vaginal birth occurred in 62% of the study population, and this rate did not differ in those with detected versus undetected SGA or according to race-ethnicity. One third of pregnancies were complicated by a hypertensive disease of pregnancy. In Non-Hispanic Whites hypertensive disease of pregnancy were more common among undetected SGA as compared to detected SGA cases. However, this effect was not appreciated in the other race-ethnicity groups. Oligohydramnios was observed in 8% of the study population, and the frequency of this complication did not differ in those with detected versus undetected SGA or according to race-ethnicity. The frequency of NICU admission and composite neonatal morbidity was more common in detected versus undetected SGA pregnancies in Non-Hispanic Whites. This effect was not observed in the other race-ethnicity groups or in the interaction model (Table 3).

Preterm birth occurred in 17% of the study population, with higher rates in those with an antenatal diagnosis of SGA as compared to those without (25% versus 12%). Rates of labor induction were higher in those with an antenatal diagnosis of SGA as compared to those without (88% versus 55%). Median birthweight was slightly lower in those with, as compared to those without, an antenatal diagnosis

of SGA (2230g versus 2241g). The observed trends in the frequency of preterm births, labor induction rates and average birthweight were consistent across the race-ethnicity groups (Table 3). This trend was not observed when results were controlled for several potentially confounding factors in examining differences in various perinatal outcomes in antenatally detected versus undetected SGA according to race-ethnicity (Table 3).

Discussion

In this study, the antenatal detection rate of SGA was found to be 38%. The antenatal detection rate, while not statistically different, ranged from 28-40% according to race-ethnicity with Asians having the lowest detection rates. Higher rates of preterm birth, labor induction, and lower median birthweights were observed in antenatally detected versus undetected SGA pregnancies. However, no significant differences were observed with regards to perinatal outcomes when antenatally detected versus undetected SGA was compared according to race-ethnicity.

In the present study antenatal detection of SGA was defined as an antenatal diagnosis of fetal growth restriction based on an ultrasound estimated fetal weight less than the 10th percentile. Different fetal growth curves were utilized over the study period due to changes in provider preferences at the institution; however, all fetal growth curves used were population-based. The use of different population-based fetal growth curves is not unique to this investigation and is in accord with current guidelines. The American College of Obstetricians and Gynecologist and the Society for Maternal Fetal Medicine recommend the use of population-based fetal growth curves rather than customized or racial/ethnic specific curves.[16] Studies that have evaluated population-based versus race-ethnicity specific fetal growth curves have consistently demonstrated that population-based curves have higher rates of predicting SGA and neonatal morbidity, and lower ultrasound-birthweight percentile discrepancies[26-28]. Results of the present study provide additional support for this recommendation as we failed to identify differences in the antenatal detection of SGA according to race-ethnicity. Furthermore, the antenatal detection rates in

our study are consistent with the rates reported in other studies, giving additional strength to our study's support of current fetal growth curve recommendations.[29-31]

This investigation identified higher rates of preterm birth and labor induction, and lower median birthweights in cases of detected SGA as compared to undetected SGA. These findings are not surprising given that antenatal management differs in cases of fetal growth restriction and iatrogenic intervention to prevent stillbirth is not uncommon.[16] While this investigation did not observe any differences in antenatal detection or perinatal outcomes according to race, prior studies have demonstrated that the incidence and perinatal outcomes of SGA infants differs according to race-ethnicity.[32-35] Large retrospective studies have observed a higher odds of SGA in Asian ethnic subgroups, Black, and Hispanic childbearing persons.[5-7, 36] Furthermore, SGA infants of historically marginalized racial and ethnic groups have higher rates of stillbirth, morbidity, and mortality.[32, 36-38] These effects were likely not appreciated in this investigation because of the relative rarity of these adverse outcomes and the smaller sample size.

The antenatal detection of fetuses at risk for being SGA infants represents a period of potential intervention and a number of prior studies have demonstrated that antenatal detection significantly decreases the risk of adverse perinatal outcomes including neurological damage, fetal distress, and fetal or infant death.[14-15, 39] Given the racial and ethnic disparities of perinatal outcomes in SGA infants and the reduction in adverse outcomes achieved with antenatal detection, it is logical to next question the impact of race-ethnicity on antenatal detection. The results of this observation study suggest that antenatal detection may not be a key contributor to the racial and ethnic disparities observed in SGA infants. Inasmuch, further study evaluating potential areas to reduce inequities in care is warranted. The underlying etiologies for these disparities are likely multifactorial and complex involving individual and system-wide biases, psychosocial stress, and discriminations.[36,40-43]

Study Strengths and Limitations

This study has several strengths. While a number of studies have evaluated racial and ethnic disparities in obstetrics, to the best of our knowledge, differences in the antenatal detection rates of SGA

according to race-ethnicity have not been examined. An additional strength is detailed data from the electronic medical record in a contemporary and diverse cohort of pregnant individuals. The diagnosis of antenatal SGA detection was not limited to a particular fetal growth curve and only population-based fetal growth curves were utilized, consistent with recommendations from obstetrical governing societies. However, the results must be interpreted with appropriate caution based on the study's limitations. The race-ethnicity categories examined were based on self-reported fields in the medical record. While prior work has demonstrated that self-reporting of race-ethnicity is accurate, race-ethnicity can also be affected by personal and societal perception thus creating the possibility of misclassification bias.[44] Only four racial-ethnic groups were evaluated in this study, with the majority of those included being non-Hispanic White. It is possible that with a larger and more diverse cohort racial-ethnic differences may be identified. Extensive review of the medical record was performed to limit the presence of missing data and misclassification; however, the retrospective nature of this study contributes to limitations.

In summary, in this retrospective cohort study no significant difference in the antenatal detection rate of SGA infants according to race-ethnicity were identified. While antenatal detection may not be the primary solution to improving racial and ethnic disparities among SGA infants, further research to investigate the barriers to the antenatal detection of SGA is warranted for the purpose of improving perinatal outcomes and reducing disparities.

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Figure 1. Cohort flowchart of eligibility and sample size.

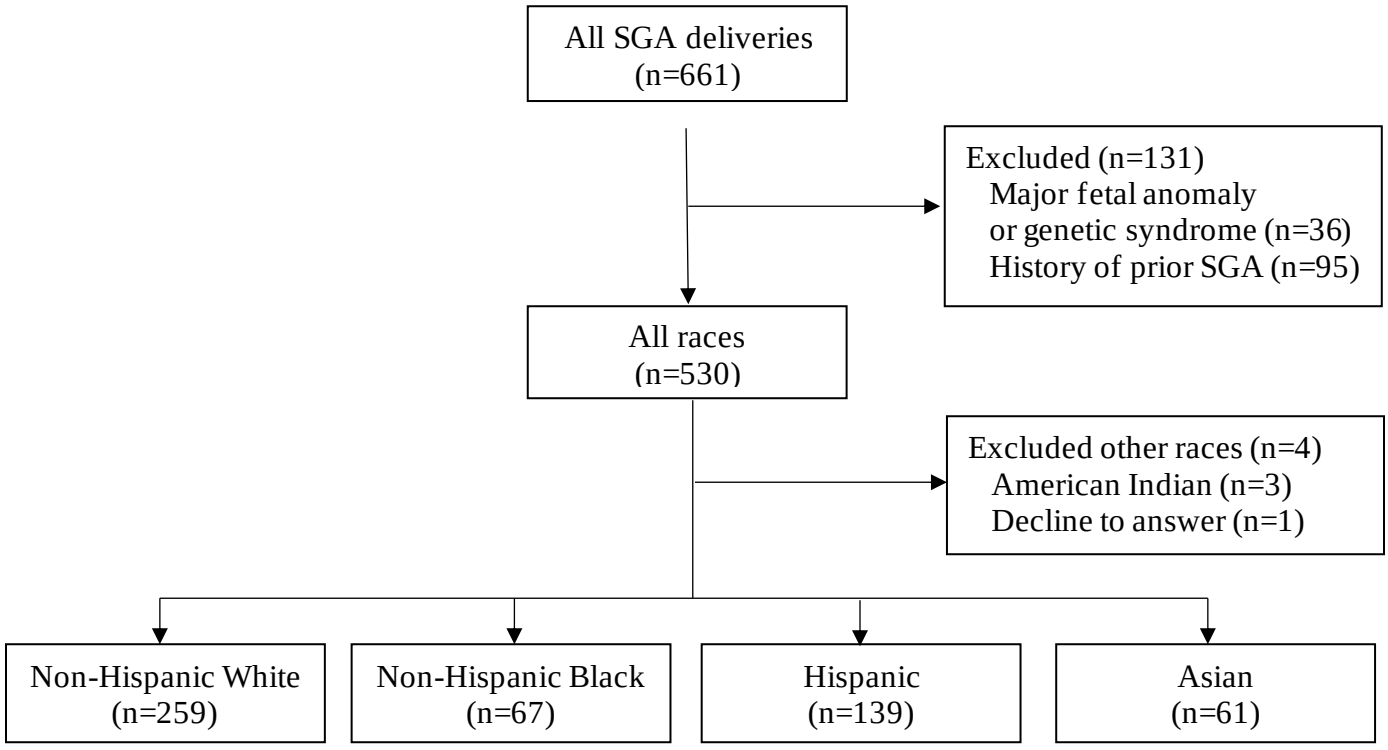

Table 1. Study population characteristics according to race-ethnicity.

	Race-Ethnicity				
Characteristic	**Non-Hispanic White (n=259)**	**Non-Hispanic Black (n=67)**	**Hispanic (n=139)**	**Asian (n=61)**	**P**
Age (y)	29.8 ± 6.0	29.9 ± 5.5	27.2 ± 6.8	31.1 ± 5.2	<0.001
Pre-gravid BMI (kg/m^2)	27.3 ± 7.2	26.5 ± 6.0	28.2 ± 7.2	24.7 ± 4.4	0.008
Nulliparous	169 (66.0)	43 (64.2)	74 (53.6)	42 (70.0)	0.22
In-vitro fertilization	12 (4.7)	1 (1.5)	2 (1.5)	3 (5.3)	0.27
Tobacco use during pregnancy	61 (24.2)	4 (6.1)	8 (6.2)	1 (1.7)	<0.001
Substance use during pregnancy	40 (15.4)	7 (10.4)	15 (10.8)	4 (6.6)	0.23
Aspirin use	17 (6.6)	8 (11.9)	11 (8.3)	4 (6.9)	0.49
No pre-existing medical conditions	96 (37.1)	32 (47.8)	62 (44.6)	35 (57.4)	0.022
Chronic hypertension	19 (7.3)	7 (10.4)	6 (4.3)	1 (1.6)	0.13
Obesity*	75 (29.9)	11 (18)	43 (32.6)	6 (10)	0.002
Hypertensive disease of pregnancy	90 (34.7)	21 (31.3)	42 (30.2)	10 (16.4)	0.042
Gestational age at delivery (wk)	37.1 ± 2.6	37.4 ± 2.1	37.4 ± 2.3	38.0 ± 1.1	0.06
Growth ultrasound performed	191 (82)	46 (76.7)	98 (77.8)	42 (70.0)	0.22
Birthweight (g)	2206.8 ± 481.0	2197.2 ± 413.7	2245.7 ± 432.4	2335.9 ± 232.3	0.10

BMI, body mass index
*Obesity defined as pre-gravid body mass index >30 kg/m^2
Data are mean ± SD, or n (%)

Table 2. Odds of antenatal detection of small for gestational age infants according to race-ethnicity.

Antenatal detection	**OR**	**95% CI**	**aOR**	**95% CI**
Non-Hispanic White	1.0	--	1.0	--
Non-Hispanic Black	0.99	0.57-1.71	1.02	0.57-1.84
Hispanic	0.85	0.56-1.30	0.88	0.55-1.41
Asian	0.57	0.31-1.05	0.59	0.31-1.14

Adjusted for: age, body mass index, tobacco use, no pre-existing medical conditions, hypertensive disease of pregnancy

Table 3. Perinatal outcomes of detected and undetected small for gestational age infants according to race-ethnicity

	Non-Hispanic White			Non-Hispanic Black			Hispanic			Asian			
Outcome	**Detected (n=105)**	**Undetected (n=154)**	**P**	**Detected (n=27)**	**Undetected (n=40)**	**P**	**Detected (n=51)**	**Undetected (n=88)**	**P**	**Detected (n=17)**	**Undetected (n=44)**	**P**	**Interaction P**
Preterm birth	29 (27.6)	24 (15.6)	0.018	7 (25.9)	5 (12.5)	0.16	10 (19.6)	7 (8.0)	0.043	4 (23.5)	2 (4.5)	0.026	0.69
Induction of labor	95 (90.5)	94 (61.0)	<0.001	24 (88.9)	18 (46.2)	0.001	43 (86.0)	42 (50.0)	<0.001	12 (75.0)	20 (48.8)	0.09	0.71
Vaginal birth	58 (56.3)	97 (63.4)	0.39	14 (53.8)	26 (65.0)	0.52	32 (62.7)	60 (68.2)	0.67	13 (76.5)	28 (63.6)	0.70	0.84
Hypertensive disease of pregnancy	24 (22.9)	66 (42.9)	0.001	9 (33.3)	12 (30.0)	0.77	13 (25.5)	29 (33.0)	0.36	4 (23.5)	6 (13.6)	0.44	0.09
Oligohydramnios	10 (9.7)	12 (8.4)	0.72	2 (7.4)	0 (0)	0.17	6 (12.2)	4 (4.9)	0.18	1 (6.3)	3 (7.3)	0.99	0.74
Intrauterine fetal demise	1 (1.0)	7 (4.6)	0.15	1 (3.7)	0 (0)	0.42	0 (0)	2 (2.4)	0.53	0 (0)	0 (0)	--	--
Birthweight (g)	2205 (1910-2440)	2445.0 (2265-2535)	<0.001	2185.0 (1990-2325)	2409.5 (2226-2495)	0.001	2245.0 (2041-2405)	2442.5 (2305-2508)	<0.001	2285.0 (2040-2465)	2468.5 (2310-2527)	0.006	0.97
NICU admission	41 (39.8)	21 (14.3)	<0.001	8 (30.8)	8 (20.0)	0.32	12 (25.0)	10 (12.0)	0.06	5 (29.4)	6 (14.6)	0.19	0.59
5-min Apgar <7	8 (7.7)	6 (4.0)	0.21	3 (11.1)	2 (5.0)	0.39	5 (10.0)	1 (1.2)	0.025	2 (11.8)	1 (2.3)	0.19	0.59
Neonatal morbidity	9 (8.6)	4 (2.6)	0.042	2 (7.4)	2 (5.0)	0.99	5 (9.8)	2 (2.3)	0.10	1 (5.9)	0 (0)	0.28	0.86

Neonatal morbidity is a composite score of: sepsis, necrotizing enterocolitis, intraventricular hemorrhage $\geq$ grade III, retinopathy of prematurity, respiratory distress syndrome, bronchopulmonary dysplasia

Data are median (IQR) or n (%) unless otherwise specified