Racial disparity in previable birth

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BACKGROUND: Extremely preterm birth of a live newborn before the limit of viability is rare but contributes uniformly to the infant mortality rate because essentially all cases result in neonatal death.

OBJECTIVE: The objective of the study was to quantify racial differences in previable birth and their contribution to infant mortality and to estimate the relative influence of factors associated with live birth occurring before the threshold of viability.

STUDY DESIGN: This was a population-based retrospective cohort of all live births in Ohio over a 7 year period, 2006—2012. Demographic, pregnancy, and delivery characteristics of previable live births at 16 0/7 to 22 6/7 weeks of gestation were compared with a referent group of live births at 37 0/7 to 42 6/7 weeks. Rates of birth at each week of gestation were compared between black and white mothers, and relative risk ratios were calculated. Logistic regression estimated the relative risk of factors associated with previable birth, with adjustment for concomitant risk factors.

RESULTS: Of 1,034,552 live births in Ohio during the study period, 2607 (0.25% of all live births) occurred during the previable period of 16—22 weeks. There is a significant racial disparity in the rate and relative risk of previable birth, with a 3- to 6-fold relative risk increase in black mothers at each week of previable gestational age. The incidence of previable birth for white mothers was 1.8 per 1000 and for black mothers, 6.9 per 1000. Factors most strongly associated with previable birth,

presented as adjusted relative risk ratio (95% confidence interval [CI]), were maternal characteristics of black race adjusted relative risk 2.9 (95% CI, 2.6—3.2), age ≥ 35 years 1.3 (95% CI, 1.1—1.6), and unmarried 2.1 (95% CI, 1.8—2.3); fetal characteristics including congenital anomaly, 5.4 (95% CI, 3.4—8.1) and genetic disorder, 5.1 (95% CI, 2.5—10.1); and pregnancy characteristics including prior preterm birth 4.4 (95% CI, 3.7—5.2) and multifetal gestation, twin, 16.9 (95% CI, 14.4—19.8) or triplet, 65.4 (95% CI, 32.9—130.2). The majority, 80%, of previable births (16—22 weeks) were spontaneous in nature, compared with 73% in early preterm births (23—33 weeks), 72% in late preterm births (34—36 weeks), and 65% of term births (37—42 weeks) (P < .001). Previable births constituted approximately 28% of total infant mortalities in white newborns and 45% of infant mortalities in black infants in Ohio during the study period.

CONCLUSION: There is a significant racial disparity in previable preterm births, with black mothers incurring a 3- to 6-fold increased relative risk compared with white mothers, most of which are spontaneous in nature. This may explain much of the racial disparity in infant mortality because all live-born previable preterm births result in death. Focused efforts on the prevention of spontaneous previable preterm birth may help to reduce the racial disparity in infant mortality.

Key words: prematurity, preterm birth, previable birth, racial disparity

E xtremely preterm birth of a live newborn before the limit of viability (less than 23 weeks of gestation) is rare but contributes uniformly to the infant mortality rate (IMR) because essentially all cases result in neonatal death.[1-3] Variations exist in gestational age ranges in which the delivery of a previable pregnancy may be considered a birth vs a miscarriage. However, because the passage of the Born-Alive Infants Protection Act of 2002, in the United States, any delivery of a living fetus is reported as a live birth, regardless of gestational age, even if born at < 20 weeks of gestation.[4-6] The US IMR is then calculated as a rate per 1000 live-born infants who die prior to 12 months of age divided by the number

of live births during the same time period.

In this study, we aim to gain a better understanding of the frequency of previable preterm births, defined as live births at 16—22 weeks of gestation as recorded in the US birth certificate.[5,7] We chose 16 weeks as the lower limit of the previable birth period rather than 20 weeks, as has been recommended recently by experts in the field of preterm birth,[8,9] considering the pathological etiologies of extremely preterm births at 16—20 weeks are similar epidemiologically compared with early preterm births that occur after 20 weeks.[10-12] Furthermore, these early deliveries of live-born babies also contribute to the IMR. We extend the gestational age range to 22 weeks in this study because essentially all live births prior to 23 completed weeks result in infant death and likewise contribute to the IMR.[5]

Our study examines a population-based statewide cohort of live birth records to assess factors associated with previable preterm birth to better

understand their underlying etiology and quantify how they may contribute to the high IMR in our state.[13]

Materials and Methods

We performed a population-based cohort study of all live births in Ohio over a 7 year period, 2006—2012, utilizing US live birth records from Ohio birth certificate data. The protocol for this study was approved, and a deidentified data set was provided by the Ohio Department of Health. This study was exempt from review by the Institutional Review Board at the University of Cincinnati (Cincinnati, OH).

The primary outcome for this study was previable preterm birth, defined as live birth at 16 0/7 to 22 6/7 weeks of gestational age in the US birth certificate.[7,14] The frequency of maternal demographic, pregnancy, and delivery characteristics of previable births were compared with later preterm births (23 0/7 to 36 6/7 weeks) and also to a referent group of term births (37 0/7 to 42 0/7 weeks). Live births with a recorded

TABLE 1
Maternal characteristics of previable compared with term births, Ohio live births 2006—2012

Characteristics	Previable, 16—22 wks (n = 2222)	Term, 37—42 wks (n = 842,488)	P value
Race/ethnicity			
White (non-Hispanic)	54.3%	79.6%	<.001
Rate incidence	0.18% 1.8 per 1000		
Black (non-Hispanic)	41.4%	15.8%	<.001
Rate incidence	0.69% 6.9 per 1000		
Hispanic	4.3%	4.6%	.50
Rate incidence	0.25% 2.5 per 1000		
Maternal age, y			
<20	15.4%	9.8%	<.001
20—34	72.5%	78.4%	<.001
≥ 35	12.1%	11.8%	.63
Unmarried	65.9%	41.2%	<.001
Medicaid	52.3%	37.7%	<.001
Less than high school educational attainment	23.7%	16.1%	<.001
BMI			
Underweight	4.7%	4.4%	.48
Normal weight	41.4%	48.8%	<.001
Overweight	23.3%	23.9%	0.55
Obese	30.6%	23.0%	<0.001
Primiparous	47.1%	40.2%	<0.001
Tobacco use	28.1%	23.8%	<0.001
Prior preterm birth	11.0%	2.7%	<0.001
Interpregnancy interval <12 mo	25.4%	19.6%	<0.001

Percentages represent the fraction within each column with the specified characteristic. Maternal characteristics were counted only once for each multifetal delivery.

BMI, body mass index.

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calculated using prepregnancy weight and height, as recorded in the medical record and categorized by the World Health Organization.[17] Other characteristics included in analyses were obtained from the birth certificate, with data obtained as outlined in the National Vital Statistics System Guide for Completing the Facility Worksheets for the Certificate of Live Birth in the United States.[14] All birth records included in this analysis utilized the most recent, 2003 version, of the US birth certificate.[7]

For maternal characteristic comparisons, only 1 birth record for each multifetal gestation was included. For birth outcomes such as pregnancy complications and delivery characteristics, each birth of a multifetal gestation was included. Births were considered indicated if complicated by preeclampsia or fetal growth restriction, delivered by cesarean without preceding labor, or delivery followed a labor induction. Those with preterm premature rupture of membranes, received tocolysis, or not classified as indicated were considered spontaneous for the purposes of this study.

Differences in baseline maternal demographic, behavioral, socioeconomic, pregnancy, and delivery characteristics among previable (16—22 weeks) and term live births (37—42 weeks) were compared. Statistical comparisons were displayed as P values, relative risk ratios with 95% confidence intervals (CIs).

The frequency of live birth at each week of gestational age was calculated and then stratified by maternal black and white race. Relative risk ratios for births to black compared with white mothers were calculated for each week of gestation. A multivariate logistic regression was then used to estimate the relative risk of various characteristics on the outcome of previable birth, compared with the term birth referent category, after accounting for coexisting risk factors. The final regression model was constructed choosing baseline factors with significant differences noted in univariate comparisons as well as factors with biologic plausibility.

Significant differences were defined as comparisons with a probability value of

gestational age at delivery of < 16 and ≥ 43 weeks were not included in analyses.

Gestational age was defined by the best obstetric estimate variable in the birth record, which takes into account a combination of last menstrual period and clinical and ultrasound parameters, as is commonly accepted in clinical practice for gestational age estimation. The exposure variable for this study, maternal race, was self-reported, which has been shown to be highly accurate when compared with ancestral genetic markers in a US population.[15]

The racial groups compared in these analyses were non-Hispanic black and non-Hispanic white. Because of the small number of births to Hispanic mothers in Ohio during the study period (< 5%), they were not included in the primary outcome comparisons. Fetal growth restriction was defined as birthweight less than the 10th percentile for gestational age.[16] Body mass index was

$P < .05$ and 95% percent CI not inclusive of the null value of 1.0. Statistical analyses were performed using STATA release 12 software (StataCorp, College Station, TX).

Results

There were 1,034,552 live births in Ohio from 2006 through 2012, with racial/ethnic distribution as follows: 76.3% non-Hispanic white, 16.3% non-Hispanic black, 4.5% Hispanic, and 2.8% other. The gestational age range of live births during this period was 12−47 weeks. There were minimal missing data on gestational age at birth, 0.22%. Previable births occurring at 16−22 weeks were uncommon (n = 2607, 0.25% of all live births) and constituted a small fraction (2.0%) of all preterm births < 37 weeks. There were few live births prior to 16 weeks recorded in Ohio during the study period (n = 14, < 0.01%).

Mothers who experienced a previable birth were more commonly of black race (41 vs 16%), < 20 years old, unmarried, primiparous, obese, had less than a high school educational attainment, and utilized Medicaid insurance. Previable births also occurred more commonly in mothers who used tobacco, had a prior preterm birth, or had a short interpregnancy interval of less than 12 months, as demonstrated in Table 1.

The rate of previable birth in black mothers (6.9 per 1000) was more than 3 times higher compared with white mothers (1.8 per 1000), risk ratio (RR) of 3.8 (95% CI, 3.5−4.1). When stratified by week of gestational age at birth, the highest relative risk of previable birth occurred at the earliest week of gestational age, 16 weeks (RR, 6.4; 95% CI, 2.6−16.0) for births to black compared with white mothers.

The relative risk was > 3.0-fold increased for all weeks of previable gestational age at birth (16−22 weeks) and remained increased for black mothers compared with white up to term gestational weeks (Figure 1 and Table 2). Previable births constituted approximately 28% of total infant mortalities in white newborns and 45% of

FIGURE 1
Relative risk of live birth at each week of gestational age
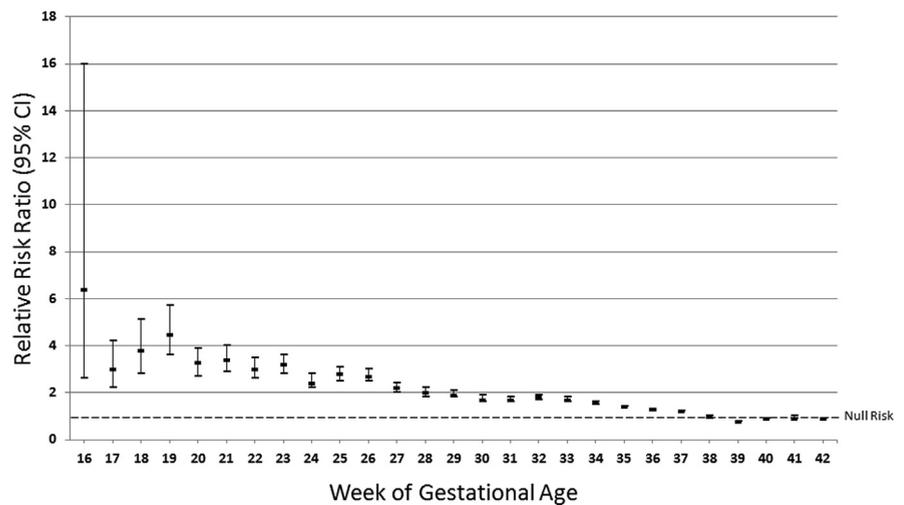
Relative risk of live birth at each week of gestational age in black compared with white mothers, Ohio live births, 2006−2012.

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infant mortalities in black infants in Ohio during the study period (Figure 2).

Multifetal births also had a significant contribution to previable births. Multifetal gestations (twins and higher order) represented 31% of previable births at 16−22 weeks, 22% of early preterm births at 23−33 weeks, 16% of late preterm births at 34−36 weeks, but only 2% of term births ($P < .001$). The relative risk for previable birth in twin gestations was 14.1 (95% CI, 12.8−15.6) and for triplets, 565.3 (95% CI, 401.9−795.0) (Table 3).

To assess the influence of racial variations in multifetal gestation on previable birth, we performed an additional analysis of previable birth stratified by plurality and race. There was a slightly higher proportion of multifetal gestations among previable births in white mothers than in black mothers. With the analysis limited to singleton gestations only, the rate of previable birth was 1.6 per 1000 live births in white mothers and 6.2 per 1000 in black mothers, a similar racial difference observed when all pluralities were included: 1.8 per 1000 in white mothers and 6.9 per 1000 in black mothers.

A larger proportion of previable births were spontaneous in nature (80%),

compared with early preterm births (73% at 23−33 weeks), late preterm births (72% at 34−36 weeks), and term births (65% at 37−42 weeks). More than 1 in 10 previable births were born by cesarean delivery (13%); however, this rate was significantly lower than the overall preterm cesarean rate (43%) and term cesarean rate (29%) ($P < .001$, Table 4).

The factors most strongly associated with previable birth are shown in Table 5. They include, in descending order of relative risk, the following: multifetal pregnancy, triplet adjusted RR, 65.4 (95% CI, 32.3−130.2); twin, adjusted RR (aRR), 16.9 (95% CI, 14.4−19.8), followed by fetal genetic disorder aRR, 5.1 (95% CI, 2.5−10.1), congenital anomaly aRR, 5.4 (95% CI, 3.6−8.1), prior preterm birth aRR, 4.4 (95% CI, 3.7−5.3), black race aRR, 2.9 (95% CI, 2.6−3.2), unmarried aRR, 2.1 (95% CI, 1.8−2.3), primiparity aRR 1.6 (95% CI, 1.5−1.8), and advanced maternal age ≥ 35 years aRR, 1.3 (95% CI, 1.1−1.6), after adjustment for co-existing risk factors.

Comment

In this study, we identified a significant racial disparity in the frequency of

TABLE 2
Frequency and relative risk ratio of Ohio live births by race, per week of gestational age at birth (2006–2012)

Week of gestational age	n, total live births, % (n = 1,034,552)[a]	Live births to white mothers, % (n = 789,871)	Live births to black mothers, % (n = 168,484)	RRR (95% CI)
12–15	14 (<0.01%)	7 (<0.01%)	7 (<0.01%)	4.7 (1.6–13.4)
16	21 (<0.01%)	8 (<0.01%)	11 (0.01%)	6.4 (2.6–16.0)
17	154 (0.01%)	87 (0.01%)	56 (0.03%)	3.0 (2.2–4.2)
18	197 (0.02%)	98 (0.01%)	80 (0.05%)	3.8 (2.8–5.1)
19	303 (0.03%)	145 (0.02%)	139 (0.08%)	4.5 (3.6–5.7)
20	484 (0.05%)	268 (0.03%)	187 (0.11%)	3.3 (2.7–3.9)
21	666 (0.06%)	360 (0.05%)	259 (0.15%)	3.4 (2.9–4.0)
22	782 (0.08%)	449 (0.06%)	289 (0.17%)	3.0 (2.6–3.5)
23	963 (0.09%)	530 (0.07%)	357 (0.21%)	3.2 (2.8–3.6)
24	1217 (0.12%)	764 (0.10%)	397 (0.24%)	2.4 (2.2–2.8)
25	1398 (0.14%)	813 (0.10%)	479 (0.28%)	2.8 (2.5–3.1)
26	1666 (0.16%)	991 (0.13%)	574 (0.34%)	2.7 (2.5–3.0)
27	1959 (0.19%)	1257 (0.16%)	586 (0.35%)	2.2 (2.0–2.4)
28	2610 (0.25%)	1713 (0.22%)	733 (0.44%)	2.0 (1.8–2.2)
29	2900 (0.28%)	1913 (0.24%)	776 (0.46%)	1.9 (1.8–2.1)
30	3994 (0.39%)	2729 (0.35%)	1006 (0.60%)	1.7 (1.6–1.9)
31	5174 (0.50%)	3511 (0.44%)	1287 (0.76%)	1.7 (1.6–1.8)
32	6969 (0.67%)	4741 (0.60%)	1782 (1.1%)	1.8 (1.7–1.9)
33	10,106 (0.98%)	6886 (0.87%)	2499 (1.5%)	1.7 (1.6–1.8)
34	16,708 (1.6%)	11,607 (1.5%)	3812 (2.3%)	1.6 (1.5–1.6)
35	25,833 (2.5%)	18,454 (2.3%)	5480 (3.2%)	1.4 (1.4–1.4)
36	46,258 (4.5%)	33,944 (4.3%)	9066 (5.4%)	1.3 (1.2–1.3)
37	92,060 (8.9%)	68,168 (8.6%)	17,111 (10.2%)	1.2 (1.2–1.2)
38	185,361 (17.9%)	142,429 (18.0%)	29,205 (17.3%)	1.0 (0.9–1.0)
39	303,103 (29.3%)	238,231 (30.2%)	43,271 (25.7%)	0.8 (0.8–0.8)
40	192,021 (18.6%)	149,153 (18.9%)	28,637 (17.0%)	0.9 (0.9–0.9)
41	76,227 (7.4%)	58,729 (7.4%)	11,798 (7.0%)	0.9 (0.9–1.0)
42	25,073 (2.4%)	19,547 (2.5%)	3751 (2.2%)	0.9 (0.9–0.9)
≥43	28,070 (2.7%)	12,114 (1.5%)	4476 (2.7%)	1.0 (0.9–1.0)

RRR, relative risk ratio.

[a] n = 2261 (0.22%) with missing data on gestational age at birth.

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previable births in black compared with white mothers, which may explain much of the racial disparity in the overall infant mortality rate in Ohio and across the United States.[13,18]

Previable live births, which ultimately result in neonatal death and contribute uniformly to the infant mortality rate, occurred in 6.9 per 1000 births to black mothers compared with only 1.8 births per 1000 in white mothers in Ohio during the study period, representing a relative risk increase of 3.8-fold for births to black mothers. Furthermore, we found that the highest relative risk increase attributed to black race occurred at the earliest weeks of previable gestational age.

This racial disparity in extremely early preterm births is particularly concerning because mothers of black race are those most likely to have recurrent episodes of preterm birth in subsequent pregnancies[19] and have concomitant risk factors for prematurity.[20]

Preterm birth is the dominant contributor to infant mortality, with deaths of preterm infants accounting for more than half of all infant deaths.[21] Previable births have a significant

contribution to the infant mortality rate, comprising approximately 20—30% of the overall IMR.[22] There is a notable racial disparity in infant mortality, with black infants incurring a 3-fold increased risk of death within the first 12 months of life compared with white infants.[21]

Despite the overall decrease in the IMR observed in recent years, the racial disparity is worsening with the relative risk increase for IMR in black infants becoming higher than that seen in white infants: increase from 2.6-fold to 3.0-fold from 1989 to 1990 to 2005 to 2006.[21,23] Likewise, the preterm birth—related IMR racial disparity is also increasing over time.[21] For black mothers, preterm-related causes of death account for most of their higher infant mortality risk and represent the largest cause-specific difference in the black-white IMR disparity, compared with differences in congenital malformations, sudden infant death, or unintentional injuries.[23]

The average IMR in the United States at the midpoint of the study period was 6.1 per 1000 live births overall, with 5.2 per 1000 for white infants and 11.6 per 1000 for black infants (2010).[24] Ohio had a higher average IMR during the study period of 7.7 per 1000 live births. In Ohio, there was a larger racial disparity in IMR compared with the national average; with the IMR for white infants of 6.4 per 1000 and for black infants 15.5 per 1000, demonstrating a 2.4-fold increased risk for black infants compared with white, a larger racial disparity as compared with the racial

FIGURE 2
Contribution of previable preterm birth to infant mortality
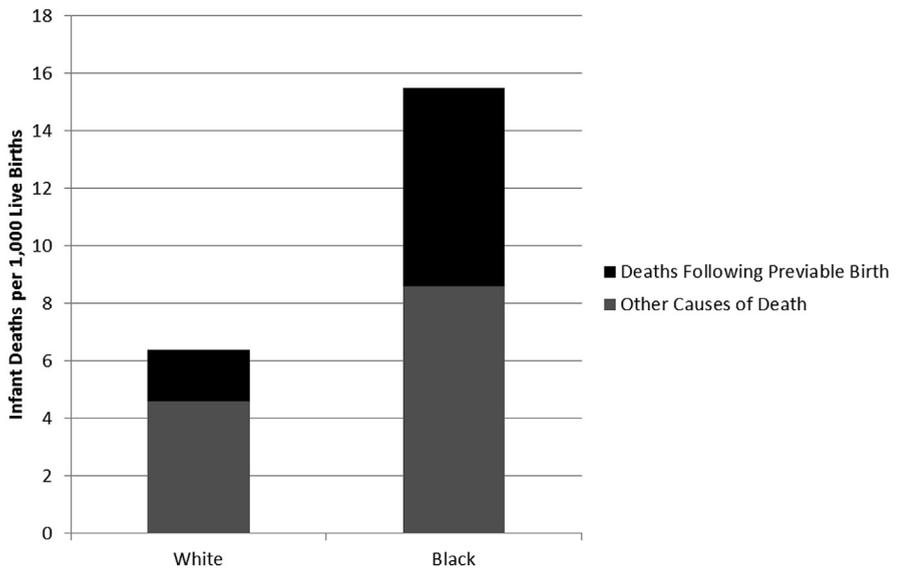
Contribution of previable preterm birth to infant mortality in Ohio in black and white mothers (2006—2012).

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disparity seen in the United States of 2.2 -old.[18]

Based on these statewide IMR rates, previable births analyzed in our study constituted approximately 28% of total infant mortalities in white newborns and 45% of infant mortalities in black infants in Ohio (Figure 2). If the rate of previable birth for black women was the same as white women, the IMR for black women in Ohio would be reduced from 15.5 to 10.2 per 1000 and the overall IMR in Ohio would be reduced from 7.7 to 6.8 per 1000 births.

The rates of preterm birth in the periviable gestational weeks of 23—25 weeks, a window in which preterm birth is also associated with a high rate of infant mortality, also were significantly higher for black compared with white mothers in our study. This would contribute additionally to the racial disparity in preterm birth—related infant mortality over and above that which we have quantified related to previable birth.

In addition to black race, we identified the following factors to be those most

TABLE 3
Contribution of multifetal pregnancy to previable live birth, Ohio live births, 2006—2012

Plurality	Previable births 16—22 wks (n = 2607)	Term births 37—42 wks (n = 873,802)	RRR (95% CI)
Singleton	77.1%	98.4%	0.06 (0.05—0.06)
Twin	18.4%	1.6%	14.1 (12.8—15.6)
Triplet	3.4%	0.01%	565.3 (401.9—795.0)
Quadruplet	0.2%	0	—
Quintuplet or higher order	0.9%	0	—

Each newborn of a multifetal gestation is counted individually.

RRR, relative risk ratio.

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TABLE 4
Pregnancy complications and delivery characteristics of previable compared with term births, Ohio live births, 2006–2012

Characteristics	Previable, 16-22 wks (n = 2607)	Term, 37-42 wks (n = 873,802)	P value	RRR (95% CI)
Maternal-fetal complication				
Fetal growth restriction	10.6%	10.0%	.383	1.1 (1.0–1.3)
Preeclampsia	3.4%	4.4%	.025	0.7 (0.6–0.9)
Major fetal anomaly	1.3%	0.3%	<.001	4.1 (2.8–6.2)
Genetic disorder	0.7%	0.1%	<.001	7.6 (4.5–12.9)
Delivery characteristic				
Cesarean delivery	13.0%	28.5%	<.001	0.4 (0.3–0.4)
Spontaneous birth	79.6%	65.1%	<.001	2.1 (1.9–2.3)
Malpresentation	26.4%	3.8%	<.001	8.6 (7.9–9.4)

Fetal growth restriction is birthweight < 10th percentile.

RRR, relative risk ratio.

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TABLE 5
Logistic regression of factors associated with previable live birth in Ohio (2006–2012), at 16 0/7 to 22 6/7 weeks of gestational age

	Adjusted RRR	95% CI
Race/ethnicity		
White (non-Hispanic)	0.74	0.60–0.91
Black (non-Hispanic)	2.88[a]	2.59–3.22
Hispanic	1.29	0.77–2.17
Maternal age, y		
<20	1.05	0.91–1.22
20–34	Referent	
≥35	1.32[a]	1.12–1.55
Unmarried	2.06[a]	1.83–2.31
Medicaid	0.95	0.73–1.25
Education less than high school	1.11	0.86–1.43
Tobacco use	1.08	0.96–1.22
Prior preterm birth	4.42[a]	3.73–5.25
Interpregnancy interval <12 mo	1.08	0.87–1.33
Primiparous	1.61[a]	1.45–1.79
Plurality		
Singleton	0.51[a]	0.44–0.59
Twin	16.89[a]	14.37–19.84
Triplet	65.44[a]	32.88–130.25
Congenital anomaly	5.38[a]	3.56–8.13
Genetic disorder	5.06[a]	2.53–10.10

Only one delivery counted for each multifetal gestation.

All relative risk ratios are adjusted for the other factors listed in the table.

RRR, relative risk ratio.

[a] Factors significantly associated with previable birth.

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strongly associated with previable birth: multifetal gestation, genetic abnormalities, congenital anomalies, and prior preterm birth. Spontaneous preterm births comprise a larger proportion of previable deliveries compared with later preterm births.

The findings of this study highlight the importance of demographic and obstetric contributors to previable birth, which results in infant mortality. The remarkable racial disparity in preterm birth rates observed at the earliest weeks of previable gestational age in our population provide insight into previable preterm birth as an important contributor to the remarkable racial disparity in infant mortality observed in Ohio and across the United States.

Preterm birth screening and preventive efforts in the United States have been associated with a declining preterm birth rate in recent years.[25] Our findings suggest that public health efforts should focus on access to prenatal care, optimizing opportunities for preterm birth screening and preventive efforts in high-risk women of black race, in an effort to close the racial disparity gap in infant mortality in our country. Considering the substantial contribution of previable birth to infant mortality, future studies of effective screening and treatment strategies for the prevention of spontaneous preterm birth before the threshold of viability are of paramount importance. ∎

Acknowledgment

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