Aberrant fetal growth and early, late, and postneonatal mortality: an analysis of Milwaukee births, 1996–2007

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OBJECTIVE: The objective of the study was to ascertain the association between fetal growth (small- [SGA], appropriate- [AGA], and large-for-gestational-age [LGA]) and early, late, and postneonatal mortality.

STUDY DESIGN: Birth certificate data for nonanomalous singletons, delivered from 1996 to 2007, were obtained for Milwaukee residents. Multivariate logistic regression analyses, adjusted for 19 covariates, determined the association between fetal growth and mortality.

RESULTS: Among the 123,383 live births, SGA was 57% higher than LGA (11% vs 7%). The infant mortality rate for SGA was 11.0, AGA, 5.3, and LGA 2.7/1000 live births. SGA was a significant risk factor for early (adjusted odds ratio, 2.66) and late (2.06) but not postneonatal mortality. The adjusted risk of mortality for LGA was not significantly different from AGA. Over 12 years, 3 types of mortality for aberrant fetal growth did not change significantly.

CONCLUSION: In the city of Milwaukee, aberrant fetal growth was variably associated with early, late, and postneonatal mortality.

Key words: early mortality, large for gestational age, late mortality, postneonatal mortality, small for gestational age

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Aberrant fetal growth encompasses small for gestational age (SGA) or large for gestational age (LGA). Whereas SGA is defined as neonatal birthweight below 10% for the gestational age, LGA is weight above 90%, with macrosomia (weight of at least 4000 g) being a subset of accelerated growth.[1,2] Fetal growth abnormalities are linked with complications. SGA, for example, is associated with fetal anomalies, oligohydramnios, stillbirth, neonatal acidosis, seizure, and death. Later in life, newborns with suboptimal growth are at increased risk of learning disabilities and cardiovascular disease.[1] On the other hand, LGA may lower or increase the likelihood of mortality. Among diabetic mothers, accelerated growth is associated with traumatic delivery and stillbirth[3]; among women with pregnancy-induced hypertension, preterm LGA has significantly lower infant mortality.[4]

The myriad complications associated with aberrant growth and the conflicting reports on mortality with LGA prompted us to inquire if SGA or LGA is associated with early (0-6 days after live birth), late (7-27 days), or postneonatal (28-364 days) mortality.

The primary purpose of this population based study was to determine whether SGA or LGA is associated with increased risk of early, late, and postneonatal mortality, and identify other risk factors; the secondary purpose was to determine whether there are temporal changes in the 3 subtypes of infant mortality.

Materials and Methods

This project was reviewed and determined exempt by the Health Sciences Institutional Review Board at the University of Wisconsin–Madison. For the years 1996-2007, we obtained vital statistics birth certificate data for the city of Milwaukee, WI, from the City of Milwaukee Health Department. The birth certificate data were linked to death certificate data, and mortality information was included. The study sample was restricted to singleton live births born to city of Milwaukee resident mothers with gestational age of 24 weeks or more.

Newborns with congenital anomaly or implausible birthweight–gestational age combinations were excluded. Implausible birthweight–gestational age data were identified by the algorithm that was developed by Alexander et al.[5] This method was based on expert opinion concerning some questionable birthweight values that may be a result of inaccurate recording of gestational age. In addition, infant death cases with unknown time of death were also excluded.

The outcomes of interest were early, late, and postneonatal mortalities. Early mortality was defined as newborns that died during 0-6 days of life; late mortality, 7-27 days; and postneonatal mortality, 28-364 days. Infant mortality rate (IMR) was the summation of early, late, and postneonatal mortality rate. Based on Alexander et al,[6] fetal growth was categorized as SGA, appropriate for gesta-

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tional age (AGA; birthweight lies within 10-90% for that gestational age), and LGA.

Nineteen covariates obtained from vital statistics birth certificate data were included in the analyses. Maternal age was categorized into 3 groups: 19 years or less, 20-34 years, and 35 years or older. Self-reported race/ethnicity was categorized into white, African American, Hispanic, and other. Maternal educational attainment was categorized into completed high school, beyond high school, and less than high school.

Paternity was coded as having a father's name listed on the birth certificate (yes/no). The father's name on the record meant one of the following: the parents were married at the time of birth; there was a statement of paternity; there was a paternity adjudication by court order (meaning paternity was established by the legal system, usually after genetic testing confirms the father's identity); or legitimation (meaning that the child is acknowledged by parents who marry after their child's birth). We used finalized birth certificate data that included amendments made by the vital records office (such as statements of paternity, adjudications, or legitimations).

Prenatal care was categorized as adequate vs inadequate, using Kotelchuck's Adequacy of Prenatal Care Utilization Index.[7] Kotelchuck's index is based on initiation of prenatal care (month prenatal care begins) and the number of visits received, and is one of the most commonly used indices of prenatal care utilization in research studies. [8-10]

Maternal behaviors and obstetric complications included reported alcohol use during pregnancy (yes/no), reported cigarette use during pregnancy (yes/no), pregestational diabetes (yes/no), gestational diabetes (yes/no), hydramnios or oligohydramnios (yes/no), gestational or pregestational hypertension (yes/no), uterine bleeding (yes/no), and premature rupture of membranes of more than 12 hours (yes/no).

Gestational age at birth was defined as the clinician's estimate of gestation (number of completed weeks) as recorded on the birth certificate. We then categorized gestational age into preterm (<37 weeks), term (37-40 weeks), and postterm (≥41 weeks). The route of delivery was categorized as spontaneous vaginal, operative vaginal, and cesarean. We also examined whether the labor was precipitous (within 3 hours vs >3 hours), abruptio placenta (yes/no), and infant sex (male/female).

Neonatal condition at birth was categorized as normal vs abnormal. Abnormal conditions included birth injury, hyaline membrane disease or respiratory distress, meconium aspiration syndrome, assisted ventilation, and seizures at birth.

We calculated corrected early, late, postneonatal, and infant mortality rate by fetal growth (SGA, AGA, and LGA). We assessed 3 year moving average mortality trends by fetal growth (SGA, AGA, and LGA) category. A χ^2 test or Fisher's exact test was used to assess the mortality trend across years. Multivariate logistic regression analyses were performed to examine the association between fetal growth and outcomes of the 3 types of mortality and adjusting for 19 potential confounding variables. The results are presented as odds ratios (ORs) and their 95% confidence intervals (CIs). Significance level was defined as $P < .05$.

For all variables, the data were complete at above 99% of the study subjects. On birth certificates, for maternal medical history, a box must be checked if a mother has a certain medical condition. We assumed that a mother did not have the condition if the box was not checked. For the frequency tables, missing values were excluded and percentages were based on the number of nonmissing values. When performing the multivariate logistic regression analyses, listwise deletion was used to remove subjects if there was a missing value on any of the variables. All statistical analyses were performed using SAS 9.2 (SAS/STAT software, version 9.2; SAS Institute, Cary, NC).

RESULTS

During the 12 years of the study period, there were 132,658 live births in Milwaukee, WI. We excluded 3879 multiple gestation births, 3559 deliveries of patients who resided outside Milwaukee, 1227 anomalous neonates, 540 newborns delivered before 24 weeks, 36 infants with implausible birthweights, 27 infant deaths with unknown time of death, and 7 others. After these exclusions, there were 123,383 (93%) live births remaining as our study population. The median number of deliveries per year was 10,257 (range, 9956–10,708). Whereas 11% of the newborns were SGA (n = 13,601), 7% were LGA (n= 8957), and the remaining 82% were AGA (n = 100,825). The 3 year moving average for the incidence of SGA (range, 10.7–11.6%; $P = .586$), AGA (range, 81.3–81.9%; $P = .987$) and for LGA (range, 6.6–7.6%; $P = .140$) was not significantly different across the 12 years. Table 1 presents the sample characteristics.

Among 123,383 newborns, there were 707 deaths within the first year of birth (IMR of 5.7 per 1000 live births), with 158 being within 0-6 days of birth (early mortality rate of 1.3), 117 within 7-27 days (late mortality rate of 0.9), and the remaining 432 within 28-364 days (postneonatal mortality of 3.5). The contribution of SGA, AGA, and LGA to early, late, and postneonatal mortality was significantly different ($P = .0005$; Figure 1).

Figure 2 depicts the 3 subtypes of infant mortality for normal and aberrant growth. The infant mortality rate is the summation of early, late, and postneonatal mortality rate, which are 11.0, 5.3, and 2.7 for SGA, AGA, and LGA, respectively.

Compared with AGA, SGA newborns had a significantly higher early (3.7 vs 1.0; $P < .001$), late (2.2 vs 0.8; $P < .001$), and postneonatal (5.1 vs 3.5; $P = .002$) mortality. Compared with LGA, SGA also had significantly higher early (3.7 vs 0.8), late (2.2 vs 0.3), and postneonatal (5.1 vs 1.6) mortality ($P < .001$ for all comparisons). The likelihood of early and late mortality for LGA vs AGA was similar ($P = .524$ and $P = .118$, respectively) but significantly different for postneonatal period ($P = .003$). The corrected infant mortality for LGA and AGA (2.7 vs 5.3, respectively) was significantly different ($P = .001$).

The infant mortality for SGA, AGA, and LGA did not change significantly

TABLE 1
Sample characteristics of Milwaukee births, 1996-2007

Characteristic	Alive (n = 122,676)	Mortality		
		Early (n = 158)	Late (n = 117)	Postneonatal (n = 432)
Maternal age, y				
≤19	19% (23,357)	23% (37)	27% (31)	28% (120)
20-34	72% (88,428)	65% (102)	67% (78)	67% (288)
≥35	9% (10,891)	12% (19)	7% (8)	6% (24)
Mother's race/ethnicity				
White	30% (36,692)	21% (33)	25% (29)	19% (81)
Black	47% (57,034)	57% (90)	62% (73)	69% (298)
Hispanic	18% (22,494)	17% (27)	9% (11)	9% (37)
Other	5% (6435)	5% (8)	3% (4)	4% (16)
Mother's education				
Less than high school	35% (42,873)	35% (51)	46% (53)	51% (218)
High school	32% (39,410)	43% (63)	34% (39)	32% (136)
Above high school	33% (39,989)	23% (34)	20% (23)	17% (74)
Paternity				
Has father on record	71% (86,835)	35% (55)	34% (40)	35% (153)
No father on record	29% (35,841)	65% (103)	66% (77)	65% (279)
Prenatal care				
Adequate or better	68% (82,894)	65% (97)	68% (78)	62% (266)
Inadequate or better	32% (39,069)	35% (53)	32% (36)	38% (166)
Alcohol use during pregnancy				
No	98% (120,672)	94% (147)	97% (114)	96% (415)
Yes	2% (1938)	6% (10)	3% (3)	4% (17)
Cigarette use during pregnancy				
No	85% (103,980)	81% (127)	73% (85)	69% (296)
Yes	15% (18,639)	19% (30)	27% (32)	32% (136)
Gestational diabetes				
No	97% (118,629)	96% (151)	96% (112)	97% (419)
Yes	3% (4047)	4% (7)	4% (5)	3% (13)
Pregestational diabetes				
No	99% (121,973)	99% (156)	99% (116)	100% (430)
Yes	1% (703)	1% (2)	1% (1)	0% (2)
Hydramnios/oligohydramnios				
No	99% (121,274)	93% (147)	95% (111)	97% (420)
Yes	1% (1,402)	7% (11)	5% (6)	3% (12)
Hypertensive disease				
No	94% (115,810)	91% (144)	91% (106)	91% (394)
Yes	6% (6866)	9% (14)	9% (11)	9% (38)

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(continued)

TABLE 1
Sample characteristics of Milwaukee births, 1996-2007 *(continued)*

Characteristic	Alive (n = 122,676)	Mortality		
		Early (n = 158)	Late (n = 117)	Postneonatal (n = 432)
Uterine bleeding				
No	99% (121,762)	98% (154)	99% (116)	98% (424)
Yes	1% (914)	3% (4)	1% (1)	2% (8)
Premature rupture of membranes (>12 h)				
No	97% (118,817)	89% (140)	92% (108)	96% (415)
Yes	3% (3859)	11% (18)	8% (9)	4% (17)
Gestational age, wks				
37 (preterm)	9% (10,709)	75% (118)	62% (72)	33% (142)
37-40 (term)	82% (100,070)	22% (35)	33% (38)	60% (261)
41 (postterm)	10% (11,897)	3% (5)	6% (7)	7% (29)
Precipitous labor (<3 h)				
No	97% (118,628)	94% (149)	97% (114)	96% (414)
Yes	3% (4048)	6% (9)	3% (3)	4% (18)
Delivery method				
Spontaneous vaginal	80% (97,489)	58% (92)	59% (69)	74% (321)
Operative vaginal	5% (5539)	2% (3)	3% (3)	5% (20)
Cesarean	16% (19,648)	40% (63)	39% (45)	21% (91)
Newborn's sex				
Male	51% (62,478)	51% (80)	52% (61)	57% (247)
Female	49% (60,198)	49% (78)	48% (56)	43% (185)
Fetal growth				
SGA	11% (13,451)	32% (50)	26% (30)	16% (70)
AGA	82% (100,292)	64% (101)	72% (84)	81% (348)
LGA	7% (8933)	4% (7)	3% (3)	3% (14)
Abruptio placenta				
No	99% (121,989)	93% (147)	92% (108)	97% (418)
Yes	1% (687)	7% (11)	8% (9)	3% (14)
Newborn's condition				
Abnormal	7% (8749)	36% (57)	37% (43)	19% (80)
Normal	93% (113,927)	64% (101)	63% (74)	82% (352)

AGA, appropriate-for-gestational-age; *LGA*, large-for-gestational-age; *SGA*, small-for-gestational-age.

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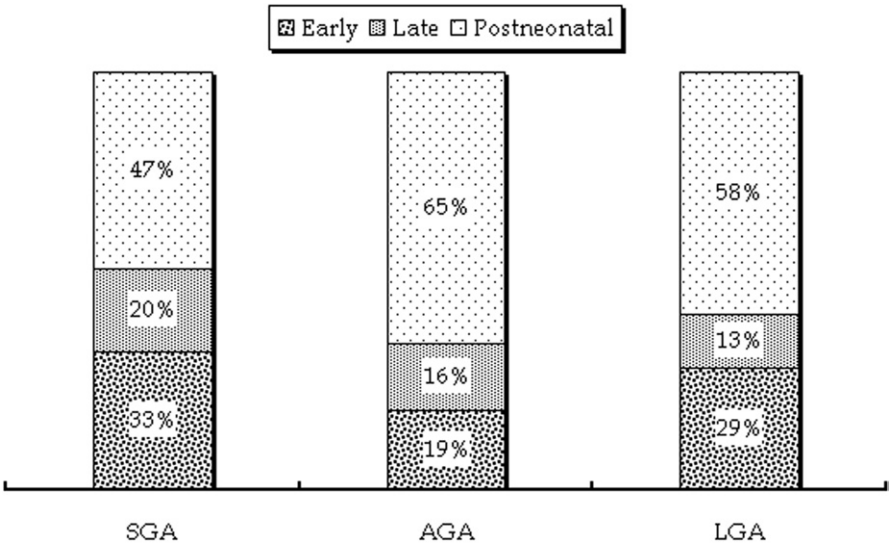
from 1996-1998 to 2005-2007 (Figure 3; $P = .999$ for all 3 comparisons). The infant mortality for all singletons also did not change significantly (range, 5.4–6.5/1000 live births; $P = .997$). The rate of early, late, and postneonatal mortality did not change during the study period ($P = .999$, $P = .976$, $P = .999$, respectively; data not shown).

Table 2 shows the multivariate logistic regression analysis for early, late, and postneonatal mortality. SGA was a statistically significant risk factor for early (adjusted OR, 2.66; 95% CI, 1.82–3.89) and late (adjusted OR, 2.14; 95% CI, 1.38–3.32) but not postneonatal mortality. LGA was not significantly associated with all 3 types of mortality, compared with AGA. Our analysis also indicated that the following 5 other factors (listed in descending order of magnitude) were statistically significantly associated with all 3 types of mortality: (1) preterm birth, (2) no father on record, (3) hydramnios or oligohydramnios, (4) cesarean delivery, and (5) abnormal condition of newborn at birth.

In addition, we found that some factors increased the risk of mortality for 1 type but not all 3. Alcohol use, for example, significantly increased the risk of early mortality but not late or postneonatal mortality. Abruptio placentae increased the risk of late mortality but not early or postneonatal mortality. Lastly, we also identified factors that decreased the risk of infant mortality. Not completing high school and hypertensive disease in pregnancy significantly lowered the likelihood of early mortality; being Hispanic or a female newborn decreased the risk of postneonatal mortality (Table 2).

FIGURE 1
Fetal growth and subtype of infant mortality



Fetal growth and subtype of infant mortality (SGA, birthweight <10% for gestational age; AGA, birthweight within 10-90%; and LGA, birthweight of >90%). Early indicates death within 0-6 days of birth; late indicates within 7-27 days, and postneonatal indicates within 28-364 days. $P = .0006$ for contribution of growth pattern to 3 types of mortality.

AGA, appropriate-for-gestational-age; *LGA*, large-for-gestational-age; *SGA*, small-for-gestational-age.

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Comment

Infant mortality has been used as a measure of the health of society as a whole as well as the well-being of the newborn.[11] The infant mortality rate for the United States has remained at 6.77 per 1000 live births from 2006 to 2007, ranking worse than many other developed countries in the world.[12] According to the Central Intelligence Agency, which tabulated the infant mortality of 224 countries, United States ranks 44th behind many European countries (Italy, Greece, the United Kingdom, Portugal, Austria, and Germany).[13]

There are many reasons for this poor ranking, such as differences in health care services, population health status and health policy differences, and maternal racial and ethnic disparities.[14,15] In addition, because other developed countries may report their infant mortality rate differently, we need to interpret the ranking with caution.[16] Nonetheless, this country's poor infant mortality ranking provides a sufficient reason to elucidate the association of obstetric factors and infant mortality in the United States.

Published reports on the topic have focused on the 3 subtypes of infant mortality and their association with obstetric factors. For example, infant mortality has been linked with maternal age[17]; no father on record[18]; pregnancy-induced hypertension and abnormal fetal growth[4]; late preterm and near-term births[19]; the effect of labor with SGA or premature rupture of membranes[20,21]; and subtypes (preterm, term, or postterm) of SGA.[22] Neonatal mortality has been linked with ethnicity and obesity[23] and postterm births[24] as well as inadequate prenatal care.[25] Late (within 27 days of birth) neonatal mortality has been associated with diabetes and LGA births,[3] and early, late, and postneonatal mortality have been associated with interracial parents.[26]

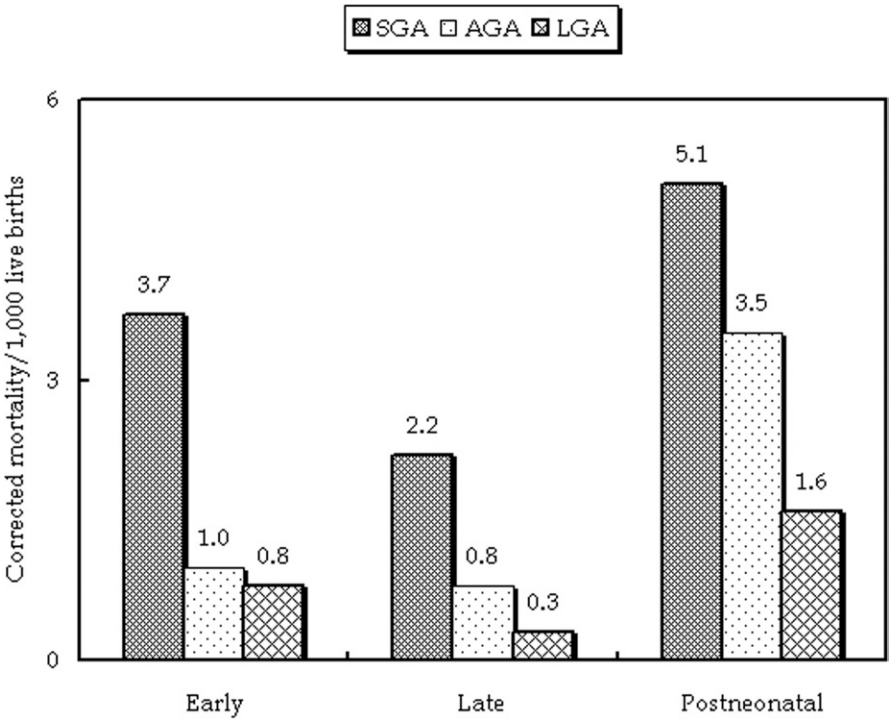
Although these studies provide invaluable insights on the relationship between obstetric factors and mortality, many of them focus on national or statewide data or focus on subpopulations.[19,24,26] Thus, we wanted to better understand antecedent factors linked with infant mortality in our city. The reason for primarily focusing on aberrant growth is that, by definition, they occur with 20% of the deliveries.

There are 4 major findings of our study. First, in our population, the likelihood of a newborn being SGA was 57% higher than being LGA (11% vs 7%, respectively), and the rate of aberrant growth did not change significantly during the 12 years. A possible reason for a much higher rate of SGA than LGA in Milwaukee is that risk factors associated with inadequate growth are more prevalent than those for excessive growth. For suboptimal growth, the predisposing factors are maternal disease (such as hypertension, renal disease, or antiphospholipid syndrome), smoking and substance use and abuse, and placental disease[1]; for excessive growth, predisposing factors include history of macrosomia, maternal weight at birth, maternal height, or prepregnancy weight.[2]

The data available on the birth certificate are insufficiently detailed to determine which risk factors increase the likelihood of SGA. It is also possible that the nomogram published by Alexander et al[5] is not applicable to Milwaukee and that each region should modify the thresholds for abnormal growth, as Seeds and Peng did.[27] We chose not to construct our own criteria for abnormal growth because we wanted to ascertain whether the national nomograms are linked to mortality.

The second finding is that the time and rate of infant mortality varied for SGA, AGA, and LGA. For SGA newborns, the

FIGURE 2
Corrected mortality rate with normal and aberrant growth



Corrected mortality rate with normal and aberrant growth (abbreviations same as in Figure 1). For all 3 types of mortality, $P < .05$ for AGA vs SGA as well as LGA vs SGA. The early and late mortality rate for LGA and AGA were similar ($P > .05$) but significantly different for the postneonatal period ($P = .003$).

AGA, appropriate-for-gestational-age; *LGA*, large-for-gestational-age; *SGA*, small-for-gestational-age.

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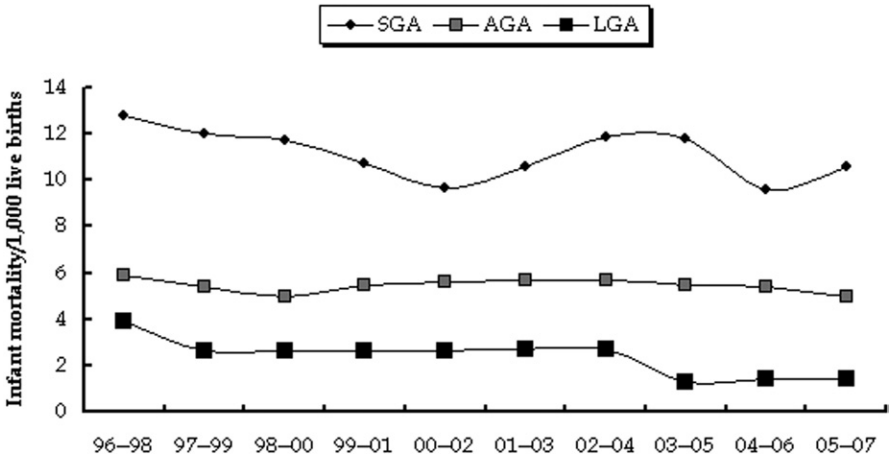
FIGURE 3
Moving average trend (3 year) for corrected infant mortality rate



For normal and aberrant growth, moving average trend (3 year) for corrected infant mortality rate (abbreviations same as in Figure 1; $P > .05$ for all 3 comparisons).

AGA, appropriate-for-gestational-age; *LGA*, large-for-gestational-age; *SGA*, small-for-gestational-age.

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majority of deaths occurred within 27 days of birth, whereas for AGA and LGA, the mortality mostly occurred in the postneonatal period (Figure 1). Newborns with inadequate growth have a significantly higher early, late, and postneonatal mortality than those with adequate or excessive growth (Figure 2). LGA newborns had a significantly lower postneonatal mortality and infant mortality than AGA. Whereas the increased risk of mortality with SGA is well documented,[1,20,22,28] the reduced mortality with LGA is less frequently reported.

Malloy[29] linked 2002 infant birth and death certificates and noted that sudden infant death syndrome (SIDS) and sudden death because of other causes were significantly higher for SGA but lower for LGA. In our study population, SIDS was the predominant cause of death in postneonatal mortality, accounting for 37%, 36%, and 49% of the postneonatal deaths among the SGA, LGA, and AGA infants, respectively. This finding could be expected, however, because SIDS by its definition rules out any other possible causes of death.[30]

We might expect that SGA or LGA infants may have other cooccurring disorders that were determined as a contributing cause of death for the infant. Chen et al[4] noted that among women with pregnancy-induced hypertension, preterm LGA had significantly lower infant mortality. Salihu et al[31] reported that among obese mothers (body mass index of 30 kg/m^2 or greater), the neonatal mortality rate for SGA or AGA newborns was significantly higher than that of nonobese mothers. But for LGA, neonatal mortality was similar for obese (6.2 in 1000) and normal-weight (4.9 in 1000) mothers (adjusted OR, 1.05; 95% CI, 0.75–1.48).

Our third finding is that in Milwaukee the rate of SGA or LGA births and infant mortality rate within SGA, AGA, or LGA births did not change significantly over the 12 years (Figure 3), which is consistent with a previous neonatal mortality trend analysis of all Wisconsin births from 1991 to 2005.[32] In contrast, other reports have noted that the rates of SGA births, macrosomia births, and perinatal mortality for preterm singletons have

TABLE 2
Adjusted odds ratios on early, late, and postneonatal mortality, Milwaukee, 1996-2007

	Early mortality			Late mortality			Postneonatal mortality		
Variables	**OR**	**(95% CI)**	***P***	**OR**	**(95% CI)**	***P***	**OR**	**(95% CI)**	***P***
Maternal age, y									
20-34	Referent			Referent			Referent		
≤19	1.18	(0.75–1.84)	.472	1.01	(0.63–1.63)	.962	1.04	(0.82–1.33)	.727
≥35	1.01	(0.57–1.79)	.964	0.57	(0.25–1.33)	.197	0.67	(0.43–1.03)	.070
Mother's race/ethnicity									
White	Referent			Referent			Referent		
Black	0.76	(0.48–1.20)	.240	0.78	(0.48–1.26)	.300	1.21	(0.93–1.58)	.160
Hispanic	1.23	(0.70–2.18)	.474	0.50	(0.23–1.07)	.072	0.60	(0.40–0.91)	.015
Other	1.42	(0.61–3.29)	.414	0.64	(0.19–2.13)	.466	1.06	(0.60–1.85)	.848
Mother's education									
High school	Referent			Referent			Referent		
Beyond high school	0.81	(0.51–1.27)	.356	0.82	(0.47–1.42)	.476	0.79	(0.59–1.07)	.126
Less than high school	0.58	(0.39–0.88)	.010	1.06	(0.67–1.67)	.803	1.20	(0.96–1.52)	.116
Paternity									
Has father on record	Referent			Referent			Referent		
No father on record	3.80	(2.60–5.56)	< .001	3.61	(2.35–5.56)	< .001	3.19	(2.57–3.97)	< .001
Prenatal care									
Adequate or better	Referent			Referent			Referent		
Inadequate or intermediate	1.04	(0.71–1.53)	.834	0.92	(0.61–1.41)	.717	1.00	(0.81–1.23)	.981
Alcohol use during pregnancy									
No	Referent			Referent			Referent		
Yes	2.56	(1.23–5.30)	.012	0.49	(0.12–2.08)	.336	1.14	(0.68–1.90)	.624
Cigarette use during pregnancy									
No	Referent			Referent			Referent		
Yes	0.74	(0.47–1.18)	.205	1.20	(0.76–1.88)	.440	1.64	(1.30–2.05)	< .001
Mother's medical history									
Gestational diabetes	1.02	(0.43–2.39)	.969	1.39	(0.55–3.50)	.487	1.10	(0.63–1.93)	.745
Pregestational diabetes	0.74	(0.17–3.15)	.681	0.64	(0.09–4.78)	.667	0.55	(0.14–2.25)	.409
Hydramnios or oligohydramnios	3.66	(1.90–7.04)	< .001	2.65	(1.13–6.22)	.026	1.90	(1.05–3.41)	.033
Hypertensive disease	0.51	(0.28–0.93)	.027	0.70	(0.36–1.35)	.284	1.20	(0.85–1.70)	.309
Uterine bleeding	1.25	(0.44–3.55)	.669	0.44	(0.06–3.24)	.420	1.82	(0.88–3.75)	.107

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decreased in the United States.[33-35] However, those reports used different inclusion criteria and time periods for analysis. For our study, potential reasons that the rate did not change significantly are the exclusion of anomalous newborns, 1 of the leading causes of infant mortality, and multiple gestations, who are at appreciable risk of mortality. In addition, our sample size may not be sufficient to detect the small improvement in corrected mortality among singletons.

Our fourth finding focuses on the multivariate logistic regression, which identified several factors that independently influence the 3 types of mortality (Table 2). When adjusted for 19 covariates and compared with AGA, SGA was a

TABLE 2
Adjusted odds ratios on early, late, and postneonatal mortality, Milwaukee, 1996-2007 *(continued)*

	Early mortality			Late mortality			Postneonatal mortality		
Variables	**OR**	**(95% CI)**	***P***	**OR**	**(95% CI)**	***P***	**OR**	**(95% CI)**	***P***
Events of labor									
Premature rupture of membranes >12 h	1.10	(0.64–1.90)	.731	0.82	(0.40–1.66)	.576	0.61	(0.37–1.01)	.052
Precipitous labor (<3 h)	1.40	(0.66–2.94)	.380	0.69	(0.21–2.21)	.529	0.98	(0.60–1.58)	.922
Abruptio placenta	1.91	(0.97–3.73)	.060	2.19	(1.04–4.63)	.040	1.54	(0.87–2.74)	.143
Gestational age, wks									
37-40 (term)	Referent			Referent			Referent		
37 (preterm)	20.19	(13.16–31.00)	< .001	10.00	(6.40–15.65)	< .001	3.44	(2.74–4.33)	< .001
41 (postterm)	1.25	(0.49–3.21)	.646	1.61	(0.71–3.63)	.251	0.94	(0.64–1.38)	.745
Delivery method									
Spontaneous vaginal	Referent			Referent			Referent		
Cesarean	2.48	(1.71–3.60)	< .001	2.23	(1.47–3.40)	< .001	1.33	(1.04–1.70)	.026
Operative vaginal	0.98	(0.31–3.13)	.971	1.05	(0.33–3.37)	.937	1.39	(0.88–2.19)	.164
Fetal growth									
AGA	Referent			Referent			Referent		
SGA	2.66	(1.82–3.89)	< .001	2.14	(1.38–3.32)	< .001	1.19	(0.92–1.55)	.195
LGA	1.72	(0.76–3.86)	.192	0.71	(0.22–2.31)	.568	0.71	(0.41–1.22)	.212
Sex									
Male	Referent			Referent			Referent		
Female	1.13	(0.81–1.58)	.469	0.96	(0.66–1.40)	.831	0.78	(0.64–0.94)	.011
Newborn's condition									
Normal	Referent			Referent			Referent		
Abnormal	2.11	(1.45–3.08)	< .001	2.74	(1.78–4.22)	< .001	1.73	(1.32–2.26)	< .001

AGA, appropriate-for-gestational-age; *CI*, confidence interval; *LGA*, large-for-gestational-age; *OR*, odds ratio; *SGA*, small-for-gestational-age.

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significant risk factor for early and late mortality but not postneonatal mortality. AGA and LGA had similar likelihoods of death. We recognized 5 other risk factors, in descending order of magnitude, as preterm birth, absence of paternity on the birth record, hydramnios or oligohydramnios, cesarean delivery, and abnormal condition of newborn at birth, which increased the risk of death for each subtype of infant mortality. Data from National Vital Statistics consistently lists preterm birth as one of the leading causes of death within the first year of birth.[36]

Consistent with our findings, other reports that linked birth and death certificates have identified absence of paternity and abnormalities of amniotic fluid as risk factors for infant mortality.[37,38] The absence of a father's name on the birth certificate may reflect an unhealthy family unit. Not reporting fathers' names could represent the lack of partner support for women to receive adequate care. It may indicate a variety of social risk factors for increased neonatal and infant mortality, such as unintended pregnancy, and the possible presence of statutory rape.[18, 37]

Some factors, such as maternal age,[17] race/ethnicity,[15,25,39] and pregnancy at 41 weeks or longer,[24] linked with mortality did not significantly contribute to deaths in Milwaukee. One factor, hypertensive disease, was found to decrease the likelihood of early but not late or postneonatal mortality. Lastly, we did confirm that certain factors, such as being Hispanic and female sexed, were protective. Although maternal race/ethnicity (particularly African American) has been a well-known risk factor for worse birth outcomes, our results demonstrated that African American maternal race was not significantly associated with worse neonatal mortality compared with whites.

Possible explanations for this finding include that our methodology excluded congenital anomalous newborns and newborns from multiple gestations. Compared with other races, we found that African American mothers had a much higher percentage of having SGA infants (14.7%) and having no father on record (44.2%), which are 2 main signif-

icant variables associated with worse neonatal mortality. Also, there may be some other unmeasured confounders that we could not adjust for. All of the aforementioned factors may have contributed to the variation between our findings and published reports.

In addition, consistent with Salihu et al,[40] our study found that cigarette use during pregnancy was significantly associated with postneonatal mortality, rather than neonatal mortality. Although smoking has been identified as a risk factor for suboptimal fetal growth, which is a contributing factor to SGA deliveries, our study was not able to account for the contribution of passive smoking. Also, in our study, prenatal care was not found to be a protective factor. However, the research literature has documented the difficulty of quantifying and measuring the effectiveness of prenatal care,[8,41] with recent studies arguing for and against the effectiveness of prenatal care in its current form.[42,43]

Several limitations of the study need to be acknowledged. First, although birth certificate data have advantages in epidemiologic research, they have known shortcomings, including but not limited to, missing data, accuracy, and validity of data.[44-46] In this study, we assumed that a mother did not have a medical condition if the box was not checked on the birth certificate; thus, we may have underestimated the prevalence of the maternal medical conditions because of unobserved missing data. Although the accuracy of vital statistics data has been examined in other states,[47-50] using combination of the terms "birth certificate, neonatal, infant, mortality, and Milwaukee, Wisconsin," we did not find any publications in the English language that assessed the validity of birth certificates in Milwaukee or Wisconsin. We additionally contacted the source of our data and they are not aware of any study that has determined the accuracy of the birth certificate data.

Second, the criteria used to determine gestational age may have varied over the 12 year period. It is possible that there were random or nonrandom misclassifications.[46] But considering we confirmed several risk factors that are known to increase mortality suggests the data are useful in exploring trends and in generating hypothesis.

Third, our analysis of the city of Milwaukee may not be representative of other cities, states, or the United States. For example, Milwaukee is one of the most segregated large metropolitan US cities.[51] Milwaukee has a higher proportion of African American births (47%) compared with the United States (16%).[52] Compared with other large Midwestern cities, Milwaukee has a higher black infant mortality rate (16.0) than Indianapolis, IN (15.4), and Columbus, OH (14.9), but lower than Chicago, IL (17.0), and Detroit, MI (18.1).[53] Also, the median household income in Milwaukee ($37,022) is lower than that of the United States ($52,175).[54] Thus, because of these shortcomings, observational and/or interventional studies are necessary before any recommendations to alter obstetric or neonatal practice are made.

In summary, our findings suggest that aberrant growth may influence early, late, and postneonatal mortality differently. When the analysis adjusts for confounding variables, SGA but not LGA is linked with increased mortality. Additional studies are needed from Milwaukee and possibly other urban settings to confirm these findings and to determine whether compliance with evidence-based medicine can decrease the risk of mortality. ■

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