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Assessing Risk Factors for Infant Mortality in the US: State of the Art

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Abstract

Objective: *To examine multiple infant and maternal risk factors for infant mortality.*

Study Design: *This cross-sectional study used data from 2017-2018 National Center for Health Statistics (NCHS) Cohort Linked Live Birth-Infant Death Files, consisting of all births occurring in 2017 and all infant deaths occurring in 2018 linked to their corresponding birth certificates.*

Results: *The 2017-2018 birth cohort linked birth/infant death data included 3,723,134 singletons in total. The number of infant deaths was 19,026, yielding an infant mortality rate (IMR) of 5.1 per 1,000 live births. We identified four most severe risk factors for infant mortality, including extremely low birth weight (< 1000 g), presence of congenital anomalies (CAs), 5-minute Apgar score <7, and extremely preterm (gestational age <28 weeks), with the associated IMRs ranging from 120-370 and associated adjusted odds ratios (AORs) ranging from 3-25. Their IMRs and AORs were, respectively, extremely low birth weight (IMR: 370.8; AOR: 24.85), presence of CAs (IMR: 119.5; AOR: 17.52), 5-minute Apgar score <7 (IMR: 140.8; AOR: 11.89), and extremely preterm (IMR: 343.6; AOR: 3.13). Other significant risk factors were infant male gender and several maternal factors, including age less than 20 years, AIAN race, high school education or less, unmarried status, inadequate or excessive GWG, smoking before or during pregnancy, lack of prenatal care, hypertension or diabetes before or during pregnancy, previous death of a live birth, and payment source for delivery as Medicaid, Self-Pay or Other, with AORs ranging from 1.1 to 2.*

Conclusions: *This study identified multiple infant and maternal risk factors for infant mortality. Identification of these risk factors could aid in infant mortality reduction by improving prenatal care, maternal and child health programs and policies through the joint collaborations between health care providers, states, communities, and partners.*

Keywords: *Infant mortality rate; risk factors; multivariate logistic regression; adjusted odds ratio.*

Introduction

Infant mortality is the death of an infant within the first year of life. The infant mortality rate (IMR) is defined as the number of infant deaths for every 1,000 live births in the first year of life. The IMR is a well-recognized indicator of maternal and infant health. According to the IMR estimates developed by the UN Inter-agency Group for Child Mortality Estimation, the IMR has been steadily declining in the US since 1960s from 25.9 to 5.6 in 2019 (https://data.worldbank.org/indicator/SP.DYN.IMRT.IN?locations=US), mainly attributed to modern improvements in basic health care, technology and medical advance.[1] Additionally, there have been public health pushes to prevent unnecessary early induced labor at <39 weeks' gestation and smoke-free legislation in several states.[2-3]

Although the IMR continues to fall, during the past decade significant infant mortality disparities persist in subpopulations depending on infant and maternal characteristics and health during pregnancy. Previous research has examined infant mortality disparities by some risk factors (e.g., infant birth weight and gestational age; maternal socio-demographics and health).[4-6] However, to our knowledge, data used in these studies might be outdated as most of them were older than 2003. Consequently, information generated from the data might be irrelevant to the research problem. Further research is needed to extend these studies by identifying and examining multiple infant and maternal risk factors using up-to-date large data to better understand, reduce and eliminate infant mortality disparities. The present study used multivariable analyses to address various risk factors that contribute to infant mortality using the recent NCHS birth cohort database. The state of the art in risk factors could help maternal and child health professionals recognize these risk factors and find opportunities to reduce the IMR.

Materials and Methods

Data Source

This cross-sectional study used data from 2017-2018 National Center for Health Statistics (NCHS) Cohort Linked Live Birth-Infant Death Files, consisting of all births occurring in 2017 and all infant deaths occurring in 2018 linked to their corresponding birth certificates. Multiple births were excluded from the study.

Infant and Maternal Factors

Infant factors included sex (female or male); birth weight (BW) with 6 categories defined according to The World Health Organization (WHO), including the extremely low birth weight (ELBW) for BW< 1000 g, very low birth weight (VLBW) for BW in 1000-1499 g, low birth weight (LBW) for BW in 1500-2499g, inadequate or insufficient birth eight (IBW) for BW in 2500-2999g, adequate or sufficient birth weight (ABW) for BW in 3000-3999g, and macrosomic for BW ≥4000g;[7] gestational age with 4 categories defined according to the WHO, including extremely preterm (< 28 weeks), very preterm (28-32 weeks), moderate to late preterm (32-37 weeks), full term (≥37 weeks); 5-minute pgar score (< 7 or ≥7);[8] presence of congenital anomalies (CAs), including anencephaly, meningomyelocele/spina bifida, cyanotic congenital heart disease, congenital diaphragmatic hernia, omphalocele, gastroschisis, limb reduction fect, cleft lip, cleft palate alone, down syndrome, suspected chromosomal disorder, and hypospadias (yes and no); presence of infections including gonorrhea, syphilis, chlamydia, or hepatitis B or C (yes or no).

Maternal factors included maternal age (≤19, 20-34, 35-39, or 40-64); race (White, Black, American Indians and Alaska Natives (AIAN), Asian, Native Hawaiians or Other Pacific Islanders (NHOPI), or Multiracial); education (≤high school or >high school including some college credit, associate degree, bachelor's degree, master's degree, doctorate or professional degree); marital status (married or unmarried); smoking before or during pregnancy (yes or no); lack of prenatal care (yes or no); hypertension or diabetes before or during pregnancy (yes or no); maternal morbidity including transfusion, perineal laceration, ruptured uterus, unplanned hysterectomy or admit to intensive care (yes or no); history of the death of a live-birth (yes or no); payment source for delivery (Medicaid, private insurance, self-pay or Other).

An additional maternal factor was the gestational weight gain (GWG). The Institute of Medicine (IOM) published guidelines on appropriate levels of GWG based on a woman's prepregnancy body mass index (BMI) as follows: 28-40 lbs for underweight women (BMI<18.5), 25-35 lbs for normal weight women (BMI:18.5-24.9), 15-25 lbs for overweight woman (BMI: 25.0-29.9), and 11 to 20 lbs for obese women (BMI≥30).[9] However, because the prepregnancy BMI was unavailable in this study, it was impossible to use the IMO guideline to calculate the appropriate GWG. We considered three GWG categories, inadequate (GWG<24), normal (24≤GWG≤40), and excessive (GWG>40), according to the conservative lower limits, 24 and 40, of the IOM recommended range.[10]

Statistical Analysis

The IMRs were calculated among groups by infant and maternal factors. The chi-square test was conducted to compare the IMRs between groups by each factor. Multivariate logistic regression was used to assess the effect of each factor on infant mortality after the adjustment of other factors. The adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were reported. All analyses were conducted using the SAS version 9.4 software (SAS Institute Inc., Cary, NC, USA).

Results

Descriptive Analysis of IMR Infant and Maternal Factors

The 2017-2018 birth cohort linked birth/infant death data included 3,723,134 singletons, and the number of infant deaths was 19,026, yielding an IMR of 5.1 per 1,000 live births. Table 1 showed IMRs among groups by infant and maternal factors. The chi-square test was significant for each factor with the p value <.0001. The IMR was the highest for ELBW (IMR: 370.8), followed by extremely preterm (IMR: 343.6), 5-minute Apgar score <7 (IMR: 140.8), presence of CAs (IMR: 119.5), VLBW (IMR: 57.7), Very Preterm (IMR: 37.9), lack of prenatal care (IMR: 23.0), previous death of a live birth (IMR: 16.3), and LBW (IMR: 15.1). The IMRs for other maternal risk factors were as follows: morbidity (IMR: 9.9), smoking status before or during pregnancy (9.7), young (<20 years; IMR: 8.4) or advanced age (40-64 years; IMR: 6.5), black (IMR: 9.2), AIAN (IMR: 8.0) or NHOPI (IMR: 6.1) race, unmarried status (IMR: 7.6), high-school education or less (IMR: 6.7), Medicaid (IMR: 6.6) or self-pay (IMR: 5.9) payment source for delivery, and hypertension or diabetes before or during pregnancy (IMR: 5.7).

Table1. *Infant mortality rate (IMR), adjusted odds ratios (AORs) and 95% confidence intervals (CIs) among groups by maternal and infant factors.*

Variable	All-cause IMR	AOR (95% CI)	Variable	All-cause IMR	AOR (95% CI)
Infant factors			**Maternal factors**		
Gender			***Race***		
F	4.7	1 (Ref)	White	4.3	1 (Ref)
M	5.5	1.18 (1.14, 1.23)	Black	9.2	1.03 (.98, 1.08)
***Birth weight* (gram)**			AIAN	8.0	1.34 (1.15, 1.56)
<1000 (ELBW)	370.8	24.85 (21.81, 28.33)	Asian	3.3	.90 (.82, .99)
1000-1499 (VLBW)	57.7	7.26 (6.45, 8.18)	NHOPI	6.1	1.05 (.75, 1.47)
1500 – 2499 (LBW)	15.1	4.37 (4.09, 4.67)	Multiracial	6.3	1.16 (1.04, 1.30)
2500 – 2999 (IBW)	3.7	1.85 (1.75, 1.96)	***Education***		
3000 – 3999 (ABW)	1.6	1 (Ref)	<=High school	6.7	1.20 (1.15, 1.25)
>4000 (Macrosomic)	1.4	.84 (.75, .94)	>High school	3.8	1 (Ref)
Apgar score			***GWG***		
<7	140.8	11.89 (11.35,12.45)	≤24	7.9	1.14 (1.09, 1.19)
≥7	2.3	1 (Ref)	25-40	3.0	1 (Ref)
			41+	4.6	1.16 (1.10, 1.23)
Gestation (week)			***Smoking***		
Extremely Preterm	343.6	3.13 (2.75, 3.55)	Yes	9.7	1.36 (1.29, 1.44)
Very Preterm	37.9	1.22 (1.09, 1.37)	No	4.7	1 (Ref)
Moderate to late preterm	9.1	1.36 (1.28, 1.44)	***Prenatal care***		
Full term	2.1	1 (Ref)	Yes	4.5	1 (Ref)
			No	23.0	1.31 (1.21, 1.42)
Presence of CAs			***Hypertension or diabetes before or during pregnancy***		
Yes	119.5	17.52 (16.22, 18.91)	Yes	5.7	1.17 (1.13, 1.22)
No	4.6	1 (Ref)	No	4.8	1 (Ref)
Infection			***Morbidity***		
Yes	8.5	1.09 (.99, 1.19)	Yes	9.9	1.09 (.96, 1.23)
No	5.0	1 (Ref)	No	5.0	1 (Ref)
Maternal factors			***Previous death of a live birth***		
Age			Yes	16.3	1.56 (1.40, 1.73)
≤19	8.4	1.19 (1.09, 1.30)	No	4.9	1 (Ref)
20-34	4.9	1 (Ref)	***Payment Source***		
35-39	4.6	1.11 (1.05, 1.18)	Medicaid	6.6	1.23 (1.17, 1.28)
40-64	6.5	1.19 (1.06, 1.33)	Private Insurance	3.6	1 (Ref)
Marital status			Self-pay	5.9	1.24 (1.13, 1.36)
Yes	3.7	1 (Ref)	Other	5.1	1.21 (1.09, 1.34)
No	7.6	1.16 (1.11, 1.22)			

Multivariate Logistic Regression Analysis of IMR Infant and Maternal Factors

As shown in Table 1, significant infant risk factors included male gender (AOR: 1.18; 95% CI: 1.14-1.23), ELBW (AOR: 24.85; 95% CI: 21.81-28.33), VLBW (AOR: 7.26; 95% CI: 6.45-8.18), LBW (AOR: 4.37; 95% CI: 4.09, 4.67), 5-minute Apgar score less than 7 (AOR: 11.89; 95% CI: 11.35-12.45), extremely preterm (AOR: 3.13; 95% CI: 2.75, 3.55), very preterm (AOR: 1.22; 95% CI: 1.09, 1.37), moderate to late preterm (AOR: 1.36; 95% CI: 1.28, 1.44), and presence of CAs (AOR: 17.52; 95% CI: 16.22,18.91).

Significant maternal risk factors were age less than 20 years (AOR: 1.19; 95% CI: 1.09,1.30), 35-39 years (AOR: 1.11; 95% CI: 1.05,1.18) or 40-64 years (AOR: 1.19; 95% CI: 1.09,1.33), unmarried status (AOR: 1.16; 95% CI: 1.11,1.22), AIAN (AOR: 1.34; 95% CI: 1.15,1.56) or multiracial race (AOR: 1.16, 95% CI: 1.04 -1.30), high school education or less (AOR: 1.20; 95% CI: 1.15,1.25), inadequate (AOR: 1.14; 95% CI: 1.09,1.19) or excessive GWG (AOR: 1.16; 95% CI: 1.10,1.23), smoking before or during pregnancy (AOR: 1.36; 95% CI: 1.29,1.44), lack of prenatal care (AOR: 1.31; 95% CI: 1.21,1.42), hypertension or diabetes before or during pregnancy (AOR: 1.17; 95% CI: 1.13,1.22), previous death of a live birth (AOR: 1.56; 95% CI: 1.40,1.73), and payment source for delivery as Medicaid (AOR: 1.23; 95% CI: 1.17,1.28), Self-Pay (AOR: 1.24; 95% CI: 1.13,1.36) or Other (AOR: 1.21; 95% CI: 1.09,1.34).

Discussion

With and without adjusting for other risk factors, we found four most severe risk factors for infant mortality, including low birth weight (ELBW, VLBW, LBW), 5-minute Apgar score <7, presence of CAs, and preterm birth, with the associated IMRs ranging from 120-370 and associated AORs ranging from 3-25. These findings were consistent with those from a cross-sectional study conducted in Brazil, which examined 9,349 births and 81 neonatal deaths (within the first 27 days of life) in 2010-2011.[5] Other significant risk factors found in our study were infant male gender and several maternal factors, including age less than 20 years, AIAN race, high school education or less, unmarried status, inadequate or excessive GWG, smoking before or during pregnancy, lack of prenatal care, hypertension or diabetes before or during pregnancy, previous death of a live birth, and payment source for delivery as Medicaid, Self-Pay or other.

Infant Risk Factors

Male Gender

Male gender is a risk factor for infant mortality. Historically, males have higher IMRs than females because they are biologically more vulnerable to infections and conditions associated with prematurity and development.[11-12] This study found that baby boys had 1.2 times odds of mortality compared to baby girls. This result was similar to that from a prospective cohort study on 297,509 births with 52 boys in India and Pakistan in 2010-2018.[13]

LBW

According to the World Health Organization (WHO), LBW accounts for approximately 15%-20% of all births worldwide, representing over 20 million births a year, and continues to be a significant global public health problem.[14] LBW babies are at risk of a range of short- and long-term health problems. This study showed that IBW, LBW, VLBW and ELBW babies had 2 to 26 times odds of mortality compared to ABW babies. A recent retrospective cohort study of live births from 2000 to 2015 in Brazil reported incidence rates of mortality associated with these BW categories ranging from 2 to 207.[15]

Presence of Congenital Anomaly (CA)

CAs were defined as conditions coded within Congenital Malformations, Deformations and Chromosomal Abnormalities (Q00-Q99) of the International Classification of Diseases (ICD), Tenth Revision (ICD-9). CAs were classified according to organ systems, and 60% of CA deaths were attributed to the nervous, cardiovascular, and respiratory systems over the last three decades.[16] This study showed that CAs were associated with 18-fold increased odds of infant mortality. Specifically, we found that the most severe CA was anencephaly (IMR: 633.0). Other important CAs were suspected chromosomal disorder (IMR: 439.8), congenital diaphragmatic hernia (IMR: 303.5), omphalocele (IMR: 239.0), cyanotic congenital heart disease (IMR: 190.7), limb reduction defect (IMR: 162.9), cleft lip (IMR: 105.1), down syndrome (IMR: 100.0), cleft palate alone (IMR: 99.3), meningomyelocele/spina bifida (IMR: 87.1), gastroschisis (IMR: 55.2), and hypospadias (IMR: 16).

Preterm Birth

According to the WHO, it is estimated that 15 million

babies are born preterm, which is more than 1 in 10 babies.[17] According to Weber et al. (2018), the US had greater prevalence and outcomes of prematurity than other developed countries, attributed partly to the higer prevalence of poverty, inadequate health care access, and racial inequalities.[18] We found that babies born extremely preterm had 3.2 times odds of morality compared to full-term babies. This finding was similar to that from a cross-sectional study in Brazil.[5] A prospective cohort study in rural Nepal followed 15,469 singleton infants for 24 weeks of age to identify risk factors for mortality within 0–7 days, 8–28 days, and 4–24 weeks after birth. They defined 5 categories of gestational age (weeks): 28-31, 32-35, 36-39, 40-42 and ≥43.[19] They found that gestational age was negatively associated with infant mortality, with the highest mortality risk occurring in the first week of life for each gestational age category. Babies with a gestational age of 28-31 weeks had 5.3 times odds of death in the first week of life compared to babies with a gestational age greater than 42 weeks.

Apgar Score

Apgar is a quick test given to a new born at 1 and 5 minutes after birth by a provider to check the baby's breathing effort, heart rate, muscle tone, reflexes, and skin color. The American College of Obstetrics and Gynecology defined a 5-minute Apgar score of 7 to 10 as reassuring, a score of 4 to 6 as moderately abnormal, and a score of 0 to 3 as low.[8] We found that a low 5-minute Apgar score (less than 7) was associated with 12 times increased odds of mortality and therefore was a severe risk factor for infant mortality. This finding was similar to that from a cross-sectional study in Brazil.[5]

Presence of Infection

According to the WHO, infections, including sepsis/pneumonia, tetanus and Diarrhoea, are one of the major causes of neonatal deaths worldwide (36%).[20] However, this study showed that the presence of infections was not a significant risk factor for infant mortality. This is possibly attributed to the quality of infection control in the US at individual and community levels.

Maternal Risk Factors

Lack of Prenatal Care

Prenatal care is important for both the mother and baby because it not only monitors the health of the mother and growing fetus, but also provides education and counseling on nutrition, exercise, and abstaining from drugs and alcohol. This study showed that babies born to mothers without prenatal care had 1.3 times odds of mortality compared to babies born to mothers with prenatal care. These results were similar to those from a cross-sectional study on 90,339 births with 11% LBW infants in New York City in 1968.[21]

Black or AIAN Race

Black and AIAN mothers were associated with higher IMRs than their white counterparts (9.2 vs 8.0). However, after adjusting for other risk factors only AIAN mothers had significantly higher odds than white mothers. This racial disparity was partly due to barriers to accessing healthcare. In 2018 AIANs were nearly twice as likely as whites to lack medical insurance.[22] In this study, the percentages of mothers who had private insurance as the payment source for delivery were, respectively, 20% for AIANs, 27% for blacks, 28% for NHOPI, 53% for whites and 64% for Asians. The percentages of mothers who did not have prenatal care were, respectively, 3.6% for AIANs, 3.2% for blacks, 4.5% for NHOPI, 1.5% for whites, and .9% for Asians. Although medical, genetic, and/or sociodemographic factors account for in part racial disparities, much remains unknown why race plays a role in infant mortality and other adverse birth outcomes.

Low Socio Economic Status (SES)

Previous research showed that low SES, measured by education, income and occupation, was associated with a higher mortality risk due to the lack of access to health services and quality care provided during pregnancy. It has been well documented that increased household income provides access to nutrients and healthcare and that increased maternal education provides mothers with connections to resources for infant health and knowledge of healthy behaviors, which in turn reduces the IMR. According to the analysis of temporal inequalities in US infant mortality by area deprivation, the adjusted relative risk of infant mortality was 41% higher for mothers with 12 or more years of education than for those with 16 years of education in 1969-2001.[23] We found that babies born to mothers with a high school education or less had 1.2 times odds of mortality compared to babies born to mothers with more than a high school education. The information on maternal income and

occupation was unavailable in this study; however, the payment source for delivery could serve as a proxy for maternal income. We found that babies whose deliveries were covered by private insurance had lower odds of mortality than babies whose deliveries were covered by other sources including Medicaid and Self-Pay. Using data on child and family well-being in the United States in 2004-2013, previous research found that the IMRs for states with low median household income (e.g., Mississippi) were up to twice as high as the IMRs for states with high median household income (e.g., Maryland).[24]

Unmarried Status

Marriage has been shown to be a protective factor against infant mortality in many studies, as it provides many benefits in social contexts.[25] The IMR is notably higher among unmarried mothers than among married mothers. This study showed that unmarried status was associated with 1.2 times odds of infant mortality and LBW compared to married status.

Smoking

Smoking during pregnancy can cause lung and brain damages in unborn babies. Previous research has shown that maternal smoking can cause adverse birth outcomes such as infant mortality, low birth weight and preterm birth.[26-28] For example, a cross-sectional study showed that maternal smoking during pregnancy was associated with a 2-fold increased risk of sudden unexpected infant death and infant mortality.[26] Another cross-sectional study in 25,102 pregnant women with 30% smokers in Denmark in 1989-1996 showed that babies born to smokers during pregnancy had a nearly 2-fold the risk of mortality compared to babies born to nonsmokers.[27] A prospective cohort study conducted in 104,415 mothers with singleton births in Japan in 2004-2010 found that smoking during pregnancy was associated with 1.5-2 times increased risk of LBW, which was similar to the finding from this study.[28]

Hypertension or Diabetes Before or During Pregnancy

Hypertension before or during pregnancy is associated with an increased risk for maternal complications such as preeclampsia, placental abruption, and gestational diabetes. We found that mothers with hypertension or diabetes before or during pregnancy had 1.2-fold increased odds of infant mortality, which was similar to the result from a prospective cohort study conducted in 822 women with chronic hypertension (22% incidence of superimposed preeclampsia).[29]

Inadequate and Excessive GWG

The amount of weight gained during pregnancy is important to maternal and infant health. Maternal GWG, combined with prepregnancy BMI, is an important predictor of birth weight. There has been evidence that excessive GWG is associated with increased BW and inadequate GWG is associated with decreased BW. We found that both inadequate and excessive GWGs were risk factors for infant mortality with AOR ranging from 1.1 to 1.2. This finding was consistent with those in three existing studies.[30-32]

Previous Death of A Live Birth

We found that the previous death of a live birth was associated with a 1.6-fold increased risk of mortality. A similar finding was reported from a cross-sectional study in rural areas of Nepal in 1976, after the adjustment of controlled for maternal age, birth order and birth interval between the death of a previously live birth and subsequent infant.[33] The study also found that babies born within 18 months of the death of a previously live born infant had twice the risk of mortality compared to babies born 36 months after the death of a previously live born infant.

Study strengths and limitations

The major strength of this study is that it used a large-scale population-based national survey consisting of all singletons occurring in 2017 and all infant deaths occurring in 2018. The data included a few infant and maternal risk factors that were not evaluated before, such as the previous death of a live birth, presence of congenital anomalies and presence of infection. The limitation of this study is that, like any typical secondary research study, it cannot derive causal relationships between the risk factors and infant mortality.

Conclusion

This study identified four most severe risk factors for infant mortality, including low birth weight (ELBW, VLBW, BW), 5-minute Apgar score <7, presence of CAs, and extremely preterm birth. Male gender was another important risk factor. Additional maternal risk factors included age below 20 years, low education, AIAN race, smoking before or during pregnancy, unmarried status,

lack of prenatal care, previous death of a live birth, hypertension or diabetes before or during pregnancy, and payment source for delivery as Medicaid or Self-Pay. Identification of these risk factors could aid in infant mortality reduction by improving prenatal care, and maternal and child health programs and policies through joint collaborations between health care providers, states, communities, and partners. For example, the recent legislative acts such as H.R. 4571 aimed to raise awareness about infant mortality by developing prevention programmes for best practices and advancing support services such as counselling and educational workshops.[34]

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