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Disparities in Health Care–Associated Infections in the NICU

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Abstract

Objectives—This study aimed to examine multilevel risk factors for health care-associated infection (HAI) among very low birth weight (VLBW) infants with a focus on race/ethnicity and its association with variation in infection across hospitals.

Study Design—This is a population-based cohort study of 20,692 VLBW infants born between 2011 and 2015 in the California Perinatal Quality Care Collaborative.

Results—Risk-adjusted infection rates varied widely across neonatal intensive care units (NICUs), ranging from 0 to 24.6% across 5 years. Although Hispanic infants had higher odds of HAI overall, race/ethnicity did not affect the variation in infection rates. Non-Hispanic black mothers were more likely to receive care in NICUs within the top tertile of infection risk. Yet, among NICUs in this tertile, infants across all races and ethnicities suffered similar high rates of infection.

Conclusion—Hispanic infants had higher odds of infection. We found significant variation in infection across NICUs, even after accounting for factors usually associated with infection.

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Author's Contributions

J.L. selected data for inclusion in analyses, executed the analysis, helped interpret the results, drafted the initial article, revised the article, and approved the final article as submitted. C.S. helped execute some of the analysis, helped interpret the results, revised the article, and approved the final article as submitted. K.S. helped interpret the results, revised the article, and approved the final article as submitted. H.C.L. helped design the analysis and interpret the results, revised the article, and approved the final article as submitted. J.P. acquired funding for this study, conceptualized and designed the study, selected data for inclusion in analyses, analyzed the data, interpreted the results, helped draft initial article, revised the article, and approved the final article as submitted. J.P. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Conflict of Interest

None declared.

Keywords

infant; health care–associated infection; disparity; risk factors

Health care–associated infection (HAI) is a serious complication among very low birth weight (VLBW; <1,500 g) preterm infants hospitalized in the neonatal intensive care unit (NICU), and infection rates in these infants have ranged from 21 to 30%.^{1–4} VLBW infants are especially susceptible to HAI. They are immune-incompetent hosts, require prolonged hospitalization, undergo frequent invasive procedures, and receive prolonged broad-spectrum antibiotics and intravenous nutrition.^{1,5–7} In addition, infection risk is conveyed by a combination of maternal health and clinical practice-related factors.^{1–3,5,6,8–11}

HAIs are associated with increases in neurodevelopmental impairment, mortality, length of stay, and as a result, increased financial costs of care.^{3,6,12–17} Payne et al reported that the occurrence of just one single type of HAI would increase costs of treating VLBW infants by \$100 million.¹² Reducing HAI has been a priority in recent years, and successful efforts have been reported from individual NICUs and through collaborative networks, such as the Vermont Oxford Network and the California Perinatal Quality Care Collaborative (CPQCC).^{7,18–20}

Vulnerable populations may be differentially affected by HAI because they may receive care in challenged hospitals, which provide lower quality of care,^{21–23} or differential treatment within hospitals.²⁴ HAI is more dependent on care processes rather than social risk, making it an intriguing measure of disparity with potential insights into the differential importance of between (i.e., receiving care at challenged hospitals) versus within (receiving differential care) NICU disparity. Our study had the following objectives:

1. To determine infant level risk factors of HAI.
2. To test for the association of race/ethnicity on within and between hospital variation in HAI rates.

Methods

Patient Sample

We performed a retrospective analysis of clinical and organizational data collected by the CPQCC data registry, which comprised 135 member NICUs (>90% of all California NICUs).²⁵ This analysis included infants who were cared for in the CPQCC network between January 1, 2011, and December 31, 2015. CPQCC collects data with variables conforming to definitions developed by the Vermont Oxford Network. We aggregated the 5-year period of data due to small numbers of VLBW infants in some NICUs. Data for infants who were transferred to CPQCC-member NICUs were included.

Infants included in this sample were between 401 and 1,500 g at birth or between 22 and 29 weeks' gestational age at birth. We further excluded infants who died in the delivery room or before 12 hours of life, and those with congenital abnormalities.

Main Outcome of Interest

The main outcome of interest was the occurrence of a late HAI (i.e., late sepsis or meningitis) in each infant, which was defined as either a late bacterial infection and/or late coagulase-negative *Staphylococcus* infection and/or late fungal infection after day 3 of life (the day of birth is day 1) at the reporting center. Any coagulase-negative *Staphylococcus* positive cultures require additional clinical criteria to be classified as an infection. Additional details can be found in the Supplementary Material (available in the online version).

Patients were evaluated for HAI at each hospital admission, and cases were coded as occurring “here,” “elsewhere,” or “here and elsewhere.” However, attributing “here” or “elsewhere” had to be standardized, as transfers may bias the NICU performance measures. A detailed algorithm was developed to correctly attribute infections to NICUs and avoid incorrectly penalizing or crediting an NICU for care delivered in another NICU. The following algorithm was internally developed in conjunction with the Vermont Oxford Network, and has been shown to be robust under other transfer scenarios. In a subset analysis attributing infections as they occurred, correlations with analyses using the algorithm below were >99%.^{22,26,27}

1. Only infants with a maximum of three admissions from two separate hospitals are included.
2. For infants who are transferred by the end of day 3 of life (day 1 is the day of birth), subsequent incidences of HAI are attributed to the receiving hospital and counted as missing for the birth hospital.
3. For infants who are transferred after the end of day 3 of life, subsequent incidences of HAI are attributed to the birth hospital and counted as missing for the receiving hospital.

Additional Covariates

We considered other factors for potential inclusion in the final risk-adjusted model, based on previous literature and clinical importance. The potential risk factors considered include the following.

Infant Level Covariates—Infant clinical characteristics included birth year, sex, small for gestational age (SGA, defined as birth weight <10th percentile for gestational age), gestational age, 5-minute Apgar score, birth at another hospital (outborn), and race/ethnicity.

Maternal Level Covariates—Maternal clinical characteristics included prenatal care, multiple gestation, cesarean birth, chorioamnionitis, any hypertension, any type of diabetes, preterm premature rupture of membranes, prolonged rupture of membranes, fetal distress, malpresentation/breech, bleeding/abruption/previa, and maternal age.

Hospital Level Covariates—Organizational factors included the hospitals’ American Academy of Pediatrics (AAP) level (level of neonatal care that a hospital provides²⁸),

number of NICU and stepdown beds, ownership type, neonatologist coverage, yearly volume of infants treated in the NICU, urban or rural status, and teaching hospital status.

Classification of Race/Ethnicity—Infants' racial and ethnic background is based on maternal race. The CPQCC race classification scheme (1) includes non-Hispanic white, Non-Hispanic black, and Hispanic; (2) combines Asian and Pacific Islander (API) groups; and (3) for this analysis, we collapsed the American Indian or Alaskan Native into an "other" category. Henceforth, we labeled these groups as white (non-Hispanic), black (non-Hispanic), Hispanic, API, and other. More information on the classification of race/ethnicity can be found in the Supplementary Information.

Analyses

For objective 1, risk factors for HAI were investigated using a multivariable mixed effect logistic regression model with NICU included as a random effect to account for hospital level clustering. An intercept-only model was first run to determine the extent of variation at the hospital level. To select a parsimonious model and prevent over-fitting, variables included in the final risk-adjusted model were selected using a Least Absolute Shrinkage and Selection Operator²⁹ (LASSO) penalized logistic regression model (package glmnet, R software).³⁰ Factors known to be associated with HAI—including birth year, SGA, race, outborn, gestational age, 5-minute Apgar Score, AAP level, and NICU volume—were forced in the model. Birth year was added to account for time varying changes in care practices. The penalization factor lambda was chosen to maximize the area under the curve of the final model. Type 3 tests were used to determine overall association of categorical covariates. Remaining variance at the hospital level after adjustment for covariates was quantified.

For the second objective, we calculated the standardized incidence ratio (SIR), and a standardized risk-adjusted infection rate for each NICU with more than 20 infants over 5 years. That adjusted rate is the ratio of observed versus expected infection rates (SIR) multiplied by the observed population mean rate. The expected infection rates were calculated from the multivariable logistic regression from above, excluding race/ethnicity. This allowed for a direct comparison between unadjusted and adjusted infection rates. Confidence intervals (CIs) for adjusted rates were calculated using the Mid-P exact method.³¹ The effects of race/ethnicity on hospital level variation were compared by examining Spearman's correlations between each NICU's overall-adjusted HAI rate and the proportion of minorities served in each NICU. Differences among adjusted infection rates in minorities versus whites were compared with each NICU's proportion of minority infants using Pearson's correlations. We divided hospitals into low, medium, and high, based on the tertile distribution of adjusted risk for HAI. Differences in SIRs and adjusted risk between tertiles were compared with analysis of variance tests. We tested differences in racial/ethnic distributions of infants across hospitals using the Kolmogorov–Smirnov's test. Sensitivity analyses were performed using infections coded as they occurred, instead of the algorithm mentioned earlier. Correlations between estimates using both attribution algorithms were more than 99.6%.

All statistical analyses were conducted with SAS Software (Version 9.4; SAS Institute, Cary, NC), and R (Version 3.2.2; R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was determined by two-tailed tests ($p < 0.05$). This study was approved by the Stanford University Institutional Review Board.

Results

Patient Characteristics

From 2011 to 2015, 26,459 eligible infants across 135 NICUs were included in the CPQCC data registry. Supplementary Fig. S1 (available in the online version) displays the cohort selection. Table 1 shows the characteristics of the 20,692 VLBW infants (21,542 admissions) who were included in this analysis. The overall infection rate across all hospital admissions between 2011 and 2015 was 8.1% (1,739 cases of infection among 21,542 admissions). Of note, 37% were $<1,000$ g at birth, 64% were less than 30 weeks' gestational age at birth, 51% were male, 23% were SGA at birth, and 11% were outborn.

Objective 1: Risk Factors for Infection

We identified candidate variables as risk factors for HAI. Table 2 shows the final multivariable mixed model for prediction of HAI at the infant level. After adjustment and inclusion of NICU as a random effect, more recent birth year was associated with a slight decrease in risk, with an adjusted odds ratio (OR) (95% CI) of 0.95 (0.92–0.99), while every week increase in gestational age was associated with a nearly 70% decrease in odds for infection (OR [95% CI]: 0.31 [0.28–0.34]). SGA status conveyed a 28% increase in odds for infection (OR [95% CI]: 1.28 [1.06–1.54]). Each one-point increase in 5-minute Apgar score was associated with a slight decrease in odds of infection (OR [95% CI]: 0.94 [0.91–0.96]). Although race/ethnicity overall was not significant ($p = 0.09$), an examination of each individual race/ethnicity showed an increased odds for HAI in Hispanic versus white infants (OR [95% CI]: 1.23 [1.06–1.41]).

Overall model prediction accuracy showed an area under the receiver operating characteristic curve of 0.79 (95% CI: 0.78–0.80). The proportion of variance in probability of HAI in infants that could be explained by NICUs was 10.3% (as calculated by the intraclass correlation coefficient), suggesting that the majority of the variance in an infant's probability of HAI can be attributed to factors other than the NICUs themselves.

Objective 2: The Role of Race/Ethnicity

Unadjusted rates of infections across the 135 NICUs ranged from 0 to 23.5% and changed only minimally with multilevel adjustment (range: 0–24.6%, mean change of 2.9%, $p = 0.91$ [Fig. 1]).

To understand the role of race/ethnicity in hospital level variation of infection rates, we compared the correlation between percentages of minorities served in each NICU to the overall risk-adjusted infection rate in each NICU. There was no significant correlation between percentage of black ($r = 0.15$, $p = 0.34$), Hispanic ($r = -0.02$, $p = 0.85$) and API

infants ($r = -0.12$, $p = 0.39$) served in each NICU and overall-adjusted infection rates in each NICU.

Differences in adjusted infection rates between each minority and white infants did not change according to the percentages of minorities served in each NICU ($r = 0.78$, 0.49 , and 0.09 for black, Hispanic and API infants; Supplementary Fig. S2A–C [available in the online version]). However, among NICUs with >10 infants of each race/ethnicity, Hispanic infants had higher adjusted infection rates than white infants in 59 NICUs, compared with just 31 NICUs in which white infants had higher infection rates than Hispanic infants ($p < 0.001$).

The adjusted infection risk was significantly different for infants receiving care in low, medium, and high infection NICUs ($p < 0.001$; Table 3). Differences in adjusted infection rates between each minority and white infants are shown within low, medium, and high infection tertiles (Fig. 2A–C). Within each tertile, Hispanic infants tended to have slightly higher rates of infection than whites (Table 3), although differences between minority and white infants within tertiles were not significant. Moreover, infants among hospitals with high infection had similarly high rates of infection across all races and ethnicities. Hispanic infants were more likely to receive care in NICUs with either high- or low-adjusted infection rates ($p = 0.01$). Black infants were more likely to receive care in NICUs with higher overall-adjusted infection rates ($p < 0.001$) and higher mortality rates (17 vs. 13%, $p < 0.001$). API infants were more likely to receive care in NICUs with low-adjusted infection rates ($p < 0.001$) (Table 3).

Discussion

This article used a multilevel population-based approach to examine HAI in VLBW infants. This study had several main findings. First, using the agnostic LASSO approach to variable selection, we constructed a model that was reasonably accurate in predicting the occurrence of HAI at the infant level. After inclusion and adjustment for various factors, birth year, gestational age, SGA, and 5-minute Apgar score were significant independent risk factors for HAI, similar to results from previous studies of risk factors for HAI in VLBW infants.^{1–3,5,10} At the infant level, Hispanic infants had significantly higher odds of HAI, compared with white infants.

We found significant variation in infection rates across NICUs in the network. Even after adjustment for previously known risk factors and taking into account clustering within NICUs, significant variation in rates remained between NICUs, with little difference between unadjusted and adjusted rates, suggesting that quality of care differs across NICUs. Variations in infection rates have been previously reported,^{32,33} and our results show that infections persist as a significant clinical problem despite widespread collaborative and individual NICU efforts to curb them.

The second objective of this study was to examine the role of race/ethnicity on HAI. At the infant level, Hispanic infants had higher odds of HAI, compared with white infants. At the hospital level, important themes emerged from our data. Similar to other studies that attributed a large proportion of racial/ethnic disparity to black infants receiving care at

challenged hospitals,^{21,34} we found that Hispanics and blacks were significantly more likely to receive care in a high HAI tertile NICU. Within NICUs, however, we found no differences in HAI rates between racial and ethnic groups. The reasons for increased infection rates in NICUs that serve vulnerable populations are not well understood but may include limited hospital resources such as equipment and staffing and less access to family-centered care, where families are included as equal partners in the care of their infant.^{5,23,24,35} Other care processes such as handwashing and infection control protocols, invasive procedures, or skin break and line entry procedures may differ across NICUs. In addition, culture measures such as teamwork and safety climate and other important environmental measures such as burnout, adequate nurse staffing, and patient crowding have been linked to risk for HAI and quality of care in the NICU, but are not currently routinely captured in this clinical database.^{11,32,36–38}

While Hispanics disproportionately received care in challenged hospitals, they also had higher adjusted infection rates than white infants in 59 NICUs, compared with just 31 NICUs in which white infants had higher infection rates than Hispanic infants ($p < 0.001$). In prior work, we demonstrated how language barriers may account for differences in family-centered care across hospitals.²⁴ Language barriers, cultural barriers, and racially biased judgment of families can lead to a family being less involved with the infant's care team, or to difficulty relaying feelings or requests, leading to less communication, which may cause processes of care to suffer (i.e., lower rates of breast milk feeding, less skin-to-skin care). In addition, certain circumstances such as transportation, employment, or access may reduce families' ability to care and advocate for their infants.

It is important to note that among hospitals with high rates for HAI, infants across all races and ethnicities had similarly high rates of HAI. Although Hispanic infants were more susceptible to infection overall, race/ethnicity was not a major driver of variations in HAI rates at the NICU level. Understanding the major drivers of variation across NICUs is crucial, and may inform future solutions that reduce HAI among VLBW infants of all races/ethnicities.

Our findings add to the literature documenting that black infants are more likely to receive care in lower quality NICUs (based on higher mortality^{21,34,39} and morbidity^{23,40}) and that NICUs with higher proportions of black infants often exhibit lower quality measures (based on lower breast milk at discharge,^{41,42} inadequate nurse staffing,⁴³ and higher rates of infection⁴²).

One key solution to this health inequity is the referral of high-risk births to hospitals with the best outcomes³³ such that black and Hispanic infants would be cared for in the highest quality NICUs. This holds promise since Profit et al found that black infants do much better when cared for in a higher quality NICU than their counterparts in lower quality NICUs.²² In addition, policy and improvement efforts to improve quality at challenged hospitals will also be crucial to reducing racial disparities in infection and overall variation in HAI rates across NICUs. Some have suggested that black infants are likely born in lower quality NICUs because of geographic and insurance barriers.⁴⁴ We would also add that the

inaccessibility of NICU quality information to the public creates a barrier to health equity. More research is needed to understand and intervene on these barriers.

This study has to be viewed in light of its design. As an observational study, our results may be influenced by unobserved confounding variables. We were unable to perform a formal competing risk analysis, as we did not have detailed time to event data for death or other morbidities. The incidence of infant death among infants with HAI was 13 versus 4% among infants without HAI. However, the direction of the bias is likely favoring white infants, given traditionally higher mortality rates among minorities.²²

In addition, we did not account for important social and neighborhood factors such as socioeconomic status, education, built environment, or social/neighborhood racial segregation patterns that may contribute to receiving care in lower quality hospitals, access to care, or differences in family-centered care. Moreover, recording of maternal race ethnicity, although based on maternal report, may suffer from misclassification. Also, larger populations often lump together heterogeneous groups, potentially obscuring effects on vulnerable populations. Moreover, the relatively small number of non-Hispanic black infants may have limited our power to detect a significant difference. Although generalization to other settings should be context specific, a major strength of our study is that it is population based in the country's most populous state, incorporating a wide range of urban and rural settings, varying types of NICUs, and a large Hispanic population.

In conclusion, we found persistent significant variation in HAI rates across NICUs in our network. Hispanic infants had significantly higher HAI rates than whites. Black infants were more likely to receive care in high HAI rate NICUs. Future policy and improvement efforts should focus on supporting challenged hospitals. Supplementary Information is available at JPER's Web site.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1. Difference between unadjusted and adjusted rates of infection among all neonatal intensive care units (NICUs) (2011–2015).

Fig. 2.

Differences in risk-adjusted infection rates between (A) non-Hispanic black versus non-Hispanic white infants, (B) Hispanic versus non-Hispanic white infants, and (C) Asian or Pacific Islander versus non-Hispanic white infants, according to low, medium, and high tertiles of infection.

Table 1Cohort characteristics ($N = 20,692$)

Characteristics	Overall n (%)
Birth weight (g)	
< 751	3,028 (15)
751–1,000	4,464 (22)
1,001–1,250	5,331 (26)
1,251–1,500	7,291 (35)
> 1,500	578 (3)
Gestational age (wk)	
27	7,449 (36)
28–29	5,852 (28)
30	7,400 (36)
Sex	
Female	10,112 (49)
Male	10,580 (51)
Multiple gestations	
No	15,168 (73)
Yes	5,506 (27)
Cesarean delivery	
No	5,363 (26)
Yes	15,325 (74)
Small for gestational age	
No	15,886 (77)
Yes	4,806 (23)
Maternal age (y)	
<20	1,377 (7)
20–29	8,304 (40)
30–39	9,556 (46)
>39	1,455 (7)
5-min Apgar score	
0–3	870 (4)
4–6	3,169 (15)
7–10	16,530 (80)
Outborn	
No	18,507 (89)
Yes	2,185 (11)
Bacterial pathogen	
None	19,595 (95)
GBS	98 (1)

Characteristics	Overall <i>n</i> (%)
<i>E. coli</i>	168 (1)
Other	831 (4)
Coagulase-negative staphylococci	
No	19,898 (96)
Yes	792 (4)
Fungal	
No	20,559 (99)
Yes	133 (1)

Table 2

Risk factors for late HAI in infants

Fixed effect ^a	Univariable odds ratio (95% CI)	p-Value for univariable analyses	Multivariable odds ratio (95% CI)	p-Value for multivariable analyses
Birth year (2011–2015)	0.96 (0.92–0.99)	0.01	0.95 (0.92–0.99)	0.01
Gestational age (weeks)	0.69 (0.68–0.71)	<0.001	0.31 (0.28–0.34)	<0.001
Small for gestational age (yes vs. no)	0.39 (0.34–0.46)	<0.001	1.28 (1.06–1.54)	0.01
5-min Apgar score	0.81 (0.79–0.83)	<0.001	0.94 (0.91–0.96)	<0.001
Outborn (yes vs. no)	1.32 (1.12–1.55)	0.001	1.06 (0.89–1.27)	0.54
Sex (male vs. female)	1.17 (1.06–1.29)	0.002	1.11 (0.99–1.23)	0.05
Maternal age (years)	0.99 (0.98–0.99)	0.001	0.99 (0.98–1.00)	0.22
Preterm premature ROM (yes vs. no)	1.07 (0.96–1.20)	0.24	0.90 (0.80–1.02)	0.10
Fetal distress	1.00 (0.89–1.13)	0.99	1.07 (0.94–1.22)	0.29
Malpresentation/breech	1.31 (1.17–1.46)	<0.001	1.07 (0.95–1.21)	0.24
Obstetrical: bleeding/abruption/previa	1.34 (1.19–1.52)	<0.001	1.06 (0.93–1.21)	0.36
Race/ethnicity				0.09 ^b
Non-Hispanic black (vs. white)	1.12 (0.93–1.36)	0.02	1.12 (0.93–1.35)	0.22
Hispanic (vs. white)	1.39 (1.22–1.59)	0.16	1.23 (1.06–1.41)	0.01
Asian or Pacific Islander (vs. white)	1.25 (1.04–1.49)	0.34	1.11 (0.90–1.35)	0.33
Other (vs. white)	1.03 (0.74–1.43)	0.27	1.09 (0.78–1.52)	0.63
No. of NICU beds	1.01 (1.11–1.02)	0.005	1.01 (0.99–1.02)	0.13
NICU volume (square root)	1.05 (0.98–1.13)	0.09	0.97 (0.93–1.01)	0.10
AAP level				0.79 ^b
3 vs. 2	2.30 (1.25–4.24)	0.008	0.81 (0.42–1.57)	0.53
4 vs. 2	3.03 (1.56–5.87)	0.001	0.69 (0.32–1.53)	0.37
Neonatologist coverage (at hospital vs. at home)	1.15 (0.87–1.52)	0.32	1.10 (0.81–1.49)	0.56
Teaching hospital (yes vs. no)	1.34 (0.98–1.84)	0.06	1.17 (0.81–1.69)	0.39

Abbreviations: CI, confidence interval; HAI, health care–associated infection; NICU, neonatal intensive care unit; ROM, rupture of membrane. Note: NICU variance for intercept only model: 0.427. NICU variance for full model: 0.377; intraclass correlation: 10.29.

^aFrom LASSO multivariable model.

b *p*-Value from type-3 test for overall significance.

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Table 3

Adjusted rates of infection and infant distribution by race/ethnicity among hospitals with low, medium, and high infection rates

Race/ethnicity	Low infection rate hospitals			Medium infection rate hospitals			High infection rate hospitals		
	No. of infants (%)	SIR	Adjusted rate (95% CI)	No. of infants (%)	SIR	Adjusted rate (95% CI)	No. of infants (%)	SIR	Adjusted rate (95% CI)
Non-Hispanic White	1,422 (25.1)	0.35	2.86 (1.93–4.07)	2,533 (44.7)	0.92	7.42 (6.32–8.67)	1,709 (30.2)	1.53	12.33 (10.63–14.25)
Hispanic ^a	2,675 (27.8)	0.53	4.28 (3.50–5.18)	3,926 (40.8)	1.06	8.60 (7.72–9.56)	3,016 (31.4)	1.78	14.33 (13.03–15.75)
Non-Hispanic Black ^a	740 (25.9)	0.37	3.03 (1.89–4.59)	978 (34.3)	0.81	6.56 (5.03–8.42)	1,135 (39.8)	1.82	14.75 (12.64–17.09)
Asian/Pacific Islander ^a	905 (33.1)	0.43	3.45 (2.22–5.14)	1,211 (44.3)	0.97	7.87 (6.22–9.88)	618 (22.6)	1.95	15.73 (12.66–19.32)

Abbreviations: CI, confidence interval; SIR, standardized incidence ratio (calculated as ratio of observed to expected cases).

^aKolmogorov–Smirnov’s test for equal distribution of infants across low, medium, high infection rate hospitals: Hispanic versus white, $p = 0.01$; non-Hispanic black versus white, $p < 0.001$.