Risk of Feeding Problems Among Infants With Neonatal Abstinence Syndrome

A Retrospective Cohort Study

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ABSTRACT

Background: The rate of infants born with neonatal abstinence syndrome (NAS) increased by more than 500% between 2004 and 2016. Although feeding problems among infants diagnosed with NAS have been documented, the risk of feeding problems among infants diagnosed with NAS has not been estimated.

Purpose: This study evaluates the extent to which feeding problems among infants diagnosed with NAS differ from thise in infants without an NAS diagnosis.

Methods/Search Strategy: A matched retrospective cohort study (2008-2017) of infants diagnosed with NAS in the United States was conducted using hospital admission data from the Cerner Health Facts Database. Multivariable logistic regressions controlling for confounders were used to assess whether an NAS diagnosis is associated with hospital admission due to feeding problems.

Findings/Results: Infants with NAS were nearly 3 times as likely (OR = 2.81; 95% CI, 2.68-2.95) to have feeding problems compared with infants without NAS after adjusting for infant and hospital characteristics. Lower birth weight, higher infant age, Hispanic ethnicity, and hospital location in the Midwest region were also associated with higher odds of feeding problems. Infants diagnosed with NAS who had feeding problems had slightly lower odds of being offered lactation services than infants without NAS who had feeding problems.

Implications for Practice: These findings suggest the need for targeted feeding interventions.

Implications for Research: Future research on infants with NAS may build on these findings by assessing the role of maternal factors such as nutrition and substance use to understand how parental characteristics also influence the risk for hospitalization.

Key Words: Cerner Health Facts, feeding problems, neonatal abstinence syndrome, substance use

BACKGROUND AND SIGNIFICANCE

Neonatal Abstinence Syndrome

Neonatal abstinence syndrome (NAS) refers to a complex withdrawal disorder prevalent in newborns who were exposed to opioids in utero.[1] Researchers estimate that NAS affects roughly 48% to 94% of exposed infants.[2] NAS is characterized by a series of conditions that stem from central nervous system and gastrointestinal (GI) disorders. The clinical manifestations of NAS typically begin within the first week of birth, and symptoms may range from poor feeding, jitteriness, high-pitched crying, diaphoresis, and diarrhea.[3-5] In addition, opioid-exposed infants may be at an increased risk for adverse outcomes such as hospital readmission.[6,7]

Over the past 2 decades, the incidence of NAS has increased considerably, in conjunction with the rise of opioid use during pregnancy.[4,8,9] For instance, data from the Centers for Disease Control and Prevention (CDC) showed that from 1999 to 2014, opioid use disorder reported among pregnant women at delivery increased more than 4-fold, from 1.5 per 1000 delivery hospitalizations to 6.5 per 1000 delivery hospitalizations.[10] Similarly, evidence from a representative sample across the United States indicates that NAS incidence increased from 1.6 per 1000 in-hospital births in 2004 to 8.8 per 1000 births in 2016, with the rates plateauing between 2014 and 2016 while remaining high.[11]

Research indicates the association between increasing NAS incidence and both high prescribing of opioids for pain management among pregnant women and increases in illicit use of heroin and prescription opioids such as oxycodone.[12-15] The

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expansion of opioid agonist treatment (ie, methadone and buprenorphine) for people with opioid use disorders has been blamed for increasing rates of NAS as well[16]; however, patient-level studies indicate these medications may reduce the risk for NAS when compared with continued illicit opioid use.[17] Similarly, ecological studies show that limited access to medications for opioid use disorders is associated with a higher NAS incidence.[18,19]

Hospital costs due to NAS have also increased in tandem with rising incidence; between 2004 and 2014, total hospital costs for births of infants diagnosed with NAS covered by Medicaid increased from $65.4 million to $462 million. In 2016, the total hospital costs for infants with NAS reached 572.7 million.[20] Likewise, the proportion of neonatal hospital costs due to NAS increased from 1.6% in 2004 to 6.7% in 2014 among Medicaid-covered births.[2] Researchers examining length of hospital stays and associated costs found that infants diagnosed with NAS spent almost 3.5 times as long in the hospital as infants without an NAS diagnosis. Consequently, the cost associated with hospital stays for infants with NAS was 3 times that of infants without NAS.[21]

Geographic and socioeconomic inequities pattern the incidence of NAS.[22-24] Data from the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project (HCUP) show the rate of NAS in rural areas of the United States was almost twice the rate of NAS in metropolitan areas between 2004 and 2013. These rural infants and mothers with opioid-related conditions are also more likely to be from lower-income families and have public insurance.[23] Higher rates of NAS are also associated with higher county-level unemployment, especially in rural regions, and with counties designated as mental health shortage areas.[19] Recent research found infants born to parents living in areas with low education and income, poor housing, high unemployment, and poor access to transportation, as measured by the Area Deprivation Index, experienced significantly longer hospital stays for NAS after controlling for pharmacologic treatment, infant custody, race, and gestational age.[25]

Feeding Problems Among Infants With NAS

Feeding problems in infants refer to a diminished oral intake of food that is not age-appropriate and often associated with a wide spectrum of underlying medical, nutritional, feeding skill, or psychosocial impairments. These underlying factors may include structural anomalies of the GI tract, neurodevelopmental delays leading to poor feeding skills, malnutrition, and distracting feeding environments.[26]

Although widely acknowledged that feeding difficulties are persistent in infants diagnosed with NAS,[27-29] the extent to which such problems affect infants born with NAS differently than such problems do to other infants remains unclear. Feeding problems observed in opioid-exposed infants comprise swallowing issues, sucking difficulties, and inefficient feeding episodes.[27,28] For instance, in demonstrating feeding challenges among infants with NAS, researchers found that infants with NAS had an immature pattern of swallow–breath interaction compared with non–drug-exposed infants.[30] Feeding difficulties in infants have been linked to increased length of hospital stays[31] and poor neurodevelopmental outcomes such as cognitive, motor, and communicative delays.[32,33]

While some research reports feeding problems among opioid-exposed infants, extant studies are limited by small sample sizes and lack of empirical evidence to characterize the overall risk of feeding problems among infants diagnosed with NAS. The purpose of this study was to use an extensive national US database to quantitatively assess the relationship between the risk for infant hospitalization due to feeding problems and NAS diagnosis while controlling for relevant sociodemographic and clinical factors to understand whether particular demographic groups face inequities in this relationship.

What This Study Adds

- Infants with NAS were nearly 3 times as likely to have feeding problems compared with infants without NAS after adjusting for infant and hospital characteristics.
- NAS diagnosed infants who had feeding problems had slightly lower odds of being offered lactation services than infants without NAS who had feeding problems.
- Lower-income families and families with Medicaid may be using other safety-net resources for parents that reduce their odds of severe feeding problems requiring hospitalization.

METHODS

Data Source

A retrospective cohort study of infants diagnosed with NAS was conducted using hospital admission data from the Cerner Health Facts Database. Health Facts is a HIPAA-compliant database that contains clinical records from more than 600 participating hospitals and health facilities across the United States. Records captured in this database include hospital procedures, diagnostic information, demographics, admission and discharge data, drug prescription, and laboratory tests. At the time of writing, Health Facts contained clinical data from more than 68 million unique patients.

The study cohort consisted of all infants in the database born from 2008 to 2017 with an NAS diagnosis within 28 days of birth. This study was reviewed by the University of New Mexico Health

Sciences (UNM-HSC) Institutional Review Board (IRB) (aka Human Research Review Committee) and was determined to be exempt from IRB review (IRB#: 16-338).

Measures

The following *International Classification of Disease, Ninth Revision* (*ICD-9*)/*Tenth Revision* (*ICD-10*) codes were used to identify infants with NAS (ie, primary exposure): *ICD-9* 779.5 (drug withdrawal syndrome in newborn), *ICD-9* 760.72 (narcotics affecting fetus or newborn via placenta or breast milk), *ICD-10* P96.1 (neonatal drug withdrawal syndrome from maternal use of drugs of addiction), *ICD-10* P96.2 (withdrawal symptoms from therapeutic use of drugs in newborn), and *ICD-10* P04.49 (newborn [suspected to be] affected by maternal use of other drugs of addiction). These diagnosis codes are used by US states to identify NAS in infants.[34] Each infant patient with NAS was matched using a "greedy matching" approach with 4 nonexposures by infant race/ethnicity, sex, age of diagnosis within 28 days of birth, hospital rural status, insurance, hospital region, and birth weight. A total of 81,790 patients were included in the final analysis.

The primary outcome was hospital admissions due to feeding problems. This was chosen because hospital admission for feeding problems implies health services utilization that has implications on healthcare costs. Feeding problems included gastroesophageal reflux, vomiting in newborns, anomalies of the larynx, and/or GI motility disorders. The conditions were identified using specified *ICD-9*/*ICD-10* codes as shown in Supplemental Digital Content Table A (available at: http://links.lww.com/ANC/A91) and were selected to be inclusive of our definition of feeding problems.[26] Patients who received at least one of these codes during a hospital admission encounter were classified as having feeding problems. The data extracted included all hospital admissions due to feeding problems including initial birth admissions and subsequent admissions due to feeding problems. Patients were excluded if they had missing values for the outcome variable. Additional explanatory variables included infant age (in days), birth weight, sex, race/ethnicity, insurance status, hospital admission diagnosis, hospital urban or rural status, and the US census region where the hospital is located.

Statistical Analysis

Greedy Matching

The SAS 9.4 statistical package (SAS Institute, Inc, Cary, North Carolina) was used to perform all analyses in this study. Each infant with NAS (ie, the primary exposure) was matched, using greedy matching with 4 nonexposed controls by infant race/ethnicity (African American, Asian/Pacific Islander, white, Hispanic, Native American, other race, and missing), sex, age of diagnosis within 28 days of birth, hospital rural status, insurance (Medicaid, private or commercial insurance, uninsured or self-pay, other, and missing), region (Northeast, Midwest, South, and West), and birth weight. Greedy matching is a type of nearest neighbor matching algorithm.[35] In this approach, we first sorted the exposed subjects (ie, patients with NAS) by their estimated propensity score and then sequentially matched each exposed subject with 4 nonexposed subjects (ie, patients without NAS) who had either the closest or an exact propensity score match. Propensity score matching technique is sequential in nature and continues until all subjects in the nonexposed group are assigned or matches are exhausted. Furthermore, since matches are obtained without consideration of whether subjects in the nonexposed group could be matched to a more suitable subject in the exposed group, the approach is termed greedy.[36] We used this type of matching for being straightforward, computationally fast, not invariant to initial order, and able to minimize the propensity score difference between those who are matched. Furthermore, greedy matching provides greater rigor to our findings of being superior in terms of bias reduction compared with other matching methods.[56] In this greedy matching scheme, we gave more weight for age and sex because of their role as the main demographic variables defining our cohort. Furthermore, lower age and male sex are known to influence feeding problems.[28,37,38] To ensure a valid match for birth weight, we allowed a possible absolute difference of 1 kg. This difference was incremented in subsequent runs of the matching by an increment of 0.5 kilogram. The greedy matching algorithm was successful in producing matched samples with balanced characteristics across the NAS group and the patients without NAS group, as shown in Table 1. In particular, the *P* values for sex, race/ethnicity, insurance, and age were 1, 1, 1, and .5958, respectively. In addition, for the matching variables where the *P* value was significant (birth weight, hospital urban–rural status, and hospital region), the effect size was significantly small ($<.1$), demonstrating acceptable balance.

Descriptive Analysis

The frequency and relative frequency of the outcome variable and the explanatory variables were stratified by patient NAS status. Sociodemographic and clinical data were extracted for infants with NAS and infants without NAS. The summary of the study cohort is provided in Table 1. The 2 groups, infants with and without NAS, were compared using chi-square tests to assess their balance with respect to

TABLE 1. Demographic Characteristics of the Study Population

Cofactors	Infants Without NAS (n = 65,432) n	%[a]	Infants With NAS (n = 16,358) n	%[a]	*P* Value for Chi-Square	Cohen's *h* Effect Size
Feeding problems						
Infants **without** Feeding problems	59,534	90.99	12,887	78.78	<.0001	0.348
Infants **with** Feeding problems	5,898	9.01	3,471	21.22		−0.348
Sex						
Female	31,076	47.49	7,769	47.49	1.0000	0.000
Male	34,356	52.51	8,589	52.51		0.000
Race/ethnicity						
African American	8,128	12.42	2,031	12.42	1.0000	0.000
Asian/Pacific Islander	252	0.39	65	0.40		0.002
White	47,610	72.76	11,901	72.75		0.000
Hispanic	488	0.75	124	0.76		0.001
Native American	2,090	3.19	522	3.19		0.000
Other race	3,433	5.25	858	5.25		0.000
Missing	3,431	5.24	857	5.24		0.000
Birth weight, kg						
<2.5	7,135	10.90	2,202	13.46	<.0001	0.078
2.5-3.9	29,524	45.12	7,023	42.93		0.044
4.0-5.9	1,171	1.79	238	1.45		0.027
Missing	27,602	42.18	6,895	42.15		0.001
Health insurance status						
Medicaid	39,824	60.86	9,956	60.86	1.0000	0.000
Private or commercial insurance	8,612	13.16	2,153	13.16		0.000
Uninsured or self-pay or other	6,464	9.88	1,616	9.88		0.000
Missing	10,532	16.10	2,633	16.10		0.000
Hospital urban–rural status						
Urban	59,994	91.69	15,159	92.67	<.0001	0.037
Rural	5,438	8.31	1,199	7.33		0.037
Hospital US census region						
Northwest	13,735	20.99	4,004	24.48	<.0001	0.083
Midwest	14,816	22.64	3,348	20.47		0.053
South	24,902	38.06	6,096	37.27		0.016
West	11,979	18.31	2,910	17.79		0.014
Covariates	**n**	**Mean**	**n**	**Mean**	***P***	
Infant age, d	65,432	0.6881	16,358	0.7025	.5958	

Abbreviation: NAS, neonatal abstinence syndrome.
[a]*Column percent.*

the explanatory variables. In addition, Cohen's h effect size measure was calculated for every category of the primary outcome and explanatory variables. Cohen's h was calculated using the equation $h = |\Phi_1 - \Phi_2|$ such that $\Phi_i = 2 \arcsin \sqrt{p_i}$ and p_i is the sample proportion of each category in all of the explanatory variables or primary outcome. The effect size is interpreted as small (where $h = 0.20$), medium (where $h = 0.50$), and large (where $h = 0.80$). In this study, Cohen's h of 0.30 or more is considered to be relevant.

Simple and Multivariable Analysis

Simple logistic regression was performed to determine unadjusted odds of hospitalization for feeding problems and corresponding confidence intervals (CIs) in infants diagnosed with NAS and for the other explanatory variables (Table 2). Multivariable logistic regression models were then utilized to assess whether the association between feeding problems and NAS persists after adjusting for potential confounders and patient characteristics. In the multivariable analysis, the initial model included the primary outcome of

TABLE 2. Crude Odds Ratios and Adjusted Odds Ratios

Independent Variables	No Feeding Problems (n = 9,369), n (%[a])	Feeding Problems (n = 72,421), n (%[a])	Unadjusted OR	95% CI	Adjusted OR[b]	95% CI
NAS status						
Infants **without** NAS	59,534 (91.0)	5,898 (9.0)	*Ref*	*Ref*	*Ref*	*Ref*
Infants **with** NAS	12,887 (78.8)	3,471 (21.2)	2.72	2.60-2.85	**2.81**	**2.68-2.95**[c]
Sex						
Female	34,502 (88.8)	4,343 (11.18)	0.95	0.91-0.99	**0.92**	**0.88-0.96**[c]
Male	37,919 (88.3)	5,026 (11.70)	*Ref*	*Ref*	*Ref*	*Ref*
Race/ethnicity						
African American	8,803 (86.6)	1,356 (13.4)	1.28	1.20-1.36	1.06	0.99-1.13
Asian/Pacific Islander	2,768 (87.1)	41 (12.9)	1.23	0.89-1.71	1.21	0.86-1.71
White	53,108 (89.2)	6,403 (10.8)	*Ref*	*Ref*	*Ref*	*Ref*
Hispanic	532 (86.9)	80 (13.1)	1.25	0.99-1.58	1.18	0.92-1.51
Native American	2,210 (84.6)	402 (15.4)	1.51	1.35-1.68	**1.46**	**1.29-1.65**[c]
Other race	3,738 (87.1)	553 (12.0)	1.23	1.12-1.34	1.00	0.90-1.10
Missing	3,754 (87.6)	534 (12.5)	1.18	1.07-1.30	1.06	0.96-1.17
Birth weight, kg						
<2.5	6,746 (72.3)	2,591 (27.8)	*Ref*	*Ref*	*Ref*	*Ref*
2.5-3.9	32,747 (89.6)	3,800 (10.4)	0.30	0.29-0.32	**0.30**	**0.28-0.32**[c]
4.0-5.9	1,258 (89.3)	151 (10.7)	0.31	0.26-0.37	**0.31**	**0.26-0.37**[c]
Missing	31,670 (91.8)	2,827 (8.2)	0.23	2.22-0.23	**0.20**	**0.19-0.22**[c]
Health insurance status						
Medicaid	44,245 (88.9)	5,535 (11.1)	0.83	0.78-0.89	**0.77**	**0.72-0.82**[c]
Private or commercial insurance	9,360 (87.0)	1,405 (13.1)	*Ref*	*Ref*	*Ref*	*Ref*
Uninsured or self-pay	3,580 (87.1)	530 (12.9)	0.98	0.89-1.10	0.90	0.81-1.01
Other	3366 (84.8)	604 (15.2)	1.20	1.08-1.33	1.05	0.94-1.17
Missing	11,870 (90.2)	1,295 (9.8)	0.73	0.67-0.79	0.70	0.64-0.76
Hospital urban–rural status						
Urban	66,430 (88.4)	8,723 (11.6)	1.22	1.12-1.33	**1.59**	**1.45-1.74**[c]
Rural	5,991 (90.27)	646 (9.7)	*Ref*	*Ref*	*Ref*	*Ref*
Hospital US census region						
Northwest	16,008 (90.2)	1,731 (9.8)	0.71	0.67-0.76	**0.62**	**0.58-0.67**[c]
Midwest	15,584 (85.8)	2,580 (14.2)	1.09	1.02-1.16	**1.18**	**1.10-1.27**[c]
South	27,902 (90.0)	3,096 (10.0)	0.73	0.69-0.78	**0.65**	**0.61-0.70**[c]
West	12,927 (86.8)	1,962 (13.2)	*Ref*	*Ref*	*Ref*	*Ref*
Cofactors	**N (Mean)**	**N (Mean)**				
Infant age, d	72,421 (0.6334)	9,369 (1.1362)	1.04	1.04 -1.05	**1.05**	**1.05-1.06**[c]

Abbreviations: CI, confidence interval; NAS, neonatal abstinence syndrome; OR, odds ratio.
Bold values indicate statistically significant odds ratios.
[a]*Row percent.*
[b]*Odds ratio adjusted for sex, race/ethnicity, hospital urban–rural status, health insurance status, US hospital region, age, and birth weight.*
[c]*Indicates statistically significant OR, 95% CIs do not contain 1.*

feeding problems, the primary exposure of NAS status, and controlled for sex, race/ethnicity, birth weight, health insurance, age, hospital rurality, and hospital region. Infant feeding method and exact gestational age variables were not available in our data source; therefore, they were not included as confounders. A second model excluded birth weight from the model because it is possible that if NAS affects birth weight, the inclusion of this variable in the model will mask the effects of NAS. The initial model showed a better fit and is presented in the final results (Table 2). An additional point of interest was to determine whether health delivery response differed between infants with NAS and infants without NAS. Therefore, we performed an additional simple logistic regression to determine the odds of being offered lactation services for infants with feeding problems and infants without feeding problems stratified by NAS status (Table 3).

TABLE 3. Lactation Services Offered Among Infants Among the Study Population Stratified by NAS Status and Feeding Problems Status

Feeding Problems Status	Not Offered Lactation Services, n (%[a])	Offered Lactation Services, n (%)	Unadjusted OR (95% CI)
Infants without NAS			
No feeding problems	58,774 (98.72)	760 (1.28)	*ref*
Feeding problems	5,593 (94.83)	305 (5.17)	**4.22 (3.68-4.83)**[b]
Infants with NAS			
No feeding problems	12,633 (98.03)	254 (1.97)	*Ref*
Feeding problems	3,270 (94.21)	201 (5.79)	**3.06 (2.53-3.69)**[b]

Abbreviations: CI, confidence interval; NAS, neonatal abstinence syndrome; OR, odds ratio.
Bold values indicate statistically significant odds ratios.
[a]*Row percent.*
[b]*Indicates statistically significant OR, 95% CIs do not contain 1.*

We used the following *Current Procedural Terminology* (*CPT*) codes to case identify infants who were offered lactation services: S9443, 99341, 99342, 99343, 99344, 93347, 93348, 93349, 93350, 99201, 99202, 99203, 99204, 99212, 99213, 99214, 99243, 99244, 99245, 99401, 99402, 99403, 99404, and 98960. A chi-squared test with Bonferroni adjustment was used to test whether infants with and without NAS have similar distributions of *ICD-9/ICD-10* codes used to indicate feeding problems, as shown in Supplemental Digital Content Table A (available at: http://links.lww.com/ANC/A91).

RESULTS

Demographic Characteristics of Study Population

A total of 81,790 infants were grouped into 2 categories for analysis: infants with NAS (20%) and infants without NAS (80%). Table 1 shows the sample characteristics stratified by NAS status. Among infants with NAS, a total of 3471 (21.2%) infants had feeding problems; 47.5% were female, and 52.5% were male. Roughly 61% of infants with NAS were insured through Medicaid, and only 6.2% were uninsured. The large *P* values and small effect sizes in Table 1 indicate strong balance on the matching variables between the primary exposure groups.

Logistic Regression

The logistic regression results showed that infants with NAS were 181% more likely (OR = 2.81; 95% CI, 2.68-2.95) to be hospitalized for feeding problems than infants without NAS after adjusting for confounding variables (Table 2). In addition to NAS status, additional characteristics were significantly associated with higher odds of hospitalization due to feeding problems. Infants who are recorded as Hispanic (OR = 1.46; 95% CI, 1.29-1.65) and infants of older age (OR = 1.05; 95% CI, 1.05-1.06) had higher odds of feeding problems. Infants being cared for at a hospital in an urban area (OR = 1.59; 95% CI, 1.45-1.74) or at a hospital in the Midwest (OR = 1.18; 95% CI, 1.10-1.27) also exhibited increased odds of feeding problems.

Several population characteristics were found to be significantly associated with a decreased risk of feeding problems. Infants who were female (OR = 0.92; 95% CI, 0.88-0.96), Native American (OR = 0.80; 95% CI, 0.65-0.97), of higher birth weight (OR = 0.20; 95% CI, 0.19-0.22), or insured by Medicaid (OR = 0.77; 95% CI, 0.72-0.82) were all significantly less likely to have feeding problems.

The results from the additional simple logistic regression (Table 3) showed that infants without NAS who had feeding problems had a 4.22 (95% CI, 3.68-4.83) higher odds of being offered lactation services than infants who did not have feeding problems. On the contrary, infants with NAS who had feeding problems had only 3.06 (95% CI, 2.53-3.69) higher odds of being offered lactation services than infants with NAS who had no feeding problems.

Infants with NAS who had feeding problems were assigned the codes P92.9 (feeding problem of newborn unspecified), P92.8 (other feeding problems of newborn), P92.09 (other vomiting of newborn), R63.3 (feeding difficulties), P92.2 (flow feeding of newborn), and P92.6 (failure to thrive in newborn) with a significantly higher percentage (after Bonferroni adjustment) than infants without NAS who had feeding problems (see Supplemental Digital Content Table A, available at: http://links.lww.com/ANC/A91). On the contrary, infants without NAS who had feeding problems were assigned the codes 779.31 (feeding problems in newborn: regurgitation of food in newborn; slow feeding in newborn; vomiting in newborn) and P92.5 (neonatal difficulty in feeding at breast) with a significantly higher percentage (after Bonferroni adjustment) than infants with NAS who had feeding problems. (see Supplemental Digital Content Table A, available at: http://links.lww.com/ANC/A91).

DISCUSSION

This is the first nationwide US study utilizing electronic medical records to examine the risk of hospitalization due to feeding problems among infants with an NAS diagnosis. Although studies have reported feeding problems among infants with NAS,[27,37,39,40] existing studies have not quantified the risk of feeding problems in this patient population. Previous studies were limited by small sample sizes,[27,37,40] drew largely on digital recordings of infants feeding instead of electronic medical records, and used mixed methods to explore feeding patterns among infants diagnosed with NAS.[27,37,39] Such study designs are unable to provide robust empirical evidence of the relative risk of feeding problems among infants with NAS compared with other infants.

The analysis presented in this study showed that infants diagnosed with NAS were almost 3 times as likely to be hospitalized for feeding problems compared with infants without NAS after adjusting for confounding sociodemographic and clinical factors. In addition to quantifying the risk of feeding problems, we found that among infants with NAS, 21% were hospitalized for feeding problems compared with 9% of infants from the matched nonexposure group. This suggests significantly greater feeding-related hospital utilization among infants diagnosed with NAS. We performed additional subgroup analysis to compare the odds of receiving lactation services. Our findings in this regard revealed that infants diagnosed with NAS and feeding difficulty were less likely to receive lactation support services than other infants with feeding problems. This difference indicates NAS diagnosis not only increases hospitalization rates but also may negatively affect whether services are offered to infants with feeding problems. A recent review of research on feeding practices among infants diagnosed with NAS indicated that infants fed with mother's own milk have improved outcomes, including shorter length of hospital stay and less NAS treatment, which mean tailoring or expanding lactation services for infants diagnosed with NAS may significantly improve health service utilization and infant outcomes.[41]

The findings of this research using national data are consistent with a large cohort study of infants admitted to neonatal intensive care units across the nation. In this study, researchers found that approximately 22% of infants with NAS had feeding difficulties.[9] Similarly, a smaller study that utilized data from a single hospital observed feeding problems among roughly 18% of infants with NAS.[42] These numbers are comparable with our finding that roughly 21% of infants with NAS had feeding problems. While these studies provide some preliminary evidence for feeding problems in infants with NAS, experts have called for more analyses indicating which infants are at a highest risk for feeding problems in order to target feeding interventions and monitor feeding progress appropriately.[29,43] Thus, improved knowledge of the risk of feeding problems among infants with NAS provides a useful tool to communicate the relative risk of feeding problems among a vulnerable infant population. Furthermore, these findings may serve to inform researchers, clinicians, therapists, and providers in understanding the level of need for evidence-based interventions that specifically target feeding problems among infants with NAS.

Our finding that infants diagnosed with NAS who had feeding problems also had slightly lower odds of being offered lactation services, which include counseling and education, warrants further investigation in future research. Infants with NAS frequently experience disruptive feeding behaviors for which researchers have demonstrated a need for parent and caregiver education and counseling to better recognize and respond to these feeding patterns.[27] A possible explanation for this health service inequity is that parents of children with NAS may be subject to stigma toward people with substance use disorders by professionals in the health sector.[44] Stigma toward pregnant people with substance use disorders is well documented[45,46] and can affect healthcare utilization.[47,48] Therefore, health providers bear an ethical responsibility to eliminate personal biases and decrease perceived and experienced stigma toward pregnant women with substance use disorders.[49] We note, however, that the extent to which this affects parental experiences with care-seeking specifically for feeding problems and the health services offered to infants is an area that future research may explore.

While the database does not include income information, the significantly lower risk of hospitalization for feeding problems among infants insured by Medicaid may indicate infants born to lower-income parents are connected to other social safety-net services such as the Special Supplemental Nutrition Program For Women, Infants, and Children (WIC) and are receiving adequate postnatal support that contributes to avoiding hospitalization due to feeding problems. On the contrary, the significance of Medicaid insurance for reducing the risk of hospitalization due to feeding problems may indicate lower-income families struggle with postnatal healthcare access and are simply more likely to try to manage feeding problems without the assistance of healthcare professionals. This is very concerning as our analyses also demonstrate that infants with feeding problems are 2.92 times (95% CI, 2.60-3.29) more likely to suffer from dehydration (ie, *ICD-9*/*ICD-10* codes 276.51 and P74.1) and 16.44 times (95% CI, 14.90-18.14) more likely to fail to

thrive (ie, *ICD-9*/*ICD-10* codes 779.34, 783.41, P92.6, and R62.51) than infants without feeding problems. To understand this, we performed additional analyses to investigate the moderating effects of health insurance status and NAS status on risk of hospitalization due to feeding problems. We found that regardless of NAS status, infants with Medicaid were significantly less likely to be hospitalized for feeding problems than their counterparts with private insurance. Furthermore, we found that compared with infants with private insurance, only uninsured infants in the NAS group were significantly less likely to be hospitalized for feeding problems. These findings support our earlier assumption that lower-income families and families with Medicaid may be using other safety-net resources for parents that reduce their odds of severe feeding problems requiring hospitalization.

Regarding uninsured infants with NAS, high medical costs and stigma may play a role in their avoidance of hospital admission to address a feeding problem. The financial burden experienced by uninsured families for healthcare-related costs[50,51] and the stigma faced by parents who use substances present significant challenges for accessing healthcare settings.[46,52] These findings suggest that environmental and social factors may play roles in the development of feeding problems. However, given the cross-sectional nature of this study, causality between significant variables and feeding problems cannot be established.

Finally, because we relied on a wide variety of diagnostic codes to capture infants with feeding problems, an additional point of interest was to understand the range of feeding problems that occurred more frequently in infants with NAS than in infants without NAS. After accounting for multiple comparisons using Bonferroni correction, one observation is worthy of mention. We found that while 6 diagnostic codes indicative of feeding problems were assigned at significantly higher rates to infants with NAS, only 2 such codes were assigned at significantly higher rates to infants without NAS. Although this finding points to a greater variety of feeding problems occurring among infants with NAS, it may also reflect provider implicit bias.[5,53] Prior research has described implicit bias among providers in the context of race as one of the sources of racial health disparities.[54,55] Here, we note that it is likely that implicit bias among providers might lead to more frequent diagnosis of feeding problems among infants with NAS than among infants without NAS; however, additional research is needed to identify the role of provider bias in the differential diagnosis of feeding problems among infants diagnosed with NAS.

Limitations

Although the findings of this study draw on a national US database with large sample sizes, there are several limitations to these findings that should be considered. NAS diagnosis and feeding problems were based on hospital billing codes, which are subject to data entry errors and misclassification. In addition, essential confounders, such as parental characteristics (nutrition, drug use, weight, comorbidities, prenatal care utilization, etc), were not available in our data source because the database does not link infant and parent electronic medical records. Databases that link parental and infant records and/or databases that include provider notes may provide

Summary of Recommendations for Practice and Research

What we know:	• Infants with NAS were nearly 3 times as likely to have feeding problems compared with infants without NAS after adjusting for infant and hospital characteristics. • Lower birth weight, higher infant age (within 28 days of birth), Hispanic ethnicity, and hospital location in the Midwest region are associated with higher odds of feeding problems. • NAS diagnosed infants with feeding problems have slightly lower odds of being offered lactation services, which includes counseling and education, than infants without NAS who have feeding problems.
What needs to be studied:	• The stigma toward parents of children with NAS and the implicit bias among providers toward them. • The social safety-net services infants born to lower-income parents are connected to and management of feeding problems without the assistance of healthcare professionals. • The association between parental characteristics (nutrition, drug use, weight, comorbidities, prenatal care utilization, etc) with infants feeding problems.
What can we do today:	• Interventions specifically directed toward NAS infants who face feeding difficulties should consider the interplay between social and economic circumstances of families, as well as stigma toward people who use drugs, and how these factors impact the likelihood of receiving needed medical services. • Expand access to lactation services to NAS diagnosed infants.

better detail on issues related to the role of gestational age, method of feeding (ie, exclusive breastfeeding, exclusive formula feeding, pasteurized donor human milk, etc), and social determinants of health (eg, parental housing status) that elaborate on the findings presented here. Finally, as this was an observational study, causality cannot be established. Despite these challenges, the findings presented were sufficiently powered to provide reliable results with relatively high precision. Future studies may utilize a different data source that allows linkage of parental characteristics to infant outcomes to understand the extent to which these variables may alter the risk for hospitalization due to feeding problems among infants diagnosed with NAS.

CONCLUSIONS

This study provides evidence that the risk of hospitalization due to feeding problems among infants diagnosed with NAS is significantly increased compared with infants without an NAS diagnosis. Environmental and social factors, such as patient insurance type and urbanicity, also appear to play a role in the risk of hospitalization due to feeding problems. Interventions specifically directed toward infants with NAS who face feeding difficulties should consider the interplay between social and economic circumstances of families, as well as stigma toward people who use drugs, and how these factors impact the likelihood of receiving needed medical services.

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