

BRIEF REPORT

An Update on the Burden of Neonatal Abstinence Syndrome in the United States

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ABSTRACT

OBJECTIVES: To provide an estimate on the most recent burden of neonatal abstinence syndrome (NAS) in the United States.

METHODS: The 2016 Kids' Inpatient Database, provided by the Healthcare Cost and Utilization Project and Agency for Healthcare Research and Quality and its partners, was used to identify patients with NAS in the United States. The data consisted of pediatric admissions from 4200 US hospitals recorded between January 1, 2016, and December 31, 2016. Data were converted to weighted form to project a national estimate on the possible number of neonates affected by NAS. Differences in sex, race, location, household income, primary payer form, length of stay, and total charges were studied.

RESULTS: The sample contained 32 128 patients with NAS (0.8%), among whom 17 164 (53.5%) were boys and 14 935 (46.5%) were girls ($P < .001$); 23 027 (80.4%) were white ($P < .001$), and 13 583 (42.3%) were from the southern parts of the United States ($P < .001$). Medicaid covered 83.8% of patients, and 40.2% had an income within the first quartile of national averages ($P < .001$). The overall mean and median length of stay were 16.45 and 12.00 days, respectively, and the mean and median total charges were calculated as \$79 937.75 and \$38 537.00, respectively. The total charges of NAS were \$2 549 098 822.

CONCLUSIONS: The incidence of NAS is on a constant rise; the number of cases rose from 21 732 in 2012 to 32 128 in 2016. Hospital charges have also tripled over the last 7 years to \$2.5 billion in 2016.

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Neonatal abstinence syndrome (NAS) is a set of postnatal withdrawal symptoms seen in infants who were exposed to illicit addictive or prescription drugs in utero.^{1,2} The major clinical findings of NAS involve autonomic and central nervous system dysfunction, such as tremors, irritability, respiratory distress, and gastrointestinal hyperactivity leading to poor feeding and growth. The severity and time of onset can vary and are believed to be multifactorial.³ Recent research has revealed that the economic burden of NAS in the United States has increased over the last 2 decades with the rise in opioid use, resulting in an increase in admission rates^{4,5} and the primary economic burden falling to Medicaid because it covered 82.0% of NAS-related births in 2014, compared with 73.7% in 2004.⁶

We sought to analyze the most recent 2016 Kids' Inpatient Database (KID) to understand changes in incidence, length of stay (LOS), and hospital charges as well as to understand racial and geographical differences compared with those in previous studies.

METHODS

Design

A retrospective study was conducted on the basis of the 2016 KID. The KID is the largest database in the United States focused on pediatric admissions, with data from 4200 US hospitals. It is provided by the Healthcare Cost and Utilization Project (HCUP) and Agency for Healthcare Research and Quality, along with their partners.^{7,8} The 2016 KID is the most recent database released and encloses discharge records from January 1, 2016, to December 31, 2016. It has information about all patients covered by different insurance policies, such as Medicaid or private insurance, as well as uninsured children. The older versions of the database have previously been used to provide national estimates of NAS in the United States.

Identification of Sample

Because the 2016 KID consisted of patients between the ages of 0 and 20, we initially filtered the ages to include admission data

from patients classified as neonates. We identified additional cases of NAS classified as "neonatal withdrawal symptoms from maternal use of drugs of addiction" with the *International Classification of Diseases, 10th Revision, Clinical Modification* code P96.1.⁹

Statistical Analysis

The original data provided by HCUP are in unweighted form. Discharge weights provided by HCUP were used to convert the data to weighted forms. Only weighted forms are suitable for national estimates.¹⁰ Differences in sex, race, location, household income, and primary payer form were compared by using Pearson's χ^2 tests. We also investigated any differences in LOS and total charges using linear regression. We further adjusted the LOS by filtering out newborns with extreme immaturity and/or preterm newborns. $P < .05$ was considered statistically significant. IBM SPSS Statistics version 24.0 (IBM Corporation, Armonk, NY) was used for all statistical analyses.

Patient and Public Involvement

According to the HCUP Data Use Agreement,¹¹ because no patients were directly involved, institutional review board approval was not required, and ethical clearance from individual institutions was also not necessary.

RESULTS

The 2016 KID consisted of 3 117 413 unweighted and

6 266 285 weighted admissions for patients between the ages of 0 and 20 years; 3 970 065 weighted admissions were of neonates, among whom 32 128 had a diagnosis of NAS (0.8%) (Fig 1, Table 1).

NAS was more common among boys (17 164; 53.5%) than girls (14 935; 46.5%) ($P < .001$). Racial and geographical differences were also noted: 23 027 patients (80.4%) were white ($P < .001$), and 13 583 (42.3%) were from the southern parts of the United States ($P < .001$). The most common primary expected payer was Medicaid (26 886; 83.8%). Household income also played an important role; 12 706 patients with NAS had an income within the first quartile of national averages (40.2%; $P < .001$).

The mean and median overall LOS were 16.45 and 12.00 days, respectively (interquartile range [IQR]: 2.00–22.00; $B = 12.712$; 95% confidence interval [CI]: 12.605–12.818; $P < .001$). A total of 5648 patients (17.6%) were classified as preterm newborns and/or newborns with extreme immaturity. The mean and median LOS of term newborns were 15.30 and 12.00 days, respectively (IQR: 5.00–21.00; $B = 11.533$; 95% CI: 11.416–11.651; $P < .001$), whereas preterm newborns and/or newborns with extreme immaturity had a mean and median LOS of 21.85 and 16.00 days, respectively (IQR: 9.00–25.00; $B = 18.038$; 95% CI: 17.784–18.292; $P < .001$). The mean and median total charges were

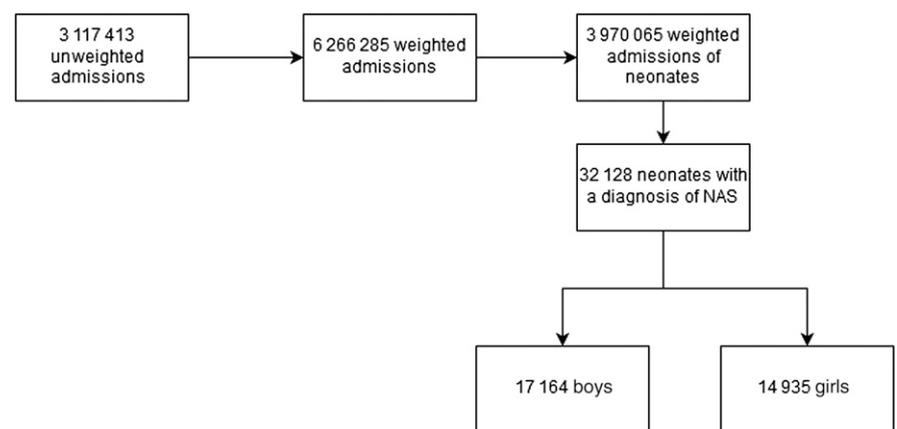


FIGURE 1 Analysis of the 2016 KID.

TABLE 1 Admissions of NAS in the United States

	NAS, <i>n</i> (%)	Non-NAS, <i>n</i> (%)	Patients Missing Data, <i>n</i> (%)	<i>P</i>
Sex			2313 (0.1)	<.001
Male	17 164 (53.5)	2 023 576 (51.4)		
Female	14 935 (46.5)	1 912 077 (48.6)		
Race			409 546 (10.3)	<.001
White	23 027 (80.4)	1 820 343 (51.5)		
African American	1972 (6.9)	515 017 (14.6)		
Hispanic	2021 (7.1)	716 665 (20.3)		
Other	1630 (5.7)	479 844 (13.6)		
Region of hospital			0 (0.0)	<.001
Northeast	6960 (21.7)	627 387 (15.9)		
Midwest	6719 (20.9)	841 516 (21.4)		
South	13 583 (42.3)	1 536 954 (39.0)		
West	4867 (15.1)	932 079 (23.7)		
Primary expected payer			4647 (0.1)	<.001
Medicaid	26 886 (83.8)	1 796 861 (45.7)		
Private	3143 (9.8)	1 827 682 (46.5)		
Others	2055 (6.4)	308 791 (7.8)		
Household income, percentile			41 491 (1.0)	<.001
0–25th	12 706 (40.2)	1 111 519 (28.5)		
25th–50th	8765 (27.7)	958 715 (24.6)		
50th–75th	6465 (20.5)	966 964 (24.8)		
75th–100th	3651 (11.6)	859 789 (22.1)		

—, not applicable.

calculated as \$79 937.75 and \$38 537.00, respectively (IQR: 11 919.00–90 701.29; $B = 60\,058.376$; 95% CI: 58 775.119–61 341.632; $P < .001$). The total charges of NAS were \$2 549 098 822.

Forty-five deaths during hospitalizations were found among patients with NAS; 27 (60%) were preterm newborns and/or newborns with extreme immaturity ($P < .001$).

DISCUSSION

Our aim for this study is to provide an updated analysis of the current burden of NAS in the United States by using the largest nationwide pediatric database. We found that the number of cases of NAS rose from 21 732 in 2012⁵ to 32 128 in 2016. Aggregate hospital charges have also tripled over the last 7 years; the charges increased from \$731 841 300 in 2009 and \$1.5 billion in 2012⁵ to \$2.5 billion in 2016. This rise in cases and charges reflects the increase in opioid use in the United States.¹² The higher incidence of

NAS in lower-income families and higher coverage by Medicaid also strongly suggests that a community-level approach to target families and patients at risk should be considered to educate them on the ill effects of opioid use during pregnancy.¹³

Our study revealed that NAS was more common in boys than in girls. However, because we are unable to assess for maternal exposure and treatment plans adopted by each group, the severity of NAS in each group remains unclear. Future research pertaining to in-hospital assessment of severity and sex differences should be encouraged to better address this question. It was also observed that the prevalence of NAS was higher in whites patients compared with African American and Hispanic patients despite previous reports revealing that African American women had a higher rate of illicit drug use during pregnancy.¹⁴ Although the genetic background behind these differences has not been fully

understood, this further raises concerns over possible racial and ethnic disparities of care required or provided to newborns too.¹⁵

The overall mean LOS in our study (16.45 days) also corresponds closely to data from 2009 (16.5 days) and 2012 (16.9 days), which raises the question of whether there have been any changes in treatment protocols in hospitals for neonates with NAS over the past 7 years. Rooming-in of neonates exposed to opioids with their mothers or close families has been shown to lower the need for pharmacotherapy, thereby decreasing the LOS.¹⁶ Other alternatives to inpatient care that bypass the NICU and allow for the use of pharmacologic treatments on an as-needed basis have proved to lower both LOS and hospital charges.¹⁷ Although the concept of rooming-in for NAS has been considered by some physicians and hospitals for more than a decade, the nationwide change in LOS may only be reflected in the future as more hospitals gradually transition to nonpharmacologic alternatives.

The HCUP data have some limitations, and errors in coding and input cannot be ruled out. The criteria for using the diagnosis code for NAS vary across different hospitals. Some hospitals require the presence of maternal exposure to opioids, whereas some limit NAS diagnosis to patients who were treated in neonatal care or required extensive treatment only. In their study on NAS, Milliren et al¹⁸ highlighted that using diagnosis codes to identify possible cases of NAS can underestimate the actual prevalence of NAS. Major hospital databases, such as the KID, rely heavily on *International Classification of Diseases* codes. Future *International Classification of Diseases* codes should be more specific to different maternal causes of NAS and to different types of treatment received as we gradually transition to pharmacologic and nonpharmacologic care for NAS.

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