Neonatal Abstinence Syndrome: An Epidemic

Kara Barlow, MD; Alexis Cannon, MD; Kindal Dankovich, MD; Alysa James, MD; Madison Merritt, MD; and Jennifer A. Hudson, MD

From the University of South Carolina School of Medicine Greenville, Greenville, SC (K.B., A.C., K.D., A.J., M.M., J.A.H.), and Children’s Hospital of Greenville Health System, Greenville, SC (J.A.H.)

Sales of opioid pain medications in the United States (US) have increased nearly fivefold since 2000.1,2 Pregnant women as a distinct population have also experienced a threefold to fourfold increase in prescription opioid use.3 These data are concerning because chronic opioid use is associated with significant adverse effects, including cardiac complications, depression, and drug dependence.4,5 For pregnant women, however, concerns are not limited to the mother, since numerous studies have shown opioid use to adversely impact fetal development6-9 and can often result in neonatal abstinence syndrome (NAS).4,10

The National Library of Medicine defines NAS as “problems that occur in a newborn who was exposed to addictive opiate drugs while in the mother's womb.”11 Manifestations of this group of “problems” vary, as do the severity and duration of symptoms that infants with NAS experience post-birth. Between 2000–2012, national rates of NAS increased 383% from 1.2 per 1000 births to 5.8 per 1000 births.2,12 Hospital costs associated with the diagnosis and treatment of NAS have also increased, with infants with NAS averaging a longer hospital stay of 12.4 days when compared to infants without NAS (Table 1).12

Currently, no national standard of care for managing NAS exists, and there is no consistency in laws or regulations on reporting substance misuse in pregnancy or NAS cases. Several individual states, however, have implemented measures to address and treat their rising NAS rates. This report aims to increase awareness surrounding the rise in opioid use in pregnant women and the subsequent danger of NAS and to provide several prevention strategies to reverse this growing epidemic.

Neonatal Abstinence Syndrome

As of 2012, an infant with NAS was born every 25 minutes in the US, accounting for more than $1.5 billion in national healthcare expenditures.12 The rate of NAS in South Carolina (SC) has also increased significantly—from 0.9 per 1000 births in 2000 to 3.9 per 1000 births in 2013.13,14 These data are troubling for several reasons: they represent the unnecessary suffering many infants are experiencing post-birth, the increasing number of pregnant women (and Americans in general) potentially experiencing complications of chronic opioid use/misuse, and the significant financial burden this epidemic is placing on payers, hospitals, and the US.

In 2000, the mean total charges generated for hospitalization of a newborn with NAS was $39 400. By 2012, that total had increased to $68 700 for infants with NAS and $93 400 for pharmacologically treated NAS infants, compared to $3500 for uncomplicated infant births (Table 1).12 Although median hospital length of stay for an infant with NAS has not changed significantly over time, it does remain more than 5 times longer than non-NAS infants (17 days vs. 3 days). Also of note, approximately 81% of all NAS-related hospital charges are billed to Medicaid.12

Neonatal abstinence syndrome primarily results from chronic late-gestation exposure to opioids.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>2000</th>
<th>2009</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate of NAS per 1000 hospital births</td>
<td>1.2</td>
<td>3.39</td>
<td>5.8</td>
</tr>
<tr>
<td>NAS newborn hospitalization costs</td>
<td>$39 400</td>
<td>$53 400</td>
<td>$68 700</td>
</tr>
</tbody>
</table>

Patrick et al12
Withdrawal symptoms can begin as early as birth but may not peak in severity until day 3 or 4 of life. Neurologically, infants with NAS may exhibit tremors, hypertonia, hyperreflexia, irritability, sleep disturbance, a high-pitched cry, and/or seizures. They may also experience autonomic dysfunction, manifesting as sweating, fever, nasal congestion, sneezing, or skin mottling. Gastrointestinal manifestations include poor feeding, vomiting, diarrhea, and failure to thrive. Tachypnea, apnea, and skin excoriations can also be present. Symptoms have been found to persist for as long as 4–6 months, with neurologic irritability occasionally extending into the seventh or eighth month of life.

Clinical presentation of NAS differs from infant to infant in manifestation, severity, and duration, and is often based on the type and amount of opioid exposure, gestational age, maternal nicotine use, and other maternal medications. Unfortunately, no clear correlation between the prenatal dose or duration of exposure and the severity of symptoms has been established, which makes it difficult to predict how an infant with NAS will appear in the first few days of life. Also, manifestations of NAS involving autonomic dysfunction, such as tachypnea and fever, are characteristic of many newborn illnesses and can make it challenging to distinguish the presence of withdrawal if the prenatal history of substance use/misuse is not known.

Previous studies have shown infants with NAS to have a significantly higher rate of post-birth complications compared to non-NAS infants. Additional conditions associated with NAS include preterm delivery, low birth weight, and a prolonged hospital stay. Few studies have examined the long-term impact on developmental outcomes, but further research is warranted.

**Prescription Opioid Use**

The majority of women will experience some pain during pregnancy. The most common complaints are back pain, abdominal pain, headaches, and/or joint pain. As a result, it is not surprising that pain relievers are desired. Prescription opioid use during pregnancy, however, can be strongly associated with neonatal complications, especially in the presence of additional risk factors, such as alcohol, smoking, antidepressant use, or other drug misuse. Despite the known risks associated with opioid use during pregnancy, the rates of opioid prescriptions being dispensed are increasing. National studies show between 14%–22% of all women will fill a prescription for an opioid medication during pregnancy, with the most common being hydrocodone, followed by codeine, oxycodone, and propoxyphene.

Challenges abound in reducing opioid use in pregnant women. First, many women may be unaware that they are pregnant; approximately 50% of US pregnancies are unplanned. Moreover, 86% of pregnancies in women who misuse opioids are unintended. Opioid use during pregnancy, however, is not limited to lack of awareness. In 2015, Palmsten et al found that 82% of pregnant women enrolled in Medicaid were dispensed at least 1 opioid prescription. Study results showed that the proportion of prescriptions dispensed increased from 52% before pregnancy to 57% through the third trimester, with 2 out of 5 pregnancies including at least 1 prescription for a Pregnancy Category D or X drug.

In 2013, approximately 52% of women of reproductive age (ages 15–44) in SC filled an opioid prescription. The 5 most common prescriptions included fentanyl transdermal, morphine, hydrocodone-acetaminophen, oxycodone-acetaminophen, and buprenorphine sublingual. Most of these drugs were prescribed for 6 months continuously, with 67% of hydrocodone-acetaminophen users being prescribed for the entire year.

**Preventing NAS**

**Primary Prevention**

At the practitioner level, office strategies can be implemented to improve education surrounding factors that increase the risk of an infant experiencing NAS. Primary prevention in the “pre-conception” phase should minimize prescription opioid use before pregnancy. Open dialogue and promotion of family planning, including effective contraception pre-pregnancy and post-delivery, are important; so is education surrounding the potential impact short- and long-term opioid use may have on future pregnancy, health, and wellness. Other strategies also include offering brochures in waiting rooms and restrooms that describe risks of opioid use, as well as utilizing social media and public education campaigns to raise awareness.

**Secondary Prevention**

**Prescription Drug Monitoring Program**

A Prescription Drug Monitoring Program (PDMP) is a state-level database that monitors controlled prescription drugs dispensed by pharmacies. Currently, 49 states have a PDMP, including SC. Data for specific patients are available to practitioners with access, and the PDMP is a helpful resource
for reporting other medications the patient has recently been prescribed, and by whom.

The PDMP in SC is known as the South Carolina Reporting and Identification Prescription Tracking System (SCRIPTS). SCRIPTS requires all dispensing practitioners and pharmacists to collect and report distribution of all class II–IV controlled substances. According to SC’s Department of Health and Environmental Control, only 28% of physicians in SC are currently using this valuable tool. Obtaining SCRIPTS access requires the practitioner and/or pharmacist to complete an online-training module, complete a notarized database access request form, sign a privacy statement, and submit a copy of his or her driver’s license. The process is free and takes approximately 15 minutes to complete. Access is typically granted by email in 3–5 business days. Although there are limitations to the database, 72% of SC prescribers may be missing opportunities to detect and prevent prescription misuse.

Screening Tools

Substance use disorders affect all genders, races, ages, and socioeconomic groups. As such, screening should not be limited to supposed “high-risk” patients. The Screening, Brief Intervention, and Referral to Treatment (SBIRT) is an evidence-based screening tool that can be used in the office setting to detect and treat patients struggling with substance misuse. Originally, SBIRT was used as a screen for alcohol and tobacco misuse, but the current version also screens for family violence, prescription, and illicit substance use problems.

Few studies have examined the effectiveness of SBIRT on lowering substance misuse. However, a large federally funded study by Madras et al saw significant improvements in illicit substance use (68% lower) and heavy alcohol use (39% lower) following implementation of SBIRT.

The American Medical Association (AMA) has approved billing codes that will allow hospital systems to be reimbursed by third-party payers for implementing SBIRT. South Carolina’s Department of Health and Human Services (DHHS) has been reimbursing obstetric providers since 2012 for SBIRT screening of pregnant women funded by Medicaid. Reimbursement ranges from $26.78 (SBI Code 99408, 15–30 minutes) to $52.29 (SBI Code 99409, >30 minutes). Taking the time to screen all pregnant women and provide brief intervention or referrals to those patients in need can potentially decrease substance misuse during pregnancy and ultimately lead to fewer cases of NAS and fewer maternal health complications.

Urine drug testing during pregnancy may also provide benefit within prevention models. The American Congress of Obstetricians and Gynecologists (ACOG) currently states that maternal urine drug testing is indicated in the setting of late or no prenatal care in the hospital setting and with diagnosis of stillbirth or placental abruption. Positive history, physical exam findings, and concerning behaviors may also prompt providers to order a urine drug test. Detection of substance use can help direct appropriate care for both infants and mothers. However, maternal testing should be done only with her knowledge and consent, including an understanding of the consequences of a positive test, which can vary from state to state.

Several states require physicians to report suspected substance misuse during pregnancy. The results of these reports and prenatal drug tests can then be used in criminal proceedings. Currently, 18 states consider substance misuse during pregnancy to be child abuse. The SC Supreme Court considers a viable fetus to be a “person”; maternal acts that endanger the life, comfort, or health of that “person” are considered criminal child abuse.

Criminal prosecution of substance misuse during pregnancy has historically led pregnant women to avoid prenatal care, leading the AMA to reject the idea of criminalizing pregnant women using drugs. ACOG experts have also stated that such legal actions “have proved to be ineffective in reducing the incidence of alcohol or drug abuse.” Colorado has implemented a bill—HB12-1100—that prohibits information gained from drug screening or testing to be used in criminal proceedings. This bill may serve as a model for other states, as women with substance use disorders may be more willing to disclose issues without fear of criminalization, allowing for physicians to provide treatment options sooner and optimize clinical outcomes for the mother and the fetus and/or infant.

Managing NAS

Currently, no nationwide standard of care exists for managing NAS. Reporting of NAS, as well as medical treatment for NAS, varies by state and often by medical provider. Tennessee was among the first to begin to address the NAS epidemic, targeting multiple levels of prevention, data collection, and treatment. One of Tennessee’s initial interventions included collaboration with other states to petition the US Food and Drug Administration for a black box warning on certain opioids related to their use during pregnancy. The state
also made NAS a reportable condition and established a web-based reporting system, requiring physicians to report an NAS case within 30 days of diagnosis. As opposed to the initial surveillance through Medicaid and hospital discharge data, the web-based reporting portal system now allows Tennessee to gather data in real time, which provides greater insight into the source of NAS and geographic hotspots. Additional intervention strategies in the state allow infants diagnosed with NAS to qualify for several assistance programs including Tennessee Early Intervention Services, Help Us Grow Successfully, and Children’s Special Services.

In 2013, Maine established the Centers for Disease Control and Prevention Snuggle ME Guidelines, which addressed screening for substance use during pregnancy, and provided information related to intrapartum, postpartum, and newborn management; educational resources for families; and additional resources for medical providers. Through a unified approach, these guidelines were distributed to all birthing hospitals in the state.

Other states and organizations have implemented quality improvement projects for NAS to help improve standards of care. In Ohio, the Nationwide Children’s Hospital (NCH) sought to enhance managing NAS by establishing a pharmacologic protocol for initiating and weaning morphine and appropriate use of adjunctive therapy. NCH implemented training for nurses to accurately use abstinence scoring and initiated monthly interdisciplinary meetings to evaluate needs for staff education. Following protocol implementation, NCH experienced a reduction in length of stay for infants with NAS (31 days to 24 days), improved reliability of abstinence scores, and added educational resources for patients and staff. The Vermont Oxford Network, an alliance of neonatal intensive care units around the world, has also created an internet-based quality improvement project focused on standardizing prevention and management strategies.

**NAS Care in SC**

In 2011, the SC DHHS established the SC Birth Outcomes Initiative (BOI)—a statewide collaboration of stakeholders aiming to improve health outcomes for newborns. Core objectives of the BOI include reducing preterm births and neonatal intensive care days and increasing SBIRT use by obstetric providers during prenatal care. Developing a management model for NAS care in low-acuity nurseries has also been an area of focus since the initiative’s inception.

One management model called MAiN (Managing Abstinence in Newborns) was developed and studied at Greenville Health System in Greenville, SC. MAiN involves a multidisciplinary and coordinated approach that targets collaboration among clinicians caring for opioid-dependent mothers and their newborns. More specifically, MAiN combines standardized early treatment, inpatient stabilization (while rooming-in with mother), and outpatient weaning in a medical home. The MAiN model has been shown to be safe, effective, and cost-efficient, generating less than $11 000 in hospital charges per case.

**Conclusion**

Substance use disorders are treatable conditions, similar to other chronic diseases encountered in pregnancy. With heightened practitioner awareness, effective prevention and screening strategies, and operational treatment and support systems, the NAS epidemic can be addressed in SC and nationwide.

**References**


