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Background

- An estimated 1 in 3 women of reproductive age filled an opioid prescription every year from 2008 to 2012 in the United States.
- The number of women admitted for L&D with Opioid Use Disorder (OUD) quadrupled from 1999 to 2014.
- Neonatal Abstinence Syndrome (NAS) diagnoses increased in the United States from 3.4 to 5.8 per 100 hospital visits between 2009 and 2012, totaling over 21,000 infants affected during these three years.
- Neonatal Opioid Withdrawal Syndrome (NOWS), a specific form of NAS, presents with unique clinical features including dysfunction in the following four domains: state control and attention, motor and tone control, sensory integration, and autonomic functioning.
- Recent studies suggest that children diagnosed with NOWS are more likely to have lower intelligence quotient scores, educational disabilities/deficits, and visual disorders.
- Children diagnosed with NOWS are more likely to require re-hospitalization or frequent healthcare follow up. Common reasons for re-hospitalization include respiratory disease, infections, and injuries.
- Preclinical models have revealed the presence of pro-inflammatory markers in the peripheral circulation and brain following prenatal opioid exposure (POE), which may in turn alter the developing immune system.
- Asthma is a heterogeneic chronic inflammatory disease that varies in the type and intensity of airway inflammation.
- The specific underlying inflammatory mechanisms involved in the progression of asthma remain unknown.

Objectives

- To determine whether POE increases the likelihood of an altered immune response, measured by the development of asthma, by eight years of age.

Methods

- A retrospective cohort design utilizing a comprehensive CERNER HealthFacts® U.S. national database.
- CERNER HealthFacts® is a clinical database that captures de-identified, longitudinal electronic health record data from 800 hospitals across the country.
- ICD-9-CM and ICD-10-CM diagnosis codes were used to identify infants born at term with known prenatal opioid exposure or NOWS and were compared to healthy control infants with no diagnoses at birth other than normal newborn codes.
- Data analysis was conducted with IBM Statistical Package for Social Sciences (version 26) and P values less than 0.05 were considered statistically significant.
- Descriptive statistics for frequencies and percentages were calculated. Pearson's Chi-Square test analysis was conducted to examine whether there was an association between POE and asthma diagnosis as well as other variables of interest.

Results

Table 1. Characteristics of Study Participants ($N = 3021$)

|	n	%
Demographics		
Gender		
Female	1420	47
Male	1531	50.7
Unknown	70	2.3
Race/ethnicity		
African American	468	15.5
Caucasian	1843	61
Hispanic	165	5.5
Other	545	18
Insurance		
Medicaid	1265	41.9
Other commercial	619	20.5
Self-Pay	106	3.5
Not Specified	1031	34.1
Community		
Urban	2795	92.5
Rural	226	7.5
Opioid Exposure		
Exposed	1523	50.4
Not Exposed	1498	49.6
Asthma Diagnosis		
Yes	172	5.7
No	2849	94.3

Table 1 shows the characteristics of the study participants, in which a total of 3,021 records from 2000 to 2016 were reviewed. The chart of each patient was reviewed until 8 years of age. A total of 50.4% of patients had POE and 49.6% had no known exposure.

- There was no difference in the percentage of patients that were male compared to female.
- Sixty-one percent of patients were identified as Caucasian, 15.5% as African American and 5.5% as Hispanic.
- The majority of patients had Medicaid insurance and resided in urban locations.

Of infants diagnosed with asthma (n = 172), 66.3% were prenatally exposed to opioids while 33.7% were not exposed.

Results

Percentage of Patients with Asthma Diagnosis with POE Compared to Control
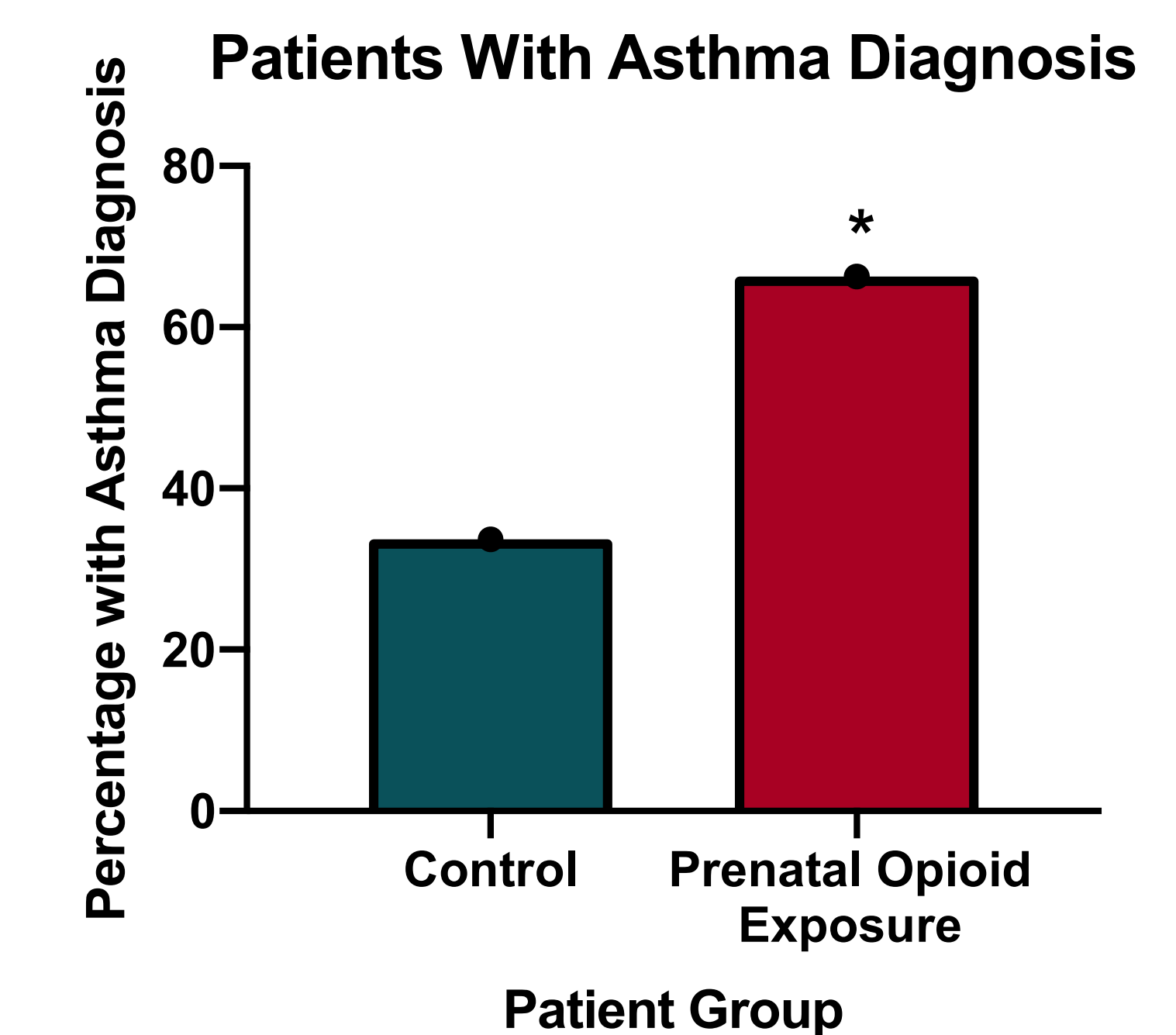
Figure 1: Asthma diagnosis differed significantly by group (X^2 [1, n = 3,021] = 18.36, $p<0.001$). **The odds of an infant developing asthma were two times higher for the group exposed to opioids prenatally** (OR 2.1, 95% CI: 1.4-3.0) and this was statistically significant ($p<0.0001$). After controlling for race, gender, demographics and payment type, we observed that infants with POE had twice the odds of diagnosis of asthma compared to infants who did not have POE.

Conclusions

- Our findings show an increased incidence of asthma in children prenatally exposed to opioids. This is consistent with previous investigations of the association between maternal drug use and risk of childhood asthma.
- This association highlights the importance of close follow up care within this patient population.
- A major strength of this study was the ability to query a national database which covers a wide area and a vast patient population. Therefore, we would expect the results from this study to be applicable to other areas in the United States.
- Limitations are present in this study as we had to assume the codes used were accurate and truly represented the patient. The diagnostic codes used to identify infant with prenatal opioid exposure were not exclusive to opioids only (such as Drug Withdrawal Syndrome in Newborn) so there may be some infants included in the study that had prenatal exposure to a drug other than an opioid. Additionally, there are confounding characteristics, such as smoking in the household, that we are unable to account for.
- A future aim is to complete a longitudinal, prospective, multisite study to address the weaknesses we have identified.