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Congenital CMV-Coded Diagnosis among American Indian and Alaska Native Infants in the United States, 2000–2017

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Abstract

To assess prevalence of congenital cytomegalovirus (CMV)-coded diagnosis among American Indian/Alaska Native (AI/AN) infants who received Indian Health Service (IHS)-funded care during 2000–2017. Using data from the Indian Health Service National Data Warehouse, we identified AI/AN infants with congenital CMV-coded diagnosis, defined as presence of a diagnostic code for congenital CMV disease or CMV infection (International Classification of Diseases, Ninth Revision or Tenth Revision, Clinical Modification 771.1, 078.5, P35.1, B25.xx) within 90 days of life. We calculated prevalence of congenital CMV-coded diagnosis overall, by age at first CMV-coded diagnosis, and by geographical region. During 2000–2017, 54 (1.5/10,000) of 354,923 AI/AN infants had a congenital CMV-coded diagnosis; 32 (0.9/10,000) had their first CMV-coded diagnosis within 45 days of life, and 22 (0.6/10,000) between 46 and 90 days of life. Prevalence of congenital CMV-coded diagnosis varied by region (range 0.9/10,000 in Southern Plains to 3.7/10,000 in Alaska, $P = 0.0038$). Among the 54 infants with a congenital CMV-coded diagnosis, 48% had clinical signs such as jaundice, petechiae, or microcephaly, compared to 25% of 354,869 infants without a CMV-coded diagnosis ($P < 0.01$); and 1 (2%) vs. 277 (0.1%), respectively, died ($P < 0.05$). The prevalence of congenital CMV-coded diagnosis among AI/AN infants who received care at IHS facilities was slightly lower than in other studies based on health claims data and varied by geographical region.

Keywords

Congenital cytomegalovirus; CMV; American Indian; Alaskan Native; Infants

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Introduction

In the United States, congenital cytomegalovirus (CMV) infection occurs in up to 20,000 (4.5 per 1000) live births annually; 10–15% of infected infants will present with symptomatic congenital CMV disease at birth [1, 2]. In the absence of universal newborn CMV screening, most congenital CMV diagnoses are likely to occur among infants with symptomatic disease. Congenital CMV disease has been reported in 2.5–3.3 per 10,000 live births, based on national U.S. health care claims data [3]. During 1990–2006, congenital CMV-associated infant mortality rate was 8.3 per 1 million infants annually, with age-adjusted mortality rates among Native Americans and African Americans twice as high as among non-Hispanic whites [4]. However, data on prevalence of congenital CMV infection or disease among minority groups, such as American Indian and Alaska Native (AI/AN) infants, are lacking. We assessed prevalence of congenital CMV-coded diagnosis among AI/AN infants who received care from Indian Health Service (IHS) facilities during fiscal years 2000–2017.

Methods

In the United States, approximately 5 million persons self-identified as being AI/AN in the 2010 Census [5]. The Indian Health Service (IHS) National Data Warehouse (NDW) database includes National Patient Information Reporting System data from approximately 1.6 million eligible AI/AN persons who receive healthcare from IHS-operated or IHS-contracted health facilities. The database includes inpatient, outpatient, and emergency department visit data. Deaths that occurred in an IHS facility are captured in the database but there is no information on deaths that occurred outside an IHS facility. AI/AN persons are assigned a unique numerical identifier, which allows linkage of claims over time. This analysis only included de-identified data; it was therefore deemed by the Centers for Disease Control and Prevention (CDC) and the IHS not to be human subjects research and did not require CDC Institutional Review Board nor IHS National Institutional Review Board approvals.

Our study population included all infants with ≥ 1 health visit in an IHS facility within the first 90 days of life, from 1 October 2000 to 30 September 2017. We defined congenital CMV-coded diagnosis as presence of a diagnostic code for congenital CMV disease or infection [International Classification of Diseases (ICD), Ninth Revision or Tenth Revision, Clinical Modification, 771.1, 078.5, P35.1, B25.xx] within the first 90 days of life. A diagnosis of congenital CMV infection or disease requires laboratory testing within 3 weeks of birth. However, we were not able to assess laboratory test results. We used an interval of 90 days of life to account for possible delays between reporting laboratory results and diagnostic coding.

We calculated prevalence of congenital CMV-coded diagnosis overall using as a denominator the total number of infants with ≥ 1 health visit in an IHS facility within the first 90 days of life. Since not all infants in our study population were born at an IHS facility, we also calculated the prevalence of congenital CMV-coded diagnosis among a

subset of infants with a live birth code, indicating they were born in an IHS facility. IHS was categorized into six regions for analysis: Northern Plains, Southern Plains, Southwest, East, Alaska, and West [6]. Data from the East and Northern Plains regions were combined into one region for analysis due to small sample sizes. To compare prevalence by region, we used a Poisson regression model and results with a P-value < 0.05 were considered statistically significant.

Among infants with congenital CMV-coded diagnosis, we assessed age of first CMV-coded diagnosis (within 45 days vs. 46–90 days) and the following clinical signs, based on ICD-diagnostic codes: jaundice, petechiae, hepatomegaly, splenomegaly, and thrombocytopenia within the first 28 days of life; and microcephaly, chorioretinitis, and brain abnormalities at any time period. Because these are associated but not specific to congenital CMV disease, we used the Pearson chi square test to compare their proportions among infants with and without congenital CMV-coded diagnosis.

Results

Among 354,923 infants with ≥ 1 health visit within the first 90 days of life, 54 had a CMV-coded diagnosis, corresponding to a prevalence of 1.5/10,000 infants. In the subset of 167,923 infants born in an IHS facility, 20 had a CMV-coded diagnosis, for a prevalence of 1.2/10,000 live births. Prevalence of congenital CMV-coded diagnosis within the first 90 days of life was 0.9/10,000 in the Southern Plains, 1.1/10,000 in the East and Northern Plains, 1.1/10,000 in the Southwest, 2.5/10,000 in the West, and 3.7/10,000 in Alaska. Using the Southern Plains region as the referent group, prevalence was significantly higher only in Alaska (P = 0.0038).

Among 54 infants with a congenital CMV-coded diagnosis, 32 (59%) infants had their first CMV-coded diagnosis within 45 days of life, and 22 (41%) between 46 and 90 days of life. The proportion of infants with ≥ 1 clinical sign among those with their first CMV-coded diagnosis within 45 days of life was 50% and between 46 and 90 days, 46%. Among the 54 infants with congenital CMV-coded diagnosis and 354,869 without, 26 (48%) compared to 89,216 (25%), respectively, had ≥ 1 clinical sign (P < 0.01); 6 (11%) vs. 740 (0.2%) infants had microcephaly; and 1 (2%) vs. 277 (0.1%) died (P < 0.05, Table 1).

Discussion

The prevalence of congenital CMV-coded diagnosis among AI/AN infants who received care at an IHS facility was between 1.2 and 1.5 per 10,000 infants during 2000–2017, lower than the 2.5–3.3 per 10,000 infants reported in a previous study based on large national health care claims data also using ICD-diagnostic codes in the United States during 2009–2015 [3]. The low prevalence suggests that not all infants with symptomatic congenital CMV disease, and likely a much smaller fraction of those with asymptomatic infection would be captured using CMV-diagnostic coding [7, 8]. Although our numbers were small compared to studies using health claims data, we found similar proportions of infants with ICD-diagnostic codes for clinical signs associated with congenital CMV disease, including microcephaly [1, 3].

Our study had some limitations. IHS dataset only includes data on persons eligible to receive care in an IHS facility and might not represent all AI/AN infants in the United States. IHS has data on 1.6 million AI/AN persons, whereas the US census reports that approximately 5 million self-identify as AI/AN; the overlap between these sources is unknown [5]. IHS NDW data provide AI/AN-specific data whereas other data systems may omit, misclassify, or categorize AI/AN populations into an “other” race group. As our study relied on use of diagnostic codes without laboratory test results or medical charts, there may have been instances of missed or miscoded diagnostic-coding of congenital CMV disease and clinical signs. Although postnatal CMV infection is less likely to be symptomatic and prompt laboratory testing, we may still have included some cases of symptomatic postnatal CMV. We were unable to capture deaths that occurred outside of the hospital.

The prevalence of permanent hearing loss among AI/AN infants is not well described. Although > 98% of AI/AN newborns are screened for hearing loss, they have the lowest follow-up rates for diagnostic evaluation after not passing hearing screening and for receiving interventions after diagnosed with hearing loss [9]. One study of AI infants in Minnesota found a high rate of hearing screening failure, which was associated with otitis media [10]. Data from population-based birth defects surveillance systems indicate significantly higher prevalence of birth defects such as cleft lip, cleft palate and anotia/microtia in AI/AN infants compared to non-Hispanic white infants, which can lead to recurrent middle ear disease and hearing loss, and an increased need for hearing, speech and language evaluation and rehabilitation [11, 12].

The prevalence of congenital CMV-coded diagnosis among AI/AN infants was significantly higher in Alaska compared to the Southern Plains region. Whether this finding is related to differences in population prevalence, or provider awareness resulting in increased testing of infants in Alaska with suspected congenital CMV-associated clinical signs is unknown. Data from newborn CMV screenings with a large number of AI/AN infants are lacking. Thus, studies with larger representation of these populations will be helpful in assessing congenital CMV disease burden and potential health disparities. Increasing congenital CMV awareness among medical providers caring for AI/AN populations will be essential for appropriate diagnosis and management of affected infants.

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Table.

Clinical characteristics of infants with congenital CMV-coded diagnosis

	Infants with congenital CMV-coded diagnosis (first CMV-coded diagnosis (0–90 days) N = 54		Infants without CMV-coded Diagnosis (0–90 days) N = 354,869	
Characteristic[a]	**n**	**%**	**n**	**%**
Jaundice	15	27.8	86,163	24.3
Petechiae [b]	---	---	1,778	0.5
Hepatomegaly [b]	---	---	33	0.0
Splenomegaly [b]	---	---	9	0.0
Thrombocytopenia	6	11.1	465	0.1
Microcephaly	6	11.1	740	0.2
Chorioretinitis [b]	---	---	138	0.0
Brain abnormalities [b]	---	---	1,548	0.4
Any of the above	26	48.1	89,216	25.1
Death	1	1.9	277	0.1

[a]We assessed jaundice, petechiae, hepatomegaly, splenomegaly, and thrombocytopenia within the first 28 days of life; microcephaly, chorioretinitis, and brain abnormalities at any time period with ICD-9-CM or ICD-10-CM codes[3]; and in-hospital deaths.

[b]If the number of infants with petechiae, hepatomegaly, splenomegaly, chorioretinitis, and brain abnormalities were < 5 infants, the numbers in these cells could not be displayed.