Journal of Pediatric Nursing (2015) **30**, 346–352

Hospitalization Cost per Case of Neonatal Herpes Simplex Virus Infection From Claims Data[1,2,3,4]

Kwame Owusu-Edusei Jr. PhD*, **Elaine W. Flagg PhD**, **Thomas L. Gift PhD**

Division of STD Prevention, Centers for Disease Control and Prevention, Atlanta, GA

Received 17 April 2014; revised 7 August 2014; accepted 8 August 2014

Key words:
Herpes simplex virus;
Neonates;
Inpatient cost;
Insured population

The purpose of this study was to estimate the average excess inpatient cost of neonatal herpes simplex virus (NHSV) infection from 2005 to 2009 insurance claims data. The estimated adjusted average excess inpatient cost for neonate admissions with HSV diagnosis and >7 days of hospitalization was $40,044 [95% confidence interval (CI), $33,529–$47,775]. When disaggregated by the days of admission, cost estimates were: 8–13 days, $23,918 [CI, $19,490–$29,282]; 14–21 days, $44,358 [CI, $34,654–$56,673]; >21 days, $68,916 [CI, $49,905–$94,967]). Although these estimates are not representative of the entire US, they can inform future economic evaluation studies on NHSV interventions.
Published by Elsevier Inc.

NEONATAL HERPES SIMPLEX virus (NHSV) infection is typically caused by the perinatal transmission of herpes simplex virus, most frequently through contact with herpes simplex virus (HSV) infected genital secretions from the mother at the time of delivery (Bradford, Whitley, & Stagno, 2008; Lawrence Corey & Wald, 2008). Mothers who acquire HSV during pregnancy have a substantially higher risk of transmission than mothers with established disease (Lawrence Corey & Wald, 2008; L. Corey & Wald, 2009). However, a large proportion (over 70%) of HSV-infected neonates are born to mothers without symptoms or signs of HSV lesions at the time of delivery (Corey & Wald, 2008), making detection very challenging.

In the US, reporting of NHSV cases is not required and we are not aware of any trend analysis studies of the burden of NHSV. Therefore, it is not known whether the incidence of disease has changed over time. The estimated rate of NHSV among live births in 2006 was 9.6 per 100,000 (Flagg & Weinstock, 2011). Most incidence estimates from managed care populations and from population-based state and local studies have ranged from 8.4 to 28.2 per 100,000 births (Flagg & Weinstock, 2011). Incidence data for NHSV are similar to those for perinatal human immunodeficiency virus (HIV) before the advent of routine use of antiretroviral therapy during pregnancy, and the incidence is similar to, or higher than, that of congenital syphilis, toxoplasmosis, and congenital rubella in years in which the virus was not epidemic (Corey & Wald, 2009).

A case series of 8538 pregnant women receiving care in two hospitals from 1989 to 1993 used serum samples obtained at the first prenatal visit and at the time of labor and found that 24% were HSV-negative at entry. Of the 7046 women who were HIV-negative at entry, 1.3% became seropositive for either HSV-1 or HSV-2 (Brown et al., 1997). In a recent study, 24.5% of cases identified in 2006 were admitted for inpatient stay with NHSV diagnosis at birth, and 86.9% of cases identified were admitted for inpatient stay after birth, but within 30 days of birth (Flagg & Weinstock, 2011).

In newborns, HSV infection can manifest as (1) disseminated disease involving multiple organs in about 25% of cases, (2) localize central nervous system (CNS) disease in about

[1] Funding: None.
[2] Conflicts of interest: None.
[3] Previous presentation: A version of the results from this study was presented as a poster at the National STD Prevention Conference in Minneapolis, Minnesota, 12–15 March, 2012.
[4] Commercial financial support: None.
* Corresponding author: Kwame Owusu-Edusei Jr. PhD.
E-mail address: Kowusuedusei@cdc.gov.

http://dx.doi.org/10.1016/j.pedn.2014.08.004
0882-5963/Published by Elsevier Inc.

30% of cases, or (3) disease localized to the skin, eyes and/or mouth (SEM) in about 45% of cases (American Academy of Pediatrics, 2012). Although the majority (approximately two-thirds) of neonates with disseminated or CNS disease have skin lesions, the lesions may not be present at the time of initial presentation. Thus, the diagnosis of NHSV is difficult in the absence of lesions. Consequently, disseminated infection should be considered in neonates with sepsis syndrome, negative bacteriologic culture results, and severe liver dysfunctions (American Academy of Pediatrics, 2012). NHSV should also be considered in neonates with fever, irritability, and abnormal cerebrospinal fluid (CSF) findings, especially in the presence of seizures or during a time of year when enteroviruses are not circulating in the community. Although asymptomatic HSV infection is common in older children, it rarely, if ever, occurs in neonates (American Academy of Pediatrics, 2012). Studies have reported that the mortality rates among untreated severe cases can range from 50 to 85% (Whitley, Nahmias, Visintine, Fleming, & Alford, 1980; Whitley et al., 1980).

The test for NHSV comprises the isolation of HSV by viral culture from specimen obtained from skin vesicles and other sites (such as CSF, stool, urine, throat, nasopharynx and conjuctivae). Additionally, the detection of HSV-DNA in CSF by polymerase chain reaction (PCR) is the typical diagnostic method for CNS (American Academy of Pediatrics, 2012; Bradford et al., 2008). However, in administrative claims data, *International Classification of Diseases, Clinical Modification* (*ICD-CM*) codes for herpes simplex virus infection in neonates indicate NHSV diagnosis (Flagg & Weinstock, 2011).

The recommended regimen for NHSV involves 14 to 21 days of intravenous acyclovir (Workowski & Berman, 2010). Thus, besides the pain and suffering endured by neonates infected with HSV, the treatment can be very costly due in part to the relatively longer admission time required for treatment. However, estimates of the hospitalization cost due to NHSV in the US are limited. In this study, we estimate the excess/additional inpatient cost attributable to HSV diagnosis in neonates using US insurance claims data for 2005–2009.

Materials and Methods

Data Source and Case Definition

Claims data on inpatient admission from the *Truven Health Analytics MarketScan® Commercial Claims and Encounters Database* (Truven Health Analytics, Ann Arbor, MI) for 2005 through 2009 were assessed and used in this study. In 2005, the MarketScan database contained claims data on over 17 million people who had employer-sponsored health insurance from more than one hundred payers, including large employers, health plans, government and public organizations (Truven Health Analytics, 2011). The records comprise information on fully adjudicated and paid claims for persons with employer-sponsored health plans, including their spouses and dependents (Adamson, Chang, & Hansen, 2006).

Details on the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes for single or multiple liveborn infants who were identified as "healthy/uncomplicated normal newborns" is provided elsewhere (Owusu-Edusei, Introcaso, & Chesson, 2013). We used *ICD-9-CM* codes 054.0–054.9 (Buck, 2011) to identify admissions with a HSV diagnosis. Liveborn admissions that were not coded as "normal newborns" and which did not have a HSV diagnosis were excluded from our analyses. Also, because codes for fever or seizures can be symptoms of other viral or bacterial infections (Caviness, Demmler, Swint, & Cantor, 2008), neonates with codes for fever or seizure, but without *ICD-9-CM* codes for herpes simplex infection (054.0–054.9) were excluded.

Estimating Total and Excess Inpatient Costs Attributable to NHSV

In the MarketScan database, inpatient total costs were the total gross payments to all providers who submitted claims for covered services rendered during admission (Truven Health Analytics, 2011). Records with total payments less than $1 were deleted because most were likely due to data entry errors, although we found very few cases where the total payment was less than $1 (<0.1%).

We first estimated total costs associated with NHSV without regard to length of hospital admission (i.e., length of stay). Then, following Flagg and Weinstock (2011), we estimated total NHSV cost for those with length of stay > 7 days. Finally, we re-estimated the hospitalization costs for NHSV by disaggregating the estimated cost based on the length of stay as follows: 8–13, 14–21 and > 21 days (Caviness et al., 2008).

Following Owusu-Edusei et al. (2013), we computed simple summary statistics on the total payments for those with and without HSV diagnosis to determine excess costs (referred to as unadjusted estimates). Second, following previous studies (Bateman, Phibbs, Joyce, & Heagarty, 1997; Owusu-Edusei et al., 2013; Shrestha, Zhang, Albright, & Imperatore, 2011), we transformed the total costs into natural logarithm (to reduce the influence of outliers) of total costs and applied a semi-log regression model (i.e., the dependent variable was the natural logarithm of total cost) to determine costs while controlling for enrollee characteristics (i.e., independent variables) provided in the database (referred to as adjusted estimates). This approach was used because the total inpatient admission costs are largely dependent on (or are determined by) the patient and insurance characteristics provided in the claim record. Thus, we investigated the available characteristics that were influential (statistically significant) in determining the total inpatient cost. Then, we used the regression results to determine the adjusted cost—the mean inpatient cost after controlling for the available characteristics.