Pneumococcal and Meningococcal Vaccination among Michigan Children with Sickle Cell Disease

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Objectives To determine the proportion of Michigan children with sickle cell disease (SCD) who were vaccinated according to pneumococcal vaccination recommendations and, secondarily, to examine uptake of meningococcal vaccine, and to compare up-to-date (UTD) vaccination status between children with and without SCD.

Study design Children with SCD who were born in Michigan were matched to controls without SCD using age, sex, race, and zip code. Using data from the state immunization registry, we assessed the significance of SCD status on UTD vaccination in logistic regression models.

Results By 36 months, substantially more children with SCD had completed the pneumococcal conjugate vaccine series (68.8%) than children without SCD (45.2%), and 59% of children with SCD had received a meningococcal vaccine. Compared with children without SCD, children with SCD had higher odds of UTD pneumococcal status at 5, 7, and 16 months. However, a large proportion of children with SCD were missing key vaccination targets: of those who received a full 7-valent pneumococcal conjugate vaccine series, 29.1% had not received a 13-valent pneumococcal conjugate vaccine dose, and 21.8% had not had pneumococcal polysaccharide vaccine administered.

Conclusions The pneumococcal and meningococcal vaccination schedules have become increasingly complex in recent years. Assessment algorithms programmed to forecast doses due based on high-risk conditions, such as SCD, could provide a useful reminder to healthcare providers in the context of increasingly complex and changing recommendations. *(J Pediatr 2018;■■:■■-■■).*

As many as 100 000 people in the US have sickle cell disease (SCD).[1] Children with SCD have functional asplenia,[2] placing them at increased risk for meningococcal disease and invasive pneumococcal disease.[3-5] Average mortality among children with SCD because of SCD-related causes in the pre-pneumococcal vaccine era was 6.4% by age 18 years.[6] The US Advisory Committee on Immunization Practices (ACIP) has, therefore, developed pneumococcal and meningococcal vaccine schedules that are different for children with and without SCD.[3,7,8]

The 23-valent polysaccharide vaccine (PPSV23) has been available since 1983, and the ACIP recommends its administration in childhood only to specific high-risk groups.[3,7] A universal recommendation for pneumococcal vaccination started in October 2000, when the ACIP advised all children aged 2 through 23 months to receive a 7-valent pneumococcal conjugate vaccine (PCV7).[9] In February 2010, the 13-valent pneumococcal conjugate vaccine (PCV13) replaced PCV7 in this recommendation.[10]

Children with SCD have a more complicated vaccine schedule than the one recommended for children without SCD. In addition to the standard schedule, children with SCD are recommended to receive 2 PPSV23 doses, the first administered when the child is aged 2 years.[3] Children with SCD should also be prioritized for receiving for receiving a PCV13 dose through age 18 years, even if the PCV7 schedule was completed.[7]

The ACIP recommendations for pediatric pneumococcal and meningococcal vaccinations are complex, have changed over time, and are different for children with certain underlying medical conditions, such as SCD, compared with the majority of children who do not have functional asplenia. The Michigan Care Improvement Registry (MCIR), the state's immunization information system, assesses children for routinely recommended vaccines but does not provide tailored recommendations for children with high-risk conditions such as SCD. The aims of this study were (1) to determine the proportion of Michigan children with SCD who have been

ACIP	Advisory Committee on Immunization Practices
LBF	Live birth file
MCIR	Michigan Care Improvement Registry
MCV4	4-Valent meningococcal conjugate vaccine
PCV13	13-Valent pneumococcal conjugate vaccine
PCV7	7-Valent pneumococcal conjugate vaccine
PPSV23	23-Valent pneumococcal polysaccharide vaccine
SCD	Sickle cell disease
UTD	Up-to-date

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vaccinated according to pneumococcal vaccination recommendations from ACIP, and, secondarily, to examine meningococcal vaccination uptake; (2) to compare up-to-date (UTD) vaccination status between children with and without SCD; and
(3) to identify parental-level and provider-level factors for children with SCD that are associated with UTD vaccination. Findings from this study could be used to support the development of vaccination algorithms for immunization information systems that highlight the special requirements for children with high-risk conditions such as SCD.

Methods

This cohort study included children with and without SCD who were born in Michigan between April 1, 1995, and January 1, 2014. Data for the study came from MCIR, the Michigan Newborn Screening Program (which screens all infants born in Michigan for over 50 metabolic and other disorders, including SCD), and the Michigan Vital Records live birth file (LBF). Records were matched between these datasets by the LBF identification number. Since 1998, all vaccination providers in Michigan have been required by law to submit comprehensive information about vaccinations administered to children age <20 years to MCIR. As of 2000, providers can report this information using a web-based portal. Providers can also input historical records into the system if a previous vaccination was not entered into MCIR.

All children with confirmed SCD in Newborn Screening Program records were included in the analysis. Since 1987, Michigan newborns have been screened for hemoglobinopathies, including SCD, with a high performance liquid chromatography assay. SCD is subsequently confirmed diagnostically with a hemoglobin electrophoresis test, usually before the infant is 3 months of age.[11] We attempted to match each confirmed child with SCD to 4 controls from the LBF dataset who did not have SCD. The cases and controls were matched on 4 characteristics: age (birth in the same month), sex, race, and mother's zip code at the child's birth. Zip code was not included in the dataset used for analysis to limit our ability to identify individuals within this small group of individuals. A total of 138 (13.5%) of the 1022 children with SCD were matched to fewer than 4 controls because an insufficient number of children with the same matching characteristics.

Derived Variables

Demographic variables were available in the LBF. We created a race/ethnicity variable with 3 categories: non-Hispanic black, Hispanic, and non-Hispanic other. Mother's education was divided into 3 categories: less than high school education, high school education, and more than high school education. Mother's age at birth was collapsed into 4 categories: <20 years of age, 20-24 years of age, 25-29 years of age, and 30 or more years of age.

Vaccine administration information was obtained from MCIR. Facility categories were publicly funded clinics (which included Federally Qualified Health Centers, Rural Health Clinics, local health departments, and Women, Infants, and Children clinics), pediatric departments, family medicine clinics, other private providers (including private hospitals and other private clinics), and historical or unknown facilities. The "historical or unknown" category refers to facilities that reported vaccinations to MCIR that they themselves did not administer.

We examined UTD vaccination status at different milestone ages to document trends in vaccination uptake. By selecting several milestone ages, we also could include children who had vaccinations administered on the catch-up schedule.[9,12] For example, to be considered UTD at 3 months of age, a child born between June 7, 2000, and December 12, 2009, would require 1 dose of PCV7; a child born between December 13, 2009, and January 11, 2010, could have either 1 dose of PCV7 or 1 dose of PCV13, and after this latter date, the child would need 1 dose of PCV13. To be considered UTD at 5 months, the infant could have 2 doses of PCV7 or PCV13, depending on the date of administration. Alternatively, if the child started the series after 3 months, they only need 1 dose of PCV7 or PCV13 to be UTD by 5 months of age according to the catch-up schedule. In general, children who started the series before 7 months of age should have received 3 primary doses and 1 booster after 12 months, children starting the series between 7 and 12 months of age should have received 2 primary doses and 1 booster after 12 months, and children starting the series between 1 and 2 years should have received 2 doses of PCV. After 2 years, children with SCD, but not children without SCD, should additionally receive 1 dose of PPSV23.

All children under 59 months of age who had received a complete series of PCV7 were recommended by ACIP to receive a dose of PCV13. We created a dichotomous variable limited to children with a complete series of PCV7 comparing those with and without a PCV13 dose.

The extended meningococcal vaccination schedule for individuals with SCD at the time of this study was a combination *Haemophilus influenzae* type b, meningococcus groups C and Y vaccine (Hib-MenCY-TT) (after November, 2012) in a 4-dose primary series for children aged 2 through 18 months or, alternatively, if that was not available, a 2-dose primary series of meningococcal conjugate vaccine (4-valent meningococcal conjugate vaccine [MCV4]) at age 2-55 years. A first booster dose of MCV4 was recommended 3 years after completion of either series and every 5 years thereafter.[8] To assess meningococcal vaccination uptake, we separately examined children with SCD who were born between October 14, 2009, and January 24, 2013, who were age-eligible for a first dose of MCV4 at age 2 years and a second dose 2 months later. Children born after November 24, 2012, were also eligible to receive Hib-MenCY-TT.

Statistical Analyses

All analyses were performed in SAS v 9.3 (SAS Institute Inc, Cary, North Carolina). The multivariable conditional logistic regression models separately regressed the UTD status at each milestone age on the child's SCD status, the child's sociodemographic characteristics, and provider facility type. The independent variables were selected a priori.

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