Low rates of transfusion-transmitted infection screening in chronically transfused adults with sickle cell disease

Vignesh Chidambaram1 | Jennifer M. Jones2 | Parvez M. Lokhandwala3,4 | Evan M. Bloch3 | Sophie Lanzkron2 | Rosalyn Stewart5 | Lydia H. Pecker2

1Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA
2Division of Hematology, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA
3Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA
4Division of Biomedical Services, American Red Cross, Baltimore, Maryland, USA
5Division of General Internal Medicine, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Abstract

Background: Adults with sickle cell disease (SCD) on chronic transfusion therapy are exposed to a large volume of blood products, thus increasing their risk of transfusion-associated human immunodeficiency virus (HIV), hepatitis C (HCV), and hepatitis B (HBV).

Methods: We performed a systematic chart review of chronically transfused SCD subjects at the Johns Hopkins Sickle Cell Center for Adults between October 2014 and September 2019 to determine our Center’s adherence to the 2014 National Heart, Lung and Blood Institute (NHLBI) SCD guidelines for annual screening for Transfusion Transmitted infections (TTI) and assessed HBV immunity and HBV vaccination rates.

Results: The study included 85 subjects with a median age of 34 years (23–63); 52% were female. No subject received annual screening; 68 subjects (80%) were screened for HIV, 60 subjects (71%) for HCV and 53 subjects (62%) for HBV infections at least once in the study period. Of those screened, one patient was newly diagnosed with HCV infection, and none with HIV or HBV infection. Among 31 subjects tested for anti-Hepatitis B surface antibody, 16 subjects (52%) tested negative. Nineteen (20%) subjects had HBV vaccination documented.

Conclusions: Low adherence to the NHLBI TTI screening guidelines, especially for HBV, highlights the resource intensiveness of this patient population. The low rates of anti-Hepatitis B surface antibody positivity highlight the need

Abbreviations: Ag/Ab, antigen/antibody; Anti-HBc, hepatitis B core antibody; Anti-HBs, hepatitis B surface antibody; EIA, enzyme immunoassay; ELISA, enzyme linked immunosorbent assay; EMR, electronic medical records; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; NAT, nucleic acid testing; NHLBI, National Heart, Lung and Blood Institute; PCP, primary care provider; pRBC, packed red blood cells; SCD, sickle cell disease; TTI, transfusion transmitted infections.
to confirm vaccination, provide boosters as indicated, and investigate the adults with SCD’s immune response to HBV vaccination.

**KEYWORDS**
guidelines, hepatitis B, hepatitis C, HIV, NHLBI, screening, sickle cell disease, transfusion transmitted infection, vaccination

1 | **INTRODUCTION**

Many adults with sickle cell disease (SCD) receive chronic packed red blood cell (pRBC) transfusions for diverse indications including stroke prevention, chronic pain, pulmonary hypertension, recurrent acute chest syndrome, and leg ulcers.\(^1\)\(^2\) Chronically transfused adults with SCD may receive simple or exchange transfusions, and are usually exposed to 2–10 units of pRBC every 3–5 weeks.\(^3\) In the United States (USA), the routine blood product screening by nucleic acid tests (NAT) reduces the risk of Human Immunodeficiency virus (HIV), hepatitis C (HCV), and hepatitis B (HBV) transmission per pRBC unit to 1 in 1.5 million, 1.1 million, and 1 million, respectively.\(^3\)\(^4\) This low risk of transfusion-transmitted infections (TTI) may not reflect the risk for adults with SCD who receive many transfusions.\(^5\)–\(^7\)

The extent to which transfusion contributes to the increased risk of HIV, HCV, and HBV in adults with SCD is not established.\(^5\)–\(^7\) Nevertheless, the 2014 National Heart, Lung and Blood Institute (NHLBI) SCD guidelines recommend annual TTI screening for chronically transfused patients.\(^2\) No citations support this recommendation that was presumably made based on this population’s theoretically elevated TTI risk from frequent pRBC exposure. Routine screening promptly identifies new infections and facilitates treatment. TTI screening for HBV may also identify HBV nonimmune individuals who require (re)immunization. Performing annual screening imposes a burden on clinical staff who must track annual screening; order and follow-up on testing and may increase healthcare costs. The potential for false positive tests has both logistical and psychological ramifications. Adherence to the TTI testing recommendation is unknown and evidence is needed to define optimal approaches to TTI screening for people with SCD in the USA.

The Johns Hopkins Sickle Cell Center for Adults cares for over 600 adults with SCD. The purpose of this study was to determine our center’s adherence to the NHLBI guidelines that chronically transfused patients receive annual HIV, HCV, and HBV screening, to assess the rates of HBV immunity, and to determine whether patients without evidence of HBV immunity are subsequently immunized.

2 | **METHODS**

The Institutional Review Board at the Johns Hopkins School of Medicine approved this single-center, systematic, retrospective cohort study.

2.1 | **Subjects**

We included adults with SCD, aged 18 years or older, with 12 or more months since initiation of chronic transfusion therapy between October 1, 2014 and September 30, 2019. We defined “years” in the study period as October to September. We excluded subjects who only received on-demand transfusions.

2.2 | **Data collection**

We performed a systematic chart review from our electronic medical record (EMR) and stored data in a REDCap database.\(^8\) We collected basic demographics (age, sex and race), the number of transfusions per month, and total number of months on a chronic transfusions. We excluded on-demand transfusions received at our center or elsewhere. We captured the screening interval, and results of all HIV, HCV, and HBV testing. We considered subjects screened for HIV, HCV, or HBV if a test result for the corresponding TTI was available during the study period. The TTI tests used were a fourth-generation enzyme linked immunosorbent assay (ELISA) for HIV1/2–Ag/Ab, an Enzyme Immunoassay (EIA) for IgG anti-HCV antibody, EIA for HBV surface antigen (HBsAg), EIA for HBV core antibody (anti-HBc), and immunochemiluminescent assay for HBV surface antibody (anti-HBs). To establish baseline HIV, HCV, or HBV infection, we collected results
available from the soonest HIV, HCV, and HBV tests preceding the study period.

2.3 | HBV immunity

HBV is a vaccine-preventable TTI. We evaluated subjects’ HBV vaccination status. Since 1991, most USA-born infants receive the HBV vaccine because acceptance is high.9 We assumed that all subjects born after 1991 received the HBV vaccine in infancy.9 We collected anti-HBs, a marker of HBV immunity from vaccination or past infection. Vaccination records were collected from the EMR and if those records were incomplete, we contacted the primary care providers (PCPs) for records and/or approached the subjects directly for this information. For anti-HBs negative subjects, we collected documentation of subsequent HBV vaccination and immune response. Anti-HBc antibody distinguishes the immune response from infection rather than vaccination, and helps identify individuals who do not express hepatitis B antigen, but have occult HBV (HbsAg mutants i.e. HBV infection).10 We classified subjects as being (1) actively infected (HbsAg positive), (2) immune after infection (anti-HBc positive and anti-HBs positive), (3) immune after vaccination (anti-HBc negative and anti-HBs positive), (4) nonimmune (anti-HBc negative and anti-HBs negative), or (5) unknown (tests unavailable). To calculate the vaccine seroconversion rate, we correlated vaccination records with serologic testing.

2.4 | Statistical analysis

Descriptive statistics were used for subjects’ annual HIV, HCV, and HBV tests, and HBV vaccination rates and immune status. We performed linear regression to determine the association between chronic transfusion duration, adherence to scheduled transfusions, and TTI screening. We calculated adherence to chronic transfusion protocol as a proportion of the number of months a subject received transfusions out of total number of months on the protocol in the study period. Statistical analyses were performed with STATA IC 16.0.11

3 | RESULTS

3.1 | Demographics

Among 144 chronically transfused adults at our center, 85 (59%) who were chronically transfused during the study period were included (Figure 1). Subjects were 23–73 years old (median 34 years [interquartile range—IQR 23–63]), 52% female, and all African American (Table 1). During the study period, eight subjects (9%) received monthly partial manual exchange transfusions, 47 (55%) received monthly automated exchange transfusions and 30 (35%) received partial manual or automated exchanges. The number of subjects on chronic transfusion regimens increased every year. There were 49 chronically transfused subjects in year 1 (Y1) and 85 subjects in Y4 and Y5. Forty-nine subjects (57.6%) received chronic transfusions for more than 4 years. The median number of units transfused per subject per month was 4.3 units (IQR 3.1–6.1). The average annual blood exposure varied. Twelve subjects (14%) received fewer than 25 units per year, 68 (80%) 25–100 units per year, and 5 (6%) over 100 units per year. At the beginning of the study period (baseline), two subjects had positive HIV tests, two had positive HCV tests, two had positive HCV tests, and none were HBV positive and 15 had HBV immunity.

3.2 | TTI screening

Over 5 years, no subjects were screened annually for HIV or HCV; 68 (80%) were screened at least once for HIV and 60 (71%) at least once for HCV (Table 2). No new HIV infections were identified. One subject without previous HCV testing tested positive for HCV. The mode of HCV transmission was unclear and may have preceded initiation of chronic transfusions. HBV testing varied. Fifty-three subjects (62%) were tested for HBsAg, 32 (38%) for anti-HBc and 31 (36%) for anti-HBs. The proportion of subjects screened for HIV, HCV, and HBV decreased over time (Figure 2). Linear regression analysis showed an inverse association between the transfusion duration and receiving annual HIV and HCV testing. Each additional year of transfusion decreased the probability of testing for HIV by 15% (p = .005), for HCV by 14% (p = .001), but not for HBsAg (p = .28) (Figure 3). There was no association between adherence to transfusion and testing rates for HIV, HCV, or HbsAg (Figure 4).

3.3 | HBV serological status, vaccination, and seroconversion

The HBV serologic status and vaccination data are summarized in Tables 3 and 4. Fifty-eight subjects had serologic data and 17 subjects had vaccination data available. For subjects without vaccination data in the EMR, we used PCP and subject records which provided no additional evidence of HBV vaccination.

Among the 58 subjects with HBV testing, 30 (35.3%) had immunity attributable to vaccination, 5 (6%) had evidence of past infection and 23 (27%) had no immunity.
Among the 17 subjects with HBV vaccination documented, 12 had anti-HBs testing and 6 were anti-HBs positive. The time from vaccination to testing did not differ by anti-HBs status (14.2 ± 8.3 years vs 19.5 ± 5.9 years, \( p = .451 \)).

Among subjects born after 1991 (\( n = 19 \)), who were likely vaccinated as infants, 10 had anti-HBs testing and 3 were anti-HBs positive. Another vaccinated after 1 year of age was also positive. Among 66 subjects born before 1991, 12 subjects had vaccination records, 6 had anti-HBs testing and four were anti-HBs positive. Twenty-three subjects were anti-HBs negative, two were subsequently vaccinated, and one of the two demonstrated seroconversion.

4 | DISCUSSION

In this study of chronically transfused adults with SCD, no subjects received annual HIV, HCV, or HBV testing. Screening for HBV immunity was low, and few non-immune subjects were then vaccinated. Screening identified one new HCV infection. These data indicate suboptimal adherence to the 2014 NHLBI SCD guidelines and highlight the need for further studies to define the (1) true risk of TTI in chronically transfused adults with SCD in the USA, (2) clinical resources required to adhere to existing guidelines, and (3) approach to HBV testing to identify new infections, confirm HBV immunity and, when indicated, provide initial or boosting vaccinations.

This study raises the question of whether annual TTI screening targeting only chronically transfused adults with SCD is necessary. No new HIV or HBV infections were identified. The subject with a first, new positive HCV test likely had a community-acquired infection as the Blood Bank did not identify transfusion transmission. These data are consistent with the published low TTI risk from pRBC units in the USA. Patients with SCD have a higher prevalence of HCV and HBV than the general population, but this risk is not specific to chronically transfused patients.5 Chronically transfused patients may, however, have more opportunities to receive screening because of their regular health care system contact.5–7

Our sample size is too small to draw definitive conclusions about the efficacy of annual TTI screening and suggests that less frequent screening may be reasonable. Large population-based studies and economic analyses are needed to spur a thoughtful examination of the efficacy of annual TTI screening for adults with SCD.

Barriers to TTI testing for adults with SCD require consideration.7–11 Annual TTI testing may be ordered separately from standing monthly transfusion labs and may be missed during phlebotomy because the patient

---

**TABLE 1** Baseline characteristics for the study participants (\( N = 85 \))

| S. no. | Characteristics                        | All patients (\( N = 85 \)) |
|--------|----------------------------------------|----------------------------|
| 1.     | Age: Median (IQR)                      | 34 (23–63)                 |
| 2.     | Female (%)                             | 44 (51.8%)                 |
| 3.     | African-American, \( N \) (%)          | 85 (100%)                  |
| 4.     | Cumulative no. of patients on chronic transusions by year |
|        | Y1                                      | 49 (57.6%)                 |
|        | Y2                                      | 66 (77.6%)                 |
|        | Y3                                      | 81 (95.3%)                 |
|        | Y4                                      | 85 (100%)                  |
|        | Y5                                      | 85 (100%)                  |
| 5.     | Duration of chronic transfusion, \( N \) (%) |
|        | 1–2 years                               | 4 (4.7%)                   |
|        | 2–3 years                               | 15 (17.6%)                 |
|        | 3–4 years                               | 17 (20.0%)                 |
|        | >4 years                                | 49 (57.6%)                 |
| 6.     | Average number of pRBC units received per year, \( N \) (%) |
|        | <2 units                                | 12 (14.1%)                 |
|        | 3–8 units                               | 68 (80%)                   |
|        | >8 units                                | 5 (5.9%)                   |

Abbreviations: IQR, interquartile range; pRBC, packed red blood cells; Y, year.
does not know to ask for this additional testing or the phlebotomist does not recognize this as part of the orders. At some centers, lack of knowledge of the guideline may be a barrier to implementation. At our center, it is more often that providers who know this recommendation must prioritize more acute concerns or are not consulted during blood draws that occur away from the center. A “Best Practice Advisories” is now implemented in our EMR to prompt providers about indicated and overdue TTI screening. Lack of systematic use of this prompt, “alert fatigue” and decisions to override such reminders impede successful implementation of this EMR-based strategy.

This study raises several issues related to HBV testing and vaccination. First, the NHLBI guidelines do indicate an approach to HBV testing or clarify whether HBV vaccination is the province of the SCD specialist or primary care doctor. Testing in our population was inconsistent and (re)vaccination infrequent. At our center, we usually defer this vaccine to PCPs. Second, whether measures of immune response to vaccination are valid for individuals with SCD is unclear. In the general population, anti-Hbs seroconversion after vaccination does not always occur and can be lost over time. SCD may lead to impaired seroconversion to vaccinations due to abnormalities in lymphocyte subsets and functional asplenia. In one study, children with SCD had lower rates of seroconversion after HBV vaccination than unaffected children. This study, fewer than 50% of vaccinated subjects had positive anti-HBs and HBV-vaccinated adults averaged

### TABLE 2 Screening and test results for HIV, HBV, and HCV

| S. no. | Tested for                      | Status at baseline (n = 85) | Tested at least once during the study period (n = 85) | Never tested (n = 85) |
|--------|--------------------------------|-----------------------------|-----------------------------------------------------|---------------------|
|        |                                | Positive (%) | Negative (%) | Unknown (%) | No. tested (%) | Positive |       |       |
| 1.     | HIV infection                  | 2 (2.2)      | 74 (87.1)    | 9 (9.7)     | 68 (80.0)     | 0        | 9 (9.7) |
| 2.     | HCV infection                  | 2 (2.2)      | 74 (87.1)    | 9 (9.7)     | 60 (70.5)     | 1        | 9 (9.7) |
| 3.     | HBV infection (HBsAg)          | 0 (0)        | 70 (82.3)    | 15 (16.1)   | 53 (62.4)     | 0        | 15 (16.1) |
| 4.     | HBV infection (anti-HBc)       | 1 (1.1)      | 45 (52.9)    | 39 (41.9)   | 32 (37.6)     | 5        | 39 (41.9) |
| 5.     | HBV immunity (anti-HBs)        | 15 (1.6)     | 34 (40.0)    | 36 (38.7)   | 31 (36.4)     | 15       | 36 (38.7) |

Abbreviations: Anti-HBc, hepatitis B core antibody; Anti-HBs, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

### FIGURE 2 Trends of testing for the transfusion transmitted infections in the last 5 years (n = 85). Anti-HBc, hepatitis B core antibody; Anti-HBs, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; Y1-5, Year1-5 [Color figure can be viewed at wileyonlinelibrary.com]
16 years between HBV vaccination and testing. Young people with SCD born after implementation of HBV vaccination in infancy continue to age into adult care, it is reasonable to expect that many more will have been vaccinated as infants.9 Interpreting a negative anti-HBs test result in this setting is complex as this may occur among vaccinated individuals in need of a booster, never-vaccinated individuals in need of vaccination and vaccine nonresponders. Economic analysis would help quantify the cost utility of different approaches to HBV testing and vaccination, which could strengthen policy and clinical guidelines. Of course, there is an ethical argument for optimizing vaccine efforts as vaccine-preventable HBV infection in individuals with SCD is unacceptable.

This study highlights that complex SCD care requires a high level of clinical coordination and resources.26,27 Adults with SCD require resource intensive care and are underserved, a consequence of improved pediatric survivorship and long-standing inequities in funding for research and clinical care.27,28 In the pediatric setting, quality improvement interventions for high-stakes SCD guideline adherence require patient tracking programs, information sessions for parents, and specialized ancillary staff.29 These resources, which are often inadequate in pediatric SCD settings, are woefully missing from most of adult SCD care settings. Nonadherence to the NHLBI guidelines may be partly attributable to our Center’s clinical load: TTI testing rates declined as the number of individuals on chronic transfusions expanded. This concern highlights why some centers support nurses, advanced practice providers and/or physicians who may even be double boarded in hematology and transfusion medicine to focus on the complex care of chronically transfused adults with SCD.
Our study has several limitations. This is a single-center study in a high-income country with a small number of patients. Given that viral testing was not undertaken routinely, this study may underestimate the prevalence of TTI in adults with SCD. HIV, HCV, and HBV may be community acquired, and we did not assess patients’ high-risk behaviors. We excluded on-demand transfusions, precluding assessment of the risk of

![Figure 4](https://example.com/figure4.png)

**Figure 4** Scatter plot of subject adherence (%) to regular transfusions and average number of TTI tests per year. Each dot represents a study subject. The x-axis shows the subject adherence (%) to regular transfusions. Adherence was calculated as a proportion of number of months the subject received transfusion over the total number of months the subject was on transfusions. The y-axis shows the average number of (A) HIV (B) HCV and (C) HBV tests performed for each subject per year during the study period. There was no association of TTI testing with subject adherence to regular transfusions ($p > .05$). HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HIV, human immunodeficiency virus; TTI, transfusion transmitted infections [Color figure can be viewed at wileyonlinelibrary.com]

**Table 3** Serological status of hepatitis B in the study subjects raises concern for suboptimal testing and vaccination ($N = 85$)

| Serological status          | HBsAg | Anti-HBc | Anti-HBs | Born after 1991 ($n = 19$) | Born in 1991 or before ($n = 66$) |
|----------------------------|-------|----------|----------|---------------------------|----------------------------------|
| Current infection           | +     | –        | –        | 0                         | 0                                |
| Past infection              | –     | +        | +        | 0                         | 5                                |
| Immunity following vaccination | –   | –        | +        | 3                         | 27                               |
| Absence of immunity         | –     | –        | –        | 6                         | 17                               |
| Unknown status              | NA    | NA       | NA       | 10                        | 17                               |

Abbreviations: Anti-HBc, hepatitis B core antibody; Anti-HBs, hepatitis B surface antibody; HBV, hepatitis B virus.
infections from sporadic transfusions. Complete vaccination data were not available, so we could not calculate vaccine seroconversion rates for all the subjects. We did not study why TTI serological tests that were ordered were not performed. Finally, regional context determines blood supply safety. Separate studies could address TTI testing strategies for individuals with SCD living in countries where TTI risk from blood products is higher.4,30

In conclusion, adherence to the NHLBI Screening guidelines for TTI in adults with SCD on chronic transfusion was low as was the diagnosis of new TTI. This evidence forms the basis for our ongoing effort to determine best practice for TTI screening and highlights the need for further information about HBV vaccine immunogenicity, and the cost-effectiveness of the NHLBI guidelines recommendation.

CONFLICT OF INTEREST
The authors have disclosed no conflicts of interest.

ORCID
Vignesh Chidambaram https://orcid.org/0000-0002-4240-1027
Evan M. Bloch https://orcid.org/0000-0001-8181-9517

REFERENCES
1. Howard J. Sickle cell disease: when and how to transfuse. Hematology Am Soc Hematol Educ Program. 2016;2016:625–31.
2. National Heart, Lung, and Blood Institute. Evidence-based management of sickle cell disease: expert panel report. Washington, DC: National Institutes of Health; 2014.p. 161.
3. Kleinman S, Stassinopoulos A. Risks associated with red blood cell transfusions: potential benefits from application of pathogen inactivation. Transfusion. 2015;55:2983–3000.
4. Busch MP, Bloch EM, Kleinman S. Prevention of transfusion-transmitted infections. Blood. 2019;133:1854–64.
5. Master S, Patan S, Cingam S, Mansour RP. Prevalence of chronic hepatitis B, hepatitis C and HIV in adult patients with sickle cell disease. Blood. 2016;128:4863–3.
6. Hassan M, Hasan S, Castro O, Giday S, Banks A, Smoot D. HCV in sickle cell disease. J Natl Med Assoc. 2003;95:864–74.
7. Nouraei M, Nekhai S, Gordeuk VR. Sickle cell disease is associated with decreased HIV but higher HBV and HCV comorbidities in US hospital discharge records: a cross-sectional study. Sex Transm Infect. 2012;88:528–33.
8. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42:377–81.
9. Yusuf H, Daniels D, Mast EE, Coronado V. Hepatitis B vaccination coverage among United States children. Pediatr Infect Dis J. 2001;20:530–3.
10. Ramachandran S, Groves JA, Xia G-L, Saá P, Notari EP, Drobeniuc J, et al. Recent and occult hepatitis B virus infections among blood donors in the United States. Transfusion. 2019;59:601–11.
11. StataCorp. Stata statistical software: release 16. College Station, TX: StataCorp LLC; 2019.
12. Belamarich PF, Gandica R, Stein REK, Racine AD. Drowning in a sea of advice: pediatricians and American Academy of Pediatrics policy statements. Pediatrics. 2006;118:e964–78.
13. Bejanki H, Mamba L, Beal S, Radhakrishnan N, Bishnoi R, Shah C, et al. The role of a best practice alert in the electronic medical record in reducing repetitive lab tests. ClinicoEconomics Outcomes Res. 2018;10:611–8.
14. with the HITEC Investigators, Ancker JS, Edwards A, Nosal S, Hauser D, Mauer E, et al. Effects of workload, work complexity, and repeated alerts on alert fatigue in a clinical decision support system. BMC Med Inform Decis Mak. 2017;17:36.
15. Lunyera J, Jonassaint C, Jonassaint J, Shah N. Attitudes of primary care physicians toward sickle cell disease care, guidelines, and comanaging hydroxyurea with a specialist. J Prim Care Community Health. 2017;8:37–40.
16. Shepard CW, Simard EP, Finelli L, Fiore AE, Bell BP. Hepatitis B virus infection: epidemiology and vaccination. Epidemiol Rev. 2006;28:112–25.
17. Middleton AB, Baker CJ, Kozinetz CA, Kamili S, Nguyen C, Hu DJ, et al. Duration of protection after infant hepatitis B vaccination series. Pediatrics. 2014;133:e1500–7.
18. Sahana HV, Sarala N, Prasad SR. Decrease in anti-HBs antibodies over time in medical students and healthcare workers after hepatitis B vaccination. Biomed Res Int. 2017;2017:1–5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5634973/
19. Pondé RA de A. Expression and detection of anti-HBs antibodies after hepatitis B virus infection or vaccination in the context of protective immunity. Arch Virol. 2019;164:2645–58.
20. Nagant C, Barbezange C, Dedeken L, Besse-Hammer T, Thomas I, Mahadeb B, et al. Alteration of humoral, cellular and cytokine immune response to inactivated influenza

| TABLE 4 Documented HBV vaccination and anti-HBs positivity rates among these in the study participants (N = 85) |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Time of birth                  | Presumed HBV vaccination (infancy) | Documented HBV vaccination (>1 year old) |
| Total                          | Tested for anti-HBs       | Anti-HBs+        | Total                          | Tested for anti-HBs       | Anti-HBs+        |
| Born after 1991 (n = 19)       | 19                        | 10              | 3                              | 1                             | 1                |
| Born in 1991 or before (n = 66)| 0                         | 0               | 0                              | 12                           | 6                |

Abbreviations: Anti-HBs, hepatitis B surface antibody; HBV, hepatitis B virus.
21. Balandya E, Reynolds T, Obaro S, Makani J. Alteration of lymphocyte phenotype and function in sickle cell anemia: implications for vaccine responses. Am J Hematol. 2016;91:938–46.

22. William BM, Corazza GR. Hyposplenism: a comprehensive review. Part I: basic concepts and causes. Hematology. 2007;12:1–13.

23. Sarnaik SA, Merline JR, Bond S. Immunogenicity of hepatitis B vaccine in children with sickle cell anemia. J Pediatr. 1988;112:429–30.

24. Cotte C, Szczepanek SM. Peritoneal B-1b and B-2 B-cells confer long-term protection from pneumococcal serotype 3 infection after vaccination with Prevnar-13 and are defective in sickle cell disease mice. Vaccine. 2017;35:3520–2.

25. Hord J, Windsor B, Koehler M, Blatt J, Janosky J, Mirro J. Diminished antibody response to hepatitis B immunization in children with sickle cell disease. J Pediatr Hematol Oncol. 2002;24:548–9.

26. Kanter J, Jordan LB. Improving the healthcare model for management of adults with sickle cell disease in the PPACA era. J Hematol Transfus. 2015;3(1037):1–3.

27. Kanter J, Smith WR, Desai PC, Treadwell M, Andemariam B, Little J, et al. Building access to care in adult sickle cell disease: defining models of care, essential components, and economic aspects. Blood Adv. 2020;4:3804–13.

28. National Academies of Sciences, Engineering, and Medicine. Addressing sickle cell disease A strategic plan and blueprint for action National Academies. https://www.nationalacademies.org/our-work/addressing-sickle-cell-disease-a-strategic-plan-and-blueprint-for-action

29. Eckrich MJ, Wang WC, Yang E, Arbogast PG, Morrow A, Dudley JA, et al. Adherence to transcranial Doppler screening guidelines among children with sickle cell disease. Pediatr Blood Cancer. 2013;60:270–4.

30. Alkindi S, Al-Umairi N, Pathare A. Prevalence of hepatitis B, hepatitis C and HIV in sickle cell disease patients from Oman. Blood. 2018;132(Supplement 1):4916–6.

How to cite this article: Chidambaram V, Jones JM, Lokhandwala PM, et al. Low rates of transfusion-transmitted infection screening in chronically transfused adults with sickle cell disease. Transfusion. 2021;61:2421–2429. https://doi.org/10.1111/trf.16547