

Vaccination rates among adults with sickle cell disease: a single-center study from the Eastern Mediterranean region of Turkey

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ABSTRACT

Objective: Being vaccinated against encapsulated bacteria is the most efficient way to reduce painful crises and mortality in patients with sickle cell disease (SCD). Although guidelines strongly recommend vaccination, vaccination rates remain under the desired levels. In this study, we aim to determine vaccination rates and understand the reasons for non-vaccination in patients with SCD.

Material and methods: We included 76 patients with SCD in this study. We administered a questionnaire consisting of 21 questions and examined the electronic vaccination records of these patients.

Results: The vaccination rates were 36.5% for the pneumococcal vaccine, 22.4% for the Hemophilus influenza type b vaccine, and 19.7% for the meningococcal vaccine. Residence in rural areas and annual control visits were found to increase the pneumococcal vaccination rates (OR: 11.90, 95% CI: 2.549–56.107, $p = 0.002$ and OR: 9.08, 95% CI: 1.120–73.624, $p = 0.039$, respectively) and meningococcal vaccination rates (OR: 2.75, 95% CI: 1.464–5.186, $p = 0.002$ and OR: 1.36, 95% CI: 1.159–1.610, $p < 0.001$, respectively). Thirty-four (44.7%) of the cases stated that their doctors did not give any information about these vaccinations.

Conclusion: Vaccination rates are low in patients with SCD. Residence in rural areas, annual control visits, educational level, and doctor recommendations affect these vaccination rates.

Keywords: Vaccination rates, sickle cell disease, reasons for non-vaccination

INTRODUCTION

Sickle cell disease (SCD) is the most common hemoglobinopathy worldwide. Impaired splenic functions, complement activation and opsonization cause increased susceptibility to infections in this disease (1). Infections, especially those caused by encapsulated microorganisms (Streptococcus pneumonia, Neisseria meningitidis, Hemophilus influenza), are the leading causes of painful crises and mortality in SCD (2).

Various studies reveal that vaccinations against encapsulated bacteria significantly decrease both infections and mortality in pediatric patients with SCD (3, 4). Current guidelines also strongly recommend vaccinations in adults with SCD (5).

However, despite the evidence regarding the importance of these vaccines for individuals with SCD, adherence to the recommended immunization schedule remains a concern around the world (6). A retrospective cohort study on a Medicaid sample shows that patients with SCD have an adherence rate of 43.4% for the 23-valent pneumococcal polysaccharide vaccine (PPSV23) (7).

Subsequent studies in the pediatric age group also state that patients with SCD still have low immunization rates (8, 9). The situation is even worse in Turkey. According to Korur et al., only 21.5% of adult patients with SCD are vaccinated against S. pneumonia (10).

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There are insufficient studies in the adult age group about this vital topic, and these works are only about influenza and pneumococcal vaccinations. There are no studies about other vaccinations in adult patients with SCD, especially those against *N. meningitidis* and *H. influenzae* type b (11). Therefore, we aim to determine such vaccination rates and identify the reasons for non-vaccination in these patients.

MATERIAL and METHODS

The study comprises 76 patients with SCD admitted to the Mersin University hematology outpatient clinic between January 2020 and March 2020. The participants were asked to complete a questionnaire, which is described in Supplemental file. A hematologist was available to address their questions concerning the questionnaire. In addition to the questionnaire, the patients' hospital electronic health records regarding vaccinations were evaluated. The demographic characteristics, SCD phenotype, clinical visits per year, and replies of the patients were documented. Patients who were in vaso-occlusive crises and younger than 18 years were excluded. This study was performed in accordance with the Declaration of Helsinki, and the ethics committee of Mersin University approved this work (Approval number: 2020/13/439). Written consent was obtained from all participants.

Statistical Method: Statistical analysis was performed with SPSS Statistics 22.0 for Windows. The categorical parameters were expressed as numbers (n) and percentages (%). Whether the numerical parameters had a normal distribution was determined using a histogram, variation coefficients, and the Kolmogorov-Smirnov test. The chi-square or Fisher's exact test was used to compare the categorical variables. We performed univariate analyses to detect variables associated with the vaccination rate of each vaccine type. Parameters with a p-value of < 0.200 were included in a multivariate analysis to identify factors that were independently associated with the vaccination rates. A p-value of < 0.05 was considered statistically significant.

RESULTS

A total of 76 patients were included in this study. Some characteristics of the patients are listed in Table 1. The vaccination rates were 36.5% for the pneumococcal vaccine, 22.4% for the Hib vaccine, and 19.7% for the meningococcal vaccine. The 11 (14.5%) patients with a history of splenectomy had all three vaccines. There was no difference between genders in the vaccination rates.

In total, 42 (55.3%) of the patients stated that their doctors gave information about the vaccinations. Twenty-six (61.9%) of these 42 patients had at least one dose of the pneumococcal vaccine. A total of 26 (51%) of the 51 patients living in rural areas had at least one dose of the pneumococcal vaccine. Individuals living in rural areas had a significantly higher vaccination rate compared with those who resided in urban areas ($p < 0.001$). Ten of the 16 patients who had educational levels of college or higher received the pneumococcal vaccine. The difference between this group and those with other educational levels was significant ($p = 0.022$).

While 14 (27.5%) of the 51 patients living in rural areas had the meningococcal vaccine, only 1 (4%) of the 25 patients

living in urban areas had the same vaccine ($p < 0.001$). Twelve of the patients who received vaccination recommendations from their doctors had the meningococcal vaccine. The difference between this group and those who were not recommended vaccination was significant ($p = 0.007$). No significant difference was noticed between educational levels in meningococcal vaccination.

Residence in rural areas and doctors' recommendations did not significantly differentiate Hib vaccination. The only significant point in terms of Hib vaccination was the educational level. Seven of the 16 patients who had an educational level of college or higher received the Hib vaccine ($p = 0.049$).

Findings showed that as the number of people living in the same house decreased and the number of annual control visits increased, the rates of pneumococcal and meningococcal vaccination increased significantly ($p < 0.001$), but the change in the Hib vaccination rate was insignificant. Variables that significantly affected the vaccination rates in the univariate analyses were then included in a multivariate analysis, and the results are summarized in Table 2.

Regarding the reasons for not being vaccinated against *S. pneumoniae*, 34 (44.7%) of the patients answered, 'I did not know its necessity,' which was the most common reason (Figure 1). Figures 2 and 3 show the responses of the patients who did not have the Hib and meningococcal vaccines, respectively.

Table 1: Some characteristics of the patients (N = 76)

Characteristics	Value
Gender, n (%)	
Female	44 (57.9%)
Male	32 (42.1%)
Age, yr, mean (range)	34.3 (18–58)
SCD phenotype, n (%)	
HbSS	67 (88.1%)
HbSB	9 (11.9%)
Educational status, n (%)	
Elementary school graduate	29 (38.2%)
Middle school graduate	9 (11.8%)
High school graduate	22 (28.9%)
College or higher graduate	16 (21.1%)
Living area of the patient	
Urban area	25 (32.9%)
Rural area	51 (67.1%)
Splenectomy	11 (14.5%)
Number of people living in the same house	
1	1 (1.3%)
2	8 (10.5%)
3	15 (19.7%)
4	22 (28.9%)
5	22 (28.9%)
6	7 (9.2%)
7	1 (1.3%)
Control visits per year	
0	12 (15.8%)
1–3	31 (40.8%)
4–7	22 (28.9%)
8–12	11 (14.5%)
Vaccination rates	
<i>S. pneumoniae</i>	28 (36.8%)
<i>N. meningitidis</i>	15 (19.7%)
<i>H. influenzae</i> type b	17 (22.4%)

Table 2: Significant factors affecting vaccination rates (multivariate analyses)

	OR	%95 CI	p-value
Pneumococcal vaccination rate			
Residence in rural area	11.90	2.549–56.107	0.002
Doctor recommendation	36.23	2.690–488.270	0.007
Annual control visits	2.75	1.464–5.186	0.002
Meningococcal vaccination rate			
Residence in rural area	9.08	1.120–73.624	0.039
Annual control visits	1.36	1.159–1.610	< 0.001
H. influenza vaccination rate			
Educational level of college or higher	3.88	1.173–12.893	0.026

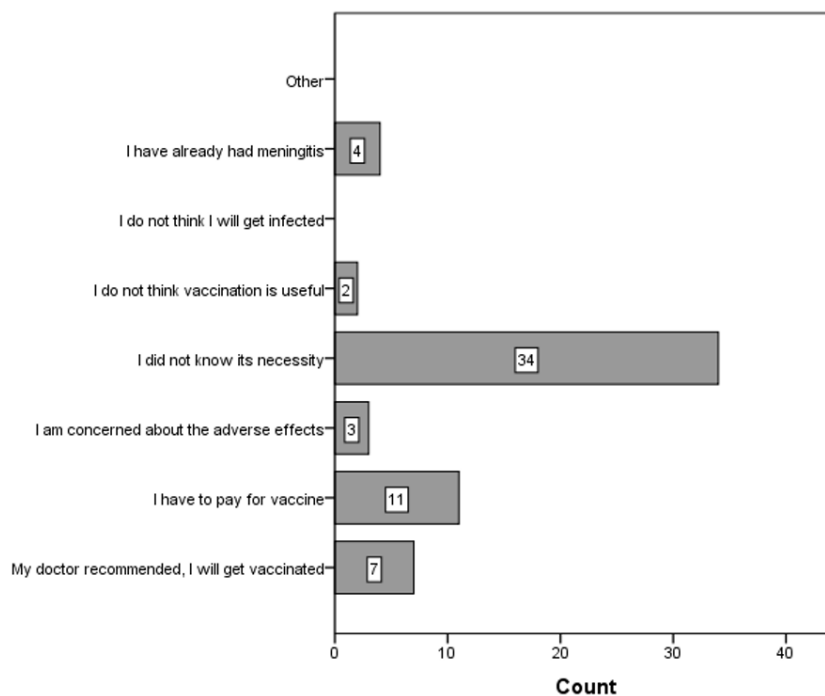


Figure 1: Reasons for not being vaccinated against S. pneumonia

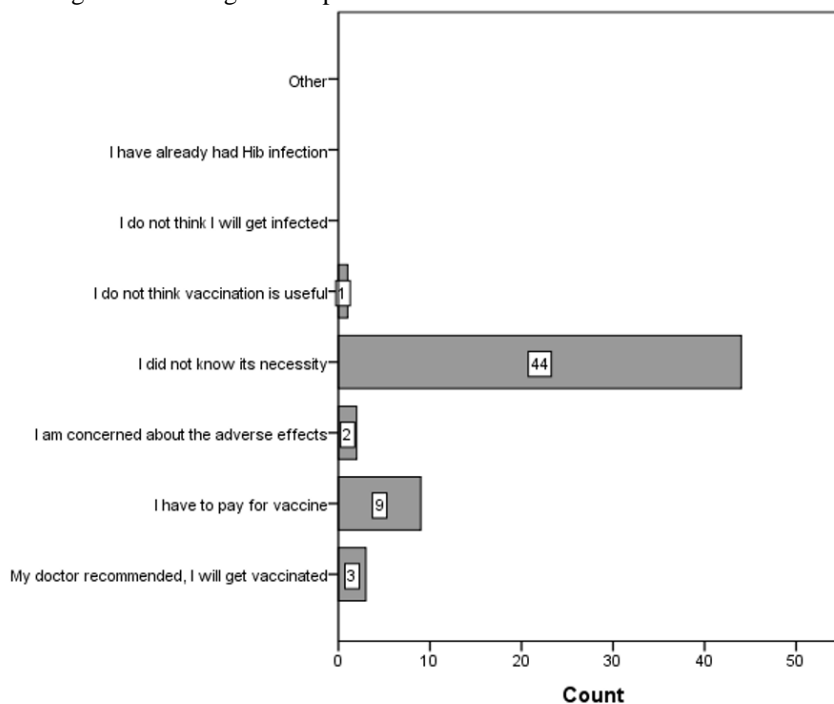


Figure 2: Reasons for not being vaccinated against H. Influenza type b

DISCUSSION

According to the National Institute of Health (NIH) expert panel report in 2014, all individuals with SCD should be immunized as recommended by the Advisory Committee on Immunization Practices (ACIP)(5). Adults aged ≥ 19 years with SCD who have not received the 13-valent pneumococcal conjugate vaccine (PCV13) or 23-valent pneumococcal polysaccharide vaccine (PPSV23) should receive one dose of PCV13 first, followed by a dose of PPSV23 at least eight weeks later. A second PPSV23 dose five years after the first PPSV23 dose is recommended. One dose of the Hib vaccine (if the patient has not received it) and the meningococcal vaccine with five-year boosters are also strongly recommended. Hepatitis B and yearly influenza vaccinations are likewise advocated. Studies show that pneumococcal infections are the leading cause of mortality and morbidity in patients with SCD; correspondingly, vaccination is effective in these patients(12). Therefore, an active immunization schedule should be maintained throughout life, beginning in infancy. In Turkey, pneumococcal vaccination was added to the routine childhood immunization schedule in 2009. In contrast, H. influenza and meningococcal vaccines are not part of the routine schedule yet.

This study demonstrates poor vaccination rates against encapsulated bacteria. According to Infanti et al., even in countries whose routine immunization schedules cover all three encapsulated bacteria, the pneumococcal and meningococcal vaccination rates are only 77% and 25%, respectively(13). A study on adult and pediatric patients in the United Kingdom revealed that only 21% of adult patients and 72% of pediatric patients are vaccinated against *S. pneumonia*(14). Nero et al. showed that children with SCD have a vaccination rate of 75% against *S. pneumonia*, and patients with SCD have higher adherence to vaccination than the normal pediatric age population(8). A recent pediatric study showed that only about 50% of patients with SCD had received both the first dose and boosters of the pneumococcal vaccine(9). According to another comprehensive study, the total dose vaccination rate against *S. pneumonia* in children is merely around 35%. Existing studies about this issue mainly include patients in the pediatric age group. There are very few works regarding vaccination profiles in the adult age group. Therefore, vaccination rates among adult patients with SCD are poor, as our study also verifies. A previous work from Turkey stated that only 21.5% of adult patients with SCD are vaccinated against *S. pneumonia*(9). The numbers are even worse for Hib and *N. meningitidis* vaccinations. Our results seem similar to those from a few published studies, including those on adults, regarding pneumococcal vaccination rates. However, we could not find studies about H. influenza or *N. meningitidis* vaccination rates in adult patients with SCD. Therefore, this study may be the first to show that vaccination rates against these two bacteria are worse than pneumococcal vaccination rates.

A survey was prepared to understand precisely the reasons for non-vaccination. The answers of the unvaccinated patients indicate massive problems in informing patients about the importance of being vaccinated. The number of patients who did not receive vaccination despite their doctors' recommendations is relatively low. Thus, a significant factor behind the low vaccination rates in these patients is lack of

information and recommendation from health care providers. Therefore, ways should be established to increase these patients' awareness of vaccination. Studies have been performed to address this issue. Korur et al. evaluated the effectiveness of electronic medical record (EMR) systems, which inform health care providers about the immunization status of patients and upcoming vaccination dates(10). In this study, the influenza vaccination rates increased to 49.2% from 23.7%, and the pneumococcal vaccination rates became 50.8% from 20.3% after the use of an alert intervention EMR system. In some studies, the use of a database to send reminders about high-risk pediatric patients, followed by recall letters for unvaccinated patients, showed increases in both influenza and pneumococcal vaccination rates(15, 16).

According to the patients' answers, another minor problem is their belief that they will have to pay for these vaccines. The general social insurance in Turkey reimburses influenza and pneumococcal vaccines for high-risk patients, whereas meningococcal and H. influenza vaccines are not repaid. This problem should be explained to these patients.

Primary care providers are a potential barrier to vaccination adherence. This may include lack of education about SCD. New studies about the knowledge of primary care providers regarding this high-risk patient population should thus be designed. In addition to lacking knowledge, primary care physicians may not be willing to follow up with these patients and refer them to tertiary care hematology centers. Bundy et al. observed an increased compliance rate for the influenza vaccine in SCD patients who visited their hematologists two or more times per year than those without a hematologist visit(17). In our study, the multivariate analysis showed that the number of annual control visits is an independent factor that increases pneumococcal and meningococcal vaccination rates (Table 2).

In this study, the main problem identified is that most patients do not have sufficient information about vaccination. In our opinion, the first problem to address should be to increase the knowledge of patients about vaccination. This can be done in three ways. First, cooperation between hematologists and primary care clinicians is essential. Since most immunizations are provided at primary care visits, initiatives should be made to increase the awareness of patients in the primary care setting. Second, time should be dedicated to educating these patients and their families about vaccination during their hematology visits. Third, vaccination schedules and notifications about upcoming vaccination dates should be integrated into medical record systems. In this manner, many patients with SCD can be referred to their primary care providers to receive the recommended immunizations.

One of the main limitations of this study is the relatively small sample size (this study is a single-center study). Moreover, the vaccination rates in this work were based on receiving at least one dose of a vaccine. Thus, the numbers do not reflect the completion of the vaccination course.

CONCLUSIONS

In conclusion, patients with SCD are at increased risks of infection and mortality due to encapsulated organisms. Hence, these high-risk patients must adhere to the recommended immunization schedule. However, vaccination

rates are evidently low in patients with SCD, and lack of information about vaccination is a significant factor. Institutions should then identify the barriers to vaccination and strive to solve them.

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