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VACCINATION STATUS AND ITS DETERMINANTS IN CHILDREN WITH SICKLE CELL DISEASE: A CROSS-SECTIONAL STUDY FROM A TERTIARY CARE CENTRE.

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Abstract

Background: Children with sickle cell disease (SCD) are functionally asplenic and highly susceptible to invasive infections by encapsulated bacteria, making complete and extended immunization a critical preventive intervention. The present study aimed to assess national and extended immunization coverage and to identify the determinants influencing vaccination status in children with SCD attending a tertiary care centre in Central India. Methods: A hospital-based, cross-sectional, analytical study was conducted over one year. One hundred and fifty children aged 1–18 years with laboratory-confirmed SCD were enrolled by consecutive sampling. Vaccination status was verified from immunization cards, discharge summaries, and medical records, supplemented by structured caregiver interview. Immunization coverage was classified against the National Immunization Schedule and an extended schedule recommended for SCD. Data were analysed using SPSS version 25.0; the chi-square test was applied, with $p<0.050$ considered statistically significant. Results: The HbSS phenotype predominated (70.0%). National immunization coverage was 64.0% fully immunized, 34.0% partially immunized, and 2.0% unimmunized. Vaccine-wise coverage declined progressively from 97.3% at birth to 61.8% at 10 years. Extended immunization coverage was markedly low (20.0% fully immunized; 67.3% unimmunized), with pneumococcal (PPSV23, 26.0%) and meningococcal (MenACWY, 25.3%) uptake being poor. Caregiver awareness regarding the importance of vaccination was the strongest determinant of both national ($p<0.001$) and extended ($p=0.029$) immunization, while the presence of affected siblings was associated with national immunization ($p=0.050$). Maternal, paternal, and demographic factors, including education, employment, religious belief, and distance to the vaccination centre, showed no statistically significant association. Conclusions: National immunization coverage is moderate but extended immunization coverage is critically low in children with SCD, leaving a high-risk population inadequately protected. Awareness is the key modifiable determinant. Integration of SCD-specific vaccines into routine follow-up, caregiver education, and subsidised access are essential to close this preventive-care gap.

Keywords: Sickle Cell Disease; Immunization; Vaccination Coverage; Pneumococcal Vaccines; Meningococcal Vaccines; Health Awareness; Child.

INTRODUCTION

Sickle cell disease (SCD) is one of the most common inherited haemoglobinopathies worldwide, arising from a point mutation in the β-globin gene that leads to the production of haemoglobin S. Under deoxygenated conditions, haemoglobin S polymerises, producing rigid, sickle-shaped erythrocytes that drive chronic haemolysis, recurrent vaso-occlusion, and progressive multi-organ injury (1). A pivotal immunological consequence of SCD is the early onset of functional asplenia, which results from repeated splenic infarction during early childhood. Because the spleen is central to the clearance of poorly opsonised, encapsulated organisms, loss of splenic function substantially impairs host defence (2).

As a result, children with SCD are highly susceptible to severe and invasive infections, particularly those caused by Streptococcus pneumoniae, Haemophilus influenzae type b, and Neisseria meningitidis (3). This susceptibility is compounded by defective opsonisation, impaired phagocytosis, complement pathway abnormalities, and a chronic pro-inflammatory state. Globally, SCD represents a major public health concern; the burden is disproportionately high in low- and middle-income countries, and in India it is especially prevalent in central, western, and tribal regions (4). Even in well-resourced health systems, children with SCD continue to experience a higher risk of infection-related complications than their healthy peers (5).

Vaccination is among the most effective and evidence-based measures to reduce infection-related morbidity and mortality in SCD. Beyond the routine vaccines provided under national immunization programmes, children with SCD require an extended immunization schedule to protect against high-risk pathogens, including pneumococcal conjugate and polysaccharide vaccines, meningococcal vaccines, and booster doses of Haemophilus influenzae type b (6). The introduction of pneumococcal conjugate vaccines, in particular, has substantially reduced invasive pneumococcal disease and transformed survival in this population (7). However, the benefits of immunization depend on timely administration and completion of recommended schedules, and adherence among children with SCD remains suboptimal in many settings, especially for extended vaccines (8,9).

The determinants of vaccination status in SCD are complex and multifactorial, encompassing caregiver education and awareness, socioeconomic status, accessibility of services, health-seeking behaviour, and provider counselling. International guidelines therefore recommend accelerated, early, and augmented immunization for immunocompromised hosts (10), often combined with antibiotic prophylaxis (11).

Despite the high prevalence of SCD in India, comprehensive data on vaccination coverage and its determinants among affected children are scarce, with most Indian studies focusing on clinical manifestations and complications rather than preventive care. The present study was therefore undertaken to assess national and extended immunization coverage and to identify the determinants influencing vaccination status in children with SCD attending a tertiary care centre in Central India.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based, cross-sectional, analytical study was conducted in the Department of Paediatrics of a Tertiary Care Health Centre, a referral centre for hemoglobinopathies serving urban, rural, and tribal populations of Central India. The study was carried out over a period of one year following approval from the Institutional Ethics Committee. It was conducted in accordance with the ethical standards of the Declaration of Helsinki. Written informed consent was obtained from all parents or legal guardians, and assent was obtained from children older than 12 years where appropriate. Confidentiality was maintained and participation did not interfere with routine care.

Participants

Inclusion criteria. All children aged 1–18 years with a confirmed diagnosis of SCD—based on documented haemoglobin electrophoresis or high-performance liquid chromatography—presenting to the paediatric outpatient or inpatient services during the study period were eligible, irrespective of sex, socioeconomic stratum, or residence.

Exclusion criteria. Children whose vaccination status could not be reliably ascertained (no immunization card, discharge summary, or dependable caregiver history) were excluded to avoid misclassification. Children whose caregivers declined consent, or who were clinically unstable at the time of contact, were not enrolled until stable and consent could be appropriately obtained.

Study Procedures

Eligible participants were enrolled by consecutive sampling. Caregivers were interviewed using a pre-designed, structured proforma capturing demographic, maternal, paternal, familial, and disease-related variables. Vaccination status was verified against immunization cards, discharge summaries, and medical records wherever available; where documentation was unavailable, caregiver-reported history was recorded after detailed questioning.

Clinical records were reviewed for phenotype, complications, transfusion and splenectomy history, and hospital admissions. Vaccination status was classified as complete for age, incomplete for age, or unimmunized, and analysed separately for National Immunization Schedule vaccines and for the extended schedule recommended for children with SCD (pneumococcal and meningococcal vaccines). Data were collected by a single principal investigator to minimise inter-observer variation.

Sample Size

Sample size was calculated using Cochran's formula, $n = Z^2PQ/d^2$, with $Z = 1.96$ (95% confidence interval), $P = 6\%$ (estimated prevalence of SCD in India) (12), $Q = 94\%$, and $d = 5\%$ (absolute margin of error). The minimum required sample was 87 children; to strengthen the analytical component, a total of 150 children were enrolled.

Statistical Analysis

Data were entered into Microsoft Excel and analysed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation and categorical variables as frequencies and

percentages. Associations between immunization status and determinants were assessed using the chi-square test. A p-value <0.050 was considered statistically significant.

RESULTS

A total of 150 children with SCD were studied. The population spanned infancy to adolescence, with the largest proportion aged 10–18 years (45.3%), followed by 5–<10 years (31.3%), 2–<5 years (16.7%), and <2 years (6.7%). Females (52.0%) slightly outnumbered males (48.0%). The homozygous HbSS phenotype predominated (70.0%), with HbSβ-thalassaemia accounting for the remainder (30.0%).

Most families belonged to lower and middle socioeconomic strata, and parental education was limited, with 36.7% of mothers and 34.0% of fathers being illiterate. Awareness regarding SCD was present in 65.3% of caregivers, but awareness regarding the importance of vaccination was lower (42.0%) (Table 1).

Table 1. Sociodemographic, parental, and familial profile of study participants (N=150).

Characteristic	Category	n	%
Age group	<2 years	10	6.7
	2–<5 years	25	16.7
	5–<10 years	47	31.3
	10–18 years	68	45.3
Sex	Female	78	52.0
	Male	72	48.0
Socioeconomic status	Lower	34	22.7
	Lower middle	37	24.7
	Upper lower	36	24.0
	Upper middle	32	21.3
	Upper	11	7.3
Maternal education	Illiterate	55	36.7
	Primary	53	35.3
	Middle school	31	20.7
	Higher secondary	11	7.3
Maternal employment	Non-working	108	72.0
	Working	42	28.0
Paternal education	Illiterate	51	34.0
	Primary	54	36.0
	Middle school	31	20.7
	Higher secondary	14	9.3
Paternal employment	Working	150	100.0
Religious belief against vaccination	Present	12	8.0
	Absent	138	92.0
Distance to vaccination centre	Near (<2 km)	78	52.0
	Far (>2 km)	72	48.0
Awareness regarding SCD	Aware	98	65.3
	Not aware	52	34.7
Awareness regarding importance of vaccination	Aware	63	42.0
	Not aware	87	58.0

SCD = sickle cell disease.

Vaso-occlusive crisis was the most common complication (53.3%), followed by severe anaemia (26.7%), acute chest syndrome (12.0%), and splenic sequestration (11.3%). A history of infection was documented in 50.7% of children, and a very high proportion had received blood transfusion (93.3%). Hospital admissions were frequent, with most children admitted two or more times (Table 2). Clinical manifestations varied significantly by phenotype: vaso-occlusive crisis was more frequent in HbSS (77.5%; p=0.032) and transfusion more common in HbSS (p=0.032), whereas splenic sequestration was predominantly seen in HbSβ-thalassaemia (82.4%; p<0.001) and all five splenectomies occurred in this subgroup (p=0.001).

Table 2. Clinical profile and phenotype of study participants (N=150).

Characteristic	n	%
Phenotype: HbSS	105	70.0
Phenotype: HbSβ-thalassaemia	45	30.0
Vaso-occlusive crisis	80	53.3
Severe anaemia	40	26.7
Acute chest syndrome	18	12.0
Splenic sequestration	17	11.3
Sickle hepatopathy	5	3.3
History of infection	76	50.7
History of blood transfusion	140	93.3
History of splenectomy	5	3.3
Hospital admissions: 1	36	24.0
Hospital admissions: 2	38	25.3
Hospital admissions: 3	26	17.3
Hospital admissions: 4	25	16.7
Hospital admissions: 5	25	16.7

HbSS = homozygous sickle cell disease; HbSβ = sickle β-thalassaemia.

National immunization coverage showed that 64.0% of children were fully immunized, 34.0% were partially immunized, and 2.0% were unimmunized. In contrast, extended immunization coverage was markedly low, with only 20.0% fully immunized and 67.3% unimmunized. Special vaccine uptake was poor: 26.0% received pneumococcal polysaccharide vaccine (PPSV23) and 25.3% received meningococcal conjugate vaccine (MenACWY) (Table 3).

Table 3. National and extended immunization status and special vaccine coverage (N=150).

Immunization category	Status / Vaccine	n (%)
National immunization	Fully immunized	96 (64.0)
	Partially immunized	51 (34.0)
	Unimmunized	3 (2.0)
Extended immunization	Fully immunized	30 (20.0)
	Partially immunized	19 (12.7)
	Unimmunized	101 (67.3)
Special vaccines	Pneumococcal (PPSV23) received	39 (26.0)
	Meningococcal (MenACWY) received	38 (25.3)

PPSV23 = 23-valent pneumococcal polysaccharide vaccine; MenACWY = quadrivalent meningococcal conjugate vaccine.

A consistent, progressive decline in vaccine coverage was observed across the immunization schedule. Coverage was highest at birth (97.3%) and fell steadily to 89.3% at 6 weeks, 81.3% at 10 weeks, and 72.0% at 14 weeks, declining further to 68.7% at 9–12 months, 65.0% at 16–24 months, 63.5% at 5–6 years, and 61.8% at 10 years. Coverage was uniform across all vaccines due at any given visit, indicating that the shortfall reflected missed follow-up visits rather than selective refusal of individual vaccines (Table 4).

Table 4. Vaccine-wise immunization coverage across the schedule (N=150).

Age / stage	Vaccines due	Eligible	Vaccinated	%
Birth	BCG, OPV-0, Hepatitis B (birth)	150	146	97.3
6 weeks	OPV-1, Pentavalent-1, RVV-1, fIPV-1, PCV-1	150	134	89.3
10 weeks	OPV-2, Pentavalent-2, RVV-2	150	122	81.3
14 weeks	OPV-3, Pentavalent-3, fIPV-2, RVV-3, PCV-2	150	108	72.0
9–12 months	MR-1, JE-1, PCV booster	150	103	68.7
16–24 months	MR-2, JE-2, DPT booster-1, OPV booster	140	91	65.0
5–6 years	DPT booster-2	115	73	63.5
10 years	Td	68	42	61.8
16 years	Td	1	1	100.0

BCG = Bacillus Calmette–Guérin; OPV = oral polio vaccine; RVV = rotavirus vaccine; fIPV = fractional inactivated polio vaccine; PCV = pneumococcal conjugate vaccine; MR = measles–rubella; JE = Japanese encephalitis; DPT = diphtheria–pertussis–tetanus; Td = tetanus–diphtheria.

On analysis of determinants, caregiver awareness regarding the importance of vaccination emerged as the strongest and only consistently significant predictor, being associated with both national ($p<0.001$) and extended ($p=0.029$) immunization; all aware caregivers had fully immunized their children under the national schedule. The presence of affected siblings was associated with national immunization status ($p=0.050$). By contrast, maternal factors (age, education, employment), paternal factors (age, education, occupation), and demographic factors (religious belief and distance to the vaccination centre) showed no statistically significant association with either national or extended immunization coverage (Table 5). Notably, despite frequent healthcare contact, uniformly low extended immunization was observed across all sociodemographic strata.

Table 5. Association of determinants with national and extended immunization status (N=150).

Determinant	National immunization, p-value	Extended immunization, p-value
Maternal age	0.314	0.810
Maternal education	0.989	0.776
Maternal employment	0.826	0.356
Paternal age	0.918	0.678
Paternal education	0.133	0.988 †
Paternal occupation	0.521	0.676
Religious belief against vaccination	0.440	0.888
Distance to vaccination centre	0.519	0.851
Number of siblings	0.313	0.692
Affected siblings	0.050 *	0.643
Awareness regarding SCD	<0.001 *	0.296
Awareness regarding importance of vaccination	<0.001 *	0.029 *

Chi-square test applied. * Statistically significant ($p<0.050$). † Value for paternal employment status (paternal education not separately significant for extended immunization). SCD = sickle cell disease.

DISCUSSION

This study evaluated immunization coverage and its determinants among children with SCD attending a tertiary care centre in Central India, spanning infancy to adolescence and thereby permitting assessment of vaccination practices across the entire schedule. The predominance of the HbSS phenotype (70.0%) reflects a cohort with a higher burden of severe disease and greater susceptibility to infection, underscoring the importance of complete immunization in this group.

National immunization coverage in the present study was 64.0% fully immunized, which is comparable to the 62.7% reported by Vohra et al. (14) and the 65.0% observed by Pandey et al. (19), but lower than the 74.7% reported by Gupta et al. (16) and 79.9% by Murhekar et al. (17), and well below the corrected coverage of Singh et al. (18). Compared with NFHS-5 (2019–21) coverage in the general population of children aged 12–23 months, coverage in this hospital-based, high-risk cohort was comparatively lower despite frequent healthcare contact (23). These variations likely reflect differences in study settings, population characteristics, and programme implementation.

A key finding was the progressive decline in vaccine coverage across the schedule, from 97.3% at birth to 61.8% at 10 years. This pattern—adequate initial access but suboptimal long-term adherence—mirrors observations by Murhekar et al. (17) and by Peng et al. (21), who reported that a substantial proportion of children with SCD fail to complete vaccination schedules despite early initiation. The uniformity of coverage within each visit stage indicates that dropout was driven by missed follow-up visits rather than selective refusal of specific vaccines.

Extended immunization coverage was strikingly low (20.0% fully immunized; 67.3% unimmunized), with poor uptake of pneumococcal (26.0%) and meningococcal (25.3%) vaccines. A major contributor is cost, as these vaccines are not included in the national programme and require out-of-pocket expenditure, which disproportionately affects the lower and middle socioeconomic groups that constituted most of this cohort. This gap is of particular concern given the heightened vulnerability of children with SCD to invasive pneumococcal and meningococcal disease, and is consistent with the low extended-vaccine uptake reported in other SCD populations (9).

Maternal and paternal sociodemographic factors did not show statistically significant associations with immunization status. This contrasts with studies such as Sahoo (13) and Srivastava et al. (20), which reported strong associations between socioeconomic variables and coverage. The difference may be explained by the relatively homogeneous healthcare access of a cohort regularly attending a single tertiary centre, which reduces between-group variability, as well as by limited subgroup sizes. Importantly, frequent healthcare contact alone—evidenced by high transfusion and admission rates—did not translate into complete immunization, signalling missed opportunities to integrate vaccination into routine clinical care (24).

Awareness emerged as the key modifiable determinant. Caregiver awareness regarding the importance of vaccination was significantly associated with both national and extended immunization, echoing findings by Vohra et al. (14) and Weiss et al. (15) on the centrality of awareness and effective communication. Together with the presence of affected siblings—likely a proxy for accumulated family experience of the disease—awareness was among the few variables that meaningfully influenced uptake, reinforcing the value of caregiver education and counselling.

Strengths and limitations. Strengths include a well-defined population, verification of vaccination status against documentary records where available, single-investigator data collection, and comprehensive assessment of both national and extended schedules alongside their determinants. Several limitations should be acknowledged. The cross-sectional design precludes causal inference. The single-centre, tertiary-care setting introduces referral and selection bias and limits generalisability. Reliance on caregiver recall where records were unavailable may introduce recall bias, and small subgroup sizes for some categories restricted statistical power. These findings should therefore be interpreted as hypothesis-generating and warrant confirmation in larger, multicentre, prospective studies.

CONCLUSION

Among children with SCD, national immunization coverage was moderate (64.0% fully immunized) but extended immunization coverage was critically low (20.0%), creating a substantial gap in protection for a population at high risk of invasive infection. A progressive decline in coverage across age groups highlights the challenge of sustaining long-term adherence, and the persistence of gaps despite frequent hospital contact indicates missed opportunities for preventive-care integration.

Awareness was the most influential determinant of vaccine uptake, while cost and the absence of extended vaccines from the national programme were major barriers. Strengthening structured follow-up, integrating immunization into routine SCD clinics, enhancing caregiver awareness, and ensuring subsidised or free availability of pneumococcal and meningococcal vaccines for this high-risk group are essential to improve coverage and reduce preventable morbidity and mortality.

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AUTHOR CONTRIBUTIONS

All authors contributed substantially to the conception and design of the study, the acquisition, analysis, and interpretation of data, and the drafting and critical revision of the manuscript for important intellectual content. All authors approved the final version to be published and agree to be accountable for all aspects of the work.

CONFLICT OF INTEREST AND FUNDING

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