

Clinico-Epidemiological Characteristics of Paediatric Sick Cell Disease in a Central Indian Tertiary Care Centre: A Cross-sectional Study.

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Abstract: This observational cross-sectional study was carried out with an intention to comprehend clinical outcome of sickle cell disease (SCD) amongst pediatrics in a central Indian tertiary care facility. Two hundred and forty patients were recruited, and the demographic, clinical complications, treatment practices and outcomes were emphasized. A high prevalence of the vaso-occlusive crises, acute anemia, and an increased dependence on hydroxyurea treatment were revealed in the course of the research. Higher fetal hemoglobin corresponding to over 20 percent was linked to an improvement in clinical outcomes. This study gives a clear indication of how much better the preventive practice is required in form of pneumococcal and meningococcal vaccines in order to prevent morbidities and deaths in this at risk group.

Keywords: Sickle cell disease, Paediatric, Hydroxyurea, Fetal hemoglobin, Vaso-occlusive crises.

INTRODUCTION

Sickle cell disease (SCD) is an inherited hemoglobinopathy that reflects point mutation of 6 position 8- globin gene (HBB) located on chromosomal region 11, which causes aberrant hemoglobin S (HbS) to be produced [1]. HbS polymerizes in deoxygenated state, deforming red blood cells into rigid, sickle-shaped type forming obstructions in the microvasculature and subsequent ischemia and hemolysis [2]. SCD is a major public health burden with more than 515,000 infants born annually with the disease and an approximation of 7.7 million SCD survivors globally [3,4]. SCD is a neglected tropical disease acknowledged by the World Health Organization especially in low- and middle-income countries where the full scope of care is less evident [4].

Sub-Saharan Africa has the greatest rate of SCD especially 1 to 3 percent of newborns not excluding the Middle East, Mediterranean region, and the Indian subcontinent. It has been estimated that there are 42,000 births of SCD babies born every year in India that makes up about 14.5 percent of total SCD births in the world [5]. The disease is concentrated on tribal populations that constitute only about 8.6 percent of the Indian population, but almost two-thirds of the victims because of high carrier rates [6]. Sickle cell trait is present in the tribal groups of central India at levels of 10-33 percent in populations like the Gonds, Bhils and Oraons that determined the so-called sickle cell belt comprising of Madhya Pradesh, Chhattisgarh, Maharashtra, Gujarat and Odisha [7].

Pediatric SCD tends to produce clinical manifestations at the age of about 56 months when the levels of fetal hemoglobin decrease. The most significant

complication, which manifested in the form of microvascular obstruction, is vaso-occlusive crises that make severe pain attacks frequent with the involvement of bones and joints, chest, and abdomen appear [8]. New pulmonary infiltrates thresholded by fever or respiratory signs defines acute chest syndrome (ACS) that occurs in more than 50 percent of children with homozygous SCD and is a frequent cause of hospitalization and death [9,10]. Children are surprisingly prone to splenic sequestration crises (with a reported incidence of up to 30 percent in children under six years), and cerebrovascular accidents (with as many as 40 percent of pediatric patients experiencing sequelae including silent cerebral infarcts) add significantly to neurocognitive morbidity [11].

The pathophysiology of SCD is more than vaso-occlusion that also involves chronic hemolytic anemia, endothelial dysfunction, inflammation and oxidative stress [12]. The onset of functional asplenia occurs early with the predisposition to overwhelming encapsulated bacteria by infections; prophylactic penicillin and pneumococcal vaccination has been proved to decrease invasive pneumococcal disease by several folds [13]. Transcranial Doppler screening and regular blood transfusion effectively reduces the risk of stroke among the children at high risk [14].

Cytotoxic agents that raise fetal hemoglobin levels and adhesion by altering leukocytes are hydroxyurea (increasing adhesion resistance), and have become the standard of disease modification pediatrics SCD regimens. Findings of the landmark Multicenter Study of Hydroxyurea included a 44 percent decrease in painful crises, and the safety and efficacy of hydroxyurea in infants was corroborated by the BABY HUG trial in children 918 months old [15,16]. December 2017 can be

considered an instrumental point in SCD care since the U.S. Food and Drug Administration approved hydroxyurea as the first drug to receive such practice in children and adolescents [17].

Even with these advances in therapy, stark inequalities remain: in sub-Saharan Africa alone, SCD has a mortality rate among children aged under five years of between 50 and 90 percent, compared with the rate of less than 5 percent which is recorded in the high-income countries due to the extensive care programs available there [18,19]. High rates of morbidity and mortality were reported at the beginning in central India, and a reduction of morbidity and mortality through micro-level planning and specific interventions is essential [20]. It is still important to address such gaps so that the outcomes of children with SCD in resource-limited places are improved. Therefore This study addresses that gap by characterizing demographic profiles, clinical complications, treatment practices, and outcomes in children admitted to a central Indian tertiary care center.

MATERIALS AND METHODS

The present observational cross-sectional study was conducted at the Department of Pediatrics, Mahatma Gandhi Memorial Medical College, Indore, Madhya Pradesh, India, from September 21, 2023, to September 21, 2024, aiming to understand the clinical outcomes of sickle cell disease in pediatric patients who met the inclusion criteria, after obtaining ethical approval from the Institutional Ethics Committee (IEC) and Scientific Review Committee.

Sample Size Calculation

The sample size was calculated based on the prevalence of sickle cell disease in India, which is reported to be 8.75% (Indian Council of Medical Research, ICMR). After calculating using the formula, the sample size was found to be 199. Given a non-response rate of 20%, the final sample size was adjusted to 240. This sample size provided an 80% power at a 5% significance level.

Sampling Technique

A convenience sampling technique was used for the recruitment of participants during the study period.

Inclusion Criteria

1. Patients diagnosed with sickle cell disease, admitted to the Pediatric Intensive Care Unit (PICU), daycare, or general wards.
2. Patients aged under 18 years.

Exclusion Criteria

1. Sickle cell disease patients with co-morbidities unrelated to sickle cell disease.
2. Patients or their guardians who did not provide consent for participation in the study.

METHODOLOGY

all eligible patients admitted to the Department of Pediatrics at Mahatma Gandhi Memorial Medical College, Indore, with a diagnosis of sickle cell disease were enrolled after obtaining written informed consent from their guardians. Data were systematically collected using a customized proforma tailored to the specific needs of the study.

Demographic information, clinical parameters (such as medical history and clinical examination findings), and anthropometric measurements (including height, weight, and Body Mass Index (BMI)) were recorded. For children under 5 years, WHO growth standards were used, while IAP growth charts were applied for those aged 5 to 18 years.

Laboratory investigations, including hemoglobin (Hb) levels, were conducted. Anemia was classified as mild, moderate, or severe according to WHO criteria based on age and hemoglobin concentration. Additional hematological parameters, such as Total Leukocyte Count (TLC), Differential Leukocyte Count (DLC), platelet count, and serum bilirubin levels, were also assessed.

Management of the patients adhered to standard treatment protocols, ensuring that the study did not interfere with the clinical care process. Data were meticulously recorded in the predesigned proforma to ensure accuracy and consistency.

Outcome Measures

The primary outcome measures of the study included factors that may influence morbidity and mortality in sickle cell disease patients. These factors were:

1. Age of the patient.
2. Nutritional status (as indicated by anthropometric measurements).
3. Use of hydroxyurea therapy.
4. Type of sickle cell disease (e.g., HbSS, HbSC).
5. Use of penicillin prophylaxis.
6. Immunization status.
7. Levels of Hemoglobin F (HbF).

These variables were analyzed to understand their relationship with the severity of disease and clinical outcomes in hospitalized pediatric patients with sickle cell disease.

Statistical Analysis Plan

Data were recorded in the proforma and subsequently transferred to Microsoft Excel for analysis. Statistical analysis was performed using IBM SPSS version 22. Descriptive statistics (frequencies, percentages) were

used to summarize the demographic and clinical characteristics of the study population. Pearson's Chi-square test was used to assess the association between categorical variables, while comparisons of means were conducted using the Unpaired t-test. A p-value of <0.05 was considered statistically significant.

Financial Implications

All treatment, diagnostic, and investigative procedures were provided free of charge by the institution, ensuring that patients or their guardians faced no financial burden.

No additional tests or procedures were performed exclusively for research purposes.

Ethical Considerations

The protocol for the study was reviewed and approved by the Institutional Ethics Committee (IEC). Informed consent was obtained from the patients or their legal guardians before enrollment in the study. All personal and clinical information was kept confidential, and only data pertinent to the study were utilized.

RESULTS-

Table 1: Baseline Socio-Demographic Characteristics of Study Participants (N=240)

Characteristic	N	Percentage (%)
Age Distribution		
≤6 years	106	44.2
>6-≤12 years	93	38.8
>12-18 years	41	17.1
Gender		
Female	132	55.0
Male	108	45.0
Socioeconomic Status		
Lower class	183	76.2
Lower middle class	42	17.5
Upper lower class	15	6.3
Caste		
Tribal	172	71.7
Non-tribal	68	28.3
Sickle Cell Disease Type		
Sickle cell anemia	208	86.7
Sickle cell β-thalassemia	30	12.5
Others (HbSC, trait)	2	0.8

This table gives the socio-demographic nature of the study participants. The age groups of the majority of patients were fewer than 6 years of age (44.2%), there was a tendency to show females predomination (55%). Majority (76.2) were born into low socio economic environments and 71.7 were tribal people. The majority of the patients were characterized by sickle cell anemia (86.7%).

Table 2: Anthropometric Profile by Sickle Cell Disease Type (N=240)

Parameter	N (%)	p-value (Pearson Chi-square test)
Weight Status (<3rd centile)		0.030
Sickle cell anemia	64 (30.8)	
Sickle cell β-thalassemia	16 (53.3)	
Others	0 (0.0)	
Height Status (<3rd centile)		0.153
Sickle cell anemia	52 (25.0)	
Sickle cell β-thalassemia	12 (40.0)	
Others	0 (0.0)	
BMI Status (Underweight)		0.697
Sickle cell anemia	49 (23.5)	
Sickle cell β-thalassemia	8 (26.7)	
Others	0 (0.0)	

This table compares the anthropometric parameters (weight, height, BMI) in the case of various types of sickle cell disease. It emphasizes that the underweight situation was quite large in patients with sickle cell beta-thalassemia (53.3%) than with that of anemia (30.8%). There were however no significant variations in height or BMI, according to the types of diseases.

Table 3: Clinical Complications and Disease Manifestations (N=240)

Complication Type	N	Percentage (%)
Infective Complications		
Acute febrile illness	65	27.1
Sepsis	10	4.1
Osteomyelitis	3	1.2
Aplastic crisis (Parvovirus B infection)	1	0.4
Non-Infective Complications		
Vaso-occlusive crisis	145	60.4
Anemia	21	8.8
Acute chest syndrome	4	1.7
Splenic sequestration	4	1.7
Thromboembolic events	4	1.7
Hepatopathy	3	1.3
Anemia Severity		
Severe (Hb <7 g/dL)	139	57.9
Moderate (Hb 7-9 g/dL)	81	33.8
Mild (Hb 9-11 g/dL)	20	8.3

This table displays the clinical complications such as those evident in the patients. The most common (75.4%) complications were non-infective complications, and vaso-occlusive crises among them were most common (60.4 percent). The burden of the disease was demonstrated by 57.9% of the patients with severe anemia (Hb <7 g/dL). Complications due to infection were not as common, making 32.9 percent of the cases.

Table 4: Treatment Characteristics and Healthcare Utilization (N=240)

Treatment Parameter	N	Percentage (%)
Hydroxyurea Therapy		
Currently using	127	52.9
Not using	113	47.1
Hydroxyurea Compliance (n=127)		
Compliant ($\geq 80\%$ doses)	114	89.8
Non-compliant (<80% doses)	13	10.2
Fetal Hemoglobin Levels		
HbF $\geq 20\%$	128	53.3
HbF <20%	112	46.7
Hospitalization Frequency		
Once	67	27.9
2-5 times	19	7.9
>5 times	154	64.2
Vaccination Status		
Routine immunization complete	218	90.8
Pneumococcal vaccine	128	53.3
HIB vaccine	206	85.8
Meningococcal vaccine	0	0.0
Penicillin Prophylaxis		
Currently using/history of use	17	7.1

This table points out the patterns of treatment and healthcare usage in the cohort. More than half of the patients (52.9%) are receiving hydroxyurea therapy with the high compliance rate (89.8%). Majority of patients (64.2%), had high rates of hospitalization (excessive to five instances). The table also indicates the vaccination status whereby the routine immunization is largely up to date although there was suboptimal use of pneumococcal and meningococcal vaccinations.

Table 5: Association Between Treatment Variables and Clinical Outcomes

Variable	N (%)	p-value (Pearson Chi-square test)
Hydroxyurea Use and Hospitalizations		0.001
No hydroxyurea: 1 hospitalization	0 (0.0)	

No hydroxyurea: >5 hospitalizations	112 (99.2)	
Hydroxyurea: 1 hospitalization	67 (52.7)	
Hydroxyurea: >5 hospitalizations	42 (33.1)	
HbF Levels and Hospitalizations		0.002
HbF<20%: 1 hospitalization	20 (17.9)	
HbF<20%: >5 hospitalizations	85 (75.9)	
HbF ≥20%: 1 hospitalization	47 (36.7)	
HbF ≥20%: >5 hospitalizations	69 (53.9)	
Sickle Cell Type and Complications		0.001
SCA: Vaso-occlusive crisis	131 (62.9)	
SCA: Anemia	11 (5.3)	
Sickle β-thalassemia: VOC	12 (40.0)	
Sickle β-thalassemia: Anemia	10 (33.3)	
Clinical Outcomes		
Mortality (overall)	4 (1.7)	0.031
Mortality in HbF<20%	4 (3.6)	
Mortality in HbF ≥20%	0 (0.0)	
Discharge rate	236 (98.3)	

This is a table that investigated the association of treatment variables (e.g., use of hydroxyurea, the level of fetal hemoglobin) and clinical outcomes. Hydroxyurea utilization and increased levels of fetal hemoglobin had a significant relationship with a high level of hospitalization rates. The mortality was quite minimal (1.7%), all occurring in those whose level of HbF was below 20 percent, in the power of fetal hemoglobin.

DISCUSSION-

The current study examining pediatric sickle cell disease (SCD) in central India closely corresponds with prior research conducted in analogous populations, particularly concerning clinico-epidemiological characteristics, significant complications, and the impacts of hydroxyurea and fetal hemoglobin. For example, Patel KG et al.[21] and Singh A et al.[22] have both reported that most of the affected children were from tribal and lower socioeconomic backgrounds, were young when they first showed symptoms, and were slightly more likely to be female. This shows that SCD disproportionately affects vulnerable groups and that it often starts early in these groups. Jain D et al.[23] reported similar barriers to care stemming from inadequate access and socioeconomic disadvantage in their study conducted in central India. The high rate of vaso-occlusive crises, which is the most common non-infectious complication that leads to hospitalizations, is in line with what Patel KG et al.[21] and Jain D et al. [23] found in their studies. They found that pain episodes and severe anemia were major causes of illness in children with SCD. Jain D et al.'s [23] work backs up the idea that sickle cell β-thalassemia patients are more likely to be underweight than people with SCD alone. They talk about the nutritional problems that people with multiple hemoglobinopathies face. The current study's results on the effectiveness of hydroxyurea, which showed fewer hospitalizations and pain episodes, are in line with the findings of Lebensburger JD et al.,[24] whose retrospective cohort study confirmed its safety and effectiveness in children of all genders and socioeconomic backgrounds. This study's finding of lower hospitalization and mortality rates in children with fetal hemoglobin levels exceeding 20% aligns with the research conducted by Estep JH et al.[25] and Adeodu OO et al.,[26] which demonstrated that sustaining HbF above this threshold significantly enhances clinical outcomes and mitigates disease severity. Moreover, the persistent gaps in pneumococcal and meningococcal vaccination coverage within this cohort reflect the inadequacies in preventive care identified by Patel KG et al.[21] and Jain D et al.[23] in their respective local studies.

CONCLUSION-

the findings of this study corroborate the conclusions of prior regional and international researchers, underscoring the critical necessity for enhanced comprehensive care strategies, the promotion of elevated HbF levels, and improved access to preventive healthcare for children afflicted with sickle cell disease.

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