Assessment of Disease Severity in Sickle Cell Disease Patients from the Nandurbar Region of Maharashtra

Abstract:

Background: Sickle cell disease (SCD) is one of the most prevalent inherited hemoglobinopathies, caused by a point mutation in the β-globin gene leading to the formation of abnormal hemoglobin S (HbS). This results in sickle-shaped red blood cells that cause chronic hemolytic anemia, recurrent vaso-occlusive episodes, and progressive multi-organ damage. Globally, over 7% of the population carries hemoglobin variants, and India ranks second in SCD burden, with a particularly high prevalence among tribal communities due to endogamous and consanguineous practices.

Aim and Objectives: This study aims to assess disease severity among SCD patients in the tribal-dominated Nandurbar district of Maharashtra, using a composite of clinical and hematological parameters. It seeks to address the lack of standardized severity scoring in rural and tribal populations and to support the development of region-specific treatment strategies.

Material and method:A cross-sectional study was conducted among SCD patients from Nandurbar. Disease severity was assessed using clinical manifestations, signs and symptoms. Hematological parameters including hemoglobin (Hb) levels and white blood cell (WBC) counts were measured to support severity classification. Data were statistically analyzed to categorize patients into mild, moderate, and severe disease groups.

Results and Observation: The majority of SCD patients in Nandurbar were found to have moderate to severe disease. The findings aligned with previous studies indicating a high burden of clinical complications in tribal populations of central and western India. Despite the extensive prevalence of the HbS gene, systematic documentation of disease severity remains limited.

Conclusion: The study highlights the need for routine application of severity scoring systems in tribal regions for effective disease management. It emphasizes the importance of region-

specific research to guide early interventions, policy planning, and improved healthcare delivery in underserved populations affected by SCD.

Keywords: Sickle Cell Disease, Sickle Cell Disease Severity Score (SCDSS), Hemoglobin S, Tribal Population, Nandurbar, Hematological Parameters, White Blood Cell Count,Clinical manifestation, Maharashtra Sickle Cell Disease, Public Health.

INTRODUCTION

Sickle cell disease (SCD) is one of the most common inherited hemoglobinopathies, characterized by chronic hemolytic anemia, recurrent vaso-occlusive episodes, and progressive multi-organ complications. The disease is caused by a point mutation in the β-globin gene, resulting in the production of abnormal hemoglobin S (HbS), which polymerizes under deoxygenated conditions, distorting red blood cells into a sickle shape. These deformed cells lead to micro vascular occlusion, ischemia, and chronic organ damage. **(1)**

Over 300 million people worldwide have genetic mutations linked to hemoglobinopathies. About 190 million carry sickle cell trait or β-thalassemia, and around 7% of the global population carries some form of hemoglobin variant. Sickle cell disease cases have increased by 41.4%, from 5.46 million in 2000 to 7.74 million.**(2)**The highest burden of SCD is seen in western and central sub-Saharan Africa and India. Thalassemias like α-thalassemia, β-thalassemia, and HbE are also common in these regions. In 2021, over half a million babies were born with SCD. Countries like Bahrain, Angola, DRC, Kenya, Ghana, Guinea, Niger, and Sao Tome had birth incidence rates of 1000–2000 per 100,000. About 90% of the global SCD population lives in Nigeria, India, and the DRC, affecting 2% of their populations. **(1)**India bears a substantial burden of SCD, particularly among certain tribal populations. India has over 20 million people affected by sickle SCD, yet it remains largely under-addressed. India ranks second in global SCD burden, with 150,000–200,000 affected births each year. SCD was first reported in India in 1952 among tribal populations in the Nilgiri Hills and Assam. The disease is especially prevalent among socio-economically disadvantaged groups like scheduled tribes, scheduled castes, and other backward classes.

Due to long-standing endogamy and consanguinity, tribal communities who form the world's largest tribal population—are particularly vulnerable to hereditary diseases like SCD. **(4, 5)**Maharashtra, particularly its tribal districts such as Nandurbar, has been identified as a high-prevalence region for SCD in India. Nandurbar, where approximately 69% of the population belongs to Scheduled Tribes, is especially vulnerable due to prevalent practices of endogamy and consanguineous marriages.**(6)** Studies from Vidarbha in eastern Maharashtra reported a sickle cell trait prevalence of around 3.58% and a confirmed SCD prevalence of 0.20%.**(6)**Broader estimates across tribal regions, including Nandurbar, suggest heterozygote frequencies ranging from 10% to 40%, particularly among communities such as Bhils, Pawaras, and Koknas, as reported by **Mohanty et al. in 2013**. **(7)** Under the National Sickle Cell Elimination Programme, Maharashtra has initiated extensive screening across 21 districts, including Nandurbar, with over 5.3 million individuals screened by January 2025, according to NHM Maharashtra in 2025. These efforts highlight the substantial public health burden of SCD in tribal Maharashtra and reinforce the need for focused interventions in high-risk regions.**(8)**The **state of Maharashtra**, especially its **northern tribal belt**, has been identified as a high-prevalence zone for the sickle cell gene. Among the tribal-dominated districts, **Nandurbar** is a recognized hotspot where the condition poses a major public health challenge. Despite significant disease prevalence, there is limited literature focusing on clinical severity, progression, or systematic scoring of disease burden in this region.**(10)**

Assessing disease severity in SCD is critical for individualized patient care, risk stratification, and allocation of health resources. While multiple clinical parameters including frequency of vaso-occlusive crises (VOCs), need for blood transfusions, clinical manifestations, hospital admissions and laboratory markers such as hemoglobin and white blood cells levels—serve as indicators of disease severity, standardized scoring systems Microsoft.QuickAction.MobileHotspotremain underutilized in rural and tribal settings.**(9)**

In India, SCD presents a distinct epidemiological pattern, with a high burden among tribal populations in central and western states such as Maharashtra, Madhya Pradesh,

Chhattisgarh, Gujarat, and **Odisha. Mohanty, Mukherjee, and Colah in 2013** described it as an emerging health concern among Indian tribal groups, while **Serjeant in 2010** emphasized India's growing contribution to the global disease burden. **(11,12)** In Maharashtra, the Nandurbar district inhabited by Bhil, Pawara, and Kokna tribes—has shown a high prevalence of the HbS gene, as reported by **Colah, Ghosh, and Nadkarni in 2015**. **(13)** Studies from Melghat, Gadchiroli, and Nagpur regions, including the work of **Karande, Kumbhar, and Wankhede in 2016**, have documented severe clinical symptoms such as pain crises, splenomegaly, and increased transfusion needs. **(14)**

Despite such findings, India still lacks a standardized and context-specific disease severity scoring system. Efforts by **Steinberg and Sebastiani in 2012** introduced genetic modifier-based indices in Western populations, while **Adegoke and Kuti in 2013** developed a clinical severity scale for Nigerian children. However, these models have limited applicability to Indian tribal populations.**(15,16)** Psychosocial and environmental contributors have also been noted—**Onu, Asinobi, and Ndu in 2025** linked higher disease severity to stress and poor social support, and Shah**, Beenhouwer, and Broder in 2020** proposed a modern severity classification framework suitable for broader use.**(17,18)**

Additionally, **Gupte and Patel in 2009**, in their study of tribal groups in Gujarat, reinforced the high burden of SCD, mirroring findings in Maharashtra. Although genetic screening in Nandurbar reveals a high HbS gene frequency, comprehensive clinical severity data remain scarce. **(19)** This gap highlights the urgent need for focused research to develop a region-specific severity scoring model, which would support early intervention strategies such as hydroxyurea therapy, nutritional support, and preventive care, ultimately improving outcomes in these high-risk tribal communities.

This study aims to fill this gap by evaluating thedisease severity score among SCD patients in Nandurbar**,** using a composite of clinical and hematological parameters. By establishing a localized understanding of disease severity, this research seeks to inform more

effective treatment strategies and guide public health policy for SCD management in underserved tribal populations. **(4)**

Material and Methods

A cross-sectional, observational study was conducted over a period from January 2024 to December 2024 among confirmed SCD patients residing in the Nandurbar district of Maharashtra. The study was carried out in rural health centres, district hospitals, and selected tribal PHCs in Nandurbar, which serves a predominantly tribal population.Random sampling was used for participant selection.

The study included a total of 86 tribal patients diagnosed with sickle cell disease. Ethical approval was obtained from the Institutional Ethical Committee prior to the commencement of the study. Informed consent was obtained from all participants before enrollment.

Inclusion Criteria:

This case study included 86 tribal SCD patients. All of whom provided informed consent. Participants (46 males, 40 females; aged 18–45) were diagnosed with SCD (HbSS) using turbidity test and HPLC methods and were under clinical management. All participants were from the native tribal community, matched for age, sex, and body weight, and confirmed by clinical screening.

Exclusion Criteria:

The study applied strict exclusion criteria to ensure data reliability and group comparability. Non-tribal individuals, those under 18 or over 45 years, and patients with acute SCD complications, other hemoglobinopathies, or hematological disorders were excluded. Individuals with hepatitis B or C, HIV, liver or thyroid diseases, a history of splenectomy, or chronic alcoholism were not included. Participants using dietary supplements or undergoing recent treatments that could affect hematological values were also excluded.

Additionally, those unwilling or unable to give informed consent were excluded to maintain ethical and methodological rigor.

Structured questionnaire was prepared on the basis of following factors

- Demographics: Age, Sex, Tribe, Socio-economic status
- Clinical Indicators:
  - Number of VOCs/year
  - Number of hospital admissions/year
  - Number of blood transfusions/year
  - Episodes of acute chest syndrome or stroke
  - Clinical manifestations

LABORATORY MEASUREMENTS USING DIAGNOSTIC REAGENTS

Blood Sample Collection

Capillary blood was collected via finger-prick into tubes containing DTT reagent. DTT-positive individuals underwent venepuncture for 2 ml of blood in EDTA tubes, which were stored on ice and sent to the central lab. CBC and HPLC for hemoglobin variants were performed using the Bio-Rad D-10 Analyzer. Diagnosed cases received counseling, and extended family screening was conducted.

Collection and Processing of Blood Samples

A trained team of physicians, lab technicians, and nurses from the government civil hospital collected data and samples. Venous blood was drawn under aseptic conditions from SCD patients into plain and heparinized tubes. Samples were allowed to clot at room temperature for 30 minutes, and then centrifuged at 3000 rpm for 10 minutes. The separated serum was used for biochemical analysis.

For primary detection and confirmation of sickle cell disease

1. Solubility Test for detection of Hemoglobin S

Sickle cell disease is caused by a point mutation in the β-globin gene (GAG → GTG), replacing glutamic acid with valine at position 6. This produces abnormal hemoglobin S (HbS), which becomes insoluble under low oxygen conditions, forming polymers that distort

red blood cells into a sickle shape. The solubility test detects HbS based on its reduced solubility in such conditions, aiding in the primary diagnosis of sickle cell disease.

Rapid Sickle Cell Solubility Test Kit (20)

This screening kit detects sickle cell trait/disease based on the solubility difference between hemoglobin S (HbS) and hemoglobin A (HbA). In the reagent mix, red blood cells lyse, and HbS precipitates, causing turbidity, while HbA remains soluble, leaving the solution clear. **(Table No.1)** Positive samples should be confirmed by High Performance Liquid Chromatography (HPLC) to avoid false positives.

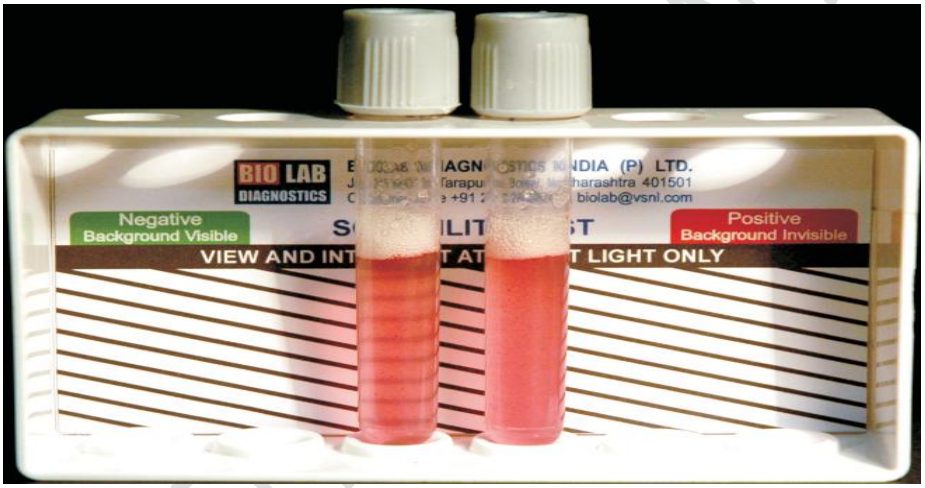


Figure No. 1. Sickle Cell Solubility Test (20)

Table No. 1

Sr. No	Turbidity	Clarity	Visibility of black lines through the tubes	Interpretation
I.	No	Yes	Yes	Normal
II.	Yes	No	No	Sickle Cell

Assessment of hemoglobin variants by High Performance Liquid Chromatography (HPLC) (21)

Method: Cation Exchange Liquid Chromatography

Equipment: BIO-RAD D-10 Hemoglobin Testing System

Specimen: Whole blood sample (EDTA)

Principle:

The D-10 system uses high-performance liquid chromatography (HPLC) to separate hemoglobins based on ionic interactions. Whole blood samples undergo automated dilution and are introduced into the analytical flow path. A buffer gradient carries the sample through an analytical cartridge, separating hemoglobins, which are then detected by measuring absorbance at 415 nm. The system processes the data using calibration factors and generates a chromatogram and report for each sample.

Procedure:

The BIO-RAD D-10 Hemoglobin Testing System operates on the principle of high-performance liquid chromatography (HPLC) using cation exchange technology. Whole blood (EDTA) samples are either run directly or pre-diluted if the volume or tube type is unsuitable. The system automatically performs a two-step dilution for whole blood samples. Once loaded into the sample rack, the barcode reader identifies the samples and the system prepares them for analysis. The diluted sample is introduced into an analytical flow path, where a buffer gradient carries it through a cartridge that separates hemoglobin fractions based on their ionic interactions. These separated components pass through a photometric detector that measures absorbance at 415 nm. The resulting data are processed and presented as chromatograms and reports. The instrument also performs internal flushing between samples to prevent carryover and maintain accuracy.

Interpretation of Results:

Results of the HPLC report were analysed based on the peak and area covered by specific hemoglobin variants in the chromatogram.

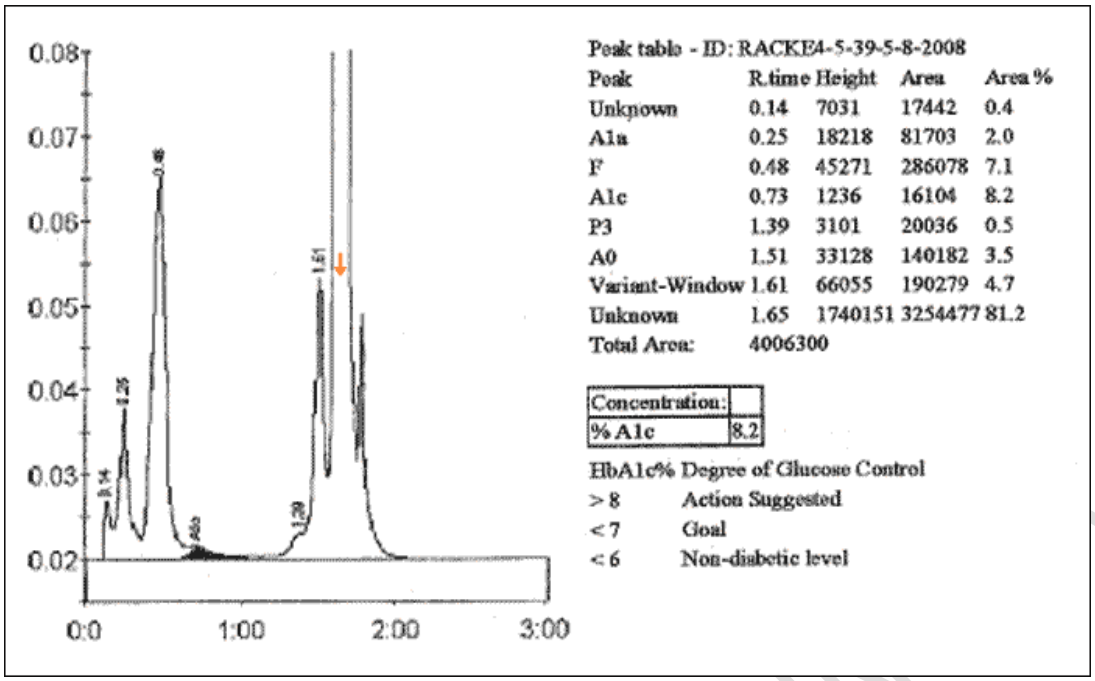


Figure No. 2. Classic Chromatogram of an HbSS patient (22)

Hemogram was measured by using cell counter.

- Hemoglobin (Hb) levels
- Reticulocyte count
- White blood cells count**(23)**

Disease Severity Score

An objective score was calculated for disease severity by using the method proposed by **Okocha et al. 2020.** Scores were assigned to the following parameters: patient white blood cell count, hemoglobin levels, and number of complications suffered from disease. Scores of ≤3 were deemed mild disease. Scores of > 3 to ≤ 5 were considered moderate disease, while scores >5 were taken for severe disease.**(24)**

Table N. 2 Hb or Anemia score

Parameter	Range	Score
	≥ 10 g/dl	**0**

Hemoglobin (Hb)	**≥ 8 g/dl < 10 g/dl**	**1**
	≥ 6 g/dl < 8 g/dl	**2**
	≥ 4 g/dl < 6 g/dl	**3**
	< 4 g/dl	**4**

Table N. 3 Complications score or Clinical features

Parameter	Range	Score
Pain crises, Fatigue, Recurrent fever, Breathlessness, Abdominal pain, Retinopathy, Icterus, Acute chest pain, Nephropathy, Priapism, Leg ulcer, Pulmonary Hypertension, Liver failure, and Heart failure	**-**	**1**
Nephropathy	**-**	**2**
Stroke	**-**	**2**

Table N. 4 White Blood Cells Score

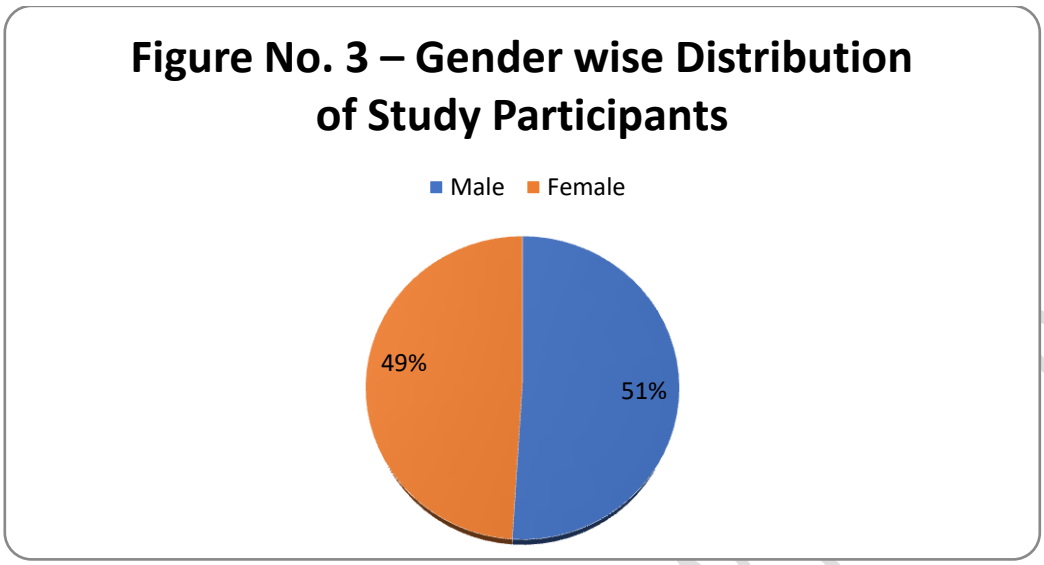
Parameter	Count Range	Score
White Blood Cells (WBC)	**< 9 x 10^9 cells/µl**	**0**
	≥ 9 < 11 x 10^9 cells/µl	**1**
	Count ≥ 11 < 15 x 10^9 cells/µl	**2**
	Count ≥ 15 x 10^9 cells/µl	**3**

Statistical analysis

Data were entered in Microsoft Excel and analyzed using Max Stat Lite v3.60 and SPSS v20. Results were presented as mean ± standard deviation (Mean ± SD). One-way ANOVA was used to compare continuous variables between SCD patients and healthy controls, followed by Bonferroni post hoc tests. A p-value < 0.05 was considered statistically significant. Pearson correlation coefficient (r) was used to assess the relationship between various haematological and biochemical parameters.

Result

As shown in **Figure 3**, out of the total SCD participants, 44 were males forming 51 %t and 42 were females forming 49 %, indicating a nearly equal gender distribution.



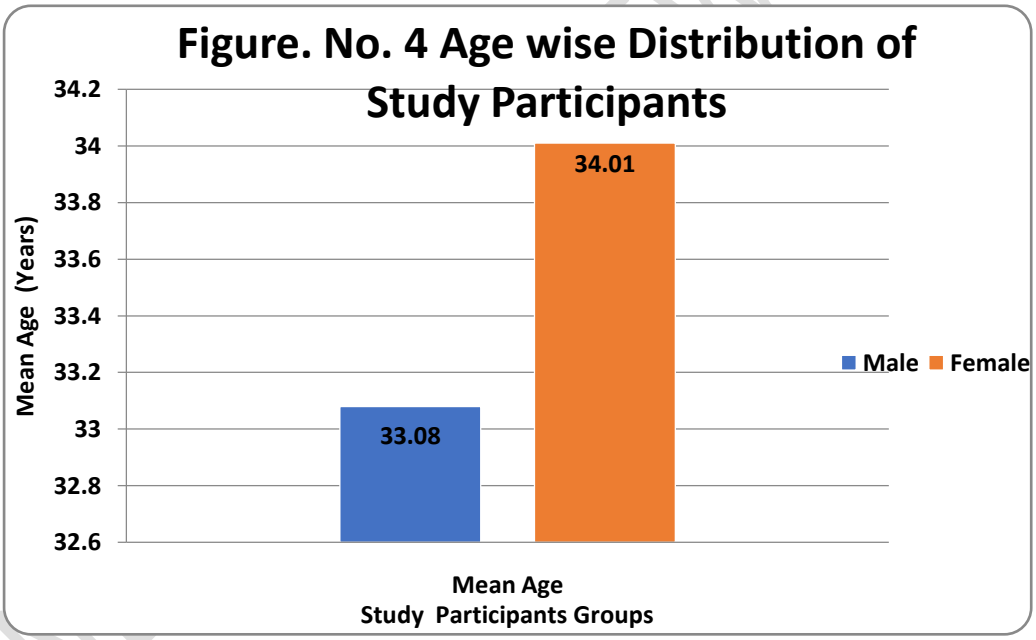


Figure No. 4presents the age distribution of SCD patients (Group I). The mean age of patients in this group was 33.08 ± 6.54 years, indicating that most individuals affected by sickle cell disease in the study were in their early thirties. This suggests that the disease predominantly affects adults in this age range. The age variation within the group, as reflected by the standard deviation, shows some spread in the ages of the patients, but overall they belong to a relatively similar age group.

Table no.5 Disease Severity Data for Sickle Cell Disease Patient

Severity Factor	Severity Score	Group I (Male n = 44)	Group II (Female n = 42)	Total (n=86)
Hemoglobin (g/dl)				
Mild Hb ≥ 10 g/dl	0	11	8	19
Moderate Hb ≥ 8 g/dl < 10 g/dl	1	13	11	24
Severe Hb ≥ 6 g/dl < 8 g/dl	2	15	17	32
Very Severe Hb ≥ 4 g/dl < 6 g/dl	3	05	06	11
Extreme Severe Hb < 4 g/dl	4	00	00	00
White Blood Cell Count (10^9 cells/µl)				
Mild (<9 x 10^9 cells/µl)	0	13	12	25
Moderate (≥9 < 11 x 10^9 cells/µl)	1	14	15	29
Severe (≥ 11 < 15 x 10^9 cells/µl)	2	11	9	26
Extreme Severe (≥ 15 x 10^9 cells/µl)	3	02	04	06
Complications or Clinical Manifestations				
Mild (1-2 complications)	1	14	15	29
Moderate (3-4 complications)	2	16	17	33
Severe (≥ 5 complications)	3	09	12	21
Nephropathy	2	02	01	03
Stroke	2	00	00	00

As stated in **table no 5**scores of ≤3 were considered mild disease. Scores of > 3 to ≤ 5 were considered moderate disease, while scores >5 were taken for disease severity scoring. Scores were calculated on the basis of above mentioned table – hemoglobin, white blood cell count, and number of complications suffered from disease.

Table no. 6. Disease Severity Score

Disease Severity	Score	Group I (Male n = 44)	Group II (Female n = 42)	Total (n=86)
Mild	**≤ 3**	**2**	**0**	**2**
Moderate	**> 3 to ≤ 5**	**21**	**20**	**41**
Severe	**> 5**	**21**	**22**	**43**

Table no. 6 shows disease severity data for sickle cell disease patients, broken down by gender and severity factors, provides important insights into the overall clinical status of the patients in this study. The findings reveal a clear distribution of severity across hemoglobin levels, white blood cell count, and complications.

The table shows the distribution of disease severity among 86 SCD patients, comprising 44 males and 42 females. Mild disease severity (score ≤ 3) was seen in only 2 male patients, with no female patients falling in this category. Moderate severity (score > 3 to ≤ 5) was observed in 21 males and 20 females, totalling 41 patients. Severe disease (score > 5) was the most common, affecting 21 males and 22 females, with a combined total of 43 patients. These findings indicate that the majority of patients, regardless of gender, experienced moderate to severe forms of the disease.

Discussion

Sickle cell disease (SCD) is a common inherited hemoglobin disorder marked by chronic hemolytic anemia, repeated vaso-occlusive crises, and gradual involvement of multiple organs. Assessing disease severity in SCD is essential for personalized care and effective resource use. **(25)**Although clinical and lab markers help indicate severity,

standardized scoring is rarely used in rural and tribal areas. This study addresses that gap by evaluating severity scores in SCD patients from Nandurbar, aiming to improve treatment strategies and inform public health planning for tribal communities.

In this study, disease severity in 86 SCD patients (44 males, 42 females) was assessed using hemoglobin levels, white blood cell (WBC) count, and clinical complications. Among them, 48 patients were classified as having moderate severity, while the rest fell into normal, mild, or severe categories. Lower hemoglobin levels indicated greater anemia and severity, while complications like pain crises, stroke, or respiratory issues were scored based on clinical impact. Elevated WBC counts were considered markers of inflammation or acute complications. Together, these factors provided a comprehensive severity score to guide treatment decisions.

The distribution of complications in this study subjects indicated that 33 patients (38.4%) experienced moderate severity, presenting with 3–4 complications. This was the most common category, highlighting that many patients had multiple clinical manifestations of sickle cell disease, such as pain crises, fatigue, or organ dysfunction. A similar trend was reported by **Smith and Penberthy in 2006 (26)**, who observed that a significant proportion of patients experienced multiple moderate complications during the course of their illness. Meanwhile, 29 patients (33.7%) had only 1–2 complications, categorized as mild, suggesting a relatively less complicated disease course. This aligns with findings from **Ballas and Smith in 1992**, **(27)** who noted that a substantial subset of patients experienced limited complications, often associated with early intervention and milder disease phenotypes.

Conversely, 21 patients (24.4%) were classified in the severe category, having 5 or more complications. This subgroup reflects the more complex and debilitating end of the disease spectrum. In studies by **Vichinsky and Platt in 2013**, similar patterns of severity were observed, particularly among patients not receiving comprehensive disease-modifying therapy. **(28)** Among the specific complications, nephropathy and stroke were especially

concerning; however, only 3 patients in the present cohort were identified with nephropathy, and none experienced a stroke. These relatively low figures suggest a positive impact of early interventions such as hydroxyurea therapy and align with observations made by **Mekonnen and Teshome in 2017**, who reported that while general complications were common among patients with sickle cell disease, life-threatening conditions like stroke occurred infrequently, likely due to preventive strategies and the younger age distribution in their study population. **(29)**

Several studies have aimed to develop or validate clinical severity scoring systems for sickle cell disease (SCD), each emphasizing different aspects of the disease's heterogeneity. **Shah et al. in 2020** introduced a three-tier classification system for SCD severity, based on expert consensus using a modified Delphi approach. Their findings emphasized that increased unscheduled acute care visits and end-organ damage were strongly associated with more severe disease, offering a practical tool to stratify patients and support clinical decision-making. **(25)**

Okocha et al. (2015) examined the relationship between hemogram parameters and disease severity in Nigerian SCD patients. They demonstrated that basic hematological markers such as high white blood cell counts, low hemoglobin levels, and increased platelet counts were significantly associated with higher severity scores, thus providing a cost-effective and accessible means of monitoring disease progression in resource-limited settings.**(30)**

Adegoke and Kuti (2013) developed a clinical severity scoring model for children with SCD in Nigeria using 15 clinical and laboratory parameters. Their study revealed that 10.4% of the children had severe disease and identified low fetal hemoglobin levels and early onset of dactylitis as significant independent predictors of severe disease. These findings highlight the value of early clinical markers in anticipating more aggressive disease courses in pediatric populations.**(31)**

In another study by **Okocha et al. in 2020,** the focus shifted to the role of biomarkers, specifically granulocyte differentiation factor 15 (GDF-15). Their research found that GDF-15 levels were significantly lower in patients with more severe disease, suggesting its potential as both a biomarker for disease severity and a target for future therapeutic intervention aimed at mitigating ischemia-reperfusion injury, which plays a key role in SCD pathology.**(24)**

Onu et al. in 2025 contributed a psychosocial dimension to SCD severity assessment. Their study revealed a significant negative correlation between disease severity and perceived social support, particularly from classmates. Interestingly, social support from peers emerged as an independent predictor of disease severity even after adjusting for fetal hemoglobin levels, highlighting the critical role psychosocial factors play in influencing clinical outcomes in children with SCD.**(32)**

Lastly, Biswas et al. (2022) evaluated the applicability of Tweel's severity scoring system in Indian patients and concluded that phenotypic variations necessitate a modified, context-specific tool. They emphasized the importance of developing a regionally appropriate severity classification system to improve patient stratification and management in Indian populations, where the clinical spectrum of SCD may differ from Western cohorts.**(33)**

Conclusion and Future Scope

This study provides key clinical insights into the severity and complication patterns of sickle cell disease among tribal patients. Most participants experienced moderate disease with common complications like pain crises and fatigue. A smaller group had mild symptoms, while others faced severe complications, highlighting the variability in disease presentation. Life-threatening issues such as stroke and nephropathy were relatively rare, possibly due to early diagnosis and timely use of hydroxyurea.

The findings emphasize the need for individualized care and regular clinical monitoring. Future research should include longitudinal studies to assess disease progression and treatment outcomes, along with genetic research to identify biomarkers for severity prediction. Expanding new-born and pediatric screening in tribal areas can aid early diagnosis. Community-based education and counseling could improve treatment adherence and reduce stigma. These insights can inform regional healthcare policies and advocate for accessible care in underserved regions. Additionally, exploring the impact of nutrition, psychosocial support, and lifestyle changes may help improve patients' overall quality of life.

Strengths and Limitations of Study

It employs a well-structured case-control design with age- and sex-matched controls, enhancing the reliability and validity of comparisons between sickle cell disease (SCD) patients and healthy individuals. The focus on tribal populations from the Nandurbar region addresses a significant gap in existing research by shedding light on a vulnerable and often neglected group. The balanced gender representation among participants allows for more inclusive analysis. Diagnostic accuracy was ensured through the use of both turbidity testing and high-performance liquid chromatography (HPLC). Furthermore, disease severity was comprehensively assessed using multiple parameters like hemoglobin level, white blood cell (WBC) count, and clinical complications offering a holistic view of disease burden. The study also applied strict inclusion and exclusion criteria, minimizing confounding factors and ensuring the integrity of the sample. Ethical standards were upheld through informed consent, and the region-specific focus enhances the relevance of findings for public health planning in tribal areas.

Despite its strengths, this study has certain limitations. Being a single-centre study focused on the tribal population of the Nandurbar region, the findings may not be generalizable to other populations or geographic areas. The relatively small sample size of 86

patients and 86 controls may limit the statistical power and the ability to detect less common clinical patterns or complications. Additionally, the cross-sectional nature of the study restricts conclusions regarding causality or long-term disease progression. Some factors that could influence disease severity such as nutritional status, socioeconomic background, genetic modifiers like fetal hemoglobin levels, and access to healthcare were not deeply explored. Self-reported data on clinical history may also introduce recall bias. Although the study evaluated disease severity using clinical and hematological parameters, the absence of a validated and universally accepted scoring system specifically adapted to the Indian tribal context may limit the consistency and comparability of severity assessment.

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Conflict of interest: The authors declare no conflict of interest related to this study.

Funding: NIL

Data availability- The data generated and analyzed during this study are not publicly available due to patient confidentiality and institutional policies, but are available from the corresponding author upon reasonable request for academic and research purposes.

Ethical Considerations- This study was conducted in accordance with ethical standards and guidelines for human research. Informed consent was obtained from all participants or their legal guardians before data collection. Patient confidentiality was strictly maintained, and all personal identifiers were removed from the dataset used for analysis. Ethical approval for the study was obtained from the Institutional Ethics Committee prior to initiation. Participation

was voluntary, and patients were free to withdraw from the study at any point without any impact on their standard medical care.

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