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Review Article: Sickle Cell Anaemia in India — Epidemiological, Clinical, and Public Health Perspectives

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Abstract:
Sickle cell anaemia (SCA) is a genetic hemoglobinopathy caused by a point mutation (Glu6Val) in the β-globin gene on chromosome 11, leading to the substitution of valine for glutamic acid and the formation of abnormal haemoglobin S (HbS). Under hypoxic conditions, HbS polymerizes, causing red blood cells to become rigid and sickle-shaped, resulting in chronic hemolytic anaemia, vaso-occlusive crises, and multi-organ damage. In India, SCA predominantly affects tribal and some non-tribal populations across Madhya Pradesh, Chhattisgarh, Maharashtra, Odisha, Gujarat, and parts of Tamil Nadu, where carrier frequencies range from 1% to 40%, posing significant regional and genetic diversity in disease burden. The autosomal recessive inheritance pattern leads to a 25% risk of disease occurrence in offspring when both parents are carriers, highlighting the urgent need for widespread premarital and antenatal genetic screening. Clinical manifestations include recurrent pain crises, splenic infarction, growth retardation, leg ulcers, and stroke, significantly impacting quality of life and life expectancy. Diagnostic approaches have evolved from solubility and sickling tests to advanced techniques such as haemoglobin electrophoresis, high-performance liquid chromatography (HPLC), capillary electrophoresis, and PCR-based molecular assays for confirmatory diagnosis and neonatal screening. Recent developments in point-of-care devices such as HemoTypeSC™ and Sickle SCAN™ have enabled cost-effective detection in rural and resource-limited settings. The Government of India's National Sickle Cell Anaemia Elimination Mission (NSCAEM) 2023–2030 has introduced systematic screening, counseling, and newborn testing programs aiming to reduce disease incidence and improve management outcomes. Despite progress, challenges remain in early diagnosis, comprehensive care, and equitable service delivery in remote areas. Ongoing research on foetal haemoglobin (HbF) induction, hydroxyurea therapy, gene editing, and stem cell transplantation continues to offer promising curative directions. This review highlights the integrated need for molecular research, public health policy, and community awareness to achieve the long-term goal of sickle cell elimination and ensure equitable health outcomes across affected populations.

Keywords: Sickle cell anaemia, India, epidemiology, anaemia, newborn screening, tribal health, hemoglobinopathy, public health

1. Introduction

Sickle cell anaemia (SCA) is one of the most common hereditary blood disorders globally and a major public health concern in India. It is caused by a single nucleotide substitution (GAG→GTG) in the β globin gene, resulting in the replacement of glutamic acid with valine at position 6. This mutation leads to

polymerization of deoxygenated HbS, causing erythrocyte deformation, Vaso-occlusion, and chronic haemolysis. In India, the HbS gene is found primarily in central, western, and southern states, with high prevalence among tribal populations.

SCA manifests with a spectrum of clinical complications including recurrent painful crises, chronic anaemia, splenic dysfunction, and increased susceptibility to infections. The severity of symptoms can vary widely depending on genetic modifiers such as co-inheritance of alpha-thalassemia or elevated foetal haemoglobin levels. Early diagnosis through newborn screening and molecular testing is crucial for timely intervention and prevention of life-threatening complications. Despite advances in clinical management, including hydroxyurea therapy and supportive care, SCA continues to impose significant morbidity and mortality. Public health efforts in India are challenged by limited awareness, socio-economic constraints, and inadequate healthcare infrastructure in tribal regions. Carrier screening and genetic counselling are essential strategies to reduce disease burden in high-prevalence communities. Furthermore, research into novel therapies, including gene editing and stem cell transplantation, offers hope for curative treatment. Integration of community-based education, improved diagnostics, and accessible care is vital to mitigate the impact of SCA in India.

2.1 Epidemiology in India

Sickle cell disease (SCD) and sickle cell trait (SCT) are major inherited hemoglobinopathies in India, predominantly affecting tribal and certain caste populations residing in malaria-endemic regions. The overall prevalence of SCD in India is estimated to be around 1.17%, while the carrier or trait frequency is about 5.9%, with HbS-β thalassemia accounting for nearly 0.37%. The sickle gene is mainly concentrated in the central, western, and parts of southern India, forming the so-called “sickle cell belt” that includes Madhya Pradesh, Chhattisgarh, Maharashtra, Gujarat, Odisha, Jharkhand, and some areas of Rajasthan, Andhra Pradesh, and Kerala. Among tribal communities such as the Gond, Bhil, Baiga, Pardhan, and Madia, the carrier rate can range from 10% to over 30%, with a variable but significant disease burden. Within states, the prevalence varies depending on specific tribal or caste groups and local environmental factors. Madhya Pradesh shows trait frequencies between 10–33%, while high rates are also seen in the Vidarbha region of Maharashtra, southern Gujarat, and tribal areas of southern Rajasthan. Recognizing the growing health burden, the Government of India launched the National Sickle Cell Anaemia Elimination Mission (NSCAEM) in 2023, aiming to eliminate genetic transmission of the disease by 2047. As of 2025, over 5.7 crore individuals have been screened across 17 high-focus states, and thousands of confirmed cases have been registered, with Odisha, Gujarat, and Madhya Pradesh reporting the highest numbers. Despite these efforts, underdiagnosis remains widespread due to limited awareness, poor access to diagnostic facilities, and socioeconomic barriers in remote tribal areas. Inconsistent newborn screening and limited access to genetic counselling further hinder disease control. Strengthening early diagnosis, public education, and community-based genetic counselling programs is crucial to reduce morbidity and to achieve a sickle cell–free India by 2047.

2.2 Case Study in Madhya Pradesh

Madhya Pradesh Population of Madhya Pradesh, where approximately 25% of tribal individuals are affected either as carriers or patients. According to the Dainik Bhaskar investigation (15 November 2021), the state’s 1.53 crore tribal population—spread across 89 tribal blocks in 27 districts—faces a significant burden of the disease, yet many areas still lack diagnostic facilities. Field data reveal alarmingly high prevalence: in Jhabua district, 36.5% of screened persons were positive for sickle cell trait or disease, while in Barwani district, screening of 8,000 people identified 1,978 patients. The 2011 Census recorded 1,53,16,784 tribal residents (77,19,404 males and 75,97,380 females), indicating that roughly every fourth tribal individual may be a carrier. To combat this, the Madhya Pradesh Sickle Cell Eradication Mission (2021–2026) was launched, targeting screening of 1.5 crore tribal individuals, including 24 lakh people in

the Nimar region (notably Khargone, Barwani, Khandwa, and Burhanpur). Pilot projects were initiated in Jhabua and Alirajpur, where community-level solubility and electrophoresis testing is being conducted for pregnant women and children aged 6 months to 18 years. The mission, supported by the Jan Abhiyan Parishad and health departments, aims to identify carriers, provide genetic counselling, and prevent disease transmission. Statewide reports estimate sickle cell positivity ranging from 0.3% to 3.4%, but local tribal clusters show much higher figures up to 40% in some villages. Despite these efforts, many of the 89 tribal blocks still lack adequate testing and treatment units, causing patients to face chronic anaemia, joint pain, and social stigma. The government's comprehensive five-year screening and awareness plan seeks to integrate laboratory facilities, patient cards, and follow-up care for sustainable control. The situation underscores the urgent need for strengthened hemoglobinopathy screening, health infrastructure, and counselling programs to mitigate the disease burden among Madhya Pradesh's tribal communities.

Table 1: Epidemiological Data on Sickle Cell Anaemia in Madhya Pradesh

Parameter	Data (as per Dainik Bhaskar Reports, 2021–2022)
Total tribal population (M.P.)	1.53 crore (2011 Census: 1,53,16,784)
Male : Female distribution	77,19,404 : 75,97,380
Total tribal blocks	89 blocks across 27 districts
High-prevalence districts	Jhabua, Alirajpur, Barwani, Dhar, Khargone, Mandla, Dindori, Shahdol
Prevalence in Jhabua	36.5% positive for trait or disease
Barwani data	1,978 patients among 8,000 screened
Overall prevalence	0.3%–3.4% (statewide average), up to 40% in tribal villages
Screening target (2021–2026)	1.5 crore tribal individuals
Nimar region coverage	24 lakh population (Khargone, Barwani, Khandwa, Burhanpur)
Screening age group	6 months – 18 years and pregnant women

2.3 Case Study in Uttar Pradesh

Sickle Cell Anaemia (SCA) is an inherited hemoglobinopathy that causes red blood cells to assume a rigid, sickle-like shape, leading to chronic haemolysis, vaso-occlusive crises, and multiorgan complications. While Uttar Pradesh (UP) is not traditionally considered a high-burden state compared to Madhya Pradesh, Chhattisgarh, or Odisha, recent screening and community-based studies reveal emerging clusters of SCA, particularly among the *Tharu tribal population* residing along the Indo–Nepal border in districts such as Lakhimpur Kheri, Balrampur, Bahraich, and Shravasti. According to the Rajya Sabha Report (December 2024) under the *National Sickle Cell Anaemia Elimination Mission (NSCAEM)*, a total of 652,404 individuals were screened in Uttar Pradesh, of which 19 were confirmed cases of Sickle Cell Disease (10 males, 9 females, and none among 117 transgender/others). Although this represents a relatively low overall state prevalence, localized studies have different prospective. A hospital-based study conducted among the Tharu community between January 2020 and June 2022 reported that out of 409 Tharu individuals tested, 60 (14.67%) were positive for sickling—45 (75%) had the sickle cell trait (HbAS) and 15 (25%) had sickle cell disease (HbSS). Genetic analyses in this population have also shown a βS allele frequency of around 10%, indicating significant hereditary transmission within endogamous groups. Media and field reports, such as the *Hindustan Times* (2023), further suggest even higher positivity rates (up to 60%) in isolated community screening camps, though these figures likely reflect selective sampling rather than true population prevalence. In Uttar Pradesh, ongoing screening targets high-risk tribal belts, with medicines and counselling services now being extended to Anganwadi and panchayat centres for better grassroots access. However, many basic challenges persist, including poor awareness, limited

laboratory infrastructure for haemoglobin electrophoresis/HPLC, and inadequate follow-up care for identified carriers and patients. Strengthening district-level genetic testing, integrating newborn screening, and establishing community-based SCA registries are essential steps toward achieving elimination goals. Despite a modest statewide burden numerically, the data from the Tharu belt underline that sickle cell anaemia remains a serious localized tribal health issue in Uttar Pradesh, warranting focused surveillance, public health interventions, and genetic counselling to break the intergenerational cycle of disease transmission.

3. Pathophysiology

Sickle Cell Anaemia (SCA) is a hereditary hemoglobinopathy resulting from a single point mutation in the β-globin gene on chromosome 11, where the substitution of valine for glutamic acid at position 6 (Glu6Val) produces abnormal haemoglobin known as haemoglobin S (HbS). Under low oxygen tension, HbS molecules polymerize, leading to the formation of rigid, sickle-shaped erythrocytes that lose deformability, become sticky, and adhere to the vascular endothelium. This polymerization process is central to the disease's pathogenesis and initiates a cascade of microvascular obstruction, haemolysis, and ischemic injury.

The sickling process is reversible initially but becomes irreversible after repeated deoxygenation–reoxygenation cycles. The rigid sickled erythrocytes have shortened lifespans of about 10–20 days compared to normal red cells (120 days), leading to chronic haemolytic anaemia. The release of free haemoglobin and heme during intravascular haemolysis results in nitric oxide (NO) scavenging, endothelial dysfunction, and oxidative stress, further exacerbating vaso-occlusion. This interplay between haemolysis and inflammation forms the pathophysiological basis of recurrent pain crises and multi-organ damage.

Microvascular occlusion occurs when sickled cells interact with leukocytes, platelets, and endothelial adhesion molecules such as VCAM-1, ICAM-1, and P-selectin, resulting in blood flow stagnation and tissue hypoxia. Repeated vaso-occlusive episodes lead to ischemia-reperfusion injury, chronic inflammation, and organ damage, particularly affecting the spleen, kidneys, lungs, and brain. Splenic infarction and fibrosis cause functional asplenia, predisposing patients to severe bacterial infections. Chronic haemolysis contributes to gallstone formation, leg ulcers, pulmonary hypertension, and stroke.

Moreover, increased red cell density and dehydration (due to K^+ and water loss via the Grados channel) enhance HbS polymerization, creating a vicious cycle of sickling. Fatal haemoglobin (HbF) plays a protective role by inhibiting polymerization; hence, therapeutic strategies such as Sickle cell anaemia (SCA) is one of the most common hereditary blood disorders globally and a major public health concern in India. It is caused by a single nucleotide substitution (GAG→GTG) in the β globin gene, resulting in the replacement of glutamic acid with valine at position 6. This mutation leads to polymerization of deoxygenated HbS, causing erythrocyte deformation, vaso-occlusion, and chronic haemolysis. In India, the HbS gene is found primarily in central, western, and southern states, with high prevalence among tribal populations.

SCA manifests with a spectrum of clinical complications including recurrent painful crises, chronic anaemia, splenic dysfunction, and increased susceptibility to infections. The severity of symptoms can vary widely depending on genetic modifiers such as co-inheritance of alpha-thalassemia or elevated foetal haemoglobin levels. Early diagnosis through newborn screening and molecular testing is crucial for timely intervention and prevention of life-threatening complications. Despite advances in clinical management, including hydroxyurea therapy and supportive care, SCA continues to impose significant morbidity and mortality. Public health efforts in India are challenged by limited awareness, socio-economic constraints, and inadequate healthcare infrastructure in tribal regions. Carrier screening and genetic counselling are essential strategies to reduce disease burden in high-prevalence communities. Furthermore, research into novel therapies, including gene editing and stem cell transplantation, offers hope for curative treatment.

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4. Clinical Manifestations

Sickle cell anaemia (SCA) is a chronic multisystem disorder arising from haemoglobin S polymerization that causes red cell deformation, haemolysis, and vascular occlusion. The disease primarily manifests as chronic haemolytic anaemia with pallor, jaundice, fatigue, and growth retardation. Laboratory findings reveal haemoglobin levels of 6–9 g/dL, reticulocytosis, and elevated bilirubin and LDH. Repeated haemolysis contributes to pigment gallstones, leg ulcers, and delayed puberty. Early splenic infarction leads to functional asplenia by the first decade of life, resulting in recurrent infections by *Streptococcus pneumoniae* and *Haemophilus influenzae*. The most frequent acute event is the vaso-occlusive (pain) crisis, caused by microvascular blockage of sickled cells. These episodes affect bones, chest, and abdomen, leading to bone infarction, avascular necrosis of the femoral and humeral heads, and osteomyelitis (often *Salmonella*-related). The acute chest syndrome, a major cause of mortality, manifests as chest pain, fever, pulmonary infiltrates, and hypoxia due to infection or infarction.

Neurological complications such as stroke and transient ischemic attacks occur from large-vessel vasculopathy, particularly in children, and are mitigated by transcranial Doppler screening and transfusion therapy. Renal involvement includes haematuria, proteinuria, and sickle nephropathy progressing to renal failure. Chronic anaemia induces cardiomegaly and pulmonary hypertension, while recurrent ischemia causes hepatic, splenic, and skeletal damage. Additional features include priapism, retinopathy, and pregnancy-related complications with increased maternal–foetal risk. The clinical heterogeneity depends on foetal haemoglobin (HbF) level, α-thalassemia co-inheritance, and environmental factors. Modern management—hydroxyurea to raise HbF, L-glutamine, voxelate, transfusion programs, and hematopoietic stem-cell transplantation—has improved survival and quality of life. Thus, SCA's manifestations reflect a complex interplay between haemolysis, Vaso-occlusion, and inflammation affecting nearly every organ, underscoring the need for early diagnosis, preventive vaccination, and comprehensive care.

5. Diagnosis and Screening

Early and accurate diagnosis of Sickle Cell Anaemia (SCA) is essential for reducing morbidity and mortality through timely intervention and genetic counselling. Diagnosis is based on haematological, biochemical, and molecular methods that identify haemoglobin variants and confirm the presence of HbS (sickle haemoglobin). Routine blood examination often reveals normocytic or microcytic anaemia, reticulocytosis, and characteristic sickle-shaped erythrocytes on peripheral smear, particularly after deoxygenation. The sickling test (using sodium metabisulfite or sodium dithionite) remains a rapid qualitative method, while the solubility test using reducing agents is widely used for screening large populations. However, these methods cannot distinguish between sickle cell trait (HbAS) and disease (HbSS). Sickle cell anaemia (SCA) is one of the most common hereditary blood disorders globally and a major public health concern in India. It is caused by a single nucleotide substitution (GAG→GTG) in the β globin gene, resulting in the replacement of glutamic acid with valine at position 6. This mutation leads to polymerization of deoxygenated HbS, causing erythrocyte deformation, vaso-occlusion, and chronic haemolysis. In India, the HbS gene is found primarily in central, western, and southern states, with high prevalence among tribal populations.

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6.Genetic Inheritance Pattern of Sickle Cell Anaemia

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Punnett Square for Sickle Cell Inheritance (HbAS × HbAS)

Parents-	HbA (Parent 2)	HbS (Parent 2)
HbA (Parent 1)	HbAA (Normal)	HbAS (Carrier)
HbS (Parent 1)	HbAS (Carrier)	HbSS (Diseased)

Table: Probability of Offspring Genotypes in Different Parental Combinations

Parental Genotypes	HbAA (Normal)	HbAS (Carrier)	HbSS (Diseased)	Remarks
HbAA × HbAA	100%	0%	0%	All normal
HbAA × HbAS	50%	50%	0%	Half carriers
HbAA × HbSS	0%	100%	0%	All carriers
HbAS × HbAS	25%	50%	25%	Typical Mendelian ratio
HbAS × HbSS	0%	50%	50%	Half carriers, half diseased
HbSS × HbSS	0%	0%	100%	All diseased

7. Management

7.1 Supportive and disease-modifying therapy

Hydroxyurea remains the mainstay therapy, increasing HbF levels and reducing crises and transfusion needs. Studies in Indian cohorts confirm its efficacy and safety. Transfusion therapy is reserved for severe anaemia and acute complications. Bone marrow transplantation is curative but limited by cost and donor availability.

7.2 Public health and community care

Comprehensive care involves immunization, infection prevention, genetic counselling, nutritional support, and psychosocial assistance. The NSCAEM emphasizes community-based screening, counselling, and drug availability in tribal districts.

8.Comprehensive Conclusion

Sickle cell anaemia (SCA) is one of the most important hereditary haemoglobin disorders worldwide, caused by a single base substitution (A→T) in the β-globin gene on chromosome 11, leading to the formation of abnormal haemoglobin S (HbS). The resulting Glu6Val mutation triggers haemoglobin polymerization under hypoxic conditions, distorting red blood cells into rigid sickle shapes that obstruct microvasculature, causing haemolysis, ischemia, and multi-organ dysfunction. The disease exhibits an autosomal recessive inheritance pattern, where homozygotes (HbSS) develop severe disease and heterozygotes (HbAS) possess sickle cell trait with partial protection against *Plasmodium falciparum* malaria. The pathophysiological cascade includes red cell dehydration, oxidative stress, endothelial adhesion, and chronic haemolytic anaemia, explaining its systemic clinical picture. Patients often present with recurrent vaso-occlusive crises, anaemia, jaundice, splenic infarction, stroke, bone necrosis, delayed growth, and organ damage. The diagnosis has evolved from classical microscopic sickling and solubility tests to advanced haemoglobin electrophoresis, high-performance liquid chromatography (HPLC), and molecular assays such as PCR-based detection of the Glu6Val mutation. Capillary electrophoresis and isoelectric focusing have become the gold standards for neonatal screening in several nations. In India, SCA is predominantly found among tribal and backward communities in Madhya Pradesh, Chhattisgarh, Maharashtra, Odisha, and Gujarat, where carrier frequencies vary between 1% and 40%. Government-led initiatives, including the National Sickle Cell Elimination Mission (2023–2030) under the National Health Mission, aim for universal screening, genetic counselling, and newborn testing. Genetic inheritance studies show that when both parents are carriers (HbAS × HbAS), offspring distribution follows Mendelian ratios—25% normal (HbAA), 50% carriers (HbAS), and 25% affected (HbSS). Understanding this inheritance pattern underscores the value of premarital and antenatal screening for disease prevention. The introduction of point-of-care diagnostic kits such as Hemo TypeSC™ and Sickle SCAN™ has revolutionized rural screening, enabling rapid and affordable diagnosis. Continued research on foetal haemoglobin (HbF) regulation, hydroxyurea therapy, and gene-editing technologies such as CRISPR/Cas9 provides new hope for long-term management and potential cure. From a public health perspective,

awareness campaigns, community education, and inclusion of sickle cell screening in school and maternal health programs are pivotal. The integration of molecular diagnostics, early intervention, and preventive strategies has transformed the disease from a fatal childhood disorder to a manageable chronic condition. Thus, SCA serves as a model for integrating genetics, public health, and community engagement in controlling inherited diseases. Sustained policy commitment, accessible molecular testing, and universal awareness can lead India towards the vision of Sickle Cell Elimination by 2030 , reducing morbidity, mortality, and intergenerational transmission of this preventable genetic disorder.

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