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The Thalassemia Spectrum among India's Tribal Populations: Genetic Diversity, Epidemiology, and Public Health Implications

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Abstract*—Thalassemia remains one of the world's most prevalent inherited blood disorders, and India contributes a major share of its global burden. Within India, tribal communities constituting nearly 8.6 per cent of the population exhibit a distinctive genetic architecture owing to geographical isolation, endogamy, and unique sociocultural practices. These groups demonstrate wide heterogeneity in mutation spectrum, carrier frequency, and clinical expression. The present review synthesises available data on genetic diversity, regional distribution, diagnostic limitations, and public-health implications of thalassemia among India's tribal populations. Literature was reviewed from PubMed, Scopus, ICMR, and state health repositories from 2000 to 2025. Carrier frequencies range from 0.5 per cent in the Andaman tribes to over 18 per cent in Odisha and Gujarat. Common β-thalassemia mutations include IVS-I-5 (G→C), Codon 8/9 (+G), Codon 41/42 (−TCTT), and the 619-bp deletion, while α-thalassemia deletions ($-\alpha^{3.7}$ and $-\alpha^{4.2}$) predominate in southern and central tribes. Public-health challenges include late diagnosis, limited transfusion facilities, poor awareness, and cultural barriers to genetic counselling. Successful models such as Gujarat's community-based screening and Odisha's Thalassemia Control Programme illustrate feasible pathways for prevention. Integrating molecular diagnostics, premarital and antenatal screening, and culturally sensitive education can substantially reduce new thalassemia births. Bridging genomics and public health is essential for ensuring equitable healthcare access to India's tribal populations.*

***Keywords*—** *Thalassemia, Tribal populations, India, Genetic diversity, Epidemiology, Public health, Screening, Prevention, Haemoglobinopathy.*

I. Background

Thalassemia refers to a group of autosomal recessive disorders characterised by reduced or absent synthesis of α- or β-globin chains, leading to imbalance in haemoglobin production, microcytosis, and chronic anaemia. The condition is distributed widely across malaria-endemic regions where heterozygote advantage confers protection against severe *Plasmodium falciparum* infection. Globally, nearly seven per cent of people carry a haemoglobin variant, and India alone accounts for about 42 million carriers.

Historically, thalassemia was recognised primarily among Mediterranean and Middle-Eastern populations, but systematic surveys during the past four decades revealed significant prevalence in South Asia. The Indian Council of Medical Research (ICMR) estimates 10 000–12 000 affected births annually, making thalassemia a major contributor to childhood morbidity. The disease's impact is magnified among tribal groups because of restricted gene flow, social isolation, and limited health-care access.

India's tribal population, distributed across 700 distinct communities, represents a mosaic of genetic subgroups. Geographic isolation and centuries of endogamy have produced unique mutation patterns not seen in the general population. Yet, these communities remain under-represented in genetic studies, leaving large knowledge gaps. Understanding the thalassemia spectrum within tribal populations is therefore essential for developing precise and culturally appropriate public-health strategies.

II. Genetic Spectrum in Indian Tribal Populations

The genetic diversity of thalassemia across India's tribes reflects regional founder effects and evolutionary selection. More than 60 β-thalassemia mutations have been described nationwide, but four mutations—IVS-I-5 (G→C), Codon 8/9 (+G), Codon 41/42 (−TCTT), and the 619-bp deletion—account for almost 90 per cent of cases.

β-Thalassemia Mutations

- Eastern India (Odisha, Jharkhand, West Bengal): The IVS-I-5 (G→C) mutation predominates, occasionally accompanied by Codon 15 (G→A).
- Western India (Gujarat, Maharashtra): Codon 41/42 (−TCTT) and the 619-bp deletion are frequent among Bhil, Naikda, and Gond tribes.
- Central India (Madhya Pradesh, Chhattisgarh): Both IVS-I-5 (G→C) and 619-bp deletion coexist; compound heterozygosity is not uncommon.
- Northeastern Region: Co-inheritance of HbE and β-thalassemia mutations gives rise to HbE-β-thalassemia with variable clinical severity.

α-Thalassemia Mutations

α-Thalassemia deletions ($-\alpha^{3.7}$ and $-\alpha^{4.2}$) are common in central and southern India. Homozygosity may lead to HbH

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disease, while double-gene deletions cause mild microcytosis often misdiagnosed as iron deficiency.

Compound and Rare Mutations

Rare alleles such as IVS-II-745 (C→G) and Codon 30 (G→C) have been documented in smaller tribal pockets. Founder mutations arise from small effective population sizes, while inter-tribal marriages occasionally introduce new variants.

TABLE 1. Prevalence of β- and α-Thalassemia Mutations among Major Tribal Groups in India

State / Region	Major Tribal Groups	Carrier Frequency (%)	Predominant Mutations
Odisha	Santal, Juang, Saora, Bhumij	10–18	IVS-I-5 (G→C), Codon 8/9 (+G)
Gujarat	Bhil, Rathwa, Naikda	8–15	Codon 41/42 (−TCTT), IVS-I-1 (G→A)
Maharashtra	Gond, Warli, Madia	6–12	619-bp deletion, Codon 15 (G→A)
Madhya Pradesh	Baiga, Bhil, Gond	4–10	IVS-I-5 (G→C), 619-bp deletion
Chhattisgarh	Halba, Muria, Dhurwa	3–8	Codon 8/9 (+G), IVS-II-654 (C→T)
Jharkhand	Ho, Munda, Santhal	5–9	IVS-I-5 (G→C), Codon 15 (G→A)
Andaman & Nicobar	Onge, Jarawa	0.5–1	Rare β-thal alleles

III. Epidemiology and Regional Distribution

Epidemiological studies reveal striking inter-state variation. Odisha's tribal belt reports some of the highest carrier frequencies worldwide, with up to 18 per cent among Juang and 12 per cent among Bhumij tribes. In Gujarat, about 10 per cent of the Bhil and 15 per cent of Naikda populations carry β-thalassemia alleles. Central Indian tribes such as Gond and Baiga show intermediate frequencies of 4–10 per cent. The lowest prevalence is recorded in the Andaman and Nicobar tribes, consistent with their genetic isolation and small population size.

Regional clustering parallels historical malaria distribution, supporting the hypothesis of balanced polymorphism. In eastern India, coexistence of β-thalassemia and sickle-cell mutations further complicates clinical patterns. Compound heterozygosity can result in atypical anaemia presentations, underscoring the importance of molecular confirmation.

Nationally, ICMR's multicentric surveys (2018–2022) estimated that about 10 per cent of all tribal individuals in India are carriers of a haemoglobinopathy. The economic cost of managing transfusion dependent thalassemia remains enormous—estimated at ₹1–1.5 lakh per child annually highlighting the need for prevention rather than treatment-based strategies.

IV. Clinical and Diagnostic Challenges

Phenotypic heterogeneity among tribal patients complicates early recognition. Mild carriers may remain undetected for years, while severe forms present in infancy with pallor, hepatosplenomegaly, and growth failure. Misdiagnosis as nutritional anaemia is common at the primary-care level.

Routine screening using haemoglobin electrophoresis and red-cell indices is limited by overlap between β-thalassemia trait and iron-deficiency anaemia. High-performance liquid chromatography (HPLC) provides accurate quantification of HbA_2 and HbF fractions, yet its availability in remote tribal districts is minimal.

Molecular testing—PCR-based mutation analysis or reverse hybridisation strip assays—confirms carrier status, but costs remain prohibitive for many state programmes. Lack of trained personnel further delays diagnosis. Consequently, antenatal testing is rarely offered, and most affected infants are diagnosed only after repeated transfusions.

Infrastructure gaps are critical: fewer than 15 per cent of district hospitals in tribal regions have blood-transfusion facilities or iron-chelation services. Regular desferrioxamine or deferasirox therapy is unaffordable for most families, leading to iron overload, cardiac failure, and premature death.

V. Public Health and Socio-Cultural Determinants

Health outcomes are profoundly shaped by social context. Among many tribes, marriage within the same clan or village is customary, sustaining high carrier frequency. Awareness of hereditary transmission is minimal; illness is often attributed to spiritual or environmental causes. Stigma surrounding genetic disorders discourages families from seeking counselling.

Low literacy levels and language barriers hinder health communication. Women face double disadvantage—both as caregivers and as potential carriers subject to social blame. Many families discontinue medical treatment once financial resources are exhausted, resulting in avoidable mortality.

Sustainable prevention demands culturally adapted strategies. Community meetings led by tribal elders, pictorial educational materials, and radio campaigns in local dialects have shown success. Involving *ASHA* and *Anganwadi* workers enhances trust. Policy frameworks must integrate thalassemia control within broader tribal health and nutrition missions, ensuring equity in service delivery.

VI. Community Screening and Prevention Programmes

Recognising haemoglobinopathies as a national priority, the Government of India launched the National Haemoglobinopathy Mission under the National Health Mission (NHM). Several states have established regional models:

- Gujarat: A pioneering programme since 2006 screening school and college students, issuing carrier cards, and providing premarital counselling. Over 1.2 million individuals have been screened with measurable decline in thalassemia births.
- Odisha: The Thalassemia Control Programme (2017) expanded screening to tribal districts; mobile diagnostic vans and free chelation therapy improved accessibility.

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- Maharashtra and Madhya Pradesh: Regional genetic laboratories perform antenatal diagnosis using chorionic-villus sampling.

Despite progress, national coverage remains below 25 per cent. Screening uptake is low among remote tribes due to travel distance and apprehension about blood testing. Integrating thalassemia screening into routine antenatal care, adolescent health programmes, and *Janani Suraksha Yojana* can normalise testing and reduce stigma.

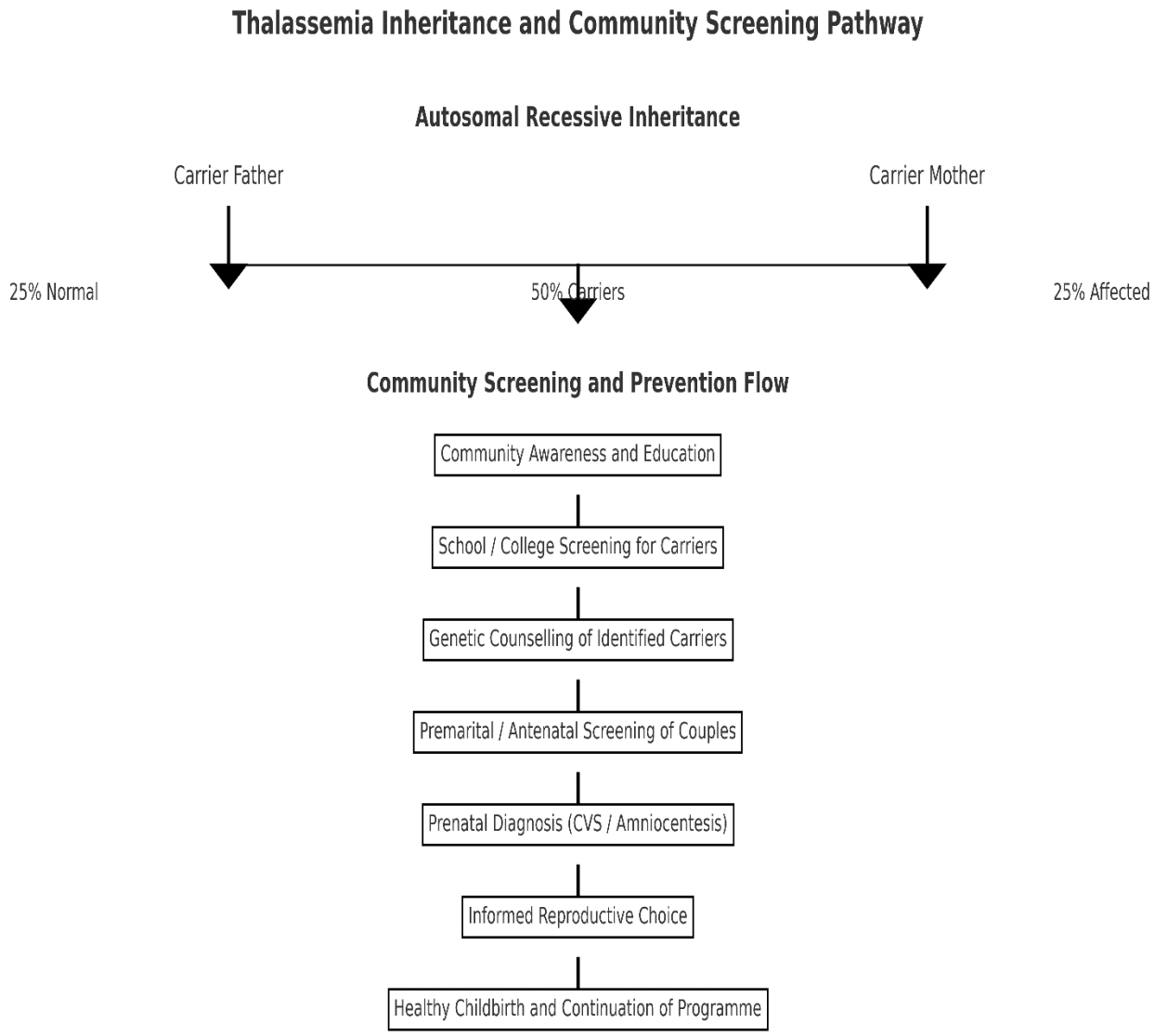

Figure 1. Thalassemia Inheritance and Community Screening Pathway

The diagram illustrates autosomal-recessive inheritance where carrier parents have a 25 per cent chance of an affected child. The lower half shows the recommended screening flow: community awareness → school/college screening → identification of carriers → premarital/antenatal counselling → prenatal testing → informed reproductive choice → healthy birth.

VII. Emerging Research and Technological Directions

Scientific advances are reshaping the management landscape:

1. Next-Generation Sequencing (NGS): Allows simultaneous detection of known and novel mutations, especially useful for heterogeneous tribal populations. NGS-based newborn screening pilots in Odisha and Gujarat demonstrated feasibility and cost reduction.
2. Gene Editing and Cell Therapy: CRISPR-Cas9 trials targeting BCL11A enhancer reactivation have produced transfusion independence in some patients abroad; Indian centres are initiating similar research.
3. Population Genomics: Projects such as the Genome India Initiative include tribal cohorts, helping trace mutation origins and guide precision prevention.

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4. Digital Health and Tele-Genetics: Mobile apps for genetic counselling and teleconsultations overcome geographic barriers.
5. Artificial Intelligence: Machine-learning models analysing HPLC chromatograms can automate carrier detection at low cost.

Collectively, these developments herald a shift from descriptive epidemiology to predictive genomics, where molecular insights directly inform community health policies.

VIII. Conclusion

Thalassemia among India's tribal populations exemplifies how biological inheritance intertwines with social and economic determinants. The disorder's persistence stems not from lack of technology but from gaps in awareness, accessibility, and political will. Expanding community screening, empowering local health workers, and ensuring affordability of diagnostic and treatment services are immediate imperatives.

Long-term success requires embedding genetic literacy within school curricula, training healthcare providers in counselling, and sustaining public funding for transfusion and chelation support. Research must continue to document regional mutation spectra so that diagnostic kits reflect India's genetic mosaic.

A multi-sectoral approach combining genomics, education, and community participation can transform thalassemia from a lifelong burden into a preventable condition. In doing so, India would set a global example of inclusive precision public health, safeguarding vulnerable tribal communities for generations to come.

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