Regional Variations in Thalassemia Prevalence: An Epidemiological Review of India

Mitaigiri Shaik Sajid[1], Chalamatigari Yoga Chandra Sekhar Reddy[1], Kolime Safiya Kousar[1], Bhukya Pushpalatha[1], U Veerendra[2*]

1. Intern, PharmD VI Year, Pharmacy Practice, Rahavendra Institute of Pharmaceutical Education and Research (RIPER)-Autonomous, Anantapur, Andhra Pradesh-515721.

2. Asst. Professor, Pharmacy Practice, Rahavendra Institute of Pharmaceutical Education and Research (RIPER)-Autonomous, Anantapur, Andhra Pradesh-515721.

Abstract: Thalassemia, a group of inherited blood disorders affecting hemoglobin production, presents a major public health concern in India. This review explores the epidemiology, burden, and challenges associated with alpha (α) and beta (β) thalassemia in the country. India carries a significant burden of thalassemia, particularly β-thalassemia, with variations across regions. Tribal communities and areas with high consanguinity rates show a concerning prevalence. β-thalassemia is more prevalent, with an estimated 3-4% carrier rate nationally. It reaches up to 17% in specific communities. α-thalassemia exhibits wider regional variations, ranging from 1% to 71%, with higher rates in the west, south, and northeast. Thalassemia leads to chronic anemia and requires lifelong medical care, imposing a strain on healthcare systems and families. Limited data, uneven access to screening and care, and inadequate infrastructure pose additional challenges. A multi-pronged approach is necessary. Strengthening carrier screening, prenatal diagnosis, and genetic counselling along with improved healthcare infrastructure and trained professionals are crucial. Research on novel therapies like gene therapy and cost-effective treatment options hold promise for improved disease management. Thalassemia necessitates a comprehensive strategy that includes addressing data gaps, strengthening prevention programs, improving access to care, and promoting research.

Keywords: Thalassemia, Prevalence, Anemia, Hereditary blood disorder.

Corresponding Author:

U Veerendra,
Assistant Professor, Pharmacy Practice, Rahavendra Institute of Pharmaceutical Education and Research (RIPER)-Autonomous, Anantapur, Andhra Pradesh-515721. E-Mail: verendras02@gmail.com

1. Introduction:

Thalassemia is a hereditary blood disorder characterized by inadequate hemoglobin production. There are two major types of thalassemia: β-thalassemia (also known as beta thalassemia), caused by similar gene abnormalities that disrupt the synthesis of the β-globin protein, and α-thalassemia (also known as alpha thalassemia), caused by a gene or genes associated with the α-globin protein that are missing or altered (mutated). There are numerous subtypes of each type. Thus, thalassaemia major, thalassaemia intermedia, and thalassaemia minor (or thalassaemia trait) are the three kinds of thalassaemia associated with both α- and β-thalassaemia.[1]

1.1 Types of thalassemia:[2,3]

Thalassemia is primarily categorized into two types: α-thalassemia and β-thalassemia.

1. **β-Thalassemia:** β-Thalassemia is caused by mutations in the HBB gene on chromosome 11, leading to reduced or absent synthesis of the beta chains of hemoglobin. This is further classified as follows.
    - β-Thalassemia Major (Cooley's Anemia): Severe form requiring regular blood transfusions.
    - β-thalassemia Intermedia: Moderate severity may require occasional transfusions.
    - β-Thalassemia Minor (Trait): Carrier state with mild anemia.
2. **α-Thalassemia**: Resulting from deletions or mutations in HBA1 and HBA2 on chromosome 16, affecting the alpha chains of hemoglobin. It includes:
    - α-thalassemia major (Hemoglobin Bart's hydrops fetalis): Usually fatal in utero or shortly after birth.
    - Hemoglobin H Disease: Moderately severe form with chronic hemolytic anemia.
    - α-Thalassemia Trait: Carrier state with mild anemia.
    - Silent Carrier State: Usually asymptomatic.

2. Global prevalence and distribution of thalassemia:

Thalassemia has a significant global burden, with its prevalence varying markedly by geographic region owing to historical patterns of migration, genetic selection, and consanguinity. The disorder is most prevalent in the Mediterranean region, parts of Africa, the Middle East, India, and Southeast Asia.[4-10]

2.1 Mediterranean Region:

In the Mediterranean, particularly in countries such as Greece, Italy, and Cyprus, thalassemia has historically been a major public health issue. The prevalence of β-thalassemia traits in these regions can reach up to 15%. This high prevalence is attributed to genetic adaptation to malaria, which has historically been endemic in these areas.

2.2 Middle East and South Asia:

These regions also exhibit high rates of thalassemia. In countries such as Iran, Pakistan, and India, the prevalence of the β-thalassemia trait is estimated to be between 4% and 10%. Cultural practices, such as consanguineous marriages, contribute to the high frequency of disorder in these regions.

2.3 Southeast Asia:

Southeast Asia, particularly Thailand and Malaysia, has a high incidence of α-thalassemia. The Hb Bart's hydrops fetalis syndrome, a severe form of alpha-thalassemia, is more common here due to the high frequency of deletions in the alpha-globin gene cluster.

2.4 Africa:

In Africa, thalassemia is less prevalent than sickle cell disease but still poses a significant health burden, particularly in North Africa. The prevalence of β-thalassemia traits in North African countries, such as Egypt, can be as high as 10%. The spread of thalassemia in sub-Saharan Africa is limited, with pockets of higher prevalence in regions with a history of malaria endemicity.

2.5 Other Regions:

In North and South America, thalassemia is less common, but has become more prevalent due to immigration from high-prevalence regions. For instance, in the United States, the prevalence of thalassemia among certain immigrant populations is high.

3. Factors influencing epidemiology:

Several factors influence the epidemiology of thalassemia, including genetic, environmental, and sociocultural factors.

- Genetic Factors: Thalassemia is an autosomal recessive disorder, in which two copies of the mutated gene are necessary for the disease to manifest. Carriers of a single gene mutation, known as thalassemia traits, are typically asymptomatic, but can pass the mutation to their offspring. The high carrier rates in certain populations result from genetic selection, where carriers had a survival advantage in malaria-endemic regions.[11-12]
- Migration: Global migration patterns significantly affect thalassemia distribution. Immigrants from high-prevalence areas have introduced disorders to regions where they were previously rare. This has implications for healthcare systems in terms of screening and management.[13]
- Consanguinity: In many parts of the Middle East and South Asia, consanguineous marriages (marriages between blood relatives) are culturally preferred, leading to a higher likelihood of homozygous thalassemia in offspring due to the increased probability of both parents being carriers.[10]
- Public Health Initiatives: The implementation of screening programs, genetic counselling, and prenatal diagnosis have significantly influenced the epidemiology of thalassemia. Countries with robust public health systems, such as Cyprus and Italy, have seen a reduction in the birth rate of affected individuals through these measures.[3,10]

4. Prevalence of different types of thalassemia in India:

India has one of the highest prevalence rates of thalassemia, with significant variations across different regions and communities.

4.1 β-Thalassemia:

β-thalassemia is particularly prevalent in regions with high rates of consanguineous marriages, which increases the likelihood of inheriting genetic disorders.[14] In India, it is

estimated that around 10,000 children are born annually with beta thalassemia major, the severe form of the disease that necessitates regular blood transfusions and chelation therapy.[15,16] The carrier rate, which indicates individuals who have one copy of the mutated gene but do not exhibit symptoms, has been reported to be between 3% and 4% across the general population.[17]

- Prevalence: Approximately 3-4% of the Indian population are carriers of β-thalassemia. The highest frequencies were reported in western and northern India, particularly in the Gujarati, Punjabi, and Sindhi communities.[15]
- Regional Distribution: States such as Gujarat, Maharashtra, and Punjab report carrier frequencies ranging from 3% to 17%.[18] Among tribal populations, the prevalence can be even higher due to genetic isolation and high rates of consanguinity.[19]
- Public Health Impact: An estimated 10,000-15,000 children are born with β-thalassemia major each year in India, necessitating lifelong medical management including blood transfusions and chelation therapy.[15,16]

4.1.1 Regional studies and findings:

In Central India, the prevalence of β-thalassemia trait ranged from 1.4 to 3.4%, with 0.94% of anemia patients having β-thalassemia major. In South India, the prevalence of β-thalassemia trait ranged from 8.50 to 37.90%, whereas β-thalassemia major was found to be between 2.30 and 7.47%. The thalassemic burden is higher in the states of Northern and Western India. The prevalence of β-thalassemia trait (0.00–30.50%), β-thalassemia major (0.36–13.20%), and other hemoglobinopathies (0.04–15.45%) was greater in tribal communities in Eastern India than in non-tribal populations. Moreover, β-thalassemia afflicted scheduled castes, scheduled tribes, and other backward classes with low socioeconomic standing and low literacy rates.[20]

4.2 α-Thalassemia:

India, with its vast and diverse population, exhibits significant regional variation in the prevalence of alpha-thalassemia. This disorder is particularly common among certain tribal and rural populations, where consanguinity and endogamy are prevalent, increasing the risk of inherited genetic conditions.

A study conducted by Desai et al. (1997) found that the prevalence of alpha thalassemia in India ranged from 1% to 15% in different regions.[21] The highest prevalence was observed in the western and southern parts of the country, notably among the tribal communities of Maharashtra and Tamil Nadu.

- Prevalence: The prevalence of the α-thalassemia trait in India varies between 11 and 71 per cent and shows regional variation.[22,23] Very high frequencies of α-thalassemia have been reported in tribals around Surat in West Central Gujarat and Nilgiris in South.[24]
- Regional Distribution: Northeastern states, such as Assam and West Bengal, show higher frequencies of α-thalassemia, influenced by ethnic and genetic factors.[25]
- Public Health Impact: Although less prevalent than β-thalassemia, α-thalassemia still poses a health burden due to its contribution to mild to moderate anemia and its role in compounding clinical severity when co-inherited with β-thalassemia.

4.2.1 Regional studies and findings:

Several regional studies have provided insights into the prevalence of α-thalassemia. Alpha thalassemia prevalence in South India is relatively high, with a study reporting a 12.9% prevalence in the Indian population.[26] This is consistent with the high prevalence of alpha thalassemia in a tribal-dominated malaria endemic area of Eastern India.[27]

5. The looming shadow: epidemiological implications of α- and β-thalassemia in India:

α- and β-thalassemia, collectively known as hemoglobinopathies, have cast a long shadow on India's public health landscape. These inherited blood disorders disrupt hemoglobin production, leading to chronic anemia and a multitude of complications. Understanding the epidemiological landscape of these diseases is crucial for the development of effective prevention and management strategies.[28-31]

5.1 High burden and geographic disparity:

India has a significant burden of thalassemia. Studies suggest a high prevalence of β-thalassemia, particularly in tribal and low socioeconomic communities. The distribution is uneven, with higher concentrations in the western and eastern regions.[20] This geographic disparity highlights the need for targeted intervention in high-risk areas.

5.2 Limited data and uneven access to care:

Despite its high prevalence, comprehensive data on thalassemia in India remain limited. Fragmented healthcare systems and lack of standardized reporting have contributed to this gap. These limited data hinder the development of effective national policies and resource allocation. Furthermore, uneven access to carrier screening and prenatal diagnosis services exacerbates the problem.[15]

5.3 Increased healthcare burden and reduced quality of life:

Patients with thalassemia require lifelong blood transfusions, chelation therapy to remove excess iron buildup, and regular medical care.[32,33] This translates to a significant strain on healthcare systems and financial hardship for families. The chronic nature of the disease also affects patients' quality of life, limiting their educational and social opportunities.

5.4 Mitigating the impact: a multi-pronged approach:

Addressing the challenges of thalassemia in India requires a multipronged approach. Strengthening carrier screening programs, particularly in high-risk communities, is crucial for preventing thalassemia births.[15] Expanding access to prenatal diagnosis and genetic counselling empowers couples to make informed reproductive choices. Additionally, improving the healthcare infrastructure, including robust blood banking systems and trained healthcare professionals, is essential for effective disease management.

5.5 Investing in research and development:

Research plays a vital role in improving thalassemia care. Studies exploring novel therapeutic options, such as gene therapy, hold promise for long-term disease management.[15] Furthermore, research on cost-effective treatment strategies and improved iron chelation therapies can significantly benefit patients and the healthcare system.

6. Conclusion:

Alpha- and beta-thalassemia represent significant public health challenges in India owing to their high prevalence and associated clinical burdens. Effective management requires a multifaceted approach, encompassing genetic screening, counselling, affordable treatment options, and public awareness campaigns. An inclusive analysis of the challenges posed can mitigate the impact and improve the quality of life of thalassemia-affected individuals and their families.

By addressing gaps in epidemiological data, strengthening prevention programs, improving access to care, and investing in research, India can take crucial steps towards mitigating the burden of these debilitating diseases. This comprehensive approach can ensure a brighter future for individuals and families with thalassemia.

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