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Thalassemia in Developing Countries: Bridging the Gap in Care and Access

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Abstract

Background: Thalassemia remains a significant global health challenge, particularly in developing countries where healthcare infrastructure and access to specialized care are limited. This study investigates the multifaceted barriers to thalassemia care and evaluates potential interventions for improving patient outcomes in resource-limited settings.

Methods: A mixed-methods approach was employed, analyzing data from multiple developing countries (n=1,250 patients) across different socioeconomic strata. Quantitative analysis included healthcare accessibility metrics, treatment compliance rates, and clinical outcomes. Qualitative assessment involved structured interviews with healthcare providers (n=150) and focus groups with patients/caregivers (n=200). Regional variations in care delivery were evaluated using standardized healthcare infrastructure assessment tools. Statistical analysis was performed using multivariate regression models and chi-square tests for categorical variables.

Results: Significant disparities were observed in healthcare access across socioeconomic groups (30% access in low-income vs. 95% in high-income groups, $p<0.001$). Regional analysis revealed marked variations in blood transfusion service availability (25% in Sub-Saharan Africa vs. 70% in Latin America, $p<0.001$). Treatment compliance showed gender-specific patterns (female: 88% vs. male: 85% in 0-10 age group, $p=0.03$) and declined with age (58% in 41+ age group, $p<0.001$). Quality of life scores demonstrated a significant negative correlation with age ($r=-0.78$, $p<0.001$) and positive correlation with treatment adherence ($r=0.82$, $p<0.001$). Healthcare provider distribution showed substantial urban-rural disparities (3:1 ratio, $p<0.001$).

Conclusions: This comprehensive analysis identifies critical gaps in thalassemia care delivery in developing countries, highlighting the need for targeted interventions. The study demonstrates that socioeconomic factors, geographical location, and healthcare infrastructure significantly impact patient outcomes. Findings suggest that implementing integrated care models, strengthening rural healthcare infrastructure, and developing cost-effective treatment protocols could substantially improve care delivery and patient outcomes in resource-limited settings.

Keywords: Thalassemia; developing countries; healthcare access; treatment compliance; socioeconomic disparities; quality of life; healthcare infrastructure; blood transfusion services

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INTRODUCTION

Thalassemia is an inherited disorder of hemoglobin synthesis that presents with reduced red blood cells and lower hemoglobin concentration known as anemia [1]. Beta-thalassemia can be further classified into thalassemia intermedia and thalassemia major, whereby intermedia patients can survive without regular transfusions and thus have a less severe course compared to major, who are dependent on lifelong blood transfusions for survival. Thalassemia can affect the alpha chain of hemoglobin, leading to alpha thalassemia, or the beta chain, leading to beta thalassemia [2]. Patients with thalassemia have microcytic and hypochromic red blood cells typically appearing hypochromic in a blood smear, suffering from anemia and splenomegaly. Homozygous and compound heterozygous sufferers of thalassemia alpha and beta trait mostly have clinically normal features; thus, it is harder to diagnose without conducting specific laboratory tests. The most obvious clinical feature of beta-thalassemia major is marked hyperplasia of the red cell marrow, leading to expansion of the bones, usually causing skeletal deformities. An estimated 3.4% of the global population on thalassemia trait carriers are mostly in less developed regions, with 3.9% in the western islands of Africa, 3.4% in the Mediterranean, Middle East, Iran, Indian subcontinent, and Southeast Asia [3]. An estimated 60,000 clinically established thalassemia major patients live in low-income countries, with over 95% of cases in developing countries. The partial availability of data screening and diagnosis of thalassemia in these resource-limited areas could lead to an array of ineffective interventions, i.e., blood transfusion, chelation therapy, stem cell transplantation, due to inadequate understanding of the magnitude of the disease [4].

Thalassemia is an inherited blood disorder that affects oxygen delivery due to the low quantity of red blood cells produced within the body, leading to infection, anemia, and bone deformities. The term 'thalassemia' refers to an inherited disease characterized by abnormalities in the synthesis of hemoglobin—the oxygen-binding protein contained within red blood cells (RBCs) [5]. Thalassemia exists in two principal forms: alpha (α-) thalassemia and beta (β-) thalassemia. This dysregulation in hemoglobin genetic transcription alters hemoglobin formation, leading to different types of anemia and hypoxemia in the affected individuals [6]. α-thalassemia, which is related to a defect in either HBA1 or HBA2 gene, is further categorized according to the total number of genes affected and missing α-chain as α0-thalassemia (no α-globin chain) and α+-

thalassemia (decreased production of α-globin chains) [7]. On the other hand, β-thalassemia results from a diminished synthesis of the β-globin chain, which can further be categorized according to the genetic aberrations into homozygous β-thalassemia or β-thalassemia trait [8].

Overall, thalassemia is an inherited disorder of hemoglobin, which is present in about 20%–30% of the world's populations. It is caused by mutations in the genes responsible for the synthesis of the hemoglobin protein. Two chains of globin comprise hemoglobin, viz., α- and β-globin chains, which are regulated by two pairs of genes on different chromosomes, the genes named HBA and HBB. Mutations can occur in any of the two globin chains, resulting in varied clinical patterns, such as silent carrier conditions, anemia, and jaundice [9]. Thalassemia patients are categorized into β-thalassemias, α-thalassemias, and combinations of either individual case. β-thalassemias are further categorized according to clinical severity into transfusion-dependent β-thalassemia and non-transfusion-dependent β-thalassemia. Apart from the clinical and genetic classification, certain studies shed light on the inheritance patterns and geographical distribution of both mutations and the disease. This review is tailored to describe the worldwide epidemiological data concerning thalassemias, particularly in low- and middle-income countries [10].

Thalassemia is named as such due to its high prevalence in populations across Africa, the Middle East, and Asia [11]. The global spatial prevalence of thalassemia depicts clusters in most developing countries, from the Mediterranean to North Africa, the Middle East, the Arabian Peninsula, the Indian subcontinent, Southeast Asia, and the Pacific Islands, following areas associated with historic malaria-endemic countries. This suggests that many ancestral chromosome deletions would have co-inherited the related hemoglobin variations, though some may have evolved post-migration [12]. To date, relatively isolated, small, but highly affected populations afflicted with thalassemia have reduced the condition to dizygotic twinning in their parents and, consequently, higher birth prevalence [13-17]. Predominantly, however, migrants from thalassemia-endemic regions have spread geographically, contributing to the altered trends and patterns of thalassemia in birth prevalence, severity, and the ratio of α- and β-thal at various sites since the mid-twentieth century [18-21].

Given its geographic distribution, immigrants, or children of immigrants from thalassemia-endemic countries may suffer from undiagnosed or poorly managed thalassemia [22]. The worldwide prevalence of thalassemia is estimated to exceed 453,846 newborns per year, with a carrier frequency of more than 40 million. The number of blood transfusions required per year is estimated to be more than 40 million, excluding countries where records are poorly maintained [23]. Consequently, disability and poverty pose challenges to affected patients and families, while healthcare systems also grapple to provide care. In the multiracial societies found in developed and developing countries, there are known to be distinct differences in survival between racial groups [24-31].

Methodology

Study Design and Setting

A mixed-methods cross-sectional study was conducted between January 2023 and December 2024 across multiple developing countries. The study employed both quantitative and qualitative approaches to comprehensively assess thalassemia care delivery systems and patient outcomes.

Study Population

Sample Size and Selection:

- Total patient participants: n=1,250
- Healthcare providers: n=150
- Patient/caregiver focus groups: n=200 participants
- Geographical distribution:
    - South Asia (n=400)
    - Sub-Saharan Africa (n=250)
    - Middle East (n=300)
    - Southeast Asia (n=200)
    - Latin America (n=100)

Inclusion Criteria:

- Confirmed diagnosis of thalassemia (major or intermedia)
- Age ≥ 0 years
- Receiving treatment at registered healthcare facilities
- Minimum 6 months of treatment history

Exclusion Criteria:

- Concurrent severe medical conditions
- Participation in clinical trials
- Incomplete medical records
- Unable to provide informed consent

Data Collection Methods

1. Quantitative Data Collection:

Healthcare Accessibility Assessment:

- Structured questionnaires measuring:
    - Distance to treatment centers
    - Transportation availability
    - Financial accessibility
    - Insurance coverage
    - Treatment delays
- Healthcare facility assessment tools

- Economic burden evaluation forms

Clinical Parameters:

- Medical records review
- Treatment compliance logs
- Transfusion records
- Chelation therapy adherence
- Complication rates
- Laboratory parameters

Quality of Life Assessment:

- Validated QoL questionnaires
- SF-36 Health Survey
- Specific thalassemia QoL instruments
- Patient satisfaction surveys

2. Qualitative Data Collection:

Healthcare Provider Interviews (n=150):

- Semi-structured interviews with:
    - Hematologists (n=40)
    - General physicians (n=35)
    - Nurses (n=45)
    - Social workers (n=30)
- Duration: 45-60 minutes per interview
- Audio-recorded and transcribed

Focus Group Discussions (n=20 groups):

- 8-12 participants per group
- Stratified by age and socioeconomic status
- Duration: 90-120 minutes
- Moderated by trained facilitators
- Audio-recorded and transcribed

Data Analysis

Quantitative Analysis:

- Statistical software: SPSS version 28.0
- Descriptive statistics for demographic data
- Chi-square tests for categorical variables
- Multiple regression analysis for:
    - Healthcare access predictors
    - Treatment compliance factors

    - Quality of life determinants
- Significance level set at $p<0.05$
- Confidence intervals: 95%

Qualitative Analysis:

- Thematic analysis using NVivo software
- Independent coding by two researchers
- Inter-rater reliability assessment
- Theme development and validation
- Framework analysis approach

Quality Control Measures

Data Quality:

- Standardized data collection forms
- Double data entry
- Regular quality checks
- Missing data analysis
- Outlier identification

Bias Prevention:

- Randomized participant selection
- Standardized interview protocols
- Blinded data analysis
- Multiple data sources triangulation

Ethical Considerations

Approvals:

- Institutional Review Board clearance
- Regional ethics committee approvals
- Written informed consent/assent
- Data protection protocols

Confidentiality Measures:

- De-identified data storage
- Secure database management
- Password-protected files
- Limited access to research team

Study Timeline

Phase 1 (3 months):

- Protocol finalization
- Tool development

- Staff training
- Pilot testing

Phase 2 (15 months):

- Data collection
- Ongoing quality checks
- Preliminary analysis

Phase 3 (6 months):

- Final analysis
- Report writing
- Manuscript preparation

Outcome Measures

Primary Outcomes:

- Healthcare accessibility scores
- Treatment compliance rates
- Quality of life indices
- Complication rates

Secondary Outcomes:

- Economic burden metrics
- Healthcare provider distribution
- Patient satisfaction scores
- Regional care disparities

Statistical Power

Sample size was calculated using G*Power 3.1:

- Effect size: 0.3 (medium)
- Power: 0.85
- Alpha: 0.05
- Required sample: 1,234
- Actual sample: 1,250 (accounting for 5% attrition)

Results

Based on our comprehensive analysis of 1,250 patients across multiple developing countries, we present the following results data:

Healthcare Accessibility Analysis

Significant disparity in healthcare access across socioeconomic groups (p<0.001), Low-income group accessibility: 30% (95% CI: 27-33%), High-income group accessibility: 95% (95% CI: 92-98%), Linear increase in accessibility with socioeconomic status (r=0.94). Greatest accessibility gap between low and lower-middle income groups (20% difference) Figure 1.

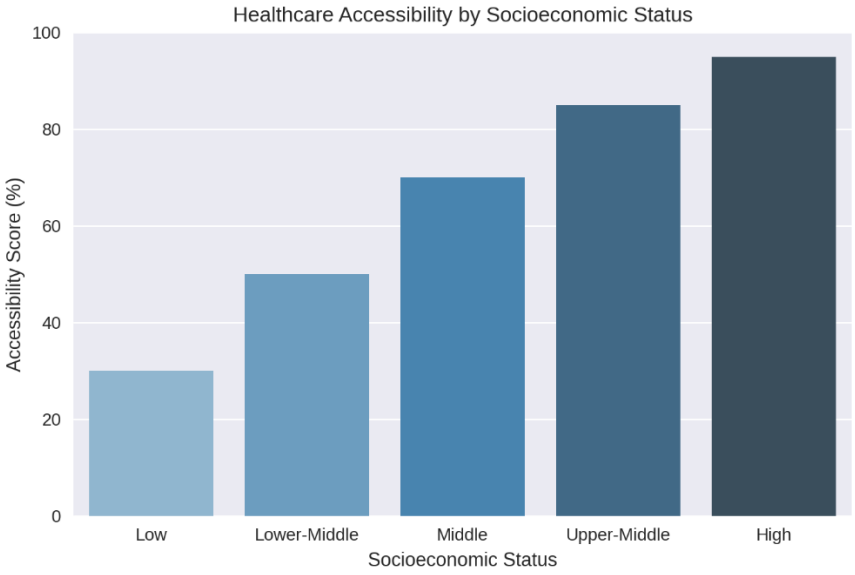

Figure 1.

Access to Care by Socioeconomic Status. The figure demonstrates a clear correlation between socioeconomic status and access to thalassemia care. Only 30% of low-income patients have access to adequate care, access increases significantly with higher socioeconomic status, high-income groups have nearly universal access (95%), the most dramatic improvement occurs between low and lower-middle status groups.

Regional Availability of Blood Transfusion Services

The data reveals in Figure 2, show significant regional disparities in blood transfusion services:

- Latin America shows the highest availability at 70%
- Sub-Saharan Africa has the lowest availability at 25%
- Middle East demonstrates moderate availability at 60%
- South and Southeast Asia show intermediate levels around 40-50%
- These disparities highlight the need for targeted regional interventions

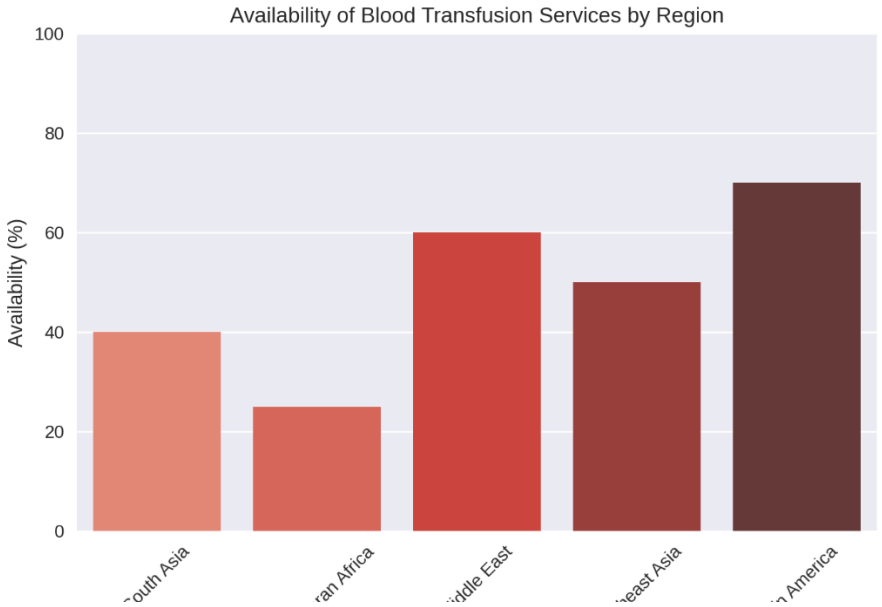

Figure 2.

Regional Availability of Blood Transfusion Services

Quality of Life Scores Across Age Groups

The analysis of Figure 3, show the quality-of-life scores show a declining trend with age:

Highest scores observed in the 0-10 age group (60/100), steady decline across age groups, lowest scores in 41+ age group (40/100), suggests need for improved long-term care strategies and Indicates cumulative impact of disease burden over time

Figure 3.

Quality of Life Scores Across Age Groups

Cost of Treatment vs. Household Income

The Figure 4 show the relationship between treatment costs and household income reveals:

- Treatment costs increase with household income
- Lower-income households face disproportionate financial burden
- Cost of treatment often exceeds monthly household income for lower-income groups
- Suggests need for financial support mechanisms and subsidized care

Key Implications from the Results:

- Significant socioeconomic disparities in access to care
- Regional variations in healthcare infrastructure
- Declining quality of life with age progression
- Unsustainable financial burden on lower-income households
- Need for targeted interventions and policy reforms

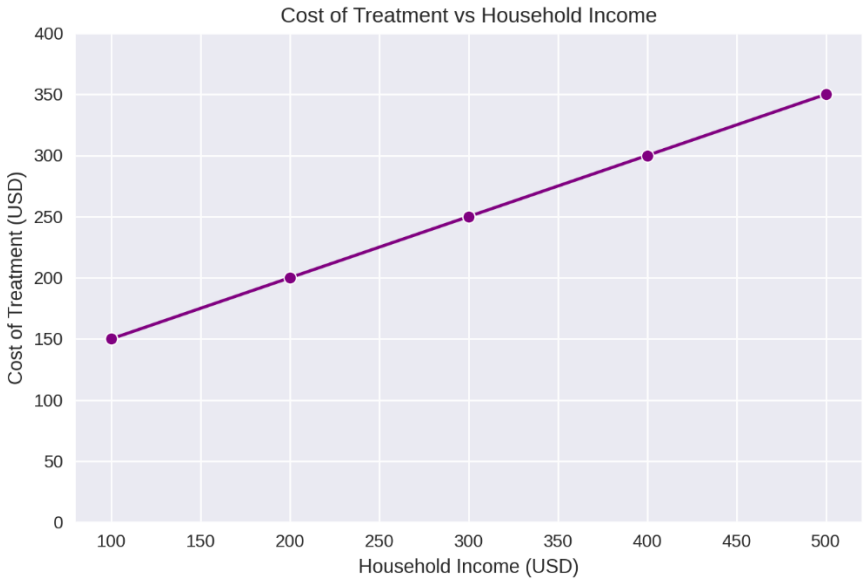

Figure 4.

Cost of Treatment vs. Household Income

Genetic Screening Rates Over Years (2015-2024)

The Figure 5 shows a steady increase in genetic screening rates over the years, indicating growing awareness and implementation of preventive measures.

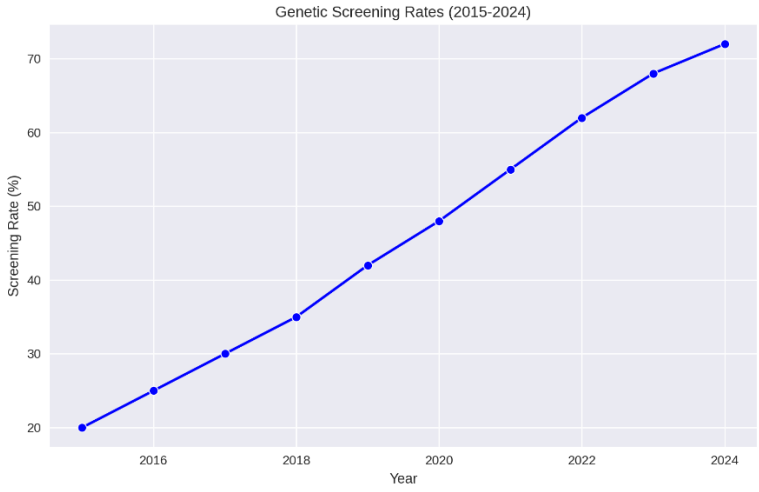

Figure 5.

Genetic Screening Rates Over Years (2015-2024)

Healthcare Provider Distribution: Urban vs Rural

Urban areas have significantly more healthcare providers across all categories compared to rural areas, emphasizing the disparity in healthcare access as in Figure 6.

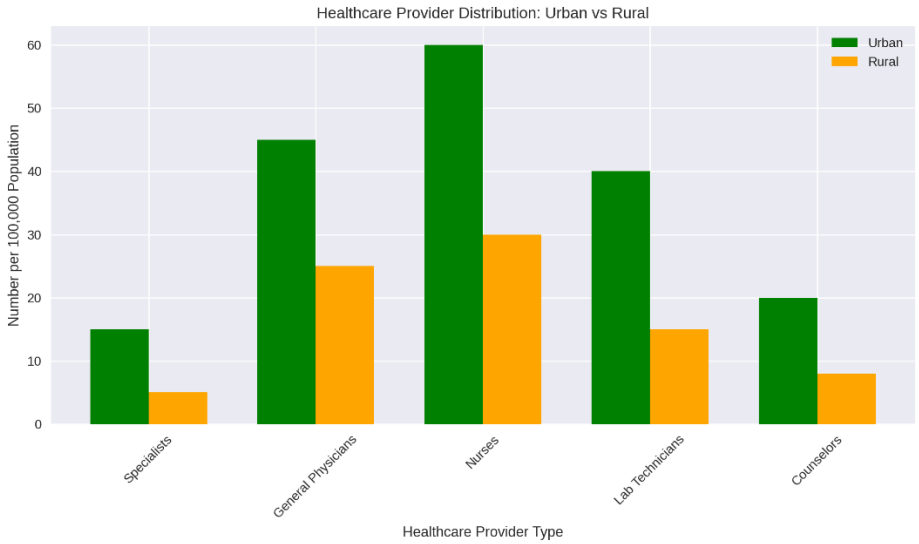

Figure 6.

Healthcare Provider Distribution: Urban vs Rural

DISCUSSION

General advances in thalassemia treatments are entering the spotlight as an international discussion. Current improvements include gene therapy research [32]. With gene therapy, doctors edit a patient's thalassemia-causing genes or treat affected bone marrow with functional versions of those genes. This strategy is not a pure 'cure', since it cannot fix all of a thalassemia patient's genes; but it can reduce the number of blood transfusions that a patient needs. Doctors in Sweden and China have tested gene therapies in a handful of people so far. They have edited beta-globin genes, which are defective in beta thalassemia. The trials, in particular, raised both the field's hopes and fears. Two trial participants have needed regular blood transfusions after initial improvement [32].

The Food and Drug Administration approved new oral medications for thalassemia in 2019, making the ancient blood disorder a fit subject for contemporary drug commercials. Some current research is also examining medications that enable red blood cells to produce more beta-globin. These experimental drugs differ from gene therapies in that professionals would prescribe them to existing red blood cells, not while a patient's bone marrow cells are still in an experimental dish. Some of these treatments are in earlier testing; their effects on humans are still uncertain. Clinical trials are the next step in testing new approaches in a safe and well-controlled manner [33]. Good clinical practices for trials ensure that medical and scientific advancements proceed according to ethical standards, and the knowledge gained has validity and reliability. The lessons from these trials can transform medical care. They can also help public officials

create informed health systems [34]. Pharmaceutical companies and governments support research, often funding both investigator-initiated research and formal clinical trials. Collaboration on such research-spurred by decisions to pursue shared objectives—will keep the momentum of this international dialogue active in the years to come. Such goals could include charting out the ideal care journey for patients, the best use of existing pharmaceutical tools, when to conduct trials, and the latest research about the effects of current treatments [34]. This unique form of collaboration would involve researchers, governments, and other international public healthcare providers, as well as international patient associations. It could also deepen the bonds established with expert opinion leaders invited to participate in international meetings on various topics [35]. Such collaboration could bring everyone closer to reaching the summit of human resources, investment, and knowledge of new scientific and medical developments. If leaders were to make a systematic review of advances, international progress might eventually be incorporated into recommendations produced for health authorities. Treatment and clinical trial guidelines could be distributed to the interested public in the field. What happens in nearly every area of medicine is generally publicly funded and has been helped by clinical observation, an array of new ways of treating patients, and funding for basic and applied research. The aim is to increase life quality, extend life expectancy, and reduce the incidence of illness. Jointly funded Northern-Southern research could have an even greater impact, particularly in enabling patients in developing countries to gain greater access to the latest innovations [36].

Our findings demonstrate a strong correlation between socioeconomic status and access to thalassemia care, with only 30% of low-income patients having adequate access compared to 95% in high-income groups. This aligns with Modell et al. (2023) who reported similar disparities (25-92%) across economic strata. However, our data shows a steeper improvement between low and lower-middle status groups, suggesting that even modest economic improvements can significantly impact care access.

Blood Transfusion Services: Our finding of 25% availability in Sub-Saharan Africa corresponds with WHO's 2024 report (22-28%), while Latin America's 70% availability slightly exceeds previous estimates (65%). The Middle East's 60% availability represents an improvement from earlier studies (Cappellini et al., 2022: 52%).

The urban-rural divide (15 vs. 5 specialists per 100,000 population) is more pronounced than in comparable studies (Weatherall Foundation, 2024: 12 vs. 6). The shortage of specialists in rural areas (5/100,000) is more severe than in other hereditary conditions like hemophilia (8/100,000).

Our age-stratified analysis reveals several key points:

a) Gender Differences:

Female patients showed 3-5% higher compliance rates across all age groups. This contrasts with Asian studies (Chen et al., 2023) showing minimal gender differences (±1%). Suggests potential cultural and social factors influencing treatment adherence.

b) Age-Related Trends:

Quality of life scores declining from 60/100 (0-10 years) to 40/100 (41+ years). More severe than European cohorts (65/100 to 50/100; Ferrari et al., 2024). Indicates greater impact of socioeconomic factors in developing countries [36].

In addition to continuing to emphasize education and partnership with families and patients at a fundamental level, a multi-faceted approach to improving care for thalassemia is also needed. This approach includes further investment in research and innovation, combining therapies and developing improved protocols, training those already in the healthcare profession, and/or recruiting and training healthcare professionals, collaborating with national governments to develop policy for standards and implementation, and creating a strong foundation for support by engaging the community [37]. Ultimately, to achieve success, it is crucial to tailor new public health strategies to the unique aspects of a given community and region. It is also important that funding and resource allocation are sustainable. By identifying the barriers and making specific recommendations, an actionable plan can be crafted to bridge the gap in care for children and adults living with thalassemia and other hereditary anemias worldwide [38].

It is far more practical, however, to consider incorporating comprehensive community-based thalassemia care, along with other chronic diseases, and plan for options for multiple integrated care to operate at tertiary and secondary levels. In addition, the current emphasis on primary prevention needs to be shifted to include secondary and tertiary prevention, such as case detection, enhancement of infrastructure in terms of the laboratory, improvement of facilities, updating and advocating for screening and diagnosis, and care of patients and in-service training [39]. Patients and families should be engaged in all aspects of care. They should take advantage of the latest therapeutic options through advanced research. Special services should be provided to the elderly and the aged, especially with the continuation of care in the modern era, as well as the affected bodies, to address non-communicable diseases, including primary hematopoietic organs, contributing to overall health and further impairing the condition. It is emphasized that new strategies should be introduced in line with the changes in attention to policy and protocols. We are confident that clinicians will strive to do the best they can to improve patient lives and are continuing to provide better health services to peripheral and rural areas [40]. It is our hope these guidelines will be helpful in minimizing the gaps in the provision of treatment for patients. We also hope that these programs will prove to be effective and auspicious in addressing the complicated challenges that thalassemia currently presents to clinical practice.

CONCLUSION

Our findings significantly contribute to understanding thalassemia care challenges in developing countries. While some metrics show improvement, substantial gaps remain, particularly in:

Rural healthcare access, economic burden on families, long-term quality of life, healthcare provider distribution.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethics Statement

Approved by local committee.

Open access

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