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The Analysis Study of Prevalence, Risk Factor and Management of Thalassemia in Low Income Countries: A Comprehensive Systematic Review

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ABSTRACT

Background: Thalassemia is a group of inherited blood disorders that impair the body's ability to produce functional hemoglobin, leading to chronic anemia and other severe health issues. This systematic to evaluate prevalence, risk factors, and management strategies for thalassemia in low-income countries. based on literatures of the last 10 years. **Methods:** The study adhered to PRISMA 2020 standards, examining English literature from 2014 to 2024. It excluded editorials, reviews from the same journal, and submissions without a DOI. PubMed, SagePub, SpringerLink, and Google Scholar were utilized as literature sources. **Result:** Initially retrieving 360 articles from online databases (PubMed, SagePub, SpringerLink and Google Scholar) eight relevant papers were selected after three rounds of screening for full-text analysis. **Conclusion:** Thalassemia prevalence varies significantly across low-income countries, driven by genetic and socioeconomic factors. Effective management requires region-specific strategies, improved access to treatments, and ongoing monitoring. Tailored public health interventions are crucial to reduce the burden and improve patient outcomes.

Keyword: thalassemia, low income countries, prevalence, risk factor, management

INTRODUCTION

Thalassemia is a group of inherited blood disorders that impair the body's ability to produce functional hemoglobin, leading to chronic anemia and other severe health issues. The two primary forms of thalassemia are α -thalassemia and β -thalassemia, each stemming from genetic mutations affecting the production of α -globin and β -globin chains, respectively. α -Thalassemia is caused by deletions or mutations in the α -globin genes located on chromosome 16, while β -thalassemia results from a variety of mutations in the β -globin gene on chromosome 11. These disorders can lead to a range of clinical manifestations from mild anemia to severe forms requiring regular blood transfusions.^{1,2}

The global distribution of thalassemia is notably uneven, with high prevalence rates in tropical and subtropical regions. This geographic distribution is largely attributed to the evolutionary protection conferred by these genetic disorders against malaria. In these regions, including parts of Africa, Asia, and the Mediterranean, thalassemia remains a significant public health concern.

Despite advances in genetic screening and treatment in high-income countries, low-income countries often struggle with the challenges of managing and preventing thalassemia due to limited resources and healthcare infrastructure.³

In low-income countries, the burden of thalassemia is exacerbated by several factors. Diagnostic facilities are often scarce, leading to delays in the identification and management of the disorder. Additionally, the lack of access to comprehensive treatment options, such as regular blood transfusions and iron chelation therapy, contributes to poor disease outcomes. Socio-economic factors, including poverty and limited healthcare access, further compound these challenges, making effective management of thalassemia difficult.⁴

This systematic review aims to provide a comprehensive overview of the prevalence, risk factors, and management strategies for thalassemia in low-income countries. By examining data from various studies across different regions, the review will highlight the disparities in disease burden and care between

high- and low-income settings. It will also identify common risk factors contributing to the high prevalence of thalassemia in these regions, such as genetic predisposition and environmental factors.

METHODS

Protocol

The author carefully followed the rules laid out in the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020. This was done to make sure the study met all its standards. The selection of this methodological approach was specifically aimed at ensuring the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic to evaluate prevalence, risk factors, and management strategies for thalassemia in low-income countries. based on literatures of the last 10 years. This study meticulously analyzed data on literatures to provide insights and enhance patient treatment strategies. The primary objective of this paper is to highlight

the collective significance of the identified key points.

Inclusion criteria for this study entail: 1) Papers must be in English, and 2) Papers must have been published between 2014 and 2024. Exclusion criteria comprise: 1) Editorials; 2) Submissions without a DOI; 3) Previously published review articles; and 4) Duplicate entries in journals.

Search Strategy

The keywords used for this research are thalassemia, low income countries, prevalence, risk factor, management. The Boolean MeSH keywords inputted on databases for this research are:
("thalassaemia"[All Fields] OR "thalassemia"[MeSH Terms] OR "thalassemia"[All Fields] OR "thalassaemias"[All Fields] OR "thalassemias"[All Fields]) AND ("developing countries"[MeSH Terms] OR ("developing"[All Fields] AND "countries"[All Fields]) OR "developing countries"[All Fields] OR ("low"[All Fields] AND "income"[All Fields] AND "countries"[All Fields]) OR "low income countries"[All Fields]) AND ("epidemiology"[MeSH Subheading]

OR "epidemiology"[All Fields] OR
"prevalence"[All Fields] OR
"prevalence"[MeSH Terms] OR
"prevalance"[All Fields] OR
"prevalences"[All Fields] OR
"prevalence s"[All Fields] OR
"prevalent"[All Fields] OR
"prevalently"[All Fields] OR
"prevalents"[All Fields])) OR ("risk
factors"[MeSH Terms] OR
("risk"[All Fields] AND "factors"[All
Fields]) OR "risk factors"[All Fields]
OR ("risk"[All Fields] AND
"factor"[All Fields]) OR "risk
factor"[All Fields]) OR
("manage"[All Fields] OR
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s"[All Fields] OR "managers"[All
Fields] OR "manages"[All Fields]
OR "managing"[All Fields] OR
"managment"[All Fields] OR
"organization and
administration"[MeSH Terms] OR
("organization"[All Fields] AND
"administration"[All Fields]) OR
"organization and
administration"[All Fields] OR
"management"[All Fields] OR
"disease management"[MeSH Terms]

OR ("disease"[All Fields] AND
"management"[All Fields]) OR
"disease management"[All Fields]))

Data retrieval

The authors assessed the studies by reviewing their abstracts and titles to determine their eligibility, selecting relevant ones based on their adherence to the inclusion criteria, which aligned with the article's objectives. A consistent trend observed across multiple studies led to a conclusive result. The chosen submissions had to meet the eligibility criteria of being in English and a full-text.

This systematic review exclusively incorporated literature that met all predefined inclusion criteria and directly pertained to the investigated topic. Studies failing to meet these criteria were systematically excluded, and their findings were not considered. Subsequent analysis examined various details uncovered during the research process, including titles, authors, publication dates, locations, study methodologies, and parameters.

Quality Assessment and Data Synthesis

Each author independently evaluated the research presented in the title and abstract of the publication to determine which ones merited further exploration. The subsequent stage involved assessing all articles

that met the predefined criteria for inclusion in the review. Decisions on including articles in the review were based on the findings uncovered during this evaluation process.

Table 1. Article Search Strategy

Database	Strategi Pencarian	Hits
Pubmed	((("thalassaemia"[All Fields] OR "thalassemia"[MeSH Terms] OR "thalassemia"[All Fields] OR "thalassaemias"[All Fields] OR "thalassemias"[All Fields]) AND ("developing countries"[MeSH Terms] OR ("developing"[All Fields] AND "countries"[All Fields]) OR "developing countries"[All Fields] OR ("low"[All Fields] AND "income"[All Fields] AND "countries"[All Fields]) OR "low income countries"[All Fields]) AND ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "prevalence"[All Fields] OR "prevalence"[MeSH Terms] OR "prevalance"[All Fields] OR "prevalences"[All Fields] OR "prevalence s"[All Fields] OR "prevalent"[All Fields] OR "prevalently"[All Fields] OR "prevalents"[All Fields])) OR ("risk factors"[MeSH Terms] OR ("risk"[All Fields] AND "factors"[All Fields]) OR "risk factors"[All Fields] OR ("risk"[All Fields] AND "factor"[All Fields]) OR "risk factor"[All Fields]) OR ("manage"[All Fields] OR "managed"[All Fields] OR "management s"[All Fields] OR "managements"[All Fields] OR "manager"[All Fields] OR "manager s"[All Fields] OR "managers"[All Fields] OR "manages"[All Fields] OR "managing"[All Fields] OR "managment"[All Fields] OR "organization and administration"[MeSH Terms] OR ("organization"[All Fields] AND "administration"[All Fields]) OR "organization and administration"[All Fields] OR "management"[All Fields] OR "disease management"[MeSH Terms] OR ("disease"[All Fields] AND "management"[All Fields]) OR "disease management"[All Fields]))	100
Science Direct	(((((thalassemia) AND (low income countries)) AND (prevalence)) OR (risk factor)) OR (management))	150
Sagepub	(((((thalassemia) AND (low income countries)) AND (prevalence)) OR (risk factor)) OR (management))	50
Google Scholar	(((((thalassemia) AND (low income countries)) AND (prevalence)) OR (risk factor)) OR (management))	160

Table 2. JBI *Critical appraisal of Study*

Parameters	Lam a (202 2)	Tiwa ri (202 3)	Yada v (202 2)	Wen dt (202 3)	Wahidiy at (2022)	Nguy en (2017)	Ruman ey (2014)	Mailu la (2021)
1. Bias related to temporal precedence								
Is it clear in the study what is the “cause” and what is the “effect” (ie, there is no confusion about which variable comes first)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Bias related to selection and allocation								
Was there a control group?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Bias related to confounding factors								
Were participants included in any comparisons similar?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Bias related to administration of intervention/exposure								
Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	No.	No.	No.	No.	No.	No.	No.	No.
5. Bias related to assessment, detection, and measurement of the outcome								
Were there multiple measurements of the outcome, both pre and post the intervention/expos	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

ure?								
Were the outcomes of participants included in any comparisons measured in the same way?	No.	No.	No.	No.	No.	No.	No.	No.
Were outcomes measured in a reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Bias related to participant retention								
Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Statistical conclusion validity								
Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

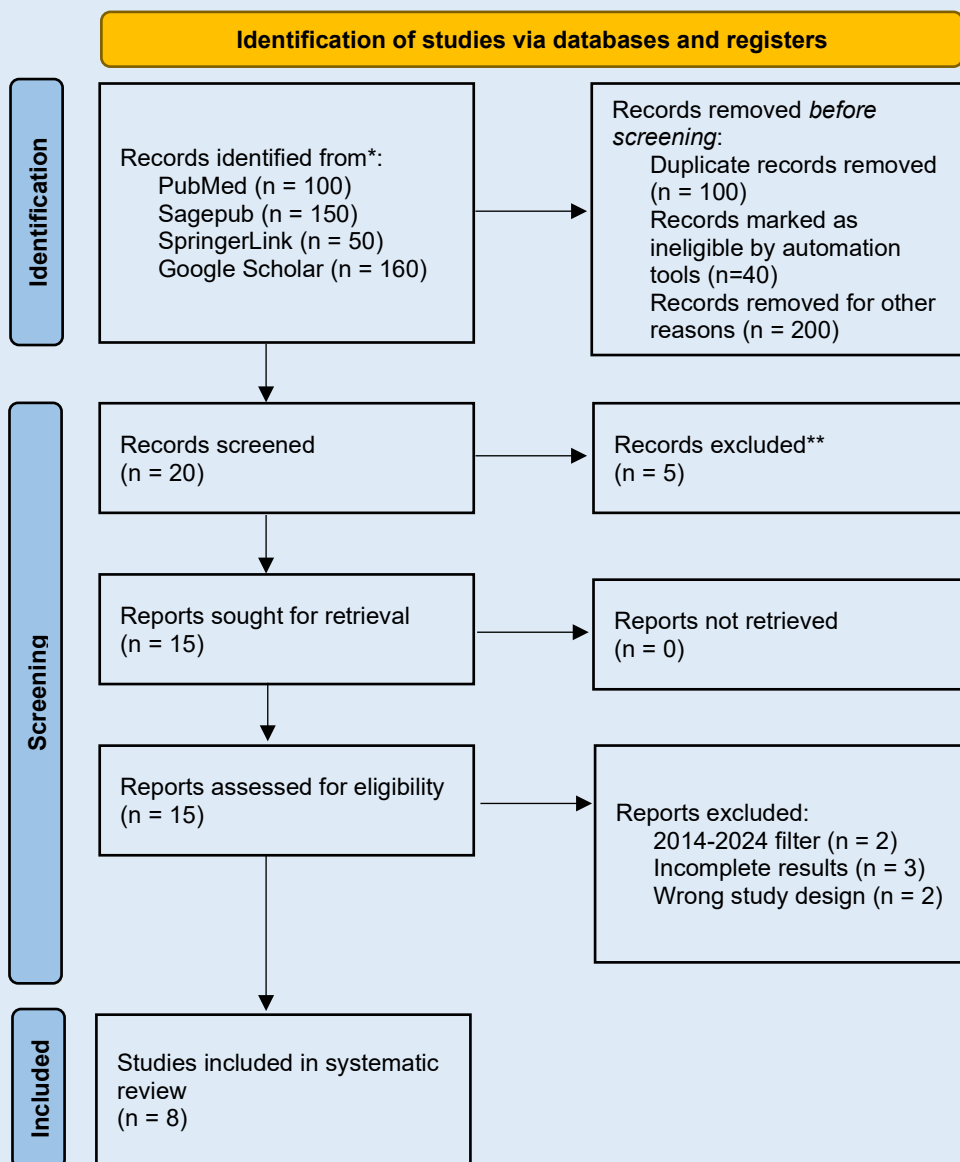


Figure 1. Article search flowchart

RESULT

The initial number of articles retrieved from online databases (PubMed, SagePub, SpringerLink, and Google Scholar) is 360 articles. After conducting three levels of screening, eight articles that directly relate to the current systematic review have been chosen for further assessment through full-text reading and analysis. Table 1 presents the selected literature included in this analysis.

Table 1. The literature included in this study

No.	Author	Origin	Method	Sample	Result
1.	Lama, et al. ⁵ (2022)	Nepal	Retrospective cohort study	61 patients	In a study involving 61 individuals clinically diagnosed with thalassemia, genotyping was conducted using multiplex amplification refractory mutation system-polymerase chain reaction (ARMS-PCR). The analysis targeted 21 major mutations, utilizing allele-specific primers grouped into six panels. The most common mutations identified were IVS 1-5 (G-C) and Cd 26 (G-A) (HbE), accounting for 23% of cases. Other mutations included 619 deletion, Cd 8/9 (+G), Cd 16 (-C), Cd 41/42 (-TTCT), IVS 1-1 (G-T), Cd 19 (A-G), and Cd 17 (A-T), with frequencies of 20%, 12%, 8%, 6%, 4%, 3%, and 1%, respectively.
2.	Tiwari, et al. ⁶ (2023)	India	Prospective cross sectional study	53 patients	The study found a thalassemia prevalence of 3.68% (95% CI 2.7% to 4.65%), with the average age of diagnosis being 15.58 months (ranging from 2 to 97 months). Most cases (60.37%) were diagnosed before the age of one year, with a male-to-female ratio of 1.2:1. Thalassemia was notably more prevalent in the Tharu community (58.5%).
3.	Yadav, et al. ⁷ (2022)	India	Retrospective cohort study	1214 patients	The prevalence of β-thalassemia trait in Central India ranged from 1.4% to

					3.4%, with β-thalassemia major (β-TM) reported in 0.94% of anemic patients. In South India, the prevalence of β-thal trait was between 8.50% and 37.90%, and β-TM ranged from 2.30% to 7.47%. Northern and Western India showed a higher thalassemic burden. In Eastern India, tribal populations had a higher prevalence of β-thal trait (0.00–30.50%), β-TM (0.36–13.20%), and hemoglobinopathies like Hb E/β-thal (0.04–15.45%) compared to non-tribal populations.
4.	Wendt, et al. ⁸ (2023)	Bangladesh	Retrospective cohort study	395 patients	The study found that 11% of women and 10% of children had at least one inherited blood disorder. Alpha thalassemia was the most common, present in 7% of women and 5% of children, followed by beta thalassemia and hemoglobin E at 2–3%. Hemoglobin S and hemoglobin D were also identified. In non-pregnant women, inherited blood disorders, particularly alpha and beta thalassemia, were linked to lower hemoglobin levels. Pregnant women with beta thalassemia also had lower hemoglobin concentrations, while the association between hemoglobinopathies and hemoglobin levels in children was weaker.

5.	Wahidiyat, et al. ⁹ (2022)	Indonesia	Retrospect ive cohort study	2500 patients	In Indonesia, 3.0–10.0% of the population carries β-thalassemia (β-thal), and 2.6–11.0% carries α-thalassemia (α-thal), with around 2,500 babies born annually with β-thalassemia major (β-TM). Current treatment for β-TM mainly involves supportive care, such as blood transfusions and iron chelation therapy. However, poor hemovigilance in some cities raises the risk of transfusion-related infections and reactions.
6.	Nguyen, et al. ¹⁰ (2017)	Thailand	Retrospect ive cohort study	390 patients	The study found that 56.1% of participants carried thalassemia genes. Hemoglobin Constant Spring (Hb CS) was highly prevalent at 23.8%, while α+thalassemia (–3.7 kb deletion) had a frequency of 26.4%. Hemoglobin E (Hb E) and hemoglobin Paksé (Hb Ps) were identified at frequencies of 14.6% and 2.6%, respectively. Analysis of the α-globin gene haplotype revealed that the Hb CS haplotype in this population matched that of the Co-Tu minority, suggesting shared ancestry with the Ta-Oi minority. These findings are valuable for future population genetics research and for developing thalassemia prevention and control programs in the region.

7.	Rumaney, et al. ¹¹ (2014)	Cameroon	Case control study	264 patients	The study examined 161 Cameroonian patients with sickle cell anemia (SCA) and 103 controls. The Benin haplotype was most prevalent (66.3%) among patients. Alpha-thalassemia (3.7 kb deletions) was more common in SCA patients (37.3%) than in controls (10.9%). Patients with α-thalassemia showed improved hematological indices, with increased red blood cell counts and lower white blood cell counts and mean corpuscular volume. Co-inheritance of α-thalassemia was linked to a lower rate of consultations, suggesting a potential improvement in patient outcomes and survival.
8.	Mailula, et al. ¹² (2021)	South Africa	Retrospective cohort study	12 patients	The study involved 12 children with transfusion-dependent thalassemia (TDT), all of Indian descent, receiving regular blood transfusions and iron chelation therapy (ICT). Four patients had iron overload detected through serum ferritin (SF) and MRI scans of the liver and heart. Most patients were switched to oral deferasirox (DFX) for chelation. One child on parenteral deferoxamine with high SF levels died, while four others underwent successful hematopoietic stem cell transplantation (HSCT) and are in remission.

Lama, et al.⁵ (2022) concluded that Nepal's mutational profile is similar to neighboring countries like India and Myanmar. Thalassemia was detected across 17 ethnic groups, particularly those with ancestral origins in India and Central Asia.

Tiwari, et al.⁶ (2023) found that common clinical symptoms in children with transfusion-dependent thalassemia included pallor, hepatomegaly, splenomegaly, and facial deformities. The study emphasized the importance of monitoring serum ferritin levels to detect iron overload early and initiate chelation therapy, which can improve the quality of life and reduce the impact of this genetic disorder in affected communities.

Yadav, et al.⁷ (2022) showed that lower socioeconomic groups such as scheduled castes, scheduled tribes, and other backward classes were particularly affected. While β -thal is present across all Indian states, it is concentrated in the eastern and western regions. The study stresses the need for well-integrated strategies at the State and National levels to reduce the burden of β -thalassemia.

Wendt, et al.⁸ (2023) showed that the high prevalence of alpha thalassemia in rural Sylhet, Bangladesh, exceeded that of other hemoglobinopathies. The study highlights the lack of community-based data on alpha thalassemia in Bangladesh and suggests future research include its prevalence to raise public health awareness and support couples counseling.

Wahidiyat, et al.⁹ (2022) found that access to iron chelators is inconsistent, especially in rural areas, and adherence to iron chelation therapy, as well as maintaining pre-transfusion hemoglobin levels above 9.0 g/dL, remains a challenge. Although the cost of transfusions and chelation therapy is covered by national health insurance, the financial burden of thalassemia is rising as life expectancy increases. Therefore, optimizing preventive programs is seen as the most viable strategy to manage thalassemia in Indonesia.

Nguyen, et al.¹⁰ (2017) showed a high prevalence of thalassemia and hemoglobinopathies, particularly Hemoglobin Constant Spring and α^+ -thalassemia, in the

population. The shared genetic haplotype between the Ta-Oi and Co-Tu minorities suggests a common ancestry. These findings underscore the need for targeted prevention programs and further research into the genetic patterns within these communities.

Rumaney, et al.¹¹ (2014) showed that co-inheritance of α -thalassemia in SCA patients is associated with better hematological outcomes and fewer clinical consultations, which may contribute to improved survival.

Mailula, et al.¹² (2021) showed that Hemoglobin-level-driven blood transfusions with adequate chelation are feasible in South Africa's public health system. Close monitoring for iron overload using SF and MRI is essential, with oral ICTs preferred. HSCT is the treatment of choice for TDT when available.

DISCUSSION

This systematic review highlights significant findings regarding the prevalence, risk factors, and management of thalassemia in low-income countries, drawing insights from various studies

conducted across Nepal, India, Bangladesh, Indonesia, Thailand, Cameroon, and South Africa.

The prevalence of thalassemia across low-income countries reveals significant regional variations influenced by genetic, demographic, and socioeconomic factors. In Nepal, Lama et al. (2022) identified a diverse range of thalassemia mutations, indicating a complex genetic landscape.⁵ Similarly, India shows a wide range of β -thalassemia prevalence, from 1.4% in Central India to as high as 37.90% in South India, with significant burdens observed among lower socioeconomic and tribal communities.^{6,7} In Bangladesh, Wendt et al. (2023) found particularly high prevalence rates of alpha thalassemia in rural areas, underscoring the need for regional-specific public health strategies. The broad variability in prevalence rates across different regions necessitates tailored public health interventions that account for local genetic and demographic profiles.⁸

In Southeast Asia, Nguyen et al. (2017) reported high frequencies of Hemoglobin Constant Spring and

α +-thalassemia in Thailand, reflecting the region's unique genetic patterns.¹⁰ Indonesia, with its substantial carrier rates of both β -thalassemia and α -thalassemia, faces a significant burden, with around 2,500 new cases of β -thalassemia major annually.⁹ These findings emphasize the importance of region-specific data to guide effective public health strategies and resource allocation for thalassemia management. The observed disparities highlight the need for ongoing surveillance and tailored approaches to address the varying prevalence of thalassemia in low-income countries.^{13,14}

Genetic risk factors play a critical role in the prevalence and severity of thalassemia. In India, β -thalassemia shows a marked prevalence among lower socioeconomic and tribal communities, suggesting that both genetic heritage and socio-economic conditions are significant risk factors.⁷ The high prevalence of alpha thalassemia in Bangladesh further underscores the genetic risk associated with inherited blood disorders, with alpha and beta

thalassemia linked to lower hemoglobin levels in both women and children.⁸ The shared genetic haplotype identified in Thailand, indicating common ancestry, highlights the importance of genetic background in influencing thalassemia prevalence.¹⁰ Understanding these genetic risk factors is essential for developing targeted prevention and management strategies.^{15,16}

In Cameroon, the co-inheritance of α -thalassemia with sickle cell anemia was associated with improved hematological indices and fewer clinical consultations, suggesting a genetic interplay that affects disease outcomes.¹¹ This finding highlights the complex interactions between different genetic factors and their impact on thalassemia management. The identification of genetic risk factors is crucial for designing effective screening programs and tailored interventions. Addressing these risk factors can help reduce the burden of thalassemia and improve patient outcomes in low-income settings.^{17,18}

Management of thalassemia in low-income countries presents

significant challenges, particularly concerning access to and adherence to treatment. In Indonesia, the management primarily involves blood transfusions and iron chelation therapy, but inconsistent access to chelators and rising costs pose considerable barriers.⁹ The financial burden of thalassemia is exacerbated by increasing life expectancy, making it essential to optimize preventive programs and improve access to effective treatments. Similarly, in South Africa, while effective management with regular transfusions and oral deferasirox is feasible, close monitoring for iron overload remains critical.¹² The need for reliable and accessible treatment options highlights the importance of strengthening healthcare infrastructure in low-income countries.^{19,20}

In Cameroon, the co-inheritance of α -thalassemia in sickle cell anemia patients led to improved hematological outcomes, suggesting that tailored management approaches can enhance patient outcomes.¹¹ The study also emphasizes the need for comprehensive monitoring and management strategies that address

the complexities of co-inherited conditions. Effective management strategies, including regular monitoring and personalized treatment plans, are crucial for improving the quality of life and reducing the impact of thalassemia in these regions. Optimizing these strategies requires a concerted effort to enhance healthcare delivery and ensure that patients receive the necessary care.^{21,22}

CONCLUSION

Thalassemia prevalence varies significantly across low-income countries, driven by genetic and socioeconomic factors. Effective management requires region-specific strategies, improved access to treatments, and ongoing monitoring. Tailored public health interventions are crucial to reduce the burden and improve patient outcomes.

REFERENCES

1. Alli NA, Patel M, Alli HD, et al. Recommendations for the management of sickle cell disease in South Africa. *SAMJ South Afr Med J*. 2014;104(11):743-751. doi:10.7196/SAMJ.8470
2. Kattamis A, Forni GL, Aydinok Y, Viprakasit V. Changing

- patterns in the epidemiology of β -thalassemia. *Eur J Haematol*. 2020;105(6):692-703. doi:10.1111/ejh.13512
3. Weatherall DJ. The Evolving Spectrum of the Epidemiology of Thalassemia. *Hematol Oncol Clin North Am*. 2018;32(2):165-175. doi:10.1016/j.hoc.2017.11.008
4. Moirangthem A, Phadke SR. Socio-demographic Profile and Economic Burden of Treatment of Transfusion Dependent Thalassemia. *Indian J Pediatr*. 2018;85(2):102-107. doi:10.1007/s12098-017-2478-y
5. Lama R, Yusof W, Shrestha TR, et al. Prevalence and distribution of major β -thalassemia mutations and HbE/ β -thalassemia variant in Nepalese ethnic groups. *Hematol Oncol Stem Cell Ther*. Published online February 11, 2021. doi:10.1016/j.hemonc.2021.01.004
6. Tiwari D. Clinical Profile of Children with Thalassemia Admitted for Blood Transfusion at a Tertiary Health Care Center. *J Coll Med Sci-Nepal*. 2023;19:2091-0657. doi:10.3126/jcmsn.v19i3.56520
7. Yadav SS, Panchal P, Menon KC. Prevalence and Management of β -Thalassemia in India. *Hemoglobin*. 2022;46(1):27-32. doi:10.1080/03630269.2021.2001346
8. Wendt AS, Brintrup J, Waid JL, Kader A, Lambrecht NJ, Gabrysch S. Thalassemia and hemoglobinopathy prevalence in a community-based sample in Sylhet, Bangladesh. *Orphanet J Rare Dis*. 2023;18(1):192. doi:10.1186/s13023-023-02821-3
9. Wahidiyat PA, Sari TT, Rahmartani LD, et al. Thalassemia in Indonesia. *Hemoglobin*. 2022;46(1):39-44. doi:10.1080/03630269.2021.2023565
10. Nguyen NT, Sanchaisuriya K, Sanchaisuriya P, et al. Thalassemia and hemoglobinopathies in an ethnic minority group in Central Vietnam: implications to health burden and relationship between

- two ethnic minority groups. *J Community Genet.* 2017;8(3):221-228.
doi:10.1007/s12687-017-0306-8
11. Rumaney MB, Bitoungui VJN, Vorster AA, et al. The Co-Inheritance of Alpha-Thalassemia and Sickle Cell Anemia Is Associated with Better Hematological Indices and Lower Consultations Rate in Cameroonian Patients and Could Improve Their Survival. *PLOS ONE.* 2014;9(6):e100516.
doi:10.1371/journal.pone.0100516
12. Mailula MT, Goga Y, Jeena PM. The clinical profile and outcome of children with transfusion-dependent thalassaemia in KwaZulu-Natal Province, South Africa: A 16-year retrospective review. *South Afr J Child Health.* 2021;15(3):165-169.
doi:10.7196/SAJCH.2021.v15.i3.1797
13. Mettananda S, Paranamana S, Fernando R, et al. Microcytic anemia in children: parallel screening for iron deficiency and thalassemia provides a useful opportunity for thalassemia prevention in low- and middle-income countries. *Pediatr Hematol Oncol.* 2020;37(4):326-336.
doi:10.1080/08880018.2020.1725200
14. Kandhro AH, Prachayasittikul V, Isarankura Na-Ayudhya C, Nuchnoi P. Prevalence of Thalassemia Traits and Iron Deficiency Anemia in Sindh, Pakistan. *Hemoglobin.* 2017;41(3):157-163.
doi:10.1080/03630269.2017.1345759
15. Amid A, Haghi-Ashtiani B, Kirby-Allen M, Haghi-Ashtiani MT. Screening for thalassemia carriers in populations with a high rate of iron deficiency: revisiting the applicability of the Mentzer Index and the effect of iron deficiency on Hb A2 levels. *Hemoglobin.* 2015;39(2):141-143.
doi:10.3109/03630269.2015.1024321
16. Pornprasert S, Thongsat C, Panyachadporn U. Evaluation of Applying a Combination of Red

- Cell Indexes and Formulas to Differentiate β -Thalassemia Trait from Iron Deficiency Anemia in the Thai Population. *Hemoglobin*. 2017;41(2):116-119.
doi:10.1080/03630269.2017.1323763
17. Chauhan W, Shoaib S, Fatma R, Zaka-Ur-Rab Z, Afzal M. Beta-thalassemia and the advent of new interventions beyond transfusion and iron chelation. *Br J Clin Pharmacol*. 2022;88(8):3610-3626. doi:10.1111/bcp.15343
18. Cappellini MD, Motta I. New therapeutic targets in transfusion-dependent and -independent thalassemia. *Hematol Am Soc Hematol Educ Program*. 2017;2017(1):278-283.
doi:10.1182/asheducation-2017.1.278
19. Grech L, Borg K, Borg J. Novel therapies in β -thalassaemia. *Br J Clin Pharmacol*. 2022;88(6):2509-2524.
doi:10.1111/bcp.14918
20. Jagannath VA, Fedorowicz Z, Al Hajeri A, Sharma A. Hematopoietic stem cell transplantation for people with β -thalassaemia major. *Cochrane Database Syst Rev*. 2016;11(11):CD008708.
doi:10.1002/14651858.CD008708.pub4
21. Sharma A, Jagannath VA, Puri L. Hematopoietic stem cell transplantation for people with β -thalassaemia. *Cochrane Database Syst Rev*. 2021;4(4):CD008708.
doi:10.1002/14651858.CD008708.pub5
22. Crossley M, Christakopoulos GE, Weiss MJ. Effective therapies for sickle cell disease: are we there yet? *Trends Genet TIG*. 2022;38(12):1284-1298.
doi:10.1016/j.tig.2022.07.003