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IRON CHELATION, VITAMINS, AND SUPPLEMENTS FOR THALASSEMIA PATIENTS: SCOPING REVIEW

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ABSTRACT
Thalassemia major and transfusion-dependent thalassemia (TDT) are hereditary hemoglobinopathies that require lifelong blood transfusions and iron chelation therapy to prevent complications related to iron overload. Despite advances in chelation therapy, patients continue to experience complications such as oxidative stress, endocrine disorders, and bone health deterioration. This scoping review aimed to synthesize evidence from research articles regarding the role of iron chelation agents, including deferoxamine (DFO), deferiprone (DFP), and deferasirox (DFX), together with vitamin and supplement interventions in the management of thalassemia patients. This study used the PRISMA-ScR guidelines to identify scientific articles published between 2016 and 2025 from the PubMed and Scopus databases. Eligible studies were selected through title, abstract, and full-text screening according to predefined inclusion and exclusion criteria. Data were extracted, categorized by intervention type, and synthesized descriptively to examine the role of iron chelation therapy, vitamin C, vitamin D, vitamin E, folic acid, calcium, and antioxidant supplements in thalassemia management. A total of 29 articles met the inclusion criteria and were reviewed. The main findings demonstrated that vitamin C enhances the effectiveness of iron chelation therapy, particularly when combined with DFO. Vitamin D and calcium supplementation improve bone mineral density and reduce the risk of osteoporosis. Vitamin E and other antioxidants help reduce oxidative stress, while appropriate folic acid supplementation prevents deficiency without causing excessive accumulation. The combination of iron chelation therapy with vitamins and supplements provides benefits in reducing complications associated with iron overload, improving bone health, and decreasing oxidative stress in patients with thalassemia. This review offers evidence-based insights to optimize nutritional management in patients with thalassemia undergoing iron chelation therapy.

Keywords: bone mineral density; iron chelation therapy; thalassemia; oxidative stress

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INTRODUCTION

Thalassemia is an inherited hemoglobin disorder characterized by reduced or absent production of α- or β-globin chains, resulting in globin chain imbalance, ineffective erythropoiesis, chronic hemolytic anemia, and a spectrum of clinical severity ranging from mild anemia to transfusion-dependent disease (Jaing TH, 2021; Sanchez-Villalobos M, 2022). Individuals with β-thalassemia major (β-TM), which is commonly classified as transfusion-dependent thalassemia (TDT), generally require lifelong regular blood transfusions every 2–5 weeks to maintain pretransfusion hemoglobin concentrations of approximately 9.5–10.5 g/dL. Maintaining hemoglobin within this target range is essential to suppress ineffective erythropoiesis and reduce complications related to chronic anemia (Forni GL, et al, 2023; Taher et al., 2025). Nevertheless, repeated transfusions contribute to excessive iron accumulation because the body has limited ability to eliminate excess iron naturally managed (Tayal A, et al, 2025). Iron overload may progressively damage essential organs such as the heart, liver, and endocrine glands, potentially causing organ dysfunction, endocrine disorders, cardiovascular complications, and increased mortality when not adequately managed (Kumfu, S., et al, 2017; Tayal A, et al, 2025).

Advances in iron chelation therapy have significantly improved the prognosis of patients with transfusion-dependent thalassemia by preventing progressive iron accumulation and reducing the risk of cardiac, hepatic, and endocrine complications. Currently, deferoxamine (DFO), deferiprone (DFP), and deferasirox (DFX) remain the most widely used iron chelators, with each agent demonstrating different pharmacological characteristics, therapeutic benefits, and safety profiles. Appropriate selection and monitoring of chelation therapy are essential for optimizing long-term clinical outcomes and quality of life in patients with thalassemia (El-Beshlawy A, Dewedar H, 2024; Sanchez-Villalobos M, 2022; Taher, 2025). Despite these therapeutic advances, patients with thalassemia still frequently experience complications such as oxidative stress, endocrine abnormalities, bone disorders, and deficiencies of essential micronutrients (Al-Sanabra et al., 2025; Aliberti et al., 2022; Rahim et al., 2016).

Recent evidence indicates that vitamins and nutritional supplements may serve as supportive therapies in reducing thalassemia-related complications. Vitamin C has been shown to improve the effectiveness of iron chelation therapy reactions (Elalfy, M. S., .et al., 2016). while vitamin D and calcium contribute to maintaining bone health and reducing bone deterioration (Giusti A, et al., 2016; Thiagarajan., et al,, 2019). Vitamin E may help decrease oxidative stress (ElLaboudy, et al., 2025), and folic acid supplementation is important in preventing deficiency in patients with increased erythropoietic activity (Agrawal, T., et al., 2022; Baghersalimi et al., 2018). Furthermore, natural antioxidant compounds derived from plants, including quercetin, grape seed extract, and green tea polyphenols, have demonstrated antioxidant and iron-chelating effects that could provide additional therapeutic advantages for individuals with thalassemia (Hezaveh, et al, 2019; Mottaghi & Abbaszadeh, 2023; Rasaei et al., 2021).

Despite advances in iron chelation therapy, patients with thalassemia continue to experience complications related to iron overload, oxidative stress, nutritional deficiencies, and impaired quality of life. Emerging evidence suggests that vitamins and nutritional supplements may provide additional benefits when used alongside conventional chelation therapy; however, findings remain fragmented and have not been comprehensively synthesized. Therefore, this review aims to critically examine the current evidence on iron chelation therapy and adjunctive vitamin and supplement interventions in patients with thalassemia, focusing on their efficacy, safety, and potential roles in improving clinical outcomes. Furthermore, this review seeks to identify existing knowledge gaps and provide recommendations for future research and clinical practice (Mottaghi & Abbaszadeh, 2023; Al-Sanabra et al., 2025). This scoping review aimed to map and synthesize the existing evidence on the use of iron chelation therapy, including deferoxamine (DFO), deferiprone (DFP), and deferasirox (DFX), as well as vitamin and nutritional supplement interventions in patients with thalassemia, with a particular focus on their effectiveness, safety, and clinical outcomes.

METHOD

This study utilized data obtained from PubMed and Scopus databases. The literature search employed the keywords “Thalassemia,” “iron,” “chelation,” “chelators,” “vitamin,” and “supplement” combined using Boolean operators. The search was restricted to original research articles published in English between 2016 and 2025 with accessible full-text availability. Review articles and non-original studies were excluded from the selection process. The initial search yielded 13 articles from Scopus and 284 articles from Google Scholar. Inclusion criteria included quantitative or qualitative studies involving patients with thalassemia, original research articles, publications written in English, accessible full-text manuscripts, and studies relevant to the synthesis of iron chelation therapy, vitamin supplementation, or supportive nutritional interventions in thalassemia management. Following the screening, duplication removal, and eligibility assessment processes, 13 articles were ultimately included in the final analysis, comprising 9 articles from Scopus and 4 articles from Google Scholar (Figure 1).

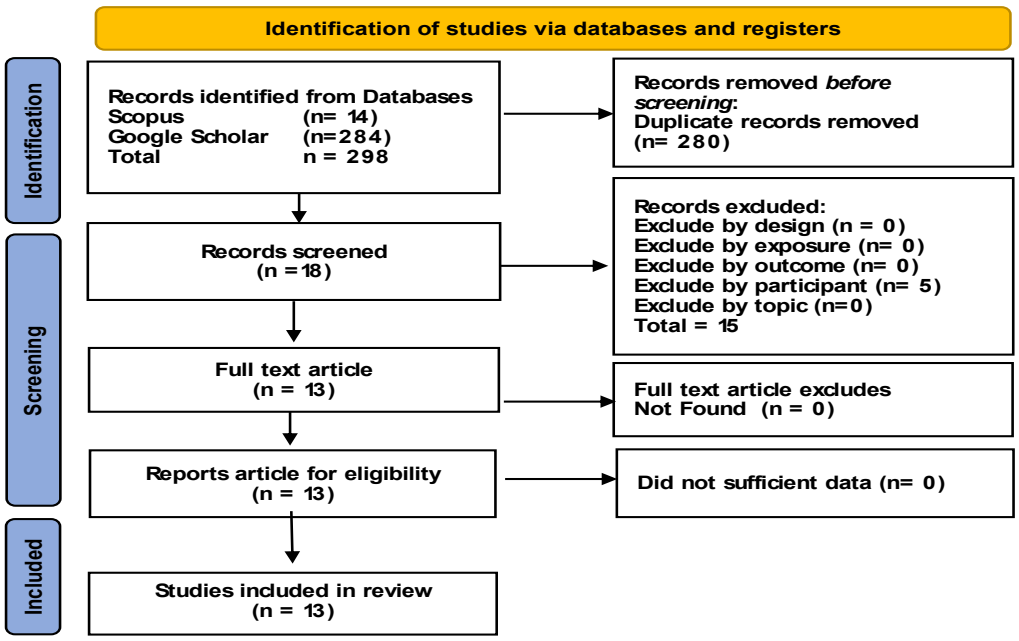

Figure 1. PRISMA flow diagram

RESULT

Table 1.
Analisys Article

No	Year	Article Title / Authors	Research Objective	Research Method	Research Findings
1	2016	Elalfy, M. S., Adly, A. A., Attia, A. A., Ibrahim, F. A., Mohammed, A. S., Sayed, A. M., & Elhenawy, Y. I.	To evaluate the efficacy and safety of vitamin C as an adjunctive therapy in patients with β-thalassemia major undergoing iron chelation therapy.	Prospective interventional clinical trial involving young thalassemia major patients receiving vitamin C in combination with iron chelators.	Vitamin C enhanced the effectiveness of iron chelation therapy, particularly when combined with deferoxamine (DFO), by reducing tissue iron overload and serum ferritin levels without causing significant adverse effects.
2	2025	Al-Sanabra, O. M., Abbas, M. A., Hazaa, A. A., & Haza, W. J.	To identify endocrine complications in β-thalassemia major patients receiving iron chelation therapy.	Case-control study assessing endocrine and metabolic parameters in thalassemia major patients.	Several endocrine complications, including hypocalcemia, hypercalciuria, vitamin D deficiency, and bone metabolism disorders, were identified despite adequate iron chelation therapy.
3	2023	Mottaghi, A., Yeganeh, M. Z., & Golzarand, M.	To assess the effects of grape seed extract combined with deferasirox on iron overload and oxidative stress in children with thalassemia.	Clinical interventional study involving children with β-thalassemia receiving deferasirox and grape seed extract.	The combination of grape seed extract and deferasirox significantly reduced oxidative stress, inflammation, serum ferritin levels, and improved liver function in thalassemia patients.
4	2025	ElLaboudy, M. A., Sabry, S. M., Farid, T. M., Hamdy, M. M., & El-Beshlawy, A.	To examine the effects of vitamin E supplementation on oxidative stress and tissue iron overload in	Randomized placebo-controlled trial conducted over 12 months in	Vitamin E supplementation significantly decreased oxidative stress markers and improved tissue iron overload parameters in patients receiving iron chelation therapy.

No	Year	Article Title / Authors	Research Objective	Research Method	Research Findings
			transfusion-dependent thalassemia patients.	children with transfusion-dependent thalassemia (TDT).	
5	2019	Hezaveh, Z. S., Azarkeivan, A., Janani, L., Hosseini, S., Shidfar, F., & Hajiaghamohammadi, A. A.	To investigate the effects of quercetin on oxidative stress and liver function in β-thalassemia major patients.	Double-blind randomized clinical trial.	Quercetin reduced oxidative stress, improved liver enzyme levels, and enhanced antioxidant status in patients treated with desferrioxamine therapy.
6	2022	Aliberti, L., Gagliardi, I., Gamberini, M. R., Ziggiotto, A., Verrienti, M., Carnevale, A., et al.	To determine the prevalence and risk factors of hypercalciuria in β-thalassemia major patients.	Multicenter observational study.	Hypercalciuria was frequently observed and associated with bone metabolism disorders, prolonged iron chelation therapy, and increased risk of osteoporosis.
7	2016	Giusti, A., Pinto, V., & Forni, G. L.	To discuss osteoporosis management in patients with β-thalassemia.	Narrative literature review.	Vitamin D and calcium supplementation, physical exercise, and antiresorptive therapy were considered important strategies in preventing and managing osteoporosis in thalassemia patients.
8	2019	Thiagarajan, N. R., Delhi Kumar, C. G., Sahoo, J., et al.	To evaluate the effects of vitamin D and calcium supplementation on bone health in children with thalassemia.	Prospective interventional study involving children with thalassemia.	Supplementation with vitamin D and calcium improved bone mineral content and contributed to the prevention of osteopenia and osteoporosis in pediatric thalassemia patients.
9	2022	Agrawal, T., Dewan, P., Gamber, S., Agarwal, R., Sharma, S., & Kotru, M.	To determine the optimal oral folic acid dosage in transfusion-dependent thalassemia patients.	Randomized controlled trial.	Adequate folic acid supplementation effectively prevented folate deficiency and supported erythropoiesis without causing excessive supplementation.
10	2025	Xu, H., Khantamat, O., Korsieporn, W., Paradee, N., Li, J., Zhong, Y., Srichairatanakool, S., & Koonyosying, P.	To investigate the effects of green tea extract on bone formation under iron overload conditions.	Experimental laboratory study using MG-63 osteoblast-like cells.	Epigallocatechin-3-gallate (EGCG) in green tea extract promoted bone formation and mineralization by reducing oxidative stress caused by iron overload.
11	2024	Rathore, V., Sharma, S., Meena, J. P., & Seth, R.	To determine the prevalence of peripheral neuropathy in children with transfusion-dependent thalassemia.	Hospital-based cross-sectional study.	Peripheral neuropathy was commonly identified in TDT patients and was associated with chronic disease complications and possible effects of iron overload.
12	2017	Kumfu, S., Chattipakom, S. C., Srichairatanakool, S., Settakom, J., Fucharoen, S., & Chattipakom, N.	To review cardiac complications associated with β-thalassemia and iron overload.	Literature review.	Iron overload increased the risk of cardiomyopathy, arrhythmias, and heart failure, whereas iron chelation therapy effectively reduced cardiovascular complications.
13	2022	Santra, G., Chakraborty, S., Patra, S., Banerjee, D., & Pradhan, S.	To assess bone mineral density, serum calcium, and vitamin D levels in adult patients with thalassemia major.	Cross-sectional study conducted at a thalassemia care center.	Most patients exhibited reduced bone mineral density, hypocalcemia, and vitamin D deficiency, which increased the risk of osteoporosis and fractures.

DISCUSSION

The findings synthesized in this review indicate that comprehensive thalassemia management should combine effective iron chelation therapy with adequate nutritional and vitamin support. While iron chelators remain the cornerstone of treatment for reducing iron overload and preventing organ damage, adjunctive supplementation with vitamins and antioxidants may help mitigate oxidative stress, improve nutritional status, and support overall clinical outcomes. These complementary interventions may address pathophysiological mechanisms that are not fully controlled by chelation therapy alone (Al-sanabra & Hazà, 2025; Jaing TH, 2021; Mottaghi S, 2023; Sanchez-Villalobos M, 2022). Vitamin C has been shown to improve the effectiveness of iron chelation therapy, particularly deferoxamine, by facilitating the mobilization of intracellular iron and promoting iron excretion (Elalfy, M. S., .et al., 2016). This beneficial effect is especially observed in patients with moderate iron overload and vitamin C deficiency, where supplementation of 100 mg/day contributed to significant reductions in iron burden indicators without notable adverse reactions (Elalfy, M. S., .et al., 2016). Nevertheless, vitamin C administration should be carefully monitored because excessive supplementation in patients with severe iron overload may increase oxidative stress rather than reduce it (Rahim, et al, 2016).

Supplementation with vitamin D and calcium is also essential in managing bone complications associated with thalassemia. These nutrients contribute to improving bone mineral density and lowering the risk of fractures by addressing the multifactorial causes of bone disease in thalassemia patients (Aliberti, L., Gagliardi, 2022; Santra et al., 2022; Thiagarajan et al., 2019).Considering the high incidence of vitamin D deficiency among thalassemia patients, regular screening and appropriate supplementation are strongly recommended (Al-sanabra & Hazà, 2025; Santra et al., 2022). Furthermore, vitamin D may provide additional benefits beyond skeletal health, including potential cardioprotective and immunomodulatory effects. Recent findings demonstrated that lower vitamin D levels were associated with increased cardiac iron uptake in patients with β-thalassemia major, suggesting that maintaining adequate vitamin D status may contribute to improved cardiac health and overall clinical outcomes (Giusti et al., 2016; Meloni et al., 2023).

Vitamin E and several antioxidant compounds such as grape seed extract, quercetin, and green tea polyphenols have demonstrated beneficial effects in reducing oxidative stress through multiple mechanisms, including scavenging free radicals, enhancing endogenous antioxidant activity, and supporting iron chelation processes (ElLaboudy et al., 2025; Hezaveh et al., 2019; Mottaghi & Abbaszadeh, 2023; Rasaei et al., 2021). When combined with conventional iron chelators, these antioxidants may provide synergistic therapeutic effects by simultaneously reducing iron overload and oxidative damage (Mottaghi S, 2023; ; Petiwathayakorn et al., 2024). Folic acid supplementation is also important in preventing folate deficiency among patients with increased erythropoietic activity. Previous studies have indicated that a weekly dose of 5 mg may provide an optimal balance between effectiveness and safety (Agrawal et al., 2022; Baghersalimi et al., 2018). In addition, monitoring and supplementation of essential trace elements and minerals may further support immune function, antioxidant defense mechanisms, and overall metabolic stability in individuals with thalassemia (Kumfu et al., 2017; Lertsuwan et al., 2018). While iron chelation therapy, vitamins, and antioxidant supplementation play important roles in controlling iron overload and its complications, optimal outcomes in thalassemia require a holistic approach that also considers patient well-being. Long-term adherence to treatment is influenced not only by clinical effectiveness but also by patients' physical comfort, psychological adaptation, and perceived quality of life. Integrated nursing interventions and psychoeducational programs may enhance treatment engagement, self-care behaviors, and overall well-being among individuals living with chronic (Priyanto et al., 2021; Priyanto, 2024). In addition, attention to physical well-being needs during repeated hospitalizations and transfusion procedures is essential for maintaining patient-centered care and improving health outcomes (Priyanto et al., 2023).

CONCLUSION

Iron chelation therapy has significantly improved the prognosis of thalassemia, transforming it from a life-threatening childhood disorder into a chronic condition with improved survival and quality of life. However, the findings of this literature review indicate that optimal thalassemia management requires not only effective iron chelation but also comprehensive nutritional and supportive interventions. Vitamins and supplements, including vitamin C, vitamin D, calcium, vitamin E, folic acid, and plant-derived antioxidants, have demonstrated important benefits in reducing iron overload, oxidative stress, bone complications, endocrine disturbances, and micronutrient deficiencies associated with chronic transfusions and thalassemia progression. Comprehensive monitoring of metabolic and endocrine complications is also essential to improve long-term clinical outcomes. Despite these advances, further large-scale and long-term studies are still needed to determine optimal dosing strategies, evaluate safety profiles, and develop individualized therapeutic approaches based on patient characteristics. Therefore, integrating evidence-based nutritional support with iron chelation therapy is recommended to optimize health outcomes, enhance quality of life, and improve the long-term prognosis of patients with thalassemia.

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