Lipids in Health and Disease

REVIEW

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Serum lipid profile abnormalities among beta-thalassemia patients: a systematic review and meta-analysis

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Abstract

Background Patients with betathalassemia have higher risk of various metabolic disturbances. The literature presents conflicting results about the patterns of abnormal lipid profile among patients with betathalassemia. This systematic review aimed to assess dyslipidemia patterns among patients with betathalassemia when compared with healthy individuals.

Methods The methods used were adherent to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines. Systematic searches of the literature were done across Medline/PubMed, Web of Science, Science Direct, and Regional Portal of the World Health Organization Virtual Health Library. Calculation of standardized mean difference (SMD) estimates and their associated 95% confidence intervals (CIs) were done through Jamovi software.

Results The systematic review included 21 studies meeting the criteria for the analyses. Patients with beta-thalassemia major displayed significantly elevated triglyceride levels (SMD: 0.448, 95% CI, 0.214 to 0.682; $P < .001$) and reduced total serum cholesterol (SMD: -2.26 (95% CI-2.834 to -1.678; $P < .001$), as well as decreased levels of both low-density lipoprotein cholesterol (SMD: -1.88, 95% CI, -2.614 to -1.147; $P < .001$) and high-density lipoprotein cholesterol (SMD: -1.32, 95% CI, -1.786 to -0.860; $P < .001$). Similarly, beta-thalassemia intermedia patients exhibited comparable lipid profile abnormalities to those with beta-thalassemia major. Conversely, beta-thalassemia minor patients only showed significantly lower total serum cholesterol levels (SMD: -0.66, 95% CI, -0.860 to -0.472; $P < .001$).

Conclusion Evidence indicates alterations in lipid profile markers among beta-thalassemia patients. The findings indicate the importance of assessing hypertriglyceridemia and hypocholesterolemia in these patients, especially those with major and intermedia forms, as these lipid profile abnormalities increase the risk of cardiovascular disease.

Keywords Betathalassemia, Lipids, Dyslipidemia, Cholesterol, Triglyceride, Meta-analysis

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Background

Beta-thalassemia is a widely occurring hereditary blood condition characterized by a deficiency of the beta-globin chains, which are vital components of hemoglobin structure [1–3]. This defect leads to a reduction in functional hemoglobin, resulting in impaired red blood cell formation and chronic anemia [2, 3]. Most thalassemias follow an autosomal recessive inheritance pattern and the various beta-thalassemia forms are broadly categorized into beta-thalassemia major, intermedia, and minor forms [2, 3]. Additionally, other variants of the disorder exist, including HbC/beta-thalassemia and HbS/beta-thalassemia, which involve hemoglobin structure abnormalities. The disease is widespread in tropical and subtropical areas such as the Mediterranean area, Africa, India, and Southeast Asia, with a notable increase in incidence of beta-thalassemia in other areas worldwide [3].

Iron overload is one of the hallmark features of the disorder, and the clinical consequences of iron overload depend on the organs affected by iron deposition, including the pituitary gland, pancreas, thyroid gland, heart, and liver. Iron overload leads to a reduction in antioxidant levels and increased oxidative stress, as well as lipid abnormalities [4–6]. Beta-thalassemia is associated with significant oxidative stress. This is because the condition leads to an accumulation of iron in the body and the breakdown of red blood cells, causing cellular damage and various complications [4, 5, 7]. In addition, beta-thalassemia patients have multiple chronic endocrine and metabolic problems [3, 8–11].

Several studies have investigated abnormalities in the levels of lipid profile markers across the spectrum of beta-thalassemia, consistently reporting impaired lipid indices in affected individuals. Though, there is limited and varied evidence regarding the specific patterns of lipid dysregulation and the potential correlations between lipid profile disturbances and underlying factors or hematological parameters. The current literature lacks a comprehensive meta-analysis to determine whether there are substantial alterations in lipid profile markers between patients with beta-thalassemia and the healthy population. Given that beta-thalassemia is associated with developing metabolic disturbances, it was hypothesized that patients with beta-thalassemia exhibit distinct pattern of dyslipidemia. This study aimed to systematically address this knowledge gap through a meta-analysis, providing new insights into the metabolic complications of beta-thalassemia.

Methods

Search approach

The methods used were adherent to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [12]. Registration of this systematic review was done beforehand on Open Science Framework platform (https://osf.io/4judx). To gather relevant literature, systematic searches of the literature were done across Medline/PubMed, Web of Science, ScienceDirect, and Regional Portal of the World Health Organization Virtual Health Library. The systematic search covered all available literature from its inception up to July 2024. The search included all available relevant studies, regardless of participant demographics or publication date. The publications that were found were uploaded to Endnote software to expedite the process of titles and abstracts screening and remove duplicate entries.

The search plan for the present systematic review involved the following terms: ((("Thalassemia"[Mesh] OR "beta-Thalassemia"[Mesh]) OR (thalassemia[Text Word] OR "beta-thalassemia"[Text Word] OR β-thalassemia[Text Word])) AND (("Cholesterol"[Mesh] OR "Cholesterol, LDL"[Mesh] OR "Cholesterol, HDL"[Mesh] OR "Hypercholesterolemia"[Mesh]) OR ("lipid profile"[Text Word] OR "cholesterol"[Text Word] OR "triacylglycerol"[Text Word] OR triglyceride[Text Word] OR "high-density lipoprotein"[Text Word] OR "low-density lipoprotein"[Text Word] OR "HDL"[Text Word] OR "LDL"[Text Word] OR "HDL-C"[Text Word] OR "LDL-C"OR "Dyslipidemia"[Text Word] OR "Dyslipidaemia"[Text Word] OR "Hyperlipidemia"[Text Word] OR "Hypolipidemia"[Text Word] OR Hyperlipoproteinemia[Text Word] OR Hypolipoproteinemia[Text Word] OR "Hypercholesterolemia"[Text Word] OR Hypocholesterolemia[Text Word]))).

Inclusion and exclusion criteria

The PICO model was used to frame the research query. The "population" included people with and without beta-thalassemia. The "intervention" was the occurrence of beta-thalassemia. The "comparison" was performed with respect to healthy controls. The assessed "outcomes" were the mean levels of lipid profile indices.

The process of selection involved a two-step method. Firstly, the titles and abstracts of all identified studies were examined to find possibly relevant articles. After that, a comprehensive full-text review of these studies was conducted to assess their eligibility based on the predefined inclusion criteria. These criteria included original human case-control, cross-sectional, or cohort studies that provided explicit data on one or more of the key indicators of the lipid profile, explicitly total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL), and high-density lipoprotein cholesterol (HDL) among patients and healthy participants. The exclusion criteria included review articles, case reports, editorials, abstracts, duplicate publications, studies lacking healthy

control groups, and studies that did not provide explicit data on variables of interest.

Quality assessment and data extraction

To assess the methodological thoroughness and potential biases in the included studies, the critical appraisal and assessment checklists prepared by the Joanna Briggs Institute were used (https://jbi.global/critical-appraisal-tools). The checklists expedite the assessment of potential bias in study conduct and data analysis. The data extraction process involved four independent reviewers, who extracted relevant information from each study. Any discrepancies or inconsistencies among the reviewers were set by discussion and agreement. The data extracted from all articles were the following: authors, region, year, number of patients, age group, and mean levels of the key indicators of the serum lipid profile. In addition, any significant associations with lipid profile abnormalities, if reported, were summarized.

Certainty of evidence

The GRADE framework (Grading of Recommendations Assessment, Development and Evaluation) was applied for weighing confidence in the estimates for all outcomes across the included studies. Confidence in the estimates was categorized into four ranks: high, moderate, low, or very low. The assessment began at low certainty of evidence because of the distinctive limitations of observational studies. The evidence certainty of was then downgraded or upgraded by one or two levels based on the GRADE domains. Further details regarding the GRADE domains and the reasons for downgrading or upgrading are described in previous reports.

Data analysis

The analyses were performed utilizing Jamovi software (https://www.jamovi.org) to calculate the pooled standar dized mean difference (SMD) estimates and their associated 95% confidence intervals (CIs). The random-effects model (DerSimonian–Laird method) was implemented to account for heterogeneity among the reviewed publications. Heterogeneity among studies was evaluated by utilizing the I^2 statistic, which quantifies the variation proportion in effect estimates because of the true heterogeneity rather than chance. Publication bias, a potential source of bias because of the overrepresentation of publications with significant results, was assessed utilizing Begg's and Egger's tests and inspection of funnel plots [13–15]. The Duval and Tweedie trim-and-fill analysis was implemented to address publication bias caused by missing articles [16].

Results

Studies characteristics

Initially, 898 studies were identified through the search. After removing duplicates, 585 studies remained for titles and abstracts screening process. Of these, a total of 547 records were omitted due to irrelevance, leaving 38 for full-text review. After further screening, 17 studies were excluded, resulting in 21 eligible studies for inclusion in the analyses. These 21 studies included data from 1,587 patients with beta-thalassemia and 1,659 healthy individuals. The studies selection process was illustrated in Fig. 1 [17–36].

The majority of the indicated that individuals with beta-thalassemia, irrespective of the specific type, tend to exhibit several lipid abnormalities (Table 1). These include hypocholesterolemia, with reduced concentrations of both LDL and HDL, and elevated concentration of TG. The key features of the reviewed publications, as well as risk of bias assessment, are illustrated in Table 1.

Lipid profile among patients with beta-thalassemia major

There were 15 studies with explicit data to calculate the SMD of TG and TC estimates. For TC, the pooled effect size showed a significant association between beta-thalassemia major and reduced serum TC levels, with SMD = -3.54 (95% CI, -4.442 to -2.632; $P<.001$) (Fig. 2). Regarding TG, the pooled effect size showed that that patients with beta-thalassemia major displayed significantly higher serum TG levels than the healthy individuals, with SMD = 1.91 (95% CI, 1.277 to 2.540; $P<.001$) (Fig. 2).

In addition, there were 13 studies with explicit data to calculate the SMD estimates of LDL and HDL. The analysis showed significantly lower LDL and HDL cholesterol levels in beta-thalassemia major patients compared to healthy people. The pooled SMD of LDL and HDL were −2.81 (95% CI, -3.654 to -1.959; $P<.001$) and −2.75 (95% CI, -3.668 to -1.837; $P<.001$) (Fig. 2).

Lipid profile among patients with beta-thalassemia intermedia

There were five studies with explicit data to calculate the SMD of TG and TC estimates. Beta-thalassemia intermedia patients exhibited comparable lipid profile abnormalities to those with beta-thalassemia major. The results showed that people with beta-thalassemia intermedia had significantly lower TC concentrations than healthy individuals, while their TG levels were significantly higher. For TC, the pooled SMD = -2.26 (95% CI-2.834 to -1.678; $P<.001$) (Fig. 3). The analysis of the serum TG levels showed SMD = 0.448 (95% CI, 0.214 to 0.682; $P<.001$) (Fig. 3).

Additionally, there were six studies with explicit data to calculate the SMD of LDL and HDL estimates. The analysis showed that both of them were significantly

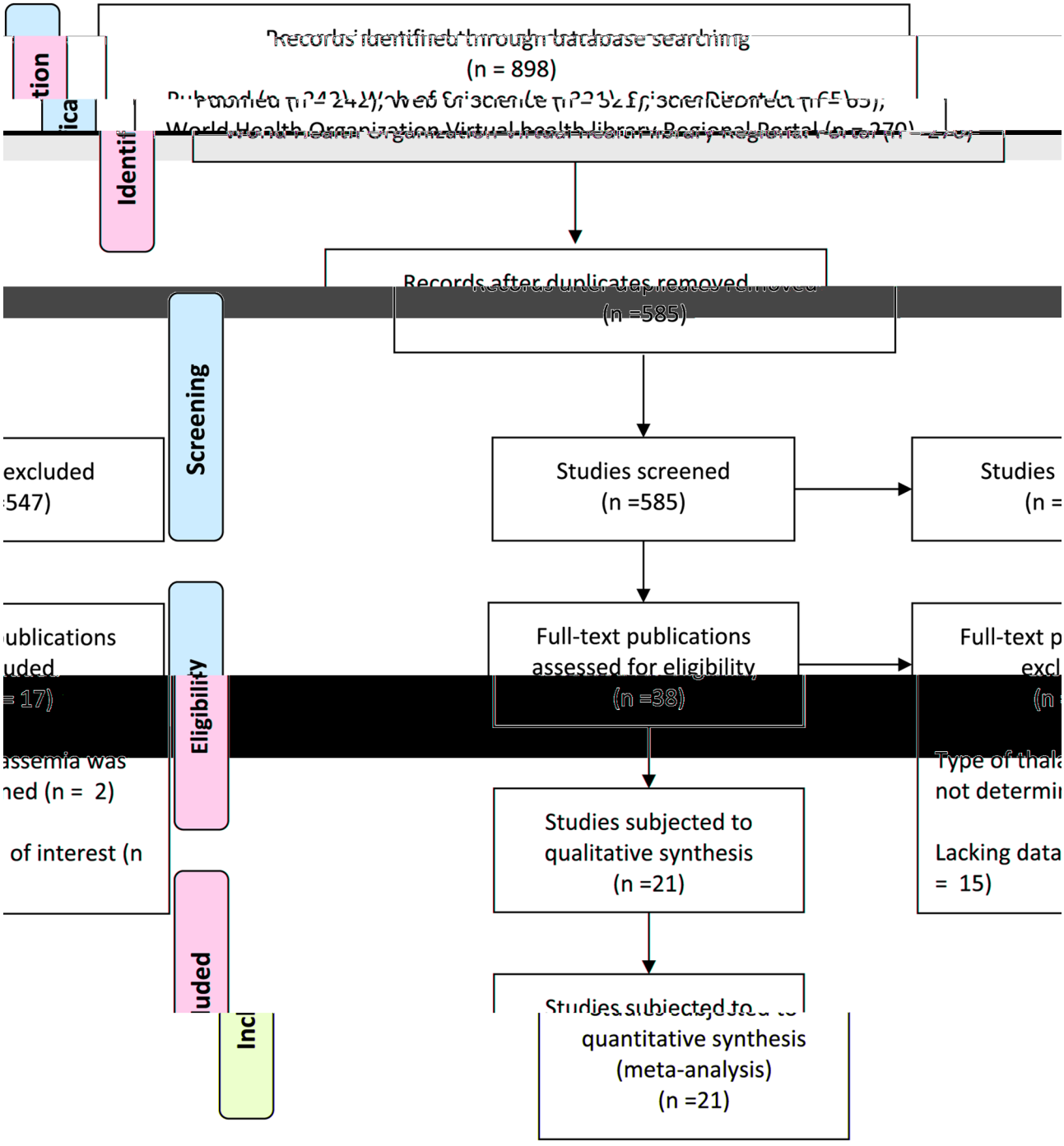

Fig. 1 Schematic of study selection

lower among beta-thalassemia patients. The pooled SMD of LDL and HDL were −1.88 (95% CI, -2.614 to -1.147; *P*<.001) and −1.32 (95% CI, -1.786 to -0.860; *P*<.001) (Fig. 3).

Lipid profile among patients with beta-thalassemia minor

There were three studies and five studies with explicit data to calculate the SMD of TC and TG estimates, respectively. For TC, the pooled effect size showed that the serum TC concentrations in beta-thalassemia minor patients were significantly lower than their controls, with SMD of -0.66 (95% CI, -0.860 to -0.472; *P*<.001) (Fig. 4). In contrast to beta-thalassemia major and beta-thalassemia intermedia, no substantial difference noted between the groups regarding TG levels, with SMD=0.08 (95% CI, −0.051 to 0.215; *P*=.228). In addition, there

Table 1 Baseline characteristics of the studies included in the review

Study	Country	Age group	No. of Patients	Type of thalassemia	Quality assessment	Main findings
Aggeli et al. [17]	Greece	Adults 24.6 +/- 0.7 years	67	β-thalassemia major	8	β-thalassemia patients had lower values TC and LDL and increased levels of parameters of endothelial dysfunction such as IL-6, sVCAM-1 and sICAM-1
Al-Quobaili et al. [19]	Syria	Children 1.5–16 years	30	β-thalassemia major	6	β-thalassemia patients had higher TG and lower TC, HDL, and LDL compared to control subjects.
Amendola et al. [20]	Italy	Adults 29 ± 12 years	23	β-thalassemia intermedia	7	β-thalassemia patients had lipid low-TC, HDL-C and LDL-C. lipid profile in was not influenced by age, sex, liver injury, hemoglobin or ferritin levels.
Ayyash et al. [21]	Palestine	All 12–42 years	65	β-thalassemia major	5	β-thalassemia patients had lower TC and higher TG levels. splenectomized β-thalassemia patients had significantly higher TC and TG levels.
Daswani et al. [22]	India	Children 1–18 years	100	β-thalassemia major	9	β-thalassemia patients had higher TG levels and lower TC and HDL. Lower TC was significantly associated with advancing age and low hemoglobin but not with chelating agents or serum ferritin. pro-atherogenic TC: HDL ratio was significantly higher in patients as compared to controls
Ghorban et al. [23]	Iran	Adults 20–30 years	70	β-thalassemia major	9	β-thalassemia patients had lower TC, HDL, and LDL compared to control subjects. In addition, cardiovascular risk parameters like apoA1 and apoB were significantly elevated in β-thalassemia patients
Goldfarb et al. [24]	Israel	Adults aged ≥ 20 years	67	β-thalassemia major, minor and intermedia	5	β-thalassemia patients had lower TC, HDL, and LDL compared to control subjects. Levels differences were independent of age, transfusion requirements, and splenectomy.
Gozashti et al. [25]	Iran	Adults aged ≥ 20 years	150	β-thalassemia minor	6	β-thalassemia patients had lower TC compared to control subjects. No significant change in TG
Haghpanah et al. [26]	Iran	All 16–30 years	105	β-thalassemia minor and intermedia	8	β-thalassemia patients had lower TC and LDL compared to control subjects
Hartman et al. [27]	Israel	Children & Adolescents aged < 20 years	56	β-thalassemia intermedia and major	8	β-thalassemia patients had higher TG and lower TC, HDL and LDL compared to control subjects. Lipid profile was not correlated with age, sex, hemoglobin, or ferritin levels.
Hashemieh et al. [28]	Iran	Adults mean age 37.5 ± 13.4	100	β-thalassemia minor	5	β-thalassemia patients had TC and LDL levels compared to controls. No significant differences in TG, HDL, and VLDL.
Ibrahim et al. [18]	Egypt	Adults 18–49 years	45	β-thalassemia intermedia	8	β-thalassemia patients had lower total cholesterol, HDL, and LDL with higher TG levels compared to the control.
Jabbar et al. [29]	Iraq	Children 6 to 16 years	79	β-thalassemia major	7	β-thalassemia patients had higher TG and lower TC, HDL and LDL compared to control subjects. Atherogenic dyslipidemia (defined as a high LDL/HDL ratio and high TG level) is common among pediatric β-thalassemia patients, it is associated with iron overload and places patients at an increased cardiovascular risk.
Keşkek et al. [30]	Turkey	Adults 35.4 ± 10.1 years	87	β-thalassemia minor	9	β-thalassemia patients had higher TG compared to control subjects and it was associated with sexual dysfunctions index.
Khubchandani et al. (2014)	India	All 9 to 24 years	50	β-thalassemia major	7	β-thalassemia patients had lower TC, HDL, and LDL with higher TG levels compared to the control.
Kirim et al. [32]	Turkey	Adults Mean age 42.2 ± 13.1 years	92	β-thalassemia minor	10	β-thalassemia patients had lower HDL and LDL with higher TG levels compared to the control. 54 patients had low HDL and 25 patients had high triglycerides. Significant correlation between HbA2 and HDL. No association was found between β-thalassemia minor and metabolic syndrome

Table 1 (continued)

Study	Country	Age group	No. of Patients	Type of thalassemia	Quality assessment	Main findings
Madani et al. [33]	Iran	Children & young adults Mean age 12.92 ± 6.06	103	β-thalassemia major	7	β-thalassemia patients had lower HDL and LDL with higher TG levels compared to the control. LDL level was higher in patients with splenectomy
Maioli et al. [34]	Italy	Adults 20.9 ± 3.5 years	70	β-thalassemia major	6	B-thalassemia patients had lower TC, LDL, HDL, apo A-I and apo-B and higher Apo B: LDL-C ratio
Saki et al. [35]	Iran	Adults 23.7 ± 5.9 years	100	β-thalassemia major	6	B-thalassemia patients had higher TG and lower TC, HDL, LDL than control groups
Setoodeh et al. [36]	Iran	All 9–32 years	48	β-thalassemia major	8	B-thalassemia patients had lower TC, HDL, LDL but higher TG than control group
Tantawi et al. [37]	Egypt	All 12–35 years	30	β-thalassemia major	9	B-thalassemia patients had higher TG and TC and lower HDL than control groups. TC was correlated with carotid intima thickness in patients.

were four studies with explicit data to calculate the SMD of LDL and HDL estimates. The analysis revealed that there was no significant variance regarding both of LDL and HDL. The pooled SMD of LDL and HDL were −0.311 (95% CI, −0.884 to 0.263; P=.289) and −0.143 (95% CI, -0.622 to 0.335; P=.556), respectively (Fig. 4).

Publication bias analyses and GRADE assessment

Potential publication bias was assessed by examining funnel plots (Supplementary Files 1–3, Figs. S1-S3) and conducting Begg's and Egger's tests (Table 2). The publication bias tests were significant mainly for results of the beta-thalassemia major analyses. To further investigate and adjust for any potentially missing articles, the Duval and Tweedie trim-and-fill analysis was utilized. However, this method did not detect any absent studies, indicating that the adjusted estimates remain consistent with the original findings across all analyses.

The quality of evidence in the GRADE assessment was judged to be low for all results related to dyslipidemia in patients with beta-thalassemia major and moderate for most results of dyslipidemia among patients with beta-thalassemia intermedia. Regarding beta-thalassemia minor, the evidence quality was assessed as moderate for the results of TC and TG and low for the results of LDL and HDL. The most common reasons for downgrading the certainty of evidence were inconsistency across included studies and publication bias. The summary of the GRADE evidence profile is presented in Supplementary File 4, Table S1.

Discussion

This systematic review revealed noteworthy alterations in the markers of lipid profiles of patients with beta-thalassemia. These alterations were observed consistently across beta-thalassemia major and intermedia, with low serum levels of TC, HDL, and LDL levels and high serum levels of TG. Likewise, this pattern of dyslipidemia (low TC, LDL, HDL, and high TG) was reported among patients with sickle cell disease [37–40].

The exact pathogenesis of hypertriglyceridemia and hypocholesterolemia in beta-thalassemia population is not fully understood. However, there are several characteristics of the disease that could contribute to the pathogenesis, such as oxidative stress and liver damage secondary to excessive iron overload in beta-thalassemia, as well as insulin resistance that can disrupts the normal regulation of fat metabolism [35, 41]. The association between ferritin and both hypertriglyceridemia and low HDL cholesterol was described by large, nationwide surveys on the general population from the United States and South Korea [42, 43].

Hypocholesterolemia in beta-thalassemia patients can arise from multiple factors: the high cholesterol

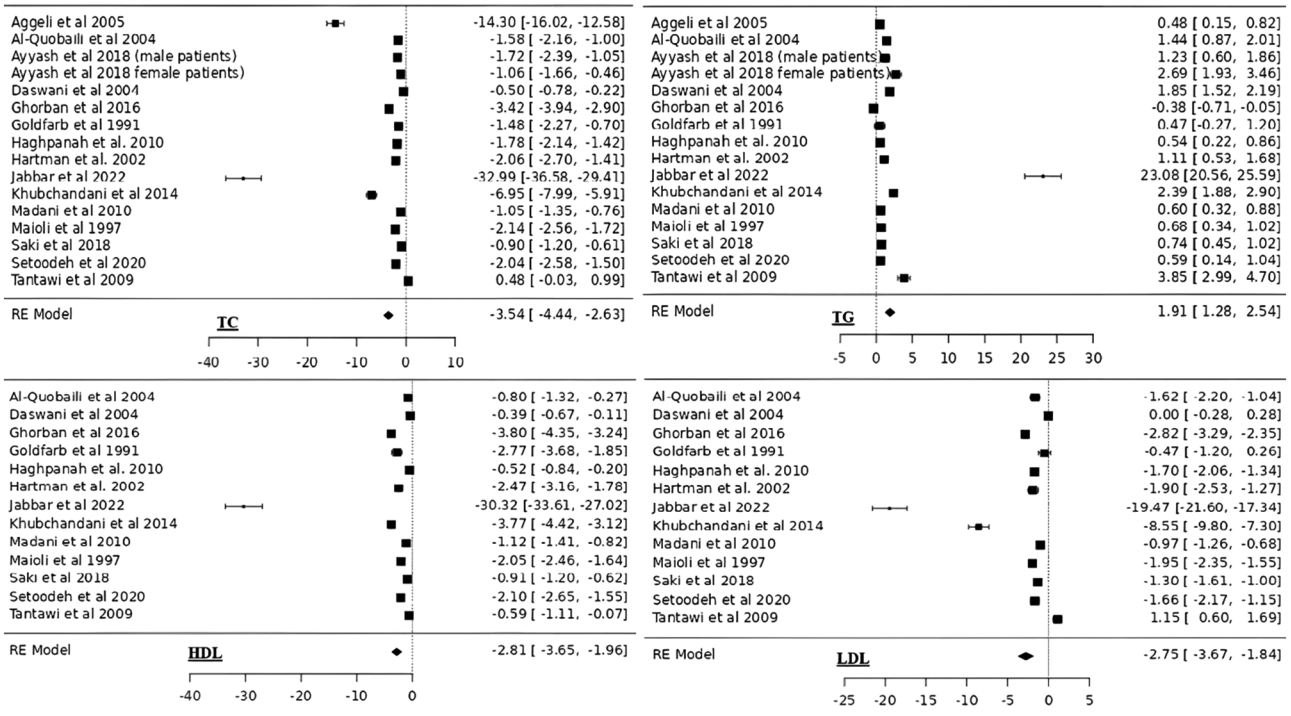

Fig. 2 Forest plot illustrating pooled SMD estimates for the analyses of beta-thalassemia major

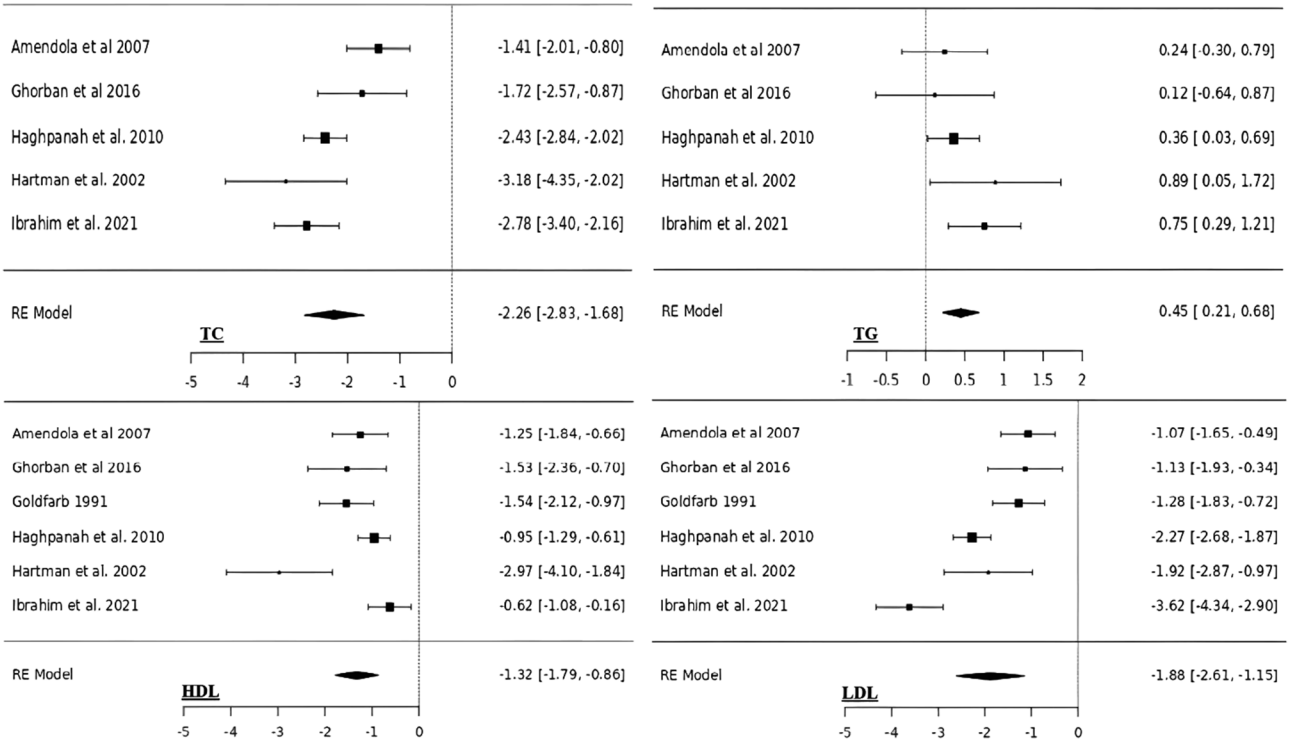

Fig. 3 Forest plot illustrating pooled SMD estimates for the analyses of beta-thalassemia intermedia

requirement due to active or amplified erythropoiesis to counteract lower survival of red blood cells or increased hemolysis; iron overload leading to decreased hepatic biosynthesis of cholesterol; plasma dilution due to anemia; and macrophage system stimulation with cytokine release which affect cholesterol synthesis [18, 19, 40, 44]. Moreover, some studies have showed that beta-thalassemia trait had a modifying and cholesterol-lowering

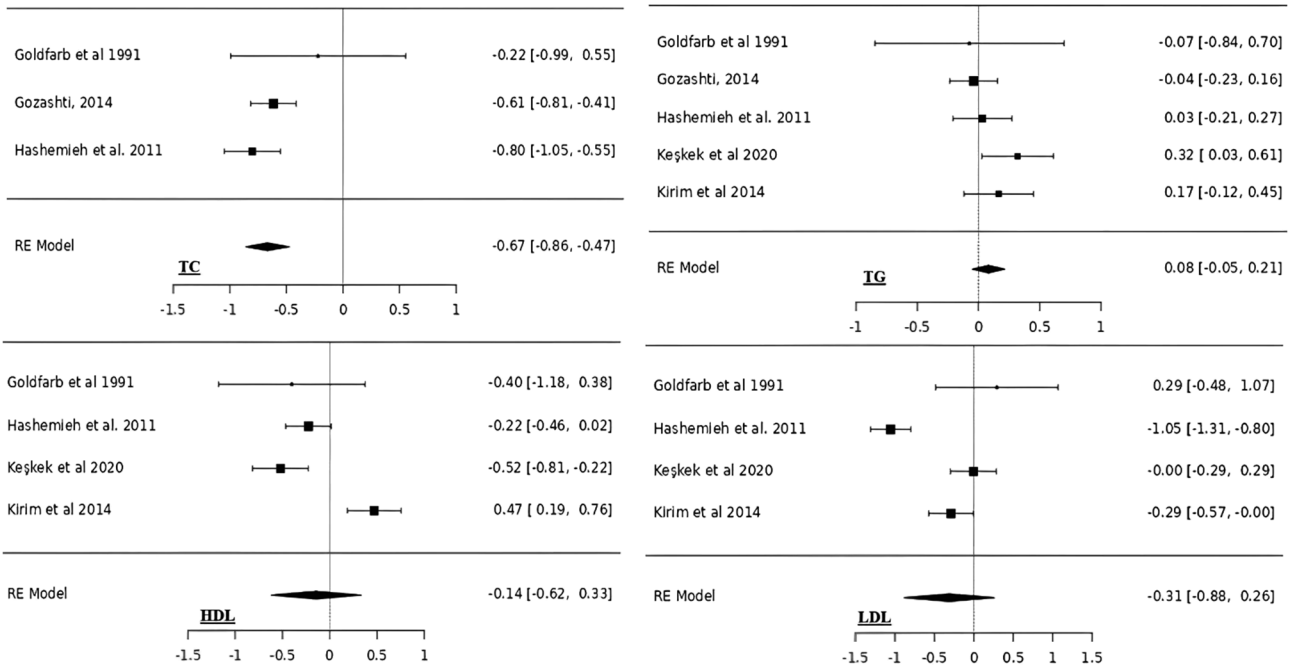

Fig. 4 Forest plot illustrating pooled SMD estimates for the analyses of beta-thalassemia minor

Table 2 Results of publication bias and heterogeneity

Population	Outcomes	Begg's test (*P*-value)	Egger's test (*P*-value)	Isquared test (%)
beta-thalassemia major	TC	0.011	< 0.001	98.17%
	TG	0.011	< 0.001	97.07%
	LDL	0.004	< 0.001	98.13%
	HDL	0.076	< 0.001	97.84%
beta-thalassemia intermedia	TC	0.817	0.597	73.19%
	TG	0.817	0.825	7.19%
	LDL	1.00	0.938	87.95%
	HDL	0.136	0.001	73.83%
beta-thalassemia minor	TC	0.330	1.00	25.19%
	TG	0.233	0.830	13.97%
	LDL	0.660	1.00	91.55%
	HDL	0.249	0.333	87.88%

effect among people with familial hypercholesterolemia [44, 45].

A few of the included studies investigated lipid profile abnormalities and their correlation with potential moderating factors. Most of them found that the altered lipid profile indicators in patients with beta-thalassemia were not depending on factors like age, sex, or ferritin levels [20, 22, 24, 27]. In addition, the relationship between lipid profiles and clinical manifestations or hematological parameters of erythropoietic activity, such as reticulocyte counts and hemoglobin levels, was not assessed by most of the included studies. However, a 2006–2018 nationwide population-based study from South Korea found that co-morbidities, including dyslipidemia, were significantly linked with the frequency of blood transfusion in beta-thalassemia patients [3]. On the other hand, studies conducted on patients with sickle cell disease did assess these clinical manifestations. These studies reported a correlation between extent of the lipid profile abnormalities and many of the clinical manifestations constituting a more severe course of the disease [37, 38, 40].

Previous studies found a high risk of cardiovascular complications, including atherosclerosis and heart failure, among individuals living with beta-thalassemia [36, 46, 47]. The finding of low cholesterol profiles in thalassemia patients suggests that the underlying mechanisms for their atherosclerosis and cardiovascular risk extend beyond the conventional understanding of cholesterol's role and point to the possibility of additional explanatory factors that may contribute to the elevated cardiovascular risk observed in this disorder.

However, the dyslipidemic profile of hypertriglyceridemia and low HDL levels found in this meta-analysis could contribute to the cardiovascular risk [35, 48]. Moreover, a few of the reviewed studies described pro-atherogenic biochemical phenotypes in patients with beta-thalassemia [22, 29, 35]. These studies and other studies indicate that atherogenic indexes, like the Castelli's risk indexes I (TC/HDL) & II (LDL/HDL), atherogenic index of plasma [log(TG/ HDL)], TC: HDL ratio, and atherogenic coefficient (AC) [(TC - HDL)/HDL], were significantly raised in beta-thalassemia patients, explaining

the high cardiovascular risk [48]. In addition, findings of Aggeli et al. of higher sVCAM-1, sICAM-1, and IL-6 levels are suggesting potential involvement of inflammation and endothelial dysfunction [17].

Strengths and limitations

The present systematic review has several strength points. One key strength is the inclusion and separate analysis of all beta-thalassemia subtypes—major, intermedia, and minor. By examining each subtype individually, this systematic review provides detailed insights into the lipid profile characteristics associated with each form of beta-thalassemia. Despite the initial detection of potential publication bias in some analyses, the application of the Duval and Tweedie trim-and-fill method did not detect missing articles, which strengthens the reliability of the results. Additionally, the application of the GRADE framework offered a structured and transparent evaluation of the certainty of evidence, adding credibility to the conclusions drawn from the findings.

Nevertheless, few limitations of this systematic review should be acknowledged. Firstly, the heterogeneity of the studies and the limitations in the available data restrict the ability to conduct further meta-analyses to explore additional aspects of dyslipidemia beyond estimating overall differences. Limited data were available regarding the clinical consequences of abnormal lipid metabolism among patients with beta-thalassemia. Most studies did not assess the impact of moderating factors influencing lipid profile abnormalities, such as disease severity, transfusion regimens, or chelation therapy, representing a knowledge gap that necessitates further research. The search primarily focused on basic lipid profile indices, excluding novel lipid indices such as small dense LDL, apolipoprotein B, and lipoprotein(a). Additionally, the omission of grey literature and the inclusion of only English-language studies could limit the overall representativeness of the findings.

Conclusion

There is evidence indicates noteworthy variations in lipid profile markers among patients with beta-thalassemia. This systematic review demonstrates that both patients with beta-thalassemia major and those with beta-thalassemia intermedia exhibit increased TG levels and decreased HDL levels compared to healthy individuals. The findings highlight the importance assessing hypertriglyceridemia and hypocholesterolemia in these patients, especially those with major and intermedia forms, particularly those with major and intermedia forms, as these abnormalities increase the risk of cardiovascular disease.

Abbreviations

TG Triglyceride
TC Total cholesterol
HDL High density lipoprotein
LDL Low density lipoprotein

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-024-02377-6.

Supplementary Material 1: Figure S1. Funnel plots illustrate the assessment of publication bias for the results of beta-thalassemia major.

Supplementary Material 2: Figure S2. Funnel plots illustrate the assessment of publication bias for the results of beta-thalassemia intermedia.

Supplementary Material 3: Figure S3. Funnel plots illustrate the assessment of publication bias for the results of beta-thalassemia minor.

Supplementary Material 4: Table S1: Detailed assessment of certainty of evidence for each outcome.

Supplementary Material 5

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Author contributions

SM conceptualized the research idea. SM, MS, and KS undertook database searches and articles screening. AEM, ASA, MAA, MGA, AGA and GAA undertook quality assessment and data extraction. SM undertook data analysis. SM, HF and NS interpreted the results and drafted the manuscript. All authors revised, edited and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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