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REVIEW ARTICLE

Prevalence of thalassemia in Saudi Arabia: a systematic review and meta-analysis

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ABSTRACT

Thalassemia, an inherited blood disorder, remains a significant public health concern in Saudi Arabia, largely due to the high prevalence of consanguinity. This systematic review and meta-analysis aimed to estimate the prevalence of thalassemia across the country and evaluate regional variations. Following Preferred Reporting Items, for Systematic Reviews and Meta-Analyses guidelines, databases including PubMed and Scopus were searched, and 10 studies were included in the final analysis. The overall pooled prevalence of thalassemia was 0.7%, with an adjusted estimate of 0.62% after excluding outliers, reflecting a slightly lower rate. The highest prevalence was recorded in the Eastern and Jazan provinces, regions with the highest rates of consanguineous marriages. Variations in thalassemia prevalence were observed between adult and pediatric populations, though pediatric data were limited. The Premarital Screening and Genetic Counseling program, introduced to reduce the incidence of genetic disorders like thalassemia, had a positive impact, yet thalassemia remains common, particularly in high-risk regions. Despite the program's implementation, some couples proceed with high-risk marriages due to familial or societal pressures, indicating the need for broader public health interventions. This study highlighted the ongoing challenges in combating thalassemia in Saudi Arabia and underscored the importance of enhancing genetic counseling, expanding awareness campaigns, and improving access to preventative services. These efforts are critical to reducing the burden of thalassemia and improving public health outcomes across the country, particularly in regions with high consanguinity rates.

Keywords: Thalassemia, Saudi Arabia, prevalence, consanguinity, genetic counseling.

Introduction

Thalassemia is a major global public health issue, especially prevalent in regions with high rates of consanguineous marriages and specific ethnic populations [1]. This hereditary blood disorder is marked by impaired hemoglobin synthesis, leading to anemia, and in severe instances, might result in life-threatening complications including organ failure and mortality.

Globally, around 56,000 children are born each year with a severe form of thalassemia, of which β-thalassemia contributes the largest burden [2]. Thalassemia is particularly common in the Mediterranean, Southeast Asia, the Indian subcontinent, and the Middle East [3]. Within these regions, Saudi Arabia has emerged as one of the countries with a particularly high prevalence of both α- and β-thalassemia, partly attributed to the cultural practice of consanguineous marriages, which increases the likelihood of recessive genetic disorders such as thalassemia being passed to offspring [4].

Thalassemia is broadly categorized into two main types. The α-thalassemia and β-thalassemia, depending on whether the α or β hemoglobin chains are affected. β-thalassemia, which includes both β-thalassemia minor (trait) and β-thalassemia major (disease), has garnered

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more attention due to its severe clinical manifestations [5]. Patients with β-thalassemia major have persistent anemia, require continuous blood transfusions, and face risks of consequences including iron excess, bone abnormalities, and cardiac failure [6]. In Saudi Arabia, recent studies showed that the prevalence of β-thalassemia traits ranges between 1.8% and 3.2% in various regions [7], with the highest prevalence observed in the Eastern and Southwestern provinces, where consanguineous marriages are most common [8].

The Premarital Screening and Genetic Counseling (PMSGC) program, which was established in 2004 and requires genetic testing for hemoglobinopathies, including thalassemia, for couples planning marriage, is one of the major actions Saudi Arabia has taken to lower the prevalence of genetic disorders. The program aimed to provide couples with informed choices, reduce high-risk marriages, and ultimately decrease the prevalence of thalassemia [9].

However, despite these efforts, the disease remains a significant health challenge. A review of data from the PMSGC program revealed that from 2011 to 2018, approximately 1.2% of individuals screened were carriers of β-thalassemia, with significant regional variations. The highest carrier rates were found in the Jazan and Eastern provinces, highlighting the need for more targeted interventions in these areas [8].

The burden of thalassemia is not only clinical but also pension physical and social. The management of patients who suffer from thalassemia and need regular blood transfusions and iron chelation therapy puts a huge burden on the healthcare systems. For example, it is believed that the lifetime cost of treating a patient with β-thalassemia major can be anywhere from £188,000 to £226,000, not including the indirect costs related to the reduced quality of life and lost productivity [10]. Moreover, patients often face social stigma, and their families bear the emotional and financial burdens associated with long-term care. In Saudi Arabia, where family structures are traditionally large and closely knit, the impact of a genetic disorder like thalassemia can be profound, affecting not just the patient but the entire family network [11].

The persistence of thalassemia in Saudi Arabia, despite the introduction of premarital screening programs, underscores the need for more robust public health strategies. While premarital screening has proven effective in identifying carriers and preventing high-risk marriages, studies showed that the uptake of genetic counseling remained low, particularly in rural areas. In some cases, couples who were identified as carriers proceed with the marriage despite the risk, due to social and familial pressures [11]. This suggested that while the PMSGC program is a crucial first step, it must be supplemented with more comprehensive public health initiatives, including enhanced public education campaigns and increased access to genetic counseling, particularly in high-risk regions.

Faced with such challenges, the systematic review and meta-analysis at hand were set to furnish a piece of updated information about the prevalence of thalassemia in Saudi Arabia. By condensing the data of many studies, this review would give information on the local distribution of thalassemia and would discover the trends over time. The results of this review would help in the continuous struggle to check the spread of thalassemia in Saudi Arabia by making public health strategies and directing future research on genetic screening and prevention programs.

Materials and Methods

This comprehensive systematic review and meta-analysis followed the guidelines outlined in the Preferred Reporting Items, for Systematic Reviews and Meta-Analyses (PRISMA) [12], with all procedures carried out in accordance, with the Cochrane Handbook [13].

Literature search strategy

A comprehensive search was performed across three major electronic databases including PubMed, Web of Science, and Scopus. The search covered studies published up to 2024 and utilized a combination of keywords, including "Thalassemia," "Prevalence," and "Saudi Arabia." No restrictions were placed on the study design, and only articles published in English were included.

Eligibility criteria

The studies included in this review focused on the epidemiological profile of thalassemia, covering aspects such as frequency, prevalence, risk factors, mortality rates, and complications. Additionally, observational studies involving populations diagnosed with thalassemia in Saudi Arabia were considered.

However, laboratory diagnostic tests, animal and experimental research, studies conducted outside of Saudi Arabia, review articles, case reports and case series, conference proceedings, and editorials were excluded from this analysis. Studies that did not align with the objectives of the review or failed to provide the necessary information to understand the epidemiological profile of thalassemia were also omitted.

Study selection and data extraction

The study selection process was carried out in three steps including finding, sorting, and checking the eligibility. The duplicate records were removed during the identification phase. The study focus was screened by the titles and abstracts of the rest of the records to exclude those irrelevant. In the end, full-text articles were checked for eligibility based on the set inclusion and exclusion criteria. Only those studies that presented thalassemia prevalence data from Saudi Arabia were included. The articles were excluded if they did not concentrate on thalassemia, were insufficient with the

data on prevalence, and were not by the study's quality standards (Figure 1).

Assessment of risk of bias

The Newcastle-Ottawa Quality Assessment Scale (NOQAS), which was originally just for cohort studies, was used to evaluate the quality of the studies retrieved [14]. Thus, the modified version of NOQAS specifically designed for cross-sectional studies was used [15]. The NOQAS score of 7 was established as the threshold for a high-quality study methodology, while a score of 5-6 was considered moderate quality. Two reviewers who were not affiliated with the study performed the quality assessment.

Data extraction

Data from the studies included in the review was independently extracted and verified. The extracted data included the following domains: the first author's name, year, and location of publication, study period, study design, characteristics of the participants, sample size, region within Saudi Arabia, and the primary outcome measures (frequency and prevalence).

Statistical analysis

Statistical data were processed for analyses using Python (version 3.9) and R (version 4.1.0). "Meta" R package was utilized to conduct meta-analysis. The estimation of relative heterogeneity among the studies led to the usage

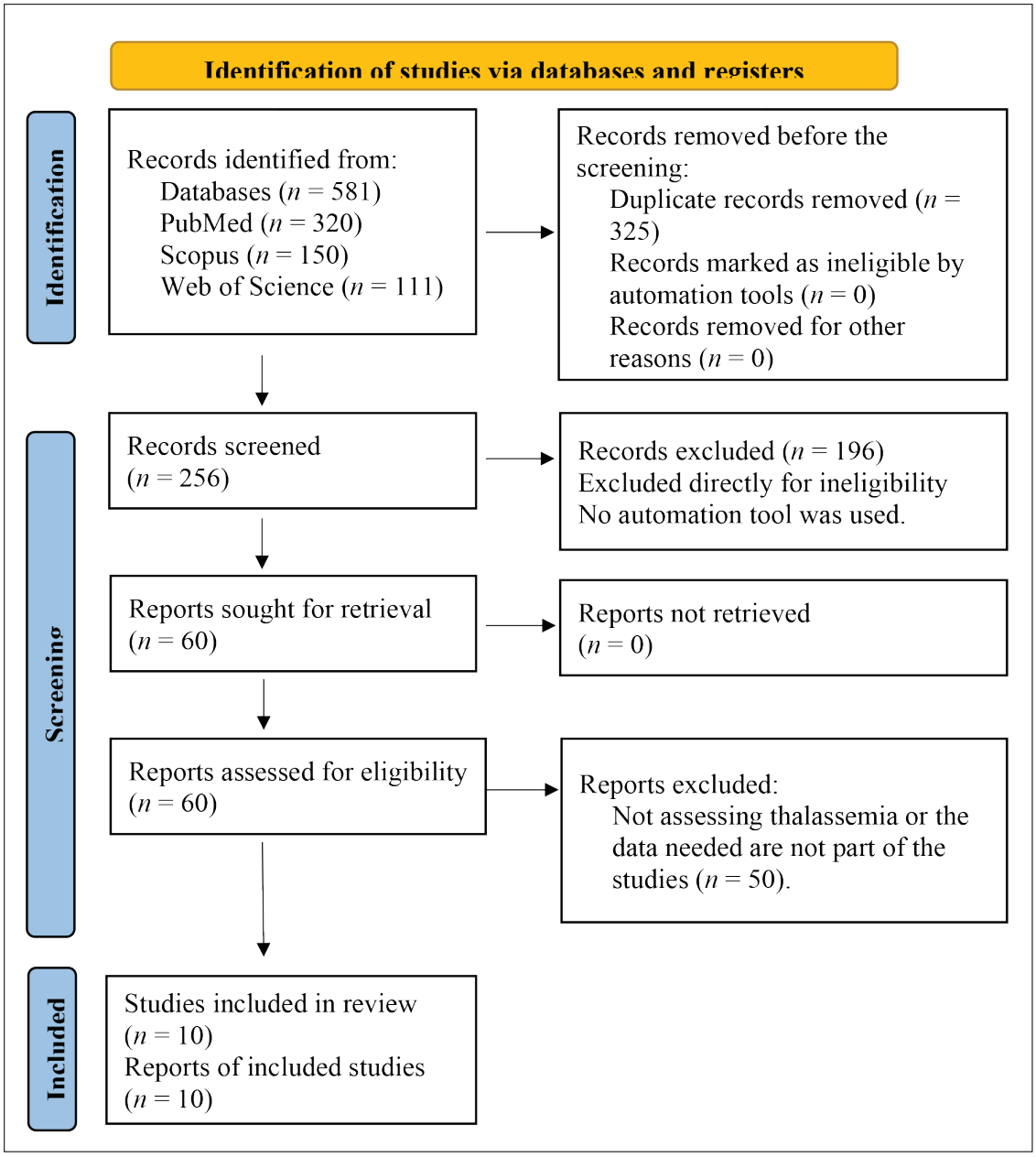

Figure 1. *Flowchart illustrates the article screening and selection process for studies.*

of a random effects model for the computation of pooled prevalence estimates. I^2 statistics were used to assess the degree of heterogeneity, where a value of 25% indicates low, 50% indicates moderate, and 75% indicates high heterogeneity, respectively.

Forest plots were generated to illustrate the prevalence estimates and their 95% confidence intervals for each study of the pooled estimate, as well as the pooled estimate. The study whose impact was the greatest among all was left out for sensitivity analysis to see how the pooled prevalence estimate would change. A Baujat plot was generated to identify the studies that were the leading contributors to the heterogeneity and the overall results. All figures were made with Python's Matplotlib and Seaborn libraries, including the PRISMA flow diagram, the forest plots, and the Baujat plot. A significance level of $p < 0.05$ was used for all analyses.

Results

Study selection and characteristics

The systematic review consisted of 581 records from different bibliographic databases, including PubMed (n = 320), Scopus (n = 150), and the Web of Science (n = 111). After dropping 325 duplicates, 256 records were screened for inclusion. A total of 196 records were excluded during the title and abstract screening, thus, the remaining 60 full-text articles were reviewed further. Among these, 50 were excluded because thalassemia was not addressed; thereby, 10 studies were included in this meta-analysis [7,8,16-23] (Figure 2).

The design of the studies included in the analysis was heterogeneous, as they were cross-sectional and retrospective in nature. The trials were carried out in various regions in Saudi Arabia, with sample sizes ranging from 329 to more than 1.8 million participants. Diagnostic techniques differed and included the following. Hemoglobin Electrophoresis, High-performance liquid chromatography (HPLC), and Agar Gel Electrophoresis. The two studies did not mention the diagnostic method used. The length of the study period was from 10 months to 10 years, with most of the studies lasting between 3 and 7 years (Table 1).

Thalassemia prevalence and population characteristics

The overall pooled prevalence of thalassemia across the studies included was estimated at 0.7% (95% CI: 0.77%-0.78%). After performing subgroup analysis and excluding the outlier study by Nasserullah et al. [16], which reported a significantly higher prevalence, the adjusted prevalence was 0.62% (95% CI: 0.62%-0.63%) [16]. This refined analysis provided a more accurate reflection of the thalassemia prevalence among the adult population in Saudi Arabia.

Most studies focused on adult populations, with only one study including children under 5 years old. Variations in prevalence rates were noted across regions and study designs, highlighting differences in β-Thalassemia and α-Thalassemia prevalence rates among the population (Table 2).

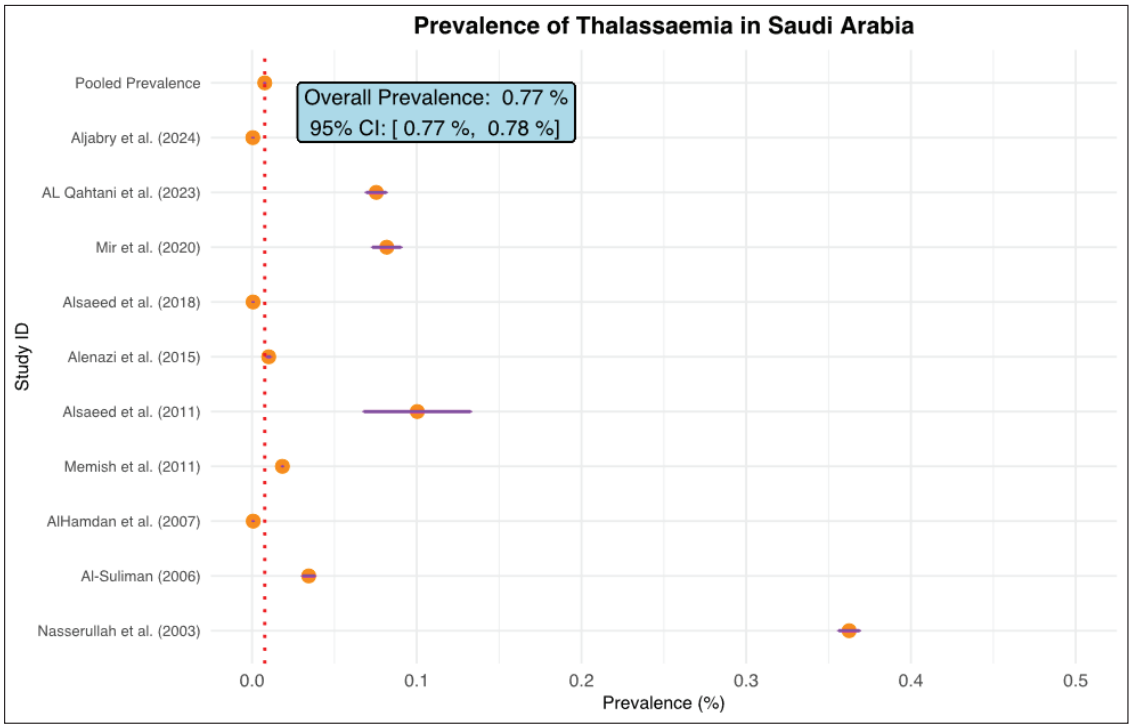

Figure 2. *Forest plot of thalassemia prevalence across screened studies in Saudi Arabia.*

Table 1. *Characteristics of Thalassemia studies: population, study design, and diagnostic techniques in Saudi Arabia.*

Study ID	Study design	Sample size	Age	Diagnostic test	Study period	Location of study (Region/City)
Memish and Saeedi [7]	Cross-sectional study	1572140	N/A	Hemoglobin electrophoresis	6 years	Across Saudi Arabia
Alsaeed et al. [8]	Cross-sectional study	1230582	Range: 13-112 years for female. Range: 17-105 years for males.	HPLC	5 years	Across Saudi Arabia
Nasserullah et al. [16]	Cross-sectional study	21858	N/A	Agar Gel electrophoresis	9 years	Qatif
Mir et al. [17]	Retrospective Study	3755	Range: From 20 to 55 years.	HPLC	3 years	Al Majma'ah
Alsaeed [18]	Cross-sectional study	329	Mean (SD): 39 (6.4)	Hemoglobin electrophoresis	5 years	Um alhammam, Riyadh
AlHamdan et al. [19]	Cross-sectional study	488315	N/A	Hemoglobin electrophoresis	2 years	Across 13 administrative regions in Saudi Arabia
Alenazi el al. [20]	Retrospective study	23522	N/A	N/A	6 years	Northern Border Region
Aljabry et al. [21]	Retrospective study	1871184	Mean (SD): 30.2 (8.0)	Hemoglobin electrophoresis	7 years	Across 13 administrative regions in Saudi Arabia
Al-Suliman [22]	Retrospective study	8918	N/A	Hemoglobin electrophoresis	10 months	Al-Hassa
AL Qahtani et al. [23]	Retrospective study	7054	Mean (SD): 33.82 (12.61)	N/A	4 years	Riyadh

*High-performance liquid chromatography (HPLC).

Table 2. *Reported Thalassemia prevalence and population characteristics across studies in Saudi Arabia.*

Study ID	Study design	Sample size	Disease type	Children below 5 years	Children above 5 years	Adults	Prevalence
Memish and Saeedi [7]	Cross-sectional study	1572140	β-Thalassemia	No	No	Yes	1.8%
Alsaeed et al. [8]	Cross-sectional study	1230582	β-Thalassemia	No	Yes	Yes	0.1%
Nasserullah et al. [16]	Cross-sectional study	21858	α-Thalassemia	Yes	No	No	36.2%
Mir et al. [17]	Retrospective study	3755	β-Thalassemia	No	No	Yes	8.2%
Alsaeed [18]	Cross-sectional study	329	β-Thalassemia	No	No	Yes	10.0%
AlHamdan et al. [19]	Cross-sectional study	488315	β-Thalassemia	No	No	Yes	0.1%
Alenazi el al. [20]	Retrospective study	23522	β-Thalassemia	No	No	Yes	1.0%
Aljabry et al. [21]	Retrospective study	1871184	β-Thalassemia	No	No	Yes	0.05%
Al-Suliman [22]	Retrospective study	8918	β-Thalassemia	No	No	Yes	3.4%
Alqahtani et al. [23]	Retrospective study	7054	β-Thalassemia and α-Thalassemia	No	Yes	Yes	7.5%

Heterogeneity and subgroup analysis

The Baujat Plot revealed high heterogeneity among studies, indicating considerable variability in prevalence estimates (Figure 3).

Sensitivity analysis and subgroup testing, which involved excluding the Nasserullah et al. [16] study as an outlier, helped reduce heterogeneity. The resulting subgroup analysis reflected a more consistent prevalence estimate of 0.62% for β-Thalassemia in the adult population (Figure 4).

Quality assessment

The ratings for quality assessment were from 6 to 8 points out of a possible 9 points, and the majority of the studies were rated very high. These studies normally had a good choice of participants and good outcome assessments. Moderate-quality studies noticed that they had issues regarding group comparability (Table 3).

Discussion

This systematic review and meta-analysis yield a new and complete report of the prevalence of thalassemia diseases in Saudi Arabia, which included measurements of both types of thalassemia. The pooled prevalence of thalassemia, according to the pooled studies, was found to be 0.7% (this was further adjusted for heterogeneity to give an estimate of 0.62%).

The highest rates were noted in the Eastern and Jazan provinces, both of which have elevated rates of consanguineous marriages, a well-documented risk factor for recessive genetic disorders like thalassemia [8]. This regional variation mirrors findings from Southeast Asia, where countries like Malaysia and Thailand exhibited high prevalence rates in specific regions, such as northern Borneo and northeastern Thailand, due to similar genetic and social factors [24,25]. In Saudi Arabia, as in these Southeast Asian countries, consanguineous marriages increase the likelihood of both α- and β-thalassemia being passed down to offspring [11].

This variability also extends to population groups. Most of the studies in Saudi Arabia focused on adult populations, leaving a gap in data for pediatric populations. The limited research on children, particularly those under 5 years, calls for additional studies to better understand the early-onset and pediatric burden of thalassemia. Similarly, countries like China and Laos also report regional and age-based disparities in thalassemia prevalence, further supporting the need for region-specific public health strategies [26-29]. For example, the Guizhou and Jiangxi provinces in China showed thalassemia prevalence rates of 12.9% and 14.5%, respectively, with variations between α- and β-thalassemia [27,28].

The differences in prevalence between adults and children in Saudi Arabia suggested the need for age-targeted interventions. In regions where consanguineous marriages are common, screening programs focusing on younger populations could offer more timely intervention. For instance, in Thailand, neonatal screening programs have proven effective in reducing the severity of thalassemia cases, highlighting the importance of early detection [24]. Therefore, understanding pediatric prevalence in

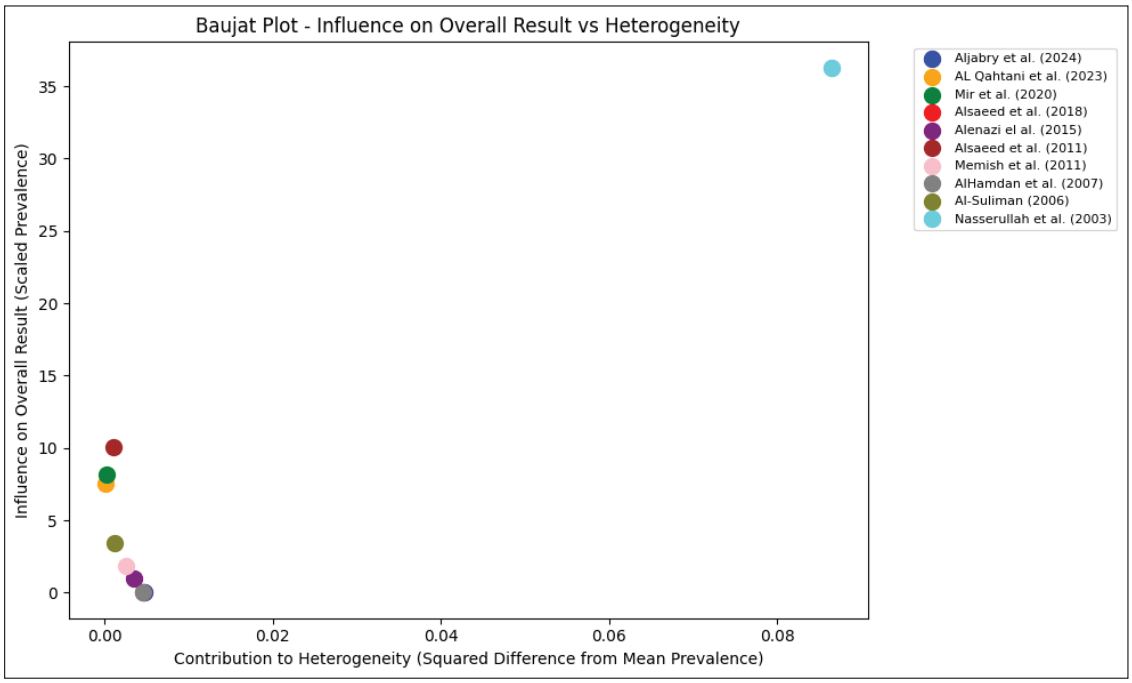

Figure 3. *Baujat plot: contribution of studies to heterogeneity.*

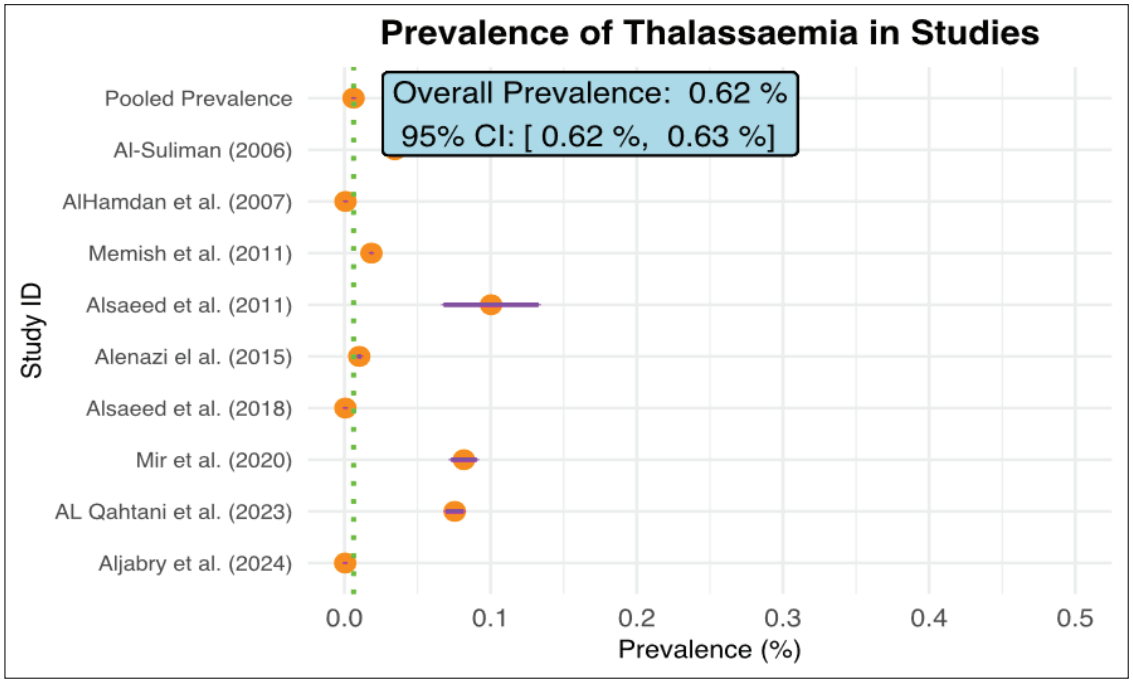

Figure 4. *Forest plot of Thalassemia prevalence across screened studies in Saudi Arabia. (After excluding outliers).*

Table 3. *Quality assessment of the included studies.*

Study ID	Participant selection (Max. 4 points)	Group comparability (Max. 2 points)	Assessment of exposure/outcome (Max. 3 points)	Cumulative score (Max. 9 points)	Quality rating
Memish and Saeedi [7]	4	2	2	8	High quality
Alsaeed et al. [8]	4	2	2	8	High quality
Nasserullah et al. [16]	4	2	2	8	High quality
Mir et al. [17]	3	2	2	7	High quality
Alsaeed [18]	3	1	2	6	Moderate quality
AlHamdan et al. [19]	4	2	2	8	High quality
Alenazi el al. [20]	3	1	2	6	Moderate quality
Aljabry et al. [21]	4	2	2	8	High quality
Al-Suliman [22]	3	1	2	6	Moderate quality
AL Qahtani et al. [23]	3	2	2	7	High quality

Saudi Arabia is essential to designing interventions that mitigate the long-term burden on the healthcare system.

In 2004, the introduction of the program PMSGC dedicated to premarital counseling and genetic screening in Saudi Arabia became a health sector-driving project aimed at reducing the rate of thalassemia and other genetic disorders [30]. Even though the PMSGC is successful in identifying the carriers, the existence of considerable thalassemia carrier rates, especially in regions with a high consanguinity rate, showed that the program is not enough to reduce and control the disease. This reflects the scenario in other countries that have similar screening programs. Countries like Cyprus, Turkey, and Greece have also come up with some robust premarital screening initiatives, which, along with public awareness campaigns, have successfully reduced the incidence of thalassemia [31-33].

However, the persistence of thalassemia in Saudi Arabia, as seen in this meta-analysis, can be attributed to several factors. Social and familial pressures often result in couples proceeding with marriages despite the known genetic risks [34]. This phenomenon is not unique to Saudi Arabia. Similar challenges have been documented in countries like Jordan and the UAE, where cultural norms sometimes override medical recommendations, leading to the continuation of at-risk marriages [35]. In contrast, countries with strong community engagement and educational campaigns, like Cyprus, have shown that

increased public awareness significantly improves the effectiveness of premarital screening [31].

Moreover, while the PMSGC program provides genetic screening, the uptake of genetic counseling remains low, particularly in rural areas [36]. This gap underscores the importance of expanding access to genetic counseling services, which are essential for helping couples make informed decisions. In Bangladesh, for instance, studies have demonstrated that proper awareness and access to counseling can substantially reduce the incidence of thalassemia in high-risk communities [31]. Therefore, enhancing genetic counseling services in Saudi Arabia could further improve the effectiveness of the PMSGC program, particularly in regions with high prevalence [37].

The findings from this review highlighted key public health implications for Saudi Arabia. First, interventions must go beyond premarital screening to include broader public education campaigns that address consanguineous marriages, improve genetic literacy, and increase access to genetic counseling. Similar approaches in Southeast Asia have successfully reduced severe thalassemia cases [38]. Second, the regional variability in prevalence suggested that tailored, region-specific strategies are more effective than a one-size-fits-all approach. Saudi Arabia could focus on high-risk areas like the Eastern and Southwestern provinces. Finally, further research is needed to assess the long-term outcomes of carriers, as seen in countries like Cyprus and Greece, where regular follow-up and counseling have reduced severe cases [39,40]. Understanding the effectiveness of the PMSGC program and exploring carrier behaviors could provide valuable insights for improving its impact.

This study had several limitations that must be highlighted. The heterogeneity among the studies included, as demonstrated by the I^2 statistics, suggested diversity in research design, diagnostic methods, and population characteristics. While sensitivity analyses reduced heterogeneity, it is the case that this variability might still affect the generalizability of the findings. In addition to this, one potential cause could be the exclusion of bibliographies in non-English languages, albeit this limitation seems minor as most thalassemia research published in Saudi Arabia is in English. The issue of scarce data regarding young patients and certain types of thalassemia (like α-thalassemia) is the last factor that could restrict the relevance of these results to all demographic groups.

Conclusion

Thalassemia initialized a grave public health problem for Saudi Arabia, especially in a certain region with high consanguinity rates. Nevertheless, PMSGC's success showed that there are still thalassemia problems that need more thorough solutions. Public health typologies should contain educational campaigns, access to genetic counseling, and region-specific approaches aimed at high-risk areas. Ongoing research on the effectiveness of the program in a long-term care facility and the long-term outcome of the carrier is vital in the improvement of prevention efforts and decreasing the illness of the population. There are various ways that thalassemia can be managed, and all of them are indispensable for the proper handling of thalassemia, and the enhancement of health results in Saudi Arabia.

List of abbreviations

HPLC High-performance liquid chromatography
NOQAS Newcastle–Ottawa quality assessment scale
PMSGC Premarital screening and genetic counseling
PRISMA Preferred Reporting Items for Systematic Review and Meta-Analysis

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Consent to participate
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Conflict of interest
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