Characterizing the Clinical, Health-related Quality of Life and Economic Burden of Alpha-Thalassemia: A Systematic Literature Review and Evidence Gaps Assessment

P1036

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BACKGROUND

- Thalassemia is a congenital hemolytic anemia which can lead to clinical complications.[1] It is estimated that approximately 56,000 children worldwide are born with thalassemia every year[2]
- Thalassemia is commonly classified into alpha and beta subtypes based on the affected hemoglobin (Hb) chain(s)[3]
- More is known about the burden of beta-thalassemia (β-thalassemia), but a knowledge gap exists on the burden of alpha-thalassemia (α-thalassemia) and associated subtypes

OBJECTIVE

- To conduct a systematic literature review (SLR) to characterize the clinical (complications, treatment patterns, and mortality), health-related quality of life (HRQoL), and economic burden associated with α-thalassemia, and to report on evidence gaps

METHODS

- The SLR was conducted in accordance with the methodological and reporting requirements outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[4] and the Cochrane Handbook for Systematic Reviews of Interventions.[5]

Inclusion Criteria (PICOS)

Population: Adult and pediatric patients with alpha-thalassemia

Intervention: Any/none

Comparator: Any/none

Outcomes: clinical burden*, treatment patterns, HRQoL, healthcare resource utilization, costs and economic evaluations

Study Design: Real-world and observational studies as well as economic evaluations

Searches

- Searches: January 2010 to September 2021
- Electronic databases (via Ovid.com):
  - MEDLINE
  - Embase
  - Cochrane Database of Systematic Reviews
  - HTA Database
  - NHS EED
  - EconLit
- Conference abstracts: January 2017 to September 2021
- Bibliography lists of existing SLRs were also screened

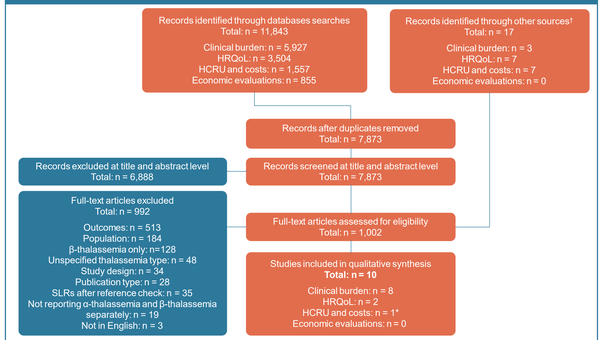
Methodology

- References screened by two independent reviewers and discrepancies resolved by a third reviewer
- Data extracted by one reviewer and validated by another

Abbreviations: HRQoL, health-related quality of life; HTA, health technology assessment; NHS EED, National Health Service Economic Evaluation Database; SLR(s), systematic literature review(s)

RESULTS

PRISMA diagram for studies reporting outcomes in α-thalassemia



*One study reported clinical burden and HCRU/cost outcomes.
†Conference websites and Health Technology Agency bodies were searched across all topics.

Ten studies reported relevant data on α-thalassemia as identified from 7,881 search hits in thalassemia.[6-15]

*One study reported clinical burden and HCRU/cost outcomes.
Abbreviations: HCRU, healthcare resource utilization; HRQoL, health-related quality of life.

All studies

- Among 10 studies that reported on HbH disease, three were in an α-thalassemia-only population,[7,9,14] and seven were in a mixed (α-thalassemia and β-thalassemia) population reporting clinical data for α-thalassemia separately (Table 1).[6,8,11-13]

Table 1. Overview of Included Studies

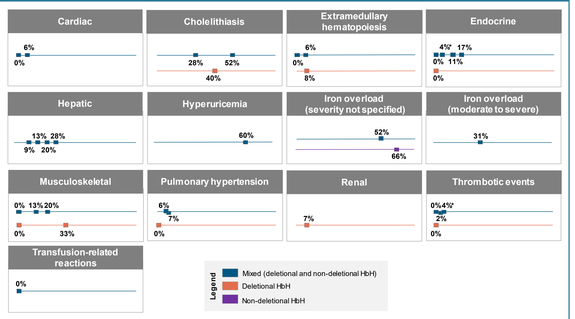
Author, Year	Outcome	Country	α-thalassemia Genotype	β-thalassemia Genotype	Transfusion Phenotype*	Age (years)	N (total)	N (α-thalassemia)
Chaloemwong 2019[6]	Clinical	Thailand	Deletional and non-deletional HbH	HbE/β-thalassemia and β-thalassemia	NTDT AND TDT	≥15	112	10
Chan 2020[7]	Clinical	Hong Kong	Deletional and non-deletional HbH	NA	NTDT	≥18	80	80
Ekwattanakit 2017[18]	Clinical	Thailand	Deletional and non-deletional HbH	HbE/β-thalassemia and β-thalassemia	NTDT	≥18	57	23
Lal 2011[9]	Clinical HCRU	United States	Deletional and non-deletional HbH	NA	Not specified	0–72	86	86
Winichakoon 2015[13]	Clinical	Thailand	Deletional and non-deletional HbH	HbE/β-thalassemia and β-thalassemia	NTDT	≥15	100	54
Zhou 2014[14]	Clinical	China	Non-deletional HbH	NA	Not specified	≥18	50	50
Ricchi 2016[11]	Clinical	Italy	Deletional HbH	β-thalassemia	NTDT	17–78	96	15
Ngim 2019[10]	Clinical	Malaysia	HbH, not further specified	HbE/β-thalassemia and β-thalassemia	NTDT AND TDT	≥18	69	2
Thavorncharoensap 2010[15]	HRQoL	Thailand	HbH, not further specified	HbE/β-thalassemia and β-thalassemia	NTDT AND TDT	5–18	315	130
Torcharus 2011[12]	HRQoL	Thailand	HbH, not further specified	HbE/β-thalassemia and β-thalassemia	TDT	2–18	49	5

*Transfusion phenotype of total study population. †With or without HbE trait.

Clinical burden

- Complication rates among patients with α-thalassemia across all studies can be seen in Figure 1.
- These studies found that HbH and/or HbH/Constant Spring (CS) demonstrated a high clinical burden, with the highest prevalence of complications including iron overload (31% to 66%, three studies[7-8,14]), hyperuricemia (60%, one study[6]), cholelithiasis (28% to 52%, three studies[8,11,13]), musculoskeletal (0% to 33%, four studies [6,8,11,13]), hepatic (9% to 28%, three studies[7-8,13]), and endocrine (0% to 17%, three studies[8,11,13]).

Figure 1. Complication Rates Among Patients with HbH Disease



*Percentages are from multiple studies.
Notes: Cardiac = cardiomyopathy, heart failure; endocrine = abnormal glucose function, adrenal insufficiency, diabetes mellitus, hypogonadism, hypothyroidism; hepatic = advanced liver fibrosis, probable cirrhosis, transaminitis; musculoskeletal = gouty arthritis, osteopenia, osteoporosis; renal = nephrolithiasis; thrombosis = leg ulcers, thrombotic event; transfusion-related reactions = serious infection

HRQoL

Two pediatric studies reported on HRQoL in patients with HbH disease:

- Pediatric patients with TD α-thalassemia and β-thalassemia had similar total and subdomains of PedsQL scores, except for physical functioning, whereby patients with homozygous β-thalassemia had higher HRQoL than those with HbH disease, and patients with HbE/β-thalassemia had the greatest HRQoL burden (p=0.008).[12]
- Another study in those with NTDT and TDT did not find differences in any PedsQL subdomain scores between patients with HbH disease, HbE/β-thalassemia, and homozygous β-thalassemia.[15]

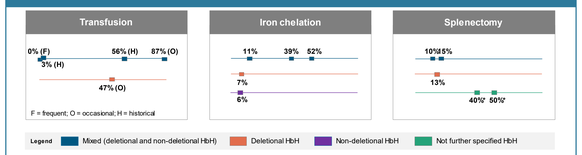
HCRU

- One study on adult and pediatric patients with deletional HbH and HbH/CS found that patients with HbH/CS had a significantly increased number of annual clinic visits, by a factor of 1.7, and hospital admissions, by a factor of 3.9, vs. those with HbH (P<0.001).[9]

Treatment Patterns

- Treatment patterns among patients with α-thalassemia across all studies can be seen in Figure 2.

Figure 2. Treatment Patterns Among Patients with HbH Disease



*TDT = 40% and NTDT = 50%; p=0.566

- Most patients with HbH and/or HbH/CS had historical (3% to 56%, two studies[7,9]), or occasional transfusion (47% to 87%, two studies[8,11]), iron chelation therapy (6% to 52%, five[7,8,13,14]), and splenectomy (10% to 15%, three[7,11,13]).
- When comparing by transfusion status, one study in unspecified HbH disease (N=50) did not find any significant difference in the rate of splenectomy between adults with TDT and NTDT (40% vs. 50.0%, respectively; p=0.566).[10]

LIMITATIONS

- There were limited data on patients with α-thalassemia, and where reported, data of interest on α-thalassemia were limited to patients with HbH disease.
- Evidence on α-thalassemia was typically limited to small subgroups, with the sample sizes ranging from two to 130 patients.[10,15]

CONCLUSIONS

- To our knowledge, this SLR was the first to investigate the clinical, HRQoL, and economic burden of α-thalassemia
- The SLR was exhaustive and searched across thalassemia to identify relevant subgroup data reported in α-thalassemia
- Complications were prevalent across a range of conditions, signaling an unmet clinical need in patients with α-thalassemia including those with HbH
- Limited data, however, were found on HRQoL, and only in children and adolescents,
  - but where reported, patients with HbH experienced similar HRQoL burden as those with β-thalassemia
- No economic evaluations were identified, and data were sparse for HCRU/costs
- This SLR highlights the need for further research to fully characterize the significant disease burden of α-thalassemia

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