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Hepatic and renal functions of paediatric patients with thalassaemia: a cross-sectional study from two large thalassaemia centres in Sri Lanka

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ABSTRACT

Objectives Thalassaemia is a genetic disorder of haemoglobin synthesis characterised by life-long chronic anaemia. Although the endocrine and cardiac complications of thalassaemia are well-studied, hepatic and renal complications are understudied. This study aims to describe the hepatic and renal functions and to understand their determinants among paediatric patients with β-thalassaemia.

Design Cross-sectional study.

Setting Two largest thalassaemia centres in Sri Lanka.

Participants All haematologically confirmed patients with β-thalassaemia aged 1–16 years attending the study sites were recruited between 1 January and 31 March 2023. Data were collected by interviewing parents and patients, performing physical examinations and perusing clinical records.

Results 72 children (girls 52.8%) were recruited. The mean age was 7.3 years (SD 3.8). A majority (44 (61.1%)) had β-thalassaemia major, while 22 (30.6%) had haemoglobin E β-thalassaemia. 55 children (76.4%) were transfusion dependent. Hepatomegaly was found in 47 (65.3%), while 28 (38.9%) had elevations of both alanine and aspartate transaminases. Haemoglobin E β-thalassaemia type (OR 13.6, 95% CI 2.0 to 92, p=0.008) and high ferritin above 1000 ng/mL (OR 6.2, 95% CI 1.0 to 38, p=0.047) were independent factors associated with high transaminases. 11 (15.5%) patients had an estimated glomerular filtration rate (eGFR) below 90 mL/min. The proportion of children with low eGFR was higher in β-thalassaemia major (23.3%), transfusion-dependent (18.5%) and deferasirox treatment (18.5%) groups.

Conclusions Elevation of hepatic transaminases is common among children with thalassaemia, especially among the subset of patients with haemoglobin E β-thalassaemia and those with high ferritin. Milder reductions in eGFR are noted in some patients with transfusion-dependent β-thalassaemia major.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study evaluates the hepatic and renal functions in a well-characterised group of children with β-thalassaemia.
⇒ This study comprehensively describes the hepatic and renal functional status among asymptomatic patients with β-thalassaemia.
⇒ Not measuring the hepatic iron overload using MRI is a limitation.
⇒ Another limitation is the relatively small number of study participants, resulting in limited statistical power.

INTRODUCTION

Thalassaemia is a disorder of haemoglobin synthesis due to autosomal recessively inherited mutations in human globin genes.[1] It is highly prevalent in the tropical belt, which extends from the Mediterranean through the Middle East to South and Southeast Asia.[2] Thalassaemia is the most common monogenic disorder in Sri Lanka, where nearly 40 new patients are diagnosed every year.[3]

The usual clinical course of β-thalassaemia starts around 6 months of age when the physiological conversion of fetal haemoglobin to adult haemoglobin occurs.[4 5] Affected children present with features like lethargy, poor feeding, failure to thrive, severe pallor, jaundice and hepatosplenomegaly.[6] The diagnosis is confirmed by qualitative and quantitative assessment of haemoglobin by high-performance liquid chromatography.[7] Definitive treatment is allogeneic haematopoietic stem cell transplantation, which is unavailable to most patients due to the cost and limitation of suitable donors.[8] Therefore, children with thalassaemia are managed with regular blood transfusions and iron chelation throughout life.[9]

Complications of thalassaemia are multifactorial and can be due to the disease, blood transfusions, iron overload and iron chelator medication.[10 11] Untreated β-thalassaemia results in excessive extramedullary

haematopoiesis and is fatal due to severe anaemia. Blood transfusions carry the risk of transfusion-related infections like hepatitis B and C and HIV. Frequent blood transfusions and increased iron absorption in patients with thalassaemia lead to iron overload. The excess iron deposits in the liver, heart and endocrine organs result in their dysfunction and failure. Iron chelator medications such as deferoxamine and deferasirox have adverse effects, including visual problems, deafness and hepatic and renal dysfunction.[12]

Although the endocrine and cardiac complications of thalassaemia are well studied, hepatic and renal complications of thalassaemia are understudied.[13 14] The studies that evaluated the renal dysfunction in thalassaemia have reported subclinical renal glomerular and tubular dysfunction; however, the exact determinant of dysfunction is not elucidated.[15 16] Studies evaluating the hepatic effects of thalassaemia have mainly focused on liver iron overload, fibrosis and steatosis.[17 18] Data on milder impairment of hepatic and renal function among asymptomatic children with β-thalassaemia are lacking. This is particularly important as newer iron chelator medications like deferasirox have adverse hepatic and renal effects not reported with traditional iron chelators.[19] Thus, it is crucial to identify the exact causes of liver and renal dysfunction, that is, whether it is due to disease, blood transfusion, iron overload or iron chelator medication.

In this study, we aim to describe the hepatic and renal function and the factors associated with abnormal hepatic and renal functions among paediatric patients with β-thalassaemia in Sri Lanka. The study investigated the following factors for hepatic function: hepatic transaminase (aspartate transaminases (AST) and alanine transaminases (ALT)), albumin, globulin, gamma-GT, alkaline phosphatase and bilirubin. Creatinine, urea, electrolytes, urine protein-to-creatinine ratio and estimated glomerular filtration rate (eGFR) were evaluated as factors related to renal function.

METHODS

Design and setting

We performed a cross-sectional descriptive study in two largest thalassaemia centres in Sri Lanka, Colombo North and Kurunegala Teaching Hospitals, from 1 January to 31 March 2023.

Study participants

All paediatric patients already diagnosed with thalassaemia aged 1–16 years attending thalassaemia centres of Colombo North and Kurunegala Teaching Hospitals for routine blood transfusion during the study period were recruited into the study. The diagnosis and classification of types of thalassaemia were based on clinical features and haemoglobin subtype quantification using high-performance liquid chromatography before the commencement of transfusions. β-Thalassaemia major was diagnosed in patients presenting with clinical features of thalassaemia between 3 and 24 months and haemoglobin F>90%. Haemoglobin E β-thalassaemia was defined as haemoglobin F>50% and haemoglobin E>30%. β-Thalassaemia intermedia was diagnosed in patients presenting with clinical features of thalassaemia after 24 months and having haemoglobin F>90% or haemoglobin A_2>3.4%. Sickle β-thalassaemia was defined as having haemoglobin S between 50 and 80%, with one parent having the β-thalassaemia trait and the other having the sickle cell trait. Parents of the participants were briefed about the study and informed written consent from guardians and assent from children over 12 years were obtained before they were recruited into the study.

Variables and data collection procedure

Data were collected using a data collection form, which included interviewing parents, perusal of clinical records and physical examination of the subjects. Trained data collectors interviewed patients and their parents to gather data on basic demographics, clinical details and iron chelator medications. Next, physical examinations were performed by trained doctors to measure anthropometric parameters and liver and spleen sizes. Weights were measured using a calibrated beam balance, and height measurements were taken using a stadiometer. Age-specific height and body mass index (BMI) SD were derived using WHO growth standards. BMI was classified as underweight (<−2 SD for age), normal weight (−2 SD to +1 SD for age), overweight (+1 SD to+2 SD for age) and obese (>+2 SD for age). Height was classified as short stature (<−2 SD for age), normal height (−2 SD to +2 SD for age) and tall stature (>+2 SD for age).

Reports of investigations done as a part of the routine care of these patients were gathered from patient records. The most recent reports of investigations done within 3–6 months of recruitment were obtained. Specifically, data on hepatic transaminase (AST and ALT), liver profile (albumin, globulin, gamma-GT, alkaline phosphatase and bilirubin), hepatitis screening and renal function tests (creatinine, blood urea and electrolytes) were collected. All biochemical tests were performed using clinically validated standard assay methods in clinically accredited laboratories of the two hospitals (online supplemental table 1). The eGFR was calculated using the Schwartz formula (eGFR=0.413× height (cm)/serum creatinine (mg/dL)). AST>40 IU/L, ALT>40 IU/L and creatinine>88 µmol/L were defined as abnormal. High serum ferritin was defined as>1000 ng/mL as per Thalassaemia International Federation guidelines.[12] The full study protocol, including the data collection form, is given as an online supplemental file.

Statistical analysis

Data were entered into a database and analysed using IBM SPSS Statistics V.29.0. Categorical variables were presented as frequency and percentages, whereas continuous variables were presented as mean with SD and median with range. Univariable analysis was performed

using the χ^2 test to determine the associations between clinical parameters related to the disease and treatment with high hepatic transaminases and low eGFR. Binary logistic regression was performed by including important clinical parameters related to the disease and treatment into a single regression model to identify independent factors associated with elevated hepatic transaminases. The following factors that could have an impact on hepatic transaminases based on the common medical knowledge were included in the binary regression model: thalassaemia type (haemoglobin E (HbE) β-thalassaemia type or not), serum ferritin (high or normal), hepatomegaly (presence or absence), deferasirox treatment (yes or no) and deferoxamine treatment (yes or no). The demographic and anthropometric parameters were not included in the regression model. The cut-off for statistical significance was set at $p<0.05$.

Patient and public involvement

Patients are neither involved in the design nor the conduct of subsequent steps of the study. The investigation results were available for participants and used in the standard management when required.

RESULTS

72 out of 76 eligible patients participated in the study (response rate 94.7%). The mean age of the population was 7.35 years (SD 3.8), and 38 (52.8%) were girls. (table 1).

Clinical characteristics of the study population

A majority (44 (61.1%)) had β-thalassaemia major while 22 (30.6%) had HbE β-thalassaemia. 55 children (76.4%) were transfusion-dependent, requiring over eight transfusions per year. The mean annual transfusion requirement of the transfusion-dependent group was 233 mL/kg/year (SD: 52), and that of the non-transfusion-dependent group was 34 mL/kg/year (SD: 60) (table 1).

Hepatic functions of patients with thalassaemia

Hepatomegaly and splenomegaly were found in 47 (65.3%) and 34 (47.2%) children, respectively. Three (4.1%) children had undergone splenectomy. All patients were negative for hepatitis B surface antigen or hepatitis C antibody. The distribution of hepatic function test values is shown in table 2.

Of the study population, 37 (51.4%) children had high (>40 IU/L) ALT, of which 9 (12.5%) had ALT elevation over three times the upper normal value (>120 IU/L). Elevation of AST above the normal range (>40 IU/L) was observed in 31 (43.1%) patients, whereas 28 (38.9%) had elevations of both transaminases. However, only 1 (1.4%) patient had hypoalbuminaemia (with serum albumin of 3.4 g/dL), and none had elevated prothrombin time.

Next, we evaluated the factors associated with high transaminases (table 3). Patients of the HbE β-thalassaemia type and those with hepatomegaly had a

Table 1 Sociodemographic and clinical characteristics of the study population

Characteristics	Frequency (n=72)	Percentage
Gender		
Male	34	47.2
Female	38	52.8
Age group		
<2 years	4	5.6
2–5 years	30	41.7
6–10 years	22	30.6
11–16 years	16	22.2
Body mass index category		
Underweight (<–2 SD for age)	21	29.2
Normal weight (–2 SD to +1 SD for age)	45	62.5
Overweight (+1 SD to +2 SD for age)	4	5.6
Obese (>+2 SD for age)	2	2.8
Height category		
Short stature (<–2 SD for age)	17	23.6
Normal (–2 SD to +2 SD for age)	53	73.6
Tall stature (>+2 SD for age)	2	2.8
Thalassaemia Centre		
Colombo North Teaching Hospital	40	55.6
Kurunegala Teaching Hospital	32	44.4
Type of thalassaemia		
β-thalassaemia major	44	61.1
Haemoglobin E β-thalassaemia	22	30.6
β-thalassaemia intermedia	5	6.9
Sickle β-thalassaemia	1	1.4
Type of thalassaemia by transfusion status		
Transfusion-dependent thalassaemia	55	76.4
Non-transfusion-dependent thalassaemia	17	23.6
Age at diagnosis		
<6 months	23	31.9
6–12 months	25	34.7
13–24 months	9	12.5
>24 months	15	20.8
Age at first transfusion		
<6 months	21	29.2
6–12 months	24	33.3

Continued

Table 1 Continued

Characteristics	Frequency (n=72)	Percentage
13–24 months	8	11.1
>24 months	16	22.2
Never transfused	3	4.2
Frequency of transfusion		
3 weekly	30	41.7
4 weekly	23	31.9
5–6 weekly	1	1.4
2–12 monthly	6	8.4
Occasionally (>annually)	9	12.5
Never transfused	3	4.2
Annual transfusion requirement		
<100 mL/kg/year	14	19.4
101–200 mL/kg/year	16	22.2
201–250 mL/kg/year	28	38.9
>250 mL/kg/year	14	19.4
Hepatomegaly		
No hepatomegaly	25	34.7
Hepatomegaly≤2 cm	19	26.4
Hepatomegaly>2 cm	28	38.9
Splenomegaly		
No splenomegaly	35	48.6
Splenomegaly≤5 cm	16	22.2
Splenomegaly>5 cm	18	25.0
Splenectomised	3	4.2
Iron chelator medication		
None	11	15.3
Deferasirox only	30	41.7
Deferoxamine only	6	8.3
Deferasirox+deferoxamine	25	34.7
Mean serum ferritin (mean of most recent three reports)		
<500 ng/mL	13	18.1
500–999 ng/mL	16	22.2
1000–2499 ng/mL	36	50.0
≥2500 ng/mL	7	9.7
Mean pre-transfusion haemoglobin (mean of most recent three reports)		
<7.0 g/dL	16	22.2
7.0–8.99 g/dL	26	36.1
9.0–10.5 g/dL	30	41.7

significantly higher prevalence of raised transaminases. Also, a higher prevalence of increased transaminases was observed among patients with high serum ferritin above 1000 ng/mL and those taking deferasirox. Among the HbE β-thalassaemia subgroup, all eight transfusion-dependent patients had high transaminases, while only 6/14 (42.9%) non-transfusion-dependent patients had high transaminases.

Then, we performed logistic regression to identify the independent associations of high transaminases (table 4). It revealed HbE β-thalassaemia type and high ferritin>1000 ng/mL as independent factors associated with high transaminases.

Renal functions of patients with thalassaemia

4 (5.5%) children had 1+proteinuria in urinalysis; however, the urine protein to creatine ratio was normal in all. None of the patients had elevated serum creatinine or blood urea (table 2). 11 (15.5%) patients had eGFR below 90 mL/min, but only 2 (2.8%) had eGFR below 60 mL/min (online supplemental table 2). A higher proportion of children with β-thalassaemia major, who are transfusion dependent and on deferasirox, had low eGFR (below 90 mL/min); however, none were statistically significant (table 5).

DISCUSSION

This study evaluated the hepatic and renal functions of children with thalassaemia in the two largest thalassaemia centres in Sri Lanka. It revealed that although major hepatic or renal dysfunctions are not common among children with thalassaemia, a significant proportion has mild abnormalities in hepatic and renal functions.

The main observation of the study is that nearly 40% of children with thalassaemia had elevated hepatic transaminases. This elevation was mainly seen among patients with HbE β-thalassaemia (OR 13.6 and 95% CI 2.0 to 92.7). This is particularly important as HbE β-thalassaemia is considered a milder disease than β-thalassaemia major with many patients remaining non-transfusion dependent.[20] The subgroup analysis showed that all patients with transfusion-dependent HbE β-thalassaemia had elevated transaminases. Although the exact mechanism for the higher prevalence of transaminase elevation in HbE β-thalassaemia is unclear, it could be related to the uncertain transfusion regimens of these patients due to the lack of definitive guidelines. Previously, we showed that patients with transfusion-dependent HbE β-thalassaemia maintained suboptimal pre-transfusion haemoglobin levels despite receiving high transfusion volumes.[14] Nonetheless, the exact reason for high transaminases among the HbE β-thalassaemia subgroup needs further research.

In addition to the HbE β-thalassaemia category, children with high serum ferritin and hepatomegaly and those taking deferasirox had high transaminases. This was partly expected as the iron overload is a recognised cause of hepatic fibrosis and dysfunction, and deferasirox is known to induce hepatic transaminases.[21–23] Liver fibrosis and cirrhosis have been reported in 20–45% and 8–9% of patients with thalassaemia, respectively, in previous studies.[24] As many patients in these studies had concurrent hepatitis B or C infection, the causation of cirrhosis

Table 2 Distribution of hepatic and renal function parameters

	N	Mean (±SD)	Median	Range
Hepatic function parameters				
Aspartate transaminases (U/L)	72	45.7 (±26.0)	37.5	11–151
Alanine transaminases (U/L)	72	59.1 (±63.6)	41.0	8–392
Albumin (g/dL)	69	4.40 (±0.80)	4.30	3.4–9.3
Globulin (g/dL)	69	2.59 (±0.62)	2.50	1.7–5.3
Gamma-GT	70	30.0 (±16.4)	26.5	12–98
Total bilirubin (µmol/L)	72	45.1 (±42.3)	38.4	4.0–340
Direct bilirubin (µmol/L)	72	14.5 (±19.3)	12.0	1.6–168
Indirect bilirubin (µmol/L)	72	30.4 (±25.5)	24.0	2.4–172
Alkaline phosphatase (U/L)	71	203.0 (±78.2)	194.0	69–428
Renal function parameters				
Urine protein: creatinine (mg/mmol)	66	14.0 (±8.5)	11.75	1.4–38
Serum creatinine (µmol/L)	71	35.9 (±10.8)	34.0	18–68
Blood urea (mg/dL)	69	21.4 (±5.6)	22.0	10–33
Na+ (mmol/L)	72	139.5 (±2.6)	140.0	133–144
K+ (mmol/L)	72	4.1 (±0.5)	4.2	2.5–5.2

was considered multifactorial.[25] However, our finding of the significant association of high serum ferritin above 1000 ng/dL with the elevated hepatic transaminases (OR 6.2 and 95% CI 1.02 to 38) supports the existing target of iron chelation that recommends maintaining serum ferritin below 1000 ng/mL.[12]

Table 3 Factors associated with high hepatic transaminases as determined by χ^2 test*

Factor	Proportion in high transaminase group	Proportion in normal transaminase group	χ^2 value	P value
Type of thalassaemia				
HbE β-thalassaemia (n=22)	14 (63.6%)	8 (36.4%)	7.05	0.008
β-thalassaemia major (n=44)	13 (29.5%)	31 (70.5%)		
Transfusion status				
Transfusion-dependent thalassaemia (n=55)	22 (40.0%)	33 (60.0%)	0.12	0.72
Non-transfusion-dependent thalassaemia (n=17)	6 (35.3%)	11 (64.7%)		
Hepatomegaly				
Hepatomegaly (n=47)	23 (48.9%)	24 (51.1%)	5.75	0.016
No hepatomegaly (n=25)	5 (20.0%)	20 (70.0%)		
Serum ferritin				
High (>1000 ng/mL) (n=43)	20 (46.5%)	23 (53.5%)	2.61	0.10
Normal (<1000 ng/mL) (n=29)	8 (27.6%)	21 (72.4%)		
Deferasirox treatment				
On deferasirox (n=55)	24 (43.6%)	31 (56.4%)	2.20	0.13
Not on deferasirox (n=17)	4 (23.5%)	13 (76.5%)		
Deferoxamine treatment				
On desferioxamine (n=31)	11 (35.5%)	20 (64.5%)	0.26	0.60
Not on desferioxamine (n=41)	17 (41.5%)	24 (58.5%)		

*High hepatic transaminases are defined as ALT>40 IU/L and AST>40 IU/L.
ALT, alanine transaminases; AST, aspartate transaminases; HbE, haemoglobin E.

Table 4 Independent factors associated with high hepatic transaminases as determined by logistic regression*

Factor	Adjusted OR for high transaminases	95% CI	P value
HbE β-thalassaemia type	13.6	2.00 to 92.7	0.008
High ferritin>1000 ng/dL	6.25	1.02 to 38.2	0.047
Deferasirox treatment	4.20	0.57 to 30.6	0.15
Hepatomegaly	1.97	0.53 to 7.35	0.31
Deferoxamine treatment	0.63	0.16 to 2.46	0.51

*High hepatic transaminases are defined as ALT>40 IU/L and AST>40 IU/L.
ALT, alanine transaminases; AST, aspartate transaminases; HbE, haemoglobin E.

The reason for the association between hepatomegaly and high transaminases is unclear. Hepatomegaly is observed in many patients with thalassaemia due to extramedullary erythropoiesis but is not associated with hepatic parenchymal alterations.[26] Whether the increasing liver size due to extramedullary haematopoiesis per se could cause high serum transaminases may need more research.

Although many children with thalassaemia had high hepatic transaminases, the exact significance of their elevation is unclear. None of the patients in the study had significant abnormalities in the synthetic functions of the liver. Although we could not perform MRI studies to assess liver iron overload or transient elastography to evaluate hepatic fibrosis due to limitations of facilities, it is unlikely that these studies would provide additional insights into mild derangements of hepatic function observed in our study.

The other important aspect examined in the study is the renal function of children with thalassaemia. Renal involvement in thalassaemia is relatively rare and is under-reported.[15] Our study did not reveal any significant elevations in serum levels of creatinine or urea in the study population. However, we observed a mild decrease in eGFR in 15% of patients. Low eGFR is more common in major patients with transfusion-dependent β-thalassaemia and those who were on deferasirox. Our results indicate that regular monitoring of eGFR may be required in thalassaemia to identify patients developing clinically significant renal dysfunction.

The relatively small number of study participants, which leads to low statistical power, is an important limitation of our study. Thalassaemia is a rare disease even in highly prevalent countries like Sri Lanka, with approximately 1700 patients of all forms of thalassaemia

Table 5 Factors associated with low eGFR as determined by χ^2 test

Factor	Proportion in low eGFR group	Proportion in normal eGFR group	χ^2 value	P value
Type of thalassaemia				
β-thalassaemia major (n=43)	10 (23.3%)	33 (76.7%)	3.62	0.05
HbE β-thalassaemia (n=22)	1 (4.5%)	21 (95.5%)		
Transfusion status				
Transfusion-dependent thalassaemia (n=54)	10 (18.5%)	44 (81.5%)	1.57	0.20
Non-transfusion-dependent thalassaemia (n=17)	1 (5.9%)	16 (94.1%)		
Serum ferritin				
High (>1000 ng/mL) (n=42)	6 (14.3%)	36 (85.7%)	0.11	0.73
Normal (<1000 ng/mL) (n=29)	5 (17.2%)	24 (82.8%)		
Deferasirox treatment				
On deferasirox (n=54)	10 (18.5%)	44 (81.5%)	1.57	0.20
Not on deferasirox (n=17)	1 (5.9%)	16 (94.1%)		
Deferoxamine treatment				
On desferioxamine (n=30)	5 (16.7%)	25 (83.3%)	0.55	0.81
Not on desferioxamine (n=41)	6 (14.6%)	35 (85.4%)		

eGFR, estimated glomerular filtration rate; HbE, haemoglobin E.

of all ages reported.[27] This study was confined to a well-characterised group of patients aged 1–16 years, and we believe our research findings should pave the way to more extensive studies involving patients in all age groups.

The study was conducted in two of the largest thalassaemia centres in Sri Lanka. As it was confined to ethnic groups in a small region of South Asia, the results of the study may not be generalisable. However, the results of this study would be an eye-opener to examine the causes and implications of milder hepatic and renal dysfunction in apparently asymptomatic thalassaemia patients worldwide.

CONCLUSION

In conclusion, this study showed that milder elevations of hepatic transaminases are common among children with thalassaemia, especially among the subset of patients with HbE β-thalassaemia type and those with high serum ferritin. Milder reductions in eGFR were noted in some patients with transfusion-dependent β-thalassaemia major.

Contributors WW, MF and SM were involved in the literature review, writing the project proposal and obtaining ethical approval. WW, RTT, HP, DB and RDS were involved in data collection. WW, RTT, HP, DB, RDS, MF, AP and SM were involved in data entry and analysis. WW, RTT and SM wrote the manuscript. All authors read and approved the final manuscript. SM is responsible for the overall content as guarantor.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the Ethical Review Committee of the Sri Lanka College of Paediatricians. The reference number for the ethical approval is SLCP/ERC/2022/41. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The datasets used and analysed during the current study are available from the corresponding author upon reasonable request.

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REFERENCES

1 Mettananda S, Higgs DR. Molecular Basis and Genetic Modifiers of Thalassemia. *Hematol Oncol Clin North Am* 2018;32:177–91.
2 Taher AT, Weatherall DJ, Cappellini MD. Thalassaemia. *Lancet* 2018;391:155–67.
3 Premawardhena A, Mudiyanse R, Jifri M, *et al*. An islandwide hospital based epidemiological survey of haemoglobinopathies and an assessment of standards of care in 23 centres. 2017.
4 Shah FT, Sayani F, Trompeter S, *et al*. Challenges of blood transfusions in β-thalassemia. *Blood Rev* 2019;37:100588.
5 Mettananda S, Gibbons RJ, Higgs DR. Understanding α-globin gene regulation and implications for the treatment of β-thalassemia. *Ann N Y Acad Sci* 2016;1368:16–24.
6 Mettananda S. Thalassaemia: In a quest towards an ultimate cure. *Sri Lanka J Child Health* 2017;46:203.
7 Mettananda S. Management of Thalassaemia. *Sri Lanka J Child Health* 2018;47:159.
8 Mettananda S, Gibbons RJ, Higgs DR. α-Globin as a molecular target in the treatment of β-thalassemia. *Blood* 2015;125:3694–701.
9 Mettananda S. Genetic and Epigenetic Therapies for β-Thalassaemia by Altering the Expression of α-Globin Gene. *Front Genome Ed* 2021;3:752278.
10 Higgs DR, Engel JD, Stamatoyannopoulos G. Thalassaemia. *Lancet* 2012;379:373–83.
11 Kattamis A, Kwiatkowski JL, Aydinok Y. Thalassaemia. *The Lancet* 2022;399:2310–24.
12 Farmakis D, Porter J, Taher A, *et al*. 2021 Thalassaemia International Federation Guidelines for the Management of Transfusion-dependent Thalassemia. *Hemasphere* 2021;6:e732.
13 Karusheva Y, Petry CJ, Yasara N, *et al*. Association of GDF15 levels with body mass index and endocrine status in β-thalassaemia. *Clin Endocrinol (Oxf)* 2023;99:182–9.
14 Mettananda S, Pathiraja H, Peiris R, *et al*. Blood transfusion therapy for β-thalassemia major and hemoglobin E β-thalassemia: Adequacy, trends, and determinants in Sri Lanka. *Pediatr Blood Cancer* 2019;66:e27643.
15 Ponticelli C, Musallam KM, Cianciulli P, *et al*. Renal complications in transfusion-dependent beta thalassaemia. *Blood Rev* 2010;24:239–44.
16 Mahmoud AA, Elian DM, Abd El Hady NM, *et al*. Assessment of Subclinical Renal Glomerular and Tubular Dysfunction in Children with Beta Thalassemia Major. *Children (Basel)* 2021;8:100.
17 Padeniya P, Ediriweera D, De Silva AP, *et al*. The association between steatosis and liver damage in transfusion-dependent beta thalassaemia patients. *Br J Haematol* 2023;200:517–23.
18 Longo F, Corrieri P, Origa R, *et al*. Changing patterns of thalassaemia in Italy: a WebThal perspective. *Blood Transfus* 2021;19:261–8.
19 Moukalled NM, Bou-Fakhredin R, Taher AT. Deferasirox: Over a Decade of Experience in Thalassemia. *Mediterr J Hematol Infect Dis* 2018;10:e2018066.
20 Premawardhena AP, Ediriweera DS, Sabouhanian A, *et al*. Survival and complications in patients with haemoglobin E thalassaemia in Sri Lanka: a prospective, longitudinal cohort study. *Lancet Glob Health* 2022;10:e134–41.
21 Ricchi P. Liver fibrosis in young patients with transfusion-dependent thalassaemia (TDT), understanding the role of steatosis. *Br J Haematol* 2023;200:399–400.
22 Padeniya P, Ediriweera DS, De Silva AP, *et al*. Using FIB-4 score as a screening tool in the assessment of significant liver fibrosis (F2) in patients with transfusion-dependent beta thalassaemia: a cross-sectional study. *BMJ Open* 2022;12:e061156.
23 Botzenhardt S, Li N, Chan EW, *et al*. Safety profiles of iron chelators in young patients with haemoglobinopathies. *Eur J Haematol* 2017;98:198–217.
24 Prati D, Maggioni M, Milani S, *et al*. Clinical and histological characterization of liver disease in patients with transfusion-dependent beta-thalassemia. A multicenter study of 117 cases. *Haematologica* 2004;89:1179–86.
25 Li CK, Chik KW, Lam CWK, *et al*. Liver disease in transfusion dependent thalassaemia major. *Arch Dis Child* 2002;86:344–7.
26 Weatherall DJ, Clegg JB. *The thalassaemia syndromes*. 4th edn. Oxford: Blackwell Science, 2001.
27 Premawardhana AP, Mudiyanse R, De Silva ST, *et al*. A nationwide survey of hospital-based thalassemia patients and standards of care and a preliminary assessment of the national prevention program in Sri Lanka. *PLoS One* 2019;14:e0220852.