Habitual Snoring in Pediatric Thalassemia Disease; Prevalence, Quality of Life and Risk Factors

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ABSTRACT

Objective: To compare the prevalence of HS and quality of life in non-transfusion dependent thalassemia (NTDT) and Transfusion dependent thalassemia (TDT) patients and to identify risk factors associated with HS in pediatric thalassemia.

Materials and Methods: We conducted a cross-sectional study of pediatric thalassemic patients aged from 6 months - 18 years between January 2020 and October 2020, at Thammasat University Hospital, Thailand.

Results: There were 141 thalassemia patients (35 TDT and 106 NTDT), aged 7 months-18 years, 73 (51.8%) were male. Sixty-eight patients (48.2%) reported snoring; 28 patients (19.9%) had HS; the remaining 40 patients (28.4%) had simple snoring. The prevalence of HS was not significantly different between TDT and NTDT group (6 (17.1%) VS 22 (20.8%); *P*= 0.527). Quality of life assessed by OSA-18 score was not significant difference between TDT and NTDT groups (51.3 ± 18.8 VS 45.7 ± 11.4; *P*=0.141). The associating risk factors for the development of HS after multivariate logistic analysis were nasal congestion, and male gender, with an adjusted OR of 5.3 and 3.0, respectively.

Conclusion: Prevalence of HS was increased in children with thalassemia. Factors such as nasal congestion and male gender were strongly associated with HS in this population. The quality of life assessment using the OSA-18 questionnaire indicated that thalassemia children generally exhibited a good quality of life. Additionally, our study observed relatively low serum ferritin levels in comparison to previous studies. The standard care provided for TDT patients, includes regular blood transfusion and effective iron chelation, may contribute to slowing down the degree of nasopharyngeal narrowing in thalassemia patients.

Keywords: Habitual snoring; obstructive sleep apnea; thalassemia; OSA-18 (Siriraj Med J 2023; 75: 546-554)

INTRODUCTION

Thalassemia disease is a common inherited hematologic disorder caused by several mutations which affect the hemoglobin synthesis. It is highly prevalent in Southeast Asia.[1-2] In Thailand, about one half of the population likely carries some sort of thalassemia gene.[3-4] It is estimated about 10,000 new cases emerge each year. The clinical spectrum of thalassemia ranges from asymptomatic to severe anemia and can cause serious complications. Ineffective erythropoiesis causes osteoporosis and expansion of marrow space in the skull and facial bone and cause extramedullary hematopoiesis (EMH). Furthermore, compensatory lymphoid hyperplasia from frequent infection by encapsulated organisms are predisposed to upper airway obstruction, especially during sleep. There have been some reports about higher prevalence of obstructive sleep apnea (OSA) in children with beta-thalassemia than healthy children.[5-9] The data also reported that adenotonsillar lymphoid hyperplasia and high serum ferritin level were associated with the occurrence of OSA.

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The majority of the complications of thalassemia major are related to iron overload, bone marrow expansion and EMH, but EMH is more prevalent in thalassemia intermedia who are non-transfusion-dependent thalassemia (NTDT) when compared to transfusion-dependent thalassemia (TDT).[5] To our knowledge, there has been no study to compare the prevalence of OSA and quality of life in both NTDT and TDT groups. Polysomnography (PSG) is the gold standard for diagnosis of OSA, but it is associated with several disadvantages, particularly in children. As a result, a timely diagnosis of OSA is not always possible. Habitual snoring is a hallmark for OSA.[10-12] A few reports have shown that habitual snoring was a strong risk factor of OSA in children with sickle cell anemia[13] and one report showed a trend of habitual snoring was increased in OSA.[8] For a resource constrained environment, history of habitual snoring may be guided for OSA screening. The aims of our study are to compare the prevalence of habitual snoring and quality of life in NTDT and TDT patients. The secondary outcome is to identify risk factors associated with habitual snoring in pediatric thalassemia.

MATERIALS AND METHODS

We conducted a cross-sectional study of pediatric thalassemic patients aged from 6 months - 18 years between January 26th 2020 and October 14th 2020, at Thammasat University Hospital, Thailand. The approval for the study was granted by the ethics committee of Thammasat University (MTU-EC-PE-1-270/63). Assent and/or informed consent forms were obtained from patient > 7 years old and all parents/guardians respectively. Children or guardians who did not understand Thai adequately or could not provide sleep data or who were cases with incomplete medical records were excluded. Clinical information was collected through a manual chart review as follows: demographic data, underlying medical conditions, nutritional status, clinical history and previous treatment of thalassemia, history during sleep and snoring, OSA-18 questionnaire, physical examination for adenoid and tonsils size, nasal congestion and hepato-splenomegaly, and laboratory data (hemoglobin and serum ferritin level).

Operational definition

Habitual snoring (HS) is defined as the presence of loud snoring at least 3 nights per week while snoring less than 3 nights per week is defined as simple snoring (SS).[7,14,15] Transfusion-dependent thalassemia (TDT) refers to the group of patients who require regular blood transfusions for survival from early life, including severe forms of hematological phenotypes of beta-thalassemia.[16] Non-transfusion dependent thalassemia (NTDT) refers to the mild group of patients or thalassemia intermedia who do not require frequent blood transfusion for survival. Obesity, for children < 5 years of age was defined as weight-for-height > 3 standard deviations (SD) above the World Health Organization (WHO) Child Growth Standard median.[17-18] Children and adolescents aged between 5 – 15 years were defined as obese if BMI-for-age was > 2 SD above the WHO Growth Reference median.[17-19] The OSA-18 score is an 18-questionnaire that uses a Likert-type scoring system to evaluate the quality of life for 2-18 years children with OSA. It has been validated as both evaluative and discriminative in Thai pediatric OSA.[20] The OSA-18 consists of 18 items grouped in 5 domains of sleep disturbance, physical suffering, emotional distress, daytime problem and caregiver concerns. On the basis of this information, a summary score is calculated that ranges from 18 (no impact on quality of life) to 126 (major negative impact). A value at or above 60 is considered abnormal.[21]

Statistical analyses

Data were analyzed using STATA for Windows v14.0. Clinical characteristics and laboratory results for continuous data were reported as mean and standard deviation (SD) or median with interquartile range (IQR); categorical data were reported as the frequency with percentage. Independent Student-t test, Wilcoxon rank-sum test, and Kruskal-Wallis test were used to compare continuous data; nominal data analysis used a Chi-square test: P-value < 0.05 was considered statistically significant. Risk factors associated with HS were analyzed using univariate and multivariate logistic regression. For univariate analysis, crude odds ratios (OR) and 95% confidence intervals (CIs) were used to consider the strength of factors associated with HS. Factors with a $p < 0.20$ or clinical significance in literature review were then entered into a multiple logistic regression model. A value of $p < 0.05$ was considered to indicate statistically significant differences, and adjusted OR and their 95% CIs were reported to consider the strength of association.

RESULTS

A total of 141 thalassemia patients (35 TDT and 106 NTDT) were enrolled. Approximately 73 patients (51.8%) were male. The median age was 8.9 years (range 7 months-18 years). Most patients were between the ages of 5-15 years. Underlying comorbidities were found in 39 children (27.7%) and there was allergic rhinitis in 13 (9.2%) children. Forty-seven patients (33.3%) had

history of passive smoking. Half of the patients were in a medium income family. For screening cognitive function, we found that the median mathematic grade was 3 and found significant lower in TDT than NTDT group (3 VS 2.5 with *P*=0.002). Sixty-eight patients (48.2%) reported snoring; 28 patients (19.9%) were HS, the remaining 40 patients (28.4%) had simple snoring. The prevalence of HS was not significantly different between TDT and NTDT group (6 (17.1%) VS 22 (20.8%); *P*= 0.527). Twenty-five patients (71.4%) in TDT group had desferrioxamine for iron chelation therapy.

Most patients had normal nutritional status; only 11 patients (7.9%) were obese and 7 patients (4.9%) had malnutrition. On physical examination, nasal congestion and tonsil enlargement were found more readily in TDT than NTDT group but of no statistical significance. Mean hemoglobin level was 9.18±1.13 g/dL, there was no significant difference between groups. The median serum ferritin level was significantly higher in TDT than NTDT group (1315 VS 62; *P*< 0.001). The detail of clinical data is shown in Table 1.

Regarding the OSA-18 questionnaire score, the mean OSA-18 score was 46.9±13.2, with no significant difference between TDT and NTDT groups (51.3 ± 18.8 VS 45.7 ± 11.4; *P*=0.141). The fifth domain (caregiver concern) revealed the highest mean total score (11.7) whereas, the fourth domain (effects on daytime function) showed the lowest mean total score (8.1). Comparison between the TDT and NTDT groups revealed that only physical symptoms including rhinorrhea and difficult in were significant higher in TDT than NTDT group. The details are shown in Table 2.

TABLE 1. Comparison of clinical data between TDT and NTDT patients.

Clinical data	All (N=141)	TDT (N= 35)	NTDT (N=106)	*P*-value
Age (year); mean (IQR)	8.9 (5.3-12.8)	10.3 (7.3-13.8)	8.3 (5-12.6)	0.127
Age group; N (%)				0.237
< 2 years	9 (6.4)	2 (5.7)	7 (6.6)	
2 years - < 5 years	24 (17.0)	4 (11.4)	20 (18.9)	
5 years - <10 years	49 (34.8)	10 (28.6)	39 (36.8)	
10 years - < 15 years	39 (27.7)	15 (42.9)	24 (22.6)	
≥ 15 years	20 (14.2)	4 (11.4)	16 (15.1)	
Male gender; N (%)	73 (51.8)	20 (57.1)	53 (50)	0.463
Nutritional status; N (%)				
Malnutrition	7 (4.9)	3 (8.6)	4 (3.8)	0.263
Obesity	11(7.9)	2 (5.7)	9 (8.6)	0.586
Passive smoking; N (%)	47 (33.6)	15 (42.9)	32 (30.5)	0.179
Median mathematic grade; median (IQR)*	3 (2.5-4)	2.5 (2-3)	3.5 (3-4)	0.002
GPA; mean (IQR)	3.5 (3-3.8)	3.2 (2.6-3.7)	3.5 (3.2-3.9)	0.095
Snoring prevalence; N (%)				0.527
Habitual snoring	28 (19.9)	6 (17.1)	22 (20.8)	
Simple snoring	40 (28.4)	8 (22.9)	32 (30.2)	
Underlying disease; N (%)	39 (27.7)	8 (22.9)	31 (29.3)	0.464
Allergic rhinitis; N (%)	13 (9.2)	3 (8.6)	10 (9.4)	0.878
Nasal congestion; N (%)	37 (26.6)	13 (37.1)	24 (23.1)	0.103
Tonsil enlargement; N (%)	9 (6.5)	3 (8.6)	6 (5.8)	0.560
Median hemoglobin level (g/dL); median (IQR) *	9.1(8.5-9.6)	8.8 (8-9.1)	9.3 (8.7-10)	<0.001
Median serum ferritin level (ng/ml); median (IQR) *	76 (73-294)	1315 (608-1650)	62 (38-95)	< 0.001

*P <0.05

Abbreviations: NTDT, non-transfusion dependent thalassemia; TDT, transfusion-dependent thalassemia; GPA, Grade point average

TABLE 2. The comparison of OSA-18 scores between HS in TDT and NTDT patients.

OSA-18 questions	All (N=28)	TDT(N=6)	NTDT(N=22)	*P*-value
Sleep disturbance	9.9±2.8	10.3±1.9	9.8±3.1	0.265
Loud snoring	4.3±1.0	4.7±1.2	4.1±0.9	0.514
Breath holding /pause	1.3±0.8	1.5±0.8	1.3±0.8	0.890
Choking or grasping	1.9±1.2	1.7±0.8	2.0±1.2	0.292
Fragmented sleep	2.3±1.3	2.5±1.0	2.3±1.4	0.474
Physical symptoms	8.9±3.8	10.3±5.7	8.5±3.1	0.068
Mouth breathing	2.5±1.3	3.2±1.5	2.3±1.3	0.679
Frequent URIs	2.1±1.1	1.7±1.2	2.2±1.1	0.745
Rhinorrhea*	2.6±1.5	3.2±2.4	2.4±1.2	0.026
Dysphagia*	1.7±.1.2	2.3±.2.2	1.6±.0.8	0.002
Emotional symptoms	8.3±3.7	8.0±3.7	8.4±3.8	0.913
Mood swing or tantrums	2.6±1.5	2.5±1.4	2.6±1.6	0.694
Aggressive or hyperactivity	2.6±1.4	2.3±1.8	2.7±1.3	0.410
Discipline problems	3.1±1.5	3.2±2.3	3.1 ±1.3	0.071
Daytime function	8.1±2.9	10±3.7	7.6±2.5	0.216
Daytime drowsiness	2.3±1.4	2.0±2.0	2.4±1.2	0.131
Poor attention span	2.7±1.4	3.0 ±1.7	2.6±1.4	0.559
Difficult awakening	3.1±1.7	5.0±1.9	2.6±1.3	0.251
Caregiver concerns	11.7±4.3	12.7±5.8	11.4±3.9	0.257
Worried over child health	4.5±1.3	5.2±1.3	4.3±1.3	0.901
Concerned not enough air	2.7±1.6	2.8±2.1	2.7±1.5	0.329
Caregiver missed activities	2.1±1.3	2.3±1.5	2.0±1.2	0.522
Caregiver frustration	2.4±.1.4	2.3±1.8	2.4±.1.3	0.422
Total OSA-18 score; mean ± SD	46.9 ± 13.2	51.3 ± 18.8	45.7 ± 11.4	0.141

*$P < 0.05$

Abbreviations: NTDT, non-transfusion dependent thalassemia; TDT, transfusion-dependent thalassemia

Regarding associated factors for HS by univariate logistical regression models, the most relevant risk factor was age group 5-10 years (OR 9.8) followed by nasal congestion (OR 4.6). Other risk factors were underlying disease (OR 2.9), male gender (OR 2.3), history of passive smoking (OR 1.7), tonsil enlargement (OR 1.3) and Serum ferritin level ≥ 1,000 ng/ml (OR 1.2. The unadjusted OR with 95% CIs of possible risk factors for HS are demonstrated in Table 3.

After multivariate logistic analysis to adjust the associating risk factors for the development of HS, we adjusted for all factors that had an odds ratio above 1 and a P < 0.20 (Table 3). The remaining factors that affected HS were nasal congestion and male gender with adjusted OR 5.3 and 3.0 respectively. The results are shown in Table 4. However, severity of thalassemia was not a significant predictor of HS both in crude and adjusted analysis OR 0.7 (95%CIs 0.22-1.93).

DISCUSSION

In our pediatric thalassemia population, 48% of patients reported to have snored in the previous year, 19.9 % had habitual snoring. The estimated prevalence of HS was high compared to a report of 6.9-8.5% in general Thai school-aged children.[22,23] However, several studies reported prevalence of HS in general children around 2.4-45%.[24-29] The prevalence rates vary according to study design, and study population characteristics, such

TABLE 3. Univariate analysis of the risk factors for the development of habitual snoring.

Clinical data	HS (N=28)	Non-HS (N=113)	OR (95% CI)	*P*-value
Age group; N (%) *				0.014
< 2 years	1(3.6)	8 (7.1)	2.3 (0.18-29.84)	
2 years - < 5 years	4 (14.3)	20 (11.7)	3.7 (0.59-23.07)	
5 years - <10 years	17 (60.7)	32 (28.3)	9.8 (1.87-51.57)	
10 years - < 15 years	2 (7.1)	37 (32.7)	1.0	
≥ 15 years	4 (14.3)	16 (14.2)	4.6 (0.72-29.78)	
Male gender; N (%) *	19 (67.9)	54 (47.8)	2.3 (0.95-5.61)	0.057
Obesity; N (%)	2 (7.1)	9 (8.0)	0.9 (0.178-4.35)	0.875
Passive smoking; N (%)	12 (42.9)	35 (31.3)	1.7 (0.70-3.88)	0.245
Median mathematic grade	3.3 (2-4)	3.0 (2.5-4)		0.749
Mathematic grade ≥ 3; N (%)	12 (66.7)	50 (73.5)	0.7 (0.24-2.20)	0.057
Severity of thalassemia; N (%)	6 (17.1)	22 (20.8)	0.8 (0.29-2.15)	0.642
TDT	6 (21.4)	29 (25.7)		
NTDT	22 (78.6)	84 (74.3)		
Underlying disease; N (%) *	13 (46.4)	26 (23.0)	2.9 (1.19-7.03)	0.013
Desferrioxamine therapy; N (%)	4 (14.8)	21 (19.8)	0.7 (0.21-2.27)	0.553
Nasal congestion; N (%) *	14 (53.9)	23 (20.4)	4.6 (1.78-11.71)	<0.001
Tonsil enlargement; N (%)	2 (7.7)	7 (6.2)	1.3 (0.24-6.49)	0.780
Median hemoglobin level (g/dL)	9.1 (8.5-9.7)	9.1 (8.5-9.6)		0.865
Hemoglobin level <10 g/dL; N (%)	22 (78.6)	88 (77.9)	1.0 (0.35-2.631)	0.937
Median ferritin level (ng/ml)	79 (40-167)	74 (45-351)		0.830
Ferritin level ≥ 1,000 ng/ml; N (%)	4 (14.8)	14 (13.1)	1.2 (0.35-3.84)	0.815

*OR >1 with $P < 0.20$

Abbreviations: NTDT, non-transfusion dependent thalassemia; TDT, transfusion-dependent thalassemia

TABLE 4. Multivariate analysis of the risk factors for the development of habitual snoring.

Variable	Coefficient OR (95%CI)	*P*-value
Age group	0.9 (0.57-1.36)	0.563
Male gender	3.0 (1.10-8.19)	0.032*
Underlying disease	2.6 (0.99-6.72)	0.051
Nasal congestion	5.3 (2.01-13.95)	0.001*

*$P < 0.05$

adjusted for age group, sex, underlying disease and nasal congestion

as age, ethnicity, environment and the description and perception of HS. Our findings of a high prevalence of habitual snoring in thalassemia disease were in accordance with the finding of Sritippayawan et al[7] who reported a high prevalence of HS and OSA in children with severe beta-thalassemia. To the best of our knowledge, there have been scanty reports regarding the prevalence of HS in childhood thalassemia. Several studies reported high prevalence of OSA or sleep disturbance in children with thalassemia major.[8-9,30] Although PSG was the gold standard method for diagnosing OSA, resulting in stronger clinical significance, there are still limitations due to incorporating young children and sparse availability of long waiting lists and high costs. Simple screening tools are needed for children. HS was a subjective assessment but a recent study showed a significant association between parental reported HS and objectively measured pathologic snoring.[31-33] It may be implied that HS must be paid close attention and should be considered that HS is an at-risk population.

The mechanism of these findings has not been well established. Kapelushnik et al[5] reported the association of pediatric OSA and thalassemia intermedia whereby they proposed EMH in the nasopharyngeal airway to be the possible cause of OSA. Sritippayawan et al[7] also reported that most pediatric OSA with thalassemia major cases had adenotonsilar hypertrophy and needed surgery. Finally, the finding from adenotonsillar lymphoid tissue showed lymphoid hyperplasia without evidence of EMH. The authors suggested lymphoid hyperplasia was the cause of nasopharyngeal airway narrowing and OSA as in the general pediatric population. The mechanism of lymphoid hyperplasia is unknown. Several mechanisms have been proposed, including repeated adenotonsillar infection or compensatory lymphoid hyperplasia in response to splenectomy or increase systemic inflammatory response from evidence of high serum ferritin in severe thalassemia cases.[5-9]

In this study, we found no significant difference in the prevalence of HS in TDT and NTDT group, although there was higher serum ferritin in TDT group. Sritippayawan et a[7] reported a higher average serum ferritin level in the OSA group than the non-OSA group. They suggested those who had more severe OSA tended to have a higher serum ferritin level than those who had a milder disease. That result was inconsistent with our study. It may be due to the mean serum ferritin level in our study being lower than their study. The mean serum ferritin level in our TDT group was 1,257 ng/ml while their study reported the mean serum ferritin level of 4,606 ng/ml in moderate to severe OSA group and 2,554 ng/ml in mild OSA group. Tarasiuk et al[6] also studied the sleep disruption among beta-thalassemia and congenital dyserythropoietic anemia. Their patients had low serum ferritin (413.7 ng/ml) and no evidence of OSA was found among any of their patients. Regular blood transfusion would have kept EMH at a minimum[34] but in NTDT as chronic anemia would still provide a stimulus for bone marrow expansion and hence a risk for airway obstruction.[35] Regular blood transfusion with adequate iron chelation may protect the patient from developing sleep order breathing.

For OSA-18 score questionnaire, its clinical usefulness for distinguishing the severity of pediatric OSA is unclear and conflicting[21,36-37] but the usefulness in determining the factor most affecting the quality of life of children with OSA was mentioned.[41] In our study, we found the mean OSA-18 score was 46.9±13.2. The result was quite low when compared to previous reports for quality of life in pediatric OSA (53-60 in non-severe OSA and ≥ 60 in severe OSA).[20-21,39] It represented a good quality of life of our thalassemia patients. This finding was consistent with Sinlapamongkolkul et al,[40] who demonstrated a better health-related quality of life (HRQoL) score of their pediatric thalassemia patients when compared to the previous decade. They stated that these findings may represent a better standard of care because the prevalence of high serum iron ferritin level was quite low (14% of patients had serum ferritin > 1,000 ng/ml) in their study when compared to the previous decade.

In our study, there was no statistically significant difference in the total score of the OSA-18 score between NDTD and TDT but we the data showed the trend of OSA-18 score in TDT was higher that NDTD group. However, we did notice a trend indicating that the OSA-18 scores were higher in the TDT group compared to the NTDT group. It is important to note that the lack of statistical significance in our findings may be attributed to the limited sample size. Therefore, further research with a larger sample size is warranted to explore this trend in more detail. Moreover, while the OSA-18 questionnaire proved to be a reliable tool for assessing the subjective aspects of OSA-related quality of life, it is essential to consider various factors that might influence the scores. These factors may include family income, guardian education, parents' perceptions, and emotional well-being, which could potentially impact the overall score. Interestingly, in our study, we observed that parents in the NTDT group exhibited higher affluence and education levels compared to the TDT group. These differences in socioeconomic status might explain the higher scores in the caregiver concern domain within the NTDT group.

Nevertheless, it is important to highlight that these scores were relatively low when compared to general pediatric OSA score.

Regarding associated factors for HS, we revealed that HS was more prevalent in age group 5-10 years than in older children. This finding can be attributed to age-dependent increases in volumetric lymphoid/cephalometric ratio, which typically peak between 2-8 years of age.[41] Our results align with previous studies that have reported similar age-related trends in HS prevalence.[15,28,42-43] However, some studies have not shown a clear trend in this regard.[44] The gender difference in the prevalence of HS among children has been variable in the literature. While several studies have reported a higher occurrence of HS in males,[15,25-26, 28,42-43] others have not found a significant gender difference.[22,24-25,46-47] Passive smoking has been identified as an important risk factor for HS in multiple studies.[15,22,28,42-43,46,48-49] Cigarette smoke induces endotoxin, resulting in a potent inflammatory reaction, mucosal swelling and increase mucous production due to goblet cell proliferation lead to nasopharyngeal narrowing.[50] Our study also found this association but no statistical significance. Furthermore, our study identified a strong association between HS and respiratory problems, including allergic rhinitis and nasal congestion. These findings are consistent with previous research.[15,26, 28,43,46,51-52] The mechanism of these findings has not been clarified, but it has been proposed that inflammatory processes resulting from allergic rhinitis or respiratory tract infections can increase airway resistance. Additionally, early exposure to respiratory viruses may induce neuro-immunomodulatory changes in adenotonsillar tissue, thereby contributing to snoring and HS.[53] Interestingly, our study did not find an association between high serum ferritin levels and HS, in contrast to a previous study reporting a negative correlation between serum ferritin and obstructive sleep apnea (OSA).[7] One possible explanation for this discrepancy could be that effective regular blood transfusion and iron chelation therapy in our study population helped maintain normal serum ferritin levels and minimize nasopharyngeal airway narrowing.

Previous studies have shown the relationship between disordered cognitive functions and anemia of any cause, including thalassemia major.[54,55] Several mechanisms were proposed, including cumulative small injuries to the central nervous system resulting from hemolysis or repeated blood transfusions, which can lead to iron overload in the brain or neurotoxicity associated with lifelong chelating therapy. All of these factors may contribute to brain dysfunction.[56,57] Monastero R et al[55] stated neuropsychological tests were significantly impaired in patients with beta-thalassemia major, particularly in those exhibiting signs of hemosiderosis but there was no correlation between desferrioxamine doses, hemoglobin and ferritin levels. Nevruz O et al[58] also reported potentials of cognitive impairment in patients with thalassemia minor. They hypothesized that chronic hemolysis may play a role in the etiology of neurological findings. Furthermore, several studies have identified an association between HS and adverse behavioral and academic outcomes, even in the absence of intermittent hypoxia[28,59-62] This may be due to increased sleep fragmentation. Consequently, thalassemia patients with sleep disorders may experience impaired cognitive function. In our study, cognitive function was assessed by screening mathematic grades as a simple measure to reflect cognitive abilities. We found significantly lower mathematic grades in TDT group. However, when focusing the association with HS, we did not observe a correlation. It is essential to recognize that our study results were based on screening questions, which may have lower reliability. In addition, some previous studies have reported no association between snoring and cognitive deficits in preschool children.[61,62] Therefore more reliable tools should be further investigated. Bottom of Form

Our study had some limitations; firstly, we were unable to perform PSG, which is considered a standard method for diagnosis OSA, due to budgetary constraints. This may have limited our ability to accurately assess the presence and severity of OSA in the study population. Additionally, both HS and OSA-18 questionnaire were recognized by the reliance on a subjective measure, which could introduce rater biases. Potential bias could occur from parental over-reporting of sleep associated problems among children. However, a recent study showed a significant association between parental reported HS and objectively measure pathologic snoring.[31-33] While the absence of PSG hindered the accuracy of OSA diagnosis, our data still indicated a trend to support the increased prevalence of sleep disturbance in thalassemia children compared to the general population. This suggests that HS in pediatric thalassemia should be closely monitored and recognized as an at-risk population for sleep-related issues. Furthermore, in our study did not find any significant associations for many variables in HS. However, this lack of significant findings may be attributed to the limited sample size utilized in the study. Therefore, further research with a larger sample size is necessary to explore this trend in greater detail and obtain more robust conclusions.

CONCLUSION

Our study reviewed a higher of HS in thalassemia children. Several factors demonstrated strong associated with HS including nasal congestion, and male gender. The quality of life of our thalassemia children assessed by OSA-18 was generally good, together with low serum ferritin levels when compared to previous studies. The implementation of standard of care protocol for TDT patients, including regular blood transfusion and effective iron chelation, may contribute to the attenuation of nasopharyngeal narrowing in thalassemia patients. The current authors believe that parent reported HS can be used as a simple indicator for early diagnosis and appropriate medical intervention for OSA.

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Conflict of Interest Statement

The authors declare no conflict of Interest.

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