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Original Research Article

Association of lung function by spirometry with serum ferritin in transfusion-dependent thalassemia patients in a tertiary care centre

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ABSTRACT

Background: β-thalassemia major is an inherited, transfusion-dependent chronic anemia which is caused by decreased production of β-globin chains required for formation of hemoglobin. Regular blood transfusion is most important factors that help in improving the survival of patients with TM; however, it leads to iron deposition in many organs such as lung. Most studied concerned about effect of iron on lung functions, revealed abnormalities, but limited data were observed. The aim of our study was to determine pulmonary function abnormalities in children with thalassemia major and assess the relation between these abnormalities and iron overload.
Methods: This study had included 51 children in each group, aged between 6 and 18 years (28 males and 23 females) with TM. All included children were subjected to full clinical examination and laboratory investigations including complete blood counts and serum ferritin. Pulmonary function tests (PFTs) were assessed in all included children using spirometry.
Results: 31.4% patients had restrictive lung functions. Spirometer parameters i.e., FEF25-75% (p value≤0.0001) and PEFR (%pred) (p value≤0.0001) had significant difference in both groups. FEF25-75% and PEFR had no effect of serum ferritin.
Conclusions: The lung may be considered a site for organ damage, and alteration of pulmonary function may be expected in transfusion-dependent patients in spite of no pulmonary symptoms or normal chest X-ray.

Key words: β-thalassemia, Ferritin, Pulmonary function

INTRODUCTION

Thalassemia is a common hematological disease in Egypt and other Mediterranean countries, resulting from a defect in globin synthesis, leading to decreased quantity of globin chains.[1]It represents a major popular health problem.[1] It is characterized by abnormal hemoglobin (Hb) production, which results in decreased delivery of oxygen to the tissues and ineffective erythropoiesis. So, to elevate capacity of the blood to carry oxygen, the patients should receive regular transfusions.[2,3] Ineffective erythropoiesis and regular blood transfusions lead to increased absorption of iron from gut, which will lead to iron overload. Although iron overload can be prevented by iron chelation therapy, iron is still deposited in many organs, especially the liver, lung, heart, and pancreas.[4] Many studies about the nature of lung function abnormality had conflicting results. Most studies on pediatric and adult patients revealed a predominant restrictive pattern on spirometry.[5] However, the specific etiology of the pulmonary dysfunction remains unknown. Several pathological mechanisms causing the pulmonary dysfunction in thalassemia had been described, such as iron overload and correlation with transfusion and allergy, but none of these had given a satisfactory explanation[4]. So far, in the literature, the most frequent

abnormal pattern had been reported in the pulmonary function test (PFT) in patients with thalassemia is the restrictive pattern.[6] With this background, we conducted this study to evaluate the pulmonary function tests in thalassemic patients with high ferritin and comparing them with non thalassemic children.

METHODS

This is cross sectional analytical study (cases transfusions dependent thallasemic children with high ferritin level. Control non thallassemic children with normal ferritin. This study was conducted in department of Paediatrics GMC Kota from April 2021 to September 2022. After taking study approval from institutional ethical committee, 51 subjects were studied in each groups.

Study population

Children with confirmed diagnosis of thalassemia and on regular transfusion attending thalassemia ward were included in study.

Exclusion criteria

Thalassemic children with co-existing congenital cardiac disease, respiratory disease congenital defects.

Statistical analysis

Descriptive statistics like Mean, Median and standard deviation were used to compare various quantitative parameters such as FVC, FEV1, FEV1/FVC, PEF (25-75%), PEFR and serum ferritin. Student "t" test were used to compare pulmonary function test parameter. Pearson's correlation analysis was used to correlate various pulmonary function test parameters with serum ferritin levels and total amount the blood transfusion. Probability value of less than equal to 0.05 was considered as statistically significant.

Children who fulfill the inclusion criteria for the study and having hemoglobin more than 9gm/dl will be selected. Informed consent was obtained from parents of all cases and controls. Details such as age, sex, age at diagnosis, age at first blood transfusion, Total No Of blood transfusions, duration of iron chelation therapy, pre transfusion hemoglobin level, ferritin level and physical examination findings will be recorded on a proforma. Pulmonary function test was done using Helios 702 spirometer. Pulmonary function test was done three times, and the best values were taken for the study. Serum ferritin level will be estimated by chemiluminescent immunoassay at the time of enrollment in study.

RESULTS

In our study there is significant (p value≤0.0001) difference between serum ferritin levels in both groups. In study group 9 paediatric patients had serum ferritin levels >2500 ng/dl, while in control group there is no such patient. Spirometer parameters i.e., FEF25-75% (p value≤0.0001) and PEFR (%pred) (p value≤0.0001) had significant difference in both groups.

Table 1: Demographic details of subjects in each group.

Parameter	Study group	Control group	P value
Total number	51	51	
Males	28	28	>0.05
Females	23	23	
Age range (years)	6-18 years	6-18 years	>0.05
Mean age±SD (years)	10.2±3.6 years	10.6 ± 3.9 years	>0.05

Table 2: Correlation between Serum Ferritin levels in both study and control groups cases.

Serum Ferritin levels (ng/dl)	Study group N (%), Mean±SD	Control group N (%), Mean±SD	P value
<2500	42 (82.35), (12.61±523.68)	51 (100), (182.37±90.68)	
>2500	09 (17.65), (2892.77±128.88)	00	<0.0001
Total	51 (100), (1549.54±788.60)	51 (100), (182.37±90.68)	
Median	1440.0	120.00	

Table 3: Spirometry parameters in both study and control cases.

Spirometry	Study group	Control group	P value
FVC (%pred)	103.29±16.08	106.74±11.31	0.213
FEV1 (%pred)	109.74±17.28	113.88±15.93	0.211
FEV1/FVC	106.19±11.73	106.49±8.30	0.884
FEF25-75%	82.94±18.51	101.01±15.13	<0.0001
PEFR (%pred)	85.98±23.98	100.45±17.93	0.0007

Mean value of FEF25-75% was less in study group (82.94), and mean value of PEFR (%pred) was also less in study group. Lung function in our study showed that 68.6% had normal lung function, while 16 patients had restrictive lung function.

Table 4: Effect on lung function.

Lung function	N	%
Restrictive	16	31.4
Within normal limit	35	68.6
Total	51	100

Table 5: Correlation of PFT parameters with serum ferritin.

Pulmonary test	Mean±SD	Serum ferritin	
		R value	P value
FVC (%pred)	103.29±16.08	-0.010	0.943
FEV1 (%pred)	109.74±17.28	-0.222	0.117
FEV1/FVC	106.19±11.73	-0.313	0.025**
FEF25-75%	82.94±18.51	-0.206	0.147
PEFR (%pred)	85.98±23.29	-0.255	0.070

*Correlation is significant at 0.05 level (2 tailed), **Correlation is highly significant at 0.01 level (2 tailed), Above table states that there is negative correlation of serum ferritin in cases and pulmonary tests.

DISCUSSION

In our study there is significant (p≤0.0001) difference between serum ferritin levels in both groups. In study group 9 paediatric patients had serum ferritin levels >2500 ng/dl, while in control group there is no such patient. Total mean serum ferritin level in study group 1549.54, and mean serum ferritin level in study group 182.37.8 patients had pre blood transfusion Hblevels 6-8 gm/dl while 43 patients had pre blood transfusion Hb levels 8-10 gm/dl. Spirometer parameters i.e. FEF25-75% (p value≤0.0001) and PEFR (%pred) (p value≤0.0001) had significant difference in both groups. Mean value of FEF25-75% was less in study group (82.94), and mean value of PEFR (%pred) was also less in study group.

Our results are comparable to Cooper et al, Keens et al, Hoyt et al.[7-9] While there is no significant difference between FVC, FEV1 and FEV1/FVC among both groups. There is negative correlation of serum ferritin in cases and pulmonary tests. Cumulative transfusions and pulmonary tests had negative correlation except FEF25-75%. FEF25-75% had weak correlation with total blood transfusion. Our findings are consistent with those of Carnelli et al, 1 Factor et al, 2 Tai et al, 5 Luyt et al,6 and Filosa et al.[7] This results were also comparable to study of Kanj et al, Cooper et al, Keens et al.[8-10] Iron chelation therapy was given to all cases. Spirometer parameters i.e., FEF25-75% (p value≤0.0001) and PEFR (%pred) (p value≤0.0001) had significant difference in both groups. Mean value of FEF25-75% was less in study group (82.94), and mean value of PEFR (%pred) was also less in study group. While there is no significant difference between FVC, FEV1 and FEV1/FVC among both groups. There is negative correlation of serum ferritin in cases and pulmonary tests.

Lung function in our study showed that 68.6% had normal lung function, while 16 patients had restrictive lung function. Our findings are consistent with those of Carnelli et al, Factor et al, Tai et al, Luyt et al and Filosa et al.[10-14] Similarly in study of Kanj studied 36 patients (17 males and 19 females) with thalassemia major by performing pulmonary function testing (PFT) and Twenty-three patients had normal PFTs, eleven patients (30.6%) showed a restrictive pattern (significant decrease in both TLC and DLCO), and only two patients (5.6%) showed an obstructive pattern.[15] A significant negative correlation was found between serum ferritin and restrictive parameters, DLCO and TLC (p=0.01 and p=0.03, respectively).

Limitations

This is a single centre hospital based study, Large no. Of thallassemic children should have been enrolled to validate our results finally and our result should not be extrapolated to all thallassemic children, which may need further validate in large cohort and longer duration of time.

CONCLUSION

Recent studies have focused on pulmonary involvement and pathophysiology of lung damage. The goal of this study was to investigate the pulmonary abnormalities in thalassemic patients and iron overload. In our study 30% patients had restrictive lung functions. Spirometer parameters i.e., FEF25-75% (p value≤0.0001) and PEFR (%pred) (p value≤0.0001) had significant difference in both groups. However, there is negative correlation of serum ferritin in cases and pulmonary tests. Hence, we can conclude that the lung may be considered a site for organ damage, and alteration of pulmonary function may be expected in transfusion-dependent patients in spite of no pulmonary symptoms or normal CXR. One way to do this is to evaluate the respiratory system by PFT to prevent the squeal of pulmonary disease.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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