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SPIROMETRIC TESTS IN PATIENTS WITH THALASSEMIA MAJOR

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ABSTRACT

Background: Pulmonary function abnormalities have been described in patients with thalassemia major. Of these, restrictive abnormalities are the most frequent. Aim: To show the effects of thalassemia on the lung functions of patients with thalassemia major. **Method:** From February to December 2021, Babil Maternity and Children Teaching Hospital in Hilla, Iraq, studied 125 individuals, 65 of whom had thalassemia major and 60 normal children as controls. Children aged 6-14 attended the hospital's hereditary blood center. Pulmonary function tests, SpO2, and serum ferritin were also performed. Results: The study found a significant decrease in forceful expiratory volume and vital capacity for thalassemia patients compared to the normal group (P value < 0.05), but no significant difference in SpO2 (P value > 0.05). Lung limitation was minor in 37% of patients, moderate to severe in 3%, and normal in 60%. The study indicates a substantial rise in serum ferritin levels compared to the control group (P < 0.05). The study found no link between serum ferritin and forceful vital capacity. Conclusion: There was a significant decrease in forceful expiratory volume in one second and forceful vital capacity. The most common pulmonary functions test effects in thalassemia patients was the restrictive pulmonary abnormality.

KEYWORDS: Spirometric, Tests, Thalassemia, Major.

INTRODUCTION

Thalassemia is a heterogeneous group of heritable hypochromic anemias varying in severity. Genetic defects include total or partial deletions of globin chain genes, nucleotide substitutions, deletions, or insertions. These genetic alterations lead to decreased or absent mRNA for one or more globin chains or the formation of defective mRNA, resulting in decreased or suppressed hemoglobin polypeptide chain synthesis.[1,2] Thalassemia major (TM) is marked by abnormal hemoglobin synthesis, which reduces oxygen delivery to tissues, causes ineffective erythropoiesis, and leads to iron overload.[3,4] To compensate, patients receive regular transfusions, which can cause generalized iron loading in organs such as the heart, liver, endocrine organs, and lungs.[3,5,6] Epidemiologically, over 200 mutations lead to reduced or absent globin production.[7,8] Although most mutations are rare, 20 common alleles account for 80% of known thalassemia cases globally. Approximately 3% of the world's population carries β-thalassemia alleles, with 5-10% of the population in Southeast Asia carrying α-thalassemia alleles. In the United States, an estimated 2,000 individuals have β-thalassemia major.[7,9] Pathophysiologic ally, the reduction (beta+) or absence (beta0) of beta globin chains results in an excess of unbound alpha globin chains, which precipitate in erythroid precursors in the bone marrow, causing their premature death and ineffective erythropoiesis. The mutation's nature at the beta globin gene on chromosome 11 determines the degree of globin chain reduction. Peripheral hemolysis, contributing to anemia, is less prominent in thalassemia major than in thalassemia intermedia but occurs when insoluble alpha globin chains damage peripheral erythrocyte membranes. Anemia stimulates erythropoietin production, leading to intensive but ineffective bone marrow expansion, which causes bone deformities, hepatosplenomegaly, and extramedullary erythropoiesis.[6,7,10] Clinically, severe β-thalassemia presents with anemia, bone marrow expansion, hepatosplenomegaly, and extramedullary hematopoiesis.[11] Patients exhibit pallor, jaundice, frontal bossing, and abdominal enlargement due to hepatosplenomegaly. Early transfusion therapy can mitigate these symptoms if hemoglobin levels are maintained at 9-10 g/dL.[12,13] Anemia and hypoxia affect serum hepcidin expression, a key regulator of intestinal iron absorption. Low hepcidin levels lead to increased iron release from macrophages and higher gastrointestinal iron absorption.[14] Iron overload manifests prominently in severe β-thalassemia, with

cardiac dysfunction being a significant cause of early death. Endocrine abnormalities such as hypogonadism, hypothyroidism, and diabetes mellitus are also common. While liver iron deposition can be substantial, functional abnormalities usually remain mild unless iron overload is severe. Chelation therapy can prevent and potentially reverse iron overload complications.[12,15] Cardiac issues include arrhythmias and congestive heart failure, with improvement seen through continuous desferrioxamine interfusion and combination therapy with deferiprone or deferasirox.[16] Endocrine abnormalities include growth retardation, hypogonadism, impaired glucose tolerance, and hypothyroidism.[7,12,17] Liver abnormalities, often mild, can become severe with hepatitis C infection, leading to cirrhosis and hepatocellular carcinoma.[18] Other complications include osteoporosis, thromboembolism, and chronic skin ulceration.[12,19] Nutritional deficiencies are also common.[12] Diagnosis typically involves clinical suspicion in infants with severe microcytic anemia, mild jaundice, and hepatosplenomegaly. Hematological diagnosis is made through RBC indices showing microcytic anemia and peripheral blood smear analysis. DNA diagnosis of the β-thalassemia mutation and testing for genetic modifiers are recommended for definitive diagnosis.[7,10] Pulmonary function tests (PFTs) are crucial in investigating and monitoring respiratory pathology in thalassemia major patients, often revealing restrictive abnormalities, although the exact etiology remains unknown.[19] Serum ferritin levels are used to diagnose iron overload; as increased levels indicate iron-related diseases.[20] This study is aimed to measure some of the pulmonary functions to show the effects of thalassemia on the lungs of patients with thalassemia major.

METHOD

This study was done in Babil Maternity and Children Teaching Hospital in Hilla / Iraq from February to December 2021 on 125 cases including 65 patients with thalassemia major and 60 normal children taken as a control group. The age range was between 6-14 years attending the hereditary blood center in the same hospital. The patients with chronic illness such as cardiac, respiratory or renal disease apart from thalassemia major and recent respiratory tract infection were excluded. **History and physical examination** were performed on patients and control. The history included age, gender, and medical diseases. The weight in Kg and height in cm were measured. The pulmonary function tests were measured by using portable spirometer; Spirotnk2 (Mir company). The children were initially trained on how to perform the test properly. Each test was performed 3 times, and we selected the best performance. The parameters were used (FEV1, FVC, FEV1/ FVC) and SpO2. Serum ferritin was measured by Minvidas Co. instrument. The data were collected, organized, and tabulated using the SPSS software version 23. The results were expressed in the form of numbers, ranges, and the mean ± standard deviation. Independent *t*-test used to analyze the difference in means between the two groups. *P* value <0.05 was considered to be statistically significant.

RESULTS

The investigation comprised 65 patients, with 46 males (71%), and 19 females (29%). The mean age of the patients was 10.26 ± 1.82 years. The pulmonary function tests were conducted on them and compared to the control group, which consisted of 60 normal children. The control group was composed of 42 males (70%) and 18 females (30%). The mean age of the children was (9.87 ± 1.8) years, as illustrated in Table 2.

Table 2: Demographic data.

Group	Age (years) Mean ± SD	Gender	
		male	female
Patients group	10.26 ± 1.82	46 (71%)	19 (29%)
Control group	9.87 ± 1.8	42 (70 %)	18 (30 %)
P value	>0.05		

The measurements of pulmonary function tests, such as FEV1 and FVC, were compared in this study. The following table 3 illustrates that there was a substantial decrease in FEV1 and FVC for thalassemia patients when compared to control patients. However, there was no significant difference in FVC/FEV1 and Spo2 between the two groups.

Table 3: FEV1, FVC, FEV1/FVC and Spo2 values.

Parameters	Group	No.	Mean ± SD	P value
FEV1	Patients	65	97.24 ± 18.32	< 0.05
	control	60	109.65 ± 12.77	
FVC	Patients	65	91.5 ± 22.20	< 0.05
	control	60	109.65 ± 19.18	
FEV1/FVC	Patients	65	108.76 ± 20.52	> 0.05
	control	60	104.93 ± 10.41	
SpO2	Patients	65	98.35± 0 .74	> 0.05
	control	60	98.40 ± 0.53	

The interpretation of the pulmonary function tests for patients with thalassemia major demonstrates that moderate to severe restriction is present in only 2 (3%), while mild restriction is present in approximately 24 (37%) patients. The remaining 39 (60%) patients are considered normal, as illustrated in Figure 5.

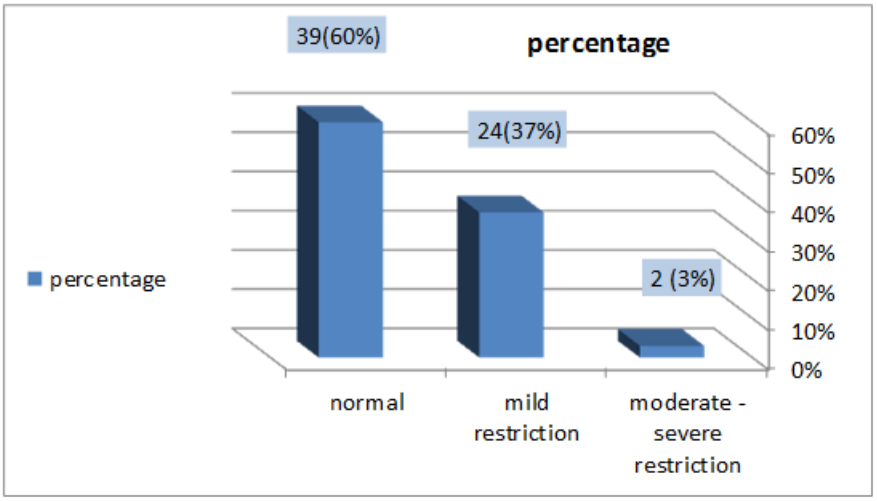

Figure 5: Shows the grading of pulmonary functions of the studied group.

The study shows significant increase in serum ferritin values in compared with control group as table (4) below.

Table 4: Serum ferritin values.

Group	No.	Serum ferritin Mean ±SD	P value
Patients	65	2981.89 ± 2523.47	< 0.05
Control	60	45.73 ± 17.93	

The study also shows no correlation between FVC and serum ferritin as illustrated in figure (6).

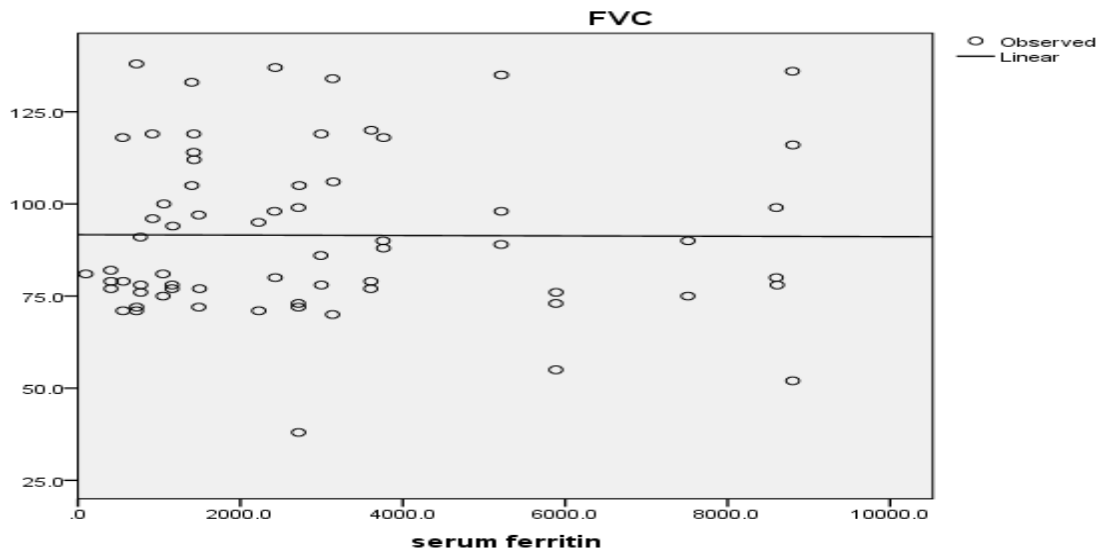

Figure 6: Relation between forced vital capacity (FVC) and serum ferritin.

DISCUSSION

In this study, pulmonary function tests, including FEV1, FVC, and the FEV1/FVC ratio, were measured. The results indicated a significant decrease in FEV1 and FVC for thalassemic patients compared to the control group (P<0.05). These findings are consistent with those of Buddu A. et al.[1], Derya and Emine[3], and Eugene Y. et al.[21], who also reported a reduction in FEV1. No

significant difference was observed in the FEV1/FVC ratio between patients and the control group (P>0.05). This result aligns with the findings of Derya Ozyourk and Emine D. Misirlioglue[3], but contrasts with those of Buddu A. et al., who noted a reduction in the FEV1/FVC ratio.[1] The SpO2 readings for the patient group showed a non-significant decrease compared to the control group (P>0.05), possibly because most patients had normal pulmonary function tests. Expanding the test to include adults might yield different results. The pulmonary function tests for patients with thalassemia major indicated mild restriction in about 37% of patients, moderate to severe restriction in 3%, and normal results in 60%. This study agrees with Buddu A. et al., who found that thalassemic patients exhibit a restrictive pattern. In their study, 95% had a restrictive pattern, with moderate restriction in 59%, mild restriction in 23.8%, and severe restriction in 12%.[1] Similarly, Azita Azarkeivan et al. reported that 72.7% had a restrictive pattern, 25.3% had normal results, and 3% had a combined pattern.[22] The variations in pulmonary function test percentages may be due to differences in patient age, as the restrictive component of the disease is mild and progresses slowly with age.[21] The study also showed a significant increase in serum ferritin levels in the patient group compared to the control group (P<0.05), consistent with findings by Amli D. et al.[23] and Azita Azarkeivan et al.[22] However, no correlation was found between FVC and serum ferritin, which is in agreement with Derya Ozyourk and Emine D. Misirlioglue[7], and Azita Azarkeivan et al.[22] Similarly, Amli D. et al.[23] found no correlation between serum ferritin and pulmonary function test parameters. This contrasts with the findings of Prapaporn Pornsuriyasak et al., who reported an inverse correlation between FVC and serum ferritin.[24]

CONCLUSION

From this study, we found there was significant decrease in FEV1 and FVC. The most common abnormality in thalassemia patients was the restrictive type.

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