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Original article

Assessment of Cardiovascular fitness in transfusion-dependent Thalassemia patients through Six Minutes' Walk Test

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Abstract:

Background- Thalassemia is a chronic disease affecting children growth & development since early age. 6MWT is easy and effective means to study cardio-vascular fitness.

Aim- To assess Cardiovascular fitness in transfusion-dependent Thalassemia patients through Six Minutes Walk Test(6MWT).

Methodology- A cross-sectional study was conducted in MGM MC & hospital Navi Mumbai, 70 transfusion-dependent thalassemia patients with an age group of 8-12(n=25), 13-17(n=24) and 18-25(n=21) years were enrolled in the study. Study parameters were measured at rest, immediately and 10 minutes after 6MWT. Total distance walked was recorded. Statistical analysis was performed applying Student's t test, one way ANOVA. A p-value of $\leq$0.05was considered significant.

Result- The mean $\pm$ SD of Pre transfusion Hb in 3 age groups are as; group I:7.1$\pm$1.2; group II: 7.3$\pm$0.82 and group III:7.42$\pm$0.77. Distance traveled during 6MWT in group III is significantly shorter than groups I & II. There is significant difference in HR and BP in all the age groups and in SpO2 in groups I & II.

Conclusion- It was concluded that there can be a lowering in performance with an increase in age.

Keywords- Thalassemia, Six minutes' walk test, cardiovascular fitness.

Introduction:

Thalassemia is a hereditary blood disorder in which globin chain production is decreased or absent,[1,2] resulting in fragile atypical red blood cells (RBCs) that are readily haemolyzed, causing persistent anemia.[3] According to the severity of the disease, thalassemia is divided into two groups: transfusion-dependent and non-transfusion dependent Thalassemia.[4]

Thalassemia is a chronic condition with health and emotional problems like physical deformities, growth retardation, and delayed puberty and bone abnormalities.[5,6] Patients with thalassemia frequently have severe problems such as cardiac iron overload, renal disease, Endocrinopathies, and infections.[7]

Children with thalassemia are much less energetic and their muscular strength, & flexibility, are often reduced.[8] Pain is an emerging consequence of thalassemia of unknown mechanism. The iron overburden, reduced haemoglobin levels, and poor bone density were probable reasons.[9]

Cardiac T2* MRI which evaluates the degree of cardiac iron overload is an expensive test and not widely available. Hence, simple test like 6MWT can be used as a screening technique for cardio-respiratory fitness in thalassemia. The Six minutes walk test (6MWT) is relatively easy and effective means of evaluating the cardiorespiratory fitness.[10] The 6MWT measures a person's endurance ability, which is related to the energy spent in various everyday activities and reflects the activity efficiency.[11]

Aim & Objective:

To assess Cardiovascular fitness in transfusion-dependent Thalassemia patients through Six Minutes Walk Test(6MWT).

Material & Method:

Study population: A cross-sectional study was conducted in MGM MC & hospital Navi Mumbai. Transfusion-dependent thalassemia children, adolescents and young adults were enrolled in the study from October 2020 to August 2021.

Sample size: 70 Transfusion-dependent thalassemia children, adolescents, and young adults with an age group of 8-25 years were enrolled and divided into three age groups I (8-12 years), II (13-17 years), and III (18-25 years). Subjects were selected using purposive sampling which satisfied inclusion criteria.

IEC Approval: The study was approved by the Ethics Committee of MGM Medical College, Navi Mumbai. Prior to participating in the study, the children and their parents were interviewed to explain the objective, methods, and possible advantages of the study, and written informed consent was taken from them.

Inclusion criteria:

1. The children who came for regular blood transfusion at the MGM hospital paediatric outpatient clinic.
2. Patients with age group of 8-25 years.

Exclusion criteria:

1. Patients who were not willing to participate.
2. Any conditions which limit exercise performance
3. Patients who were unfit for the test because of severe anaemia or cardiac failure as per the treating doctor's advice.

Tool Used:

1. The cardiovascular fitness was assessed through Six minute's walk test(6MWT), following the guidelines of the American Thoracic Society[11] pre-transfusion.
2. Anthropometric measurements like Weight (kg) and height (cm) were recorded using an anthropometric digital weighing scale (MI-120T model), Meditrin instruments, India. Body mass index (BMI) was calculated as weight (kg)/height2 (m).
3. History was collected from the patient's medical record.
4. Pre – transfusion Haemoglobin level was recorded.
5. Cardiovascular parameters measured are Systolic blood pressure (SBP), Diastolic Blood pressure (DBP), SpO2, and heart rate (HR). A digital automatic BP monitor (HEM_8712 model) Omron sphygmomanometer was used to monitor systolic (SBP) and diastolic (DBP) blood pressure; a portable pulse oximeter (Omron-CMS50N model) was used to assess SpO2, and heart rate (HR).

Procedure:

The 6MWT was conducted in a 30-meter long corridor with markings at each end indicating the start and finish of the trajectory.[11] Patients were given both theoretical and practical instruction on how to perform 6MWT. Before starting the test, patient was resting for the first 15 to 20 minutes.

Instructions given are as followed:

1. Instructor showed start and end mark of the route to patients and demonstrated before they performed.
2. Patients were asked to walk along the distance of 30 meters of corridor and back, at their own pace for six minutes.
3. At the end of six minutes, the patient was asked to sit down, the parameters were measured, the total distance walked was recorded in meters. The number of rounds noted manually, and the time was recorded using a stopwatch.[10]
4. Patients who felt tired and unable to walk for six minutes were asked to sit down.

All Cardiovascular variables were measured at rest, immediately, and 10 minutes after the 6MWT in a sitting position.[10]

Statistical analysis:

The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS). The Statistical analysis was done applying the paired Student's t-test and one-way ANOVA. The P value ≤ 0.05 was considered statistically significant. The data is presented using the mean and standard deviation (SD).

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Result:

This study assessed 70 patients with transfusion-dependent thalassemia which were divided into three age groups as groups I (8-12 years), II (13-17 years), and III (18-25 years).

Table 1: Demographic characteristics expressed in mean ±Standard deviation; for group I: Age 9.47±1.31 years, Weight 22.3±4.9 Kgs, Height 125±9.1 cm; for group II: Age 14.3±1.33 years, Weight 31.5±8.8 Kgs, Height 146±11.5 cm; for group III: Age 21.4±2.6 years, Weight 38.6±8.4 Kgs, Height 150±11.5 cm.

Table 2: The mean ± standard deviation of Pre transfusion Hb in three age groups are as; group I has 7.1±1.2; group II has 7.3±0.82 and group III has 7.42±0.77. There is no significant difference in Pre-Transfusion Hb level between different age groups (p=0.5). Distance travelled by patients during 6MWT in group III is significantly shorter than group I & II (271±29.1 < 276 ± 75, 289± 41.6 p=0.03).

Table 3: Mean± standard deviation of variables measured at rest, after a walk, and after 10 minutes of walk in three different age groups (8-12, 13-17, 18-25). Analysing the variables in 70 thalassemic patients it is found that Cardiopulmonary parameters (HR and BP) showed significant differences immediately after a walk and after 10 minutes of walk.

Table 4: Difference in variables at rest and immediately after a walk in Six minutes walk test**.** Group I: HR (p-0.01), SBP (p-0.001), DBP (p-0.01); Group II: HR (p-0.02), SBP (p-0.01), DBP (p-0.001) and in Group III: HR (p-0.03), SBP (p-0.03), DBP (p-0.05). It was observed that there is a significant increase in the parameters immediately after walk when compared with the parameters at rest. There is a increase in SpO2 in group I (significant increase immediately after walk p-0.03) & group II (increase immediately after walk p-0.06) but not in group III (no difference after walk p-0.8).

Table 5: Difference in variables immediately after a walk and 10 minutes after walk in Six minutes walk test**.** Group I: HR (p-0.001), SBP (p-0.01), DBP (p-0.01); Group II: HR (p-0.09), SBP (p-0.01), DBP (p-0.001) and Group III: HR (p-0.02), SBP (p-0.01), DBP (p-0.03). Decrease after 10 minutes when compared with parameters at the end of the exercise. There is a significant decrease in SpO2 after 10 minutes in group I (p-0.05) & group II (p-0.05) but not in group III (no difference when parameters compared at end of walk and after 10 minutes-p-0.7)**.**

Table 1 – Mean ± SD of Demographic data in Six minutes walk test in different age groups.

Age group	No of participants	Age(years)	Weight (Kgs)	Height (cm)
8-12	25	9.47±1.31	22.3±4.9	125±9.1
13-17	24	14.3±1.33	31.5±8.8	146±11.5
18-25	21	21.4±2.6	38.6±8.4	150±11.1

Table 2 – Mean±SD of Pre- transfusion Hb level and Distance walked in Six minutes walk test in the different age groups.

Age(years)	No. of participant	Pre transfusion Hb (gm/dl)	Distance travelled in 6 minutes (meters)
8-12	25	7.1±1.221	276±75.8
13-17	24	7.3±0.82	289±41.6
18-25	21	7.42±0.77	271±29.1
P-value	--	0.5	0.03*

Level of significance: Significant*; Highly significant**

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Table 3 – Mean±SD of Variables at rest, immediately after a walk and 10 minutes after a walk in different age groups in Six minutes walk test

Age	No. of participants	Variables	At rest	Immediately after walk	10 minutes after the walk
8-12 years	25	HR (beats/min)	109.1±9.4	114.9±11	97.6±11
		SBP (mmHg)	98±11	118.7±4.4	95.8±11.6
		DBP (mmHg)	62.3±9.1	66.6±6.3	60.6±8.4
		SpO2(%)	98±0.9	95.1±3.9	97±2
13-17 years	24	HR (beats/min)	95.5±9.5	100.5±10.5	93.9±5.8
		SBP (mmHg)	105±5.4	112±8.5	102±9.2
		DBP (mmHg)	66.1±6.57	73.6±6.42	64.9±8.6
		SpO2(%)	98.4±0.8	97±2.11	98±0.6
18-25 years	21	HR (beats/min)	96±6.3	100±6.9	94.8±8.0
		SBP (mmHg)	107±10.3	114±8.2	107±12.8
		DBP (mmHg)	71±9.42	75.2±7.5	69.5±9.19
		SpO2(%)	98±0.72	98.5±0.7	98.4±0.8

Table 4 – Difference in variables at rest and immediately after a walk in Six minutes walk test

Age	No. of participants	Parameters	At rest	Immediately after walk	P-value
8-12 years	25	HR (beats/min)	109.1±9.4	114.9±11	0.01**
		SBP (mmHg)	98±11	118.7±4.4	0.001**
		DBP (mmHg)	62.3±9.1	66.6±6.3	0.01**
		SpO2(%)	98±0.9	95.1±3.9	0.03*
13-17 years	24	HR (beats/min)	95.5±9.5	100.5±10.5	0.02*
		SBP (mmHg)	105±5.4	112±8.5	0.01**
		DBP (mmHg)	66.1±6.57	73.6±6.42	0.001**
		SpO2(%)	98.4±0.8	97±2.11	0.06
18-25 years	21	HR (beats/min)	96±6.3	100±6.9	0.03*
		SBP (mmHg)	107±10.3	114±8.2	0.02*
		DBP (mmHg)	71±9.42	75.2±7.5	0.05*
		SpO2(%)	98±0.72	98.5±0.7	0.8

Level of significance: Significant*; Highly significant**

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Table 5 –Difference in variables immediately after a walk and 10 minutes after walk in Six minutes walk test

Age	No. of participants	Variables	Immediately after walk	10 minutes after the walk	P-value
8-12 years	25	HR (beats/min)	114.9±11	97.6±11	0.001**
		SBP (mmHg)	118.7±4.4	95.8±11.6	0.01**
		DBP (mmHg)	66.6±6.3	60.6±8.4	0.01**
		SpO2(%)	95.1±3.9	97±2	0.05*
13-17 years	24	HR (beats/min)	100.5±10.5	93.9±5.8	0.09
		SBP (mmHg)	112±8.5	102±9.2	0.01**
		DBP (mmHg)	73.6±6.42	64.9±8.6	0.001**
		SpO2(%)	97±2.11	98±0.6	0.05*
18-25 years	21	HR (beats/min)	100±6.9	94.8±8.0	0.02*
		SBP (mmHg)	114±8.2	107±12.8	0.01**
		DBP (mmHg)	75.2±7.5	69.5±9.19	0.03*
		SpO2(%)	98.5±0.7	98.4±0.8	0.7

Level of significance: Significant*; Highly significant**

Discussion:

In this study, Cardiovascular fitness of transfusion-dependent thalassemia patients was assessed through Six Minutes walk test. Children and Adolescents with thalassemia may not have overt Cardiovascular symptoms till significant cardiac iron overload has occurred. Also, the cardiac signs & symptoms like tachycardia, tachypnoea and fatigue, breathlessness may be attributed to chronic anaemia by the parents and treating physicians.

In the literature, there were very few studies where Six Minutes walk test was used to assess cardiovascular fitness in hemoglobinopathies, especially transfusion-dependent thalassemia. As there are not many publications in the literature evaluating the cardiopulmonary efficiency in Thalassemia, the focus of this study was to assess the cardiopulmonary fitness in Thalassemia patients using Six Minutes walk test.

In the study, thalassemia patients were divided into three age groups as groups I (8-12 years), II (13-17 years), and III (18-25 years). When compared to literature, the primary findings revealed that children with thalassemia had lower exercise capacity than healthy age-matched subjects.

Reduced exercise capacity might be ascribed to increased pain and impaired physical abilities. This finding is supported by the findings of Ismail D et al.[1], who found that in patients with thalassemia, there is a decreased value of handgrip strength due to the presence of increased joint pain and decrease exercise capacity. The relative long effects of continuous transfusion on nutrition, physical strength, and development may be the cause of decreased exercise capacity in children with thalassemia.[12] "Body composition is influenced by many factors, including age, gender, gonadal status, nutrition, exercise, and hormonal factors", according to Boot et al.[13]

The majority of the patients with thalassemia had a family history and were on iron-chelation therapy. These findings are in accordance with those of Ayoub et al.[14], who found similar results in Saudi Arabia in terms of family history and chelation therapy. In terms of Hb concentration, Hb level is much lower, these findings corroborated Galanello and Origa's[15], findings that individuals with thalassemia major have reduced Hb level (7 g/dl) and low RBCs count, resulting in anemia. Furthermore, reduced haemoglobin levels are linked to a variety of symptoms, including weariness, lethargy, and decreased concentration, all of which contribute to poor quality of life in these children, as shown in Shumaker and Berzon's study.[16] Haemoglobin value, may also be linked to lower exercise capacity. Patients with group III walked significantly shorter distances than group I and

group II. This might be because with increasing age, these patients get adopt to decreased Hb level in body. Hence their exercise capacity is reduced as compared to younger age group. [10,17]

At the end of the 6MWT, a substantial rise in HR and SpO2 was seen in the age group I and II immediately after exercise. But group III shows rise in HR but no significant changes in SpO2 in the current study. Similar results were found by Lammers et al.[18] According to Lammers et al. SpO2 changes minimally during the 6MWT in healthy youngsters, but HR increases significantly. Chronic anaemia results in decreased tissue oxygenation, importantly during exercise, when the supply for oxygen is increased to satisfy the increased necessity of energy. But due to compensatory mechanisms, such as Higher heart rate during exercise, elevated systolic volume, and lower peripheral vascular resistance decreases erythrocyte resistance in capillary transit and oxygen delivery to the tissues, enabling mixed venous blood saturation to be close to normal.[10,19] This might account for the current findings, which shows rise in HR with no significant changes in SpO2.

There was an increase in SBP and DBP immediately after a walk and decreases after 10 minutes. This result is similar to observed in Barden et al. which shows increase in SBP and DBP may be linked to a drop in HR and, as a result, a decrease in cardiac output, as well as the maintenance of vasodilation for a length of time following exercise. [20]

Limitation: There are some limitations of this study as there was no control group & sample size was small. Furthermore, there is very less previous studies that have examined Six minutes walk test with thalassemia, which makes it difficult to compare our findings to those of others research.

Conclusion:

Thalassemia has a detrimental influence on individual's strength and endurance. Exercise capacity in patients with thalassemia is low compared to that suggested for their age group. Patients with age group III had performed worse in terms of distance walked after Six minutes walk test compared to age group I and II.

More studies with similar designs for assessing exercise capacity in patients with thalassemia should be done. It was concluded that there can be a lowering in performance with an increase in age. The 6MWT is a very useful tool for measuring cardiorespiratory fitness which can help us with a prognosis of disease and improving quality of life.

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