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PERVASIVENESS OF IRON DEFICIENCY IN THALASSEMIA TRAIT IN PAKISTAN

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Abstract:
Introduction: *Thalassemia is considered the most common genetic disease in the world, and about 7% of the world's population are carriers. The vast majority of such cases are iron deficient.*
Aim: *This study was undertaken to identify patterns of iron levels in the features of thalassemia, and thus to identify coexisting iron deficiency.*
Method: *This cross-sectional study was conducted at the Department of Medicine Unit-II of Services Hospital Lahore for one-year duration from June 2019 to May 2020. Adult anemia patients with hypochromic microcytic smear presenting to the outpatient clinic were screened for thalassemia based on clinical history, physical symptoms, and hemoglobin electrophoresis. A total of 50 anemia patients with thalassemia carriers were detected and selected for iron profile evaluation.*
Results: *Patients with iron deficiency detected on the basis of serum iron profile were compared with patients without iron deficiency. The mean age in the studied years was 30.38 ± 9.79 years. Among the studied population, 50% were men and 50% women. The highest incidence of coexisting iron deficiency was found in people aged 21-30 years. The frequency of iron deficiency among the b-type thalassemia trait was 30.2%. There was a statistically significant mean difference in Hb, MCV, MCH, MCHC, serum iron, TIBC, and S. saturation ferritin, indicating that subjects without iron deficiency had higher levels than subjects without iron deficiency ($p < 0.05$).*
Conclusion: *Clinical iron deficiency may occur in people with thalassemia disease / in carriers of hereditary hemoglobin disorders. A complex condition should always be suspected, and iron supplements are often needed to improve the anemia condition.*
Key words: *trait of β-thalassemia, iron deficiency anemia.*

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INTRODUCTION:

Thalassemia's are a heterogeneous group of genetic disorders of hemoglobin synthesis, all of which result from a decreased rate of production of one or more hemoglobin globin chains. Several types of thalassemia are described and named according to the affected globin chain, of which the most common clinical types are b, á, and ãâ thalassemia. Pakistan is dominated by Hb E disorders, where a single mutation in the globin gene is responsible for both reduced production of the b gene product and Hb E instead of Hb A. For this reason, it is called "thalassemic hemoglobinopathy" [1-2]. Thalassemia is considered the most common genetic disease in the world. WHO estimates that approximately 7% of the world's population are carriers? Every year, 300,000-500,000 babies are born with severe, homozygous states of the disease. The disease is very common in the Mediterranean, Middle East, South and East Asia, South Pacific and South China, with reported carrier rates ranging from 2% to 30%. In Pakistan, there are no definitive data on the status of a carrier of hereditary Hb disorders. Conservative World Health report estimates that 3% of our population are carriers of beta thalassemia, which means there are 3-6 million carriers of beta thalassemia in Pakistan [3-4]. The affected births per thousand b-thalassemia is 0.106. The microcytic hypochromic image of red blood cells is characteristic of thalassemia, but the vast majority of such cases have iron deficiency anemia. Iron deficiency is widespread worldwide, especially in developing countries such as Pakistan. Iron deficiency was found in 27.2% of beta thalassemia in northern India[5-6]. It is often impossible to distinguish between iron deficiency anemia and the trait of thalassemia either on the basis of red blood cell morphology or red blood cell markers. In this situation, this study was undertaken to establish the iron status pattern in carriers of hereditary hemoglobin disorders and to determine their coexisting iron deficiency. In this way, assessing the iron level of the thalassemia trait would assist in making decisions about iron treatment [7-8]. There are many conflicting findings regarding the link between thalassemia trait and iron stores. Some researchers have found that normal iron stores are reflected by measuring serum ferritin, others report that b-thalassemia features are often positive in iron balance and there is a high risk of iron overload. If severe iron overload has been reported in the group of patients with thalassemia disease, administration of iron in these cases may actually prove harmful and cause iron-related complications. On the other hand, some have found a higher incidence of iron deficiency in thalassemia than in the normal population. Iron deficiency is a common symptom of thalassemia in women of childbearing age and should be given adequate iron supplementation after iron stores have been assessed by measuring ferritin. Elevated hemoglobin A2 level is an important diagnostic feature of beta thalassemia [9-10]. It has been shown that coexisting iron deficiency does not affect the diagnosis of beta thalassemia on the basis of elevated Hb A2 levels. Contrary to the above observations regarding Hb A2 levels, some researchers have reported a reduction in Hb A2 levels in the presence of iron deficiency, even in the presence of the beta-thalassemia trait. In this situation, administering iron to these people increases the level of HbA2 and exposes the diagnosis of beta-thalassemia[11]. There are no previous studies that investigate iron status in the characteristics of thalassemia in Pakistan. Research was undertaken to determine the frequency of coexistence of iron deficiency and thalassemia carriers and to develop strategies for rational iron supplementation in these people.

MATERIALS AND METHODS:

This cross-sectional study was conducted at the Department of Medicine Unit-II of Services Hospital Lahore for one-year duration from June 2019 to May 2020. All patients with clinical anemia were sent for CBC with PBF, and people with microcytic hypochromic anemia were screened for Thalassemia is the basis of clinical history, physical outcomes, and ultimately hemoglobin electrophoresis. Citrate agar gel electrophoresis was performed at basic PH. People taking iron preparations or blood transfusions, suffering from acute febrile illnesses, inflammations, hematological diseases and liver diseases were excluded from the study. A total of 50 patients with anemia and carriers of thalassemia were selected for further studies. Among the subjects, the indexes of red blood cells (MCV, MCH, MCHC) and iron profile (iron levels S., ferritin, TIBC, transferrin saturation) were observed. Patients who were iron deficient in their iron profile were compared with patients without iron deficiency. The relevant information was recorded in a previously prepared data sheet. The data was analyzed using the SPSS version 19 statistical package.

RESULTS:

In total, 50 people with microcytic hypochromic anemia were selected, among whom the percentage of men and women was equal. The age range was 16-52 years.

Table I:*Distribution of the iron deficiency by carriers of thalassemia*

Iron (%)	Inherited hemoglobin disorders deficiency	Beta thalassemia E trait	Total trait (%) (%)
Present	13 (30.2)	0 (.0)	13 (26.0)
Absent	30 (69.8)	7 (100.0)	37 (74.0)
Total	43 (100.0)	7 (100.0)	50 (100.0)

The frequency of iron deficiency was 30.2% among the features of thalassemia b, but none of the features of Hb E showed iron deficiency (Table I and Fig. 1).

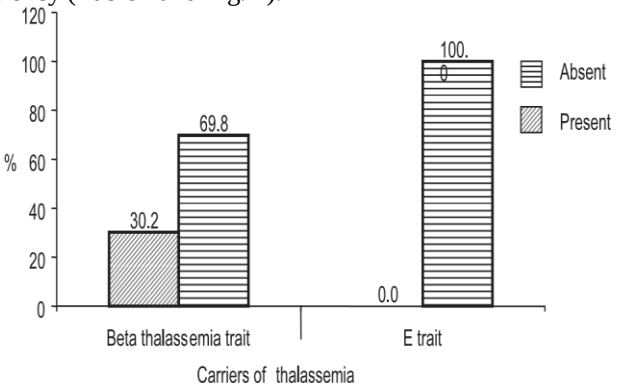

Fig.-1: *Bar chart of the iron deficiency among the carriers of thalassemia*

The mean age in the studied years was 30.38 ± 9.79 years. The highest incidence of coexistence of iron deficiency was found in people aged 21-30 (Table II).

Table II: *Distribution of the study subjects by age*

Age (in year)	Frequency(n)	Percent(%)
≤20	7	14.0
21-30	25	50.0
31-40	8	16.0
40-50	8	16.0
>50	2	4.0
Total	50	100.0
Mean ± SD (Range)	30.38 ± 9.79	(16-52)

There were statistically significant differences in the mean values of Hb, MCV, MCH, MCHC between the subjects without iron deficiency and subjects with iron deficiency (p value = 0.001) [Table III]. All these parameters were higher in iron-rich people than in iron deficient people.

Table III

Distribution of Hb, MCV, MCH, MCHC, S.Iron, TIBC, S. Ferritin, Transferrin saturation among study subjects.

	Mean	SD		p value*
Hb (g/dl)	With iron deficiency	6.88	1.17	0.001
	Without iron deficiency	10.23	1.47	
MCV (fl)	With iron deficiency	51.54	5.24	0.001
	Without iron deficiency	72.05	5.24	
MCH (pg)	With iron deficiency	15.15	2.21	0.001
	Without iron deficiency	21.65	2.69	
MCHC (g/dl)	With iron deficiency	29.69	2.21	0.923
	Without iron deficiency	29.78	2.81	

DISCUSSION:

The feature of b-thalassemia causes mild ineffective erythropoiesis associated with increased iron absorption. Thus, it can be expected to provide some degree of protection against iron deficiency, but this may not be true in all cases [11]. Most people with thalassemia trait create a microcytic hypochromic blood picture, but this change may not be solely due to abnormal globin chain production. A significant proportion of these cases are iron deficient, which affects the blood picture, and require iron supplementation to replenish the iron deficiency and raise Hb levels. Early diagnosis of Hb disorders and reduced iron intake by early adopters may play a major role in this clinical unit. On the basis of red blood cell morphology, it is often impossible to distinguish iron deficiency and the trait of thalassemia and the coexistence of both. Iron deficiency was found in a quarter of the traits, mainly in the age group 21-30 years[12-13]. A statistically significant mean Hb difference was found, indicating that subjects without iron deficiency had higher (10.23 g / dl) Hb levels than those with coexisting iron deficiency (6.88 g / dl). Mean MCV (72.05 fl vs 51.54 fl) and MCH (21.65 pg vs 15.15 pg) were also high in the non-iron deficient group and statistically significantly higher mean difference was found compared to the iron deficient group (p = 0.001) (Table III). The same was observed in another study. The results of the conducted studies indicate that in a significant number of 13 (26%) subjects with beta thalassemia trait with low (<12 µg / l) serum ferritin level, which indicates coexisting iron deficiency. On the other hand, in the study group, 7 patients had the Hb E feature and the serum ferritin level was normal. This study's finding is also in line with other studies in British Asiatic children [14-15].

Coexistence can be caused by various gastrointestinal disorders, chronic blood loss due to various worm infestations that are very common in Pakistan. Poor bioavailability and low dietary iron content, late weaning, low birth weight, prior iron deficiency should be considered as comorbid iron deficiency in the Pakistan context. Finally, fear of iron overload and its complications can lead doctors and their thalassemia patients to follow a strict iron-free diet from the time they are diagnosed.

CONCLUSION:

The phenotypic expression of the thalassemia trait varies widely and it is believed that iron absorption is increased in these individuals. However, this observation does not always exclude that iron deficiency may contribute to anemia among the features of thalassemia. Clinical iron deficiency anemia can often coexist with beta thalassemia, and iron supplementation is invariably necessary in deficient patients. Therefore, comorbid iron deficiency should always be considered in people with thalassemia anemia in the context of Pakistan's low socioeconomic status.

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