HAEMA (Αίμα) ISSN: 1108-2682
www.mednet.gr/eae/haema

Haema 2004; 7(3): 321-325
Original article

Iron status in subjects with β-thalassaemia minor

Nameer Mohammed Widad[1], Lamia Mustafa Al-Naama[3], Mea'ad Kadhum Hassan[2]

[1]Department of Paediatrics, [2]Department of Biochemistry, [3]Haemoglobinopathy Unit, College of Medicine, University of Basrah, Basrah, Iraq

Abstract. In this study, 116 patients with β-thalassaemia minor, and 142 apparently healthy control subjects were investigated for: haemoglobin, blood indices, serum iron, total iron binding capacity, transferrin saturation, and serum ferritin. Patients with β-thalassaemia minor had low Body mass index (BMI) value, but it was satistically insignificant as compared to that of the controls, being equal to 19.85±2.66 kg/m^2 compared to 20.61±4.28 kg/m^2 for the controls ($p > 0.05$). Haemoglobin level and most blood indices were significantly decreased ($p<0.001$) in patients with β-thalassaemia minor in comparison to the control group, with exception of red blood cells count that was significantly higher in β-thalassaemia minor individuals as compared with control subjects ($p<0.001$). Serum levels of iron, ferritin, and transferrin saturation were all increased significantly ($p<0.001$) in β-thalassaemia minor and in most age groups compared with controls. TIBC showed a decreased level in all age groups compared with control groups. In addition, β-thalassaemia minor subjects show about 12% increase in transferrin saturation and about 2-folds or more increase in serum ferritin levels, with a positive correlation between them ($r=0.41$, $p<0.01$). From this study we can conclude that there is a possibility of iron overload in subjects with β-thalassaemia minor; regular follow up of subjects with high levels of serum ferritin is recommended.

Key words: beta-thalassaemia minor • iron • tranferrin • ferritin • total iron binding capacity

✉ **Correspondence:** Lamia Mustafa Al-Naama, MD, Haemoglobinopathy Unit, College of Medicine, University of Basrah, Basrah, Iraq, e-mail: lamia_alnaama@yahoo.com

INTRODUCTION

Thalassaemias constitute a major health problem in many parts of the world particularly in Mediterranean basin, equatorial or near equatorial regions of Asia and Africa[1,2]. In 1999, WHO had estimated that the carrier frequency of β-thalassaemia in Iraq is about 3% and the annual births of homozygous β-thalassaemia are about 571 patients/year[2]. In Basrah, a recent premarital study on couples attending the Public Health Laboratory showed that the prevalence rate of β-thalassaemia is 4.6%[3].

The β-thalassaemia gene heterozygosity results in mild hypochromic microcytic anaemia. Most patients are asymptomatic. A mild decrease in RBC survival can be shown with a slight elevation of fecal urobilinogen, but overt haemolysis is usually absent. Peripheral blood shows typical microcytosis, hypochromasia and small target cells[4,5]. Symptomatic iron overload occurs infrequently in individuals with β-thalassaemia minor and it is attributed to either coincidental idiopathic haemochromatosis or, less commonly, inappropriate iron therapy[6]. The serum iron in a large series of heterozygous β-thalassaemia subjects shows con-

Received: December 3, 2003; Accepted: January 22, 2004

siderable variability, and there are usually no abnormalities of total iron binding capacity. Serum ferritin is either normal or slightly increased[7].

This study was carried out to determine the changes in iron status in subjects with β-thalassemia minor and compare them with subjects of a normal haemoglobin pattern.

PATIENTS AND METHODS

Patients

This study was conducted at Basrah Maternity and Children Hospital, on 116 patients with β-thalassaemia minor; mostly relatives of patients with β-thalassaemia major who attended the Thalassaemia Center at the Hospital from July 2000 to July 2001. Their ages varied from 1-60 years (47 males and 69 females). In addition to patients, 142 age-matched healthy subjects (with normal haemoglobin pattern) aged 1-61 years (69 males and 73 females) had served as a control group.

Both of patients and control groups were categorized into four main subgroups according to their age; group A (1-6 years), group B (7-12 years), group C (13-18 years) and group D (subjects >18 years). The following informations were obtained from subjects included in the study: age, sex, complaint, history of medical diseases, weight and height were recorded. Body mass index (BMI) was measured as weight (in kilograms) divided by the square of height (in meters).

Methods

The importance of the procedure was explained to all subjects participated in the study and/or their parents. Fresh venous blood (6 ml) was drawn from patients and controls. About 2 ml was collected into EDTA tubes and immediately tested for haemoglobin variant and haematological parameters. The reminder was transferred to plain tubes (without anticoagulant), centrifuged and sera was obtained for the biochemical investigations.

Haemoglobin, haematocrit (PCV), red cell counts, mean cell volume (MCV), mean cell haemoglobin (MCH) and mean cell haemoglobin concentration (MCHC) were estimated by using automated Coulter Counter MS9. Haemoglobin typing was performed quantitatively by an automated ion exchange HPLC system using β-thalassaemia short programme on the Bio-Rad VARIENT instrument (Bio-Rad Laboratories, Belgium). β-thalassaemia minor was identifi by characteristic elevation of HbA_2 ranging from 3.5 7%[4].

Serum iron and total iron binding capacity w tested within 24 hours by spectrophotometric meth transferrin saturation (%) was calculated mathem cally. The reminder sera were stored at -20°C, for later estimation of serum ferritin that was carried by CIS bio (UK) radioimmunoassay test as descri by the manufacturer.

Statistical Analysis

The results were expressed as mean±SD. The were analyzed statistically by one-way analysis of ance (ANOVA). While the correlation between data were tested statistically using simple linear gression, employing SPSS computer program. P < was considered to be the lowest limit of significa

RESULTS

The mean age of all four age groups of β-thal saemia minor individuals was 26.86±14.49 years. mean value of BMI was 19.85±2.66 kg/m^2, that lower than for the control group, but it was statisti insignificant as compared with control group. mean age of the control group was 21.01±14.21 y while the BMI value was 20.61±4.28 kg/m^2.

As illustrated in Table 1; the haemoglobin l (Hb), PCV, MCV, MCH and MCHC were all sig cantly decreased in individuals with β-thalassae minor in comparison to the control group (p<0.0 Red blood cells count was significantly higher i thalassaemia minor individuals as compared with trol subjects (p<0.001).

Regarding gender, there was a significant crease in haemoglobin concentration in female compared with males in both groups; the control thalassaemia minor (p<0.01 and p<0.001 respect ly). Concerning PCV there was a significant decr in females as compared with males in thalassae minor group only (p<0.01).

Table 2 shows the biochemical parameters w were investigated in this study for all groups. The rum levels of iron, ferritin, and transferrin satura were all increased in β-thalassαemia minor as c pared with controls. The differences between t groups were statistically significant (p<0.001).

The values of haemoglobin, serum iron, total b

Table 1. Haematological findings in patients with thalassaemia minor and their controls

		Control (n= 142)	β-thalassaemia minor (n=116)
Hb g/dl	**Male**	12.9±1.6	11.5±2.1
	Female	11.9±1.3	10.7±1.6
	Total	12.4±1.5	11.1±1.8*
PCV %	Male	42.5±3.7	38.6±4.4
	Female	38.4±3.8	34.7±3.5
	Total	40.4±3.7	36.0±4.2*
RBC counts x10⁶/µl	Male	5.4±0.5	6.1±0.4
	Female	5.1±0.4	5.8±0.7
	Total	5.3±0.5	5.9±0.7*
MCV fl	Male	78.9±5.5	70.1±6.9
	Female	78.1±7.4	69.3±8.5
	Total	78.5±3.6	69.3±3.9*
MCH pg	Male	26.8±2.7	22.4±2.8
	Female	25.8±2.7	22.1±3.5
	Total	26.3±1.4	22.2±2.58*
MCHC gm/dl	Male	32.9±1.6	30.7±5.2
	Female	32.2±2.2	30.4±4.6
	Total	32.6±1.9	30.5±3.9*

Results were expressed as mean ±SD
* Significantly different as compared with healthy subjects (P<0.001).

ing iron capacity (TIBC), transferrin saturation and ferritin in different age groups are presented in Table

Table 2. Iron status in the studied groups

Biochemical Parameters	Control (n=142)	β-thalassaemia minor (n=116)
Iron (µg/dl)	112.7±21	124.5±19.1*
TIBC (µg/dl)	279.2±33.8	286.5±39.7
Transferrin Sat. %	38.2±7.1	43.9±6.7*
Ferritin (µg/l)	63.5±48	147.1±91.9*

Results were expressed as mean±SD
* Significantly different as compared with healthy subjects (P<0.001).

3. Haemoglobin and TIBC showed a decreased level in all age groups compared with control group. However, this decrease was statistically significant only for haemoglobin levels in the first group (1-6 years) and in subjects older than 18 years (p<0.05 and p<0.001 respectively). On the other hand, serum iron, transferrin saturation and serum ferritin were higher in all age groups compared with controls. This elevation was statistically significant in the last age group (>18 years) for serum iron and transferrin saturation (p<0.05 and p<0.001 respectively). While it was statistically significant in all age groups (except in the third age group 13-18 years) for serum ferritin as compared with control groups.

Table 3. Haemoglobin and iron status in β-thalassaemia minor in different age groups

Age/years	Groups	Hb (g/dl)	Iron (µg/dl)	TIBC (µg/dl)	Transferrin saturation %	Ferritin (µg/l)
1-6	Control n=20	12.24±0.94	106.95±14.25	302.75±32.0	35.37±6.4	22.5±6.2
	β-Thal Minor n=13	10.16±2.68*	119.61±73	285.15±49.3	42.9±6.9	105.8±69*
7-12	Control n=23	11.84±1.1	111.26±23.43	307.74±35.83	36.17±6.7	32.8±21.4
	β-Thal Minor n=15	11.04±0.74	126.85±16.6	293.73±37.7	43.45±5.9	109.9±71.4*
13-18	Control n=24	12.0±1.42	113.1±19.7	300.96±27.91	37.73±6.5	75.5±49.8
	β-Thal Minor n=15	11.73±0.91	123.06±17.6	290.0±23.49	42.61±6.4	120.5±170.4
> 18	Control n=75	12.81±1.53	114.6±22.19	291.23±34.72	93.5±7.4	74.1±51.1
	β-Thal Minor n=73	11.09±1.93**	125.27±21.0*	284.47±41.3	44.41±7.0**	167.3±92.4**

Results expressed as mean ±SD
*, ** Significantly different as compared with healthy subjects (P<0.05 & P<0.001 respectively).

DISCUSSION

In Iraq, β-thalassaemia is considered as one of the important public health problems. This is because of the considerable burden on the children and their families as well as on health services. Furthermore, in Basrah, together with the presence of high prevalence of β-thalassaemia carriers (4.6%), there is also a high prevalence of other type of haemolytic anaemias, namely sickle cell anaemia (6.48%)[3] and G6PD deficiency (12.5%)[3,9].

In patients with β-thalassaemia minor, this study showed that there was no significant decrease in BMI as compared with controls. This can be attributed to that in this group only one β-gene is deleted and still there a single β-gene ready to be transcribed and compensate the defect[10].

It is well known that idiopathic haemochromatosis and thalassaemia are the most frequent genetic disorders associated with iron overload. In thalassaemia major and intermedia, the iron overload is a well defined situation. However, in thalassaemia minor, frequently an asymptomatic disease, there is no agreement about the situation of iron storage[11]. In this study although data on iron status in patients with β-thalassaemia minor seem to be within normal values, still most of these data differ from that of the control group. However, by age grouping of data, there was only a significant variation in some groups, which was mainly due to the size of the sample. We can conclude that haemoglobin level in subjects with β-thalassaemia minor was lower than that of the control group by 1-2 gm/dl. This mild anaemia is well established[7,12] and it is the result of mild ineffective erythropoiesis secondary to imbalance between α- and β-chain synthesis with the precipitation of the small excess of α-chains[7].

In addition to that, β-thalassaemia minor subjects show about 12% increase in transferrin saturation and about 2-folds or more increase in serum ferritin levels. A positive correlation between transferrin saturation and serum ferritin ($r=0.41$, $p< 0.01$) was observed (Figure 1). Findings close to our results were reported by de-Fonseca et al[11] and Barbic et al[13]. In subjects with β-thalassaemia minor, in addition to mild ineffective erythropoisis and slight increase in intestinal iron absorption, these subjects are often misdiagnosed as suffering from deficiency; therefore, they may be inappropriately treated with iron supplementation for extended periods[7,14].

From this study we can conclude that there is a possibility of iron overload in subjects with β-thalassaemia minor and there is a necessity to follow up subjects with high levels of serum ferritin. As well established genetic factors do not seem to influence siderosis in thalassaemia[15] every subject of this group should be appropriately tested regularly.

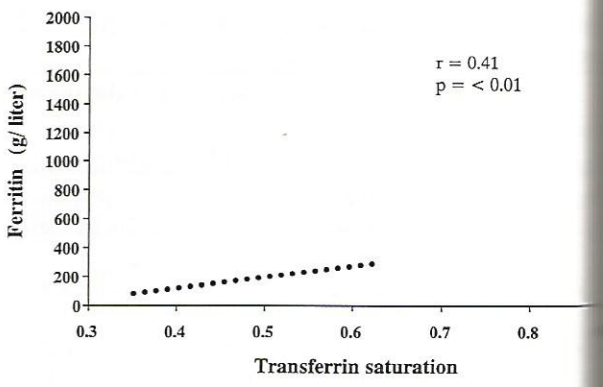

Figure 1. Correlation between ferritin and transferrin saturation in b-thalassaemia minor (n=116).

REFERENCES

1. Weatherall DJ. The thalassemias. In Williams WJ, Beutler E, Erslev AJ, Rundles RW (eds): Hematology. 2nd cond edition, 1987, pp. 391-413.
2. Thalassemia International Federation. Management of β-thalassemia. 6th International Thalassemia Federation (TIF) educational workshop on clinical, management thalassemia. 1999, pp. 18-21.
3. Hassan MK, Al-Naama LM, Widad NM et al. Prevalence of β-thalassemia, HbS and G6PD in Basrah governorate. East Mediterranean Health J 2003; In press.
4. Benz JR EJ, Schwartz E. Thalassemia syndromes. In Miller DR, Baehner RL, Miller LP (eds): Blood diseases of infancy and childhood. 6th edition, Mosby, St. Louis, 1989, pp. 428-463.
5. Beatler E. Disorder of hemoglobin. In Fauci AS, Braunwald E, Isselbacher KJ, et al (eds): Harrison's Principles of Internal Medicine. 14th Edition, McGraw Hill. New York, 1998, pp. 645-652.
6. Van der Weyden MB, Fong H, Hallam LJ et al. Red cell ferritin and iron overload in heterozygous β-thalassemia. Am J Hematol 1989; 30: 201-205.
7. Weatherall DJ. Clegg JB. The β-thalassemia. In The Thalassemia syndromes. 3rd edition, Blackwell Scientific Publication, Oxford, 1981, pp. 148-319.
8. Ceriotti F and Ceriotti G. Improved direct specific determination of serum iron and total iron binding capacity. Clin Chem 1980; 26: 327-331.
9. Al-Naama MM, Al-Naama LM, Al-Sadoon TAH. Frequencies of G6PD, PK and hexokinase deficiencies in Basrah population. Screening 1995; 4: 27-34.

11. Forget BG. Thalassemia syndrome. In Hoffman R, Benz JR EJ, Shattil SJ et al (eds): Hematology, basic principals and practice. 3rd edition, Churchill Livingstone, New York, 2000, pp. 485-510.
12. da Fonseca SF, Kimura EY, Kerbauy J. Assessment of iron status in individuals with heterozygous β-thalassemia. Rev Assoc Med Bras 1995; 41: 203-206.
13. Weatherall DJ. Genetic disorders of hemoglobin. In Hoffbrand AV, Lewis SM, Tuddenham EGD et al (eds): Postgraduate hematology. 4th edition, Butterworth-Heinemann, Oxford, 1999. pp. 91-119.
13. Brabec V, Cermak J, Sebestik V et al. Serum feritin in various hemolytic disorders. Folia Hematol Int Mag Klin Morphol Blutforsch 1990; 117: 219-227.
14. Honig GR. Hemoglobin disorders. In Behrman RE, Kliegman RM, Arvin AM (eds): Nelson Textbook of Pediatrics. 16th edition, W.B. Saunders Company, Philadelphia, 2000, pp. 1478-1487.
15. Konstantopoulos K, Theocharis S, Karagiorga M et al. Iron stores in multitransfused thalassemic patients seem not to be influenced by the HLA system. Haematologia 2000; 30: 319-323.