# PREVALENCE OF IRON DEFICIENCY IN B-THALASSEMIA TRAIT IN ERBIL GOVERNORATE

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Submitted 3 Dec 2014; accepted 31 Dec 2014

# **ABSTRACT**

Background and objectives Anemia is a common clinical disorder that could be seen by clinician in Iraqi Kurdistan hospitals and private clinics, iron deficiency anemia perform the vast majority of such cases, and the prevalence of  $\beta$ -thalassemia trait in our community is about 7.5-8%. We examined a consecutive cohort of patients with  $\beta$ -thalassemia trait to detect the frequency of iron deficiency among them.

**Method** A descriptive cross sectional study performed in Erbil-Rizgary teaching hospital, the study was conducted among 162 individuals with  $\beta$ -thalassemia trait over a period extending from October 2013 to October 2014. The individuals had their diagnosis confirmed by a combination of blood counts and High Performance Liquid Chromatography. They were then investigated for Iron status by determining Transferrin saturation and Serum ferritin.

Results Among the 162 individuals with  $\beta$ -thalassemia minor enrolled, the prevalence of iron deficiency was 34.6%. There were no significant difference in the frequency of iron deficiency between adults and children (p = 0.99) or males and females (p= 0.477). The mean haemoglobin (Hb) and mean corpuscular volume (MCV) were significantly lower in those with concomitant iron deficiency (ID) than those without it (p= 0.009, p= 0.021 respectively) while mean red cell distribution width (RDW) was higher among those with ID than those without ID (p = 0.01). However, no significant differences were noted in the Hb A2 % in those with concomitant ID (p= 0.52).

Conclusions Iron deficiency is frequent among our  $\beta$ -thalassemia trait people, serum ferritin was low in only 16% of cases while the prevalence of ID counting on both serum ferritin and transferrin saturation (Tsat%) was 34.6%; so serum ferritin shuold not be the only ultimate tool for iron assessment among such people.

Duhok Med J 2014;8(2): 38-46.

**Keywords:** Iron deficiency, β thalassemia trait, Erbil

halassemia is the most common genetic disorder worldwide.  $^{1,2}$  It affects men and women equally and occurs in approximately 4.4 of every 10,000 live births.  $^3$  They are inherited in autosomal recessive manner that cause hemolytic anemia because of the decreased or absent synthesis of a globin chain.  $^4$  In its heterozygous state  $\beta$ -thalassemia trait (minor), is asymptomatic and results in microcytosis and mild anaemia.  $^5$ 

Prevalence of  $\beta$ -thalassemia trait in Mediterranean region, Africa and Southeast Asia is about 5-30% and in Erbil is 7.7%.<sup>6,7</sup>

Thalassemia syndromes and iron deficiency anemia (IDA) are the two most microcytic common etiologies of hypochromic anemia in children and adults. It has long been considered that deficiency does not exist thalassemia syndromes, including

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thalassemia major as well as trait.<sup>8</sup> It has been suggested that the trait confers an advantage in maintaining iron balance in which case the prevalence of iron deficiency should be lower in those with this trait.<sup>9</sup> However; studies have shown the occurrence of iron deficiency in patients with beta thalassemia trait.<sup>9-11</sup>

The aim of the study: to detect the frequency of iron deficiency among  $\beta$  -thalassemia trait people, and to see the impact of iron deficiency on red cell count, RDW and RBC indices like MCV and MCH in such individual.

# **METHODS**

The study was conducted in Erbil-Rizgary teaching hospital over a period extending from October 2013 to October 2014; a total of 162 patients were enrolled in this study. These patients were seen either for assessing anemia or they were detected by chance with low mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) from complete blood count that was arranged for other reasons. Patients of both sex and all age groups with MCV below 80 fimtoliter (fL) and MCH less than 27 picogram (pg), and with HbA2 more than 3.5% and thus labeled as  $\beta$ thalassemia minor were deemed eligible for the study, while those with MCV more than 100 fl, subjects iron taking and preparation, other haemoglobinopathies were excluded from the study. The data was collected by a direct interview of patients through a special questionnaire designed for the current study containing; demographic description of each enrolled individual, chief complaint, physical findings and laboratory data then the purpose of the study was carefully explained to each participant. The study was approved by the scientific and ethical committees of the College of Medicine- Hawler Medical University. The purpose of the study was demonstrated to each participant individually or for the parent of the children during enrolled personal interviews, and an informed verbal consent was obtained from all enrolled individuals. A blood sample was taken for complete blood picture by automated haematology analyzer (Celttac alpha 6410 Japan). The following blood biomarkers reflecting iron metabolism were assessed directly: serum concentrations of iron (µg /dl), total iron-(TIBC, binding capacity μg/dl). Transferrin saturation (Tsat) was calculated as a ratio serum iron (µg/dl) and TIBC (µg/dl), multiplied by 100 and expressed in percent and serum ferritin (μg/L). The later was measured using immunoassay (Roche Diagnostics GmbH, Mannheim, Germany). Serum iron and TIBC were assessed using a substrate method with Feren S (Thermo Fisher Scientific, Waltham, MA, USA). Iron deficiency was defined prospectively as serum ferritin <15 µg/L and or Tsat <15%. High performance liquid chromatography (HPLC) (D10, Biorad USA); arranged for haemoglobin analysis and estimation of HbA2.

# Statistical Analysis

Statistical package for social sciences (SPSS) software (version 19) was used for data entry and analyzing, aided by Microsoft excel 2010 for plotting graphs and tables. Descriptive data were presented

for continuous variables as mean  $\pm$  SD, while qualitative data description done by calculating number and percentage. t-test was used to compare between two means and Chi-square(x2) tests was used to compare between proportions , p value  $\leq$  0.05 considered statistically significant.

#### **RESULTS**

Out of 162 patients with  $\beta$ -thalassemia trait enrolled in this study, 101 (62.3%) were females, and 61 (37.7%) were males with female: male ratio of (1.6:1). The Mean ( $\pm$ SD) of age was 29.6 $\pm$ 16 years ranging from 1.4-70 years, 26 (16%) of them were  $\leq$  12 years (pediatric age group), 25 (15%) of the patients belong to age group (10-19) years, followed by 43 (27%) of the patients in the age group (20-29) years, and 34 (21%) patients in the age group (30-39) years as shown in (Figure 1).

The basic haemogram parameters concerning Hb%, haematocrit (%), red cell count, MCV, MCH, RDW and HbA2 are illustrated in (Table 1). The result of iron status including serum iron, TIBC, serum ferritin and Tsat also demonstrated in (Table 1).

The prevalence of iron deficiency (ID) was 34.6% (56 patients) among the 162 enrolled individuals, with no significant difference between children and adults (p Moreover, there was no = 0.996). significant difference in prevalence of ID in relevance to gender among the enrolled individuals (p= 0.477) (Table Comparisons between the subjects with βthalassemia trait and ID and those without ID are shown in (Table 3), and revealed that there were significant difference in

mean Hb, MCV and RDW between those with ID and those without ID; the mean Hb and mean MCV were both lower while mean RDW was higher in those in the ID subgroup (p= 0.009, p= 0.021 and p= 0.01 respectively), but there were no significant difference between both subgroups regarding MCH, RBC count and HbA2.

Prevalence of anemia among the studied individuals was 88.3% but there was no significant difference between those with ID (87.5%) and those without it (88.7%) (p = 0.824) as shown in (Table 4).

Serum ferritin and transferrin saturation (Tsat %) both were assessed in all 162 studied individuals, (Table 5) shows that Transferrin saturation was more likely to detect iron deficiency than S. ferritin, and there was a significant correlation (p < 0.001).

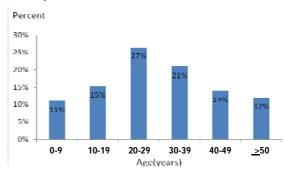


Figure 1 Distribution of enrolled patients by age

Table 1. Overall Mean and SD of the studied parameters

	Mean	SD	Mini.	Maxi.
Hb g/dl	10.74	1.38	6.6	14.3
Hct %	33.76	4.48	22	45
MCV fL	61.9	4.99	47.4	76
MCH pg	19.63	1.99	14.3	26.9
RDW %	16.43	2.52	11	25
RBC ×1012	5.51	0.61	3.3	7.45
HbA2 %	4.89	0.77	3.51	6.9
S. ferritin µg/L	78.34	78.92	0.05	424
S. iron µg/dl	67.07	35.19	8	153
TIBC µg/dl	316.37	78.54	151	576
Tsat %	22.39	12.75	2	59

Table 2. The prevalence of ID according to age and sex

			Prevalence ID%		
	N	No.	%	P value	
Age					
≤12 years	26	9	34.6	0.996	
> 12 years	136	47	34.6		
Sex					
Male	61	19	31.1	0.477	
Female	101	37	36.6		

Table 3. A comparison between β-thalassemia trait with ID and those without ID

	ID	N	Mean	SD	SE	P value
Hb_g/dl	Yes	56	10.436	1.499	.173	.009
	No	106	11.005	1.224	.131	
MCV fL	Yes	56	60.997	5.511	.636	.021
	No	106	62.801	4.356	.467	
MCH pg	Yes	56	19.447	2.401	.277	.287
	No	106	19.793	1.562	.167	
HbA2 %	Yes	56	4.941	.810	.093	.520
	No	106	4.862	.745	.080	
RBC ×1012	Yes	56	5.433	.661	.076	.125
	No	106	5.582	.573	.061	
RDW %	Yes	56	16.9747	2.68051	.30952	.011
	No	106	15.9690	2.30219	.24682	

Table 4. The prevalence of anemia among enrolled people

	Hb%						
	Low		Normal		Total		P value
Prevalence of ID	No.	%	No.	%	No.	%	
No	94	88.7	12	11.3	106	65.4	
Yes	49	87.5	7	12.5	56	34.6	0.824
Total	143	88.3	19	11.7	162	100	

Table 5. The correlation between S. ferritin and Tsat%

Ferritin		Ts	sat%				
- -	Low (ID)		Normal (No ID)		Total		
- -	No.	%	No.	%	No.	%	P value
low	23	88.5	3	11.5	26	100	
Normal	30	22.1	106	77.9	136	100	< 0.001
Total	53	32.7	109	67.3	162	100	

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#### **DISCUSSION**

Iron status in β-thalassemia trait had always been an area of interest to haematologist. The common held notion is that iron deficiency is unlikely coexist in thalassemia trait. Moreover, conflicting data came up from different studies regarding the iron metabolism in βthalassemia trait. In 1980 Economidou et al. showed that iron deficiency was a common finding in female thalassemia trait of reproductive age not receiving iron supplement.<sup>12</sup> However in 1987 Mehta and Pandya showed that the β-thalassemia an trait group had advantage maintaining iron balance. 13 In 1995 a study done among British Asian children showed that coincident iron deficiency and thalassemia trait can coexist and it should not be presumed that the trait protects iron status or that the two are in any way mutually exclusive, at least in the early years. 14 In 2000 a study in Iran concluded that, iron level should be examined in subjects with the trait especially in men, to avoid harmful effects of iron overload in early stages of the disorder.15Thus the exact role of thalassemia trait in iron metabolism still remains an area to be explored.

In the current study the prevalence of iron deficiency was 34.6% among 162 individuals with  $\beta$ - thalassemia trait, with no significant difference regarding both the age and the sex of enrolled individuals. The high prevalence of ID may be explained by the fact that ID still is the most frequent nutritional disorder in our community, and it may also be related to a

false belief among the public and even among physician that individuals with thalassemia are always iron overload and thus advised to avoid iron-rich meals and iron supplements. Our result is much higher than results of Qureshi in Pakistan<sup>10</sup> of 13.5%, Dolai et al, and Madan et al of 19.3% and 27.2% in India.<sup>11, 16</sup>

The mean Hb and MCV were lower in those with ID as compared to those without it; our finding is in consistence with Dolai et al in India11, while mean RDW was higher among traits with ID, RDW was introduced as an important parameter for differentiating IDA from  $\beta$ -thalassemia trait.<sup>17</sup>

We observed that mean HbA2 was not significantly different in those with ID versus those without it. Mean HbA2 was even marginally higher in the subgroup with ID. Our finding is in agreement with Madan et all<sup>16</sup> and Passarello et al<sup>18</sup>, this indicate that the presence of iron deficiency did not preclude the detection of thalassemia trait in this population, reduction of HbA2 has been reported to be linked to the severity of anemia<sup>9</sup> so that possibly the concomitant ID is not sufficiently severe or not sufficiently prolonged to significantly reduce the level of HbA2, but our result is in contrary to Harthoorn et al<sup>19</sup> conclude that patients with β-thalassemia trait and concomitant ID can show normal HbA2 and Steinberg et al<sup>20</sup> reported reduced HbA2 in βthalassemia trait coincident with ID.

Concerning the prevalence of anemia; the majority (88.3%) of the studied individuals were anemic but there was no significant difference between those with

ID and those without ID (p = 0.824), which means that ID contribution to the anemia in the studied cohort was not significant, on the other hand about 12% of the enrolled cases were not anemic so normal Hb level should not preclude such individual from iron state evaluation.

Diagnosis of IDA may be less straight forwards in patients with acute or chronic inflammatory conditions, since most of the biochemical markers of iron metabolism are affected by acute phase reaction.<sup>21</sup> We have estimate both serum ferritin and Tsat in all the studied cases and the correlation was significant (p < 0.001), serum ferritin was low in 26 (16%) cases only while the prevalence of ID counting on both serum ferritin and Tsat was (34.6%); so we can not consider serum ferritin alone as the only reliable ultimate tool for iron state evaluation in such individuals.

Iron deficiency is frequent among  $\beta$ -thalassemia trait in our population, and one clue to its concomitant presence is high RDW. Thus the coexistence of both should not be dismissed and the best approach to securing a diagnosis is a combination of serum ferritin and transferrin saturation.

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# يوخته

# ریژهی ههبوونی کهمی مادهی ئاسن له نیو هه لگرانی نه خوشی پالاسیمیا جوری بیتا له شاری ههوایس

پیشه کی و ئامانج: که م خوینی به ربلاوترین نه خوشیه که پزیشك روبه روی ده بیته وه له نه خوش خانه کان و کلینیکه تایبه تیه کان له کوردستانی عیراق. که م خوینی به موی که می ماده ی ئاسن ریژه یه کی روزی ئه م نه خوشانه پیک دینیت. ریژه ی ئه وکه سانه ی که هه لگری نه خوشی پالاسیمیا جوری بیتا له کومه لگه ی ئیمه نزیکه ی 8-7.5. ئیمه هه ستاین به پشکنین و لیکولینه وه ی چه ند گروپیکی یه ک له دوای یه کی ئه و که سانه ی که هه لگری نه خوشی پالاسیمیا جوری بیتا ن بو نوزینه وه ی ریژه ی که می مادده ی ئاسن له نیوانیاندا.

دەرئەنجام: كەمى مادەى ئاسن بەربلارە لە نيو ئەر كەسانەى كە ھەلگرى نەخىرشى پالاسىمىا جۆرى بىتا ن لە كۆمەلگەكەمان. لە كىنى 17٢ كەس كە ھەلگرى بىتا پالاسىمىان كەرا بە شدار بوون لەم لىكولىنەرەيە تەنھا %16يان رىپرەى فىرىتىنى ناو خوينىان كەم بو بەلام رىپرەى ھەبوونى كەمى مادەى ئاسن لە نيو ئەر كەسانە ٣٤,٦٪ بو بەپشت بەستن بەھەريەك لە رىپرەى فىرىتىنى ناو خوين و رىپرەى تىربونى ترانسفىرىن. بويە پىوانى رىپرەى فىرىتىن لە خوين بەتەنھا نابىت بە پىشكنىنى سەرەكى دابنرىت بى ھەلسەنگاندنى مادەى ئاسىن لە خوينى ئەر كەسانەى كە ھەلگرى بىتا پالاسىمىيان.

# الخلاصة

# انتشار نقص الحديد بين حاملي مرض الثلاسيما من نوع بيتا في محافظة أربيل

الخلفية والأهداف: فقر الدم هو اضطراب سريري شائع التي يمكن أن يواجه الطبيب في المستشفيات والعيادات الخاصة في كوردستان العراق ، وفقر الدم نتيجة نقص الحديد يشكل الغالبية العظمى من هذه الحالات، نسبة انتشارحامل مرض الثلاسيما (الثلاسيميا الصغرى) من نوع بيتا في مجتمعنا حوالي ٧٠٠-٨٪. قمنا بدراسة مجموعات منتالية من حاملي مرض الثلاسيما من نوع بيتا للكشف عن نسبة نقص الحديد بينهم.

المرضى والطرق: دراسة وصفية مقطعية أجريت في مستشفى رزكاري التعليمي في اربيل. وقد أجريت الدراسة بين ١٦٢ شخصا من حاملي مرض الثلاسيما نوع بيتا على مدى فترة امتدت من أكتوبر ٢٠١٣ إلى أكتوبر ٢٠١٤. لقد تم تشخيص مرض الثلاسيما عند هؤلاء الاشخاص عن طريق تحليل الدم العام و تحليل السائل الكروماتوكرافي عالي الاداء (HPLC) بعد ذلك تم التحري عن نسبة الحديد بواسطة كل من نسبة الفيرتين في مصل الدم ونسبة تشبع الترانسفيرين.

النتائج: بين ١٦٢ شخصا من حاملي مرض الثلاسيما نوع بيتا الذين شماتهم الدراسة بلغت نسبة انتشار نقص الحديد (P=.87%)، لم يكن هناك اختلاف بشكل ملحوظ بين الكبار والأطفال (P.9.9) و بين كلا الجنسين (P=.87%). معدل نسبة خضاب الدم ومعدل حجم كريات الدم الحمراء (MCV) كان أقل وبشكل ملحوظ بين حاملي مرض الثلاسيما نوع بيتا المتزامن مع نقص الحديد (ID) من تلك دون نقص الحديد (E=0.009) على التوالي)، في حين معدل توزيع خلايا الدم الحمراء (EDW) كان أعلى بين ذوي نقص الحديد (EDW) من دون تلك (EDW). على اية حال لم يلاحظ اي اختلاف ملحوظ في خضاب (EDW) عند حاملي مرض الثلاسيما نوع بيتا المتزامن مع نقص الحديد (EDW).

الاستنتاج: نقص الحديد شائع و منتشر لدى الاشخاص الحاملين لمرض الثلاسيما نوع بيتا، نسبة الفيرتين كان اقل من الحد الطبيعي عند %16 فقط من مجموع ١٦٢ شخصا اجريت عليهم الدراسة بينما بلغت نسبة انتشار نقص الحديد 7.3٪ معتمدا على كل من نسبة الفيرتين في مصل الدم ونسبة تشبع الترانسفيرين، لذلك فان قياس نسبة الفيرتين في مصل الدم لا يمكن ان تكون الفحص الاساسى الوحيد لتقييم نسبة الحديد بين هؤلاء الشخاص.