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Hypothyroidism in transfusion dependent β-thalassemia

Najla Ayoub[1], Khaleed J. Khaleel[2], Ihsan Ibrahim Mohammed[3]

1 Medical collage Al_mustansuryia unv.
2 Iraqi Centre for cancer and medical genetics research .
3 Thalassemia Centre AL-karama hospital

Abstract:

Background: beta thalassemia major is a big health problem worldwide. There are few studies dealing with prevalence and nature of thyroid dysfunction in Iraq.
Objectives: to establish the prevalence of thyroid dysfunction among patients with beta thalassemia major.
Patients and Methods: this study was conducted during Nov. 2013 and dealt with 73 Iraqi patients with beta thalassemia major attending Al-Karma thalassemia Centre in Baghdad. They included 40 males and 33 females with age ranged from 15 years to 30 years. The height and weight were measured. Thyroid function tests were performed by enzyme linked fluorescent antibodies.
Results: hypothyroidism were reported in 16 patients 10 males and 6 females out of 73 patients examined with prevalence rate of 21.9%. All cases of hypothyroidism were subclinical hypothyroidism (high TSH level with normal T4 and T3).No case was documented to have autoimmune thyroiditis.
Conclusion: there is high prevalence of thyroid dysfunction among Iraqi patients with beta thalassemia major. It is of high importance to monitor those patients at yearly intervals for early detection and replacement therapy.

Key words: *β-thalassemia major , hypothyroidism*

Introduction:

β- Thalassemia major (BTM) is sever hereditary anemia resulting from defect in beta-globin synthesis .It is commonly associated with shortened red cells life span and excessive destruction of red blood cells (1, 2).

In Iraq, thalassemia is a major health problem with prevalence of carrier range from 4.4%-6.66% (3, 4).Life-long blood transfusion therapy lead to excessive accumulation of iron in different organs which was associated with early fatalities .It is well known with introduction of iron chelators, especially the oral ones during the last decade,the rate of survival in thalassemic patients have improved (5).

The endocrine complications became more frequent in long term survivor and substantially affect the quality of their life (6).

Thyroid dysfunction is well recognized endocrine complication after long term blood transfusion in β-thalassemia major (7).

Corresponding address:
Khaleed J. Khaleel
Iraqi Centre for cancer and medical genetics research .
Email: khaleed59@yahoo.com

The clinical manifestations of hypothyroidism are non specific and usually patients are often unaware of their condition .The early diagnosis of hypothyroidism could be rapidly done using thyroid function tests (8).

In spite of the large numbers of patients attending ALkarama center for hemoglobinopthies therapy there has been no data collected on the prevalence of hypothyroidism in those patients.

Moreover, it has been little research on thyroid disease in the β-thalassemia major population in Iraq.

The present study aims to determine the prevalence of thyroid dysfunction in patients with thalassemia major using iron overload as one of the measures.

Patients and Methods:

The present study was carried out on 73 patients older than 15 years old randomly selected (40 males and 33 females) from Alkarama thalassemia center in Baghdad for the period from November 2013 to January 2014. These who had thalassemia minor and thalassemia intermedia were excluded from the study. Control group of 25 person (14 male , 11 Female)

with age range from (15-30)years.

Informed consent were obtained from each patient or their parents. The research done with agreement of the ethical committee of the ministry of health. In this research a complete questionnaire consist of age of patients , onset, frequency of blood transfusion, time of starting desferal therapy and history of endocrine problems.

The patients height and weight were measured and body mass index (BMI) calculated (weight /height 2) at different ages. For adults (>20 year aged) a BMI less than 18.5kg/m was considered as underweight , while BMI greater than 25kg/m was considered as overweight and above 30 kg/m was considered as obese .

For children and adolescents (2-20 year aged). A BMI (85th – 95th) percentile were considered as overweight .

All blood samples were collected just before blood transfusion, five ml of venous blood obtained from cubital vein and the serum was stored at -20 c until used.

A commercial kits were used for determination of serum ferritin, TSH, T3 and T4 levels (vidas ® ceritinbioMerieut Lyon –France) based on an immunoenzymetic method (enzyme-linked flouresnt assay) according to procedure.

Statistical analysis

All Values were expressed as mean ± SD.

Comparison between control and patients when performed using two tailed students t-test and were considered significant if the obtained P value was lower than 0.05.

Results:

It would be notable that the present data revealed that 16 patients (10 males) and (6 females) had subclinical hypothyroidism out of 73 patients examined with prevalence rate of 21.9 % . No case of overt hypothyroidism could be identified.

Table (1): comparison of body mass index ,Ferritin and thyroid function tests of thalassemia patients with control group

Parameters	Control (n=25) Mean ± SD	Patients (n=73) Mean ± SD	P value
BMI (kg/m^2)	27.8 ± 4.6	18.6 ± 4.1	P< 0.05
TSH(µIU/ml)	2.2 +1.4	3.8 ± 1.9	P< 0.05
T4(nmmol/L)	81.2 ± 13.4	75.2 ± 12.3	N.S.*
T3(nmmol/L)	1.65 ± 0.41	1.56 ± 0.38	N.S.*
Ferritin(ng/ml)	60 ± 11.5	1210 ± 129	P< 0.01

* Non-significant by t-test .

Table (2):serum ferritin level in thalassemic patients with hypothyroidism and thalassemic patients with normal thyroid function.

Parameter	Thalassemic patients with hypothyroidism (n=16) Mean ± SD	Thalassemic patients with normal thyroid function(n=57) Mean ± SD	P value
Serum ferritin (ng/ml)	1190 ± 113	1120 ± 95	N.S.

This study surveyed (73) patient (40 males) and (33 females) suffering from β-thalassemia major. Their ages ranged from 15 to 30 years. The averages BMI of patients group (18.6 ± 4.1) were significantly lower than control group (P< 0.05).

We regard serum ferritin as a parameter of Iron overload.

Non-significant difference in serum ferritin in those with hypothyroidism and those with normal thyroid function was noticed (as shown by table 2) .

No autoimmune thyroiditis could be noted in hypothyroid group, all cases had negative anti-thyroglobulin antibodies

and thyroperoxidaes antibodies.

Discussion:

Thyroid dysfunction in BTM patients had been reported with very variable prevalence as shown in table (3) with either low range 0-12% or high 16-35% (9,10,15).

The variation of prevalence in the fact may be related to different methods used for thyroid function, different ages in the studied population or different medications.

Primary hypothyroidism that may affect patients with β-thalassemia major from the second decade of life is mainly due to the gland being iron overload (19).

Autoimmune thyroiditis was absent in our studies group as anti-thyroglobulin antibodies were negative in all cases with hypothyroidism.

Central hypothyroidism caused by decreased secretion of TSH from anterior pituitary gland or by decreased TRH from hypothalamus was not seen in our study.

Our data revealed non-significant difference in serum ferritin level in those with subclinical hypothyroidism and those with normal thyroid function. This could be explained that the prevalence of hypothyroidism in homozygous hemochromatosis are non-significantly different from normal control where hypothyroidism was 1.9 % (20).

Moreover, high prevalence of hypothyroidism in thalassemia intermediate without high iron over load (21,22).

Wide spectrums of pathological mechanisms are involved. Tissue chronic hypoxia (23) and iron overload have a direct toxic effect on thyroid gland. High levels of labile plasma iron are regarded responsible for formation of free radicals and production of reactive oxygen spices that can lead to cell organ damage (23).

The symptoms of hypothyroidism are usually nonspecific, but the consequences affect every organ and system, early laboratory evaluation and control of thyroid dysfunction is indicated in all BTM patients (24).

Iron overload induced hypothyroid may respond to adequate chelation therapy promoting prevention or reversal of the disease and associated comorbidity (24).

It is well known that each had different efficiency and safety profile with regards to their response to chelation therapy.

Negative iron balance that ensure prevention or reversal of iron overload complications is really difficult to achieve with chelation monotherapy. Combined chelation therapy can have a better approach (25).

Our studied group had experience with the use of monotherapy chelation regimen that is usually desferroxamine.

In conclusion, the present data demonstrated that hypothyroidism in the β- thalassemia major is a frequently noticed.

In most patients there are no obvious clinical signs of hypothyroidism so regular follow up for early detection and a timely replacement therapy to be implanted specially in children and adolescents with growth failure and delayed puberty .

The use of intensive combined chelation may lead to the reversal or prevention of hypothyroidism in BTM.

Additional this treated regimen may prevent the progression of subclinical to overt hypothyroidism. Combined chelating therapy may have positive impact on quality of life.

Table (3): Showed the prevalence of hypothyroidism in different of world compared with our data.

Country	Number of patients	Prevalence of hypothyroidism	Reference
Iran	56	16	F.Najafipour (2008) (9).
Jordan	36	0	Irstaid *et al*. (2009) (10).
Indonesia	179	26.8	Rindarg K. *et al.* (2011) (11).
Greece	200	16.5	A.Zenas *et al*. (2002) (12).
Oman	30	3.3	Mula-Abed w. *et al*. (2008)(13).
Turkey	90	3.3	Pirincciogla A. *et al*. (2011) (14).
Qatar	48	35	Soliuan A. *et al*. (2013) (15).
Thailand	51	17.6	Jaruratanasirikul S. *et al.* (2007)(16).
Italy	97	21.6	Danctis V. et.al (2008) (17).
Pakistan	70	25.71	SA. Malik S.sved ,*etal*. (2008)(18).
Baghdad	73	21.9	This study.

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نقص انتاج الغدة الدرقية في مرضى الثلاسيميا المعتمد على نقل الدم

نجلة ايوب[1]، خالد جمعة خليل[2]، احسان ابراهيم محمد[3]
1 كلية الطب / الجامعة المستنصرية.
2 المركز العراقي لبحوث السرطان والوراثة الطبية/ الجامعة المستنصرية.
3 مركز الثلاسيميا /مستشفى الكرامة التعليمي / وزارة الصحة.

الخلاصه:

يعتبر مرض الثلاسيميا الكبرى نوع بيتا بأنها مشكلة صحية كبيرة في العالم .وهنالك عدد قليل من الدراسات تناولت اضطراب وظائف الغدة الدرقية في مرض الثلاسيميا في العراق .
ان الهدف من هذة الدراسة هي لمعرفة مدى انتشار اضطراب الغدة الدرقية في مرضى الثلاسيميا العراقيين.
حيث تم اخذ 73 مريض من مركز الثلاسيميا في مستشفى الكرامة التعليمي في تشرين الثاني .تتضمن 40 ذكرا و33 انثى تتراوح اعمارهم بين -15 30 سنة وتم قياس الطول والوزن وتم قياس هورمون الغدة الدرقية بواسطة انزيمات الغدة الدرقية بواسطة الانزيمات المرتبطة بالاجسام المضادة الفلورسنية.
اظهرت النتائج بأن (16) مريضا منهم 10 ذكور و(6) اناث من 73 مريض بنسبة انتشار (21.9%) كل الحالات هي عبارة عن نقص انتاج الهورمونات تحت السريري حيث TSH اعلى من الحد الطبيعي وt4 وt3 ضمن الحدود الطبيعية .
الاستنتاج بأن هنالك نسبة انتشار عالية في المرضى والذين يحتاجون الى متابعة مستمرة لغرض اعطاء هورمونات الغدة الدرقية .