Frequecy of hypothyroidism In multi-transfused thalassemic patients in AL- Diwanyia Maternity Hospital children

Abbas Mohammed hussein Al-shebani*

*Lecturer ;department of pediatrics: AlQadisyia medical college

Abstract:

Back ground: hypothyroidism in thalassemic children is not uncommon problem and need special attention and frequent patient monitoring.

Objective: to establish the frequency of hypothyrodism among multitransfused thalassemic patients depending on clinical and laboratory investigations.

Methods: A cross sectional study of thyroid function ,T3,T4, and TSH, was carried out in 120 transfusion-dependent thalassemia and sickle cell anemia patients attended the thalassemic Center in AL-Diwanyia Maternity and Children.Teaching Hospital .The inclusion criteria were 1(the age more than 5 years and 2)receiving frequent blood transfusions at least 6 times per year in the last three years.

Result: eight patients have hypothyroidism and had a prevalence of (6.66%). Two patients had low T3 and T4 and elevated TSH with signs and symptoms of hypothyroidism and was already treated with thyroxin ,which consistent with the diagnosis of primary hypothyroidism , and 6 patients had no signs and symptoms of hypothyroidism with normal T3 and T4 but elevated TSH and this was consistent with the diagnosis of subclinical hypothyroidism . No patient of these 8 have family history of hypothyroidism . All affected patients are receiving blood transfusions more than 20 times since the time of diagnosis and all the effected patients have suboptimal iron –chelating therapy as reflected by the high serum ferritin level (> 1000).

Conclusion: patient with transfusion dependent hemoglobinpathy need frequent monitoring of their thyroid function at least once yearly to detect early hypothyroidism and start early treatment .

Introduction:

The commonest hemoglobinopathies that need frequent interval , regular thalassemia an-blood transfusion are o and B (١)thalassemia-d sickle cell Where regular transfusions eliminate the complications of anemia and compensate bone marrow expansion, permit normal development and extend survival(2)In parallel transfusions result in a second disease while treating the first, that is inexorable accumulation of iron in the tissue which without treatment is fatal in the second .(٢)of life decade

As patients with thalassemia have ineffective erythropoiesis ,this results in a drastic increase inplasma iron turnover ,10-15 times that of normal subject(3) This process stimulate iron absorption ,along with the release of iron derived from red blood cell catabolism into the circulation. subsequent tissue iron overload is therefore a significant problem, which is compounded by the need for regular blood transfusions. In the absence of adequate management ,iron overload can be fatal ,as the accumulation of iron results in progressive dysfunction of the heart ,Jiver and endocrine system(4).

Iron accumulation also adversely impacts on the endocrine system Jeading to

disturbed sexual maturation , early secondary amenorrhea, diabetes mellitus, and hyperinsulinemia[5,7].Iron deposition over many years may also cause damage to the thyroid lead to hypothyroidism ,parathyroid, and adrenal glands[8].

Clearly , the removal of excess body iron is vital to improve morbidity and Mortality in patients with thalassemia Effective iron chelating therapy therefore play a key role in the management of these patients and the benefits of this approach has been established with deferoxamine ,a paranteraly administered iron chelator [9,10]. It is therefore evident that ironchelating therapy can effectively improve the morbidity and subsequent mortality of patient with iron overload[11,13].

Hypothyroidism in thalassemia is uncommon in optimally treated patients and usually appearing in the second decade of life [14].

This study was carried out to determine:

1.The prevalence of hypothyroidism in thalassemic patients in AL-Diwaniya acity .

2.The Correlationof hypothyroidism with certain variables including age, sex, Number of blood transfusions and iron chelating therapy.

Patients and methods:

1. Patients:

A total of 120 patients (74 male and46 female), known patients with β-thalassemia major and sickle cell thalassemia who were attending AL-Diwanyiah Maternity &Pediatric Teaching hospital from the period of March 2008 till December 2008 were included in this study ,the inclusion criteria are

1)the age more than 5 years.

and 2) receiving frequent blood transfusions at least 6 times per year in the last three years. 102 patients included had p-thalassemia major and 18 patients had sickle cell thalassemia.

2: Methods:

A special questionnaire designed for the purpose of the study was filled for each patient enrolled in this study and includes detailed history and physical examination with specific attention to identifying the signs and symptoms of hypothyroidism , the data collection included the type of thalassemia, the age of diagnosis, number of blood transfusions since the age of diagnosis, details about the use of chelating therapy, family history of thyroid disease the date of last blood transfusion.

A blood sample was aspirated in the morning and at least 2 weeks from the last blood transfusion for assessment of thyroid function test (T3,T4and TSH) and measurement of serum ferritin level.

assay of thyroid function test:

T3,T4 and TSH were measured by radicimmunoassay(RIA).

The normal range of T4 was 0.07-1.75 ng/dl ,T3 60-181 ng/dl and TSH 0.25-5.00m IU/L. The cut point for thyroid dysfunction were as follows :

* T3<60ng/dl,T4 <0.07 ng/dl with TSH >5.00m IU/Lwere considered overt primary hypothyroidism.

*T3 and T4 in normal range with TSH > 5.00 mIU/L was consistent with compensated hypothyroidism (subclinical hypothyroidism).[15]

Results:

A total of 120 multi-transfused thalassemic patients were included ,their age range from 5-25 years, and 85% of patients were had β-thalssemia major , 6.66%were found to have laboratory finding of hypothyroidism. (Table 1)

Tble 1:Clinical characteristics of the studied patients(120 patients) Sex (male: female) 74:46

variable	value
Sex (male:female)	74:46
Age at time of test(yr)	12.5+3.9(range 5-25)
Type of thalassemia: p-thalassemia major Sickle-thalassemia	102(85%) 18 (15%)
No.of blood transfusion(L)	40 (range 10-60)
Ferritin level(microgram/dl)	1500+ 755
Patients with hypothyroidism	8 (6.66%)

*All patients with hypothyroidism were older than 15 years of age ,female are more affected than male, most the affected patient have thalassemia major and all patients receiving freqnt blood transfusions(Table 2).

Table 2: Comparison of selected variables of thalassemic patients with normal and abnormal thyroid function .

	Abnormal Thyroid function (no=112)	Abnormal Thyroid function (no=8)	P value
Age (yr)	13.5±2.5	18±2.5	P<0.001
Male Sex: female	58% 42%	37.5% 62.5%	P> 0.05 P< 0.05
No.of transfusions	22±10	40±13	P< 0.001
Type of thalassemia Thalassemia major Sickle-thalassemia	 85% 15%	 87.5% 12.5%	P > 0.05
S.ferritin	732±200	1300±260	P>0.001

Table 3 show that all patients with hypothyroidism are have high s.ferritin level which indic ate suboptimal chelating therapy,75% of patient with hypothyroidism have no sign or sympto ms of hypothyroidism with normal T3&T4 but have elevated TSH and were classified as co mpensated hypothyroidism.

Table 3:1aboratory results of thalassemic patients with hypothyroidism.

No.of pt	s.ferritin	T4	T3	TSH m IU/L
1	1720	0.033	52	65.00
2	1655	0.035	41	67.00
3	1120	0.09	33	67.00
4	1020	0.15	34	15.00
5	1510	0.10	34	60.00
6	1100	0.09	32	60.00
7	1120	0.07	34	33.00
8	1100	0.15	46	35.00

There is strong correlation between serum ferritin concentration and the presence of thy roid dysfunction with much high level of serum ferritin among patients with abnormal thyroi d function (table 4).

Table 4.Serum ferritin of patients with normal and abnormal thyroid function

S.ferritin level	No.ofthalassemic patients with hypothyroidism	No.ofthalassemic patients with hypothyroidism	P-value
200-600	0	10(8.9%)	P< 0.001
600-800	0	92(82.1%)	
800-1000	0	8(7.1%)	
1000-2000	8(100%)	2(1.7%)	

Discussion :

Thyroid dysfunction in p-thalassemic patients has been reported in many studies high with variable frequencies ranging from a low prevalence 0-12% [16,18] to high prevalence 16-35% [19,20]. These discrepancies in frequencies in these previous studies can be related to the different methods used for thyroid Function studies (some measure serum T4 and TSH, while thers depend on measurement of thyrotropin-releasing hormone), the different ages Of the the studies patients (pediatric or adult), different amount of blood transfusion, And the different dosages of iron-chelating therapy.[16,21]. in this study the frequency of abnormal thyroid function is 6.66% which was in the low range and this result is similar to many previous studies like those done in Tehran (1.7%) and those done by Masala et al who reported aprevalence of hypothyroidism at 5%.1% However many other studies reported high prevalence rate as that done in Thailand 17.6%.(23)and Germany 16% .Also in the present study ,all thalassemic patients with abnormal thyroid function are above 15 years of age which comparable with the result of studies done in Tehran and Thailand [22,23]. The present study reported that all thalassemic patients with hypothyroidism have received blood transfusion >20 times since the time of diagnosis and all those patients had suboptimal iron-chelating therapy as reflected by serum ferritin level which was >1000 in all patients and these results are similar to many other studies done throughout the world [18,22,,24].Patients with β-thalassemia major are more liable to have hypothyroidism (87.5%) than patients with sickle cell thalassemia (12.5%) and this is may be because thalassemia major cause more severe hemolysis and patients need more frequent blood transfusion to keep their hemoglobin level >10 g/d1.[25] Lastly this study reported that 75% of thalassemic patient with hypothyroidism have subclinical disease with elevation of TSH level but no sign and symptoms and no increasing in the level of T3 and T4. also this result is similar to results of studies done in Tehran, Thailand and in Germany.[22,24]

From this study ,it can be concluded that:

*There is a low frequency of hypothyroidism (6.66%) among thalassemic patient Receiving frequent blood transfusion .All thalassemic patients with hypothyroidism are more than 15 years of age and female are affected more than male. All affected patients have receive frequent blood transfusions (>20 times) since the age of diagnosis, and all of them had suboptimal iron-chelating therapy.

thus we recommended that:

All thalassemic patients with frequent blood transfusions should have monitoring of thyroid function , particularly those received suboptimal iron-chelating therapy, and patients fol who have elevated TSH level should be up yearly to detect-lowed any decline of T3 and T4 and the need of the patient to thyroid hormones replacement.

References:

1.Antonio C.Management protocol for the treatment of thalassemia. Thalassemia International Fedration ,1997;first edition:5-18.

2. Olivieri N.T, Brittenham G.M.Iron chelating therapy and treatment of thalassemia Blood ,1997;89:739-761.

3.Hershko C,Rachmilewitz EA.Mechanism of desferrioxamine-induced iron excretion in thalassemia .Br J Hematol, 1979;42:1 25-132.

4.Wood JC,Tyszka JM,Carson S.Myocardial iron loa ding in transfusion- dependent thalassemia and Sickl e cell disease .Blood ,1985;103:1934-1936.

thalassemia major .Br J Hematol ,1998;103:911-915.

7.Jiang R,Manson JE,Meigs JB,et al : Body iron store s in relation to risk of type 2 diabetes in apparently H ealthy women :JAMA ,2004;219:711-717.

8.Olivieri N :Thalassemia:Clinical management .Baill ieres Clin Haemato,1998;11:147-162.

9.Ehlers KH, Giardina PJ,Lesser ML,et al:Prolonged survival in patients with beta-thalassemia major treate d with deferoxamine .J Ppediatr , 1991;118:540-545.

10.Barry M,Flynn DM, Letsky EA; set al: Long term chelation therapy in thalassemia major :Effect o n liver Iron concentration .Br Med J 1974;2:16-20.

11.Marcus RE,Davies SC,Bantock HM,et al:Desferri oxamine to improve cardiac function in iron-ov erload patients with thalassemia major .Lancet1,1984 :329-393,

12.Modell B,Khan M,Darlison M.Survival in beta-tha lassemia major in the UK:Data from the UK Thalasse mia Register .Lancet ,2000;355:2051-2052.

13.de Sanctis,Eleftherioou A,Malaventura C.Prevalen ce of endocrine complications and short stature in p atients with thalassemia major.Ped Endocrine Rev 2004;2(suppl.2):249-255 .

14.Mohammadian S,Bazrafshan HR,Sadeghi-nejad A. Endocrine abnormalities in thalassemia major:a brie f review .J Med Assoc Thai , 2003;86,576_82

15.Fauci.B,Kasper.H,Longo.J.L. Harrisons principle of internal medicine 17th edition,2009,chapter :laborat ory value of clinical importance;table 2.

16.Flynn DM,Fairney A, Jackson D,Clayton BE. Hor monal changes in thalassemia major.Arch Dis Chlid, 1976;51 :828-36.

17.de Luca F,Melluso R,Sobbrio Get al. Thyroid func tion in thalassemia
major.Arch Dis Child ,1980;55; 389-92.

18.Masala A,Meloni T,Gallisai D ,et al.Endocrine fun ctioning in multitransfused prepubertal patients with homozygous beta-thalassemia .J Clin Endocrinol Met a,1984;58:667-70.

5.DeSanctis V.Growth and puberty and its manageme nt in thalassemia .Horm Res ,2000;58:72-79.

6.Jensen CE,Tuck SM,Agnew JE,et al .High prevalen ce of low bone mass in
19.Sabato AR,de S V,Atti G,et al. Primary hypothyroi dism and low T3 syndrome in thalassemia m ajor. Arch Dis Child, 1983;58:120-7.

20.0erter KE, Kamp GA,Munson PJ et al. Multiple ho rmone deficiency in children with hemochromatosis .J Clin Endocrinol Metab, 1993;76:357-61.

21.De Sanctis V,Roos M,Gasser T,et al. Impact of lon g-term iron chelating therapy on growth and endocr ine functions in thalassemia.J Pediatr Endocrinol Met ab,2006;19:471-80.

22.Alireza AS,Mir Reza Bet al. Metabolic and endocr inologic complications in
beta-thalassemia major: A multicenter study in Tahra n.BMC endocrine disord
2003.

23.Somchit J,Malai W,Vichai L,et al. Thyroid functio n in β-thalassemic children receiving hyper transfusio ns with suboptimal iron-chelating therapy. J Med A ssoc Thail ,2007;19:1798-1802.

24. .Cairo H,Stahnke,Sander S,et al. Epidemiological situation and treatment of patients with thalassemia m ajor in Germany:results of the German multicenter
beta-thalassemia study .Ann Hematol ,2000;79:7-12.

25.Low LC:Growth ,puberty and endocrine function i n beta-thalassemia major .J Pediatric Endocrinol Meta b, 1997;10:175-184.