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International Journal of Pharmaceutical Research & Allied Sciences, 2016, 5(3):270-276

Research Article

ISSN : 2277-3657
CODEN(USA) : IJPRPM

The Frequency of Hypogonadism in Males with Major Beta Thalassemia Above 14 Years Old Referred to Shafa Thalassemia and Hemoglobinopathy Research Center in Ahvaz in 2010

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ABSTRACT

Major thalassemia, the hemolytic disorder lead to Iron over load in body (Hemocidrosis) and Iron deposit on pituitary gonadotropic cells, as the result leads to endocrine disorder and hypogonadism. In this study we evaluated frequency and risk factors of hypogonadism in pationts with major thalassemia. This was a descriptive study conducted on the male pationts older than 14 years old diagnosed with major thalassemia referred to Ahvaz Shafa Thalassemia Center during 2010. For all of the patients, the levels of FSH, LH rate, testosterone, thyroid function test, calcium, phosphorus, fasting blood sugar, blood lipids and ferritin were evaluated. In addition, the sexual status based on Marshal-Tanner table and clinical findings were investigated. The data were analyzed with statistical package SPSS using descriptive statistics. Thirty seven patients over 14 years old with major thalassemia were evaluated. The rate of hypogonadism was 59.46% and the average level of ferritin in these patients was 4408 ± 1918, whereas 2331±744 in normal patients. Despite recent advances in Desferal therapy for the management of major beta thalassemia, the risk of secondary endocrine dysfunction remains high and makes the hypogonadism as one of the most frequent endocrine complications. Endocrine evaluation in patients with major thalassemia must be carried out regularly, especially in the patients older than 14 years old .

Keywords: Major thalassemia, Hypogonadism, Hemocidrosis

INTRODUCTION

Major thalassemia is a form of hereditary anemia in which natural growth of individuals due to complication resulting from disease get disorder. Its severe forms was less but is along with mortality and disability (1). These patiens did not have much life before using therapy method of blood transfusion and often died in early decade of life, but with blood transfusion for every 3 to 4 weeks and maintaining sustainably hemoglobin, added on their lifetime and significant improvement has occurred in physical form of body especially on the head and face area and also reduction of growth disorder. The accumulation problem of iron overload resulting from blood transfusion, transferred growth disorder into the third decade of life and growth of the patients decreased from age 11 to 12 years old to next suddenly that the problem also using iron repellent drugs such deferral is greatly disappeared (2, 3). Overall, different complications resulting from increased iron accumulation in the body, threaten the health of these patients. Identification of the complications and risk factors and also evaluation of prophylactic agents, and

treatment ways of the complications are nessesary. Khuzestan province in southern west of Iran is one of the affected areas by Thalassemia. According to the statistics of 1993, over 950 people in Ahvaz and about 2000 persons in Khuzestan province wrer affected by Thalassemia. This study aimed to investigate the frequency and the main risk factors of hypogonadism among over 14 years old male patients with major thalassemia referred to Ahvaz Shafa Thalassemia Center during 2010.

MATERIALS AND METHODS

This was a descriptive study conducted on the male pationts older than 14 years old diagnosed with major thalassemia referred to Ahvaz Shafa Thalassemia Center during 2010. Low numbers of patients in this age group as well as not completing some addresses or changing the patients location, lack of awareness of patients from addresses change made it impossible to conduct this study on the larger sample size patients. Therefore, surveillance and the sampling were performed during April to May 2010 in the thalassemia department of the healthcare center and finally 37 patients were enrolled in the study..

Inclusion criteria of the study were as follows:
1. Tendency to participation in study
2. The definitive diagnosis of major beta thalassemia
3. The boy of above 14 years old
4. Absence of maturity signs or maturity delay based on tanner criteria (The patients who their age with their maturity has been differenciated over SD2 with natural mean).
5. LH and FSH of up or down along with testosterone of lower than normal simultaneously

The form including patient formation was determined for visitors about name, age, height, weight, maturity and clinical symptoms of completed endocrine glands diseases and maturity level based on tanner criteria. Patients' height and weight was compared with charts of the National Center of Vital Statistics (NCHS). The evaluation of sexual status is including pubarche symptoms (growth of pubic area hairs) and SMR (Sexual maturation steps). The cases with clinical and diagnosed symptoms were considered by doctor; the possible cases of subclinical were not considered.

Also, for all patients with inclusion criteria, was performed hormone tests including LH, FSH, and testosterone and also other blood tests were done such as measurement of Ca, P, Alkp, blood glucose, serum ferritin, blood lipids and thyroid function tests to endocrine ways, and RIA. The serum ferritin level was measured with ELISA method and with Tecan-A-5582 and Ferritin EIA kit. Above tests were used for patients routinely and had been mentioned in individuals' record. So, from existent information in records was used for performed study.

Then, patients based on performed tests and their maturity status were classified to cases of Central and Peripheral maturity delay. Other patients characteristics in term of endocrine status and internal diseases such as heart diseases, liver involvement, mellitus diabetes, thyroid diseases, and other endocrine glands diseases were studied using the contents of patients' records. All data were recorded on information forms and were used for survey and study.

c. Variables
LDL ،HDL و TG
1. Height: Based on centimeter expressed and is obtained with measurement by tape measure.
2. Weight: Based on kilogram expressed and is obtained the patient's weight with measurement by balance.
3. Testis growth: Based on clinical examination and was evaluated the comparison with Tanner standard table.
4. Growth of pubic area hairs: Based on clinical examination and was evaluated the comparison with Tanner standard table.
5. LH: Based on unit per liter expressed and was considered for diagnosis of primary and secondary hypogonadism type.
6. FSH: Based on unit per liter expressed and and was considered for diagnosis of primary and secondary hypogonadism type.
7. Testosterone: Based on picogram per milliliter expressed and sexual hormone is secreted from the testis. Testosterone concentration was considered less than 30 Pg/ml as hypogonadism index.
8. Thyroid function tests (T4, TSH): Based on microunit per milliliter are expressed.
9. Ferritin: Based on microgram per liter expressed and its normal for men is 15-400.

10. Blood glucose: Based on milligram per deciliter expressed and was considered for diagnosis of Diabetes.
11. Calcium: Based on milligram per deciliter expressed and its normal is 8.5-10.2 milligrams per deciliter.
12. Phosphorus: Based on milligram per deciliter espressed and its normal is 3- 4.5 milligrams per deciliter.
13. Alkaline phosphatase, cholesterol, LDL, HDL, TG all of them are expressed based on milligrams per deciliter.

Data was reported with descriptive statistics and processing was performed by SPSS statistical software. The results are expressed as mean, standard deviation, and percent. The statistical differences degree between proportions was determined using Chi-square test at 95% (p= 0.005).

RESULTS

In total of 37 patients who had inclusion criteria to the study, 22 persons (59.46%) of them had testis length less than 2.5 ml which is deemed as hypogonadism criterion or maturity delay and 15 persons (40.54%) had been shown maturity signs (Figure 1).

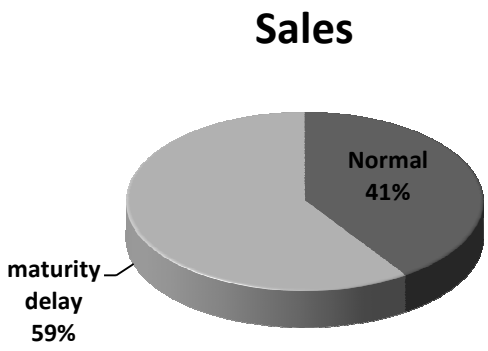

Figure 1. Maturity status in studied patients major thalassemia patients

The average of sex hormones level in patients is came in figure 2.

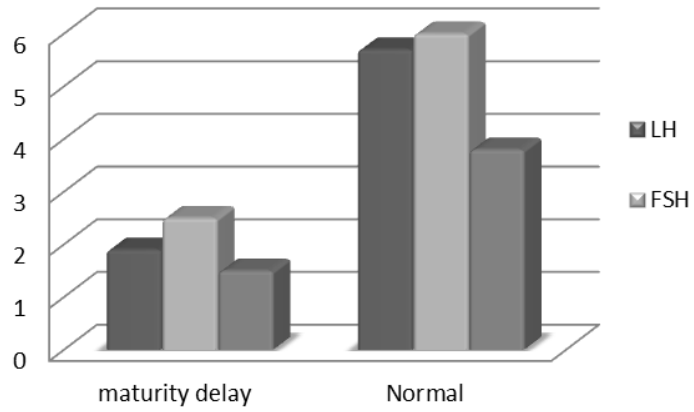

Figure 2. The average of LH, FSH, and testosterone in patients with and without maturity delay

Fasting blood sugar (FBS) from 37 studied patients, in 10 persons was between 100- 126 that are accounted component of patients with glucose tolerance disorder (IFG) (Table 1).

Table 1. Classification of the patients in term of fasting blood sugar

FBS	Frequency	Frequency percent
< 100	23	62.16%
100 - 126	10	27.02%
< 126	4	10.81%

In term of investigation FBS between two group of hypogonadism and individuals with maturity signs: IFG (FBS between 100- 126) between two group with P_{Value}= 0.033 was not seen a significant difference. In FBS> 126 also between two groups with P_{Value}> 0.05 was not seen a significant difference (Table 2).

Table 2. Analysis based on frequency, frequency percent of FBS in both groups of patients

FBS	Hypogonadism	Frequency	Frequency percent in group
>100	+	16	72.7
	-	7	46.6
100 - 126	+	4	18.2
	-	6	40
>126	+	2	9
	-	2	13.3

In table 3 Frequency and frequenct percent of calcium rate show primary hypothyroidism and hypocalcemia in both groups of patients who 4 patients with Ca< 8.5 mg/dl simultaneous had maturity delay. Hypocalcemia did not have a significant difference in both groups (P> 0.05).

Table 3. Analysis based on frequency and precent frequency of calcium rate in both groups

Ca	Hypogonadism	Frequency	Frequency percent in group
Ca < 8.5 mg/dl	+	18	81.8
	-	11	73.3
Ca > 8.5 mg/dl	+	4	18.2
	-	4	26.7

The phosphorus average of all patients was 4.92 ± 0.61 mg/dl which shows mentioned patients have phosphorus average higher than the general population. Also, 8 persons (21.6%) of patients had hepatomegaly in examination whose their liver 3 Cm was touch under the ribs edge. Also, 12 persons (32.4%) of patients had been splenectomy and 10 persons (27.02%) of patients has palpable spleen in examination as well.

The hemoglobin average has been classified before blood transfusion during 6 months.

Table 4. Classification of patients in term of hemoglobin before blood transfusion

pretransfusion Hb	Frequency	Frequency percent
5 - 7	21	56.8%
9	12	32.4%
>9	4	10.8%

Pearson-Chi Square test was not shown a significant difference for assessing between maturity delay with hemoglobin before blood transfusion (P= 0.09) (Figure 3).

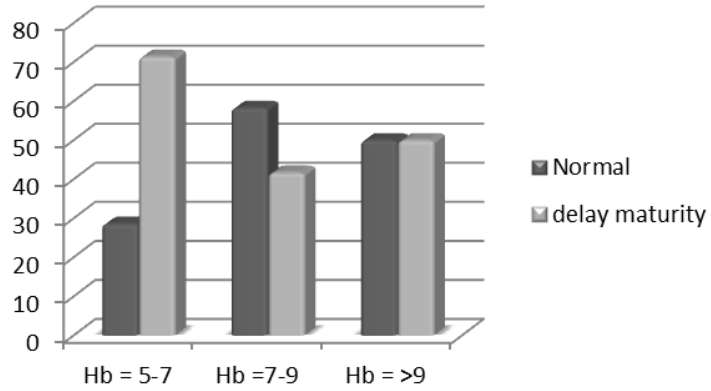

Figure 3. The average of hemoglobin before blood transfusion with and without delay maturity

The average of serum ferritin of patients during 6 months is referred in table 5.

Table 5. Classification of patients in term of serum ferritin in 6 months

The average of serum ferritin in 6 months	Frequency	Frequency percent
2000 >	9	24.3%
2000-4000	16	43.2%
4000 <	12	32.4%

The average of serum ferritin in two groups of hypogonadism and patients with natural maturity, in hypogonadism group was 4408 ± 1918 and in healthy group was 2331 ± 744 and independent t test was not shown a significant difference (P≤ 0.0001) (Figure 4).

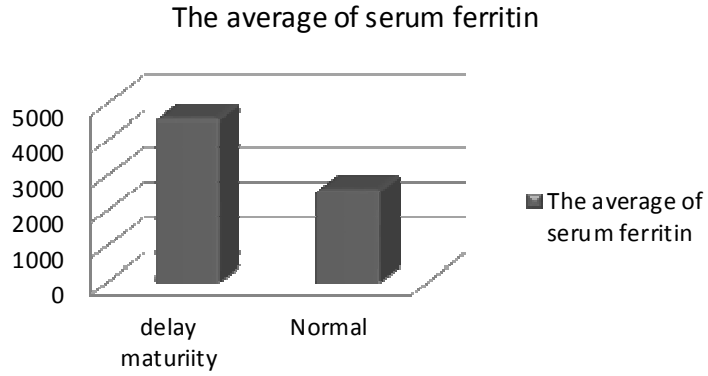

Figure 4. The average of serum ferritin in 6 months in patients with and without delay maturiity

Table 6. Analysis based on mean and standard deviation of sexual hormones in both groups of patients

Variable	Hypogonadism	Mean	Standard deviation
LH (U/lit)	+	1.90	1.117
	-	5.57	0.87
FSH (U/lit)	+	2.17	1.09
	-	5.70	1.42
Testosterone (Pg/ml)	+	1.24	1.59
	-	3.50	1.74

Table 7. Laboratory values of 33 patients affected by major thalassemia

Variable	Standard Deviation	Mean	Minimum	Maximum
LH (U/lit)	2.11	3.48	0.45	7.71
FSH (U/lit)	1.86	3.79	0.8	8.45
Testosterone (Pg/ml)	1.99	2.21	0.2	9.1
TSH (мU/ml)	0.96	1.68	0.6	7.9
Ca (mg/dl)	1.13	8.96	6.7	10.4
P (mg/dl)	0.61	4.92	4.1	7.0
Alkp (mg/dl)	121	361	96	715

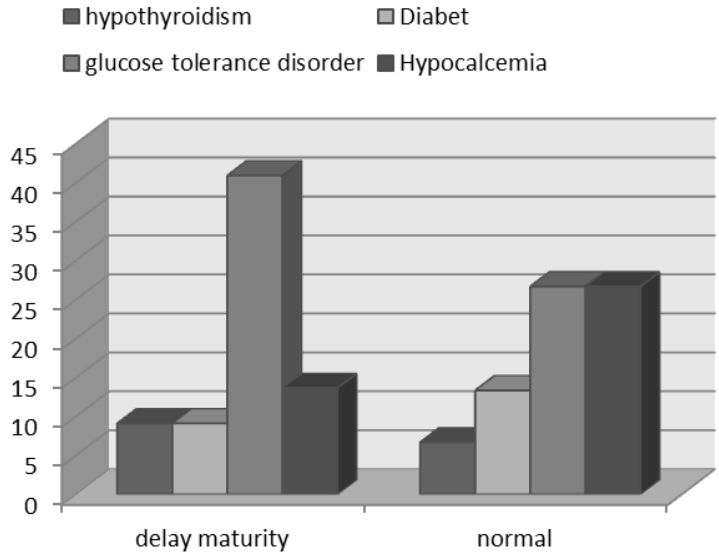

Figure 5. Frequency percent of compeer disorders in patients with and without delay maturity

The height average of patients was 154 ± 10.2 cm. Considering the height less than 2 standard deviations as height short, 64.86% had height short and the prevalence of height short and hypogonadism in these patients was almost close together.

CONCLUSION AND DISCUSSION

The study shows that there is a clear relationship between growth disorder and weight loss in patients with thalassemia and with age increase, determines growth disorder rate so that the highest growth disorders rate is in age group over 14 years and hypogonadism (6.63% in total of patients) introduced it is that hypogonadism and delay maturity play a key role in process of short stature patients.

In our study, existence of patients in affection risk to diabetes in the future shows thet only fasting blood sugar measurement can not be sufficient in follow up and thalassemic patients control and glucose tolerance test should be taken to be diagnosed in the early stages of their diabetes. In our study, 8 persons (21.6%) of patients had been affected by hypocalcemia as 5.8 mg/dl > Ca who 4 persons of them simultaneous had delay maturity. The phosphorous average of total patients was higher than phosphorous natural average (3.75 ± 0.75) that can be said the serum calcium average of the patients less and their phosphorous average is higher than the international standard that likely iron sediment hypocalcemia in the parathyroid gland and lack of appropriate response of this gland with hypocalcemia or is due to nutritional.

In a study, 22.7% of patients were affected by hypocalcemia who 70% of them simultaneous had hyperphosphatemia (4). In another study on 112 patients, 12.4% of them had thalassemia (5). Although not measured parathyroid hormone in this study, according to others' studies and lowing the prevalence of hypo-parathyroid from hypocalcemia, it seems hypocalcemia has also other causes except hypoparathyroidism (6). In studied population, any secondary hypothyroidism cases did not find. Prevalence of hypothyroidism in some studies,

was reported 18% and in other some from zero to 9%. In addition, in other research, 7.7% and 10.8% of patients were affected by clear hypothyroidism (7). Based on the study results , poor control of plasma ferritin has a important role in maturity delay, so nutritional status improvement and adequate control of ferritin with regular use of deferoxamine in effective in growth improvement and sexual maturity status of major thalassemia patients.

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