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Distribution of BMI, Blood Groups, and Secretory Status Among Iraqi Patients with Beta Thalassemia Major

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Abstract
Background: Beta-thalassemia is an inherited disorder of hemoglobin synthesis characterized by deficient synthesis of the ß-globin chain that causes severe anemia. One of the complication is internal organ damage due to iron over load resulted from long life blood transfusion leading to growth retardation, delay of sexual maturation, and later involvement of the heart, liver, and endocrine system.**Aim of study**: This study was designed to determine the status of Iraqi TM patients in respect to their body mass index (BMI), blood groups, as well as secretory status in comparison to healthy subjects as control. **Methodology:** Sixty nine TM patients were recruited from the thalassemia center / Ibn-Albalady hospital/ Baghdad/ Iraq, and twenty normal subjects with matched age and sex. The height and weight of all subjects was measured to determine the BMI categories, blood and saliva samples were obtained to determine blood groups and secretory status respectively.**Results:** Non-significant difference in the distribution of blood groups was recorded between patients and normal subjects, while frequency of non-secretors was significantly elevated (P= 0.019) from 20% among normal subjects up to 49.3% among TM patients. However, BMI was significantly decreased ($P < 0.00001$) from (23.2 ± 5.1 kg/m^2) with only 5% underweight cases in control group down to (17.9 ± 2.8 kg/m^2) with 14.5% underweight cases among TM patients.**Conclusion:** This study suggested that status in TM patients may play an important role as risk factor that associated with severity of iron overload complications and need further investigation.
Keywords: Beta-thalassemia, Blood groups, Secretory status, Body mass index

Introduction:

Thalassemia major presents as a progressive anemia during 6-24 months of age as γ-chain synthesis diminishes without a concomitant increase in β-chain synthesis due to genetic abnormalities involving both β genes[1].Three of the general allele combinations are responsible for this thalassemia phenotype;B^0/B^0,B^0/B^+, and sometimes B^+/B^+ [2]. In thalassemia major, the excess unpaired alpha-globin chains aggregate to form inclusion bodies that damage RBC membranes, leading to intravascular hemolysis and premature destruction of RBC precursors, causing ineffective erythropoiesis[3,4]. The commonest form of life-long treatment for individuals with beta-thalassemia major is regular blood transfusions in order to maintain Hb blood concentration and to compensate for ineffective erythropoiesis[5]. However, multiple blood transfusions can result in several adverse effects which include iron overload, serious infections such as hepatitis B or C, and hypersensitivity reactions[6]. Moreover, iron overload can result in multiple progressive organ damage grouped together under a condition called hemosiderosis that involved heart, liver, and endocrine system lead to growth retardation and delay of sexual maturation in children[1].

On the other hand, it was found that individuals could be classified as 'secretors' and 'non-secretors' according to their ability to secrete ABO blood group antigens in saliva[7]. H antigen that is present on the cells of individuals with O blood group is base for A and B antigens, but A&B antigens differ only in their added terminal sugars, which are controlled by specific enzymes called fucosyltransferase enzymes (FUT). These enzymes are under the control of inherited genes, which are(*FUT1*)gene for ABH blood group system, (*FUT2*) gene for secretor status, and (*FUT3*) gene for Lewis antigen system[8,9].

Generally, about 80% of the world's population are secretors of ABH antigens and only 20% are non-secretors but with some racial differences[10].Determining ABH secretor phenotype may be useful as risk factor determinates for a number of conditions including heart disease, diabetes, insulin resistance, and certain types of cancer, autoimmune diseases, celiac disease, chronic urinary tract infections, and others[9].

Since most of researches doesn't focused on secretory status in TM patients, therefore the present study was conducted to investigate this feature and its association with some complications in those patients.

Material and methods

This study has been designed upon Iraqi patients with β thalassemia major in the thalassemia center / Ibn-Albalady hospital/ Baghdad/ Iraq during the period from December 2014 up to July 2015. Subjects involved in this study include eighty nine; 69 of them were patients with homozygous beta-thalassemia major (TM) (44 males, and 25 females) at age range 4-30 years, all of them were blood transfusion-dependent, also all of them

were on iron chelation therapy. Twenty normal subjects (10 males, and 10 females) with age range corresponding to that of patients were involved and considered as control group. For adults (> 20 years aged), a BMI of less than 18.5 is considered underweight, while a BMI greater than 25 is considered overweight and above 30 is considered obese[11]. However, for children and adolescents (2-20 years aged), a BMI that is less than the 5th percentile is considered underweight and above the 95th percentile is considered obese, while those with a BMI between the 85th and 95th percentile are considered to be overweight[12]. Blood and saliva samples were collected from all subjects (normal and TM patients). The ABO blood groups were determined according to the tube method by using Anti-A, Anti-B (Biotec, Germany) [13], and the secretory status of all subjects were determined according to inhibition of hemagglutination test by using tube technique by using anti-H lectin (Biorex, UK) [14].

Results:

Sixty nine subjects with β-thalassemia major (patients group) and twenty normal subjects (control group) were involved in this study. The homogeneity of age and gender in both groups were recorded without significant differences as shown in (Table -1).

Table -1: Frequency of age and gender in control and patients groups

Character		Groups		Significance (P =)
		Control	Patients	
Age (years)	N	20	69	0.322
	M±SD	15.9 ± 5.5	14.1 ± 7.1	
Gender	Male (n), (%)	(10), (50%)	(44), (63.8%)	0.267
	Female (n), (%)	(10), (50%)	(25), 36.2%)	
Age analyzed by t-test, while gender by Pearson Chi-square				

The statistical analysis of blood groups and secretory status showed non-significant difference in the distribution of blood groups between the control and patients groups as shown in (Table -2). However, the frequency of non-secretors was significantly elevated (P= 0.019) from 20% in control group up to 49.3% in thalassemic patients group.

Table 2: Frequency of blood groups and secretory status distribution in control and patients groups

Groups		Blood Groups				Secretory status	
		A	B	AB	O	Secretors	Non-secretors
Control	**n**	8	5	2	5	16	4
	%	40%	25%	10%	25%	80%	20%
Patients	**n**	21	16	1	31	35	34
	%	30.4%	23.2%	1.5%	44.9%	50.7%	49.3%
Chi-square		***(P= 0.148)***				***P=0.019***	

The results revealed that there is significant difference (P < 0.00001) in the BMI between the control (23.2 ± 5.1 kg/m^2) and patients (17.9 ± 2.8 kg/m^2). Depending on the standard reference of BMI categories, the frequency of each category was calculated for male and female at different age of all subjects. By using Chi-square test, statistical analysis of results showed that 14.5% of the patients have underweight body stature and the remainder having normal (72.5%), overweight (5.8%), and obesity (7.2%) with high significant association (P < 0.004) from those in subjects of control group (5%, 45%, 25%, and 25% respectively) as shown in (Figure -1).

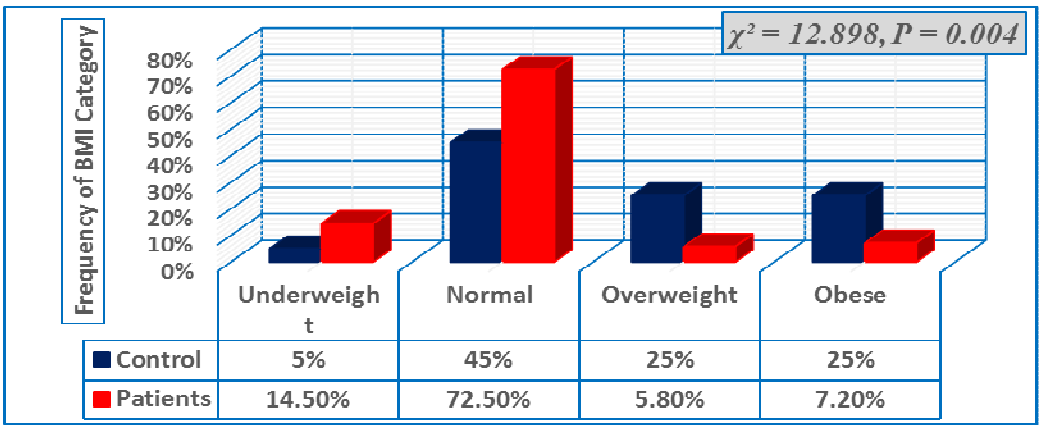

Figure -1: Frequency of BMI categories in patients and control groups

Discussion

On the other hand, this study demonstrated non-significant difference in the distribution of blood groups between the control and patients, although 'O' group was the most frequent (44.9%) among TM patients (Table-2). Similarly to this result, other studies found that blood group O was the highest percentage distribution (42.86%) among TM patients[15] and 35.8% among patients with hemoglobinopathy[16]. According to previous study carried on 24063 Iraqi people, the normal distribution of ABO blood groups recorded that blood group O constitute about 34.7% [17]. The relationship between ABO blood group and susceptibility to chronic disease as an example of genetic basis for family predisposition has been discussed, and the results showed that some diseases like hematological malignancies [18] and ischemic heart disease[19] had significant association. Furthermore, Orstavik and colleagues found that 66 percent of the total variation in plasma von Willebrand factor (VWF) levels was genetically determined and that 30 percent of this genetic component was explained by ABO blood group [20,21]. Other study has been reported that group O subjects have lower plasma VWF levels than non-O individuals [22].

The present study not claimed that there is a direct relationship between thalassemia disease and ABO blood groups distribution, but may be indirect association via the expression of gene responsible for specific enzymes called fucosyltransferase enzymes (FUT) because the results of this study reported high significant frequency of non-secretors (49.3%) in thalassemic patients group in comparison with those in control group (20%) as shown in (Table -2). These enzymes are under the control of inherited genes, which are (*FUT1*) gene for ABH blood group system, (*FUT2*) gene for secretor status, and (*FUT3*) gene for Lewis antigen system[8,9]. It is generally known that about 80% of the world's population are secretors of ABH antigens and only 20% are non-secretors but with some racial differences [23]. Determining ABH secretor phenotype and/or Lewis blood group status may be useful as risk factor determinates for a number of conditions including heart disease, diabetes, insulin resistance, certain types of cancer, autoimmune diseases, and others [9]. It has been reported that secretor and non-secretor status as well as certain blood group makes somebody prone to communicable and non-communicable diseases [24,25]

As growth disturbances are a major clinical feature of patients with beta-thalassemia major [26], the result of this study showed significant difference ($P < 0.00001$) in the BMI between the control and patients and about (14.5%) of the patients have underweight body stature in comparison to those in subjects of control group (Figure -1). Several other studies also found that the weight of (31%) of TM patients was below the 3rd percentile [27], and (52%) of their cases were below the 3rd percentile [28], but according to the age of TM patients, it has been found that (12.4%) of TM patients under (10) years have underweight BMI up to (46.5%) in patients with age above (10) years [29]. This finding has many possible etiologies, the most important of which are possibly the presence of multiple endocrinopathies, under-nutrition as well as other complications of thalassemia such as tissue hypoxia, and side effects of chelating therapy with desferrioxamine [26,30,31]. The toxic effect of deferoxamine on linear growth could be due to excess deferoxamine accumulating in tissues and interfering with iron-dependent enzymes which are involved in the post-translational modification of collagen [32], additionally, low rate of growth and BMI and delayed or absent pubertal spurt in thalassemic patients were related to low hemoglobin and high ferritin levels and sub-optimal iron chelation therapy [33]. Recently, it was found that the thalassemic patients had low BMI, and nearly two third of them (60%) are underweight, but non-splenectomized TM patients revealed lower BMI (16.5 kg/m^2) and higher percentage of underweighted patients (77.3%) in comparison with splenectomized patients (18.2 kg/m2, (38.9%) respectively [34]. it has been postulated that the developed endocrinopathies secondary to iron overload, and also possibly side effects of chelating therapy in long term are major contributing factors in producing underweight patients [26,29]. Also it may be due to iron overload resulting in multiple progressive organ damage which includes growth retardation and delay of sexual maturation in children, and later involvement of the heart, liver, and endocrine system [35,36].

In conclusion. This study suggested that status in TM patients may play an important role as risk factor that associated with severity of iron overload complications and need further investigation.

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