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Original Research Article

Assessment of Humoral Immunity of Patients with β- Thalassemia

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ABSTRACT

Background: Infectious complications form an important cause for morbidity and mortality in thalassemia patients. Many studies tried to investigate any possible defect or change in immune state that can be responsible for increase susceptibility to infections in these patients.
Objective: To assess the humoral immunity in thalassemia patients and evaluate its possible role in high rate of infections in these patients.
Methods: Cross-sectional study of 34 β-thalassemia patients and 10 control case in period from first of March to end of May of 2015 in Wasit Provenance in Iraq.
Results: Mean serum level of IgM was significantly higher in patients than control only in age group ≥ 15 years. However, it did not reach the significant level in age group < 15 years. Mean serum level of C3, C4, IgG, and IgA did not show significant difference between patients and control in both age groups. Iron overload appeared to have no role on humoral immunity of our patients.
Conclusion: Although our study did not show significant change in humoral immunity, the study of complement and immunoglobulin level can be useful in evaluating the function of immune system and explaining the high rate of infection in thalassemia patients.

Key words: Complement system, Humoral immunity, Immunoglobulin, Thalassemia.

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INTRODUCTION

Thalassemia is one of the most prevalent hematologic disorders worldwide[1]. Beta-thalassemia is a hereditary anemia due to defects in the production of β-globin chain. Patients with β-thalassemia major are prone to several complications including tendency to develop infections[2]. Many studies have been done to evaluate the possible changes of immune system in thalassemia patients, considering the humoral and cellular immune systems; but no consistent defect in white cells or immune function had been documented yet[3].

The susceptibility to infections in thalassemia is multifactorial and appears to be related to the disease itself, altered immune system secondary to blood transfusions, iron overload and splenectomy[4]. A wide range of abnormalities of the humoral and cell mediated immunity, along with other aspects of immune system have been reported in patients with thalassemia major[5].

Various immunological abnormalities are reported in previous studies such as, decreased opsonization and granulocyte phagocytosis, increased serum immunoglobulin levels and alterations in B and T cell number and function[6]. Immune deficiencies have been suggested as a precipitating factor for the fourth most common cause of death in beta-thalassemia, i.e. malignancies. Of course severe anemia, itself, is a risk factor for bacterial infections in thalassemia, predominantly pneumonia[7].

Some studies have revealed a decreased activity of T and B lymphocytes, neutrophils, macrophages and complements. Some studies have revealed an increased activity of B-lymphocytes and other studies reported normal levels[8].

MATERIALS AND METHODS

Cross-sectional study of 34 β-thalassemia major and intermediate patients and 10 control case in period from first of March to end of May of 2015. The patients were treated in thalassemia center in Wasit provenience in Iraq.

All patients and control were free form signs of infection. Blood samples were collected for assays before the monthly blood transfusions. Clinical and laboratory information was retrieved from the patients' notes files. Five ml of blood samples were centrifuged immediately and used.

Serum levels of immunoglobulin were determined using Radial immunodiffusion (RID) method. C3 and C4 level were detected by immunoassay method using MISPA-i2 (AGAPPE diagnostics Switzerland GmbH). The patients and control group were classified according their age (more or less than 15 years) as comprise the effect of age on immunoglobulin complement levels. SPSS software (version 20) was used to do statistical analysis of the data. Unpaired t test used to compare data with mean and SD.

RESULTS

The demographic data of the patients and control is shown in table 1. Male to female ratio was 1.4:1 for the patients while it was 1:1 in the control. The mean age for patients was 17.3 year with median 14.5 year with range (11-40) years. For the control, the mean of the age was 19 years with median 20 years with range (11-28) years.

Table 2 shows the demographic data of the patients, thalassemia major was reported in most the patients (73.5%) while thalassemia intermedia reported in six patients (26.5%). Splenectomy was done for 9 patients (26.5%). The mean of serum ferritin was 5000 ng/dl and the median 5300 ng/dl with range (227-11400 ng/dl). More than half the patients using X jade as iron chelator, 20 patients (58.8%). And twelve patients were using desferoxamine as iron chelators, (35.5%).

Comparison between mean serum level of IgG, IgM, IgA, C3, C4 levels in patients and control group according to age group is shown in table 3: mean serum level of IgM was significantly higher (p= 0.001) in patients than control only in age group ≥ 15 years . However in age group < 15 years it did not reach the significant level. Other humoral components (IgG, IgA, C3, and C4) did not show significant difference between patients and control in both age groups.

To evaluate the effect of iron overload on humoral immune parameters result, we classified our patients into two groups: one include patients with serum ferritin level < 2500 ng/dl and the second group with serum ferritin level ≥ 2500 ng/dl. Table 4 shows the mean serum level of C3, C4, IgG, IgM and IgA of both groups: no significant difference was found in serum immunoglobulin and complement level of both groups.

Table 1: Demographic data of the patients and control.

Item	Patients (%)	Control (%)
Male	20(58.8)	5(50)
Female	14(41.2)	5(50)
Age in years		
mean	17.3	19
median	14.5	20
Minimum	11	11
maximum	40	28

Table 2: Clinical and laboratory finding of the patients.

Item	No. (%)
Thalassemia type	
Major	25(73.5)
Intermedia	9(26.5)
Splenectomy	9 (26.5)
Serum ferritin (ng/dl)	
Mean	5000
Median	5300
Minimum	227
Maximum	11400

Table 3: Comparison of serum Ig levels and C3, C4 of thalassemia patients with matched controls and age group.

	Less than 15 years		
Item	**Patients (mean ±SD)(N)**	**Control (mean ±SD)(N)**	**P value**
C3 (mg/dl)	81.7(±19)(27)	93(±8.2)(4)	0.2
C4 (mg/dl)	24(±1.2)(27)	18.5(±3.1)(4)	0.3
Ig M (mg/dl)	77.5(±4.1)(13)	72.5(±6)(4)	0.07
Ig G (mg/dl)	1402(±751)(13)	1193(±78)(4)	0.6
Ig A (mg/dl)	322(±173)(13)	343(±78)(4)	0.9
	Equal or more than 15 years		
C3 (mg/dl)	85.7(±15.6)(7)	100(±10)(6)	0.07
C4 (mg/dl)	19.8(±9.7)(7)	26.3(±3.4)(6)	0.3
Ig M (mg/dl)	99.9(±5.7)(5)	87.3(±8.1)(6)	0.01
Ig G (mg/dl)	1311(±340)(5)	1470(±340)(6)	0.1
Ig A (mg/dl)	400(±219)(5)	340(±154)(6)	0.6

Table 4: Comparison of serum Ig and complement level in patients with high and low serum ferritin level

Item	< 2500 ng/dl	≥2500 ng/dl	P value
C3 mean ± SD (n)	81.2±11.9 (12)	83.3±21.2(22)	0.7
C4 mean ± SD (n)	18.5±9.9(12)	25.8±12 (22)	0.08
IgG mean ± SD (n)	1368.2±864.3(7)	1301.5±548.8(11)	0.8
IgM mean ± SD (n)	98.9±47.5 (7)	74±44.5(11)	0.2
IgA mean ± SD (n)	358.8±213.6(7)	333.9±172.8(11)	0.7

DISCUSSION

Patients with β- thalassemia suffer from many complications rather than the severe anemia, including increase rate of infection. Many studies investigated possible defect or change in humoral and cellular immunity that could be responsible for this high rate, but nothing was documented yet.

Some studies suggested that iron overload plays role in altering the immune system of β- thalsemia patients[6,9]. By enhancing migration of T-helper cells to the lymph nodes and gut, leading to increase IgG level[6]. According to our study, iron overload appear to have no role on immunoglobulin and complement levels. This finding agrees with other studies as Ahmed Amin study in Iran[10] and Najdat study in Iraq[11].

The humoral immune system is an important constituent of the immune system that fights infection in β-thalasemia patients, so that evaluation of immunoglobulin and complements level is vital in assessing the immune state of these patients.

Our study revealed intact humoral immunity in thalassemia patients except for IgM level which was significantly higher in thalassemia patients than control only in age group ≥ 15 years and this probably reflects the effect of age on immunoglobulin levels .The increasing level of IgM and non-increasing level of IgG may be due to many factors as repeated blood transfusions, recent infections rather than remote infection.

Many other studies on humoral immunity revealed heterogeneous results, some showed significant increase in IgM, IgG and IgA level and significant decrease in C3, C4 level as in Ahmed Amin study in South Iran[10]. Zuhair study in our country revealed results similar to Amin study in Iran[12]. Wafaa Sadoon study recorded significant increase only in IgG with no significant difference in other humoral components[13]. Mojgan Kiani-amin study in Iran revealed increase level of IgA in non splenctomized patients aged less than 5 years as well as splenctomized patients aged more than twenty while other immunoglobulins and complement levels were normal[14].

Others as Vergin study demonstrated that there was no significant abnormalities in immunoglobulins or complements[3].similar results was shown by Najdat Shukur study who studied immunoglobulins by immunofixation electrophoresis and revealed no abnormal immunoglobulin band[11].

This variation in studies results reflect the heterogeneity of thalassemia patients in different studies, this heterogeneity involve race, socioeconomic class, nutritional status, stage of the disease and environmental factors[3].

CONCLUSION

Many factors play role in significant abnormalities of immune parameters in patients with thalassemia. These abnormalities are variable with age of the patient and clinical state.

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