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Assessment of Some Immunological Parametrs in Respect to Glycemic Control in Type 1 and 2 Diabetes Mellitus: Comparative Study

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Abstract: Changes in immunological parameters are observed in Type 1 (T1D) and Type 2 (T2D) diabetes. Some of them are linked with diabetic complications this study aimed to assess some components of complement system (notably C3 and C4) and immunoglobulins (IgA, IgG, IgM) in T1D and T2D in reference to their glycemic control. A total number of 160 (70 male and 90 female) T1D and 75 T2D (25 male and 50 female) patients who allocated randomly as well as 40 healthy subjects are enrolled in the study. Glycosylated hemoglobin (HbA1c%) and serum glucose, complements C3, C4 and immunoglobulins IgA, IgG and IgM were measured. On 4 out of 160 T1D patients have HbA1c >7% and none of T2D patients havely than HbA1c >11%. Serum C3 and C4 of T1D patients is significantly less than corresponding value of healthy subjects and the lowest value of C3 is observed in patients with HbA1c >11%. Only serum IgM is significantly decreased in T1D and T2D patients compared with healthy subjects and there is no significant differences between T1D and T2D patients. Some immunological parameters are depressed in poor-controlled diabetes. The difference in immune response between T1D and T2D patients is observed in serum C3.

Key words: Complement, immunoglobulin, diabetes, complement system, patients, Iraq

INTRODUCTION

Disturbances of immune system may be the cause and/or associated with diabetes mellitus. Type 1 Diabetes (T1D) is the result of a breakdown in immune regulation that leads to expansion of autoreactive CD4+ and CD8+T cells, autoantibody-producing B lymphocytes and activation of the innate immune system (Coppieters and von Herrath, 2010; Meier-Stiegen and Ziegler, 2011). In Type 2 Diabetes (T2D), the immunity is deteriorated and the inflammatory process is enhanced in term of increased level of immunoglobulins. Also, T2D is inked by coincident presentation and alterations in Toll-Like Receptor (TLR)-dependent B cell cytokine production (Nikolajczyk, 2010). Morimoto *et al.* (1988a, b) studied the status of some components of complement system in both T1D and T2D and found significant increase in serum level of CH50, C3, C4 and C3bINA compared with non-diabetic healthy controls (Morimoto *et al.*, 1988b). Moreover, higher level of complements particularly C4 was reported in T2D complications (retinopathy and neuropathy) compared without complications (Morimoto *et al.*, 1988a, b). Recently, Awartani F reported that IgA and IgG levels were found to be significantly higher in poorly controlled T2D (HbA1c≥9%) as compared with those having HbA1c<9% (Awartani, 2010). In children with T1D the significant high serum level of IgG is attributed to the interaction of IgG with anti-cow immunoglobulins (Haroun and El-Sayed, 2007). Serum Ig A level in T1D is either within normal value or decreases and it is not well correlated with HbA1c% (Sayarifard *et al.*, 2010). Therefore, it is worth trial to assess some components of complement system (notably C3 and C4) and immunoglobulins (IgA, IgG, IgM) in T1D and T2D in reference to their glycemic control.

MATERIALS AND METHODS

This study is conducted in Martyr Layla Qasm center for diabetes mellitus in Erbil, Iraq during the period of 1st of August 2008 to 30 December 2009. The study is approved by the local scientific committee of College of Pharmacy, Hawler Medical University. A consent form was obtained from each participant prior to the study. A total number of 160 (70 male and 90 female) T1D and 75 T2D (25 male and 50 female) patients who allocated randomly are enrolled in the study. An apparent healthy subjects (n = 40) were also included in this study as control group. A fasting venous blood samples were obtained from participants and the sera were separated for determination of glucose, glycosylated hemoglobin (HbA_{1c}%). Single Radioimmunoassay (SRIA) based determination of serum IgA, IgG, IgM antibodies and the components of C3 and C4 complements were used.

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Statistical analysis: The results are expressed as number and mean±SD. The data were analyzed using two tailed unpaired student's t-test and simple correlation test taking $p \leq 0.05$ as the lowest limit of significance.

RESULTS AND DISCUSSION

Table 1 shows the characteristics of patients enrolled in the study. The duration of disease in T2D is significantly longer than corresponding T1D. Poor glycemic control as assessed by fasting serum glucose and HbA1c% is observed in T1D and T2D and significant higher values are observed in T1D compared with T2D patients (Table 1). Only 4 out of 160 T1D patients have HbA1c <7% and none of T2D patients havely than HbA1c >11%. There is significant direct correlation ($r = 0.38$, $p<0.001$) between duration of diabetes and HbA1c% in T2D patients while the correlation in T1D is inverse and does not reach to the level of significant ($r = -0.153$, $p>0.05$). Table 2 shows the serum C3 and C4 of T1D patients is significantly less than corresponding value of healthy subjects and the lowest value of C3 is observed in patients with HbA1c >11%. In T2D patients, the serum C3 is significantly higher than healthy subjects and T1D while the serum C4 is non-significantly higher than healthy subjects and significantly higher than corresponding value of T1D patients. Regarding the immunoglobulin level, only serum IgM is significantly decreased in T1D and T2D patients compared with healthy subjects and there is no significant differences between T1D and T2D patients (Table 3).

The results reported in this study show that the immune response in patients with T1D patients is differed from that of patients in T2D and the decreased serum C3 level is related to the poor glycemic control in T1D and T2D. The decreased serum levels of C3 and C4 indicated that the adaptive and innate immunity are declined in T1D patients and to less extent in T2D (Carroll, 2004; Botto *et al*., 2009). The association of decreased serum C3 level and poor glycemic control in T1D may herald the susceptibility of those patients to the life threatening susceptibility to pyogenic infection (Botto *et al*., 2009). On the other hand, the decreased serum C4 level pointed out the existence of immune complex disease which is clearly observed in T1D (Nicoloff *et al*., 2004). Therefore, these results show that T1D patients with poor glycemic control are more vulnerable to pyogenic infection compared with T2D and the autoimmune etiological factor is not solely related to T1D and it may shared in type T2D (Yeung *et al*., 2011; Husebye and Anderson, 2010). On the other hand, the status of serum immunoglobulin is shifted to significant decrease in serum IgM in T1D and T2D. The lowest serum IgM is associated with the higher HbA1c%. The clinical significance of this observation is related to presence of occult chronic infectious disease (Shin *et al*., 2006). Recent studies show that increased urinary IgM excretion is an increase in urinary IgM excretion in patients with type 1 diabetes is associated with an increased risk for cardiovascular mortality and renal

Table 1: The characteristics of the T1D and T2D patients enrolled in the study

Factors	Healthy subjects (n = 40)	T1D patients (n = 160)	T2D patients (n = 75)
Gender			
Male	20	70	25
Female	20	90	50
Age (year)			
Mean±SD	27.1±7.8	22.2±9.3	41±4.2*
Median	17.4	21	41
Duration of diabetes (year)		6.01±2.86	8.21±1.42*
Fasting serum glucose (mg dL^{-1})	91.4±5.9	336.4±77.8†	211.2±26.0
Glycosylated hemoglobin (HbA_{1c} %)	5.282±0.484	9.486±1.193†	8.65±0.72

*p<0.001 compared with T1D patients and healthy subjects. †p<0.001 compared with T2D patients and healthy subjects

Table 2: Serum level of C3 and C4 (mg dL^{-1}) in respect to HbA1c % T1D and T2D patients

	Healthy subjects			T1D patients			T2D patients		
HbA1c %	n	C3	C4	n	C3	C4	n	C3	C4
≤7	40	131.9±70.9	39.4±10.5	4	-	-	-	-	-
7.1-9.0	-	-	-	61	94.8±24.2*	26.4±10.3*	56	165.8±56.38*†	32.8±12.4*
9.1-11.0	-	-	-	73	91.2±26.9*	26.9±10.5*	19	157.7±49.60†	30.9±10.8*
≥11.1	-	-	-	62	85.5±18.1**	28.5±9.10*	-	-	-

*p<0.01, **p<0.001 compared with healthy subjects. †p<0.001 compared with T1D

Table 3: Serum level of immunoglobulins Ig A, IgG and IgM (mg dL^{-1}) in respect to HbA1c % in T1D and T2D patients

	Healthy subjects				T1D patients				T2D patients			
HbA1c %	n	IgA	IgG	IgM	n	IgA	IgG	IgM	n	IgA	IgG	IgM
≤7	40	370.6±114.4	1364.5±285.3	219±44	3	-	-	-	-	-	-	-
7.1-9.0	-	-	-	-	61	360.7±149.1	1045.0±352.4	179.5±56.3†	56	376.3±136.5	1112.3±360.6	185.1±51.7†
9.1-11.0	-	-	-	-	73	383.9±132.0	1115.2±346.9	184.3±64.2†	19	323.6±124.0	1051.8±395.8	179.7±62.2*
≥11.1	-	-	-	-	62	339.4±141.0	1087.3±327.1	175.9±58.8†	-	-	-	-

*p<0.02, †p<0.001 compared with healthy subjects

failure (Tofik *et al*., 2009). Although, celiac disease is commonly associated with diabetes and accompanied with significant changes in serum and intestinal IgA neither celiac disease non-significant changes in serum IgA in T1D or T2D are found in this study (Uibo *et al*., 2011).

CONCLUSION

The results of this study clearly defined that some components of humoral immunity particularly C3 and IgM are significantly reduced in presence of poor glycemic control. Further study is recommended to assess serum C3 and IgM as abiomarkers to detect the latent complications of diabetes. It concludes that some immunological parameters are depressed in poor-controlled diabetes. The difference in immune response between T1D and T2D patients is observed in serum C3.

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