

RELATIONSHIP BETWEEN ANTICARDIOLIPIN AND DIABETES MELLITUS PATIENTS TYPE 2

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Abstract

An Anticardiolipin antibody, oxidatively modified low-density lipoproteins is humoral factor that has been linked to vascular damage. To analyze their possible role in the complication in type 2 diabetes mellitus, we investigated (22) patients with diabetes mellitus type 2 of ages (35-68) years.

The patients were also compared with (20) healthy individuals. The level of anticardiolipin antibody was measured by using Enzyme Linked Immuno Sorbent Assay test (ELISA), there was a highly significant elevation in IgM and IgG anticardiolipin concentration in patient with diabetic mellitus than in controls group ($P < 0.001$). The prevalence of IgM and IgG anticardiolipin antibody was (13.6% and 9.1%) respectively. There were highly significant differences between study groups than in control groups.

The higher levels of anticardiolipin Abs of both type IgG and IgM suggests that these humoral factors might be involved in the pathogenesis and complications of type 2 diabetes mellitus.

Introduction

Type 2 Diabetes mellitus (DM) occurs when pancreas produce insufficient amounts of the hormone insulin and/or the body's tissues become resistant to normal or even high levels of insulin, this causes high blood glucose levels which can lead to a number of complications [1]. Whereas cardiolipin (biphosphotidyl glycerol) is an important component of the inner mitochondrial membrane where it constitutes about 20% of the total lipid and it is typically present in metabolically active cells of the heart and skeletal muscle in the membrane of their mitochondria[2]. Anticardiolipin(ACL)antibod ismay play a role in the enhancement of platelet

Aggregation and/or progression of the macro vascular diabetic complications, Also (ACL) antibodies may cause or promote ischemia and thrombosis [3]. Cardiolipin has recently been found to be deficient in the heart at the earliest stages of diabetes, possibly due to a lipid-digesting enzyme that becomes more active in diabetic heart muscle[4]. ACA antibodies divided into two groups, antibodies dependant about B2-glycoprotein 1(B2GP1) and independent (B2GP1) and these antibodies dependent (B2GP1) related with Antiphosphlipid antibodies syndrome (APS)[5]. In anti-

cardiolipin mediated autoimmune disease there is a dependency on the apolipoprotein H for recognition [6].

Diabetes has been shown to be an independent risk factor for the development of atherosclerosis [7]. Some humoral factors like anti-cardiolipin antibodies (ACL), other negatively charged phospholipids, are associated with accelerated atherosclerosis [8].

The purpose of this study was to investigate the possible contribution of the humoral factor ACL in type 2 diabetes mellitus and compare their prevalence with a healthy control group.

Materials and Methods

The study included (22) patients with type 2 diabetes mellitus of ages 35-68 years treated at National Center for diabetes in Al-Mustansiriya University; and 20 healthy blood donors taken as a healthy control group.

Individuals with another autoimmune disease were excluded. IgG and IgM anticardiolipin antibodies were measured in both serum samples by using Enzyme Linked Immuno Sorbent Assay (ELISA). This was performed and described in the leaflet of the kit (AESKULISA Germany).

Statistical Analysis

Comparison of paired data from the three groups of subjects was done using T-test (t), while correlations between groups were analyzed using person correlation coefficient (r) formula. Statistical tables including observed frequencies with their percentage. SPSS and Microsoft Excel Programs were used for T-test and correlation coefficient calculations respectively. [9]

Results

The levels of ACL in patient with diabetic mellitus and controls are reported in Tables & Figs. (1-4).

There was a highly significant elevation in IgM and IgG ACL concentration in patient with diabetes mellitus than in negative and control groups ($P < 0.001$).

The prevalence of IgM and IgG was 13.6% (3/22) and 9.1% (2/22) respectively. There was highly significant difference between study groups.

Table (1)
Anti-cardiolipin Ab (IgG) in sera of diabetic patient.

Diseases	Anti- Cardioplin Ab. (IgG)	No.	%	Chi-square (χ^2)	
				P-value	Sig.
DM	Positive	2	9.1	0.00	Highly Sig. ($P < 0.01$)
	Negative	20	90.9		

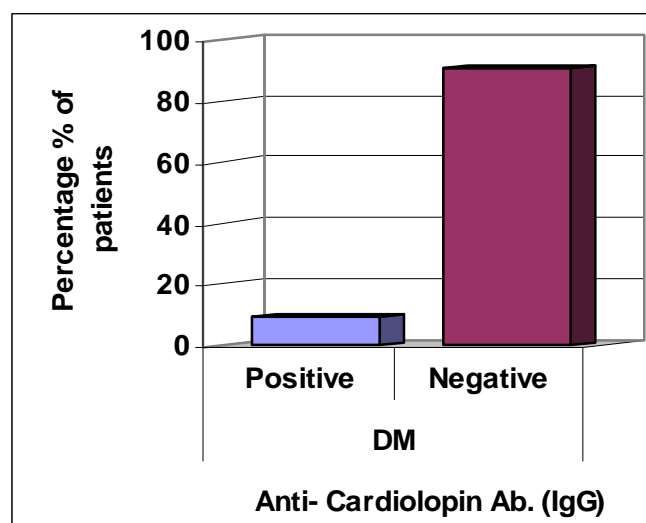


Fig. (1): Anti- cardiolipin Ab (IgG) in sera of diabetic patient.

Table (2)
Anti- cardiolipin Ab (IgM) in sera of diabetic patient.

Diseases	Anti- Cardiolipin Ab. (IgM)	No.	%	Chi-square (χ^2)	
				P-value	Sig.
DM	Positive	3	13.6	0.001	Highly Sig. (P<0.01)
	Negative	19	86.4		

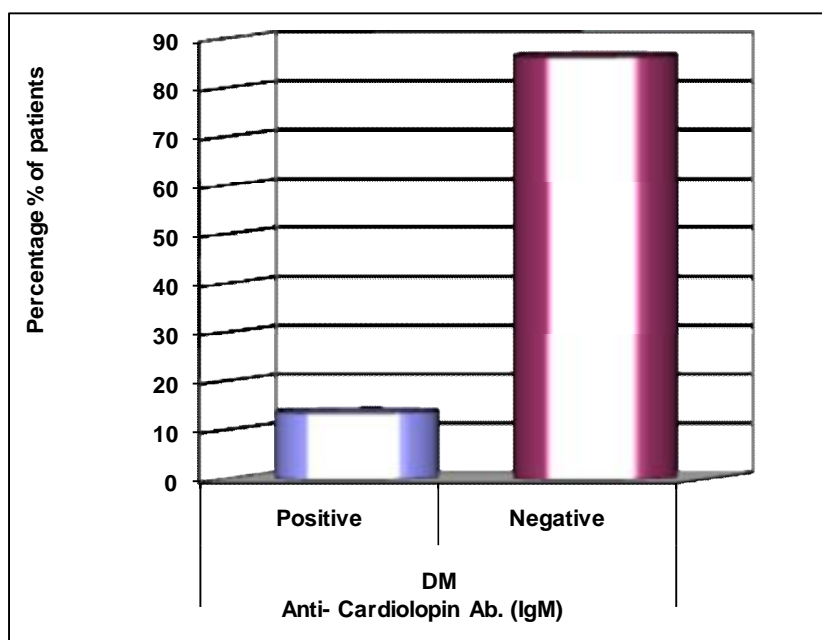


Fig. (2): Anti- cardiolipin Ab (IgM) in sera of diabetic patient.

Table (3)
Mean distribution of anti-CLP Ab-IgG (GPL/ml) level among studied group (Control & diabetic patients).

Studied group	N	Mean	SD	Std. Error	Min.	Max.	Student test (t-test)		
							P-value	Sig.	
Control	20	8.65	2.37	0.53	4	13	-	-	
Anti-CLP Ab. (IgG)	Positive	2	26.1	11.31	8	18	34	0.00	HS
	Negative	20	7.45	2.31	0.52	4	13	0.203	NS
Total	42	Positive Vs Negative					0.00	HS	

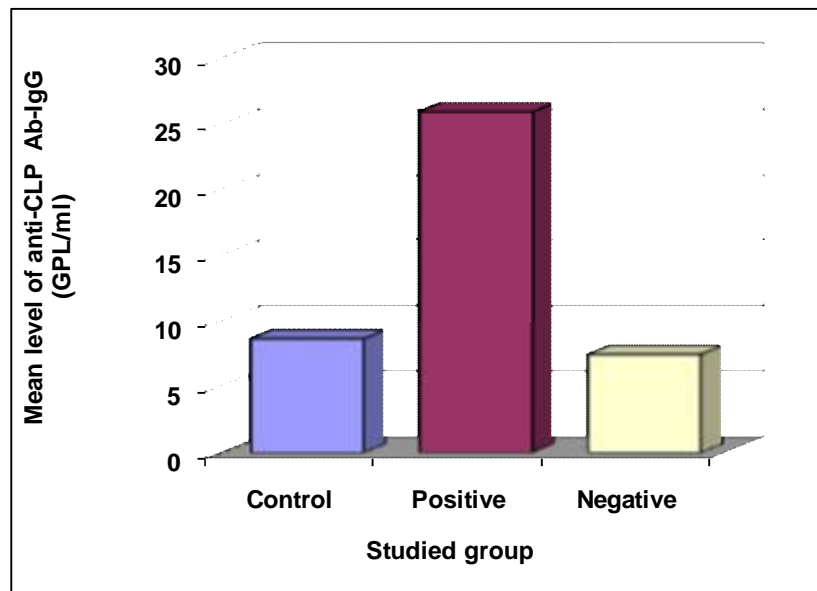


Fig.(3): Mean distribution of anti-CLP Ab-IgG (GPL/ml) level among studied group (Control & diabetic patients).

Table (4)
Mean distribution of anti-CLP Ab-IgM (MPL/ml) level among studied group (Control & diabetic patients).

Studied group	N	Mean	SD	Std. Error	Min.	Max.	Student test (t-test)	
							P-value	Sig.
Control	20	9.2	2.13	0.48	6	13	-	-
Anti-CLP Ab. (IgM)	Positive	3	29.3	4.36	24	32	0.00	HS
	Negative	19	7.47	1.50	5	11	0.026	S
Total	42	Positive Vs Negative					0.00	HS

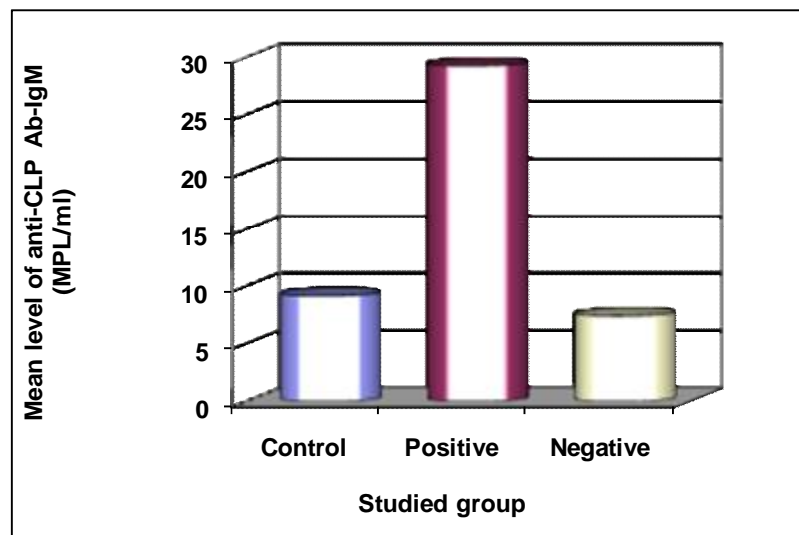


Fig. (4): Mean distribution of anti-CLP Ab-IgM (MPL/ml) level among studied group (Control & diabetic patients).

Discussion

In this study, we have tried to analyze their association with anticardiolipin antibody in type 2 diabetes mellitus. There are few reports on ACL in association with diabetes mellitus. In one study, the frequency of anticardiolipin antibodies in NIDDM was 51% and the predominant isotype of the antibodies were IgG and IgA [10]. In another report, low titers of ACL were observed in a mixed patient with type 2 and NIDDM [11].

In another report, the prevalence of anticardiolipin antibodies was similar in uncomplicated type 2 diabetes (19.5%); control (4.6%) [12, 13]. In another study, IgG anticardiolipin antibodies were found in 7 patients (24%), while IgM anticardiolipin antibodies were absent in all [14, 15].

Our results show ACL of both IgM and IgG type with increased prevalence in patients with diabetes mellitus and with differences in patients with controls group.

The high levels of IgG might related to along period of exposure to autoantibody resulted from a chronic infection with diabetes mellitus [16] and the higher levels of IgM might indicate an ongoing and they a more achieve immune/ inflammatory reaction against cardiolipin in patient with diabetes mellitus [17].

Several hypotheses have been proposed to explain the cellular and molecular mechanisms by which antiphospholipid antibodies thrombosis. The first implicates activation of endothelial cells. Binding of antiphospholipid antibodies induces activation of endothelial cells as assessed by up-regulation of the expression of adhesion molecules, the secretion of cytokines, and the metabolism of prostacyclins. Antiphospholipid antibodies recognize β_2 -glycoprotein I bound to resting endothelial cells, although the basis for the interaction of β_2 -glycoprotein I with viable endothelial cells remains unclear [18, 19].

A second theory focuses on oxidant – mediated injury of the vascular endothelium, oxidized low-density lipoprotein (LDL), a major contributor to atherosclerosis, is taken up by macrophages, leading macrophage to activation and subsequent damage to endothelial cells. Auto antibodies to oxidized LDL occur in association with anticardiolipin

antibodies, and some anticardiolipin antibodies cross-react with oxidized LDL. Moreover , anticardiolipin antibodies bind to oxidized but not reduced, cardiolipin, suggesting that anticardiolipin antibodies recognize oxidized phospholipids, phospholipids-binding proteins, or both [20, 21].

A third theory proposed that antiphospholipid antibodies interfere with or modulate the function of phospholipids-binding protein involved in the regulation of coagulation. Although little is known about the biologic function of β_2 -glycoprotein I. It is thought to act as a natural anticoagulant [22, 23].

Conclusion

The higher prevalence and levels of ACL in type 2 diabetes mellitus patients point towards a possible role of those antibodies in the pathogenesis and/or progression of complications in this disease.

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الخلاصة

أن أضداد شحميات القلب هي بروتينات دهنية واطئة الكثافة محورة مؤكسدة ولها القابلية على التحطم الوعائي. ولتحليل الوظيفة المحتملة لهذه الأضداد في داء السكر من النوع الثاني فقد تمت الدراسة على (22) مريض بداء السكر من النوع الثاني بأعمار تتراوح بين (35-68) سنة. وكذلك قد تمت المقارنة بين مجاميع المرضى والأشخاص الأصحاء والذين يعتبرون مجاميع سيطرة والبالغ عددهم (20) شخص. لقد كانت هناك زيادة معنوية في تراكيز أضداد IgM و IgG في المرضى بداء السكر من النوع الثاني مقارنة مع السيطرة ($P < 0.001$)، وأن ظهور هذه الأضداد لشحميات القلب (IgM و IgG) كان بنسبة (13.6%) و (9.1%) على التوالي. وقد كانت هناك فروق معنوية بين مجموعة الدراسة. أن المستويات العالية لهذه الأضداد IgM و IgG من المحتمل أن لها علاقة بامراضية ومشاكل داء السكر ومن النوع الثاني.