Evidence of Correlation between Some Auto Antibodies with Complement Component in Lupus Nephritis

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ABSTRACT:

BACKGROUND:

lupus nephritis is a fatal complication of systemic lupus erythematosus (SLE), the serological hallmark of SLE is the presence of circulating autoantibodies directed against a wide variety of nuclear, cytoplasmic and plasma membrane antigens among which are anticardiolipin (ACL),anti-B2glycoprotein and anti-C1q antibodies, together with the consumption of complement component (C3 &C4) by immune complex mediated reaction.

AIM OF STUDY:

To shed light on the relations among these autoantibodies and with complement component in lupus nephritis patients.

METHODS:

Tthe study was conducted on 25 patients with lupus nephritis, attended the renal clinic in specialized surgical hospital/ medical city /Baghdad, 25 lupus patients without nephritia and 25 healthy controls. Enzyme linked immunsorbant assay was used for detection for ACL, anti-B2GP, anti-C1q, while single radial immundiffusion plates used for the estimation of C3& C4.

RESULTS AND CONCLUSION:

Anticardiolipin antibodies correlated significantly with anti-B2GP IgG & IgM ($P<0.05$), anti-C1q antibodies ($P<o.o1$) respectively, also anti-C1q correlated with C3, C4 complement respectively.

KEY WORD: Autoantibodies, C3, C4 complement , lupus nephritis.

INTRODUCTION:

Renal involvement is the most common cause of ill health and death in patients with SLE [(1)]. This result from autoantibody mediated pathogenecity, two theories were implicated to explain this impact. First one suggests the cross reactivity between them and glomerular basement membrane complex [(2)], while second accused circulating immune complex, However, autoantibody may lead to tissue injury by Fc receptor mediated inflammation, as well as by direct cytotoxicity which is usually complement dependant [(3)].These are heterogeneous group of immunoglobulins (autoantibodies) with specificity toward negatively –charged phospholipids, including cardiolipin (diphosphatidylgycerol), phosphatidyl serine and phospholipids-protein complexes [(4)], which need B2 glycoprotein as cofactor for binding [(5)], principally B2GPI may function as an-vivo anticoagulant [(6)]. Recently, it has been suggested that presence of anti-C1q is a required condition for the development of lupus Nephritis [(7,8)]. AntiC1q antibodies serve as an aquired mechanisim of classical pathway amplification [(9)]. The presence of anti-C1q promote development of autoantibodies that target DNA, which similar to what occur when C1q is absent due to genetic deficiency [(10)] . In this study we try to find a possible correlation between anticardiolipin (ACL), anti-B2glycoprotein (B2GPI) and anti-C1q antibodies with C3, C4 complement component in lupus nephritis patients.

PATIENTS:

The study was conducted on 25 patients with lupus nephritis, 25 patients without nephritis as patient control, they fulfilled four or more of the ACR criteria for classification of SLE and compared with 25 healthy control.

METHODS:

Enzyme linked immunesorbant assay (ELISA) was used for detection of ACL, anti- B2GPI and anti-C1q antibodies. Single radial immune diffusion plates for detection of serum complement C3 and C4. Micro plates are coated with highly purified ACL, B2GP antigen and human C1q respectively, and the principles of the tests based on formation of complex and enzymatic color reaction.

1-Anti-ACL ELISA kit (Biomaghreb Kit Ref.80515s).

2-Anti-B2GP ELISA kit (BINDAZYME Kit Ref: k991801).

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3- anti-C1q ELISA kit (BINDAZYME CIC Kit, MK021). (Ref .213267B).
4. Single radial immune diffusion plates for serum complement C3 and C4 (Biomaghreb n.795, 813).

RESULTS:

When possible correlations (Pearson correlation coefficient {r} test) between pairs of individual auto antibodies and complement C3, C4 , were investigated, in lupus nephritis, ACL was high significantly (P<0.01) correlated with anti-B2GP IgG, CIC respectively, while anti-C1q correlated high significantly (P<0.01) with anti-B2GP IgM, C3, C4, respectively. Also high significant correlation was found between C3, C4 complements. . The only two significant correlations (p<0.05) were seen between ACL and anti-B2GP IgM.

Table (1) Correlation of immunological parameters for Lupus nephritis.

Correlation		B2 GPI (IgM)	B2 GPI (IgG)	C1C level	C3 level	C4 level
Anti-cardiolipin Ab.(ACL)	Pearson(r)	0.485	0.618	0.780	-0.384	-0.330
	P-value	0.014	0.001	0.00	0.058	0.107
	C.S	S	HS	HS	NS	NS
B2 GPI (IgM)	Pearson(r)		-0.163	0.744	-0.259	-0.229
	P-value		0.437	0.00	0.212	0.270
	C.S		NS	HS	NS	NS
B2 GPI (IgG)	Pearson(r)			0.271	-0.301	-0.235
	P-value			0.191	0.143	0.257
	C.S			NS	NS	NS
C1C level	Pearson(r)				-0.628	-0.526
	P-value				0.001	0.007
	C.S				HS	HS
C3 level	Pearson(r)					0.877
	P-value					0.00
	C.S					HS
C4 level	Pearson(r)					-0.769
	P-value					000
	C.S					HS

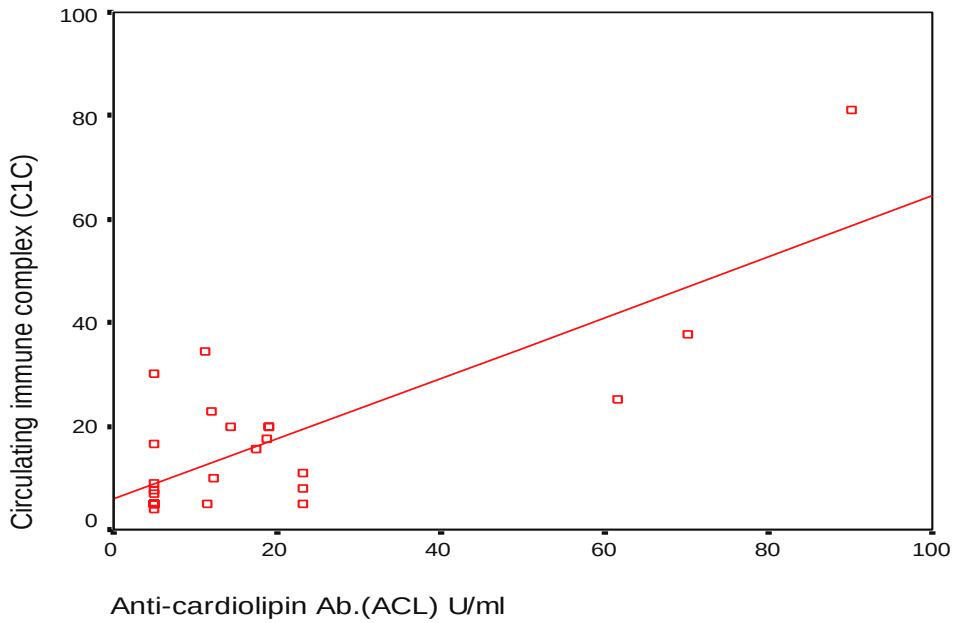

Figure (1) Correlation between ACL U/ml & anti-C1q antibodies (C1C) for Lupus nephritis.

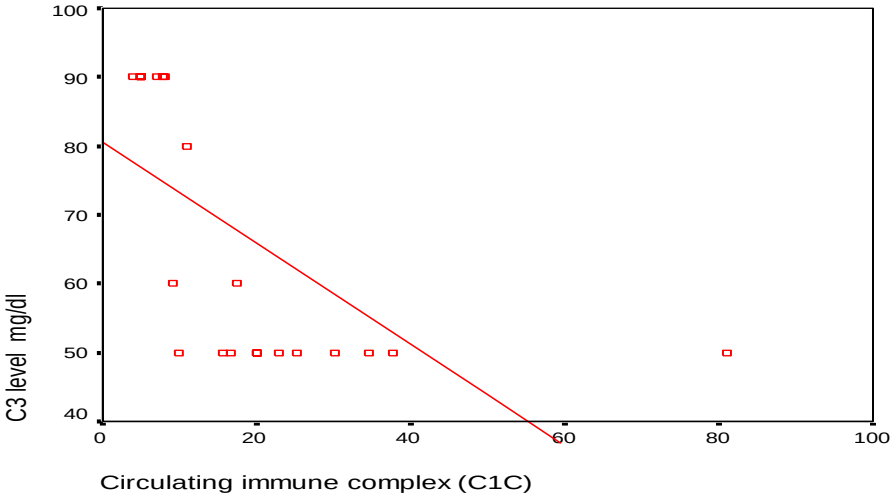

Figure (2) Correlation between circulating immune complex & C3 level (mg/dl) for Lupus nephritis.

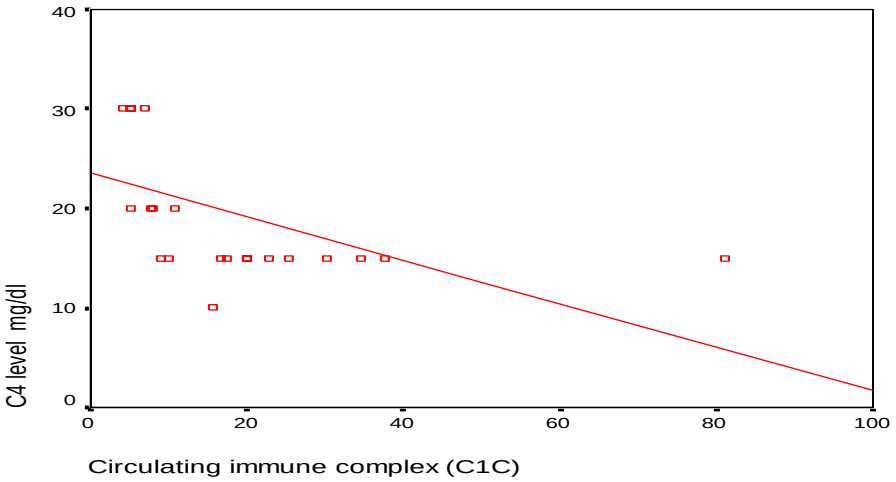

Figure (3) Correlation between circulating immune complex & C4 level (mg/dl) for Lupus nephritis.

DISCUSSION:

On examining the relationship between ACL and anti-B2GP levels there was highly significant correlation between ACL and anti-B2GP IgG (P<0.01) and significant (p< 0.05) with anti-B2GP IgM in lupus nephritis. These findings are similar to some studies which had also found significant correlations between ACL and anti- B2GP antibodies [11,12]. Some believe that these observations imply that both IgM and IgG ACL can bind to B2GP without the presence of cardiolipin if structure of B2GP is altered by factors such as oxygen atom present on the irradiated plates, so that antibodies against a normally cryptic epitopes of B2GP are the pathogenic anticardiolipin antibodies [12]. Although, ACL anti-B2GP IgM, IgG not significantly correlated with C3, C4 complement component in lupus nephritis, so it agree with suggestion that anti-B2GP level can be to some extent reflect disease activity in SLE [13]. There was highly significant correlation between ACL and anti-C1q antibodies (P<0.01) in lupus nephritis.

This association found for ACL, but not for anti-B2GP with lupus nephritis activity was strengthened by the strong association seen when ACL positivity in conjunction with positivity for anti-ds DNA and anti-C1q antibodies was examined; their presence and levels in serum could act as useful marker for the severity of renal disease [14].the correlations of anti-C1q with C3, C4 complement component are agree with many who denote activation of classical pathway lead to consumption of C3, C4 complement and a decrease of the complement classical pathway was associated with active renal disease [15,16].

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