IMpact of AntiCardiolipin Antibodies and Hyperprolactinemia on Laboratory, Immunological and Histopathological Parameters of Lupus Nephritis

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Key words: ACL ABS & Hyperprolactinemia in SLE Nephritis.

Abstract

Objective: Hyperprolactinemia and anticardiolipin antibodies (ACL) have been involved in the pathogenesis of systemic lupus erythematosus (SLE). However, the significance of both has not yet been fully investigated in lupus nephritis. So this study was planned to evaluate the impact of both ACL and prolactin on laboratory, immunological and histopathological findings in such patients.

Material: The study included 28 female SLE patients (Group I). Their mean age was 27.3 ± 8.87 years and mean disease duration was 5.2 ± 2.36 years. Ten apparently normal subjects, matched for age and sex served as controls (Group II).

Methods: SLE patients were classified into two subgroups: G1a (14 patients with renal affection) and G1b (14 patients without renal affection). All patients were subjected to full history taking with stress on clinical manifestations of renal dysfunction, laboratory investigations for SLE, serum prolactin and IgG ACL. Light and electron microscopic examination of renal biopsies from G1a patients and controls were done.
Results: There was a statistically significant difference of both serum prolactin and IgG ACL between G1 & GII (p < 0.01 & p < 0.05 respectively) with a higher level of GlA as compared to Glb patients (p < 0.05). There was a positive correlation between serum prolactin and both proteinuria (p < 0.05), and anti-ds DNA (p < 0.05). On the other hand, there was a positive correlation between IgG ACL and proteinuria (p < 0.05) Lupus nephritis activity index was found to correlate with ACL (p < 0.05), serum prolactin, (p< 0.001), serum creatinine (p < 0.01), proteinuria, (p < 0.05) and anti ds-DNA (p < 0.05). Serum prolactin was found to be a sensitive (64.2 %) and a specific (100 %) marker in the diagnosis of lupus nephritis while IgG ACL is a specific one (100%).

Conclusion: Hyperprolactinemia and IgG ACL might play a role in the pathogenesis of lupus nephritis. Prolactin not only has a direct effect, but it also stimulates the production of some antibodies like ACL and anti-ds-DNA. So, a possible novel role of dopamine receptor agonists in down-regulating the autoimmune phenomena should be investigated in such patients. In evaluation of lupus nephritis, we may consider serum prolactin as a sensitive and a specific marker while IgG ACL as a specific one.

INTRODUCTION

Clinical evidence of kidney involvement is found in one half to two thirds of patients with systemic lupus erythematosus (SLE) (Isenberg, 1984). Treatment is guided by activity of the renal lesion, the greater the activity, the more important the need to treat patients aggressively (Lahita, 1997). The presence of antiphospholipid antibodies (APL) in SLE was shown to be related to several clinical and analytical alterations (Love & Santoro, 1990). APL was found to be associated with the presence of glomerular thrombi in patients with lupus nephritis, probably in the context of thrombotic microangiopathy (Frampton, et al., 1991 and Farrugia et al., 1992).
Prolactin has been involved in the pathogenesis of SLE. Hyperprolactinemia favored the autoimmune processes that are reflected by the presence of high titers of autoantibodies. Elevated levels of IgG anticardiolipin antibodies (ACL) were accompanied by increased prolactin in SLE (Neidhart, 1996).

**Aim Of Study:**

Accordingly this study was designed to evaluate the impact of IgG ACL and hyperprolactinemia on the activity of lupus nephritis. We also aimed at correlating these factors with the laboratory, immunological and histopathological findings in SLE patients.

**SUBJECTS AND METHODS**

**Subjects:**

Twenty-eight subjects were examined at the Outpatients and Inpatients Clinics of the Rheumatology & Rehabilitation and Internal Medicine Departments, Zagazig University Faculty of Medicine Hospitals. They were divided into two groups:

**Group I (G1):** Included 28 female SLE patients. Their age ranged from 19 to 35 years with a mean value of 25.8 ± 8.87 years. The disease duration ranged from 2 to 9 years with a mean value of 5.2 ± 2.36 years. Patients were diagnosed according to the American College of Rheumatology Association (ACR) criteria (Tan et al., 1982).

GI patients were subdivided into two groups according to renal impairment (proteinuria/24 hour urine collection, serum urea, serum creatinine and creatinine clearance).

**Gla:** included 14 patients with renal affection, all were females, their mean age was 25.8 ± 7.8 years, mean disease duration was 1.92 ± 0.47 years and mean values ± SD of serum urea, serum creatinine, creatinine clearance and protein in 24 hour. Urine collection were 54 ± 21.4, 1.03 ± 0.27, 77.5 ± 12.5 and 1.47 ± 0.79 respectively. Assessment of lupus nephritis activity was done according to parameters of activity index (Lahita, 1997).

**Glb:** included 14 patients without renal affection, all were females. Their mean age was 24 ± 5.8 %, mean value of disease duration was 2.5 ±
1.4 years and mean values ± SD of serum urea (mg/dL) serum creatinine (mg/dL) creatinine clearance (ml/minute) and protein in 24 hour urine collection (gm/dl) were, 26.3 ± 4.9, 0.66 ± 0.26, 94.6 ± 8.19 and 0.26 ± 0.18 respectively.

**Group II (GII):** included 10 apparently healthy individuals. They were selected from the Urology Department Zagazig University Hospitals. All were females, their age ranged from 20 to 36 years with a mean value of 26.9 ± 4.11 years. They served as controls for normal renal tissues samples. Practically, it is not permitted to take renal biopsy from a completely healthy subject. Previous researchers used to take open renal biopsies from tumor nephrectomy specimens, from sites, which are remote from tumor-bearing tissues (Wagner et al., 1999). In this work, 10 control kidney samples were obtained from tumor nephrectomy specimens. Pre-operative clinical, laboratory, and radiological data proved that they were free from other diseases apart from early renal masses. They had undergone total nephrectomy and histopathological examination. Part (about 5-10g) of the neighboring unaffected tissue of the kidney (by naked eye) was sent for histopathological examination and only those that proved normal renal tissues were used as controls.

**Methods:**

**SLE patients were subjected to**

**I- FULL HISTORY TAKING WITH STRESS ON:**

a) Specific manifestations of thrombosis including deep venous thrombosis peripheral gangrene, Raynaud’s phenomenon, angina pain and cerebra-vascular thrombosis & history of recurrent abortions and stillbirths in married females.

b) Other causes of hyperprolactinemia were excluded as: pregnancy, hypothyroidism, chronic renal failure, pituitary tumors and drugs known to be associated with hyperprolactinemia, [anti-emetic (metecloropromide), psychotropic drugs (chlorpromazine), oral contraceptive, opiates, haloperidol, cimetidine, and alpha methyl dopa]. Also, no SLE patients were on chloroquine therapy (drug known to decrease prolactin level).

**II: CLINICAL MANIFESTATIONS OF RENAL DYSFUNCTION:**

Such as hypertension, lower limb oedema, and hematuria.
III: Full Clinical Examination With Detailed Locomotor System Examination.

IV: Full Neurological Examination.

V: Laboratory Investigations:

* Complete blood picture.
* Erythrocyte sedimentation rate (Westergren, 1957).

Sampling:

Venous blood was withdrawn with a sterile syringe. The first portion was used for LE cell and anti-ds DNA antibodies testing. This portion is not suitable for complement assay since the sampling process may initiate complement activation. The blood used for assaying complement was collected then centrifuged to obtain serum, stored at -40°C. Sera were obtained after blood clotting, centrifugation and stored at -20°C for assaying other parameters.

- **LE cells**: LE cell latex slide test for detection of deoxyribonucleic acid antibodies associated with SLE (Human Gresell Schaft, Fur, Biochemica and Diagnostica GmbH Germany).
- **Anti-ds DNA antibody**: With indirect immunofluorescent kits that were obtained from Human GmbH D-5205, WUiesbaden.
- **Detection of antinuclear antibody**: With indirect immunofluorescence test using Kallestad Diagnostic kit.
- **Determination of third components of complement**: (C3c): Performed with immunofixation according to Cooper et al. (1983). In that method we use specific antisera to neoantigen (C3c) to avoid over estimation. Reference value of C3c is 64-115 IU/ml in females.
- **Detection of IgG anti-cardiolipin antibodies (ACL)**: With enzyme-linked immunosorbent assay (ELISA) according to Harris et al. (1987). Normal level of IgG ACL up to 23 GPL.
- **Detection of serum prolactin (PRL)**: Was performed with immuno-radiometric method according to Mansbach, et al. (1988) using DSL-4500 supplied by diagnostic system laboratory (DSL) 440 medical center, Wetester, Texas USA.
- **Assessment of renal affection was done as follows**: 

c) Urine analysis for RBC’s/HPF, cellular casts and protein in 24 hours urine collection (gm/dL).

d) Serum urea and creatinine (mg/dL).

e) Creatinine clearance (ml/minute).

f) Renal biopsy: percutaneous renal biopsy was performed under ultrasound control for patients who showed signs of renal dysfunction (14 out of 28 SLE patients) (GIa). Each renal biopsy was dissected into minute pieces and fixed in 2% glutaraldehyde in phosphate buffer (pH 7.2) for 24 hours then post fixed in osmium tetroxide (pH 7.2) for four hours. Semi-thin sections were stained and examined with Yeal TEM 100 CX (transmission electron microscope) and light microscope in the electron microscope center of Zagazig University.

Statistical methods:

All data were coded, entered and analyzed using EPI-INFO (version 6.1) software computer package (Dean et al., 1994).

RESULTS

Table (1): Comparison between the mean values ± SD of serum prolactin and IgG anticardiolipin antibodies (ACL) in SLE patients (GI) and controls (GII).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group I (n = 28) X ± SD</th>
<th>Group II (n = 10) X ± SD</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum prolactin (ng/dL)</td>
<td>15.6 ± 7.1</td>
<td>8.3 ± 3.1</td>
<td>3.09</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>IgG ACL (GPL)</td>
<td>19.2 ± 11.1</td>
<td>11.1 ± 4.1</td>
<td>2.24</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

p < 0.05 = significant  N.B.: Normal level of IgG ACL up to 23 GPL

Table (2): Relation between clinical, laboratory and immunological data among patients groups.

<table>
<thead>
<tr>
<th>Data</th>
<th>GIa</th>
<th>Gib</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>25.8 ± 7.8</td>
<td>24 ± 5.8</td>
<td>0.71</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Duration/Years</td>
<td>1.92 ± 0.47</td>
<td>2.5 ± 1.4</td>
<td>1.84</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Blood pressure /mmHg</td>
<td>Systolic</td>
<td>130.3 ± 13.0</td>
<td>3.93</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Diastolic</td>
<td>82.1 ± 8.7</td>
<td>2.58</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Serum Urea (mg/dL)</td>
<td>54 ± 21.4</td>
<td>26.3 ± 4.9</td>
<td>4.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Serum Creatinine (mg/dL)</td>
<td>1.03 ± 0.27</td>
<td>0.66 ± 0.26</td>
<td>3.68</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Creatinine clearance (ml/min.)</td>
<td>77.5 ± 12.5</td>
<td>94.6 ± 8.19</td>
<td>4.28</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Protein in 24/ hour (g/dL)</td>
<td>1.74 ± 0.79</td>
<td>0.26 ± 0.18</td>
<td>5.56</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>C3c (IU/ml)</td>
<td>39.2 ± 26.2</td>
<td>77.2 ± 29.7</td>
<td>2.99</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Ant. Ds DNA (titre)</td>
<td>52.2 ± 50.4</td>
<td>31.11 ± 23.6</td>
<td>6.64</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Serum Prolactin (ng/dL)</td>
<td>18.7 ± 7.3</td>
<td>12.5 ± 5.6</td>
<td>2.53</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>IgG ACL (GPL)</td>
<td>27 ± 15.4</td>
<td>11.2 ± 4.4</td>
<td>3.71</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

p < 0.05 = Significant  N.B.: Normal level of IgG ACL up to 23 GPL
Table (3): Serum prolactin (PrL) and IgG anti-cardiolipin (IgG ACL) levels among the study groups.

<table>
<thead>
<tr>
<th></th>
<th>GIa X ± SD</th>
<th>Gb X ± SD</th>
<th>GIi X ± SD</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum PrL (ng/dL)</td>
<td>18.7* ± 7.3</td>
<td>12.5 ± 5.6</td>
<td>8.3 ± 3.1</td>
<td>9.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>IgG ACL (GPL)</td>
<td>27.1* ± 15.4</td>
<td>11.2 ± 4.4</td>
<td>11.1 ± 4.4</td>
<td>11.2</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

LSD

*p < 0.05 when compare GIa with Gb patients or with GIi.

N.B. Normal level of IgG ACL up to 23 GPL

Table (4): Number and percentage of hyperprolactinemia and positive IgG ACL in GIa, Gb, and GIi.

<table>
<thead>
<tr>
<th></th>
<th>GIa (n = 14)</th>
<th>Gb (n = 14)</th>
<th>GIi</th>
<th>X²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Hyperprolactinemia</td>
<td>9</td>
<td>64.3</td>
<td>2</td>
<td>14.3</td>
<td>0</td>
</tr>
<tr>
<td>Positive IgG ACL</td>
<td>6</td>
<td>42.9</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Yates corrected X²

Table (5): Correlation between serum prolactin and IgG ACL and some parameters of renal affection.

<table>
<thead>
<tr>
<th>Variables</th>
<th>GIa</th>
<th>Gb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p</td>
</tr>
<tr>
<td>PrL VS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum creatinine (gm/dl)</td>
<td>0.74</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Serum urea (gm/dl)</td>
<td>0.17</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Creatinine clearance (ml/minute)</td>
<td>-0.24</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Protein/24 hour urine collection (gm/dl)</td>
<td>0.53</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>IgG ACL VS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum creatinine (gm/dl)</td>
<td>0.19</td>
<td>&gt; 0.005</td>
</tr>
<tr>
<td>Serum urea (gm/dl)</td>
<td>0.34</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Clearance creatinine (ml/minute)</td>
<td>-0.08</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Protein/24 hour urine collection (gm/dl)</td>
<td>0.52</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

p < 0.05 = significant

Table (6): Correlation between serum prolactin (PrL) and IgG ACL and some Immunological parameters.

<table>
<thead>
<tr>
<th>Variables</th>
<th>GIa</th>
<th>Gb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p</td>
</tr>
<tr>
<td>Serum PrL VS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C3c (IU/ml)</td>
<td>0.01</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Anti-ds. DNA (titre)</td>
<td>0.04</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>IgG ACL VS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C3c (IU/ml)</td>
<td>0.01</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Anti-ds DNA (titre)</td>
<td>0.18</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

p < 0.05 = significant

Table (7): Correlation between lupus nephritis activity index (AI) and some laboratory data.

<table>
<thead>
<tr>
<th>Lupus nephritis AI</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG ACL (GPL)</td>
<td>0.63</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Serum prolactin (ng/dl)</td>
<td>0.96</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Serum urea (mg/dl)</td>
<td>0.02</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>0.71</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Creatinine clearance (ml/minute)</td>
<td>-0.19</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Protein/24 hour urine collection gm/dl</td>
<td>0.63</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>C3c (IU/ml)</td>
<td>-0.7</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Anti-ds DNA (titre)</td>
<td>0.64</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

p < 0.05 = significant
Photo (1): Normal renal biopsy stained with toludin blue showing normal glomeruli and tubules (light microscopic examination).

Photo (2): Renal biopsy from SLE patient (G1a) showing:
   a) Degenerative changes in the form of different sized vacuoles filling the tubular and glomerular cavities (one arrow)
   b) Interstitial mononuclear infiltration (two arrows) (light microscopic examination).
Photo (3): Renal biopsy form SLE patient (G1a) stained by toludin blue showing necrosis of tubular epithelial cells (light microscopic examination).

Photo (4) Renal biopsy from SLE patient (G1a) showing thickening in the basal lamina, disfigurement of podocytes (one arrow) and dilatation of intertubular spaces. Different sized vacuoles are present (two arrows) (Electron microscopic examination).
Photo (5): Renal biopsy form SLE patient (G1a) showing extensive degenerative changes in the form of replacement of the normal tissue with fat cells (one arrow) and precipitation of different sized granules (two arrows) (Electron microscopic examination).

Photo (6): Renal biopsy form SLE patient (G1a) showing 3 red blood cells in the lumen. The blood cells are adherent with the endothelial cells (en). The latter cells lost their cytoplasmic membrane. Peri-endothelial fibrosis indicated by many newly formed collagen fibrils (F). The destructed cytoplasmic membranous endothelial cells and adhesed red blood cells are focal areas of latter formed thrombosis.
Table (8): Validity of Prolactin (PrL) and IgG ACL in the diagnosis of lupus nephritis.

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Predictive Value</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>%</td>
<td>+ve %</td>
<td>-ve %</td>
</tr>
<tr>
<td>Serum PrL (ng/dl)</td>
<td>64.2</td>
<td>100</td>
<td>100</td>
<td>66.6</td>
</tr>
<tr>
<td>IgG ACL (GPL)</td>
<td>42.8</td>
<td>100</td>
<td>100</td>
<td>55.5</td>
</tr>
</tbody>
</table>

DISCUSSION

Renal involvement in systemic lupus erythematosus (SLE) may be quite diverse and may vary from no clinical abnormalities to rapidly progressive renal failure (Hurtado et al., 1999).

SLE has been associated with ACL, the relation between these antibodies and lupus nephropathy is not clear (Perdiguero et al., 1995). Renal biopsies from SLE patients with positive ACL showed thrombotic microangiopathy (Kincaid-smith et al., 1988 and Amigo et al., 1992). On the other hand, prolactin has been involved in the pathogenesis of SLE and hyperprolactinemia has been connected to systemic activity (Miranda et al., 1998). Accordingly this study was planned to evaluate the impact of both ACL and prolactin on laboratory, immunological and histopathological aspects in lupus nephritis patients.

Our results showed a significant difference between SLE patients (GI) and controls (GII) as regards prolactin p < 0.01 (table 1). It was higher in Gl a (patients with renal affection as compared with patients in GII b p < 0.001 (table 3). Our results were in agreement with Miranda et al. (1998), who reported hyperprolactinemia in SLE and higher levels in lupus nephritis patients.

The possible source of hyperprolactinemia in SLE might include stimulation of prolactin synthesis and release by estrogen. A high estrogen level has been reported in both SLE males and females with (Inman, 1978). Also, hyperprolactinemia can result from stimulation of the pituitary gland by cytokines and inflammatory mediators (IL1β, IL-6 and TNF-α), which have been found to stimulate prolactin secretion (Kennedy & Jones, 1991).

The association between renal disease and serum prolactin level is of great importance because renal disease has been known to contribute very significantly with morbidity and mortality in SLE (Walker et al., 1998). The kidney has receptors for prolactin (Posner et al., 1994) and kidney damage or nephrectomy leads to hyperprolactinemia (Biasioli et al., 1988). On the
other hand, prolactin stimulates phagocytic function which mediates immune complex kidney damage (Davila et al., 1990).

Our results showed a significant difference between SLE patients (GI) and controls (GII) as regard IgG anticardiolipin antibodies (ACL) p< 0.05 (Table 1). ACL was found to be higher in Gla patients as compared with those in Glb p< 0.001 (table 3).

In this study 6 out of 14 patients in Gl (42.9%) had positive IgG ACL (table 4). Our results were nearly in agreement with the results of Frampton et al. (1991) who found that the incidence of ACL was higher in patients with lupus nephritis as compared with those without lupus nephritis.

In this study there was a significant positive correlation between serum prolan and some parameters of renal affection in Gla patients (serum creatinine p< 0.001 and protein in 24 h urine collection p< 0.05) (table 5). Our results were in accordance with Miranda et al. (1998) who demonstrated a positive correlation between hyperprolactinemia and severe renal disease according to serum creatinine, creatinine clearance and albuminuria (Davila et al., 1990).

In this study we found a significant positive correlation between IgG ACL and proteinuria in Gla patients as compared with those in Glb p < 0.05 (table 5). Our results were in accordance to Perdiguero et al. (1995) who found that proteinuria was significantly higher in IgM and IgG ACL positive SLE patients compared with ACL negative patients.

Renal function tends to deteriorate more quickly in ACL positive SLE patients due to renal ischemia secondary to non-inflammatory vascular pathology with these antibodies (Leaker et al., 1991). Imbalance of prostacyclin thromboxane A2 ratio (Carreras and Vermylen 1982), inhibition of protein C (Carriou et al., 1988) or plasminogen activation (Angeles-cano et al., 1979) and a low level of free protein S (Parke et al., 1992) may be possible mechanisms whereby ACL is associated with recurrent thrombosis and renal microangiopathy.

In the present study, there was a positive correlation between serum prolactin and anti-ds DNA antibodies in Gla patients p < 0.05 (table 6). On the other hand, there was a positive correlation between lupus nephritis AI and both serum prolactin and anti-ds DNA p < 0.001 & < 0.05 respectively
(table 7) in patients with renal dysfunction (GlA). These findings could be explained by a possible triangular relationship that exists between prolactin, anti-ds DNA and the development of glomerulonephritis (Niedhart, 1996).

Our results showed an insignificant correlation between IgG ACL and C3c and anti-dsDNA (table 6). These findings agreed with those of other authors (Farrugia et al., 1992 and Harris et al., 1983). The relatively low number of patients in this study could explain the absence of statistical association between the presence of ACL and these immunological parameters.

Histopathological examination of renal biopsies of GlA examined with light and electron microscope (L & E/M) showed a positive correlation between lupus nephritis AI and IgG ACL p < 0.05 (Table 7). These findings suggest a pathogenic role for these autoantibodies in lupus nephritis (Perdiguero, et al., 1995). Our findings support those of Domrongkitchaiporn et al., 1994 who found a trace or no immunoglobulin or complement in kidney biopsy specimens, which provides evidence against an immune-complex-induced nephropathy.

Our results showed a positive significant correlation between lupus nephritis AI and some parameters of renal dysfunction [serum creatinine p < 0.01, protein in 24 hour urine collection p < 0.05]. Several authors have reported that activity index correlates with proteinuria and renal function (Mitjavila et al., 1997 and Hurtado et al., 1999).

Comparing the validity of serum prolactin and IgG ACL with lupus nephritis AI, our results revealed that prolactin was more sensitive (64.2 %) and more accurate (79.1) than IgG ACL (42.8 % & 66.1 % respectively). But both were specific (100 %) in evaluating patients with lupus nephritis (table 8).

The specificity of ACL might be explained by that all positive IgG ACL had thrombi in their renal biopsies, while the sensitivity and specificity of prolactin could be related to the more prevalence of serum hyperprolactinemia in patients with lupus nephritis.

Conclusion:

1- Hyperprolactinemia might play a role in the pathogenesis of lupus nephritis not only due to its direct effect, but also through stimulation of
prolactin to produce some antibodies like ACL and anti-ds-DNA. Accordingly a possible novel role of dopamine receptor agonists in down regulating the autoimmune phenomena should be investigated in such patients.

2- In the evaluation of lupus nephritis we may consider serum prolactin as a sensitive and a specific marker while IgG ACL as a specific one.

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تأثير كل من الأجسام المنضادة للكارديويليين وارتفاع مستوى البرولاكتين على
المعايير المعملية والمناعية والهستوبيولوجية في الالتهاب الكلوي الذئبي

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لعل ذلك من البرولاكتين والأجسام المنضادة للكارديويليين دوراً هاماً في مرضي الذئبي
الحمار، ولكن لتم دراسة مستفيضة لهذه العاملين في الالتهاب الكلوي الذئبي. ولذا تم إجراء
هذا البحث لتقييم تأثير هذين العاملين على المعايير المعملية والمناعية والهستوبيولوجية في هؤلاء
المرضى.

اشتمل هذا البحث على 38 شخصاً (28 أنثى مصابة بمرض الذئبي الحماراء متوسط
أعمارهن 27.3 سنة ومتوسط زمن المرض 5.2 سنة بالإضافة إلى 10 أشخاص كمجموعة
ضابطة). تم تقسيم مرضى الذئبي الحماراء إلى مجموعتين طبقاً لوظائف الكلى: مجموعة 1-أ
اشتملت على 14 مريض يعانون من اختلال في وظائف الكلى. ومجموعة 1- ب (اشتملت على
14 مريض كانت وظائف الكلى لديهم طبيعية). تم اخذ تاريخ مرضي للحالات مع التركيز على
المظاهر الإكلينيكية لإختلال وظيفة الكلى، وقد تم عمل فحوصات عامة وفحص عيونات الكلى لكل
من المرضى والمجموعة الحاكمة بال mikroskop الضوئي والألكتروني

وقد أظهرت نتائج البحث وجود علاقة ذو داله إحصائية بين كل من البرولاكتين
والأجسام المنضادة للكارديويليين في المجموعات المدرجة مع ارتفاع نسبة كل
منهما بصورة واضحة في المرضى الذين يعانون من اختلال وظائف الكلى مقابلتهم بالمرضى الذين لديهم
وظائف كلها طبيعية. وجدت أيضاً علاقة ذات دالة إحصائية بين كل من البرولاكتين والأجسام
المضادة للكارديويليين وكل من الزائدة البولية والأجسام المنضادة لـ D-د. كما كانت هناك علاقة
ذات دالة إحصائية بين داله شؤب الالتهاب الكلوي الذئبي بكل من الأجسام المنضادة للكارديويليين
والبرولاكتين والزائدة البولية والأجسام المنضادة لـ D-د. كما وجد أن مستوى
البرولاكتين في المصل يمكن اعتباره دالة حساسة ومتينة في تشخيص الالتهاب الكلوي الذئبي
بينما الأجسام المنضادة للكارديويليين ذو داله مميزة في تشخيص هؤلاء المرضى.

وقد خلصنا هذا البحث إلى أن ارتفاع مستوى البرولاكتين وجود الأجسام المنضادة
للكارديويليين لهما دور محتمل في إحداث الالتهاب الكلوي الذئبي وأن البرولاكتين له تأثير مباشر
لإحداث المرض بالإضاـفة إلى أن يؤدي إلى إنتاج بعض الأجسام المنضادة مثل الأجسام المنضادة
كلم من الكارديويليين بدو أن هذا يمكن استنبط دور جديد ومحتمل لمنشآت مستقبل
الدوبامين في تنظيم الظاهرة المناعية من خلال دراـسات مستقبلية.