

## **AIM OF THE WORK**

The aim of this work was to determine toll like receptor 7 (TLR7) in peripheral blood monocytes and serum IL-29 in patients with SLE, and their correlation to disease activity and lupus nephritis.

## SUBJECTS

This study was conducted on 45 subjects. They were divided into three groups:

- Group I:** Fifteen patients with SLE without laboratory evidence of lupus nephritis. Their ages ranged between 22-42 years with a mean of  $30.13 \pm 6.74$  years. They were 3 males (20%) and 12 females (80%).
- Group II:** Fifteen patients with SLE with laboratory evidence of lupus nephritis. The age ranged between 18-44 years with a mean of  $27.13 \pm 7.38$  years. They were 2 males (13.3%) and 13 females (86.7%).
- Group III:** Fifteen normal subjects as a control. Their age ranged between 20-41 years with a mean of  $31.20 \pm 6.72$  years. They were 6 males (40%) and 9 females (60%).

The patients of the studied groups and controls were matched of age ( $F = 1.38$ ,  $P = 0.263$ ) and sex ( $\chi^2 = 3.128$ ,  $P = 0.209$ ).

All patients and controls were sero-negative for HCV, HBV, cytomegalovirus (CMV) and HIV. Patients with chronic liver disease, diabetes mellitus, systemic infection, malignancy, cardiac, respiratory or other autoimmune diseases were excluded. Also, patients who have received previous anti-viral drugs were excluded from the study

The study was conducted in accordance with the provisions of the Declaration of Helsinki and Good Clinical Practice guidelines. An informed consent was obtained from all subjects included in the study.

## METHODS

All subjects were subjected to:

### I- Thorough History Taking:

It included; age of onset, duration of the disease, number of flares, presence of fever, fatigue, photosensitivity, weight loss, anorexia, hair fall, skin lesion, joint pain and eye problems, precipitating factors such as sun exposure, stress or infection. Complaints related to renal or other systems. Any drug history with special stress on drugs associated with lupus like syndrome.

### II- Clinical Examination:

It was done especially for the assessment of disease activity in SLE patients using SLE disease activity index 2000 (SLEDAI) such as the presence of seizure, psychosis, organic brain syndrome, visual disturbance, cranial nerve disorders, cerebro-vascular accident, vasculitis, arthritis, myositis, rash, alopecia, mucosal ulcers, pleurisy and pericarditis. (Table VI)<sup>(57)</sup>

**Table VI: SLEDAI 2000 (SLEDAI– 2K) data collection form:** <sup>(57)</sup>

SLEDAI 2K		Descriptor	Definition
Weight	Score		
8	_____	Seizure	Recent onset, exclude metabolic, infectious or drug causes.
8	_____	Psychosis	Altered ability to function in normal activity due to severe disturbance in the perception of reality. Include hallucinations, incoherence, marked loose associations, impoverished thought content, marked illogical thinking, bizarre, disorganized, or catatonic behavior. Exclude uremia and drug causes
8	_____	Organic brain syndrome	Altered mental function with impaired orientation, memory, or other intellectual function, with rapid onset and fluctuating clinical features, inability to sustain attention to environment, plus at least 2 of the following: perceptual disturbance, incoherent speech, insomnia or daytime drowsiness, or increased or decreased psychomotor activity. Exclude metabolic, infectious or drug causes.
8	_____	Visual disturbance	Retinal changes of SLE. Include cytooid bodies, retinal hemorrhages, serous exudate or hemorrhages in the choroid, or optic neuritis. Exclude hypertension, infection, or drug causes.
8	_____	Cranial nerve	New onset of sensory or motor neuropathy

*Methods*

		disorder	involving cranial nerves.
8	_____	Lupus headache	Severe, persistent headache; may be migrainous, but must be nonresponsive to narcotic analgesia.
8	_____	cerebro-vascular accident	New onset of cerebrovascular accident(s). Exclude arteriosclerosis.
8	_____	Vasculitis	Ulceration, gangrene, tender finger nodules, periungual infarction, splinter hemorrhages, or biopsy or angiogram proof of vasculitis.
4	_____	Arthritis	≥ 2 joints with pain and signs of inflammation (i.e., tenderness, swelling or effusion).
4	_____	Myositis	Proximal muscle aching/weakness, associated with elevated creatine phosphokinase/aldolase or electromyogram changes or a biopsy showing myositis.
4	_____	Urinary casts	Heme-granular or red blood cell casts.
4	_____	Hematuria	>5 red blood cells/high power field. Exclude stone, infection or other cause.
4	_____	Proteinuria	>0.5 gram/24 hours
4	_____	Pyuria	>5 white blood cells/high power field. Exclude infection.
2	_____	Rash	Inflammatory type rash.
2	_____	Alopecia	Abnormal, patchy or diffuse loss of hair.
2	_____	Mucosal ulcers	Oral or nasal ulcerations.
2	_____	Pleurisy	Pleuritic chest pain with pleural rub or effusion, or pleural thickening.
2	_____	Pericarditis	Pericardial pain with at least 1 of the following: rub, effusion, or electrocardiogram or echocardiogram confirmation.
2	_____	Low complement	Decrease in CH50, C3, or C4 below the lower limit of normal for testing laboratory
2	_____	Increased DNA binding	Increased DNA binding by Farr assay above normal range for testing laboratory.
1	_____	Fever	>38° C. Exclude infectious cause.
1	_____	Thrombocytopenia	<100,000 platelets/x10 <sup>9</sup> /L, exclude drug causes.
1	_____	Leukopenia	< 3,000 white blood cells / x10 <sup>9</sup> /L, exclude drug causes.

**TOTAL SCORE**

### **III- Laboratory Investigations:**

- 1- Complete blood picture. <sup>(186)</sup>
- 2- Renal function tests; Blood urea, serum creatinine <sup>(187)</sup> and estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease (MDRD) formula. Where serum creatinine, age, sex and race were considered: <sup>(188)</sup>  
$$\text{eGFR (ml/min/1.73 m}^2\text{)} = 186 \times \text{serum creatinine (mg dl}^{-1}\text{)}^{-1.154} \times [\text{age (years)}]^{-0.203} \times (0.742 \text{ if female}) \times (1.21 \text{ if black}).$$
- 3- Complete urine analysis and estimation of albumin to creatinine ratio in urine to assess albumin excretion rate (AER). <sup>(187)</sup>
- 4- Estimation of erythrocyte sedimentation rate (ESR) 1<sup>st</sup> hour. <sup>(186)</sup>
- 5- Determination of C-reactive protein (CRP). <sup>(186)</sup>
- 6- Estimation of serum complement 3 and 4 (C<sub>3</sub> and C<sub>4</sub> respectively). <sup>(189)</sup>
- 7- Antinuclear antibody (ANA) <sup>(189)</sup> and anti-double stranded DNA antibodies (anti ds-DNA). <sup>(190)</sup>

### **8- Measurement of Serum Levels of Interleukin-29 by Using Enzyme Linked Immunosorbent Assay Kit (ELISA): <sup>(191)</sup>**

#### ***Principle of the test:***

Quantitative determination of IL-29 in serum was performed using an in vitro using a commercially-available ELISA kit (eBioscience Inc, Bender MedSystems GmbH, Vienna, Austria and North America). This assay employs an antibody specific for human IL-29 coated on a microwell plate. Standards and samples were pipetted into the wells, human IL-29 present in the diluted samples binds to antibodies adsorbed to the microwells. A biotin-conjugated anti-human IL-29 antibody was added and binds to human IL-29 captured by the first antibody. Following incubation unbound biotin-conjugated anti-human IL-29 antibody was removed during a wash step. Streptavidin-horseradish peroxidase (HRP) conjugated anti-human IgG was added and binds to the biotin-conjugated anti-human IL-29 antibody. Following incubation unbound Streptavidin-HRP was removed during a wash step, and substrate solution reactive with HRP was added to the wells. A coloured product was formed in proportion to the amount of human IL-29 present in the sample or standard. The reaction was terminated by addition of acid and absorbance was measured at 450 nm. A standard curve was prepared from 7 human IL-29 standard dilutions and human IL-29 sample concentration was determined.

#### ***Test procedure:***

- 1-The number of microwell strips required was determined.
- 2- Microwell strips were washed twice with wash Buffer.
- 3- A 100 µl Sample diluent was added, in duplicate, to all standard wells to make the standard dilution on the microwell plate. A 100 µl prepared standard was pipette into the first wells and standard dilutions were created by transferring 100 µl from well to well. A 100 µl was discarded from the last wells and alternatively, a 100 µl of these standard dilutions was pipette in the microwell strips to make an external standard dilution in tubes.
- 4- 100 µl of sample diluents was added in duplicate to blank wells and 50 µl was added to sample wells.

## *Methods*

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- 5- Biotin-Conjugate was prepared and 50  $\mu$ l was added to all wells. Microwell strips were covered and were incubated 2 hours at room temperature (18° to 25°C). Then microwell strips were emptied and washed 6 times with wash buffer.
- 6- Streptavidin-HRP was prepared and 100  $\mu$ l of diluted streptavidin-HRP was added to all wells including the blank wells. Microwell strips were covered and were incubated 1 hour at room temperature (18° to 25°C). Microwell strips were emptied and washed 6 times with wash buffer.
- 7- A100  $\mu$ l of 3,3',5,5'- tetramethylbenzidine (TMB) substrate solution was added to all wells, and incubated for about half hour at room temperature (18° to 25°C).
- 8- A100  $\mu$ l stop solution (1M- Phosphoric acid) was added to all wells.
- 9- Absorbance of each microwell was read on a spectrophotometer at 450 nm as a primary wave length. A standard curve was prepared from seven human IL29 standard dilutions and human IL29 sample concentrations were determined.

Samples have been diluted 1: 2 (50  $\mu$ l sample + 50  $\mu$ l sample 34 iluents) so; the concentration read from the standard curve was multiplied by the dilution factor (x 2).

### **9- Enumeration of Toll Like Receptor 7 In Peripheral Blood Monocytes By Flow Cytometry:** <sup>(192)</sup>

The cells expressing TLR7 within mononuclear cells in the peripheral blood detected using color flow cytometric assay. The direct immunofluorescence technique was employed using labeled antibodies according to the manufacturer instructions and also cytoplasmic staining was employed. Viable mononuclear cells were incubated with the fluorescein-labeled monoclonal antibodies and immunofluorescence on the cells was analyzed on a flow cytometry.

### ***Reagents and Equipments:***

1. **Monoclonal Antibodies:** the fluorochrome-conjugated monoclonal antibodies used for detection of TLR7 included:
  - Fluorescein isothiocyanate-conjugated anti-CD14 (CD14-FITC) antihuman MoAb antibody, FC application [Clone: 47-3D6, Cat. Ref.: 14F-100T, Fluorochrome: Fluorescein isothiocyanate (Molecular Probes), Product of Immunostep, Spain].
  - Phycoreythrins-conjugated anti-TLR7 (TLR7-PE) antihuman MoAb antibody, FC application [Clone: 533707, Cat. No.: IC5875P, Product of R&D Systems, USA].
2. **Lysing solution:** was formed of 0.037g sodium ethylene diamine tetraacetic acid (Na EDTA), 1.0g potassium bicarbonate (K HCO<sub>3</sub>) and 8.3g ammonium chloride (NH<sub>4</sub> CL) in 1 liter distilled water.
3. **Phosphate buffered saline (PBS):** obtained in the form of tablets (Gibco BRL, USA, cat No. 18912-014). It is formed of potassium dihydrogen phosphate (KH<sub>2</sub> PO<sub>4</sub> 0.1 mol/L) and disodium monohydrogen phosphate (Na<sub>2</sub> H PO<sub>4</sub> 0.1 mol/L). One tablet was dissolved in 500 ml distilled water to give pH 7 and was thus ready to use.
4. **Falcon tubes:** 5 ml polystyrene round-bottom tubes, 12×75mm style (BD Biosciences) (Ref 352052).
5. **Flow cytometer:** Becton Dickinson, FACs caliber flow cytometer equipped with Cell Quest software.

### ***Assay procedure:***

Whole blood samples were collected in pyrogen/endotoxin free collecting tubes containing EDTA:

1. 100 $\mu$  EDTA-treated whole blood was added to each falcon tube.

## *Methods*

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2. 10  $\mu$ l of CD14-FITC antihuman MoAb were added, mixed well and incubated for 10 minutes at room temperature.
3. After incubation, the cells were washed twice with wash buffer PBS, and centrifuged at 2000 rpm for two minutes each at room temperature
- 4- 200  $\mu$ l of lysing solution were added, mixed well and left for ten minutes in the dark, then centrifuged at 2000 rpm for five minutes, and the supernatant discarded. Again, the cells were washed twice with wash buffer PBS.
- 5- 200  $\mu$ l of PBS with 4% PFA were added and mixed well. The cells were incubated for ten minutes at room temperature.
- 6- After incubation, the tubes were centrifuged at 2000 rpm for two minutes at room temperature, and the supernatant discarded.
- 7- The cells were then re-suspended in 200  $\mu$ l of PBS with 0.2% T20, vortexed and centrifuged again at 2000 rpm for two minutes, and the supernatant discarded.
- 8- Another wash in 0.2% T20 was performed for complete permeabilization of the cells. The cells were then fixed and permeabilized and ready for immunostaining.
- 9- The fixed cells were incubated with 10  $\mu$ l of TLR7-PE antihuman MoAb for ten minutes in the dark at room temperature.
- 10- After two washes with 0.2% T20 as above, the cells were incubated for ten minutes at room temperature.
- 11- The cells were then washed twice with PBS and re-suspended in 500  $\mu$ l of PBS, and were ready for analysis by flow cytometry. During analysis, a gate was set around the mononuclear cell population
- 12- Isotopic antibodies were used as negative controls in order to compensate for auto-fluorescence of the cells and the non-specific binding of the antibodies.
- 13- The cut-off point of positivity was considered when more than 20% of the cells stained with a particular antibody in excess of the background fluorescence in the negative controls.
- 14- Cells expressing TLR7 within mononuclear cells were identified as CD14<sup>+</sup>TLR7<sup>+</sup> cells were expressed qualitatively as percentage of total monocyte count. This specific percentage of positive cells was converted into the absolute number of positive cells/ $\mu$ L using the following formula: the percentage of positive cells x Monocyte blood cell count/100.

## **IV- Histopathological Examination:**

Renal biopsy for patients with LN was done. <sup>(193)</sup>

## STATISTICAL ANALYSIS

The data collected from the present study were analyzed using Statistical Package for the Social Sciences (SPSS) software package version 18.0 (SPSS, Chicago, IL, USA). Quantitative data was expressed using range, mean, standard deviation (SD) while qualitative data was expressed as number (n) and percentage (%).<sup>(194)</sup>

Qualitative data was analyzed using Chi-Square test ( $\chi^2$ ) and Fisher exact test. Comparison between the means of quantitative variables was performed using the student t-test (t-test). Not normally distributed quantitative data was analyzed using non parametric tests, Mann Whitney and Kruskal Wallis tests. Comparison between the means of quantitative variables was performed using the one-way ANOVA (F-test) for comparison between more than two means. Pearson coefficient was used to analyze the correlation between the different parameters. Statistical significance was considered at  $p \leq 0.05$ .<sup>(194)</sup>

The sensitivity and specificity of IL29 and TLR7 in discriminating patients with LN from patients with SLE was assessed by plotting a receiver-operating characteristic (ROC) curve and determining its cut-off value.<sup>(194)</sup>

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## RESULTS

### **I- Clinical Results:**

In the present study, different clinical manifestations were reported, some of which are parameters of the SLEDAI score as fever, hair fall and skin lesions, while others may indicate part of the clinical sequelae of the disease as photosensitivity, anorexia, weight loss, lymphadenopathy and serositis. (Table VII)

In group I, one patient presented by fever or had a history of fever during the past 10 days (6.67 %), 13 with photosensitivity (86%), 5 with skin lesions (33.33%); five patients suffered from malar rash, 12 with hair fall (80%), 2 with alopecia areata (13.33%); 15 with anorexia (100%) although nine patients only alleged actual weight loss (60%), one with deep cervical lymphadenopathy (6.67%), their size decreased dramatically after institution of pulse steroids. None of the patients had serositis. (Table VII)

In patients with group II, 6 patient presented by fever (40%), 14 with photosensitivity (93%), 5 with skin lesions (33.33%); five patients suffered from malar rash, and only one of them also had discoid lupus, 12 with hair fall (80%), 6 with alopecia areata (40%), 14 with anorexia (93%), 13 alleged actual weight loss (86%), 2 with serositis (13.33%); one patient suffered from mild pericardial effusion, mild right pleural effusion and moderate to severe ascites that only responded well to oral mycophenolate mofetil (MMF) 2 g plus oral prednisolone daily, while the other patient suffered from aseptic pericardial tamponade that required pericardiocentesis, this responded well to pulse steroids then oral prednisolone plus monthly intravenous infusion of 1 gm cyclophosphamide. None of the patients had lymphadenopathy (0%). (Table VII)

### **II- Laboratory Results:**

#### **1- Hematological Data:**

##### ***a- Hemoglobin Concentration:***

In group I, it ranged from 7.40-13.90 g/dl with a mean of  $11.31 \pm 1.87$  g/dl. In group II, it ranged from 7.20-14.30 g/dl with a mean of  $9.39 \pm 2.10$  g/dl. In group III, it ranged from 12.50-14.60 g/dl with a mean of  $13.22 \pm 0.63$  g/dl. There was a statistically significant difference in hemoglobin concentration between the three studied groups ( $F = 19.847$ ,  $P < 0.001$ ). There was a statistically significant decrease in hemoglobin concentration in both group I and group II than group III, also it was significantly lower in group II than group I. (Tables VIII, IX, X, XIV) (Figure 6)

##### ***b- Total White Blood Cell Count:***

In group I, it ranged from  $2.20-9.90 \times 10^3/\text{mm}^3$  with a mean of  $5.67 \pm 2.11 \times 10^3/\text{mm}^3$ . In group II, it ranged from  $2.60-8.50 \times 10^3/\text{mm}^3$  with a mean of  $5.24 \pm 1.94 \times 10^3/\text{mm}^3$ . In group III, it ranged from  $5.50-10.20 \times 10^3/\text{mm}^3$  with a mean of  $8.37 \pm 1.46 \times 10^3/\text{mm}^3$ . There was a statistically significant difference in total white blood cell count between the three studied groups ( $F = 12.550$ ,  $P < 0.001$ ). There was a statistically significant decrease in total white blood cell count in both group I and group II than

group III, however there was no statistically significant difference in total white blood cell count between group I and group II. (Tables VIII, IX, X, XIV) (Figure 7)

***c- Monocytes Count:***

In group I, it ranged from 0.09-0.56  $\times 10^3/\text{mm}^3$  with a mean of  $0.33 \pm 0.14 \times 10^3/\text{mm}^3$ . In group II, it ranged from 0.13-0.84  $\times 10^3/\text{mm}^3$  with a mean of  $0.37 \pm 0.19 \times 10^3/\text{mm}^3$ . In group III, it ranged from 0.28-0.69  $\times 10^3/\text{mm}^3$  with a mean of  $0.52 \pm 0.14 \times 10^3/\text{mm}^3$ . There was a statistically significant difference in monocyte count between the three studied groups ( $F = 6.366$ ,  $P = 0.004$ ). There was a statistically significant decrease in monocyte count in both group I and group II than group III. There was insignificant statistical difference between group I and group II (Tables VIII, IX, X, XIV) (Figure 7)

***d- Platelets Count:***

In group I, it ranged from 103.00-350.00  $\times 10^3/\text{mm}^3$  with a mean of  $233.47 \pm 77.42 \times 10^3/\text{mm}^3$ . In group II, it ranged from 88.00-241.00  $\times 10^3/\text{mm}^3$  with a mean of  $179.20 \pm 54.94 \times 10^3/\text{mm}^3$ . In group III, it ranged from 210.00-335.00  $\times 10^3/\text{mm}^3$  with a mean of  $253.60 \pm 35.48 \times 10^3/\text{mm}^3$ . There was a statistically significant difference in platelet count between the three studied groups ( $F = 6.489$ ,  $P = 0.004$ ). There was a statistically significant decrease in platelet count in group II than both group I and group III, with statistically insignificant difference in platelet count between group I and group III. (Tables VIII, IX, X, XIV) (Figure 8)

**2- Renal Function Tests:**

***a- Blood Urea:***

In group I, it ranged from 17.00-38.00 mg/dl with a mean of  $27.27 \pm 6.64$  mg/dl. In group II, it ranged from 19.00-199.00 mg/dl with a mean of  $63.20 \pm 54.54$  mg/dl. In group III, it ranged from 28.00-39.00 mg/dl with a mean of  $32.73 \pm 3.15$  mg/dl. There was a statistically significant difference in blood urea between the three studied groups ( $F = 5.570$ ,  $P = 0.007$ ). There was a statistically significant increase in blood urea in group II than both group I and group III. There was no statistically significant difference in blood urea between group I and group III. (Tables XI, XII, XIII, XIV) (Figure 9)

***b- Serum Creatinine:***

In group I, it ranged from 0.70-0.80 mg/dl with a mean of  $0.75 \pm 0.04$  mg/dl. In group II, it ranged from 0.70-6.40 mg/dl with a mean of  $2.09 \pm 2.25$  mg/dl. In group III, it ranged from 0.65-0.80 mg/dl with a mean of  $0.75 \pm 0.05$  mg/dl. There was a statistically significant difference in serum creatinine between the three studied groups ( $F = 5.371$ ,  $P = 0.008$ ). There was a statistically significant increase in serum creatinine in group II than both group I and group III. However there was no statistically significant difference in serum creatinine between group I and group III. (Tables XI, XII, XIII, XIV) (Figure 10)

***c- Estimated Glomerular Filtration Rate:***

In group I, it ranged from 90.07-122.34  $\text{mL min}^{-1} 1.73\text{m}^{-2}$  with a mean of  $103.50 \pm 9.27 \text{mL min}^{-1} 1.73\text{m}^{-2}$ . In group II, it ranged from 7.97-113.39  $\text{mL min}^{-1} 1.73\text{m}^{-2}$  with a mean of  $74.28 \pm 33.99 \text{mL min}^{-1} 1.73\text{m}^{-2}$ . In group III, it ranged from 90.51-137.17  $\text{mL min}^{-1} 1.73\text{m}^{-2}$  with a mean of  $117.33 \pm 13.77 \text{mL min}^{-1} 1.73\text{m}^{-2}$ . There was a

statistically significant difference in e-GFR between the three studied groups ( $F=15.199$ ,  $P<0.001$ ). There was a statistically significant decrease in e-GFR in group II than both group I and group III. There was statistically insignificant difference in e-GFR between group I and group III. (Tables XI, XII, XIII, XIV) (Figure 11)

#### ***d- Urinary Albumin/ Urinary Creatinine Ratio:***

In group I, it ranged from 8.70-29.00 mg/g with a mean of  $20.24\pm7.92$  mg/g. In group II, it ranged from 950.00-18500.00 mg/g with a mean of  $5055.33\pm5137.42$  mg/g. In group III, it ranged from 6.30-28.00 mg/g with a mean of  $12.05\pm5.45$  mg/g. There was a statistically significant difference in urinary albumin/urinary creatinine ratio between the three studied groups ( $F = 14.432$ ,  $P<0.001$ ). There was a statistically significant increase in urinary albumin/urinary creatinine ratio in group II than both group I and group III. There was no statistically significant difference in urinary albumin/urinary creatinine ratio between group I and group III. (Tables XI, XII, XIII, XIV) (Figure 12)

### **3- Erythrocyte Sedimentation Rate:**

In group I, it ranged from 12-133 mm with a mean of  $55.45\pm40.97$  mm. In group II, it ranged from 11.00-120.00 mm with a mean of  $77.07\pm35.10$  mm. In group III, it ranged from 7.00-10.00 mm with a mean of  $8.93\pm0.96$  mm. There was a statistically significant difference in erythrocyte sedimentation rate between the three studied groups ( $F = 18.737$ ,  $P<0.001$ ). There was a statistically significant increase in ESR in both group I and group II than group III, with statistically insignificant difference in ESR between group I and group II. (Tables XV, XVI, XVII, XVIII) (Figure 13)

### **4- C- Reactive Protein:**

In group I, it ranged from 1.96-31.00 mg/l with a mean of  $10.69\pm7.84$  mg/l. In group II, it ranged from 2.36-45.90 mg/l with a mean of  $15.78\pm13.78$  mg/l. In group III, it ranged from 1.19-2.80 mg/l with a mean of  $2.08\pm0.50$  mg/L. There was a statistically significant difference in CRP in between the three studied groups ( $F = 8.577$ ,  $P = 0.001$ ). There was a statistically significant increase in CRP in both group I and group II than group III, with statistically insignificant difference in CRP between group I and group II. (Tables XV, XVI, XVII, XVIII) (Figure 14)

### **5- Immunological Tests:**

#### ***a- Complement 3:***

In group I, it ranged from 0.46-1.66 mg/ml with a mean of  $1.04\pm0.39$  mg/ml. In group II, it ranged from 0.14-1.90 mg/ml with a mean of  $0.88\pm0.48$  mg/ml. In group III, it ranged from 1.00-1.70 mg/ml with a mean of  $1.37\pm0.26$  mg/ml. There was a statistically significant difference in C3 between the three studied groups ( $F = 6.156$ ,  $P = 0.005$ ). There was a statistically significant decrease in C3 in both group I and group II than group III, with statistically insignificant difference in C3 between group I and group II. (Tables XV, XVI, XVII, XVIII) (Figure 15)

***b- Complement 4:***

In group I, it ranged from 0.06-0.44 mg/ml with a mean of  $0.22\pm 0.10$  mg/ml. In group II, it ranged from 0.05-0.35 mg/ml with a mean of  $0.18\pm 0.10$  mg/ml. In group III, it ranged from 0.19-0.38 mg/ml with a mean of  $0.31\pm 0.05$  mg/ml. There was a statistically significant difference in C4 between the three studied groups ( $F = 7.456$ ,  $P = 0.002$ ). There was a statistically significant decrease in C4 in both group I and group II than group III. There was no statistically significant difference in C4 between group I and group II. (Tables XV, XVI, XVII, XVIII) (Figure 15)

***c- Antinuclear Antibody titer:***

In group I, it ranged from 40.00-640.00 with a mean of  $162.67\pm 161.75$ . In group II, it ranged from 40.00 – 640.00 with a mean of  $229.33\pm 224.99$ . In group III, it ranged from 40.00–40.00 with a mean of  $40.00\pm 0.00$ . There was a statistically significant difference in antinuclear antibody between the three studied groups ( $F = 5.405$ ,  $P = 0.008$ ). There was a statistically significant increase in ANA titer in both group I and group II than group III. There was a statistically insignificant difference in ANA titer in group I and group II. (Tables XIX, XXIV) (Figure 16)

***d- Anti-double stranded DNA Antibody:***

In group I, it ranged from 33.00-175.00 IU/ml with a mean of  $83.21\pm 38.93$  IU/ml. In group II, it ranged from 33.00-178.00 IU/ml with a mean of  $84.02\pm 33.65$  IU/ml. In group III, it ranged from 8.10-27.00 IU/ml with a mean of  $18.13\pm 6.23$  IU/ml. There was a statistically significant difference in anti-ds.DNA antibody between the three studied groups ( $F = 23.947$ ,  $P < 0.001$ ). There was statistically significant increase in anti-ds.DNA antibody in group I and group II than group III, with a statistically insignificant difference in anti-ds.DNA antibody in group I than group II. (Tables XX, XXIV) (Figure 17)

**6- Systemic Lupus Erythematosus Disease Activity Index (SLEDAI):**

In group I, it ranged from 4-31 with a mean of  $18.33\pm 7.74$ . In group II, it ranged from 8-40 with a mean of  $25.60\pm 10.40$ . There was a statistically significant increase in SLEDAI in group II than group I ( $t = 2.170$ ,  $P = 0.039$ ). (Tables XXI) (Figure 18)

**7- Enumeration of Toll-Like Receptor 7:**

In group I, it ranged from 16.00-33.00 cell/ $\mu$ l with a mean of  $19.93\pm 4.64$  cell/ $\mu$ l. In group II, it ranged from 31.00-143.00 cell/ $\mu$ l with a mean of  $89.73\pm 38.26$  cell/ $\mu$ l. In group III, it ranged from 0.00-5.00 cell/ $\mu$ l with a mean of  $2.87\pm 1.64$  cell/ $\mu$ l. There was a statistically significant difference in TLR7 between the three studied groups ( $F = 64.053$ ,  $P < 0.001$ ). There was a statistically significant increase in TLR7 in both group I and group II than group III, with a statistically significant increase in TLR7 in group II than group I. (Tables XXII, XXIV) (Figure 19)

By plotting a ROC curve, the sensitivity and specificity of TLR7 in discriminating patients with LN from patients with SLE were found to be 100% and 93.33% respectively, at a cut-off value of 28 cell/ $\mu$ l. The area under curve = 0.996. (Figure 20)

**8- Serum Interleukin-29:**

In group I, it ranged from 12.10-86.40 pg/ml with a mean of  $45.95 \pm 24.34$  pg/ml. In group II, it ranged from 22.60-108.60 pg/ml with a mean of  $65.05 \pm 29.62$  pg/ml. In group III, it ranged from 12.50-26.40 pg/ml with a mean of  $18.53 \pm 4.09$  pg/mL. There was a statistically significant difference in IL-29 between the three studied groups ( $F = 16.560$ ,  $P < 0.001$ ). There was a statistically significant increase in IL-29 in group I and group II than group III. Also, there was a statistically significant increase in IL-29 in group II than group I. (Tables XXIII, XXIV) (Figure 21)

By plotting a ROC curve, the sensitivity and specificity of IL-29 in discriminating patients with LN from patients with SLE were found to be 93% and 40% respectively, at a cut-off value of 29.8 pg/ml. The area under curve = 0.687. (Figure 22)

**Table VII: Clinical manifestations in patients with systemic lupus erythematosus with and without nephropathy**

Clinical manifestations	Group I		Group II	
	Number of patients	Percentage of patients	Number of patients	Percentage of patients
Presence of fever	1	6.67	6	40
Photosensitivity	13	86	14	93
Skin lesions	5	33.33	5	33.33
Hair fall	12	80	12	80
Alopecia	2	13.33	6	40
Anorexia	15	100	14	93
Weight loss	9	60	13	86
Lymphadenopathy	1	6.67	0	0
Serositis	0	0	2	13.33

**Group I = Patients with systemic lupus erythematosus without nephropathy**

**Group II= Patients with systemic lupus erythematosus with nephropathy**

**Table VIII: Haemoglobin concentration, total white blood cell count, monocytes count and platelets count in patients with systemic lupus erythematosus without nephropathy:**

No	Hb (g/dl)	T. WBC's ( $\times 10^3/\text{mm}^3$ )	Monocytes ( $\times 10^3/\text{mm}^3$ )	Platelets ( $\times 10^3/\text{mm}^3$ )
1	12.4	5.0	0.38	323
2	12.2	5.3	0.25	283
3	9.8	5.2	0.33	242
4	13.1	4.4	0.28	186
5	8.8	2.2	0.09	103
6	12.8	7.9	0.43	214
7	12.1	6.3	0.44	339
8	11.7	3.8	0.22	350
9	12.7	5.1	0.19	149
10	12.2	7.4	0.38	273
11	7.4	6.5	0.49	237
12	10.0	2.2	0.09	266
13	8.9	6.0	0.37	158
14	13.9	9.9	0.56	120
15	11.6	7.9	0.38	259
<b>R</b>	<b>7.40-13.90</b>	<b>2.20-9.90</b>	<b>0.09-0.56</b>	<b>103.00-350.00</b>
<b>Mean</b>	<b>11.31</b>	<b>5.67</b>	<b>0.33</b>	<b>233.47</b>
<b>±SD</b>	<b>1.87</b>	<b>2.11</b>	<b>0.14</b>	<b>77.42</b>

**Hb = Haemoglobin**

**T.WBC's = total white blood cell count.**

**R = Range**

**SD = Standard deviation**

**Table IX: Haemoglobin concentration, total white blood cell count, monocytes count and platelets count in patients with systemic lupus erythematosus with nephropathy:**

<b>No</b>	<b>Hb (g/dl)</b>	<b>T. WBC's (x10<sup>3</sup>/mm<sup>3</sup>)</b>	<b>Monocytes (x10<sup>3</sup>/mm<sup>3</sup>)</b>	<b>Platelets (x10<sup>3</sup>/mm<sup>3</sup>)</b>
1	14.3	7.50	0.53	241
2	8.7	2.90	0.30	88
3	8.4	8.10	0.56	239
4	7.5	4.70	0.19	232
5	9.8	4.70	0.26	223
6	8.1	6.30	0.47	221
7	11.7	8.50	0.84	214
8	8.9	3.30	0.22	183
9	12.9	7.00	0.36	224
10	8.2	4.80	0.42	102
11	7.8	3.36	0.16	135
12	8.5	2.60	0.13	98
13	8.2	5.95	0.39	175
14	7.2	5.44	0.53	131
15	10.7	3.41	0.18	182
<b>R</b>	<b>7.20-14.30</b>	<b>2.60-8.50</b>	<b>0.13-0.84</b>	<b>88.00-241.00</b>
<b>Mean</b>	<b>9.39</b>	<b>5.24</b>	<b>0.37</b>	<b>179.20</b>
<b>±SD</b>	<b>2.10</b>	<b>1.94</b>	<b>0.19</b>	<b>54.94</b>

Abbreviation as table VIII

**Table X: Haemoglobin concentration, total white blood cell count, monocytes count and platelets count in control subjects**

No	Hb (g/dl)	T. WBC's ( $\times 10^3/\text{mm}^3$ )	Monocytes ( $\times 10^3/\text{mm}^3$ )	Platelets ( $\times 10^3/\text{mm}^3$ )
1	12.8	10.1	0.63	215
2	13	9.5	0.46	246
3	13.4	10.2	0.67	308
4	14.6	8.8	0.58	232
5	13.5	9.7	0.62	216
6	12.5	5.5	0.39	266
7	12.7	7.6	0.41	285
8	12.9	6.3	0.28	246
9	12.6	9.8	0.64	276
10	13.0	7.5	0.4	225
11	12.9	6.7	0.38	243
12	13.3	8.5	0.69	256
13	14.2	9.5	0.59	245
14	12.8	7.8	0.41	335
15	14.1	8.1	0.68	210
<b>R</b>	<b>12.50-14.60</b>	<b>5.50-10.20</b>	<b>0.28-0.69</b>	<b>210.00-335.00</b>
<b>Mean</b>	<b>13.22</b>	<b>8.37</b>	<b>0.52</b>	<b>253.60</b>
<b><math>\pm</math>SD</b>	<b>0.63</b>	<b>1.46</b>	<b>0.14</b>	<b>35.48</b>

Abbreviation as table VIII

**Table XI: Blood urea, serum creatinine, estimated glomerular filtration rate and urinary albumin/urinary creatinine ratio in patients with systemic lupus erythematosus without nephropathy:**

No.	Bld.urea (mg/dl)	S.Cr (mg/dl)	eGFR (MDRD) (ml/ min/ 1.73m <sup>2</sup> )	U.Alb/U.Cr ratio (mg/g)
1	28	0.70	105.15	11.3
2	25	0.70	119.07	8.8
3	21	0.75	102.70	12.7
4	35	0.80	91.89	28.0
5	18	0.80	92.89	28.0
6	32	0.75	105.90	18.0
7	29	0.80	90.07	29.0
8	31	0.70	122.34	8.7
9	19	0.75	97.80	26.1
10	29	0.70	113.80	22.0
11	30	0.75	100.91	25.6
12	22	0.73	105.96	14.4
13	35	0.75	102.40	14.0
14	38	0.80	99.89	28.0
15	17	0.75	101.78	29.0
<b>R</b>	<b>17.00-38.00</b>	<b>0.70-0.80</b>	<b>90.07-122.34</b>	<b>8.70-29.00</b>
<b>Mean</b>	<b>27.27</b>	<b>0.75</b>	<b>103.50</b>	<b>20.24</b>
<b>±SD</b>	<b>6.64</b>	<b>0.04</b>	<b>9.27</b>	<b>7.92</b>

**Bld.Urea = Blood urea.**

**S.Cr = Serum creatinine**

**eGFR = Estimated glomerular filtration rate**

**MDRD = Modification of Diet in Renal Disease**

**U.Alb/U.Cr = Urinary albumin/Urinary creatinine ratio**

**Abbreviation as table VIII**

**Table XII: Blood urea, serum creatinine, estimated glomerular filtration rate and urinary albumin/urinary creatinine ratio in patients with systemic lupus erythematosus with nephropathy**

No.	Bld.urea (mg/dl)	S.Cr (mg/dl)	eGFR (MDRD) (ml/ min/ 1.73m <sup>2</sup> )	U.Alb/U.Cr ratio (mg/g)
1	19	0.7	113.39	1336
2	86	2.7	31.57	18500
3	199	6.4	7.97	7376
4	71	1.2	62.19	5750
5	22	1.0	99.31	3485
6	26	0.7	102.43	1102
7	84	1.1	62.86	3480
8	20	0.7	109.27	950
9	29	0.9	83.22	2262
10	81	6.3	8.73	14848
11	36	0.9	81.76	3250
12	34	0.9	82.47	1885
13	21	0.9	96.62	4520
14	165	6.3	75.73	5750
15	55	0.7	96.62	1336
<b>R</b>	<b>19-199</b>	<b>0.70-6.40</b>	<b>7.97-113.39</b>	<b>950-18500</b>
<b>Mean</b>	<b>63.20</b>	<b>2.09</b>	<b>74.28</b>	<b>5055.33</b>
<b>±SD</b>	<b>54.54</b>	<b>2.25</b>	<b>33.99</b>	<b>5137.42</b>

Abbreviation as table VIII, XI

**Table XIII: Blood urea, serum creatinine, estimated glomerular filtration rate and urinary albumin/urinary creatinine ratio in control subjects**

No.	Bld.urea (mg/dl)	S.Cr (mg/dl)	eGFR (MDRD) (ml/ min/ 1.73m <sup>2</sup> )	U.Alb/U.Cr ratio (mg/g)
1	31	0.70	103.74	13.20
2	30	0.75	137.17	7.23
3	34	0.80	121.47	11.50
4	28	0.65	122.37	12.00
5	35	0.80	130.99	6.30
6	37	0.80	113.80	8.00
7	32	0.80	127.33	28.00
8	36	0.75	126.71	12.00
9	29	0.70	98.01	14.00
10	30	0.70	110.22	17.00
11	33	0.70	102.43	10.10
12	39	0.80	116.92	8.50
13	33	0.75	129.97	9.00
14	30	0.75	90.51	16.00
15	34	0.75	128.28	7.90
<b>R</b>	<b>28-39</b>	<b>0.65-0.80</b>	<b>90.51-137.17</b>	<b>6.30-28.00</b>
<b>Mean</b>	<b>32.73</b>	<b>0.75</b>	<b>117.33</b>	<b>12.05</b>
<b>±SD</b>	<b>3.15</b>	<b>0.05</b>	<b>13.77</b>	<b>5.45</b>

Abbreviation as table VIII, XI

**Table XV: Mean  $\pm$  standard deviation and statistical analysis of haemoglobin concentration, total white blood cell count, monocytes count, platelets count, blood urea, serum creatinine, estimated glomerular filtration rate and urinary albumin/urinary creatinine ratio in patients with systemic lupus erythematosus with and without nephropathy and control subjects.**

Parameter	Group I	Group II	Group III	F	P	LSD		
						GI/GII	GI/GIII	GII/GIII
<b>Hb (g/dl)</b>	11.31 $\pm$ 1.87	9.39 $\pm$ 2.10	13.22 $\pm$ 0.63	19.847*	<0.001	*	*	*
<b>T. WBC's count (x10<sup>3</sup>/mm<sup>3</sup>)</b>	5.67 $\pm$ 2.11	5.24 $\pm$ 1.94	8.37 $\pm$ 1.46	12.550*	<0.001	N.S.	*	*
<b>Monocytes count (x10<sup>3</sup>/mm<sup>3</sup>)</b>	0.33 $\pm$ 0.14	0.37 $\pm$ 0.19	0.52 $\pm$ 0.14	6.366*	0.004	N.S.	*	*
<b>Platelets count (x10<sup>3</sup>/mm<sup>3</sup>)</b>	233.47 $\pm$ 77.42	179.20 $\pm$ 54.94	253.60 $\pm$ 35.48	6.489*	0.004	*	N.S.	*
<b>blood urea (mg/dl)</b>	27.27 $\pm$ 6.64	63.20 $\pm$ 54.54	32.73 $\pm$ 3.15	5.570*	0.007	*	N.S.	*
<b>S.Cr (mg/dl)</b>	0.75 $\pm$ 0.04	2.09 $\pm$ 2.25	0.75 $\pm$ 0.05	5.371*	0.008	*	N.S.	*
<b>eGFR (MDRD) (ml/ min/ 1.73m<sup>2</sup>)</b>	103.50 $\pm$ 9.27	74.28 $\pm$ 33.99	117.33 $\pm$ 13.77	15.199*	<0.001	*	N.S.	*
<b>U.Alb/U.Cr ratio (mg/g)</b>	20.24 $\pm$ 7.92	5055.33 $\pm$ 5137.42	12.05 $\pm$ 5.45	14.432*	<0.001	*	N.S.	*

Abbreviation as tables VII, IX, XII

F= ANOVA test for comparing between the three studied groups.

LSD= least significance difference (Post Hoc test) for multiple comparisons.

\* =Significant P value at 5% level.

N.S. = not significant.

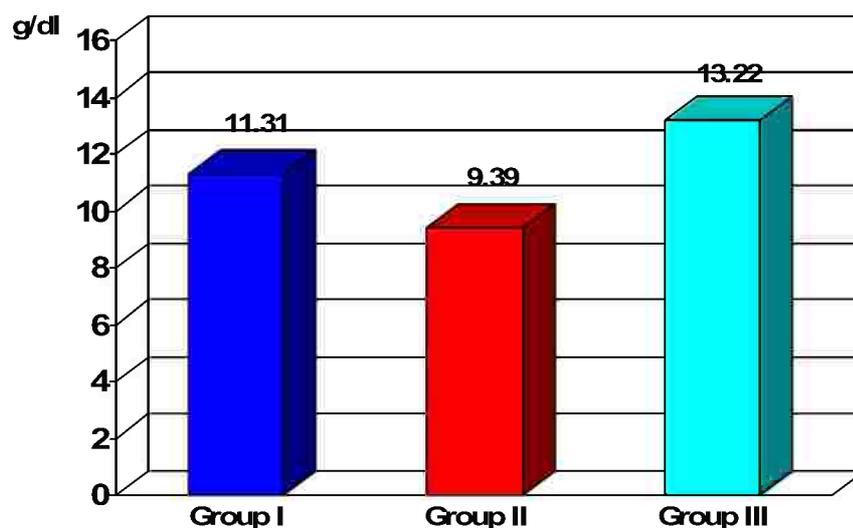


Figure 6: Haemoglobin concentration (g/dl) in patients with systemic lupus erythematosus without (Group I) and with nephropathy (Group II) and control subjects (Group III).

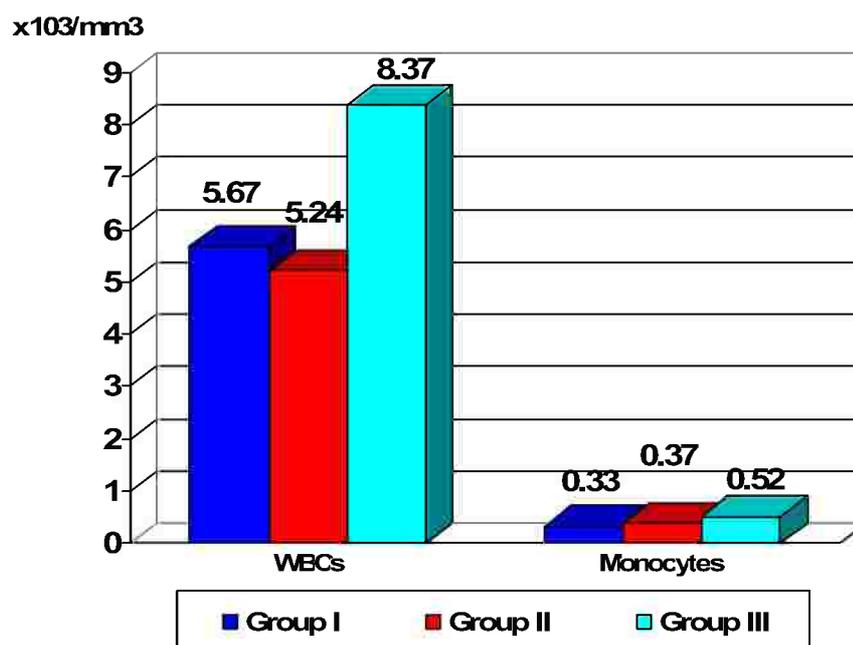


Figure 7: Total white blood cell count and monocyte count ( $\times 10^3/\text{mm}^3$ ) in patients with systemic lupus erythematosus without (Group I) and with nephropathy (Group II) and control subjects (Group III).

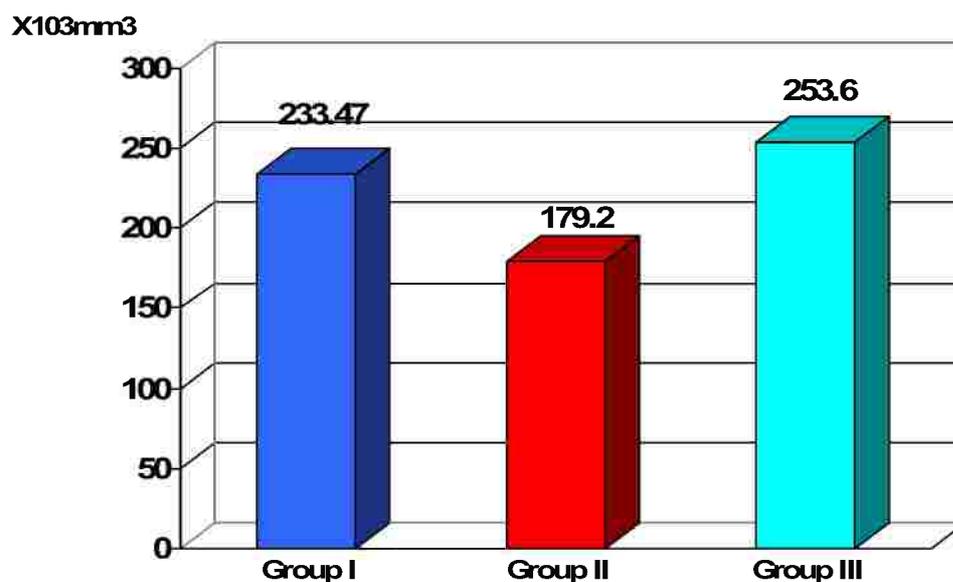


Figure 8: Platelet count (cell x 10<sup>3</sup>/mm<sup>3</sup>) in patients with systemic lupus erythematosus without (Group I) and with nephropathy (Group II) and control subjects (Group III).

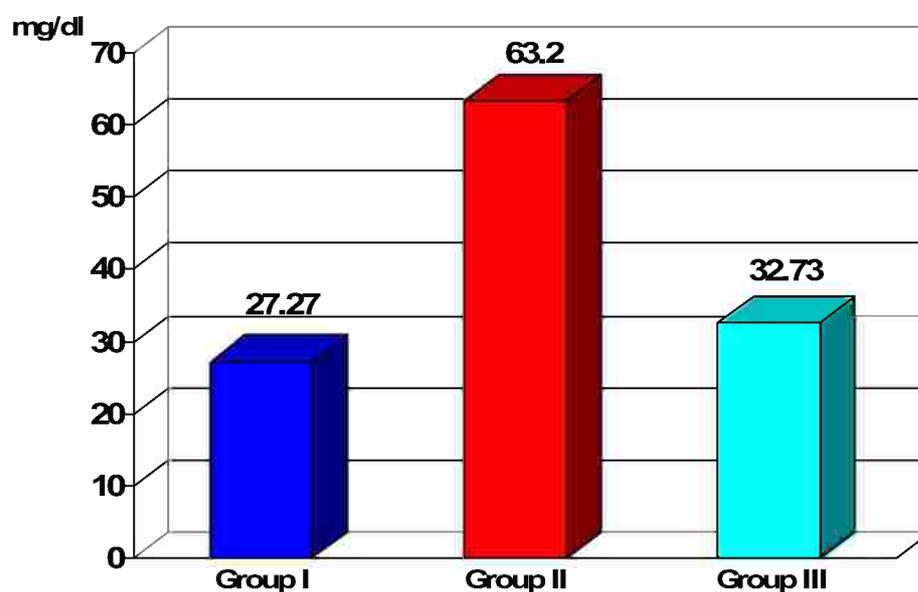


Figure 9: Blood urea (mg/dl) in patients with systemic lupus erythematosus without (Group I) and with nephropathy (Group II) and control subjects (Group III).

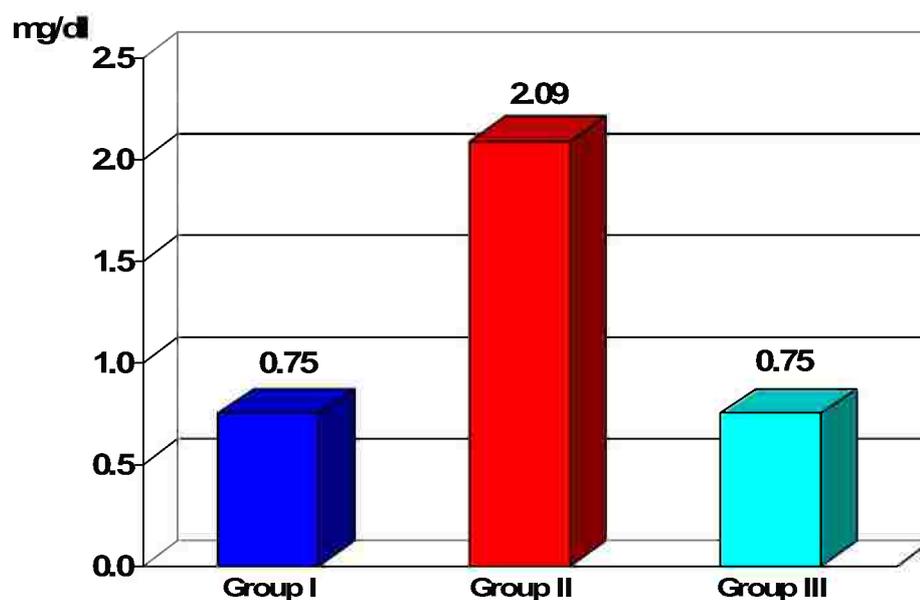


Figure 10: Serum creatinine (mg/dl) in patients with systemic lupus erythematosus without (Group I) and with nephropathy (Group II) and control subjects (Group III).

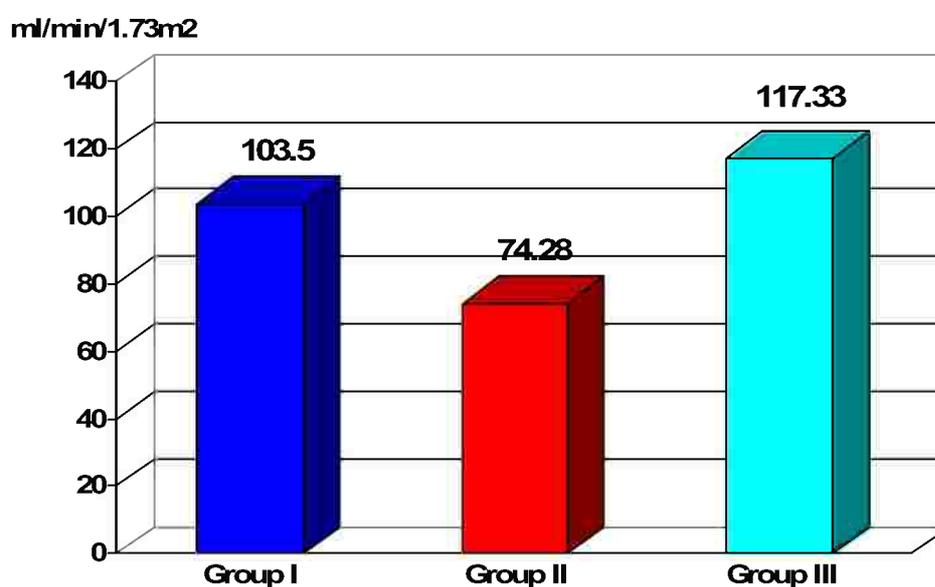
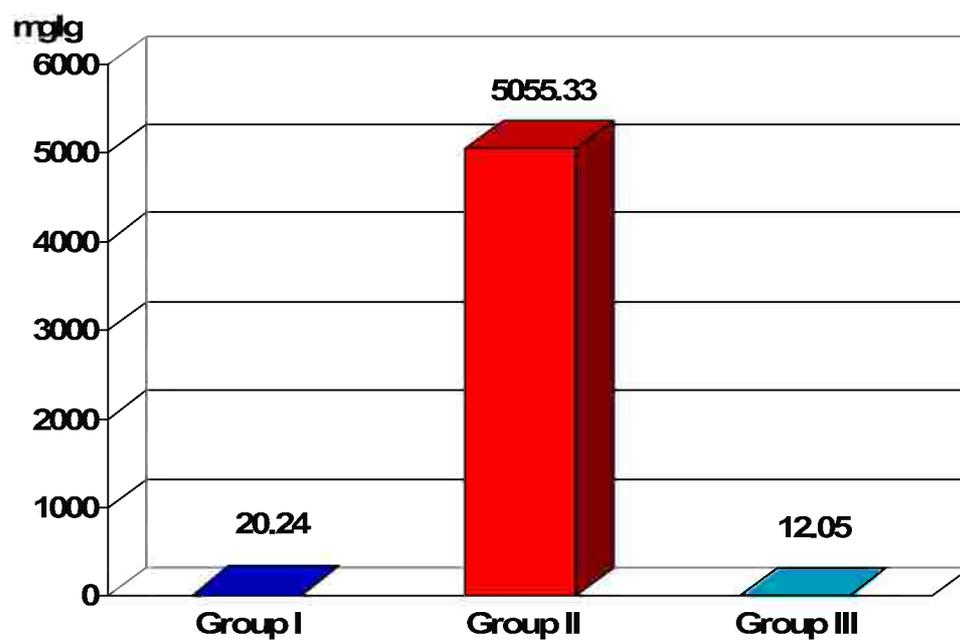


Figure 11: Estimated glomerular filtration rate (ml/min/1,72m<sup>2</sup>) in patients with systemic lupus erythematosus without (Group I) and with nephropathy (Group II) and control subjects (Group III).



**Figure 12: Urinary albumin/creatinine ratio (mg/g) in patients with systemic lupus erythematosus without (Group I) and with nephropathy (Group II) and control subjects (Group III).**

**Table XV: Erythrocyte sedimentation rate, C-reactive protein, complement 3 and complement 4, in patients with systemic lupus erythematosus without nephropathy**

<b>No.</b>	<b>ESR (mm)</b>	<b>CRP (mg/l)</b>	<b>C3 (mg/ml)</b>	<b>C4 (mg/ml)</b>
1	15.0	2.25	1.66	0.44
2	13.6	3.30	1.23	0.31
3	44.2	10.40	1.20	0.23
4	133.0	16.70	0.96	0.18
5	68.0	14.00	0.50	0.13
6	16.3	1.96	1.20	0.36
7	99.3	14.60	0.46	0.13
8	12.0	2.15	1.24	0.29
9	47.0	15.80	1.35	0.18
10	12.0	3.30	1.50	0.27
11	65.3	12.30	0.65	0.14
12	36.0	6.70	1.35	0.28
13	75.0	31.00	0.66	0.06
14	130.0	13.60	0.51	0.12
15	65.0	12.30	1.06	0.19
<b>R</b>	<b>12-133</b>	<b>1.96-31.00</b>	<b>0.46-1.66</b>	<b>0.06-0.44</b>
<b>Mean</b>	<b>55.45</b>	<b>10.69</b>	<b>1.04</b>	<b>0.22</b>
<b>±SD</b>	<b>40.97</b>	<b>7.84</b>	<b>0.39</b>	<b>0.10</b>

**ESR = Erythrocyte sedimentation rate**

**CRP = C-reactive protein**

**C3 = Complement 3**

**C4 = Complement 4**

**Abbreviations as Table VIII**

**Table XVI: Erythrocyte sedimentation rate, C-reactive protein, complement 3 and complement 4, in patients with systemic lupus erythematosus with nephropathy**

<b>No.</b>	<b>ESR (mm)</b>	<b>CRP (mg/l)</b>	<b>C3 (mg/ml)</b>	<b>C4 (mg/ml)</b>
<b>1</b>	11	2.36	1.90	0.35
<b>2</b>	110	30.00	0.23	0.10
<b>3</b>	120	45.90	0.50	0.05
<b>4</b>	92	18.00	0.94	0.13
<b>5</b>	66	9.23	1.35	0.15
<b>6</b>	105	11.00	0.60	0.14
<b>7</b>	110	12.20	0.72	0.13
<b>8</b>	18	2.45	0.87	0.33
<b>9</b>	56	7.50	1.22	0.25
<b>10</b>	72	20.50	0.14	0.05
<b>11</b>	80	8.10	1.20	0.26
<b>12</b>	90	9.23	0.69	0.14
<b>13</b>	28	7.40	1.40	0.32
<b>14</b>	110	44.00	0.46	0.06
<b>15</b>	88	8.80	1.03	0.25
<b>R</b>	<b>11-120</b>	<b>2.36-45.90</b>	<b>0.14-1.90</b>	<b>0.05-0.35</b>
<b>Mean</b>	<b>77.07</b>	<b>15.78</b>	<b>0.88</b>	<b>0.18</b>
<b>±SD</b>	<b>35.10</b>	<b>13.78</b>	<b>0.48</b>	<b>0.10</b>

Abbreviation as table VIII, XV

**Table XVII: Erythrocyte sedimentation rate, C-reactive protein, complement 3 and complement 4 in control subjects**

<b>No.</b>	<b>ESR (mm)</b>	<b>CRP (mg/l)</b>	<b>C3 (mg/ml)</b>	<b>C4 (mg/ml)</b>
1	10	2.24	1.20	0.30
2	8	2.48	1.50	0.25
3	9	1.61	1.60	0.28
4	10	2.32	1.10	0.33
5	9	2.80	1.60	0.19
6	10	2.37	1.00	0.27
7	9	1.51	1.70	0.29
8	8	1.93	1.21	0.35
9	7	1.19	1.10	0.22
10	8	2.33	1.65	0.38
11	10	2.40	1.30	0.36
12	8	1.22	1.70	0.34
13	9	1.95	1.10	0.33
14	10	2.66	1.15	0.35
15	9	2.16	1.60	0.34
<b>R</b>	<b>7-10</b>	<b>1.19-2.80</b>	<b>1.00-1.70</b>	<b>0.19-0.38</b>
<b>Mean</b>	<b>8.93</b>	<b>2.08</b>	<b>1.37</b>	<b>0.31</b>
<b>±SD</b>	<b>0.96</b>	<b>0.50</b>	<b>0.26</b>	<b>0.05</b>

Abbreviation as table VIII, XV

**Table XIX: Mean  $\pm$  standard deviation and statistical analysis of erythrocyte sedimentation rate, C-reactive protein, complement 3 and complement 4 in patients with systemic lupus erythematosus with and without nephropathy and control subjects.**

Parameter	Group I	Group II	Group III	F	P	LSD		
						GI/GII	GI/GIII	GII/GIII
<b>ESR (mm)</b>	55.45 $\pm$ 40.97	77.07 $\pm$ 35.10	8.93 $\pm$ 0.96	18.737*	<0.001	N.S.	*	*
<b>CRP (mg/l)</b>	10.69 $\pm$ 7.84	15.78 $\pm$ 13.78	2.08 $\pm$ 0.50	8.577*	0.001	N.S.	*	*
<b>C3 (mg/ml)</b>	1.04 $\pm$ 0.39	0.88 $\pm$ 0.48	1.37 $\pm$ 0.26	6.156*	0.005	N.S.	*	*
<b>C4 (mg/ml)</b>	0.22 $\pm$ 0.10	0.18 $\pm$ 0.10	0.31 $\pm$ 0.05	7.456*	0.002	N.S.	*	*

Abbreviation as tables VII, XV, XVI

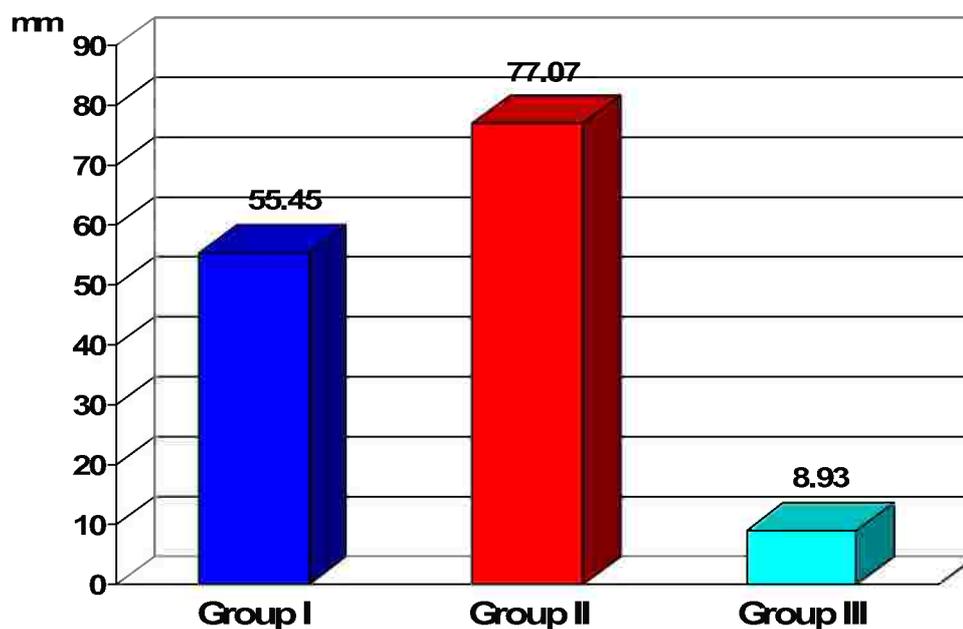


Figure 13: Erythrocyte sedimentation rate (ESR) in patients with systemic lupus erythematosus without (Group I) and with nephropathy (Group II) and control subjects (Group III)

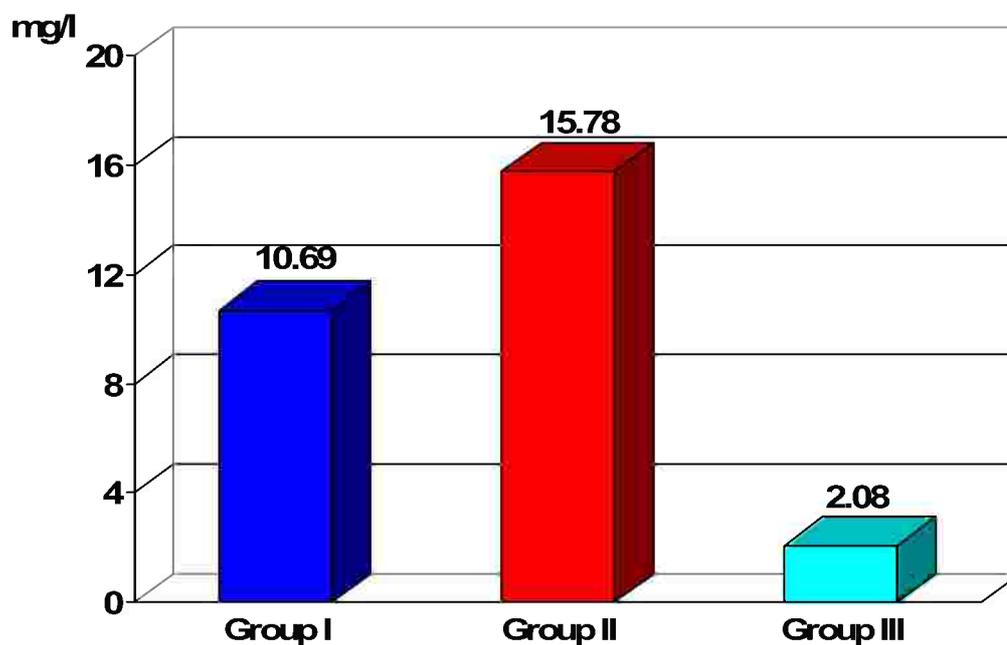


Figure 14: C-reactive protein (CRP) in patients with systemic lupus erythematosus without (Group I) and with nephropathy (Group II) and control subjects (Group III).

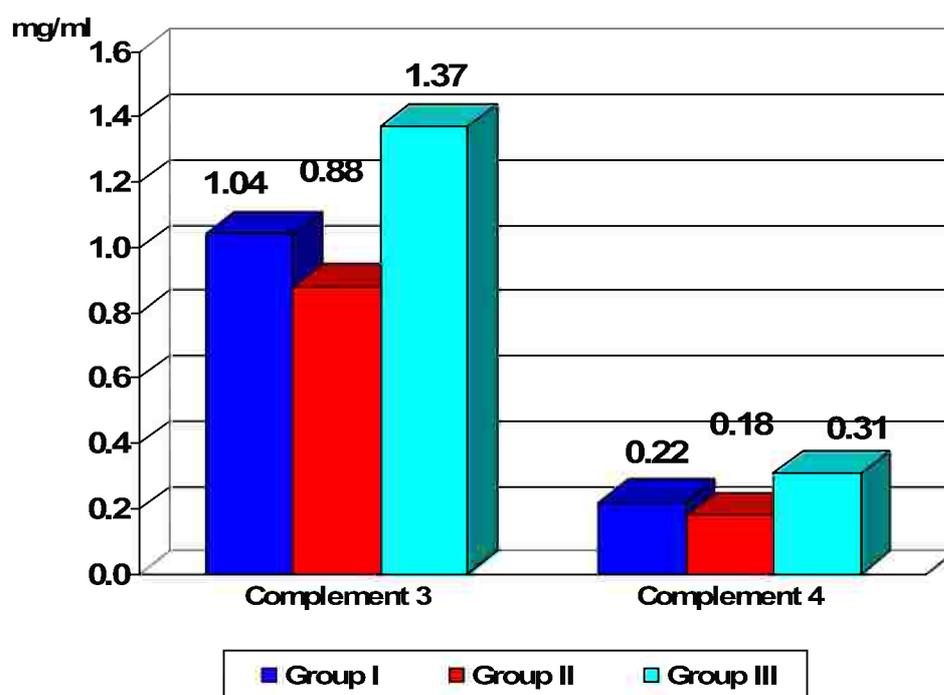


Figure 15: Complement 3 and complement 4 (mg/ml) in patients with systemic lupus erythematosus without (Group I) and with nephropathy (Group II) and control subjects (Group III).

**Table XIX: Antinuclear antibody (ANA) titer in patients with systemic lupus erythematosus with and without nephropathy and control subjects.**

<b>No</b>	<b>Group I</b>	<b>Group II</b>	<b>Group III</b>
<b>1</b>	1/40	1/40	1/40
<b>2</b>	1/40	1/640	1/40
<b>3</b>	1/160	1/640	1/40
<b>4</b>	1/160	1/320	1/40
<b>5</b>	1/80	1/40	1/40
<b>6</b>	1/40	1/160	1/40
<b>7</b>	1/160	1/40	1/40
<b>8</b>	1/40	1/160	1/40
<b>9</b>	1/160	1/40	1/40
<b>10</b>	1/40	1/160	1/40
<b>11</b>	1/320	1/160	1/40
<b>12</b>	1/80	1/160	1/40
<b>13</b>	1/320	1/80	1/40
<b>14</b>	1/640	1/640	1/40
<b>15</b>	1/160	1/160	1/40
<b>R</b>	<b>40-640</b>	<b>40-640</b>	<b>40-40</b>
<b>M</b>	<b>162.67</b>	<b>229.33</b>	<b>40.00</b>
<b>±SD</b>	<b>161.75</b>	<b>224.99</b>	<b>0.00</b>

Abbreviation as table VIII, XIV

**Table XX: Anti-double stranded DNA (Anti-ds DNA IU/ml) in patients with systemic lupus erythematosus with and without nephropathy and control subjects.**

<b>No</b>	<b>Group I</b>	<b>Group II</b>	<b>Group III</b>
<b>1</b>	68.0	33.0	8.1
<b>2</b>	35.0	98.4	20.4
<b>3</b>	82.3	178.0	12
<b>4</b>	129.0	94.1	25
<b>5</b>	81.7	53.4	9.4
<b>6</b>	33.0	72.5	11
<b>7</b>	78.0	58.0	23
<b>8</b>	35.0	88.0	26
<b>9</b>	94.9	45.2	22
<b>10</b>	45.7	85.6	13.6
<b>11</b>	99.5	85.6	19
<b>12</b>	89.6	95.0	27
<b>13</b>	120.7	72.0	14.5
<b>14</b>	175.0	102.5	21
<b>15</b>	80.8	99.0	20
<b>R</b>	<b>33-175</b>	<b>33-178</b>	<b>8.10-27.00</b>
<b>M</b>	<b>83.21</b>	<b>84.02</b>	<b>18.13</b>
<b>±SD</b>	<b>38.93</b>	<b>33.65</b>	<b>6.23</b>

Abbreviation as table VIII, XIV

**Table XXI: The activity index in patients with systemic lupus erythematosus with and without nephropathy**

No.	SLEDAI (Total score=105)	
	Group I	Group II
1	12	9
2	10	40
3	18	35
4	22	35
5	26	12
6	10	16
7	22	24
8	8	8
9	24	24
10	4	38
11	24	33
12	20	29
13	31	22
14	24	30
15	20	29
<b>R</b>	4-31	8-40
<b>Mean</b>	<b>18.33</b>	<b>25.60</b>
<b>±SD</b>	<b>7.74</b>	<b>10.40</b>
<b>t</b>	<b>-2.170*</b>	
<b>P</b>	<b>0.039</b>	

**SLEDAI =Systemic Lupus Erythematosus Disease Activity Index**

**t = Test for comparing between the two studied groups.**

**Abbreviation as table VII, VIII**

**Table XXII: Toll like receptors 7 (TLR 7 cell/ $\mu$ l) in patients with systemic lupus erythematosus with and without nephropathy and control subjects.**

<b>No</b>	<b>Group I</b>	<b>Group II</b>	<b>Group III</b>
<b>1</b>	16	31	5
<b>2</b>	17	133	1
<b>3</b>	18	143	1
<b>4</b>	19	70	4
<b>5</b>	20	46	4
<b>6</b>	21	96	4
<b>7</b>	20	110	1
<b>8</b>	16	78	0
<b>9</b>	20	66	3
<b>10</b>	17	122	4
<b>11</b>	18	50	4
<b>12</b>	18	136	1
<b>13</b>	33	95	3
<b>14</b>	28	130	3
<b>15</b>	18	40	5
<b>R</b>	<b>16-33</b>	<b>31-143</b>	<b>0-5</b>
<b>Mean</b>	<b>19.93</b>	<b>89.73</b>	<b>2.87</b>
<b><math>\pm</math>SD</b>	<b>4.64</b>	<b>38.26</b>	<b>1.64</b>

Abbreviation as table VIII, XIV

**Table XXIII: Serum interleukin 29 (IL-29 pg/ml) in patients with systemic lupus erythematosus with and without nephropathy and control subjects**

<b>No</b>	<b>Group I</b>	<b>Group II</b>	<b>Group III</b>
<b>1</b>	12.1	22.6	16.4
<b>2</b>	20.6	108.6	12.6
<b>3</b>	33.6	87.3	21.6
<b>4</b>	48.6	67.3	22.7
<b>5</b>	65.7	30	18.4
<b>6</b>	24.2	85.5	26.4
<b>7</b>	78.5	67.9	12.5
<b>8</b>	26.2	43.2	18.3
<b>9</b>	56.1	43.7	17.8
<b>10</b>	20	104.2	18.6
<b>11</b>	74.8	42.4	15.2
<b>12</b>	29.8	86	16.8
<b>13</b>	86.4	47.2	23.6
<b>14</b>	68.8	106.3	22.3
<b>15</b>	43.8	33.6	14.7
<b>R</b>	<b>12.10-86.40</b>	<b>22.60-108.60</b>	<b>12.50-26.40</b>
<b>Mean</b>	<b>45.95</b>	<b>65.05</b>	<b>18.53</b>
<b>±SD</b>	<b>24.34</b>	<b>29.62</b>	<b>4.09</b>

Abbreviation as table VIII, XIV

**Table XXV: Mean  $\pm$  standard deviation and statistical analysis of antinuclear antibody titer, anti-double stranded DNA, toll-like receptor 7 and serum interleukin-29 in patients with systemic lupus erythematosus with and without nephropathy and control subjects.**

Parameter	Group I	Group II	Group III	F	P	LSD		
						GI/GII	GI/GIII	GII/GIII
<b>ANA (Titer)</b>	162.67 $\pm$ 161.75	229.33 $\pm$ 224.99	40.00 $\pm$ 0.00	5.405*	0.008	N.S.	*	*
<b>Anti-ds.DNA (IU/ml)</b>	83.21 $\pm$ 38.93	84.02 $\pm$ 33.65	18.13 $\pm$ 6.23	23.947*	<0.001	N.S.	*	*
<b>TLR7 (cell/<math>\mu</math>l)</b>	19.93 $\pm$ 4.64	89.73 $\pm$ 38.26	2.87 $\pm$ 1.64	64.053*	<0.001	*	*	*
<b>IL-29 (pg/ml)</b>	45.95 $\pm$ 24.34	65.05 $\pm$ 29.62	18.53 $\pm$ 4.09	16.560*	<0.001	*	*	*

Abbreviation as tables VII, XV, XX, XXI, XXII, XXIII, XXIV

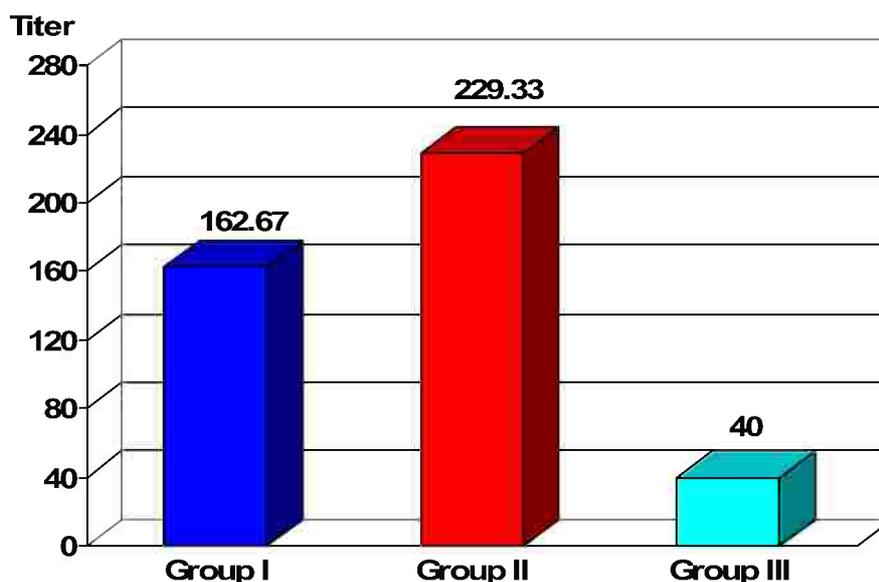


Figure 16: Antinuclear antibody (ANA) titer in patients with systemic lupus erythematosus without (Group I) and with nephropathy (Group II) and control subjects (Group III).

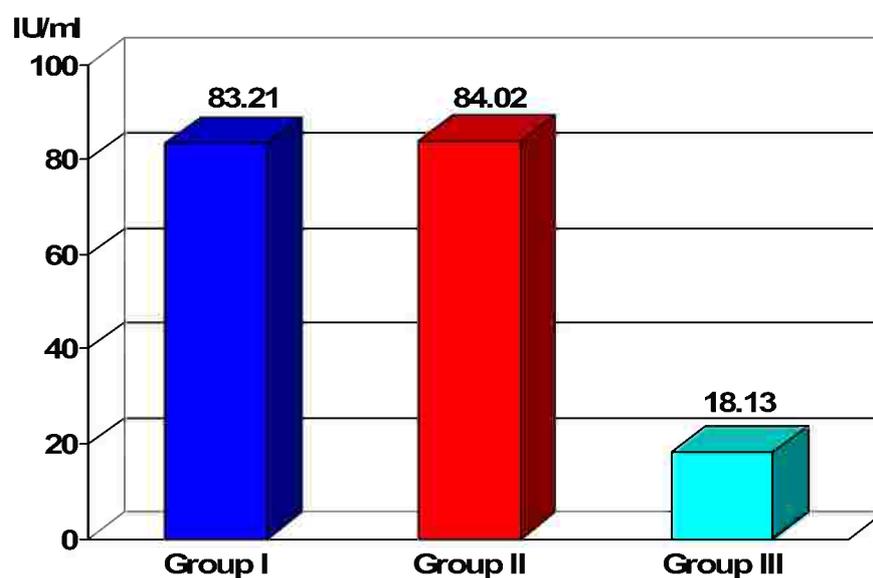
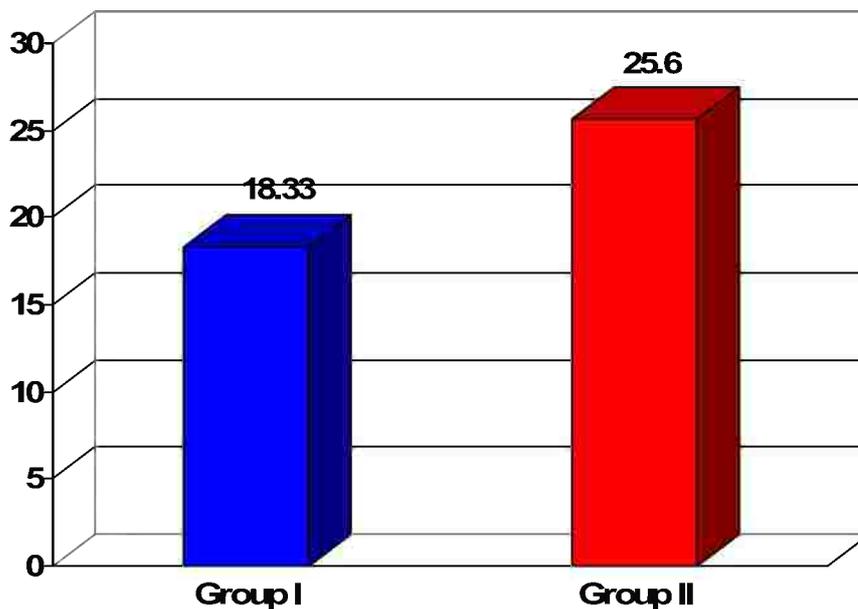
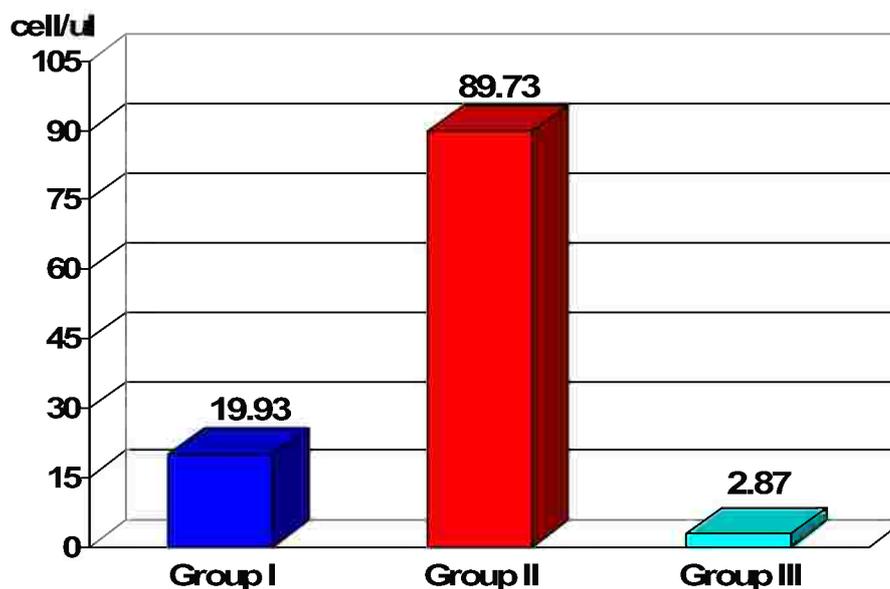


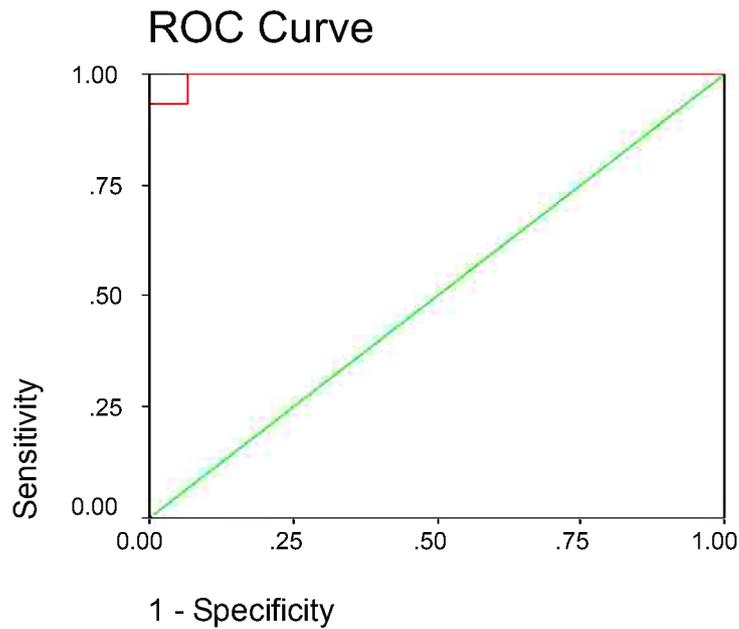
Figure 17: Anti double stranded DNA (IU/ml) in patients with systemic lupus erythematosus without (Group I) and with nephropathy (Group II) and control subjects (Group III).



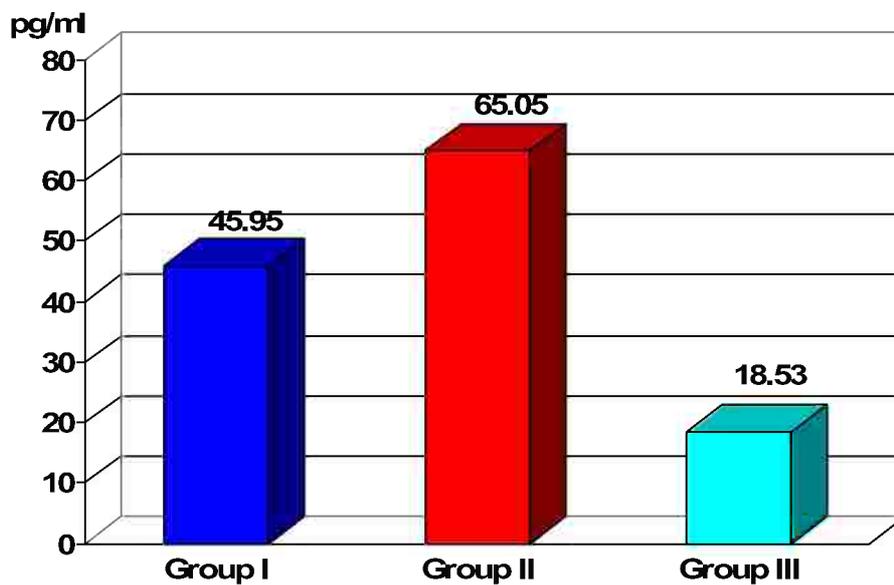
**Figure 18: Systemic lupus erythematosus disease activity index (SLEDAI) in patients with systemic lupus erythematosus without (Group I) and with nephropathy (Group II)**



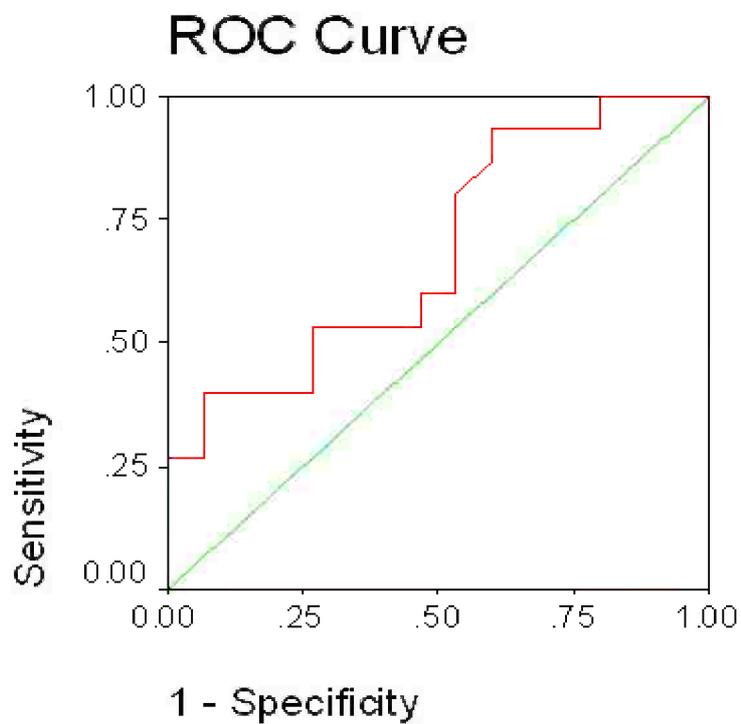
**Figure 19: Toll-like receptor 7 (cell/μl) in patients with systemic lupus erythematosus without (Group I) and with nephropathy (Group II) and control subjects (Group III).**



**Figure 20: Receiver operating characteristic curve (ROC) for Toll-like receptor 7 for discrimination of patients with lupus nephritis from patients with systemic lupus erythematosus. Area under curve = 0.996, cut-off value = 28, at sensitivity =100% and specificity =93.33%.**



**Figure 21: serum interleukin 29 (pg/ml) in patients with systemic lupus erythematosus without (Group I) and with nephropathy (Group II) and control subjects (Group III).**



**Figure 22: Receiver operating characteristic curve (ROC) for interleukin 29 for discrimination of patients with lupus nephritis from patients with systemic lupus erythematosus. Area under curve = 0.687, cut-off value = 29.8 at sensitivity = 93% and specificity = 40%.**

### V- Histopathology Results:

Renal biopsy was done for 14 out of 15 patients who represent group II (patients with lupus nephritis). Renal biopsy was not performed for one patient as it was contraindicated for the small size of both kidneys as shown by ultrasound.

According to ISN/RPS classification, consensus 2003, <sup>(80)</sup> renal biopsy of four patients showed class II LN; one of each was (IIC), (IIA/C), (IIA) and (II) LN. Three biopsies showed class III LN; one of each was class (III A), (III A/C) and one (III) LN. Seven biopsies showed class IV LN, one of them class (IV A). Eight biopsies showed class V LN, six of them was class (V A), one (V A/C) and one class (V). Eight patients had combined classes, one class III + IV (A), one class III (A/C) + V and six class IV + V (A) LN. (Table XXV)

The activity index was in one of each biopsy with 0/24, 4/24 and 7/24, in two biopsies of each with 1/24, 2/24, 6/24, 8/24, and in three with 5/24. The chronicity index was 0/12 and, 1/12 in five biopsies each, in three biopsies 2/12 and one 4/12. (Tables XXV) As regards walls of blood vessels; seven biopsies were within normal range of thickness, three were mildly thickened and four were thickened and hyalinized.

**Table XXV: Renal biopsy of patients with systemic lupus erythematosus with nephropathy**

No	ISN/RPS Class 2003	Activity Index	Chronicity Index
1	Class II (C) lupus nephritis	0/24	1/12
2	Class IV + V (A) lupus nephritis	8/24	0/12
3	-----	-----	-----
4	Class IV + V (A) lupus nephritis	6/24	1/12
5	Class II(A/C) lupus nephritis	4/24	2/12
6	Class III + IV (A) lupus nephritis	6/24	0/12
7	Class IV + V (A) lupus nephritis	1/24	0/12
8	Class IV + V (A) lupus nephritis	5/24	2/12
9	Class III (A/C) + V lupus nephritis	5/24	4/13
10	Class III (A) lupus nephritis	8/24	0/12
11	Class II (A) lupus nephritis	2/24	1/12
12	Class IV + V (A) lupus nephritis	5/24	2/12
13	Class V (A/C) lupus nephritis	2/24	1/12
14	Class IV + V (A) lupus nephritis	7/24	0/12
15	Class II lupus nephritis	1/24	1/12

**ISN/RPS= International Society of Nephrology/Renal Pathology Society classification of lupus nephritis (2003)**

## Statistical Correlations

### **I-Patients With Systemic Lupus Erythematosus Without Nephropathy:** **(Table XXVI - XXVII)**

#### **1 -Toll-like Receptor 7:**

The TLR7 was positively correlated with CRP, ANA, anti-ds.DNA antibody SLEDAI and IL-29 ( $r = 0.761$ ,  $P = 0.001$ ), ( $r = 0.697$ ,  $P = 0.004$ ), ( $r = 0.632$ ,  $P = 0.011$ ), ( $r = 0.627$ ,  $P = 0.012$ ) and ( $r = 0.669$ ,  $P = 0.006$ ) respectively, and was negatively correlated with platelets count, C3 and C4 ( $r = -0.615$ ,  $P = 0.015$ ), ( $r = -0.568$ ,  $P = 0.027$ ) and ( $r = -0.626$ ,  $P = 0.013$ ) respectively. (Figures 23, 24, 25, 26)

#### **2- Interleukin 29:**

The IL-29 was positively correlated with S.Cr, urinary albumin/urinary creatinine ratio, ESR, CRP, ANA antibody, anti-ds.DNA antibody and SLEDAI ( $r = 0.728$ ,  $P = 0.002$ ), ( $r = 0.589$ ,  $P = 0.021$ ), ( $r = 0.736$ ,  $P = 0.002$ ), ( $r = 0.855$ ,  $P < 0.001$ ), ( $r = 0.671$ ,  $P = 0.006$ ), ( $r = 0.663$ ,  $P = 0.007$ ) and ( $r = 0.872$ ,  $P < 0.001$ ) respectively, and was negatively correlated with platelets count, e-GFR, C3 and C4 ( $r = -0.513$ ,  $P = 0.050$ ), ( $r = -0.667$ ,  $P = 0.007$ ), ( $r = -0.885$ ,  $P < 0.001$ ) and ( $r = -0.931$ ,  $P < 0.001$ ) respectively. (Figure 27, 28)

#### **3- Systemic Lupus Erythematosus Disease Activity Index:**

The SLEDAI was positively correlated with S.Cr, ESR, CRP, ANA antibody and anti-ds.DNA antibody ( $r = 0.717$ ,  $P = 0.003$ ), ( $r = 0.723$ ,  $P = 0.002$ ), ( $r = 0.885$ ,  $P < 0.001$ ), ( $r = 0.606$ ,  $P = 0.017$ ) and ( $r = 0.770$ ,  $P = 0.001$ ) respectively, and was negatively correlated with platelets count, e-GFR, C3 and C4 ( $r = -0.636$ ,  $P = 0.011$ ), ( $r = -0.752$ ,  $P = 0.001$ ), ( $r = -0.706$ ,  $P = 0.003$ ) and ( $r = -0.816$ ,  $P < 0.001$ ) respectively. (Figure 29)

#### **4- C- Reactive Protein:**

The CRP was positively correlated with S.Cr, ESR, ANA antibody and anti-ds.DNA antibody ( $r = 0.591$ ,  $P = 0.020$ ), ( $r = 0.678$ ,  $P = 0.006$ ), ( $r = 0.553$ ,  $P = 0.032$ ) and ( $r = 0.690$ ,  $P = 0.004$ ) respectively, and was negatively correlated with platelets count, e-GFR, C3 and C4 ( $r = -0.580$ ,  $P = 0.024$ ), ( $r = -0.612$ ,  $P = 0.015$ ), ( $r = -0.637$ ,  $P = 0.011$ ) and ( $r = -0.861$ ,  $P < 0.001$ ) respectively. (Figure 29)

#### **5- Complement 3:**

The C3 was positively correlated with e-GFR and C4 ( $r = 0.583$ ,  $P = 0.023$ ) and ( $r = 0.832$ ,  $P < 0.001$ ) respectively, and was negatively correlated with S.Cr, urinary albumin/urinary creatinine ratio, ESR, ANA antibody and anti-ds.DNA antibody ( $r = -0.799$ ,  $P < 0.001$ ), ( $r = -0.562$ ,  $P = 0.029$ ), ( $r = -0.749$ ,  $P = 0.001$ ), ( $r = -0.628$ ,  $P = 0.012$ ) and ( $r = -0.552$ ,  $P = 0.033$ ) respectively. (Figure 30, 31)

#### **6- Complement 4:**

The C4 was positively correlated with platelets count and e-GFR ( $r = 0.567$ ,  $P = 0.028$ ) and ( $r = 0.576$ ,  $P = 0.025$ ) respectively, and was negatively correlated with S.Cr, urinary albumin/urinary creatinine ratio, ESR, ANA antibody and anti-ds.DNA

antibody ( $r = -0.701$ ,  $P = 0.004$ ), ( $r = -0.607$ ,  $P = 0.016$ ), ( $r = -0.745$ ,  $P = 0.001$ ), ( $r = -0.651$ ,  $P = 0.009$ ) and ( $r = -0.669$ ,  $P = 0.006$ ) respectively. (Figure 30, 31)

#### **7- Antinuclear Antibody:**

The ANA antibody was positively correlated with S.Cr, ESR and anti-ds.DNA antibody ( $r = 0.528$ ,  $P = 0.043$ ), ( $r = 0.712$ ,  $P = 0.003$ ) and ( $r = 0.864$ ,  $P < 0.001$ ) respectively, and was negatively correlated with platelets count ( $r = -0.520$ ,  $P = 0.047$ ).

#### **8- Anti-Double Stranded DNA Antibody:**

The anti-ds.DNA antibody was positively correlated with S.Cr and ESR ( $r = 0.667$ ,  $P = 0.007$ ) and ( $r = 0.857$ ,  $P < 0.001$ ) respectively, and was negatively correlated with platelets count and e-GFR ( $r = -0.627$ ,  $P = 0.012$ ) and ( $r = -0.613$ ,  $P = 0.015$ ) respectively.

#### **9- Serum Creatinine:**

Serum creatinine was positively correlated with urinary albumin/urinary creatinine ratio and ESR ( $r = 0.762$ ,  $P = 0.001$ ) and ( $r = 0.881$ ,  $P < 0.001$ ) respectively, and was negatively correlated with e-GFR and platelets count ( $r = -0.875$ ,  $P < 0.001$ ) and ( $r = -0.597$ ,  $P = 0.019$ ) respectively.

#### **10- Estimated Glomerular Filtration Rate:**

The e-GFR was negatively correlated with urinary albumin/urinary creatinine ratio and ESR ( $r = -0.758$ ,  $P = 0.001$ ) and ( $r = -0.757$ ,  $P = 0.001$ ) respectively.

#### **11- Urinary Albumin/Urinary Creatinine Ratio:**

Urinary albumin/urinary creatinine ratio was positively correlated with ESR ( $r = 0.699$ ,  $P = 0.004$ ).

### **II-Patients With Systemic Lupus Erythematosus With Nephropathy:** **(Table XXVIII, XXIX, XXX)**

#### **1- Toll-like receptor 7:**

The TLR7 was positively correlated with S.Cr, urinary albumin/urinary creatinine ratio, ESR, CRP, ANA antibody, anti-ds.DNA antibody, SLEDAI and IL-29 ( $r = 0.647$ ,  $P = 0.009$ ), ( $r = 0.541$ ,  $P = 0.037$ ), ( $r = 0.567$ ,  $P = 0.028$ ), ( $r = 0.690$ ,  $P = 0.004$ ), ( $r = 0.621$ ,  $P = 0.014$ ), ( $r = 0.581$ ,  $P = 0.023$ ), ( $r = 0.523$ ,  $P = 0.046$ ) and ( $r = 0.899$ ,  $P < 0.001$ ) respectively, and was negatively correlated with e-GFR, C3 and C4 ( $r = -0.669$ ,  $P = 0.006$ ), ( $r = -0.819$ ,  $P < 0.001$ ) and ( $r = -0.711$ ,  $P = 0.003$ ) respectively. (Figure 23, 24, 25, 26)

#### **2- Interleukin 29:**

IL-29 was positively correlated with S.Cr, urinary albumin/urinary creatinine ratio, ESR, CRP, ANA antibody, anti-ds.DNA antibody and SLEDAI ( $r = 0.695$ ,  $P = 0.004$ ), ( $r = 0.671$ ,  $P = 0.006$ ), ( $r = 0.681$ ,  $P = 0.005$ ), ( $r = 0.737$ ,  $P = 0.002$ ), ( $r = 0.693$ ,  $P = 0.004$ ) and ( $r = 0.514$ ,  $P = 0.050$ ) ( $r = 0.645$ ,  $P = 0.009$ ) respectively, and was negatively correlated with platelets count, e-GFR, C3 and C4 ( $r = -0.548$ ,  $P = 0.034$ ), ( $r = -0.704$ ,  $P = 0.003$ ), ( $r = -0.913$ ,  $P < 0.001$ ) and ( $r = -0.831$ ,  $P < 0.001$ ) respectively. (Figure 27, 28)

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### 3- Systemic lupus erythematosus disease activity index:

The SLEDAI was positively correlated with S.Cr, urinary albumin/urinary creatinine ratio, ESR, CRP, ANA antibody and anti-ds.DNA antibody ( $r = 0.542$ ,  $P = 0.037$ ), ( $r = 0.684$ ,  $P = 0.005$ ), ( $r = 0.661$ ,  $P = 0.007$ ), ( $r = 0.613$ ,  $P = 0.015$ ), ( $r = 0.590$ ,  $P = 0.021$ ) and ( $r = 0.579$ ,  $P = 0.024$ ) respectively, and was negatively correlated with platelets count, e-GFR, C3 and C4 ( $r = -0.527$ ,  $P = 0.043$ ), ( $r = -0.798$ ,  $P < 0.001$ ), ( $r = -0.628$ ,  $P = 0.012$ ) and ( $r = -0.628$ ,  $P = 0.012$ ) respectively. (Figure 32)

### 4- C- Reactive Protein:

The CRP was positively correlated with S.Cr, urinary albumin/urinary creatinine ratio, ESR, ANA antibody and anti-d.s.DNA antibody ( $r = 0.867$ ,  $P < 0.001$ ), ( $r = 0.561$ ,  $P = 0.030$ ), ( $r = 0.679$ ,  $P = 0.005$ ), ( $r = 0.914$ ,  $P < 0.001$ ) and ( $r = 0.739$ ,  $P = 0.002$ ) respectively, and was negatively correlated with e-GFR, C3 and C4 ( $r = -0.713$ ,  $P = 0.003$ ), ( $r = -0.650$ ,  $P = 0.009$ ) and ( $r = -0.772$ ,  $P = 0.001$ ) respectively. (Figure 32)

### 5- Complement 3:

The C3 was positively correlated with platelets, e-GFR and C4 ( $r = 0.538$ ,  $P = 0.038$ ) ( $r = 0.721$ ,  $P = 0.002$ ) ( $r = 0.808$ ,  $P < 0.001$ ) respectively, and was negatively correlated with S.Cr, urinary albumin/urinary creatinine ratio, ESR, ANA antibody and anti-d.s.DNA antibody ( $r = -0.646$ ,  $P = 0.009$ ), ( $r = -0.639$ ,  $P = 0.010$ ) ( $r = -0.700$ ,  $P = 0.004$ ) ( $r = -0.618$ ,  $P = 0.014$ ) and ( $r = -0.582$ ,  $P = 0.023$ ) respectively. (Figure 33, 34)

### 6- Complement 4:

The C4 was positively correlated with e-GFR ( $r = 0.752$ ,  $P = 0.001$ ) and was negatively correlated with S.Cr, urinary albumin/urinary creatinine ratio, ESR, ANA antibody and anti-d.s.DNA antibody ( $r = -0.710$ ,  $P = 0.003$ ), ( $r = -0.573$ ,  $P = 0.025$ ), ( $r = -0.836$ ,  $P < 0.001$ ), ( $r = -0.604$ ,  $P = 0.017$ ) and ( $r = -0.518$ ,  $P = 0.048$ ) respectively. (Figure 33, 34)

### 7- Antinuclear antibody:

The ANA antibody was positively correlated with S.Cr, urinary albumin/urinary creatinine ratio, ESR, anti-ds.DNA antibody ( $r = 0.691$ ,  $P = 0.004$ ) ( $r = 0.569$ ,  $P = 0.027$ ), ( $r = 0.600$ ,  $P = 0.018$ ) and ( $r = 0.765$ ,  $P = 0.001$ ) respectively and was negatively correlated with e-GFR ( $r = -0.586$ ,  $P = 0.022$ ).

### 8- Anti-Double Strand DNA Antibody:

The anti-ds.DNA antibody was positively correlated with S.Cr and ESR ( $r = 0.618$ ,  $P = 0.014$ ) and ( $r = 0.561$ ,  $P = 0.030$ ) respectively, and was negatively correlated with e-GFR ( $r = -0.617$ ,  $P = 0.014$ ) respectively.

### 9- Serum Creatinine:

Serum creatinine was positively correlated with urinary albumin/urinary creatinine ratio ( $r = 0.596$ ,  $P = 0.019$ ) and was negatively correlated with e-GFR ( $r = -0.763$ ,  $P = 0.001$ ).

**10- Estimated Glomerular Filtration Rate:**

The e-GFR was negatively correlated with urinary albumin/urinary creatinine ratio and ESR ( $r = -0.801$ ,  $P < 0.001$ ) and ( $r = -0.568$ ,  $P = 0.027$ ) respectively.

**11- Urinary Albumin/Urinary Creatinine Ratio:**

Urinary albumin/urinary creatinine ratio was negatively correlated with platelets count ( $r = -0.549$ ,  $P = 0.034$ ).

**12- Activity Index of Renal Biopsy:**

The activity index of renal biopsy was positively correlated with S.Cr, urinary albumin/urinary creatinine ratio, CRP, ANA, TLR7 and IL-29 ( $r = 0.615$ ,  $P = 0.019$ ), ( $r = 0.623$ ,  $P = 0.017$ ), ( $r = 0.640$ ,  $P = 0.014$ ), ( $r = 0.628$ ,  $P = 0.016$ ), ( $r = 0.640$ ,  $P = 0.014$ ) and ( $r = 0.786$ ,  $P = 0.001$ ) respectively, and was negatively correlated with C3 and C4 ( $r = -0.771$ ,  $P = 0.001$ ) and ( $r = -0.690$ ,  $P = 0.006$ ) respectively. (Figure 35)

**13- Chronicity Index of Renal Biopsy:**

The chronicity index of renal biopsy was negatively correlated with IL-29 ( $r = -0.551$ ,  $P = 0.041$ ). (Figure 36)

**Table XXVI: Statistical correlation between TLR7, IL-29 and the different studied parameters in patients with systemic lupus erythematosus without nephropathy.**

Parameters		TLR7	IL-29
Platelets	r	-0.615*	-0.513*
	p	0.015	0.050
S.Cr	r	0.440	0.728*
	p	0.101	0.002
e-GFR (MDRD)	r	-0.305	-0.667*
	p	0.269	0.007
U.Alb/U.Cr ratio	r	0.156	0.589*
	p	0.578	0.021
ESR	r	0.507	0.736*
	p	0.054	0.002
CRP	r	0.761*	0.855*
	p	0.001	<0.001
C3	r	-0.568*	-0.885*
	p	0.027	<0.001
C4	r	-0.626*	-0.931*
	p	0.013	<0.001
ANA	r	0.697*	0.671*
	p	0.004	0.006
Anti-ds.DNA	r	0.632*	0.663*
	p	0.011	0.007
SLEDAI	r	0.627*	0.872*
	p	0.012	<0.001
IL-29	r	0.669*	-----
	p	0.006	-----

Abbreviation as tables VIII, XI, XV, XIX, XX, XXI, XXII, XXIII

r = Pearson coefficient.

\* = Significant P value at 5% level

**Table XXVIII: Statistical correlation between the different studied parameters in patients with systemic lupus erythematosus without nephropathy**

Parameters		Platelets	S.Cr	eGFR (MDRD)	U.Alb/U.Cr ratio	ESR	CRP	C3	C4	ANA	Anti-ds.DNA
S.Cr	r	-0.597*									
	p	0.019									
eGFR (MDRD)	r	0.496	-0.875*								
	p	0.060	<0.001								
U.Alb/U.Cr ratio	r	-0.462	0.762*	-0.758*							
	p	0.083	0.001	0.001							
ESR	r	-0.497	0.881*	-0.757*	0.699*						
	p	0.059	<0.001	0.001	0.004						
CRP	r	-0.580*	0.591*	-0.612*	0.397	0.678*					
	p	0.024	0.020	0.015	0.142	0.006					
C3	r	0.449	-0.799*	0.583*	-0.562*	-0.749*	-0.637*				
	p	0.093	<0.001	0.023	0.029	0.001	0.011				
C4	r	0.567*	-0.701*	0.576*	-0.607*	-0.745*	-0.861*	0.832*			
	p	0.028	0.004	0.025	0.016	0.001	<0.001	<0.001			
ANA	r	-0.520*	0.528*	-0.358	0.408	0.712*	0.553*	-0.628*	-0.651*		
	p	0.047	0.043	0.190	0.131	0.003	0.032	0.012	0.009		
Anti-d.s.DNA	r	-0.627*	0.667*	-0.613*	0.503	0.857*	0.690*	-0.552*	-0.669*	0.864*	
	p	0.012	0.007	0.015	0.056	<0.001	0.004	0.033	0.006	<0.001	
SLEDAI	r	-0.636*	0.717*	-0.752*	0.490	0.723*	0.885*	-0.706*	-0.816*	0.606*	0.770*
	p	0.011	0.003	0.001	0.064	0.002	<0.001	0.003	<0.001	0.017	0.001

Abbreviation as tableXII, XVI, XX, XXI, XXII, XXVII

**Table XXVIII: Statistical correlation between TLR7, IL-29 and the different studied parameters in patients with systemic lupus erythematosus with nephropathy.**

Parameters		TLR7	IL-29
Platelets	r	-0.479	-0.548*
	p	0.071	0.034
S.Cr	r	0.647*	0.695*
	p	0.009	0.004
e-GFR (MDRD)	r	-0.669*	-0.704*
	p	0.006	0.003
U.Alb/U.Cr ratio	r	0.541*	0.671*
	p	0.037	0.006
ESR	r	0.567*	0.681*
	p	0.028	0.005
CRP	r	0.690*	0.737*
	p	0.004	0.002
C3	r	-0.819*	-0.913*
	p	<0.001	<0.001
C4	r	-0.711*	-0.831*
	p	0.003	<0.001
ANA	r	0.621*	0.693*
	p	0.014	0.004
Anti-ds.DNA	r	0.581*	0.514*
	p	0.023	0.050
SLEDAI	r	0.523*	0.645*
	p	0.046	0.009
IL-29	r	0.899*	-----
	p	<0.001	-----

Abbreviation as tables VIII, XI, XV, XIX, XX, XXI, XXII, XXIII, XXVI

**Table XXX: Statistical correlation between the different studied parameters in patients with systemic lupus erythematosus Withnephropathy.**

Parameters		Platelets	S.Cr	eGFR (MDRD)	U.Alb/U.Cr ratio	ESR	CRP	C3	C4	ANA	Anti-ds.DNA
S.Cr	r	-0.293									
	p	0.289									
eGFR (MDRD)	r	0.309	-0.763*								
	p	0.262	0.001								
U.Alb/U.Cr ratio	r	-0.549*	0.596*	-0.801*							
	p	0.034	0.019	<0.001							
ESR	r	-0.193	0.428	-0.568*	0.344						
	p	0.491	0.111	0.027	0.210						
CRP	r	-0.196	0.867*	-0.713*	0.561*	0.679*					
	p	0.484	<0.001	0.003	0.030	0.005					
C3	r	0.538*	-0.646*	0.721*	-0.639*	-0.700*	-0.650*				
	p	0.038	0.009	0.002	0.010	0.004	0.009				
C4	r	0.269	-0.710*	0.752*	-0.573*	-0.836*	-0.772*	0.808*			
	p	0.332	0.003	0.001	0.025	<0.001	0.001	<0.001			
ANA	r	-0.298	0.691*	-0.586*	0.569*	0.600*	0.914*	-0.618*	-0.604*		
	p	0.280	0.004	0.022	0.027	0.018	<0.001	0.014	0.017		
Anti-ds.DNA	r	-0.180	0.618*	-0.617*	0.321	0.561*	0.739*	-0.582*	-0.518*	0.765*	
	p	0.522	0.014	0.014	0.244	0.030	0.002	0.023	0.048	0.001	
SLEDAI	r	-0.527*	0.542*	-0.798*	0.684*	0.661*	0.613*	-0.628*	-0.628*	0.590*	0.579*
	p	0.043	0.037	<0.001	0.005	0.007	0.015	0.012	0.012	0.021	0.024

Abbreviation as table XII, XVI, XX, XXI, XXII, XXVII

**Table XXX: Statistical correlations of the activity and chronicity indices in renal biopsy in patients with lupus nephritis:**

Parameters		Activity Index	Chronicity Index
Activity index	r	-----	-0.133
	p		0.650
Chronicity index	r	- 0.133	-----
	p	0.650	
S. creatinine	r	0.615*	-0.463
	p	0.019	0.096
U.Alb/U. Cr ratio	r	0.623*	-0.452
	p	0.017	0.105
CRP	r	0.640*	-0.520
	p	0.014	0.056
C3	r	-0.771*	0.488
	p	0.001	0.076
C4	r	-0.690*	0.467
	p	0.006	0.092
ANA	r	0.628*	-0.455
	p	0.016	0.102
Anti-ds.DNA	r	0.489	-0.371
	p	0.076	0.191
SLEDAI	r	0.441	-0.335
	p	0.114	0.242
TLR7	r	0.640*	-0.403
	p	0.014	0.153
IL-29	r	0.786*	-0.551*
	p	0.001	0.041

Abbreviation as tables XI, XV, XIX, XX, XXI, XXII, XXIII, XXVI

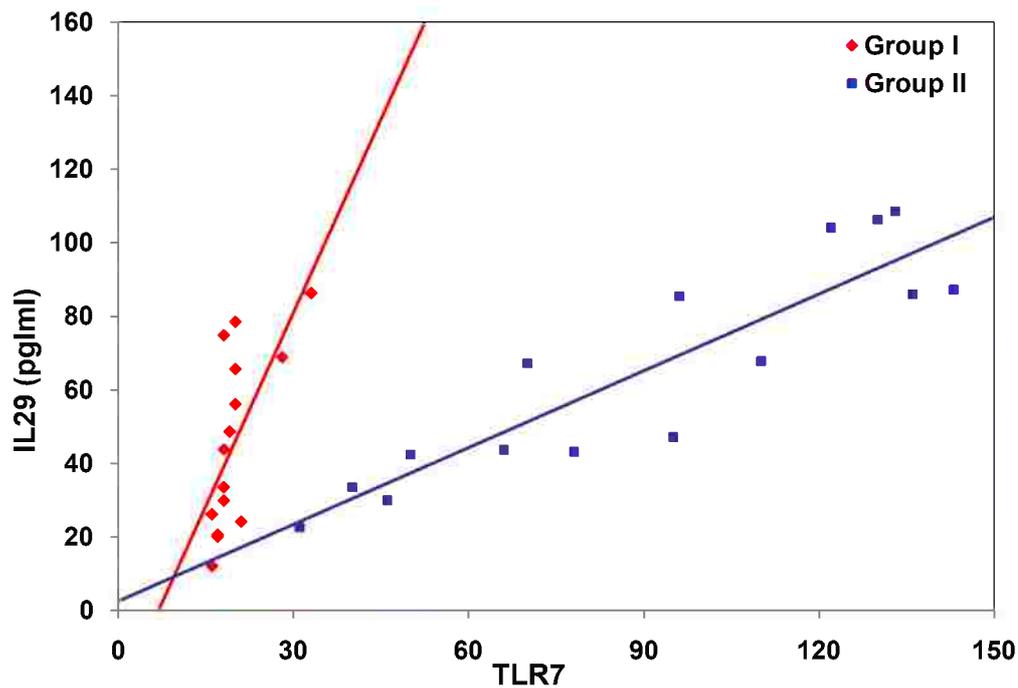


Figure 23: Correlation between toll like receptor 7 (TLR7) (cell/ $\mu$ l) and interleukin 29 (IL-29) (pg/ml) in patients with systemic lupus erythematosus without nephropathy (Group I) and patients with lupus nephritis (Group II).

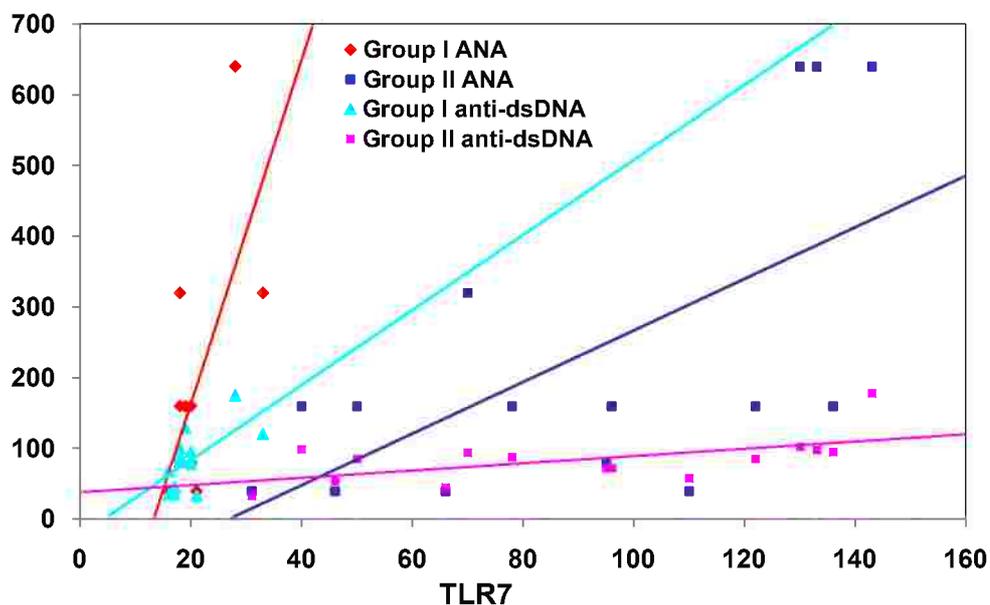


Figure 24: Correlation between toll like receptor 7 (TLR7) (cell/ $\mu$ l) and both antinuclear antibody (ANA) (titer) and anti-double stranded DNA (anti-ds DNA) (IU/ml) in patients with systemic lupus erythematosus without nephropathy (Group I) and patients with lupus nephritis (Group II).

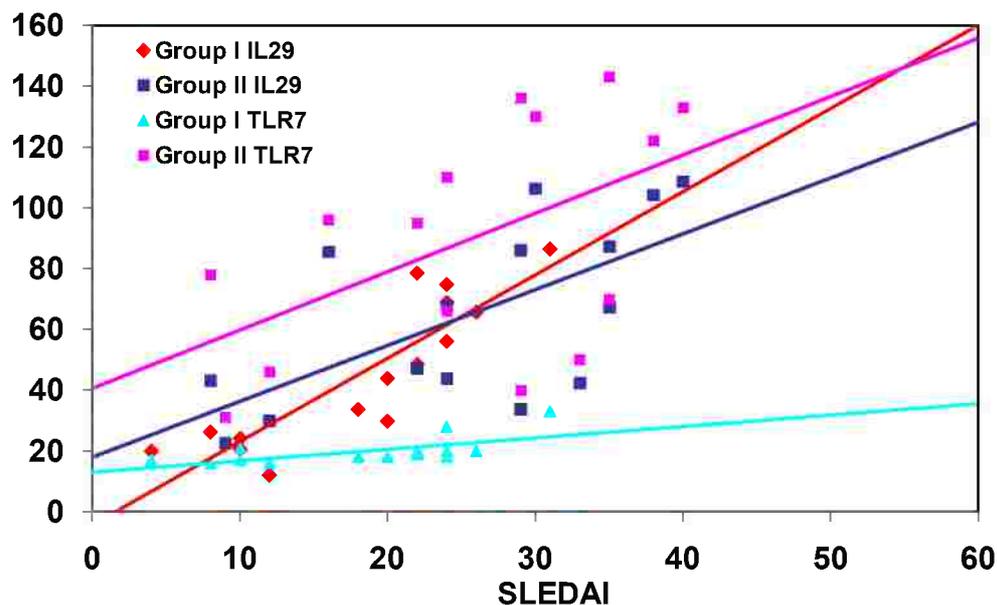


Figure 25: Correlation between Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and both interleukin 29 (IL-29) (pg/ml) and toll like receptor 7 (TLR7) (cell/ $\mu$ l) in patients with systemic lupus erythematosus without nephropathy (Group I) and patients with lupus nephritis (Group II).

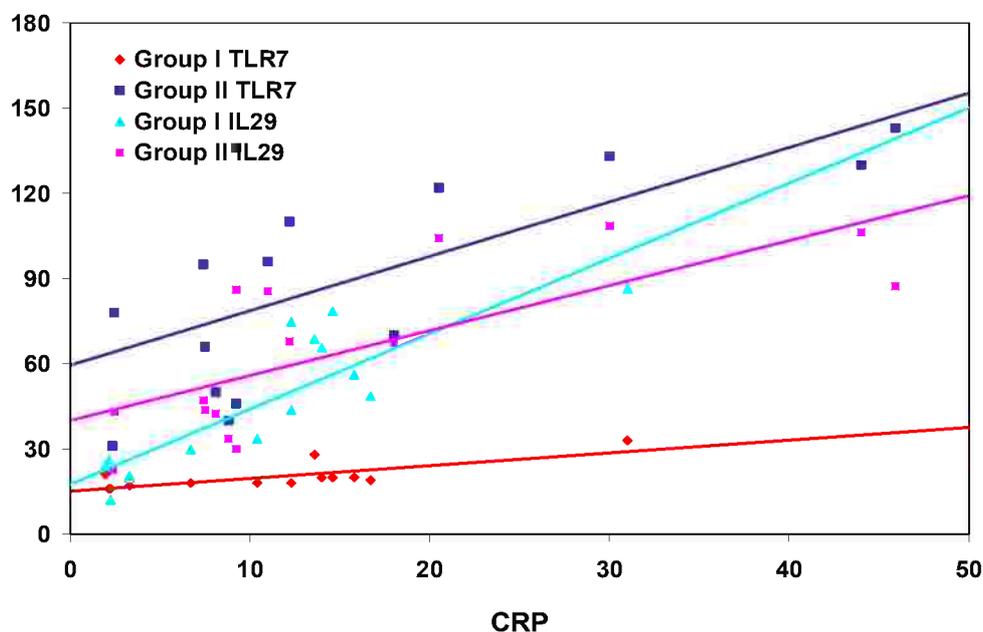


Figure 26: Correlation between C-reactive protein (CRP) (mg/l) and both toll like receptor 7 (TLR7) (cell/ $\mu$ l) and interleukin 29 (IL-29) (pg/ml) and in patients with systemic lupus erythematosus without nephropathy (Group I) and patients with lupus nephritis (Group II).

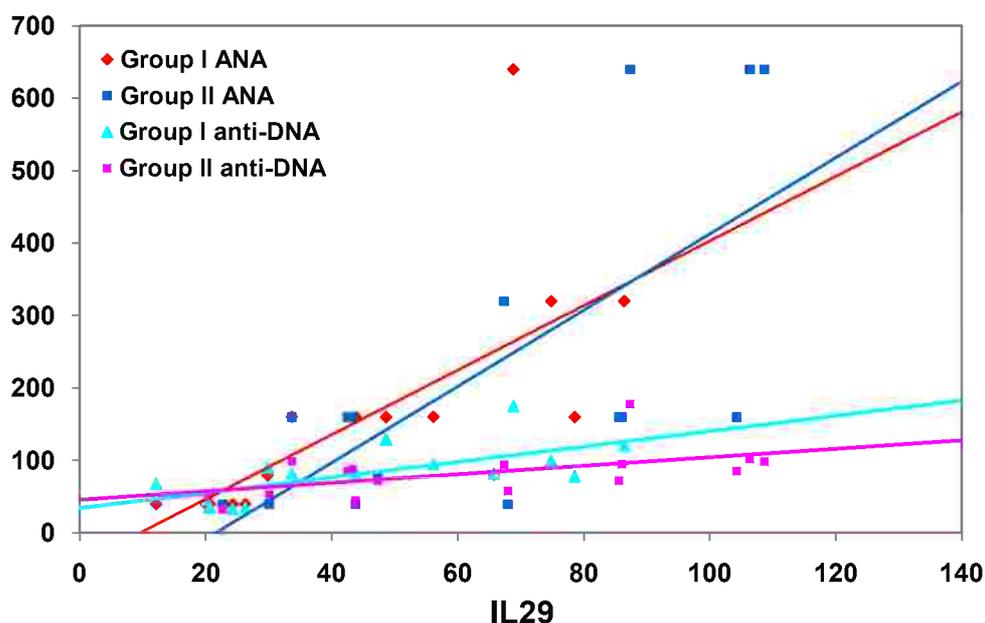


Figure 27: Correlation between interleukin 29 (IL-29) (pg/ml) and both antinuclear antibody (ANA) (titer) and anti-double stranded DNA (anti-ds DNA) (IU/ml) in patients with systemic lupus erythematosus without nephropathy (Group I) and patients with lupus nephritis (Group II).

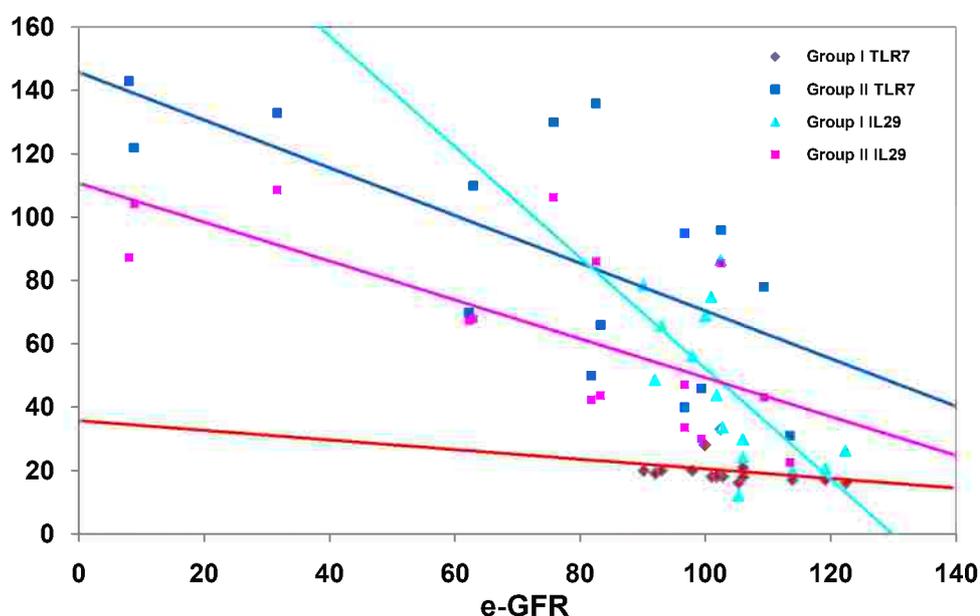


Figure 28: Correlation between estimated glomerular filtration rate (e-GFR) (ml/min/1.73m<sup>2</sup>) and both toll like receptor 7 (TLR7) (cell/ $\mu$ l) and interleukin 29 (IL-29) (pg/ml) in patients with systemic lupus erythematosus without nephropathy (Group I) and patients with lupus nephritis (Group II).

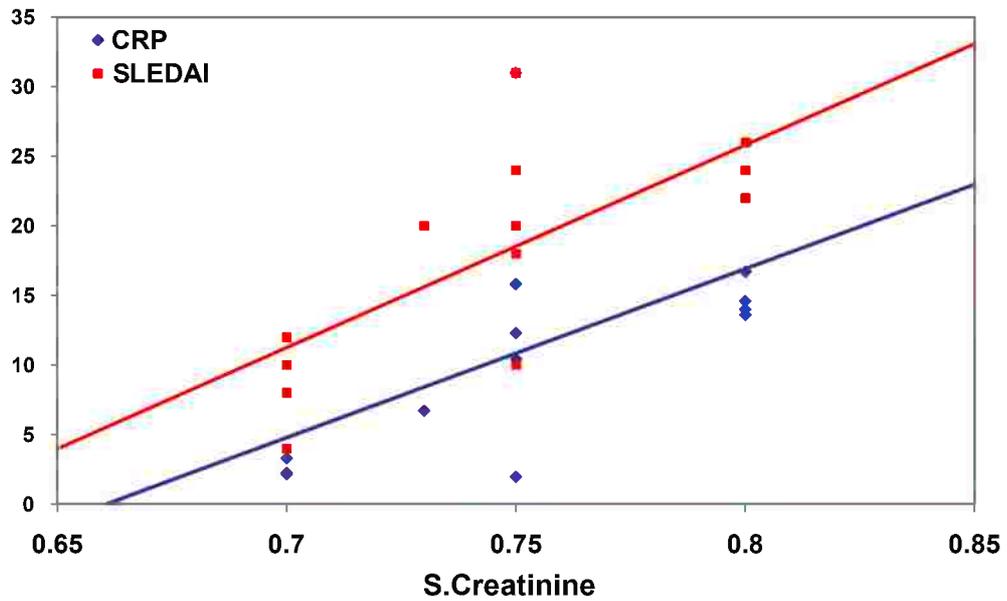


Figure 29: Correlation between serum creatinine (mg/dl) with both C-reactive protein (CRP) (mg/l) and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) in patients with systemic lupus erythematosus without nephropathy (Group I).

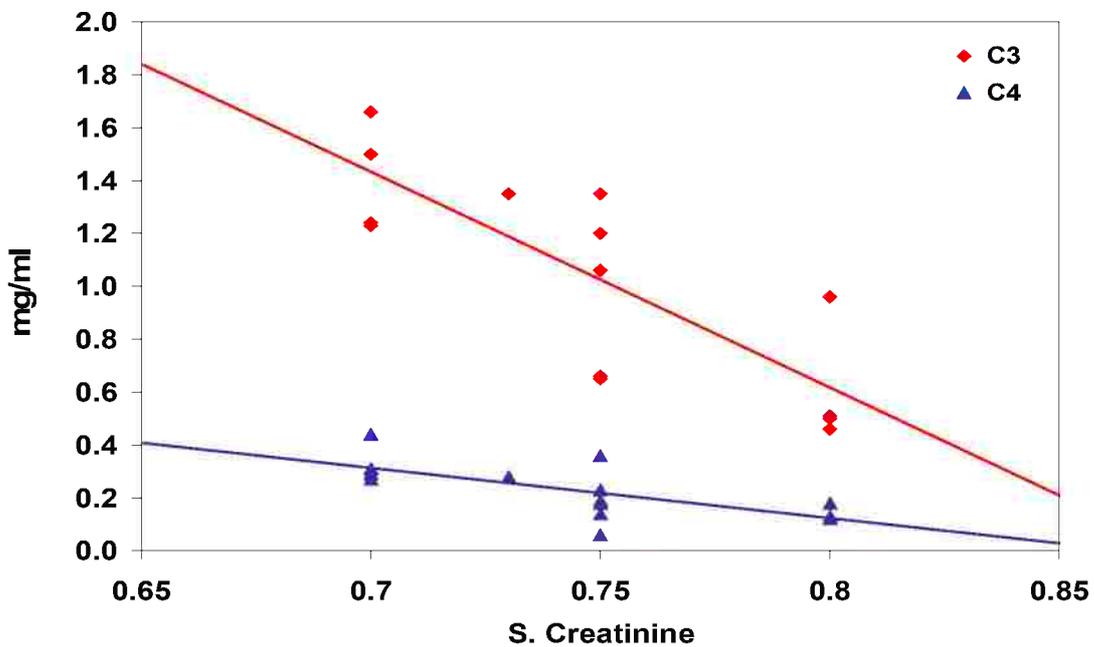


Figure 30: Correlation between serum creatinine (mg/dl) with both complement 3 (C3) (mg/ml) and complement 4 (C4) (mg/ml) in patients with systemic lupus erythematosus without nephropathy (Group I).

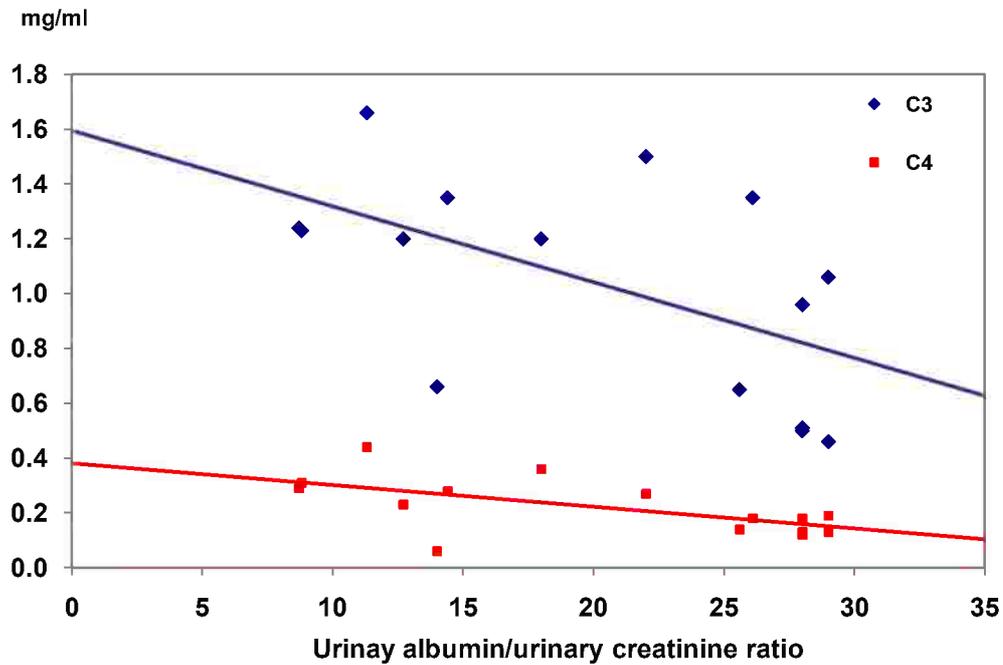


Figure 31: Correlation between urinary albumin/urinary creatinine ratio (mg/g) and both complement 3 (C3) (mg/ml) and complement 4 (C4) (mg/ml) in patients with systemic lupus erythematosus without nephropathy (Group I).

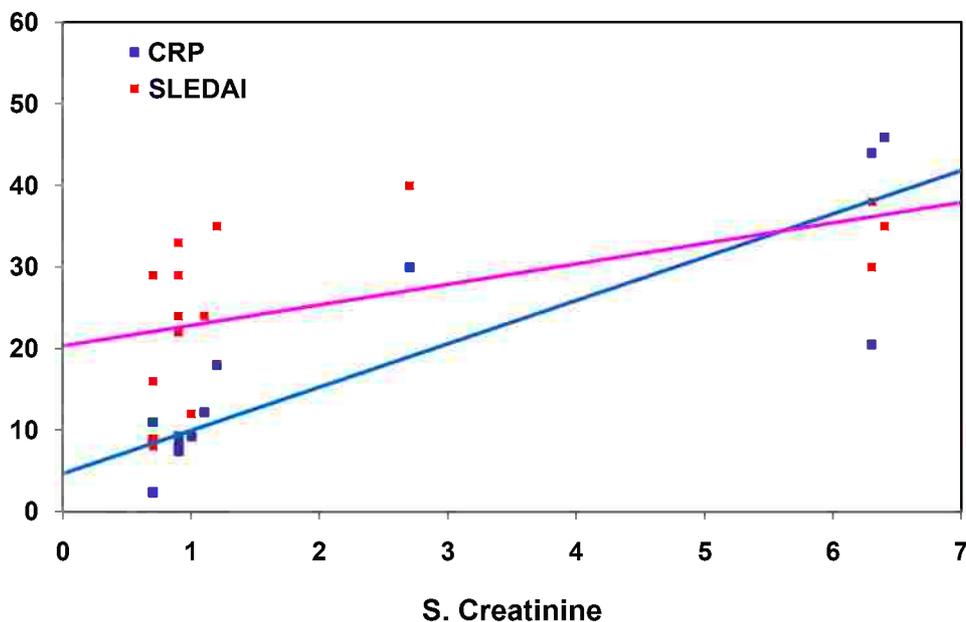


Figure 32: Correlation between serum creatinine (mg/dl) with both C-reactive protein (CRP) (mg/l) and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) in patients with lupus nephritis (Group II).

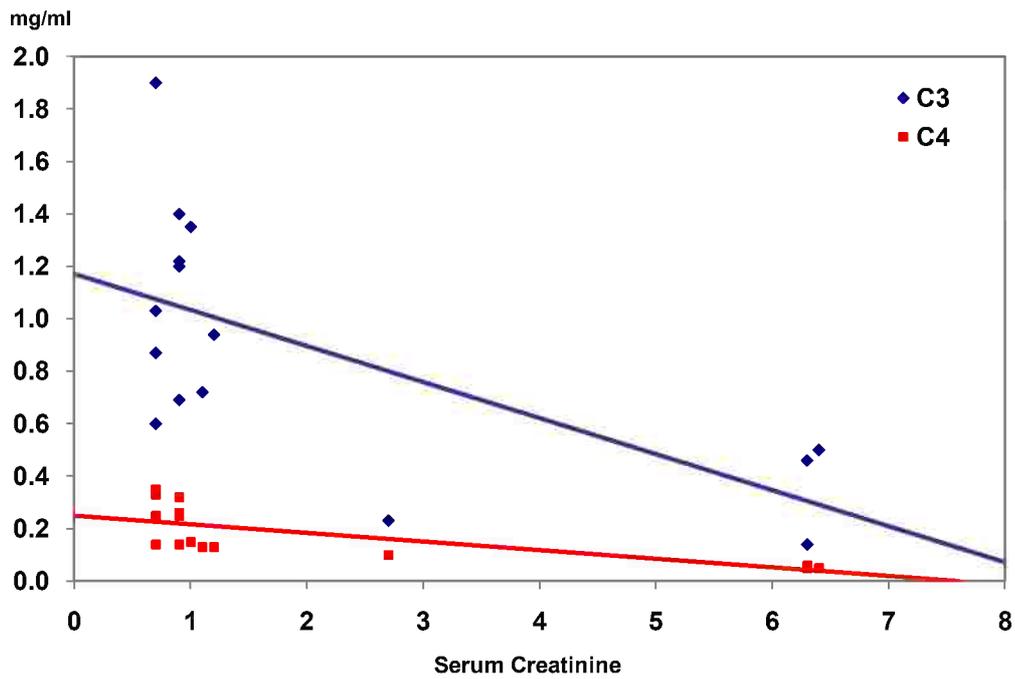


Figure 33: Correlation between serum creatinine (mg/dl) with both complement 3 (C3) (mg/ml) and complement 4 (C4) (mg/ml) in patients with lupus nephritis (Group II).

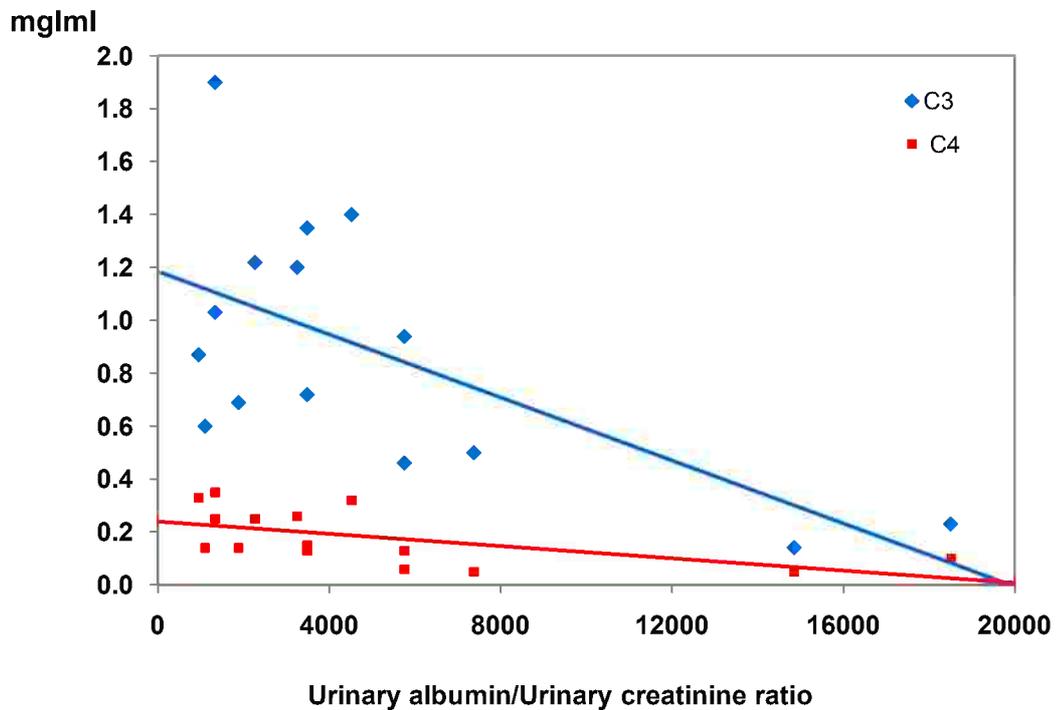


Figure 34: Correlation between urinary albumin/urinary creatinine ratio (mg/g) and both complement 3 (C3) (mg/ml) and complement 4 (C4) (mg/ml) in patients with lupus nephritis (Group II).

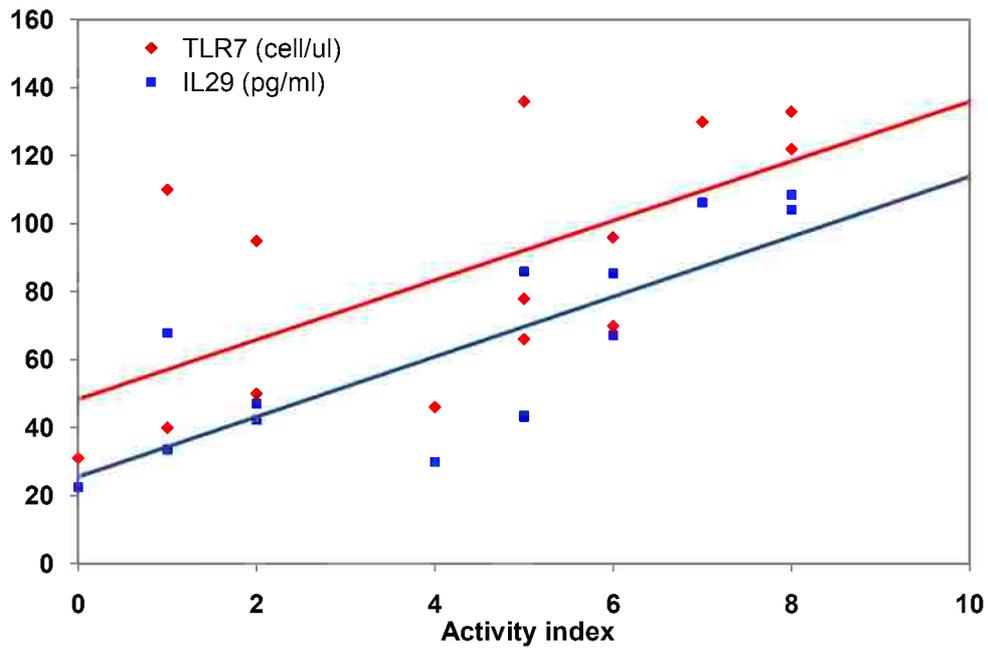


Figure 35: Correlation between the activity index in renal biopsy and both toll like receptor 7 (TLR7) (cell/ $\mu$ l) and interleukin 29 (IL-29) (pg/ml) in patients with lupus nephritis (Group II).

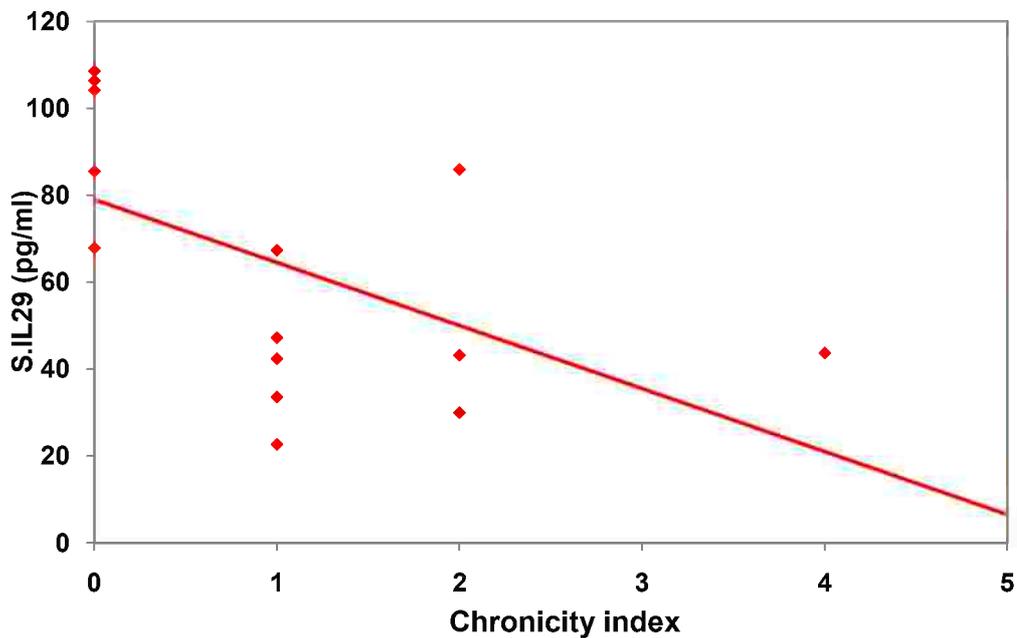


Figure 36: Correlation between the chronicity index in renal biopsy and interleukin 29 (IL-29) (pg/ml) in patients with lupus nephritis (Group II).