ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

Clinical, laboratory, histopathology characteristics and correlations of lupus nephritis patients- A single Center experience

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Manuscript Info

Manuscript History:

Received: 10 January 2016
Final Accepted: 25 January 2016
Published Online: January 2016

Key words:

Lupus nephritis, kidney biopsy, histopathology, clinical, laboratory, correlation

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Abstract

Background: Lupus nephritis (LN) is one of the most serious complications of systemic lupus erythematosus (SLE).The world Health Organization (WHO) and International Society of Nephrology/Renal Pathology Society (ISN/RPS 2003) can correlate the histopathology pattern with clinical renal syndrome and provide valuable information regarding diagnosis, prognosis and management guidelines.

Objective: To evaluate the main clinical, laboratory and histopathological characteristics of lupus nephritis (LN), and find the clinicopathologic correlation of renal biopsy lupus classification.

Patients and methods: This study comprised a total of 38 adults LN patients, 36Females (94.7%), and 2 males (5.3%) with female to male ratio (18:1), mean age of 26.7 ± 8.95ys, urban patients 24 (63.2%) and rural 14 (36.8%)**.** All patients were subjected to complete clinical, laboratory, and native renal biopsy histopathological evaluation through one year. Biopsies were examined and categorized according to ISN/RPS 2003 classifications.

Results: The most frequent presenting features of SLE were mucocutaneous found in (78.9%), serositis (47.4%) and hematological disorders (23.7%).The frequencies of LN histopathological patterns were as follow**:** diffuse proliferative LN (class IV) found in 21 cases (55.3%), followed by class III found in 12 patients (31.5%) then class V in 4cases (10.5%) and lastly class II found in 1case (2.6%). A significant association found between nephrotic syndrome, edema and class V LN (p = 0.016 & p=0.024) respectively, also a significant associations between nephritic syndrome, hypertension, decreased estimated GFR and microscopic hematuria and class IV LN (p =0.048, p =0.01, p = 0.04 & p=0.02) respectively**.** While no significance found between LN class III or IV and each of arthritis, CNS, serositis, SLE disease activity index (SLEDAI), antiphospholipid syndrome (APS) and cutaneous manifestations**.**

Conclusion: Our study demonstrated that diffuse proliferative LN class IV was the predominant pattern followed by class III. Obvious correlation found between clinical, laboratory and renal histopathology of lupus nephritis. Renal biopsy remains the corner stone in diagnosis, management and prognosis of the disease.

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disorder characterized by multisystem inflammation with the generation of autoantibodies.[1]SLE encompasses a wide spectrum of severity, ranging from relatively mild manifestations (e.g. skin rash or non-erosive arthritis) to seriously disabling or even life threatening complications, such as lupus nephritis, neuropsychiatric disorders and other major organs involvement.[2] The disease course is milder and survival rate is higher in persons with isolated skin and musculoskeletal involvement than in those with renal disease and CNS disease.[3] Mortality in patients with SLE has decreased over the past few decades.[4]

The kidney is the most commonly involved visceral organ in SLE , however only approximately 50% of patients develop clinically evident renal disease , biopsy studies demonstrate some degree of renal involvement in most patients.[5] LN is one of the most serious SLE complications since it is the major predictor of poor prognosis.[6] Careful screening tests are critical because most patients present with asymptomatic urine abnormalities(AUA), such as hematuria or proteinuria, or with new onset or worsening hypertension, however the clinical presentation does not always predict the underlying histologic class of nephritis.[7]

In general, patients with mesangial nephritis have small amounts of proteinuria (<1 g/day) with hematuria but typically no cellular casts. Patients with proliferative nephritis have hypertension, nephritic urine sediment with various degrees of proteinuria (often at nephritic range), low C3 and typically high titers of anti-DNA antibodies, whereas patients with membranous glomerulopathy have proteinuria often at nephrotic range but otherwise bland urine sediments; C3 tends to be normal, and anti-DNA Abs when present are usually found in low titers. [7]

The aim of this study is to evaluate the main clinical, laboratory and histopathology characteristics of LN, and find the clinicopathologic correlation of renal biopsy lupus classification through one year study.

Patients and Methods

Study design and population

This retrospective cross sectional study was carried out, in Zagazig nephrology unit and renal Pathology departments in the period from December 2013 to December 2014, in accordance with Helsinki Declaration and institutional review board of our faculty of medicine, informed written consent was obtained.

Eligible participants included 38 adults' patients, 36Females and 2males with female to male ratio (18:1), age ranged from 17 to 48 years, mean age of 26.7 ± 8.95years, presented with LN, and meeting at least 4 items of SLE diagnostic criteria, updated by American college of Rheumatology 1997.

Exclusion Criteria

Young's (<16years old), lupus patients with end stage renal disease (ESRD) on regular hemodialysis , overlapping syndromes, kidney transplant recipients, bleeding diathesis, uncontrolled hypertension, solitary kidney, morbid obesity (BMI>40%), well known diabetic nephropathy and uncooperative patients .

All patients included in this study are subjected to the following

Thorough Clinical examination

Detailed history taking with special stress on age, sex, BMI, nephrotoxic and SLE induced drugs, duration of disease, full menstrual history (including miscarriage or repeated abortions), and family history with covering all clinical criteria, presence of HPN, edema, volume overload, skin pigmentation or neuropsychiatric manifestations and assessment of renal disease activity by SLEDAI scores.

Laboratory measurements

Taken Peripheral venous blood samples subjected to hematologic and biochemical analysis including: Complete

blood picture(CBC) [hemoglobin (HB)(g/dl), hematocrit % (HCT)] , ESR, uric acid, fasting blood sugar(FBS), serum albumin, blood urea nitrogen (BUN), creatinine (SCr), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP),Calcium(Ca),phosphorus(P) ,bleeding time , clotting time, sodium , potassium, lipid profile,HA1c ,C-reactive protein (hsCRP),urinalysis, 24 h protein according to standard methods used in routine clinical laboratory**.** HBsAg and HCV Ab are measured by ELISA technique. Immune profile [ANA, Anti dsDNA Ab, ANCA and rheumatoid factor (RF)] by both immunoassay and indirect fluorescent antibody (IFA). C3 & C4, measured by standard immunochemical methods and (ELISA), anti cardiolipin antibodies IgG and IgM by immunoassay or by (IFA). Estimation of GFR using (CKD- EPI equation) (ml /min/m²).[8]ECG, and when indicated computed tomography (CT) for brain. Pelvi-abdominal US, using Acuson 128XP 110 to evaluate kidney size, echogenicity, cortical thickness.

Kidney biopsy performance

Prior to biopsy taken, clotting profile [platelets count, bleeding time, clotting time, and prothrombin time] were assisted. Ultrasound guided renal biopsy is performed. [9, 10] Biopsy cores processed according to standard techniques; paraffin sections processed and stained with hematoxylin and eosin (H/E), periodic acid Schiff (PAS) and Masson trichrome stains. [11] Slides examined by LM, at least 11 glomeruli were reviewed by a single nephropathologist**.** Histopathological assessments studied according to ISN/RPS 2003, with calculation of activity and chronicity indices **.**[12] Patients remained flat on their back for 24 with frequent monitoring of blood pressure, pulse, urine flow & lion pain. Also patients encouraged to drink a lot of fluids. Fortunately no complications reported.

Statistical analysis

Collected data were computerized and statistically analyzed using SPSS program (Statistical Package for Social Science) version 18.[13]Quantitative data were expressed as mean ± SD .Independent t test was used to calculate difference between quantitative variables. Qualitative data were represented as frequencies and relative percentages, Chi square test was used to calculate difference between qualitative variables, and ANOVA test. P value <0.05 indicates significant results.

Results

Demographic characteristics

Characteristics of studied patients illustrated in table1.A total of 38 adults LN patients included, 36Females (94.7%), and 2 males (5.3%) with female to male ratio (18:1), age ranged from 17 to 48 years, mean age of 26.7 ± 8.95ys, 24 cases (63.2%) urban and 14 (36.8%) rural**.** A 42 renal biopsies (first and second) taken.

Admission presentations

Different clinical admission presentations of SLE patients showed in table 2. Where, 19 (50%) of cases were in emergency situations, due to disturbed conscious level in 6 (15.8%) [2 post ictal confusion & 4 acute confusional state), rapidly progressive glomerulonephritis (RPGN) in 6 (15.8%), adults respiratory distress syndrome (ARDS) in 4 (10.5%), hypertensive emergency (acute left ventricular failure) in 2(5.3%) and thrombotic thrombocytopenic purpura (TTP) in one case (2.6%). While non-emergent, 19 (50%) cases, generalized edema 15 (39.5%), acute DVT 3 (7.8%) and prolonged fever in one case (2.6%). As regard clinical characteristics of SLE patients were as follow; mucocutaneous manifestations found in 30 (78.9%) [Malar rash, photosensitivity, discoid rash and oral ulcers found in 19 (50%), 10 (26.3%), 1(2.6%) and 20 (52.6%)] respectively. Musculoskeletal manifestations in 26(68.8%) [Arthritis 8 (21%) and arthralgia 18 (47.8%)]. Serositis in 18 (47.4%), normocytic normochromic anemia in 36 (94.8%), leucopenia and/or thrombocytopenia in 9 (23.7%) and hemolytic anemia with negative comb's test in one case (2.6%), seizures and delirium in 7 (18.4%), and antiphospholipid syndrome (APS) in 3 (7.9%). Regarding SLE complications, Hypertension in 24 (63.2%), diabetes mellitus 3 (7.9%), valvular heart disease 2 (5.3%) and Vasculitis complicated by foot amputation in one case (2.6%).

Laboratory characteristics

Laboratory and immunological characteristics of SLE patients are showed in table 3. Mean values, of WBC was 6.5 ± 5.1(× 10 ³/ mm3), Platelets count 172 ± 85.1(× 10 ³/ mm3), HB was 9.2 ± 1.3gm/dl, PT 13.2 ± 1.5sec., 24 h

urinary protein 4.8 ± 3 gm, ESR 105 ± 13.5, eGFR 40.8 ± 34.3 ml/min/m², S. albumin 2.3 ± 0.5gm/dl , microscopic hematuria 21(55.3%) , RBC casts in 7(18.4%). Positive ANA found in 36 (94.4%), +ve anti dsDNA in 31 (81.5%), [cases with -ve ANA were +ve for anti dsDNA]. Low C3 in 23 (60%), low C4 in 24 (63%).Positive Anticardiolipin IgG& IgM in 7 (18.4%), where a suspicion of APS was high, criteria of APS fulfilled in 3 cases, lupus anticoagulant was +ve in 4 (10.5%) and (P ANCA) +ve in one case (2.6%). Lastly, base line SLEDAI score was 16. Eight patients (21.1%) needed urgent hemodialysis and one case (TTP) (2.6%) needed urgent Plasmapheresis beside steroid and cyclophosphamide pulse therapy.

Kidney biopsy histopathology patterns

Frequency of LN patterns according to ISN/RPS classification 2003 showed in table 4. Where**,** Class II found in 1case (2.6%), class III in12 (31.5%), class IV in 21 (55.2%), class V in 4 (10.5%) cases, with predominance of active and chronic lesion in 27 (71%) and global lesion in 10 (47.6%) of class IV

Clinicopathologic correlation

Correlation between LN classes, renal syndromes and some clinical , and laboratory finding showed in Table5: A significant association found between nephrotic syndrome , edema and class V LN (p = 0.016& p=0.024) respectively, also significant associations between nephritic syndrome, hypertension, decreased estimated GFR and microscopic hematuria and class IV (p=0.048 , p =0.01 , p = 0.04 & p=0.02) respectively**.** While no significant difference found between classes III or IV LN and each of arthritis, CNS manifestations, serositis, SLEDAI, APS and cutaneous manifestations. RPGN patterns showed crescent and fibrinoid necrosis and picture of thrombotic microangiopathy (TMA) in two cases of class IV.

Difference between died and survived patients regarding some clinical and laboratory characteristics showed in table 6. 80 % of the 5 the deceased were LN class IV and one case LN class III. Also, there was a significant difference between deceased and survived patients regarding ARDS (p = 0.01), need for urgent hemodialysis (p =0.02), leucocytosis (p = 0.001), elevated creatinine & BUN (p = 0.024& p=0.045) respectively. Meanwhile, no significant association found regarding age, SLEDAI, and CNS manifestations.

Table 1: Demographic characteristics of SLE studied patients.

Parameters		
Age (ys) Mean ± SD / (Range)	26.7 ± 8.95 / (17 – 48)	
Sex	No	(%)
Female/ Male	36/2	94.7/5.3
Residence	No	(%)
Urban/ Rural	24/14	63.2/36.8
Marital state	No	(%)
Married / Single/ Divorced	20/14/4	52.6/36.8/10.5

Table 2: Admission presentations, clinical characteristics and complications of SLE patients.

Emergent lupus presentation	No	(%)
Disturbed conscious level	6	15.8
RPGN	6	15.8
ARDS	4	10.5
Hypertensive emergency	2	5.3
TTP	1	2.6
Non emergent lupus presentation	No	(%)
Generalized edema	15	39.5
Acute DVT	3	7.8
Prolonged fever for investigation	1	2.6
Clinical characteristics of SLE patients	No	(%)
Mucocutaneous manifestations	30	78.9
Malar rash	19	50
Photosensitivity	10	26.3
Discoid rash	1	2.6
Oral ulcers	20	52.6
Musculoskeletal manifestations	No	(%)
Arthritis	8	21
Arthralgia	18	47.4
Serositis	18	47.4
Pleural effusion	16	42.1
Pericarditis	1	2.6
Peritonitis	1	2.6
Hematological disorders	9	23.7
Leucopenia and/or Lymphopenia	2	5.3
Thrombocytopenia	4	10.5
Mixed leucopenia and thrombocytopenia	3	7.9
Hemolytic anemia with negative comb's test	1	2.6
Anemia (normocytic normochromic)	36	94.8
CNS disorders	7	18.4
Seizures	3	7.9
Delirium (acute confusional state)	4	10.5
Antiphospholipid syndrome	3	7.9
Complications of SLE	No	(%)
Hypertension	24	63.2
Diabetes	3	7.9
Cardiovascular	2	5.3
Vasculitis	1	2.6

Table 3: Basic laboratory and immunological characteristics of SLE patients.

Variables	Mean ± SD	
WBCs (× 10 ³/ mm3)	6.5±5.1	
Platelets (× 10 ³/ mm3)	172.0 ± 85.1	
Hemoglobin (gm/dl)	9.2 ± 1.3	
Prothrombin time (secs.)	13.2 ± 1.5	
24 hours protein in urine	4.8 ± 3.0	
24 hours protein in urine levels	No	(%)
< 1 gm/dl /24h	2	5.2
1 – 3 gm./dl/24h	24	63.1
> 3 gm/dl/24h	12	31.6
Other variables	Mean ± SD	
ESR 1st hour	105.0 ± 13.5	
Serum creatinine (mg/dl)	3.3 ± 2.5	
Serum BUN (mg/dl)	39.0 ± 25.9	
eGFR	40.8 ± 34.3	
Serum albumin (gm/dl)	2.3 ± 0.5	
Urine analysis	No	(%)
RBCs in urine (microscopic hematuria)	21	55.3
Granular casts	14	36.8
RBCs casts	7	18.4
Auto antibodies	No	(%)
ANA +ve	36	94.4
Anti-ds DNA +ve	31	81.5
Low C4	24	63
Low C3	23	60
Anticardiolipin Ab IgG and / or IgM	7	18.4
Lupus anticoagulant +ve	4	10.5
P ANCA +ve	1	2.6
Urgent dialysis	8	21.1
Plasmapheresis	1	2.6
SLEDAI score Mean ± SD	16.15 ± 5.9	

Table 4: Frequency of LN histopathological classes according to ISN/RPS classification 2003.

LN biopsy classes		No	(%)	Gender		Age (ys) (range)
				F	M	
Class II		1	2.6	1	0	(26ys)
Class III	III (A)	4	10.5	4	0	(16 – 30)
	III (A/C)	8	21	8	0	(17 – 30)
	Total	12	31.5	12	0	(16 – 30)
Class IV	IV S (A)	2	5.3	2	0	(19 – 45)
	IV S (A/C)	9	23.7	9	0	(18 – 38)
	IV G (A/C)	10	26.3	8	2	(17 – 48)
	Total	21	55.3	19	2	(17 – 48)
Class V		4	10.6	4	0	(19 – 26)

Table 5: LN classes, renal syndrome, clinical, and some laboratory finding

Variable	LN Biopsy class						X2	P value
	Class III / n=12		Class IV / n= 21		Class V / n= 4			
	No	(%)	No	(%)	No	(%)		
Acute Nephritic syndrome	5	41.6	15	71.4	0	0	3.7	0.048 S
RPGN	2	16.6	4	19	0	0	0.16	1.82
Nephrotic syndrome	2	16.6	4	19	4	100	12.1	0.016 S
Hypertension	4	33.3	19	90.4	1	25	13.2	0.01 S
Generalized edema	2	16.6	9	42.8	4	100	11.2	0.024 S
Arthralgia	5	41.6	11	52.3	2	50	0.02	0.99
Arthritis	3	21.4	4	20	1	25	0.052	0.97
CNS manifestations	2	14.3	5	25	0	0.0	0.17	1.63
Antiphospholipid syndrome	0	0.0	3	14.2	0	0.0	2.8	0.64
Serositis	6	42	10	50	2	50	0.18	0.91
Cutaneous manifestations	8	35.7	19	60	3	50	2.94	0.56
Low C3	7	58.3	15	71.4	1	25	4.5	0.1
Low C4	7	58.3	16	76.1	1	25	4.1	0.38
Leucopenia/ thrombocytopenia	3	25	4	19	1	25	0.051	0.96
Microscopic hematuria	3	25	17	80.1	1	25	11.5	0.02 S
Anti dsDNA	9	75	19	90.4	3	75	3.7	0.65
	Mean ± SD		Mean ± SD		Mean ± SD			
eGFR	54.6 ±45.1		28.4 ± 18.8		75.1± 15.4		6.103	0.04 S
SLEDAI (mean ± SD)	14.6±7.5		16.4 ±6.39		8.25±1.70		1.078	0.351

Table 6: Comparison between died and survived regarding some clinical and laboratory characteristics.

Variable	Survive (n=33)	Died (n=5)	t. test	P value
Age	26.9 ± 8.6	25.6 ±12.3	0.294	0.770
ARDS No (%)	0(0.0%)	4 (80%)	14.5	0.01 S
CNS manifestations No (%)	6 (18.1%)	1 (20%)	1.078	0.41
Urgent dialysis No (%)	5(15.2)	3 (60%)	5.2	0.02 S
SLEDAI Score	14.6 ±5.5	17.8 ±6.2	1.020	0.315
	mean ± SD	mean ± SD		
WBCs (×10³/cmm)	5.50 ± 2.64	13.0 ± 11.18	3.48	0.00 S
S. Cr. (mg/dl)	2.94 ± 2.21	6.52 ± 5.28	2.35	0.024 S
BUN	35.8 ± 23.8	60.6 ± 32.5	2.07	.045 S
eGFR	44.0 ± 34.8	23.3 ± 16.8	1.29	0.20
Platelets (×10³/cmm)	167.2 ± 87.0	204.2 ± 70.4	0.90	0.37

Discussion

SLE is a systemic autoimmune disorder characterized by multi organ damage with heterogeneous clinical manifestations. [14] Several studies have shown that ethnicity plays a vital role in determining clinical features and outcomes in SLE patients. [15] LN is one of the most serious SLE complications since it is the major predictor of poor prognosis. [6] Glomerular lesions frequently accompany SLE have been the subject of intense investigation and after several revisions LN WHO classification, the recent ISN/RPS 2003 one aims to enhance the quality of communication among renal pathologists and nephrologists.[12]

In our study, regarding demographic characteristics of a total 38 adults LN patients included,36Females (94.7%), and 2 males (5.3%) with female to male ratio (18:1), age ranged from 17 to 48 years , mean age of 26.7 ± 8.95ys, 24 (63.2%) , urban and 14 (36.8%) rural cases. The mean age of 26.7 ± 8.95ys was similar to reported by Neumann K

et al [16], but higher than finding of Wafaey et al, (mean age of 24 ± 3.2ys)[17], and less than Raouf et al, (mean age of 31 ± 4.2 ys)[18], this may be due to different types of studies. Regarding sex, it was consistent with other studies [19, 20], but higher than reported by others [21, 22], where the ratios (6.6:1) and (9.9:1) respectively. Studies durations may played a role. The increased frequency of LN in urban than rural areas was similar to Laurent et al [23],which may due to increased triggering factors. [24]

As regard to clinical admission presentation, 19 cases (50%) of cases presented in emergency due to CNS disorders, 6 cases 15.8% [2 post ictal confusion & 4 acute confusional state], acute renal insufficiency18.4% [RPGN & TTP] and cardiopulmonary [acute pulmonary edema & severe pneumonia complicated by ARDS in (15.8%). These finding in contrast to YI et al [14], who found that fever (39.7%), cardiopulmonary (18.3%) and digestive system disorders (11.5%) respectively, as emergency causes. Moreover Rojas-Serrano et al [25], reported that (26%), (25%) and (18%) of patients presented by fever, polyarthralagia and abdominal pain respectively as emergency causes. This may be attributed to degree of SLE activity, complications, and/or immunosuppressive treatment.

Regarding general clinical manifestations of SLE, the most frequent, mucocutaneous found in (78.9%), serositis (47.4%) and hematological disorders (23.7%), in agreement with Hamdy et al. [19]Also findings of other authors [18, 20], reported that mucocutaneous finding of (77.8%) & (78.1%) respectively. While Cervera et al [26], reported (60%) in his thesis but Niang et al [27], found that commonest extra renal manifestations were hematological followed by mucocutaneous and musculoskeletal disorders. On the other hand, Rabbani et al[28] in Pakistan reported the lowest incidence of malar rash (29%) and photosensitivity (6%).These variations may be due to the higher level of sunshine in Egypt and other Arab countries compared with Europe and less dark skin of Egyptian people compared with Pakistanis.

The CNS manifestations were present in (18.4%) in the current study similar to Raouf et al[18], who reported (17.8%) of patients. Hypertension found in (63.2%) in agreement with Wafaey et al[17,] who reported (62.9%), but higher than reported (28%), by Al Arfaj et al. [22] However, diabetes found in (7.9%) close to other study [17] (6.1%), mostly, steroid induced hyperglycemia. Secondary APS criteria found in (7.9%) close to that of Mina Dawood et al[29] who reported (5.4%), but in contrast to others[30,31], who reported APS in (32.4%) and (21%) of patients respectively.

Regarding hematological disorders in this study, leucopenia found in (5.3%) and thrombocytopenia in (10.5%) which in disagreement with that obtained by other authors [21, 19], who recorded leucopenia in (64.4% &55.9%)) and thrombocytopenia in (44.6% &32.9%) respectively. The explanation may be due to disease activity and cytotoxic medications used. Normochromic anemia was presented in all patients with mean hemoglobin 9.2 gm/dl similar to Niang et al, in Senegal. [27] But other work, reported that (89.3%) anemic. [29] However, hemolytic anemia present in (2.6%) in consistent with Frigui et al[32].

In this study, 24hours protein in urine was 4.8 ± 3.0 gm similar to Nezhad et al[33,]but more than of other study[18] , 2.7 ± 0.96 gm. Proteinuria > 3.5 gm found in (26.3%) of patients, in contrary to other study reported (38.5%) of patients.[33] This different range may due to different durations , starting treatment or collection errors. Hematuria found in (53.3%) of patients in contrast to Wafaey et al[17],who reported a ratio (88.6%) which may be related to different sample sizes or disease activity.

Positive ANA found in (94.7%) close to Wafaey et al[17], but higher than (66.7%) reported by Raouf et al [18].This could be explained by technical inaccuracy. Also anti dsDNA found positive in (81.5%) similar to reported by other, [22] but contrary to Mina Dawood et al who found that (100%) of patients positive to anti dsDNA where no explanation found .[29]

Regarding low C4 & C3 found in (63%) and (60%) respectively, was similar to other study [18], who reported low C3 & C4 in (68.9%) and (73.3%) respectively in acute LN patients. but contrary to, Wafaey et al [17], who found low C3 & C4 in (19.5%) and (13.3%) respectively, and Jallouli et al [34], who reported significantly low C3 .
Regarding the significant decrease of mean value of eGFR in this study, 40.8 ± 34.3 ml/min/m² which was lower than that e GFR of 72.6 ± 43.6 ml/min/m² reported .[33] As some of our patients presented by acute renal impairment while others with chronic one so high SD while low mean, which agree with the fact that GFR is a bad marker for

assessment of acute kidney disease. The baseline SLDAI score, it was 16 in consistent with Al Saleh et al, who reported a score of17 as a baseline for SLEDAI in his study.[20]

As regard to LN histopathology biopsy classes, diffuse proliferative LN (class IV) was the predominant one (55.3%) followed by LN class III (31.5%), in agreement with many previous studies. [34,35,36,37] but in contrary to other studies [30, 38], reported higher incidence of class III. Moreover global lesions of class IV according to ISN/RPS 2003 were higher than segmental lesions with predominance of active and chronic ones in agreement with Wafaey et al .[17]

Regarding clinicopathologic correlations of LN patients, the commonest clinical syndromes was acute nephritic syndrome found in (39.5%) in consistent with Mina Dawood et al, who reported (46.6%) nephritic syndrome.[29] Regarding the significance of nephritic syndrome, some have found that the presence of heavy proteinuria and or nephritic syndrome were predictive of unfavorable prognosis.[16] Nephrotic syndrome found in (26.3%) close to Frigui et al ,who reported a ratio of (20%).[32] .A significant correlation between hypertension and edema with class IV and V lupus nephritis respectively which was similar to that obtained by other work. [33] Daisuke et al, reported that frequency of LN, including ISN/RPS class III and IV, was high in SLE patients without clinical renal involvement and LN patterns could be hidden with a high titer of anti-dsDNA antibody and a low C3.[39] Our results was similar to Nezhad et al regarding a significant associations between lowest eGFR and class IV LN[33], explained by predominant class IV global lesions in this work , moreover microscopic hematuria was significantly present in class IV LN in disagreement with other study[33], reported no significant association.

Surprisingly a new case of SLE presented with all criteria of a typical TTP with negative comb's test. Plasmapheresis was started before evident diagnosis. Whether certain antiphospholipid antibodies or lupus anticoagulant play a pathogenic role in triggering TTP in SLE patients, although neither of these present, may be associated with TTP. [40] Connective tissue disorders, including SLE, can present with low levels of ADAMTS-13, suggesting a possible pathophysiology. [41]

Regarding the mortality, Five patients deceased (13.2%) of all (38), two in the second hospitalization due to severe pneumonia , they were subjected to urgent dialysis on first hospital admission due to severe LN plus immunosuppressive therapy, while other three cases died in first hospitalizations [one case, severe pneumonia complicated with septic shock , one case RPGN with AKI treated by pulse therapy & urgent dialysis also suffered severe pneumonia and septic shock , one case with severe lupus activity presented with CNS disorders].This was in contrary to Rojas-Serrano et al, who reported five deceased patients but with different underlying causes of death [two cases pneumonia, one case pancreatitis, one case pulmonary hemorrhage, and one case pulmonary thromboembolism].[25] While infection specially pneumonia was the main cause of mortality in this study, YI et al, reported that pulmonary hypertension was the most frequent cause of mortality followed by invasive infections mainly pneumonia in (79.1%) of cases ,followed by renal failure.[14]

Regarding SLEDAI score in deceased patients was nearly equal to survived ones in this study, in contrast to lower SLEDAI in deceased patients reported [14], an issue which need further investigation to evaluate prognostic role of SLEDAI in LN patients. The high mean serum creatinine, BUN, leucocytosis plus the need for urgent hemodialysis therapy, significantly associated with deceased, reflected the severity of LN states.

Conclusion

This study concludes that the most frequent presentig features of SLE, were mucocutaneous, serositis and hematological disorders .Diffuse proliferative class IV LN was predominant pattern followed by class III LN. A significant association found between nephrotic syndrome, edema and class V LN and a noticeable correlation found between, nephritic syndrome, hypertension, microscopic hematuria, elevated serum creatinine, elevated BUN and, decreased estimated GFR and proteinuria with the worse class IV LN. ISN/RPS 2003 classification is charachterized by its clear definitions; clinically relevant sub classification and good communication between pathologists and nephrologist. Renal biopsy is of utmost value in evaluation of renal status, determination of LN class and management guidelines.

Further prospective in depth studies on large sample population, focusing on patient's outcome with determination of mortality independent risk factors, of sure will yield more clear, conclusive and beneficial results.

Acknowledgment
The authors acknowledge Prof.Dr. Khaled Lakouz, Prof.of intervention radiology for his kind help in biopsy taken.

Conflict of interest
No conflict of interest has been declared by the authors.

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