ORIGINAL ARTICLE

FREQUENCY OF BIOPSY PROVEN CLASS I-V LUPUS NEPHRITIS – A TERTIARY CARE HOSPITAL EXPERIENCE

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ABSTRACT

Background and Objective: Systemic lupus erythematosus (SLE) is fairly common immunologic disorder, more common in females. Renal involvement in the form of nephritis is frequent with proteinuria, haematuria and even renal failure in uncontrolled cases. The objective of the present study was to assess the frequency of biopsy proven class I-V Lupus Nephritis at Fatima Memorial Hospital Lahore, which is a tertiary care teaching hospital.

Methods: A descriptive study was conducted in the Department of Pathology at Fatima Memorial Hospital Lahore from January to December 2015. Both male and female patients with clinical suspicion of lupus nephritis having serum ANA and Anti-ds DNA level investigations were included. The staining methods performed for light microscopy were Hematoxylin and Eosin (H&E) in order to study the morphology and determine the frequency of five classes of Lupus Nephritis.

Results: Among 38 patients, 18.4% were males and 81.6% were females which makes the male to female ratio, 1:5. Mean age of the patients was 26.55 ± 8.13 years with age range of 14 – 49 years. When the patients were assessed on the basis of biopsy by H&E staining, out of 38 patients, n = 05 belonged to class III, n = 32 belonged to class IV and n = 1 belonged to class V.

Conclusions: Maximum number of the patients i.e. 84.21% were in class IV, then 13.16% were in class III and only 2.63% were in class V lupus nephritis.

Key Words: SLE, Biopsy proven, Activity of Lupus nephritis, Chronicity of Lupus nephritis H&E. Diffuse proliferation, Interstitial edema, Tubular damage.

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is not an uncommon autoimmune systemic disorder. Its prevalence is close to 1:500-1000 population worldwide.[1] Lupus nephritis is known complication of SLE which has wide range of clinical presentations like poteinuria, hematuria and even renal failure. The diagnosis of lupus nephritis is made on histological findings. Lupus nephritis involvement is 20% to 75% in pediatric SLE patients.[2] The prevalence of lupus nephritis is 3.64 cases per 100,000 children. It is 4.46 times higher among girls than boys, highest among girls ages 15–18, and highest among Asians, African-Americans, Hispanics and Native Americans.[3]

The renal functions evaluation is important in all the patients diagnosed with SLE to detect the renal involvements earlier. As laboratory investigations, clinical features and morphological information of renal biopsy give complete knowledge about the diagnosis. Therefore, earlier the detection and treatment, better is the improvement in renal outcome.[4]

For the purpose of diagnosis, lupus nephritis is divided in to six classes. The Table 1 shows classification of lupus nephritis. This was revised by the International Society of Nephrology (ISN) and the Renal Pathology Society (RPS) in 2003. This classification is based on the findings of hematoxylin and eosin staining, site, pattern and intensity on immunofluorescence staining, and features seen on electron microscopy from renal biopsy specimens.[10] This study however excluded Class VI lupus nephritis.

The Table 2 shows the activity and chronicity indices of lupus nephritis. These help along with the other histological patterns to elaborate the diagnosis of class III & IV lupus nephritis which helps in tailoring the proper treatment.

During regular follow-up, various laboratory findings such as urinary protein or sediment, low albumin levels or raised serum creatinine levels also suggest active lupus nephritis. While in contrast, some patients of lupus nephritis may be totally asymptomatic.[9-12]

In patients of active lupus nephritis in class III and

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Table 1: *International Society of Nephrology/Renal Pathology Society 2003 Classification of Lupus Nephritis.*[10]

Classes	*Light Microscopy*	*Immunofluorescence*	*Clinical Features*
I. Minimal mesangial lupus nephritis	Normal	Mesangial immune deposits	Mild proteinuria
II. Mesangial proliferative lupus nephritis	Purely mesangialhypercellularity or mesangial matrix expansion with mesangial immune deposits	Mesangial immune deposits; few immune deposits in subepithelial or subendothelial deposits possible	Asymptomatic hematuria or proteinuria. No treatment required.
III. Focal lupus nephritis	Active or inactive focal, segmental, or global glomerulonephritis involving < 50% of all glomeruli	Subendothelial and mesangial immune deposits	Active generalized SLE and mild-to-moderate hematuria and moderate proteinuria in most patients.
IV. Diffuse lupus nephritis	Diffuse, segmental or global glomerulonephritis involving = 50% of all glomeruli	Subendothelial immune deposits	Renal complications like edema, hypertension, active urinary sediment, worsening renal function, and nephrotic range proteinuria in most cases and active extrarenal SLE in many patients
V. Membranous lupus nephritis	Diffuse thickening of glomerular basement membrane and no inflammatory infiltrate, may be subepithelial deposits and basement membrane spikes	Subepithelial and intramembranous immune deposits; subendothelial deposits are usually not seen but present only when associated proliferative component is present	Usually no features of active SLE but clinical and laboratory features of nephrotic syndrome.
VI. Advanced Sclerosing lupus nephritis	Involvement of over 90% glomeruli with no residual activity		Progressive decrease in renal function associated with protienuria and normal urinary sediments

Table 2: *Activity and Chronicity Index for Class III & Iv Lupus Nephritis.*[10]

Activity Index	*Chronicity Index*
• Endocapillaryhypercellularity leukocyte infiltration may or may not be seen; luminal reduction	Glomerular sclerosis; segmental, global
• Karyorrhexis	Fibrous adhesions
• Fibrinoid necrosis	Fibrous crescents
• Rupture of glomerular basement membrane	
• Cellular or fibrocellular crescents	
• Subendothelial deposits on light microscopy	
• Intraluminal immune aggregates	

IV, the symptoms of active SLE like fever, fatigue, serositis, rash, arthritis or the feature of CNS involvement are more common.[5] Some patients of lupus nephritis may be totally asymptomatic, seen in the class II and V of lupus nephritis.[6]

In Class IV lupus nephritis other symptoms related to hypertension include headache, visual disturbances, dizziness and cardiovascular events. In class III and IV lupus nephritis, there are oral or nasal ulcers and rash. However synovitis or serositis can also be present.[7]

In Class V lupus nephritis signs of an isolated nephrotic syndrome are more common. These include effusions in various cavities like peritoneal, pleural and pericardial. Peripheral edema is also seen but usually no hypertension.[11]

In SLE patients who have clinically active disease or their laboratory findings are suggestive of active nephritis, should be advised for the renal biopsy. As it is the gold standard for diagnosis.[12] By the help of histological patterns we can now active or chronic stage of disease and thus renal biopsy is very helpful in the treatment and prognosis of lupus nephritis.[13]

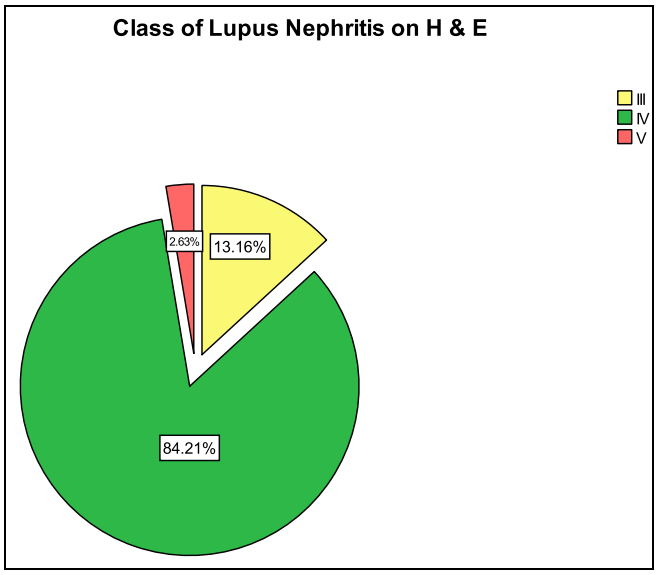

Fig. 1: *Class of 38 Lupus Nephritis Patients.*

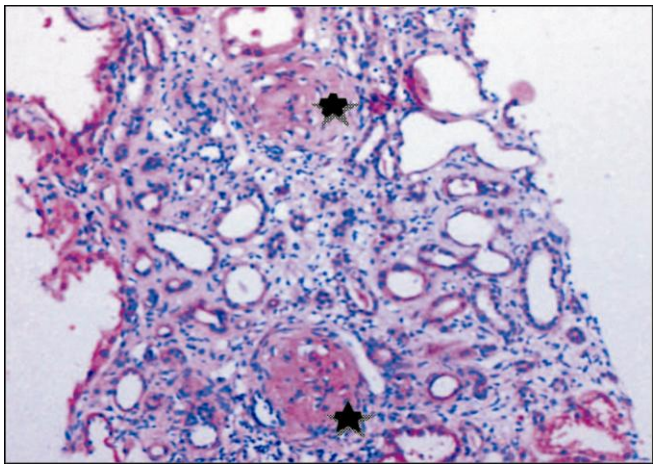

Fig. 2: *This shows a Lupus nephritis class III, 2 glomeruli showing global diffuse proliferation as well as sclerosis. (Stars) there is tubular atrophy, interstitial inflammation and edema present. (10X) (H&E)*

During a renal biopsy, there are chances of sampling error. Hence, the results of the biopsy are always correlated with the history, examination, radiological and laboratory findings of the patient.[8]

METHODOLOGY

A descriptive study was conducted in the Department of Morbid Anatomy and Histopathology, at University of Health Sciences, Lahore. Informed consents of patients and parents in case of minors were taken. Ethical approval from institutional board was taken. The ANA was detected by indirect immunofluorescence antinuclear antibody test (IF-ANA) and Anti-dsDNA by Enzyme-linked immunosorbent assay (ELISA) method. Findings of the laboratory investigations like serum creatinine, ANA, anti-dsDNA, serum complement levels in relevant proformas.

Total 38 renal core biopsies from both genders of 1-65 years of age, were taken by well-trained nephrologists at Fatima Memorial Hospital Lahore. Two cores of renal biopsies were obtained from each patient under real-time ultrasound guidance to localize the kidney, using a needle biopsy gun. The core for light microscopy was sent in the 10% formol saline. The biopsies were transported under controlled condition to the department of Morbid Anatomy & Histopathology at University of Health Sciences Lahore. The fixed section was made in paraffin for hematoxylin and eosin staining techniques. However, inadequate renal biopsies (less than 5 glomeruli), patients with urinary tract infections, severe chronic debilitating co-morbidities and pregnant females were excluded.

RESULTS

The mean age of the patients was 26.55 ± 8.13 years with age range of 14-49 years. Mean age of the female patients was 27.93 ± 9.68 years with a range of 12-56 years, while for the males it was 34.67 ± 12.64 years (range of 17-56 years). In gender distribution, female preponderance (81.6%) was noted as compared to male (18.4%) so a male to female ratio was 1:5. A total of 97.37% of the patients were having proteinuria and 81.58% were having the either complaint of gross haematuria or they had microscopic haematuria.

On the basis of biopsy interpretation by Hematoxylin and Eosin staining maximum number of the patients (84.21%) was in class IV, 13.16% were in class III and only 2.63% were in class V lupus nephritis.

DISCUSSION

This study included a total of 38 patients. The biopsies were taken from the Department of Pathology, Fatima Memorial Hospital Lahore, Pakistan, from January to December, 2015. All the biopsies were examined microscopically and reviewed by consultant pathologists for changes.

The classes of lupus nephritis predicted on clinical basis were different when assessed microscopically on H&E. As the renal biopsy interpretation on H&E is the gold standard for confirmation of actual class of lupus nephritis. Upon the first episode of nephritis, the renal biopsy should be done in all the patients with SLE who have either clinical or laboratory evidence of active lupus nephritis.[1] However the treatment is started only when detailed clinical features, laboratory investigations and morphology is correlated. So according to the present study, the class IV lupus nephritis was the most common 84.21% on hematoxylin and eosin staining. This result was quite in accordance with the study conducted in USA.[14]

Various laboratory findings like proteinuria, its intensity, haematuria, its intensity, ANA, Anti dsDNA, serum C3 and C4 were taken to assess their association

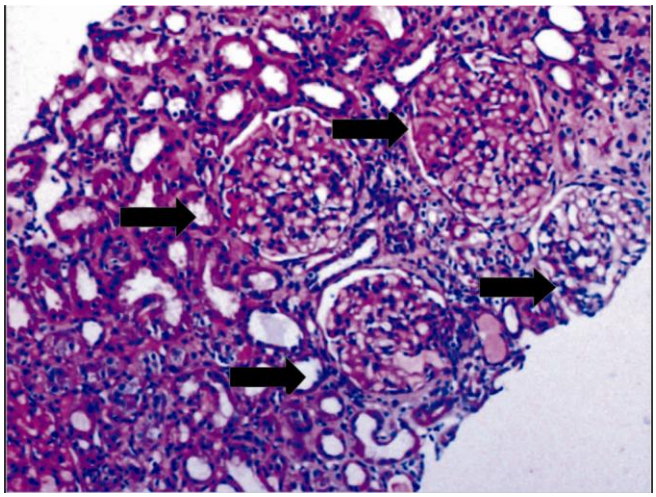

Fig. 3: *Lupus nephritis class IV, 4 glomeruli showing global diffuse proliferation. (arrows). Note the moderate tubular damage and interstitial fibrosis. (10X) (H&E).*

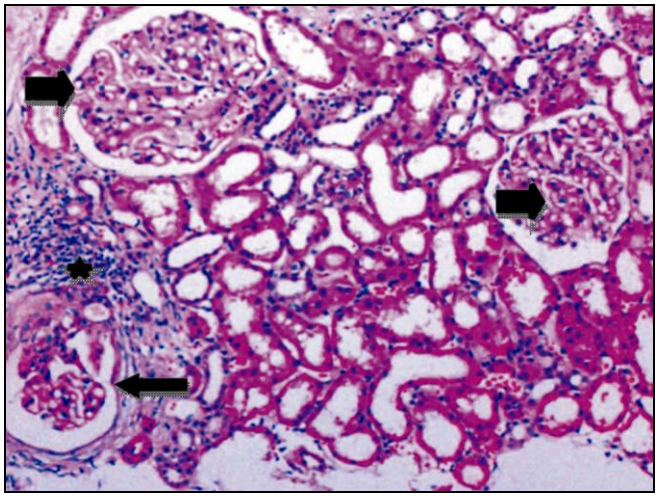

Fig. 4: *This figure shows class V lupus nephritis. There is diffuse proliferation (big arrows) and segmental sclerosis with synechae formation (small arrow). The tubules are back to back. Also note the focal interstitial damage. (star) (H&E) (10X).*

with the clinical features like age group, gender and clinical class of lupus nephritis. Pearson chi-square and Fisher Exact tests were applied to see the results but none of the association was found to be statistically significant.

Different laboratory findings like serum creatinine, proteinuria, proteinuria intensity, haematuria, haematuria intensity, ANA, Anti-dsDNA, serum C3 and C4 were used to assess their association with the biopsy findings on hematoxylin and eosin staining like class of lupus nephritis, global and segmental distribution of lupus nephritis and activity of the disease. Pearson chi-square and Fisher Exact tests were applied to see the results but none of the association was found to be statistically significant. It is ***concluded*** that renal biopsy remains the gold standard for diagnosis and prognosis of class of lupus nephritis. Some features seen on biopsy are very important and when correlated with history and labo-ratory findings, these help to decide, the kind of treat-ment required. Such features are activity and chroni-city scoring done on Hematoxylin and Eosin stained slides in Class III & IV lupus nephritis. This feature in most centers of renal biopsy reporting are not included as priority due to which, detailed pathogenesis of a class of lupus nephritis gets ignored.

Conflict of Interest

No conflict of interest was declared.

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Authors' Contribution

SK: Paper writing and literature review. ZW: Literature review. MJM: Data collection. NN: Proof reading. AHN: Proof reading. SR: Sampling and research methodology.

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