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Study of Renal Biopsy in Systemic Lupus Erythematosus

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ABSTRACT

Background: *Systemic Lupus Erythematosus (SLE) is a chronic inflammatory multisystem autoimmune disease primarily affecting women of reproductive age. It is a disease characterized by the production of auto antibodies to components of the cell nucleus in association with a diverse array of clinical manifestations. The primary pathological findings are those of inflammation, immune complex deposition, vasculopathy and very rarely vasculities*[1,2].

Objective: *The main purpose of this study is the role of renal biopsy for the diagnosis of LN, interpretation of activity and chronicity indices for the staging of LN to know its prognostic importance in subsequent management of SLE.*

Materials and Methods: *3 year study of renal biopsy in 101 cases of SLE was conducted in tertiary care hospital in Mumbai. Tissue were processed, stained and studied under microscope. Results were analysed and tabulated.*

Results: *Most commonly found in females (93.9%), amongst young adults between 21-30 years age group, Class IV/diffuse lupus nephritis (84.84%) followed by Class III/focal lupus nephritis (6.06%) are most commonly evident, activity index in class IV were Interstitial Inflammation (67.86%).*

Conclusion: *Kidney biopsy helps to diagnose the disease process, assess the course of progression and to decide the treatment plan of SLE.*

KEYWORDS : Systemic Lupus Erythematosus (SLE), autoimmune disease, Lupus nephritis (LN)

INTRODUCTION: Systemic Lupus Erythematosus (SLE) is a chronic inflammatory multisystem autoimmune disease primarily affecting women of reproductive age. Renal lesions i.e. Lupus nephritis (LN) is a common but one of the serious manifestation of (SLE), occurring in up to 60% of affected adults during the course of their disease and may lead to the development of end stage renal disease (ESRD) in 20% to 25% of those with lupus nephritis, even if properly treated[3-6].

The renal symptoms show good correlation with the classification of LN. Patients with SLE should have kidney biopsy as soon as clinical signs of nephritis are evident in order to accelerate treatment decisions and minimize risk of inflammation-induced irreversible kidney damage[7-9]. The primary purpose of renal biopsy in lupus patients is not only to confirm the presence of LN but also to determine the severity and type of renal involvement providing an aid to therapeutic decisions[10, 11].

The main purpose of this study is the role of renal biopsy for the diagnosis of LN, interpretation of activity and chronicity indices for the staging of LN and its prognostic importance in subsequent management.

MATERIAL AND METHODS: This is a retrospective analysis of kidney biopsies received in the Uropathology division of a tertiary health care centre and referral hospital over a period of three years (from January 2009 to December 2011).

Among the 101 adequate biopsies, 89 were definite cases of SLE fulfilling ARA criteria. 33 patients with clinical diagnosis of SLE and biopsy with immunofluroscense and/or electron microscopy were included in this study.

Renal biopsy cores were fixed in 10% buffered formalin and subjected to routine processing - paraffin sections were cut at 2-3 microns thickness and stained with multiple staining techniques. Examination was carried out under light microscope to record histopathological features and kidney biopsy was studied under the headings of glomerulus, tubules, interstitium and vessels. Wherever feasible immunofluorescence and electron microscopic findings were obtained from clinical records and a final diagnosis was given after correlating these findings with light microscopy and clinical findings.

OBSERVATION & RESULTS:
There were 2 males (6.1%) and 31 females (93.9%) & Male to female ratio was 1:15.5.

Table no. 1 showed the mean age of patients was 24.55 years (range: 10 to 40 years). Majority of the cases 18 (54.55%) were young adults between 21-30 years age group, followed by 8 cases (24.24%) from age group of 13-20 years.

On observing **Table no. 2** denotes that the 33 study patients who underwent renal biopsy, maximum number of patients had renal lesion of ISN/RPS Class IV/diffuse lupus nephritis (84.84%) followed by Class III/focal lupus nephritis (6.06%).

No patient with class I or class VI was seen in our study.

Table no.3 suggests that Class III and class IV LN were given activity and chronicity index according to the ISN/RPS 2003 Classification. Majority of patients belonged to class IV (28 out of 30).

The most frequently seen features in activity index in class IV were Interstitial Inflammation 19 (67.86%) followed by Leukocyte infiltration 13 (46.43%) and endocapillary-hypercellularity 8 (28.57%). Subendothelial deposit was not seen in any patients under this study.

Most common histologic parameter in Chronicity Indices in class IV was Glomerulosclerosis seen in 14 out of 28 (50%) patients, and the fibrous Crescents as least common in 3 patients (10.71%).

DISCUSSION:

Our analysis showed that cases of biopsy proven lupus nephritis contributed 6.33% of our total renal biopsies examined over a 3-year period from 2009 to 2011.

This is comparable to study by Yong J et al[12] where he found 5.4% of lupus nephritis patients out of the total number of patients subjected to renal biopsy over a 15-year period. Similar result was seen in study by Srija M et al[13] in a Tertiary care Hospital in Kerala which showed 7.75% of lupus nephritis cases among total 400 studied patients.

There was a preponderance of female patients in the study. We found female to male as 15.5:1. This finding was slightly more than many studies where female to male ratio is between 8 and 13. A recent study of Farid E et al[14] in 2013 showed female-to-male ratio of 13.6:1, closer to our present study.

Maximum number of cases i.e 18 (54.55%) are from age group of 21-30 years with the mean age of 24.55 years. Followed by 8 cases (24.24%) from age group of 13-20 years. This is almost similar to studies by a number of groups[15-17].

However, a study by Uramato K et al[18] reported the mean age at diagnosis as 49.2 years out of 48 SLE patients.

The most common pathology in given studies including our present study was Class IV diffuse proliferative lupus nephritis.

Our present study showed class III more common than class II and class V, as seen in studies by Rajaee et al[15] and Torabi et al[19]. This is in contrast to other studies where class II is more common. Though class IV is most common, there is some variation between class II and class III frequency among lupus nephritis patients. These differences may be due to small number of the cases or it may reflect the pattern of the disease in central India.

In all the above studies (including present study) class I and class II patients were least in number. Study by Austin et al[20] found that class IV patients were at modestly, but significantly, increased risk of end stage renal disease compared to those with other classes. Similarly study by Rajaee et al[15] reported worse prognosis of the patients in the class IV group than the patients in other groups.

Lesions in classes III and IV are progressive unless the activity of the acute inflammatory process can be arrested by appropriate therapy. Hence it is very important to recognise these classes of LN and initiate necessary therapy.

In our present study, 30 cases were belonged to class III and IV and thus activity and chronicity scores were calculated in 30 cases.

In the study of Austin et al[21] on renal outcomes in severe LN, endocapillary proliferation was the most common parameter in activity index seen in almost all study patients followed by fibrinoid necrosis (75%). Interstitial inflammation was seen only in 29.7% of cases.

In a similar study also done by Austin et al[20] they found endocapillary proliferation as the most common (91.7%) parameter in activity index followed by interstitial inflammation (87.5%) in his study group of 72 patients. Our present study findings are more or less similar to this study.

In our study 66.66% out of 30 patients had interstitial inflammation as the most common parameter.

Hsieh at el[22] highlighted the importance of interstitial processes in determining prognosis in LN. As interstitial inflammation is potentially reversible, the presence of severe interstitial nephritis is an important histologic findings that may identify high risk patients who would benefit from aggressive or directed therapeutic interventions and many warrant more focus in drug development and clinical trials.

In our present study, glomerulosclerosis was the most common parameter in chronicity index (46.67%). Comparing the chronicity indices in our present study with the studies by Austin at el[21], it is seen that Glomerular Sclerosis is most common parameter in chronic indices.

CONCLUSION:

There was a preponderance of female patients in the study with male to female ratio of 1:15.5.

A wide age range of patients was seen from 10 years to 40 years with the mean age of 24.55 years. Maximum cases were seen in the age group of 21 to 30 years (54.55%).

Among the 33 study patients who underwent renal biopsy, the largest number was in Class IV (84.84%) followed by Class III (6.06%).

Interstitial Inflammation (66.66%) was the most common parameter seen in activity index and glomerulosclerosis (46.67%) most common in chronicity index.

Class IV had the highest activity and chronicity score.

Kidney biopsy helps to diagnose the disease process, assess the course of progression and to decide the treatment plan. For an accurate diagnosis correlation with immunofluorescence, electron microscopy and clinical features is essential.

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Conflict of Interest: None

Table No. 1 : Distribution of kidney biopsies according to age

Age in years	No. of cases (n)	Percentage (%)
0 to 12	1	3.03
13 to 20	8	24.24
21 to 30	18	54.55
31 & above	6	18.18
Total	33	100

Table No. 2: Distribution of histopathological lesions in kidney biopsy specimens according to ISN/RPS classification

Histopathological findings	No. of cases (n=33)	Percentage (%)
Class I: Minimalmesangial LN	0	-
Class II: Mesangial proliferative LN	1	3.03
Class III: Focal LN	2	6.06
Class IV: Diffuse LN	28	84.84
Class V: Membranous LN	1	3.03
Class V+IV: Membranous with diffuse LN	1	3.03
Class VI: Advanced sclerotic LN	0	-

(LN=Lupus Nephritis)

Table No. 3: Study of Activity – Chronicity index in cases of lupus nephritis

Indices	Class III (n=2)	Class IV (n=28)	Total (n=30)
Activity index			

1. EndocapillaryHypercellularity	1 (50%)	8 (28.57%)	9 (30%)
2. Fibrinoid Necrosis/ karyorrhexis	-	1 (3.57%)	1 (3.33%)
3. Subendothelial deposits	-	-	-
4. Cellular crescents	-	1 (3.57%)	1 (3.33%)
5. Leucocyte Infiltration	-	13 (46.43%)	13 (43.33%)
6. Interstitial Inflammation	1 (50%)	19 (67.86%)	20 (66.66%)
Chronicity index			
Glomerulosclerosis	-	14 (50%)	14 (46.67%)
2. Fibrous crescent	-	3 (10.71%)	3 (10%)
3. Tubular atrophy	1 (50%)	10 (35.71%)	11 (36.67%)

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