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Original Research Article

Assessment of renal involvement in patients with systemic lupus erythematosus in a tertiary care hospital

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ABSTRACT

Background: Renal involvement in SLE is common. Lupus Nephritis is the major cause of mortality in SLE patients. Renal involvement is a severe form of the disease and subsequent management is planned according to the histopathological class of lupus nephritis. Thus, this study was planned to assess the clinical profile and the extent of renal disease in SLE patients.
Methods: A prospective observational study was conducted among SLE patients who got admitted in the Department of General Medicine and Nephrology in Thanjavur Medical College Hospital, Thanjavur from July 2012 to October 2013. Fifty SLE patients who had renal symptoms were included in this study.
Results: SLE is Common among females. Common renal presentations were haematuria and proteinuria. 42% of the patients had Class IV lupus nephritis, followed by 24%, 16%, 16%, and 2% of Class III, II, Class V and Class I lupus nephritis respectively. No case of class VI lupus nephritis was reported in this study. ANA was positive among 66%, Anti ds DNA was positive in 64% and C3 level was found to be reduced in 50% of patients. Antiphospholipid antibodies were seen in 2% of the patients.
Conclusions: Proteinuria, haematuria, a lower serum C_3 level and need for aggressive hypertension management were prominently seen with a worse class of lupus nephritis. Patients with active and proliferative forms of lupus nephritis had a severe course of illness and required aggressive management with immunosuppressants.

Keywords: Clinico-pathological correlation, Lupus nephritis, Systemic lupus erythematosus

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a multi- system disease that is caused by tissue damage resulting from autoantibodies and complement fixing immune complex deposition. Spectrum of clinical presentation varies, characterised by remissions and exacerbations.[1,2]

Updated American College of Rheumatology criteria for Classification of Systemic Lupus Erythematosus (1997) includes Malar rash, Discoid rash, Photosensitivity, Oral ulcers, Non-erosive arthritis, Serositis in the form of pleuritis or pericarditis, Renal involvement in the form of Persistent proteinuria and Cellular casts, Neurological involvement in the form of seizures and Psychosis, Hematological involvement in the form of Hemolytic anemia, Leukopenia, Lymphopenia and thrombocytopenia and presence of Anti-DNA, Anti-Smith, Anti Phospholipid antibodies and Antinuclear Antibodies immunologically. A patient is said to have SLE if any 4 or more out of 11 criteria are present,

serially or simultaneously, during any interval of observation.[3]

The prevalence of SLE varies from region to region. In United States the prevalence varies from 20 to 150 per 100,000 populations and it is more common in blacks than whites, whereas in India, it is 14 to 16 per 100,000 populations, the lowest in the world. SLE is more common in urban population than rural population. Also prevalence varies among different races and ethnic groups.[4]

Women were more commonly affected by SLE than men. Among the SLE affected women, 90% belong to childbearing age group with female to male ratio of about 7-15:1. Children, men and elderly can also be affected, but the prevalence in these populations is comparatively low.

In men, highest incidence is seen between the age group of 20 and 50 years whereas in females, incidence is higher between the age group of 20 and 30 years.[5]

Renal involvement in SLE is called as Lupus Nephritis (LN) and is a very common occurring in about 90% of patients with SLE. It is characterized by anti dsDNA positivity, decreased C3 and C4 levels and a normal or increased c-RP. Patients develop proteinuria >500mg/day, oliguria, anuria, haematuria, granular or RBC casts, hypertension and end stage renal disease eventually.

Clinical evidence of kidney involvement is found in one half to two thirds of patients with SLE. Renal biopsy shows immune complex deposition in the kidneys of all patients with SLE, regardless of the presence of urine sediment.[6]

The major clinical point is that each renal lesion has activity. The greater the activity, the more important is the need to treat the patient aggressively, with large doses of steroids or immunosuppressive agents. Those patients with inactive lesions like membranous nephropathy, sclerotic glomeruli, fibrous crescents, tubular atrophy, or interstitial fibrosis do not require aggressive therapy. Thus assessment of renal involvement plays a central role in deciding upon the further line of management. The objective of the study was to study the clinical profile and the extent of renal involvement in patients with lupus nephritis.

METHODS

A prospective observational study was conducted to assess the clinical profile and the extent of renal involvement in patients with SLE among the patients who got admitted in the department of General Medicine and department of Nephrology in Thanjavur Medical College Hospital, Thanjavur from July 2012 to October 2013.

Inclusion criteria

SLE patients with renal symptoms between age group of 13-45 years of age, who satisfied 4 out of 11 criteria according to modified American College of Rheumatology Criteria were included in this study.

Exclusion criteria

- Patients with mixed connective tissue disorder, nephritic syndrome, nephrotic syndrome and renal failure of other causes were excluded
- Patients who underwent re-evaluation renal biopsy were also excluded from this study.

After assessing the inclusion and exclusion criteria, fifty patients with SLE who had renal symptoms were included in this study.

Diagnosis of SLE was done using Updated American College of Rheumatology criteria for Classification of Systemic Lupus Erythematosus (1997) and diagnosis of Lupus Nephritis was done using WHO classification (Table 1).[3,7]

Table 1: WHO classification of Lupus Nephritis.[7]

WHO classification of Lupus Nephritis	
Class I LN	No histological changes by light microscopy
Class II LN	Mesangio Proliferative Glomerulo Nephritis
Class III LN	Focal Proliferative Glomerulo Nephritis
Class IV LN	Diffuse Proliferative Glomerulo Nephritis
Class V LN	Membranous Glomerulo Nephritis
Class VI LN	Scarred glomeruli- ESRD

This study is registered with Institutional Research Ethical Committee. The principal investigator explained the purpose of the study to each participant and a written consent was obtained from the participants prior to the commencement of the study. The participants were also informed that their participation was voluntary and that they could withdraw from the interview at any time without consequences. Every effort was made, to be sure that all information collected from the participants, was kept highly confidential. The study was conducted using a proforma which includes the clinical details of the patients.

A detailed history was taken and examination was done by the principal investigator. Following which blood samples were collected in order to assess Serum C3 levels, Antinuclear antibody (ANA), Anti dsDNA antibody, Anti phospholipid antibodies and urine samples were collected to assess the presence of haematuria and proteinuria.

Also, after assessing the haematological parameters and ultrasonogram, renal biopsy was done for the patients who had SLE with any of the following:

- 24 hrs urinary protein >500 mg/day and/or
- Haematuria >5 RBCs/ cu.mm and/or
- Renal failure.

In all these patients, ultrasound guided real time core needle, renal biopsy was done with Trucut needle and two bits were taken and sent for histopathological examination and immunofluorescence. It was preferred to do biopsy in the lower pole of the left kidney to reduce the risk of inadvertent passage of the biopsy needle through the major vessels like renal artery or vein. Formalin preserved samples were sent for histopathological examination and glutaraldehyde preserved samples were sent for immunofluorescence. Glomerular lesions were classified according to the World Health Organisation criteria. It was established that the patients had normal platelet count and prothrombin time before the procedure was undertaken.

After the procedure, patients were instructed strict bed rest for 18 to 24 hours. Vitals were monitored periodically. Haematocrit and haemoglobin values were obtained within 24 hrs after the procedure.

Statistical analysis

The collected data was entered in Microsoft excel and all statistical analyses were performed using the SPSS (Software package used for statistical analysis) package, version 17.

RESULTS

Age

Among 52% of the study participants in the age range of 15-25 years, maximum (85%) were females. Of the 32% patients in the age group of 26-35 years 75% were females and 25% were males. One case was found to be below 15 years of age (Table 2).

Table 2: Proportion of cases with respect to age and gender.

Age	Male	Female	Total
<15 years	0	1 (100%)	1 (2%)
15-25 years	4 (15%)	22 (85%)	26 (52%)
26-35 years	4 (25%)	12 (75%)	16 (32%)
>35 years	0	7 (100%)	7 (14%)

Duration

Among the cases, the duration of SLE was found to be less than 1 year in 44% of patients, 1-3 years in 50% of the patients and more than 3 years in 6% of the patients in the study population.

Urine analysis

Proteinuria was common and was seen in 90% of the cases and Hematuria was observed in 56% patients. Among 50 lupus nephritis patients, Nephrotic range proteinuria was observed in 54% cases and the remaining had non-Nephrotic range proteinuria (Figure 1).

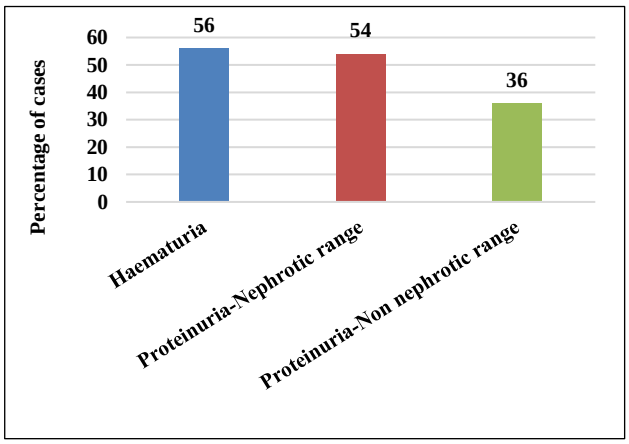

Figure 1: Proportion of cases with haematuria and proteinuria.

Class

In this study, 42% of the patients were diagnosed to have Class IV lupus nephritis, followed by 24%, 16%, 16% and 2% of Class III, Class V, Class II and Class I lupus nephritis respectively. Also, there were no case of class VI lupus nephritis reported in this study (Table 3). Renal failure was more common in patients with Class IV (61.8%) lupus nephritis.

Renal failure was also seen in 23.5% of patients with Class V patients lupus nephritis and 11.8 % of patients with Class III lupus nephritis. Renal failure was less common (2.9%) in Class II lupus nephritis and there were no case of renal failure reported among the patients with class I LN. Ultrasonography of kidneys showed evidence of scarred kidneys in all patients with class V lupus nephritis (Table 5).

Table 3: Proportion of cases based of classification of LN.

Classification of LN	Frequency	Percentage
Class I	1	2%
Class II	8	16%
Class III	12	24%
Class IV	21	42%
Class V	8	16%
Class VI	NIL	NIL

Antibodies

ANA was positive among 66% of the patients, Anti dsDNA was noted in 64% of the cases. C3 level was found to be reduced in half the number of study population (50%). APL antibody was seen in 2% of the study patients (Table 4). All anti dsDNA positive patients had a clinically severe course. Anti dsDNA positivity correlated well with class IV lupus nephritis ($p<0.003$) and renal failure ($p <0.001$). Thus, there was a statistically significant association of anti dsDNA positivity and renal failure with class IV lupus nephritis. One patient tested positive for antiphospholipid antibody.

Table 4: Proportion of cases with positive antibodies.

Antibodies	Frequency	Percentage
ANA	33	66%
Anti dsDNA	32	64%
APL	1	2%
Decreased C3	25	50%

Table 5: Proportion of cases with renal failure.

Renal failure in LN	Frequency	Percentage
Class I	0	-
Class II	1	2.9
Class III	4	11.8
Class IV	21	61.8
Class V	8	23.5
Total	34	100

In this study, the clinical profile, renal manifestations and biopsy reports of 50 patients with SLE was analysed, to bring out the clinico-pathological findings in lupus nephritis.[8]

Fifty SLE patients with renal symptoms who satisfied criteria underwent renal biopsy, out of which 86% were females and 14% were male patients. This observation revealed that the disease had female preponderance. Study included patients from 13-45 years. According to a study on progression of lupus nephritis mean age of presentation was 18-35 years. Mean age of patients with lupus nephritis in this study was 25±5 years.[9]

Age and sex distribution was studied in which 52% of the patients belonged to the age group of 15-25 years, of which 38% had class IV lupus nephritis. Males predominantly had class IV and class V lupus nephritis. Disease was aggressive in the younger age group and male patients.[9]

On analysing the incidence of urinary abnormalities in our study, 90% of patients had proteinuria, out of which 54% had nephrotic range of proteinuria. Proteinuria, haematuria, a lower serum C_3 levels and a need for hypertension management were prominently seen with a worse class of lupus nephritis.

In this study of 50 patients, 42% had class IV DPGN accounting for the most common class of presentation in lupus nephritis and it was the predominant class in the study group. Clinico pathologic studies reveal that class IV LN is a severe form of illness and it is the predominant class of presentation in lupus nephritis. It was seen in age group of 15-35 years.

Disease activity markers like dsDNA and serum C_3 levels were also studied. Among the patients who had decreased C_3 levels 76% of patients had class IV LN. Decreased C_3 levels correlated well with class IV lupus nephritis. 90.4% of patients, who had class IV DPGN, were anti dsDNA positive and had renal failure.[10]

In patients with clinically severe illness 64% had class IV lupus nephritis. 42% of the patients with lupus nephritis had hypertension and 62% of patients with hypertension had class IV lupus nephritis.

In Lupus nephritis, the prognostic information was offered by renal biopsy and patients with active histological changes required aggressive immunosuppressive therapy. Renal biopsy had a major role in deciding the type and intensity of immunosuppressive therapy. Best overall predictor appeared to be the extent of tubulointerstitial disease in renal biopsy. Thus, renal biopsy in lupus nephritis helps in evaluation, instituting therapy and in predicting prognosis in patients with SLE and renal involvement.[11]

Correlation between clinical manifestation and histopathology of renal biopsy was revealed in a study by Bald et al. Likewise in our study overall severity correlated well with anti dsDNA positivity, class IV lupus nephritis, renal failure, hypertension, decreased C_3 levels and a disease flare. Histologically severe forms result in more severe manifestation.[10]

DISCUSSION

In this study the clinical profile, renal manifestations and biopsy reports of 50 patients with SLE was analysed, to bring out the clinico-pathological findings in lupus nephritis.[8] Fifty SLE patients with renal symptoms who satisfied criteria underwent renal biopsy, out of which 86% were females and 14% were male patients. This observation revealed that the disease had female preponderance. Study included patients from 13-45 years. According to a study on progression of lupus nephritis mean age of presentation was 18-35 years. Mean age of patients with lupus nephritis in this study was 25±5 years.[9] Age and sex distribution was studied in which 52% of the patients belonged to the age group of 15-25 years, of which 38% had class IV lupus nephritis. Males predominantly had class IV and class V lupus nephritis. Disease was aggressive in the younger age group and male patients.[9] On analysing the incidence of urinary abnormalities in our study, 90% of patients had proteinuria, out of which 54% had nephrotic range of

proteinuria. Proteinuria, haematuria, a lower serum C3 levels and a need for hypertension management were prominently seen with a worse class of lupus nephritis.

In this study of 50 patients, 42% had class IV DPGN accounting for the most common class of presentation in lupus nephritis and it was the predominant class in the study group. Clinico pathologic studies reveal that class IV LN is a severe form of illness and it is the predominant class of presentation in lupus nephritis. It was seen in age group of 15-35 years. Disease activity markers like dsDNA and serum C3 levels were also studied. Among the patients who had decreased C3 levels 76% of patients had class IV LN. Decreased C3 levels correlated well with class IV lupus nephritis. 90.4% of patients, who had class IV DPGN, were anti dsDNA positive and had renal failure.[10] In patients with clinically severe illness 64% had class IV lupus nephritis. 42% of the patients with lupus nephritis had hypertension and 62% of patients with hypertension had class IV lupus nephritis. In Lupus nephritis, the prognostic information was offered by renal biopsy and patients with active histological changes required aggressive immunosuppressive therapy. Renal biopsy had a major role in deciding the type and intensity of immunosuppressive therapy. Best overall predictor appeared to be the extent of tubulointerstitial disease in renal biopsy. Thus, renal biopsy in lupus nephritis helps in evaluation, instituting therapy and in predicting prognosis in patients with SLE and renal involvement.[11] Correlation between clinical manifestation and histopathology of renal biopsy was revealed in a study by Bald et al. Likewise in our study overall severity correlated well with anti dsDNA positivity, class IV lupus nephritis, renal failure, hypertension, decreased C3 levels and a disease flare. Histologically severe forms result in more severe manifestation.[10]

CONCLUSION

Observation shows that there is a significant clinico-pathological correlation in lupus nephritis. Proteinuria, haematuria, a lower serum C_3 levels and a need for aggressive hypertension management were observed in patients with a worse class of lupus nephritis. Patients with active and proliferative forms of lupus nephritis had a very severe course of illness. Though clinico-pathological correlation is reasonable, it is always far from perfect. Patients with aggressive lesions were started on immunosuppressive therapy and kept under close follow up.

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