Original Article

Frequency of histopathological patterns of Lupus Nephritis according to WHO classification – Report from a tertiary referral centre from Central Lahore

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ABSTRACT

Background: Renal involvement in Systemic Lupus Erythematosus (Lupus Nephritis) carries high morbidity and mortality. It is important to classify Lupus Nephritis to ensure appropriate management for improved long-term prognosis. This study was conducted to determine the frequency of histopathological patterns of lupus nephritis according to World Health Organization (WHO) classification on renal biopsy in patients presenting at a Tertiary referral centre in Central Lahore.

Patients and methods: This cross-sectional study was done at Division of Rheumatology, Fatima Memorial Hospital, Lahore from January 2017 till July 2017. Eighty-three consecutive patients, fulfilling 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for Systemic Lupus Erythematosus (SLE), and having evidence of nephritis were enrolled. An informed consent was obtained from the subjects to include their data in the study. Renal biopsy was done by the same Consultant Nephrologist and biopsy specimens sent to the Pathology Department were reported by the same Consultant Pathologist. Patterns of Lupus Nephritis according to WHO classification criteria were recorded on a pre-designed proforma. Data was analysed using SPSS version 22.0 for Windows. Frequency of each class of nephritis was calculated.

Results: Total of 83 diagnosed patients were evaluated. Majority of patients (69%) were between 31-50 years (n=57). Mean age was 43.76±4.74 years. There were 49 females (59.03%). Patterns of Lupus Nephritis according to WHO classification showed that 9.63% (n=8) had Class I, 21.68% (n=18) Class II, 26.50% (n=22) Class III, 32.53% (n=27) Class IV, 6.02% (n=5) Class V and 3.61% (n=3) had Class VI.

Conclusion: The frequency of WHO Class III and Class IV is high among patients with Lupus Nephritis. So, every patient who presents with nephritis should be sorted out for class of the disease in order to start early treatment to limit renal failure.

Keywords:

Lupus Nephritis, renal biopsy, histopathological patterns, SLICC (Systemic Lupus International Collaborating Clinics)

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an autoimmune, multisystem disease mostly affecting young women.[1] It can affect multiple organ systems. Kidneys are one of the commonest organs affected by SLE. Every part of kidney can be affected, but glomeruli are the most common target.[2] Abnormal urine analysis with normal or raised creatinine is present in most patients at the time of diagnosis or later. Most frequently observed abnormality is proteinuria.[3] Studies have shown that Lupus Nephritis is an important predictor of poor outcome.[4] Renal involvement is seen in 50-75% of patients and nephritis is suspected when there is presence of significant proteinuria (>500mg/24 hours).[3-5] There are a several types of renal diseases associated with SLE and these are usually differentiated on renal biopsy. If not treated appropriately 10-15% of Lupus Nephritis patients eventually develop end stage renal disease, requiring renal replacement therapy or renal transplantation.[5] Major histopathological findings for classification for nephritis in SLE includes focal and/or diffuse involvement of glomerulus, the degree and site of hyper cellularity, immune complex deposition and the presence of sclerosis or active lesions.[6] The classification of Lupus Nephritis is very important in decision making about patient care and for assessing outcome.[5] International data shows that according to WHO classification, the most common form of Lupus Nephritis in USA, UK, Saudi Arabia, Jordan and

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Lebanon is Class IV, 48.6%, 37%, 37.1%, 46.8% and 38% respectively followed by Class V.[7] Previous study from Pakistan showed that using WHO classification criteria, Class IV Lupus Nephritis is the most common form (40%) followed by Class III (20%).[8] This study aims to find out the frequency of various classes of Lupus Nephritis in local population represented at a Tertiary care private sector hospital in Central Lahore.

PATIENTS AND METHODS

This cross-sectional descriptive study was carried out at the Division of Rheumatology, Fatima Memorial Hospital, Lahore, from January to July 2017, after prior approval from Institutional Review Board (IRB) of Fatima Memorial Hospital, Lahore. The centre receives patients from various parts of the Central Punjab region. Total of 83 patients who fulfilled 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for Systemic Lupus Erythematosus (SLE) were enrolled from Out-Patient Department of Rheumatology, Fatima Memorial Hospital, Lahore. This classification criterion has two components, Clinical criteria (total 11 like oral ulcers, alopecia, serositis, renal, neurological etc.) and Laboratory criteria (total 6 like ANA, Anti ds DNA etc.) and at least one is needed from each with minimum total of four criteria.[9] Renal biopsy was done by same Consultant Nephrologist by admitting the patient in medical ward, taking written informed consent and in local anaesthesia under ultrasound guidance using Dr. Japan semiautomatic biopsy needle. After renal biopsy, all patients were advised strict bed rest for 24 hours (2 hourly BP monitoring was done) and they were seen by both Rheumatology and Nephrology teams. First post biopsy day renal ultrasound was done to look for any per-nephric collection and early morning urine complete was also done to look for haematuria. All biopsy specimens were reported by same Consultant Pathologist. After renal biopsy, patients were pulsed with intravenous Methylprednisolone 1g for three days and were started on Mycophenolate mofetil or Cyclophosphamide after combined decision of Rheumatology and Nephrology consultants and treatment was modified as per biopsy report. Patterns of Lupus Nephritis according to latest WHO classification criteria (revised in 2003 by International Society of Nephrology/Renal Pathology Society (ISN/RPS) were recorded on a pre-designed proforma.[10] This criteria classifies Lupus Nephritis into 6 classes, Class I (Minimal meningeal lupus nephritis), Class II (Mesangial proliferative lupus nephritis), Class III (Focal/ focal proliferative lupus nephritis), Class IV (Diffuse / diffuse proliferative lupus nephritis), Class V (Membranous lupus nephritis) and Class VI (Advanced sclerosis).[10] The collected data was analysed by using SPSS version 22. Qualitative data (gender and patterns of lupus nephritis) were presented as frequency and percentage. Mean and standard deviation were calculated for age of the subjects. Stratification for age and gender was done to control the effect modifiers. Frequency of each class of nephritis was evaluated.

Table 1. Patterns of Lupus Nephritis according to WHO classification on renal biopsy

Classification on Renal Biopsy	No. of Patients	%
Class I	8	9.63
Class II	18	21.68
Class III	22	26.50
Class IV	27	32.53
Class V	5	6.02
Class VI	3	3.61
Total	83	100

RESULTS

Total of 83 patients were diagnosed and enrolled during the period under study. There were 49 (59%) females and 34 (41%) male patients, with male to female ratio 1:1.7. Age distribution showed majority of the patients (69%) were between 31-50 years (n=57), 25.3% (n=21) between 51-70 years, and 6% (n=5) between 15-30 years of age. Mean age of patients was 43.8 $\pm$ 4.74 years. Class IV nephritis was the most common type found in 27 patients (32.5%) followed by Class III (26.5%) and Class II (22%). Patterns of Lupus Nephritis according to WHO classification on renal biopsy observed in 83 patients are summarized in Table 1.

DISCUSSION

Systemic Lupus Erythematosus (SLE) is an autoimmune disease that can affect any organ of the body and is usually seen in childbearing women.[11,12] Renal involvement is seen in approximately 60% patients throughout life with at least 25–50% patients having kidney involvement at presentation. Lupus Nephritis presents in a variety of ways, starting from as mild as asymptomatic proteinuria to rapidly progressive glomerulonephritis with haematuria and red cell casts.[12] The results of this study revealed that majority of the patients were between 31-50 years (69%) and mean age was 43.76 $\pm$ 4.74 years reflecting that the morbidity is more prevalent in this age group. There is slight female predominance (1:1.7). These findings are different from

the results of a previous local study, male to female ratio 1:14 and most frequent age group 20-30 years but that study had a very small sample size (30 patients).[8] Patterns of lupus nephritis according to WHO classification were recorded which showed that 9.63% (n=8) had Class I, 21.68% (n=18) Class II, 26.50% (n=22) Class III, 32.53% (n=27) Class IV, 6.02% (n=5) Class V and 3.61% (n=3) had Class VI. The findings of the study are in agreement with previous two studies from this region by showing Class IV as the commonest class (40% Junejo and 42.8% Chakrabarti).[8] The findings are different from those of Dhakal and co-authors from Nepal concluded that according to WHO 1995 revised classification of Lupus Nephritis grade II (35%) and grade III (24%) were the most common types of lupus nephritis in a study of 38 patients (grade and class are interchangeable terms).[13] This difference might be due to their small sample size or different disease expression and genetics in both patient populations and needs further large scale studies. Literature has shown that the prevalence, incidence and severity of Lupus Nephritis varies among different ethnic groups.[14] The main advantage of this study is that internationally recognised WHO criteria for classification was used, so the results can be compared with other studies both nationally and internationally. One limitation is that this study was done at a single centre; a multicentre study may produce different results.

CONCLUSIONS

The frequency of Class III and Class IV (according to WHO classification) on renal biopsy is high among patients with Lupus Nephritis. So, it is recommended that every patient who presents with Lupus Nephritis should be sort out for class of the disease. However, it is also required that every setup should have their surveillance in order to know the frequency of the problem and to initiate early therapy to prevent the progression of disease.

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