



LUPUS NEPHRITIS; CATEGORIZATION OF PROTEINURIA AND HEMATURIA IN PATIENTS WITH LUPUS NEPHRITIS AT A TERTIARY CARE CENTER IN LAHORE.

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ABSTRACT... Categorization of proteinuria and hematuria in patients with lupus nephritis at a tertiary care center Lahore. **Objectives:** Distribution of proteinuria and hematuria has a pivotal role in renal complications of systemic lupus erythematosus (SLE). Proteinuria and hematuria has been included as an independent descriptor in the SLE disease activity index (SLEDAI). Hence this study aims to categorize the proteinuria and hematuria in local population. **Data Source:** Fatima Memorial Hospital. **Design of Study:** Descriptive study. **Setting:** This study was conducted in the Department of Morbid Anatomy and Histopathology, at University of Health Sciences, Lahore. Samples were collected from the department of pathology at Fatima Memorial Hospital Lahore. **Period:** In 2015 from January till December. **Methods:** Urine was collected from 38 cases both male and female patients immediately prior to biopsy for evaluation of lupus nephritis. Relevant laboratory investigations, serum Antinuclear antibody (ANA) and Anti-double stranded DNA (Anti dsDNA) levels and renal function tests were recorded. The proteinuria and hematuria were detected and categorized by dipstick methods. Proteinuria was categorized on the following scale: 1+ = 200 - 500 mg/24 hours, 2+ = 500 - 1500 mg/24 hours, 3+ = 2500-3500 mg/24 hours and 4+ = >3500 mg/24 hours. Microscopic hematuria is categorized via RBC/HPF: 0-2 (negative), 3-10 (1+), 11-50 (2+), 51-100 (3+), and 100+ (4+). Microscopic hematuria was categorized as RBC/HPF: 0-2 (negative), 3-10 (1+), 11-50 (2+), 51-100 (3+), and 100+ (4+). **Results:** Among 38 patients the male to female ratio was 1:5. Mean age of the patients was 26.55 ± 8.13 years with age range of 14-49 years. A total of 37 (97.3 %) cases had proteinuria. The intensity of proteinuria was graded as 1+ in 4 (10.53%), 2+ in 14 (36.84%) and 3+ in 19 (50%) patients. Haematuria was present in 31 (81.58%) cases. Among these patients, the intensity was graded as 1+ in 11 (28.95%), 2+ in 9 (23.68 %) and 3+ in 11 (28.95%) cases. Serum ANA and anti dsDNA were positive in all cases regardless of disease progression. None of the variable showed any significant association when compared statistically. **Conclusions:** The grade of proteinuria increases rapidly with progression of the lupus nephritis in SLE which may be partly due to delayed diagnosis and brisk activity of the renal flares and partly as complication in SLE treatment in our population. Hematuria in the presence of proteinuria alone can suggest glomerular disease progression without the need for extensive urological investigations.

Key words: Proteinuria, Hematuria, Systemic Lupus Erythematosus, Lupus Nephritis, SLEDAI.

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INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease worldwide with prevalence close to 1:500-1000 population.¹ There are a number of systemic complications among which renal complications are seen in 30%-90% of SLE patients by published studies. It is called lupus nephritis in which there is proteinuria, hematuria and even renal failure. In last few

years, children have more frequently presented with this complication and more kidney damage is seen secondary to the severity and treatment associated complications of the disease.² As a complication it occurs within 5 years of diagnosis. The diagnosis of lupus nephritis is however finally made on histological findings in the patients with SLE. Renal functions evaluation is important in all the patients diagnosed with SLE to detect the

Lupus Nephritis	Clinical and Laboratory Information
Class I. Minimal mesangial lupus nephritis	Normal serum creatinine and urine laboratory results. Incidental finding.
Class II. Proliferative mesangial lupus nephritis	Normal serum creatinine, with microhematuria or non-nephrotic proteinuria. If nephrotic syndrome develops, podocytopathy should be ruled out.
Class III. Focal lupus nephritis	Proteinuria and hematuria
	Occasionally: Nephrotic Syndrome, Hypertension, increased serum creatinine
	Progression towards renal failure depends on the percentage of affected glomeruli
	May evolve towards class IV
Class IV. Diffuse lupus nephritis	The most frequently biopsied form
	Hematuria, Proteinuria, Nephrotic Syndrome, renal failure, arterial hypertension
	Associated with anti-nDNA titre and hypocomplementemia
	May evolve towards renal failure
Class V. Membranous lupus nephritis	Proteinuria or nephrotic syndrome with normal renal function, hypertension and microhematuria
	In general, little immunological activity
Class VI. Sclerosing lupus nephritis	Progressive decrease in renal function associated with proteinuria and normal urinary sediments

Table-I. Clinical classes of lupus nephritis.³

renal involvements earlier. As earlier the detection and treatment, better is the improvement in renal outcome.

Lupus Nephritis can be early and life threatening presentation, especially in women in 3rd decade of life. A female to male ratio is found to be 9:1. However in male SLE patients, the active renal complications are more common as well as have worst prognosis.¹

There are six classes of lupus nephritis on the basis of clinical and laboratory information. (Table-I)

Whenever there is glomerular injury particularly mesangial and membranous there is albuminuria which leads to peripheral edema. These symptoms are more observed in patients of class IV or V lupus nephritis due to heavy proteinuria.⁴ Hematuria in the presence of proteinuria typically represents the glomerular and/or tubular injury and is usually followed by proteinuria.⁵

Proteinuria and hematuria not only predict the renal disease activity but have also been included as independent descriptors in the SLE disease activity index (SLEDAI). These are validated indices for the measurement of renal damage and

disease activity in SLE. Hence proteinuria and hematuria are judged by a panel of experienced rheumatologists with an expertise in SLE.⁶

The main causes of death in SLE are usually the severe renal disease and the complications due to treatment, including various cardiovascular diseases. Further complications of the progressive renal disease are uremia, anemia, acid-base imbalances and electrolyte imbalances. Coronary artery disease and stroke can proceed as a complication of hypertension. Nephrotic syndrome can cause complications like hyperlipidemia, ascites and edema. These further increase the chances of cardiovascular events. Keeping in view the worst clinical outcome of lupus nephritis, this study was designed to categorize proteinuria and hematuria in patients of lupus nephritis in local population.⁷

METHODOLOGY

This descriptive study was conducted in the Department of Morbid Anatomy and Histopathology, at University of Health Sciences, Lahore from January - December 2015. Informed consents of patients and parents in case of minors were taken. Ethical approval from institutional board was taken. Urinary samples of 38 clinically

suspected male and female patients of age range 1-65 years of lupus nephritis were collected from the Department of Pathology at Fatima Memorial Hospital Lahore. Patients with benign and pre-existing genitourinary causes of proteinuria or hematuria (medical renal disease, urolithiasis, kidney cancer, bladder cancer, prostate cancer, BPH) were identified and excluded. Patients with positive or equivocal urine cultures for urogenital pathogens at the time of urinalysis were also excluded.

The proteinuria and hematuria were detected by dipstick methods. The intensity of proteinuria was assessed by the quantitative method. In this method the amount of proteins is measured in 24 hour. Proteinuria is described based on the following scale: 1+ = 200 - 500 mg/24 hours, 2+ = 500 - 1500 mg/24 hours, 3+ = 2500-3500 mg/24 hours and 4+ = >3500mg/ 24 hours.⁸ Microscopic hematuria was categorized via RBC/HPF : 0-2 (negative), 3-10 (1+), 11-50 (2+), 51-100 (3+), and 100+ (4+).⁹ The ANA was detected by indirect immunofluorescence antinuclear antibody test (IF-ANA) and Anti-ds DNA by Enzyme-linked immunosorbent assay (ELISA) method. Findings of the laboratory investigations like serum creatinine (0.6 to 1.2 mg/dL in adult males and 0.5 to 1.1 mg/dL in adult females), ANA (+ve or -ve), anti-dsDNA (cut off value is <1:10), serum complement levels C3:21-50U/ml and C4:22-45U/ml were recorded in relevant proformas.

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).

As regard the gender distribution, female preponderance (81.6%) was noted as compared to male (18.4%) males with a male to female ratio of 1:5.

A total of 37 (97.3 %) had proteinuria with intensity as shown in Figure-1.

Note that 1+ in 4 (10.53%), 2+ in 19 (50%) and

3+ in 14 (36.84%) patients. Note that n=1 (2.63%) patient had no complaints of proteinuria.

A total of 31 (81.58%) cases presented with haematuria. Among the patients having haematuria, the intensity was graded as shown in Figure-2.

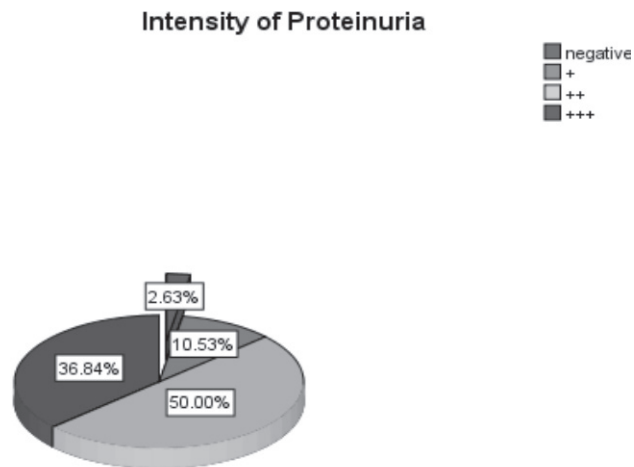


Figure-1. Intensity of proteinuria in n=38 Lupus Nephritis Patients.

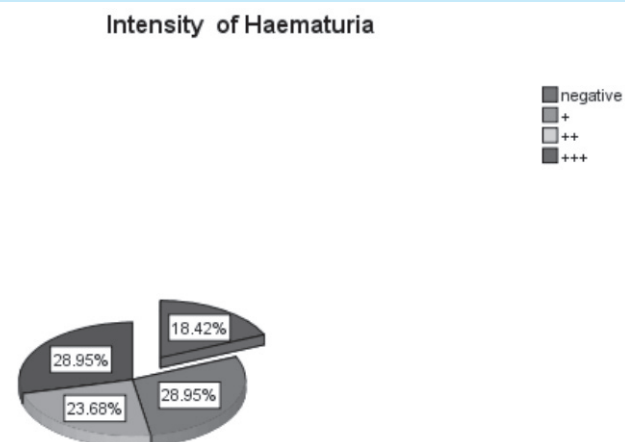


Figure-2. Intensity of hematuria in n=38 Lupus Nephritis Patients.

Note that 1+ in 11 (28.95%), 2+ in 9 (23.68 %) and 3+ in n=11 (28.95%), patients.

Various laboratory findings like proteinuria, proteinuria intensity, haematuria, haematuria intensity, ANA, Anti dsDNA, serum C3 and C4 were taken to assess their association with the clinical features in our study like age group, gender and clinical class of lupus nephritis. Pearson chi-square and Fisher Exact tests were

applied to see the associations among different variables but none of the association was found to be statistically significant.

DISCUSSION

This study included a total of 38 patients of lupus nephritis where they were classified on the basis of proteinuria and hematuria.

Systemic lupus erythematosus is a chronic autoimmune disease in which females are affected more due to multifactorial reasons. Lupus nephritis is one of the most dangerous complications of SLE. The percentage of people with SLE that are diagnosed with lupus nephritis is 60 % and these patients end up in severe renal complications and even death.¹⁰

In present study there were 81.6% female patients and 18.4% male patients so the male to female ratio turned out to be 1:5. This result was in accordance with a study conducted in China in which male to female ratio was similar (1:5).¹¹ The mean age of the patients was 26.55 ± 8.13 years with age range of 14-49 years. This finding was also in accordance with a study conducted in the department of rheumatology at Santa Casa de Misericórdia de São Paulo by Melo et al 2009.¹²

Mean age of the female patients was 27.93 ± 9.68 years with a range of 12-56 years and this result was closer to a study conducted in Saudi Arabia by Nehzad et al 2008.¹³ While for the males, the mean age was 34.67 ± 12.64 years and range was 17-56 years that is highly concordant with a study conducted in United Kingdom by Patel et al (2006).¹⁴

Most of the patients presented with the complaint of frothiness of urine which is a clear picture of proteinuria in simple terms. A total of 97.37% patients had proteinuria, which was confirmed by the dipstick method so this result was in accordance with a study conducted in Philadelphia by Dooley, 2007.⁴

Total 50% of the patients had 2+proteinuria, 36.84% of the patients had 3+ proteinuria, 10.53 % of the patients had 1+ proteinuria. It was

found that patients with class IV lupus nephritis more frequently had 2+ and 3+proteinuria. These results were in accordance with a study conducted in the department of rheumatology at Santa Casa de Misericórdia de São Paulo by Melo et al 2009.¹²

Haematuria was not as common as proteinuria though. Haematuria was either clinical which is gross haematuria or it was microscopic which means it was confirmed by the dipstick method which detects hematuria at a concentration of more than 3 RBCs/HPF and its sensitivity is more than 90%.^{5,15} A total of 81.6% of our patients had haematuria.¹⁶ As most of the patients belonged to class III and IV and the haematuria can be variable in these two classes of lupus nephritis.¹⁷

The associations proved to be insignificant showing that there is no significant p value seen when various laboratory findings like proteinuria, proteinuria intensity, haematuria, haematuria intensity, ANA, Anti dsDNA, serum C3 and C4 were assessed for their association with the clinical features in our study like age group, gender and clinical class of lupus nephritis and the results in the references of various studies were also according to these.^{18,19,20,21}

CONCLUSIONS

Serum ANA and Anti dsDNA are positive in every case of SLE being the diagnostic markers of SLE. The grade of proteinuria increases rapidly with progression of the lupus nephritis in SLE. The main reason is delayed diagnosis and the renal flares. However proteinuria can also progress as complication of SLE treatment. Early diagnosis of the lupus nephritis is possible if the SLE patients are regularly followed with clinical and laboratory workups. Patients can also be made aware of the earliest sign and symptom of proteinuria which is frothiness of urine and any color changes. Hematuria in the presence of proteinuria reveals progression of the renal disease and suggests glomerular disease otherwise the patients are asked for extensive urological investigations. Patients can be taught to use dipsticks at home and to interpret the color coding at least for proteinuria and hematuria. As these two signs

denoting lupus nephritis getting worst if assessed earlier can give prompt diagnosis of renal insult and can prevent progression into renal failure. This in return can help in having an early treatment and patient's survival.

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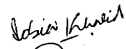






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The hardest prison to escape is in your mind.

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