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Relationship of Histological Classes with Renal Functional Status of Lupus Nephritis Patient

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ABSTRACT: ***Background:*** Lupus nephritis is one of SLE's more common and serious manifestations. It is regarded as both a strong predictor and a leading cause of morbidity and mortality. The presence of lupus nephritis reduces survival from 92% to 88% in 10 years. So, it is very important to know the histological classes for appropriate therapeutic intervention of lupus patients. Therefore, this study has been conducted to determine the relation between the histological classes and renal functional status. ***Methods:*** This was a cross-sectional descriptive type of study carried out in the Department of Nephrology, Rajshahi Medical College Hospital, from January 2013 to December 2014. After taking history, clinical examination, and relevant investigations, including biopsy, 30 (thirty) lupus patients who fulfilled inclusion and exclusion criteria were enrolled in this study. The data were analyzed with the help of SPSS software program version 16.0. Descriptive analytical techniques involving frequency distribution, computation of percentage, mean, SD, etc., were applied. Association between variables was conducted by applying the chi-square & ANOVA test. P-value <0.05 is considered statistically significant. ***Results:*** Mean (±SD) age of the patients were 26.07 (±10.29) with a range from15-29 years, male-female ratio was 1:14. Histological classes were class-IV (46.7%), class-III & class-V both were (20%) and class-II (13.3%) no patient of class-I & class IV. The mean urinary total protein was 4.3(±4.57) with a range of 0.2 to 14.7, and the mean serum creatinine level was 1.24 (±0.52) mg/dl with a range of 0.6 to 2.9. The difference in histological classes about UTP & serum creatinine was not significant (p>0.05). ***Conclusion:*** The relationship between histological classes and renal functional status was found to be insignificant, indicating that occult lupus nephritis may exist even without typical laboratory findings that suggest renal disease.

Keywords: Lupus Nephritis, Histological Class, Renal Functional Status.

Article at a glance:

Study Purpose*: To investigate the relationship between histological classes and renal functional status in lupus nephritis patients.*
Key findings: *No significant relationship was found between histological classes and renal functional status in lupus nephritis.*
Newer findings: *The study suggests that occult lupus nephritis can exist without typical renal laboratory findings.*
Abbreviations: *SLE - Systemic Lupus Erythematosus, UTP - Urinary Total Protein*

INRODUCTION

Systemic lupus erythematosus (SLE) is a multiystem autoimmune disease primarily occurring in young women. It is characterized by chronic immune complex formation and variable manifestations that include multiple organ involvement, accompanied by multiple laboratory abnormalities and frequent exacerbations.[1] Involvement of the kidney in SLE is known as lupus nephritis (LN). Lupus nephritis is one of the more common and severe manifestations of SLE. It is regarded as both a strong predictor and a leading cause of morbidity and mortality. Nearly 70-80% of all causes of SLE have some clinical manifestations of lupus nephritis, mostly glomerulonephritis Martins L *et al*., The presence of lupus nephritis reduces survival from 92% to 88% at 10 years. So, knowing the histological classes for appropriate therapeutic intervention of lupus patients is very important. If it is possible to avoid renal biopsy to determine the histological classes, it would be very helpful both for the patients & for the doctors. Patients would get early treatment so that they would be able to hold off or delay End Stage Renal Disease. On the other hand, poor patients have many difficulties in undergoing renal biopsies due to economic conditions. We must treat the Class III and IV diseases, and Class V, among Class III or IV diseases, should be treated with

aggressive immunosuppression because there is a high risk for End end-stage renal disease if patients are untreated or undertreated. In my study, each biopsy will be classified according to the WHO and ISN/RPS 2003 classification system. Class I: Minimal Mesangial Lupus Nephritis. Class II: Mesangial Proliferative Lupus Nephritis, Class III: Focal Lupus Nephritis, Class IV: Diffuse Lupus Nephritis, Class V: Membranous Lupus Nephritis, Class VI: Advanced Sclerotic Lupus Nephritis. The study was done to determine the histological classes of the lupus patients & the relation between the histological classes and renal functional status. The primary objective of this study was to classify the histological types of lupus nephritis based on kidney biopsy findings and to analyze urinalysis parameters, including 24-hour total protein estimation and serum creatinine levels. Renal functional status in this study was assessed through urinalysis, which included 24-hour total urinary protein measurement and serum creatinine level evaluation.

MATERIALS AND METHODS

A cross-sectional descriptive type of study was carried out in the Department of Nephrology, Rajshahi Medical College Hospital, from January 2013 to December 2014. After taking history, clinical examination, and relevant investigation, 30 (thirty) lupus patients who fulfilled both inclusion and exclusion criteria were enrolled in this study. After obtaining informed written consent from the patient, data was collected with the help of a predetermined questionnaire and data collection form. The patients had undergone percutaneous renal biopsy with all aseptic precautions. After proper labeling, one core of tissue was collected in a normal saline-containing pot for Direct Immunofluorescence (DIF), and another core was collected in a containing pot for histopathological examination. Then, both pots were preserved in the refrigerator at 4°c before being taken to a parcel service for sending the specimen to Dhaka to Lab aid Ltd. During transport; an icebox was used to maintain appropriate sample preservation. Histopathology reports were collected and analyzed. After renal biopsy, each patient was observed in the hospital for at least 24 hours. The data were analyzed with the help of SPSS software program version 16.0. Descriptive analytical techniques involving frequency distribution, computation of percentage, mean, SD, etc., were applied. The association between variables was determined by applying chi-square and ANOVA tests. P-value <0.05 is considered statistically significant.

RESULTS

The age of the 30 lupus patients was categorized into four groups ranging from 12 years to 60 years. Of 30 lupus patients, 18 (60%) patients were in the 15-29 years group, and 8 (26.7%) were in the 30-45 years group. 2 (6.7%) patients were in less than 15 years group, and 2 (6.7%) patients were in more than 45 years group. The mean (±SD) age was 26.07±1o.29. The age distribution of lupus patients is shown in Table.

Table 1: Age Distribution of Lupus Nephritis Patients (N=30)

Age Group	Frequency (%)	Mean±SD
<15	2(6.7)	
15-29	18(60)	26.07±10.29
30-45	8(26.7)	
>45	2(6.7)	

Out of 30 lupus nephritis patients, only 2(6.6%) patients were male, and 28(93.3%) patients were female in sex. The male-female ratio was 1:14. Shown in table-2.

Table- 2: Sex Distribution of Lupus Nephritis Patients (N=30)

Sex	**Frequency (%)**
Male	2(6.6)
Female	28(93.3)
Male:female = 1:14	

Table 3: Histological classes of lupus nephritis patients.

Histological Class	Frequency	Percent (%)
Class I	0	0
Class II	4	13.3
Class III	6	20
Class IV	14	46.7
Class V	6	20
Class VI	0	0
Total	30	100

The histological classes were class IV (46.7%), class III and class V (both 20%), and class II (13.3%), with no patients of class I and class V.

Table 4: Urinary total protein (UTP) in different histological classes of lupus patients. (N=30)

	UTP (gram)							
Histological class	<3 N (%)	3-5.9N (%)	6-8.9 N (%)	9- 11.9 N (%)	>12 N (%)	Total N (%)	Mean (±SD)	F (p)
class II	3 (18.75)	0	0	0	1 (25)	4 (13.33)	4.05 (±7.00)	
class III	2 (12.5)	1 (25)	1 (20)	1 (100)	1 (25)	6 (20)	5.58 (±5.14)	0.287
class IV	7 (43.75)	3 (75)	2 (40)	0	2 (50)	14 (46.67)	4.36 (±.41)	(>0.05)
class V	4 (25)	0	2 (40)	0	0	6 (20)	3.05 (±3.23)	
Total						30 (100)		

Urinary total protein (UTP) of the 30 lupus patients were categorized in 5 groups of them in <3 gram group: 3 (18.75%) patients were of class II, 2 (12.5%) patients of class III, 7 (43.75%) patients of class IV, and 4 (25%) patients of class V; in 3 to 5.9-gram group: no patient of class II, 1 (25%) patients of class III, 3 (75%) patients of class IV and no patient of class V. In the 6-to-8.9-gram group: the number of patients of class II was 1 (20%) patients of class III, 2 (40%) patients of class IV, and 2 (40%) patients of class V. In the 9-to-12-gram group, there number of class II patients, 1 (100%) patients of class III, and no patients of class IV and class V. In the>12-gram group: 1(25%) patient of class II, 1(25%) patient of class III, 2(50%) patients of class IV, and no patient of class V. Mean (±SD) UTP in class II was 4.05±7.00, in class III 5.58±5.14, in class IV 4.36±4.41, in class V 3.05±3.23 (Table 4). The difference in histological classes in urinary total protein was not significant (F=0.287, df =3, p>0.05).

Table 5: Serum creatinine (mg/dl) in different histological classes of lupus patients. (N=30)

Histological	Serum creatinine (mg/dl)					F(p)
Class	<1N (%)	1--2N (%)	>2N (%)	Total N (%)	Mean(±SD)	
Class II	2(22.2)	2(11.1)	0	4(13.33)	1.00(±0.39)	0.659 (>0.05)
Class III	3(33.4)	1(5.5)	2(66.7)	6(20)	1.43(±0.94)	
Class IV	2(22.2)	12(66.7)	0	14(46.67)	1.27(±0.32)	
Class V	2(22.2)	3(16.7)	1(33.3)	6(20)	1.12(±0.45)	

Serum creatinine of the 30 lupus patients were categorized into three groups in <1mg/dl group: 2 (22.2%) patients were of class II, 3(33.4%) patients of class III, 2 (22.2%) patients of class IV and 2 (22.2%) patients of class V; in 1 to 2mg/dl group: 2 (11.1%) patients were of class II, 1(5.5%) patient of class III, 12 (66.7%) patients of class IV and 3(16.7%) patients of class V; in > 2mg/dl group: no patient was of class II, 2 (66.7%) patients of class III, no patient of class IV and 1(33.3%) patient of class V. Mean (±SD) serum creatinine in class II 1.00±0.39, class III 1.43±0.94, class IV 1.27± 0.32, class V 1.12±0.45 (Table 5). The difference in histological classes in urinary total protein was not significant (F=0.659, df =3, p>0.05).

DISCUSSION

In this study, we found no significant relationship between histological classes UTP and serum creatinine level, which is similar to the studies

carried out by several world-renowned researchers. [2, 6, 8, 9, 10, 3,4, 11]. Regarding 24-hour urinary total protein (UTP), 36% of diffuse proliferative lupus nephritis (class IV) patients presented with <1-gram UTP, and 25% of class II patients presented with nephrotic range proteinuria. There was no statistically significant relation between histological classes and UTP. This observation is consistent with other studies examining 27 patients, showing that 24 hours of urine protein levels were unrelated to WHO class.[10] A retrospectively studied 144 patients with biopsy-proven lupus nephritis at Shiraj Nephrology Center, Shiraj, Iran, from 1999-2003. There was no significant correlation between proteinuria and WHO histological classification.[6] A retrospective study from January 2000 to 31 December 2009 at Groote Schuur Hospital, Cape Town, South Africa, among 251 patients. Proteinuria (UPCR) showed no statistically significant difference between proliferative and non-proliferative LN 7. A retrospective study from 2008 to 2014 on 84 consecutive cases of biopsy-proven LN at a nephropathology laboratory in Iran showed no significant difference in 24-hour proteinuria between the two classes (class IV & class III).[5] In one study, Jacobsen and coworkers retrospectively reviewed the biopsies of 94 patients with active lupus. They found no correlation between the degree of proteinuria and the underlying histology except for patients with class V membranous disease, who tended to have higher levels of proteinuria [3].

In the cage of serum creatinine, a minority of lupus patients in this present study presented with renal impairment, and serum creatinine levels were above the normal reference range only in 20% of lupus patients at the time of diagnosis. Renal impairment was observed in 23% of patients with proliferative (class III, IV, V) lupus nephritis & 21% of patients with Diffuse proliferative (class IV) lupus nephritis. The relation between histological classes and serum creatinine was not significant. These findings are consistent with those of Tsai C S and coworkers (2000), who investigated 27 patients and showed that serum creatinine was unrelated to WHO class. A study on 13 patients with a clinical diagnosis of SLE with active no renal manifestations but without signs of chronic renal failure or abnormal urinalysis.[2] Interestingly, 7 of the 13 patients were found on renal biopsy to have focal (class III) or diffuse proliferative (class IV) lupus nephritis. These observations suggested that occult lupus nephritis could be present without typical laboratory findings indicating renal disease. An important report mentioned that ten cases of Mesangial Lupus Nephritis (WHO Class II) were associated with Nephrotic Syndrome in the Division of Nephrology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan, and Department of Pathology, National Taiwan University Hospital, Taipei, Taiwan.[9] Another cross-sectional study of 40 patients of lupus nephritis from 2003 to 2006 concluded that it is impossible to predict the types, severity, and activity of lupus based only on clinical and laboratory findings 8. No significant correlation between histological findings and laboratory data was demonstrated. Here, we found no significant relationship between histological classes and urinary abnormalities or serum creatinine levels, similar to the studies by several world-reputed researchers .[2, 3, 8, 9, 10, 11]

CONCLUSION

The predominant histological class of lupus patients was IV, the next class III & IV, and the least was class II. The relationship between histological classes and renal functional status was not significant. One of the main aims of this study was to determine how we avoid renal biopsy. So, we correlated urinary total protein (UTP) protein with each- histological pattern and the serum creatinine level with all the histological patterns. However, a significant correlation was not found. So, we can conclude that to determine histological class, it is essential to do a renal biopsy.

Limitations: The study was conducted over a short period, with a small sample size and financial constraints.

Recommendation: A renal biopsy is necessary to determine the histological class. But further large-scale study can then be carried out.

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Conflict of Interest: None declared.

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