INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic disease with autoimmune pathogenesis and manifests as a low-grade inflammation and may advance to multiorgan fatal damage [1]. The disease prevalence differs globally. The annual incidence of SLE in relatively low-to-high-risk groups varies from 6 to 35 cases per 100,000 populations [2,3]. The first case of SLE was reported from India in 1963. Reported prevalence in northern Indian population ranges from 14 to 60/100,000 [4].

The inflammatory involvement of SLE virtually affects every organ including the joints, skin, kidney, brain, serosa, lungs, heart, and gastrointestinal tract. Renal involvement of SLE, known as lupus nephritis (LN) is a common manifestation and often determines the course of the disease. It is also an important cause of morbidity and mortality in SLE patients. The incidence of LN in SLE is divergent around the world and may be related to different ethnic and genetic backgrounds.

Nearly 70-80% of all cases of SLE have some clinical manifestations of LN mostly glomerulonephritis [5]. Proteinuria and deterioration of renal function were the main indications for renal biopsy. Although diagnosis of LN is straight forward in a patient with SLE and proteinuria, and an active urine sediment and perhaps renal insufficiency, still renal biopsies are required at diagnosis to enable classification of nephritis severity, to provide prognostic information, and to guide treatment. Hence, the objective of this study is to determine the frequency of distribution of different classes of LN based on renal biopsy reports and to correlate it with various laboratory findings.

METHODS

A retrospective study was done in all patients with LN who had at least one representative renal biopsy and evaluated in Nephrology Department of SCB Medical College, Cuttack, in 6-month duration. Various laboratory values were recorded and correlated with histopathological lupus classifications.

RESULTS

Out of 35 patients enrolled, 33 (94.28%) were females and 2 (5.71%) were males. Mean age was 27.53±12.26 years. Majority of cases belong to Class IV followed by Class V. Patients of Class IV LN have a significantly low hemoglobin level. Similarly, serum urea and creatinine are higher in Group IV than other groups, and serum creatinine was found to be significant. 24 hrs urinary protein excretion has a significant correlation with the classes of LN.

CONCLUSION

This study suggests some meaningful correlation between laboratory findings and histopathological lupus classification. This study also suggests that renal biopsies are still beneficial for better evaluation of renal status and determination of LN classes.

Keywords: Clinico-pathological correlation, Lupus nephritis, Biopsy.

As there generally exist a good correlation between clinical and hematological presentations with renal biopsy in patients with LN, so it is of utmost importance to correlate the clinical and pathological data in patients with LN for the proper management and prognostication. Again this type of correlative study will help in better understanding of the pathophysiology of renal involvement in this disease.

Numerous studies are available on the clinico-pathological correlation in LN patients mainly from developed countries. However, regarding this, there are very few publications currently available in a developing country in India and probably no such data has been published in Odisha (an Eastern state of India) till date.

Therefore, this study was aimed to assess the basic laboratory features of LN patients of eastern zone of India with biopsy-proven LN class, according to ISN/RPS 2003 classification.
urea, creatinine, triglycerides, cholesterol, urinalysis, and 24 hrs urine protein excretion.

For statistical analysis SPSS computer program was used to determine whether there was an association between the laboratory parameters and ISN/RPS classification. Values were calculated by student’s t-test and analysis of variance. p<0.05 was considered to be statistically significant.

RESEARCH

Total 35 patients who fulfilled the American Rheumatism Association criteria for SLE and underwent renal biopsy were included in the study. There was a female preponderance in the studied patients, and only two of them were found to be male. Age of the patients ranges from 6 years to 55 years with a mean age of 27.5±12.26 years.

As per Table 1, maximum number patients fall in the age group of 21-40 years and only 4 were >40 years of age.

Table 2 shows the distribution of renal biopsies according to ISN/RPS 2003 classification. It is apparent from the study that majority of cases belong to Class IV followed by Class V. No patient was found to be having Class I or Class VI.

Distribution of various laboratory tests including hematology, biochemistry, and urine analysis among different stages of LN has been shown in Table 3. As no patient was found to be having Stage I and VI in our study population, so these two groups were not included in this table.

Anemia was observed mainly in Class IV and V. Severe anemia in Class IV (8.5±1.2) was statistically significant (p=0.03) when compared with other 3 groups. Serum urea and creatinine were studied as renal parameters. These two parameters are higher in Group IV than other groups, and serum creatinine was found to be significant. Serum protein and albumin levels were low in all groups.

Albuminuria was observed in all 4 Classes of LN ranging from traces to +4. There was a significant correlation between 24 hrs proteinuria and ISN/RPS 2003 classification (p=0.04).

DISCUSSION

LN remains one of the most severe manifestations of SLE and associated with substantial morbidity and mortality. The glomerular lesions that frequently accompany SLE have been the subject of intense investigation by clinicians and pathologists for nearly a half of century.

This study was conducted to find out the frequency of distribution of various stages of LN and to correlate different laboratory parameters with these stages.

Out of 35 subjects, 33 were females and 2 were male patients with a female:Male ratio of 16:1. In the present study, the female preponderance might be due to small sample size which was only 35 due to lack of registry of male patients during last 6 months study period. In another study conducted Sanker et al., all the patients were found to be females [8]. Various other studies also showed female preponderance in the study population [9-11]. Increased frequency of SLE among women may be attributed to differences in the metabolism of sex hormones and/or gonadotropin-releasing hormones.

Mean age of the study group patients at presentation was found to be 27.5±12.26 years. Approximately similar results were obtained in different parts of India by Shobha et al. [12], where mean age of SLE patients was found to be 28±10±62 years and Sanker et al. [8] (mean age = 28.42). In fact, SLE is a disease of childbearing age. Some authors such as Esdaile et al. and Austin et al. have found out that younger age (<23 years) is one of the indicators associated with increased rate of renal failure and a more rapid progressive course [10,13].

| Laboratory parameters | Histopathological classifications (mean±SD) | p    |
|-----------------------|------------------------------------------|------|
|                       | Grade II (n=3)          | Grade III (n=6)      | Grade IV (n=19)     | Grade V (n=7)       |
| Hemoglobin (g%)       | 12.4±2.38                | 10.58±1.5              | 8.57±1.2             | 9.28±1.5             | 0.03*          |
| TLC                   | 10100±3833               | 9933.3±2056.5           | 7755.5±1749.3        | 8742.8±2349.3        | 0.10          |
| Serum urea (mg/dl)    | 20±10.3                  | 59±35.8                | 91.3±35.9            | 452±218.8            | 0.19          |
| Serum creatinine (mg/dl) | 0.97±0.47             | 1.56±1.40              | 3.13±1.7             | 1.13±0.55            | 0.02*         |
| Serum protein (g%)    | 5.8±1.2                  | 4.83±1.39              | 5.02±0.78            | 5.1±0.68             | 0.78          |
| Serum albumin (g%)    | 2.7±0.6                  | 2.6±1.09               | 2.28±0.53            | 2.37±0.37            | 0.70          |
| Serum cholesterol (mg/dl) | 168±56.5               | 257±36.27              | 227.7±87.7           | 216.2±26.1           | 0.63          |
| Serum triglyceride (mg/dl) | 134±29.2               | 216.1±45.6             | 224.7±216.2          | 168.4±33.6           | 0.7           |
| Urine analysis        |                          |                        |                      |                      |               |
| Urine albumin         |                          |                        |                      |                      |               |
| Urine RBC (+)         | 1 (33.3%)                | 5 (83.3%)              | 10 (52.6%)           | 4 (57.14%)           |               |
| Urine WBC (+)         | 1 (33.3%)                | 3 (50%)                | 12 (63.1%)           | 5 (71.4%)            |               |

*p<0.05 - significant

Table 3: Histopathological classification of laboratory parameter
On observing Table 2, we found none of the subjects were included in Class I or VI. Class IV is the most common histological type (54.28%) of LN in this zone. This finding is in agreement with some previous studies where Group IV was found to be the most common variety [5,12,14,15]. Neumann et al. in his study on 150 LN patients found out a frequency of 10%, 17%, 53%, and 14% for the Class of II, III, IV, and V, respectively [16]. Similarly, Polak and Pirani conducted their study on 376 LN patients and observed the overall frequency of Class II, III, IV, and V to be 26%, 19%, 37%, and 15%, respectively [17]. On the other hand, some researchers such as Apple et al. and Austin et al. found Class II and III as the more frequent groups [18,19].

On studying Table 3, anemia was found to be statistically significant in Class IV as compared to other classes. Similar findings were observed by Shobha et al. [12]. In the study by Austin et al. [19], anemia was found to be individually associated with an increased probability of renal insufficiency as seen in Class IV. This is probably explained by a higher risk for development of anemia secondary to renal failure and active hematuria in Class IV. No significant correlation was seen in the case of leukocyte count with any class of LN. However, according to Esdaile et al., low platelet count was associated with renal insufficiency (p=0.04) on multivariate analysis.

Serum urea level was found to be higher, whereas serum creatinine was found to be significantly higher in Class IV similar to the study by Nezhad and Sepaskhah [5] and Mok et al. [20], who also observed a significant correlation of WHO classification and renal function. This could be explained by the severity of renal lesion in Class IV. One previous study reported that creatinine >2.4 mg/dl is associated with poor survival outcome reflecting more severe renal damage [21]. According to another study by Yoo et al., more cases of Class IV showed progression to severe lesion on subsequent biopsy with an increase in serum creatinine level [22].

In our study, the highest protein excretion was found in Class IV. Correlation between 24 hrs urinary protein excretion and ISN/RPS 2003 classes was found to be statistically significant and is in agreement with the study by Nezhad and Sepaskhah [5], who also found significantly elevated 24 hrs urine protein excretion. Our study contradicts the result of Mok et al. where no significant correlation was found between 24 hrs urinary protein excretion and WHO classes [20]. Our study also showed a higher incidence of leukocyturia in Class IV as compared to other classes.

We conclude that our study suggests some meaningful correlation between laboratory findings and histopathological lupus classification on renal biopsy. This study also suggests that renal biopsies are still beneficial for better evaluation of renal status and determination of LN classes. However, there are some limitations of the present study mainly the small size of the study population, and patients were not followed up for long to see further clinical, laboratory, and histopathological changes of renal status.

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