Original research article

To study of the signs and symptoms of lupus nephritis in a tertiary care center: A prospective study

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Abstract

Background and Objective: Systemic lupus erythematosus is a persistent inflammatory disorder characterized by the involvement of multiple organs. The primary aims of this study were to investigate the histopathological abnormalities observed in patients who have received a diagnosis of lupus nephritis.

Material and Methods: The study covers a total of 40 participants. The present study was conducted at the Department of General Medicine, RVS Institute of Medical Sciences, Chitoor, Tirupati Road, and Andhra Pradesh. This study included patients diagnosed with systemic lupus erythematosus who met the American College of Rheumatology criteria. The patients were hospitalized to the medicine and nephrology wards of medical college between February 2016 to February 2017.

Results: Lupus nephritis is a significant contributor to both mortality and morbidity in individuals with systemic lupus erythematosus. The timely detection of renal involvement and prompt beginning of treatment has been shown to significantly extend the lifespan of patients. Our study observed a predominance of female patients. This finding aligns with the majority of studies that have demonstrated a higher representation of females in research on systemic lupus erythematosus.

Conclusion: Lupus nephritis is a prevalent factor contributing to mortality in systemic lupus erythematosus. Therefore, it is advisable to assess all patients with systemic lupus erythematosus for urine abnormalities and renal function, and subsequently provide treatment based on the classification of lupus nephritis.

Keywords: clinical profile, lupus nephritis, tertiary care centre, renal

Introduction

Systemic lupus erythematosus (SLE) is a chronic inflammatory disorder characterized by the involvement of multiple organs. SLE is characterized by the presence of inflammation, which has a significant impact on several organs inside the body ^[1]. These organs include the skin, joints, kidneys, brain, lungs, heart, serosa, and gastrointestinal tract. The renal signs observed in SLE are commonly referred to as "lupus nephritis." SLE has a wide range of clinical and immunological symptoms. The condition is distinguished by the existence of antinuclear antibodies. SLE is diagnosed using many sets of diagnostic criteria, namely the American College of Rheumatology (ACR), the European League Against Rheumatism (EULAR), and the Systemic Lupus International Collaborating Clinics (SLICC) criteria ^[2, 4].

Renal involvement in SLE manifests in approximately 40-75% of patients during a five-year timeframe following the initial beginning of the disease. Lupus nephritis and infections have been identified as significant indicators of unfavorable prognosis in SLE. Patients diagnosed with SLE who also have lupus nephritis experience a reduced lifespan compared to those without nephritis. The standard mortality ratio in individuals with lupus nephritis is reported to be between 6 and 6.8 times higher compared to those without nephritis ^[5, 6]. The timely identification of renal involvement is crucial in order to anticipate the occurrence of permanent renal damage and subsequent renal failure. The clinical presentations of lupus nephritis (LN) are frequently characterized by modest symptoms. All four renal compartments, including the glomeruli, interstitium, tubules, and blood vessels, have the potential to be impacted. The urine study reveals the presence of proteinuria, hematuria, urinary casts, and pyuria. Certain individuals may exhibit indications of renal failure, including the presence of edema resulting from the nephrotic syndrome, as well as the manifestation of severe hypertension ^[7, 9].

The term "silent lupus nephritis" is employed to characterize patients who do not exhibit any discernible clinical manifestations of renal involvement, despite the presence of active proliferative lesions as indicated by biopsy. Hence, it is imperative to conduct an assessment of renal involvement in all

individuals diagnosed with SLE during the first evaluation and subsequently on an annual basis, irrespective of the absence of overt manifestations of renal pathology $^{[10,\ 11]}$. Furthermore, it is advisable to do a reassessment of patients for LN) in the event of SLE flares. The evaluation process encompasses urinalysis as well as the measurement of kidney function, namely the assessment of serum creatinine concentration or estimated glomerular filtration rate (eGFR). The glomerular filtration rate (GFR) exhibits a progressive decline that is commensurate with the severity and nature of renal disease. The management of LN is contingent upon the specific histological classifications $^{[12,\ 14]}$.

Lupus nephritis is categorized into six histological classifications in renal biopsy according to the guidelines established by the International Society of Nephrology and the Renal Pathology Society. Despite many investigations, there remains considerable debate surrounding the significance of clinical, demographic, laboratory, and histologic markers in the prediction of renal outcomes in SLE. The objective of this study was to investigate potential associations between clinical and laboratory characteristics during renal biopsy, as well as to provide a comprehensive description of renal abnormalities in patients with SLE who undergo renal biopsy [15, 17].

The primary aims of this study were to investigate the histopathological abnormalities observed in patients who have been diagnosed with lupus nephritis. The objective of this study is to establish a correlation between the clinical and laboratory data and the histopathological classification of Lupus nephritis.

Materials and Methods

The study covers a total of 40 participants. The present study was conducted at the Department of General Medicine, RVS Institute of Medical Sciences, Chitoor, Tirupati Road, and Andhra Pradesh. This study included patients diagnosed with systemic lupus erythematosus who met the American College of Rheumatology criteria. The patients were hospitalized to the medicine and nephrology wards of medical college between February 2016 to February 2017.

Inclusion Criteria

- Patients meeting all four ACR requirements
- Individuals meeting at least one immunological or clinical requirement
- Biopsy-verified ANA-positive or anti-double stranded DNA lupus nephritis

Exclusion Criteria

- Patients who satisfy each of the four ACR criteria
- People who satisfy at least one clinical or immunological criteria
- ANA-positive or anti-double stranded DNA lupus nephritis confirmed by biopsy

Methodology

All patients who have been diagnosed with SLE based on the criteria established by the American College of Rheumatology (ACR) and the European League against Rheumatism (EULAR) should undergo a comprehensive assessment. This assessment should include a full medical history, thorough physical examination, and relevant investigations, with a specific focus on identifying any renal abnormalities. The information gathered during this process should be documented using a standardized proforma. The historical aspects encompass several elements such as the presentation of symptoms related to SLE, manifestations affecting the kidneys, previous medical history, the course of treatment received, and any concurrent comorbid illnesses. A comprehensive physical examination was conducted. The studies conducted encompassed a comprehensive blood count, a thorough study of urine, a measurement of protein excretion in urine over a 24-hour period, assessments of blood urea and serum creatinine levels, an estimation of glomerular filtration rate, and a kidney biopsy.

Statistical Methods

The chi-square test has been employed to assess the statistical significance of the study parameters within the LN classes. The Odds Ratio has been employed to assess the magnitude of the association between the variables under study and the categories of patients with lymph node involvement.

Results

This study has a cohort of 40 individuals who met the American College of Rheumatology (ACR) criteria for systemic lupus erythematosus (SLE). The present study involved the collection of various observations.

Table 1: Age Distribution

Sr. No.	Age (Yrs.)	Total patients	%
1.	< 20	10	25%
2.	21-30	08	20%
3.	31-40	20	50%
4.	>40	02	05%

In our study, the majority of the population fell within the age range of 31 to 40 years, accounting for 50% of the total sample.

Table 2: Sex Distribution

Sr. No.	Gender	Patients	%
1.	Male	08	20%
2.	Female	32	80%

In the conducted survey, a majority of the participants (80%) identified as female, while a minority (20%) identified as male.

Table 3: Pedal Edema

Sr. No.	Pedal edema	Patients	%
1.	Present	20	45%
2.	Absent	20	50%

In our investigation, a total of 20 patients had symptoms of pedal edema. A total of 20 patients exhibited no signs of pedal edema.

Table 4: Decreased Urine Output

Sr. No.	Decreased urine output	Patients	%
1.	Present	19	47.5%
2.	Absent	21	52.5%

In our investigation, a total of 19 individuals exhibited oliguria, while 52.5% of the patients did not manifest this condition.

Table 5: Arthralgia

Sr. No.	Arthralgia	Patients	%
1.	Present	17	42.5%
2.	Absent	23	57.5%

Within the examined cohort, a notable proportion of patients, specifically 42.5%, exhibited the presence of arthralgia in the context of lupus nephritis.

Discussion

Lupus nephritis is a significant contributor to both mortality and morbidity in individuals with systemic lupus erythematosus. The timely detection of renal involvement and prompt beginning of treatment has been shown to significantly extend the lifespan of patients. Our study observed a predominance of female patients. This observation aligns with the majority of existing studies that have consistently reported a higher representation of females in systemic lupus erythematosus SLE research [18, 20].

The average age of presentation in the present study was 26.2 years. This phenomenon bears resemblance to numerous prior investigations. According to the research conducted by Austin *et al.* and Esdaile study groups, it has been observed that individuals who are younger than 23 years of age tend to have a poorer prognosis. The prevailing clinical manifestation observed in this study was edema. This bears resemblance to previous research endeavors [21, 22]. A prevalence rate of 38% was observed for the occurrence of oliguria among the patients. Out of the whole sample size, 27 patients exhibited the absence of edema, whereas 31 patients shown the absence of oliguria. The clinical manifestations indicative of renal illness in patients with systemic lupus erythematosus are predominantly characterized by a lack of noticeable symptoms. This suggests that when a patient exhibits obvious clinical manifestations of renal illness, it signifies the presence of an advanced stage of the disease, resulting in a delay in its detection [23, 26].

In the conducted investigation, a total of 26 patients were identified as having hypertension. This bears resemblance to previous research conducted by Austin *et al.* and the study conducted by Esdaile. Moreover, a significant proportion of individuals diagnosed with class IV lupus nephritis exhibited

hypertension [27].

According to the research conducted by Suchitha $\it et~al.$, it has been demonstrated that hypertension exacerbates the severity of glomerular inflammation in cases with proliferative lupus nephritis, hence accelerating the progression of the disease. This study aims to compare the additional renal symptoms observed in our research with those reported in other relevant studies. The presence of anemia was determined to have a statistically significant association with class IV when compared to the other categories. Anemia in Class IV LN may likely be attributed to subsequent renal failure and concurrent active hematuria. This bears resemblance to the research conducted by Austin $\it et~al~^{[28,~30]}$.

Proteinuria is a prevalent manifestation observed in cases of lupus nephritis. The findings of our investigation revealed that a significant proportion of patients exhibited proteinuria in their urine. A statistically significant correlation was seen between the presence of proteinuria and the classification of lupus nephritis. Patients with Class IV lupus nephritis typically exhibit a predominance of proteinuria in the nephrotic range. This finding exhibited resemblance to other prior studies. In our investigation, all patients exhibited a urine protein creatinine ratio over 0.2. The occurrence of hematuria was seen in 24% of the participants in our study. The presence of hematuria in our study shown a statistically significant positive connection with proliferative lupus nephritis. The findings align with previous research. The research population exhibited an elevated blood urea level in 52% of cases [31, 32].

The study population exhibited an elevated serum creatinine level in 74% of cases. There is a positive correlation between an elevated serum creatinine level at the time of renal biopsy and an increased likelihood of developing renal failure. Hill *et al.* identified interstitial inflammation as a highly significant factor associated with elevated serum creatinine levels.

Elevated levels of blood urea and serum creatinine were seen in patients with class V and IV lupus nephritis. The study conducted by Too *et al.* revealed that a higher number of individuals in class IV had a suboptimal survival result when their serum creatinine levels exceeded 2.4. A debate has arisen regarding the efficacy of laboratory measurements as potential prognostic indicators compared to non-laboratory clinical factors in the assessment of lupus nephritis. Numerous studies have demonstrated that serum creatinine is a robust predictive indicator for the course of lupus nephritis. The study observed a decrease in glomerular filtration rate across all participants [33, 35].

The research undertaken by Pollack and Pirani encompassed a comprehensive investigation of biopsy samples obtained from 376 patients with lupus nephritis. This study identified and summarized five primary analytical approaches employed in the examination of these biopsy specimens. The researchers have recorded the respective frequencies of class II, III, IV, and V as 26%, 19%, 37%, and 15% in their observations. In a study conducted by Neumann *et al.*, a total of 150 patients were examined, revealing frequencies of 10%, 17%, 53%, and 14% for each of the relevant classes. The current investigation, together with the aforementioned research, identified class IV as the prevailing lesion. The results of our investigation indicated that class IV had the greatest levels of activity and chronicity scores [36, 37].

Conclusion

In our study, it was observed that lupus nephritis exhibits a higher prevalence among females in comparison to males. The predominant age range observed in our study for those seeking presentation is between 31 and 40 years of age. The majority of the patients had no symptoms, with the diagnosis of lupus nephritis being made during routine evaluation. However, a subset of patients presented with symptoms such as pedal edema, oliguria, nonspecific symptoms, malar rash, arthralgia, photosensitivity rash, anemia, and hematuria. Proteinuria is a prevalent manifestation observed in cases of lupus nephritis. All participants in our research investigation exhibited substantial proteinuria. In order to ensure correct classification for treatment purposes, it is crucial to establish the specific class using renal biopsy. Lupus nephritis is a prevalent etiological factor contributing to mortality SLE. Therefore, it is advisable to assess all patients diagnosed with SLE for urine abnormalities and renal function, and subsequently provide appropriate treatment based on the classification of lupus nephritis.

Funding

None

Conflict of Interest

None

References

- 1. Manzi M, Goldman R, Star KV. Epidemiology of systemic lupus erythematosus. in Rheumatology, 3rd Edition, MC Hochberg, AJ Silman (eds), Philadelphia: Mosby. 2003, 1295-1296.
- 2. Ward MM, Pyun E, Studenski S. Long term survival in systemic lupus erythematosus. Patient characteristics associated with poorer outcomes. Arthritis Rheum. 1995;38:274-283.
- 3. Mevorach D. The role of death –associated molecular patterns in the pathogenesis of systemic lupus erythematosus. Rheum Dis Clin North Am. 2004;30930:487-504.

- 4. Arbuckle MR, Mc Clain MT, Rubertone MV, Scofield RH. Development of autoantibodies before the clinical onset of SLE. NEJM. 2003;349(16):1526-33.
- 5. Hoffman BI, Katz WA. The gastrointestinal manifestations of systemic lupus erythematosus: review of the literature. Semin Arthritis Rheum. 1980;9:237-247.
- 6. Nossent JC, Swaak AJG. Prevalence and significance of Haematological abnormalities in patients with systemic lupus erythematosus. QJ Med,1991 July;80(291):605-612.
- 7. Fransisco P, Quismono JR. Hemic and lymphatic abnormalities in SLE. In Dubois Systemic Lupus Erythematosus, 4th ed. D Wallace, BH Hahn (eds), Philadelphia, Lea and Febiger. 1993, 418-430.
- 8. Das S, Das MK, Jarouliya U, Ahire ED. Plant Metabolites as Immunomodulators. InAdvances in Flavonoids for Human Health and Prevention of Diseases. Apple Academic Press; c2024. p. 239-264.
- 9. Budman DR, Steinberg AD. Haematologic aspects of systemic lupus erythematosus. Current concepts. Ann Int Med. 1977;86:220-229.
- 10. Gladman DD, Urowitz MB. Clinical features in SLE. in Rheumatology, 3rd Edition, MC Hochberg, AJ Silman (eds), Philadelphia: Mosby. 2003:1359-1381.
- 11. Surana KR, Ahire ED, Mahajan SK, Patil DM, Khairnar SJ. Nutrition, Malnutrition, Infection, And Immunity. InImmune-Boosting Nutraceuticals for Better Human Health; c2024 Jan 2. p. 355-367. Apple Academic Press.
- 12. Pollak VE, Pirani CL. Lupus nephritis: Pathology, pathogenesis, clinical pathologic correlations and prognosis. In Dubois Systemic Lupus Erythematosus, 4th ed. D Wallace, BH Hahn (eds), Philadelphia, Lea and Febiger. 1993, 525-541.
- 13. Kokande AM, Surana KR, Mahajan SK, Ahire ED, Patil SJ. Functional Foods for Microbial Infections. InApplications of Functional Foods in Disease Prevention; c2024 Jan 9. p. 165-189. Apple Academic Press.
- 14. Pistiner M, Wallace DJ. Lupus erythematous in the 1980s: A survey of 570 patients. Seminars Arthritis Rheum. 1991;21:55-64.
- 15. Appel GB, Silva FG, Pirani CL. Renal involvement in systemic lupus erythematosus (SLE): a study of 56 patients emphasizing histologic classification. Medicine (Baltimore). 1978;57:371-410.
- 16. Brauhn JA, Dinklo JCM. Distinct patterns of expression of ICAM- 1, VCAM-1 and ELAM-1 in renal disease. Lab Invest. 1993;69(37):329-335.
- 17. Magh AB, Putterman NL. Prognostic factors in diffuse lupus glomerulonephritis. Kidney Int. 1988;34:511.
- 18. Pathan AS, Wagh PP, Jain PG, Sonawane GB, Ahire ED. Functional Foods in Health and Diseases. InApplications of Functional Foods in Disease Prevention; c2024 Jan 9. p. 103-117. Apple Academic Press.
- 19. Neumann K, Wallace DJ. Lupus in 1980s: Influence of clinical variables, biopsy and treatment on the outcome in 150 patients with lupus nephritis seen in a single centre. Arthritis and Rheum. 1995:25:47-55.
- 20. Pollak VE, Pirani CL. Lupus nephritis: Pathology, pathogenesis, clinicopathological correlations and prognosis, in Wallace DJ, Hahn BH (eds): Dubois Lupus Erythematosus, ed 4. Philedelphia. PA, Lea & Febigerr. 1993, 525-541.
- 21. Mc Laughlin J, Gladman DD. Kidney biopsy in systemic lupus erythematosusII: survival analysis according to biopsy results. Arthritis rheum. 1991;21:55-64.
- 22. Austin III, Muenz: prognostic factors in Lupus nephritis: contribution of renal histologic data, Am J Med. 1983;75:382-391.
- 23. Wallace DJ, Podell T. Systemic lupus erythematosus survival patterns; experience with 609 patients. JAMA. 1981:245;934-938.
- 24. Baldwin BS, Lowenstein J. The clinical course of the proliferative and membranous forms of lupus nephritis. Ann Int Med. 1970;73;929-942.
- 25. Hans C N, Swaak T J G *et al.* Contribution of renal biopsy data in predicting outcome in Lupus Nephritis. Arthritis Rheumat. 1990:33: 7: 970-977.
- 26. Whiting-O'Keefe, Henke JE. The information content from renal biopsy in systemic lupus erythematosus; Stepwise linear regression analysis. Ann Intern Med. 1982;96:718-723.
- 27. Magil AB, Ballon HS. Diffuse proliferative lupus glomerulonephritis; Determination of prognostic significance of clinical laboratory and pathologic factors. Medicine (Baltimore). 1984;63:210-220.
- 28. Zweiman B, Kornblum J. The prognosis of lupus nephritis; role of clinico pathologic correlations. Ann Intern Med. 1968;69:41-462.
- 29. Hardin JA, Cronlund M. Activation of blood clotting in patients with systemic lupus erythematosus; Relationship to disease activities. Am J Med. 1978;65:430-436.
- 30. Pollak VE, Pirani CL. The natural history of renal manifestations of systemic lupus erythematosus. J Lab Clin Med. 1964;63:537-550.
- 31. Wallace DJ, Podell T. Systemic lupus erythematosus survival patterns experience with 609 patients. JAMA. 1981;245:934-938.

- 32. Wilkinson RG. Ed. Class and Health; Research and longitudinal data. New York; Tavistock Publications; c1986.
- 33. Pirani CL, Pollak VE. The reproducibility of semiquantitative analysis of renal histology. Nephron. 1964;1;230-237.
- 34. Morel-Margoer L, Mery JP. The course of lupus nephritis; contribution of serial renal biopsies. Adv Nephrol. 1976;6:79-118.
- 35. Ballow JE. Clinico pathologic correlation in lupus nephritis; evolving concepts. Ann Intern Med. 1979;91:587-604.
- 36. suchitha S, Deka P, Shetty MS. A clinico-pathological study of lupus nephritis basedon the International Society of Nephrology-RenalPathology Society 2003 classification system. J LabPhysicians. 2017;9:149-55.
- 37. Sharma M, Das HJ, Doley PK, Mahanta PJ. Clinical and histopathological profile of lupus nephritis and response to treatment with cyclophosphamide: A single center study. Saudi J Kidney Dis Transpl. 2019;30:501-7.
- 38. Devadass CW, Mysorekar VV, Eshwarappa M, Mekala L, Siddaiah MG, Channabasappa KG, *et al.* Clinical features and histological patterns of lupus nephritis in a single center of South India. Saudi J Kidney Dis Transpl. 2016;27:1224-30