

FREQUENCY OF RENAL INVOLVEMENT IN PATIENTS OF SYSTEMIC LUPUS ERYTHEMATOSUS

ABSTRACT

Objective: To determine the frequency of renal involvement in patients of systemic lupus erythematosus.

Methodology: This cross-sectional study was conducted at Department of Medicine, Ghulam Muhammad Mahar Medical College Teaching Hospital Sukkur, Pakistan, during six months after the approval of synopsis from October 30, 2018 to April 29, 2019. All the inclusion criteria fulfilling patients who visited above stated study setting were included in the study. Well-versed written consent was obtained after explaining the risks, procedure, and benefits of this study. Proven cases of Systemic Lupus erythematosus will be assessed for renal involvement indicated by proteinuria >0.5 gm/24 hrs. or cellular casts (tubular, red, and granular cells) or serum creatinine >1.3 mg/dl. The study data was recorded electronically using proforma attached as appendix.

Results: Mean of patients' age was 29.11 ± 5.80 years. Mean \pm SD of serum urea, serum creatinine, and serum albumin was 48.58 ± 18.61 , 1.28 ± 0.43 and 3.44 ± 0.42 mg/dL respectively. Mean of urine protein was 1448.88 ± 1278.76 mg. Out of 95 patients, 37 were male and 58 were female. Renal involvement was noted in 34 (35.8%) patients.

Conclusion: In conclusion, renal involvement is very prevalent in people with systemic lupus erythematosus. Systemic lupus erythematosus patients should get a kidney biopsy as early as clinical indications of nephritis appear in order to expedite treatment decisions and reduce the risk of irreparable kidney damage caused by inflammation.

Key words: Renal Involvement, Systemic Lupus Erythematosus, Prognosis

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disorder that causes a wide range of immunologic and clinical symptoms in virtually every body organ, with renal involvement, known as lupus nephritis (LN), being the most serious [1]. According to the common agreement, 60 percent of lupus patients will suffer clinically significant nephritis at some time throughout their disease's natural course [2]. A conclusive diagnosis of SLE is normally made if at least four of the eleven American Rheumatism Association diagnosis criteria are satisfied, either sequentially or concurrently [3]. The pathogenesis of LN and SLE is caused by the interaction of many variables, most notably epigenetic, genetic, and environmental factors. It is distinguished by a lack of self-tolerance that results in polyclonal antibody stimulation, which is traditionally seen as positive ANA as well as a fullhouse pattern on immunofluorescence in kidney biopsy specimens [4]. The pathology of immune-complex LN is addressed using the 2003 Renal Pathology Society/International Society of Nephrology (RPS/ISN) nomenclature [5]. The RPS/ISN system classifies LN based on the location of immune complexes accumulation in glomeruli, the absence/presence of endocapillary or mesangial proliferation, the overall degree of glomeruli participation (diffuse or focal) and glomerular impairment (segmental or global), and whether glomerular impairment is active or chronic (inflammatory or sclerotic respectively). Even though the decision to undertake a kidney biopsy in SLE cases with clinical evidence of kidney damage appears clear, it has become rather contentious due to a prevalent belief that all forms of LN can be

satisfactorily treated with immunosuppressive/cytotoxic agents and corticosteroids [7]. However, a renal biopsy is required to determine the extent of renal damage. Even though immune-complex GN remains the most prevalent trigger of renal disorder in SLE, several other processes are involved in renal impairment and involve a distinctive management approach than those used in immune-complex LN; such as lupus podocytopathy and thrombotic microangiopathy (TMA), which can be noticed in roughly 1.3% and 24% cases of LN, respectively [8,9]. As a result, in an SLE patients with any level of clinical renal impairment, renal biopsy contributes significantly in diagnosis as well as management [10,11]. It is effective in obtaining an early pathologic diagnosis of SLE, encompassing the numerous glomerular lesions as well as the parameters suggesting severity, chronicity, activity, and other concurrent lesions, early during disease process. Such kidney biopsies can serve as a reference range for eventual renal disease progression and association with clinical symptoms [12]. The usual indicators for performing the first kidney biopsy are persistent proteinuria $>0.5\text{g}/24$ hours active urine sediment (≥ 5 red/white blood cells per high power field, mostly dysmorphic without evidence of infection) or rising serum creatinine $>1.3\text{mg}/\text{dl}$ [13,14]. One local study on renal involvement in systemic lupus erythematosus found 45% prevalence of immune mediated lupus nephritis in SLE patients [15]. Despite significant advances in management, lupus nephritis stays the most common cause of SLE-related morbidity, and to the best of the investigators' knowledge, local data regarding characteristics of SLE appear scarce. As a result, the primary goal of this study is to review clinic laboratory data, and timely identification and treatment of kidney impairment is critical, as early response to therapy is associated with better outcome.

METHODOLOGY

This cross-sectional study was conducted after getting by CPSP and approval ethical review committee of the hospital, at Department of Medicine, Ghulam Muhammad Mahar Medical College Teaching Hospital Sukkur, Pakistan, during six months after the approval of synopsis from October 30, 2018 to April 29, 2019. All the inclusion criteria fulfilling patients who visited above stated study setting were included in the study. Well-versed written consent was obtained after explaining the risks, procedure, and benefits of this study. All the patients with Mixed connective tissue disease (MCTD) labelled by positive anti-UI-RNP antibodies on ENA profile, renal impairment secondary to cause other than the primary SLE disease like urinary tract infection, and renal stone disease and cystic disease of kidney were excluded. The inclusion criteria included the proven cases of Systemic Lupus erythematosus by fulfilling the diagnostic criteria attending either in patient or outpatient department. Those patient with renal involvement indicated by proteinuria >0.5 gm/24 hrs or cellular casts (red cells, granular, tubular) or serum creatinine $>1.3\text{mg}/\text{dl}$ was considered for renal biopsy after informed consent. Expenditure was afforded by researcher himself. These tests were done free of costs and the results of these tests were collected on reporting date and entered on the Performa by researcher himself. All the data was entered and analyzed using SPSS software version 21.0.

RESULTS

In this study 95 patients were included and males were in majority 58(61.1%). Mean \pm SD of age was 29.11 ± 5.80 years, mean of serum urea was 48.58 ± 18.61 mg/dL, mean of serum creatinine was 1.28 ± 0.43 mg/dL, mean of serum albumin was 3.44 ± 0.42 mg/dL and mean of urine protein was 1448.88 ± 1278.76 mg as shown in TABLE 1.

Renal involvement was found in 34 (35.8%) patients as shown in FIGURE 1.

Stratification of age, gender, serum urea, serum creatinine, serum albumin and urine protein were done with respect to renal involvement in from [TABLE 6-11]

Table 1. Descriptive statistics of age, serum urea, creatinine, albumin and urine protein n=223

Statistics	Age	Serum urea	Serum creatinine	Serum albumin	Urine protein
Mean	29.11	48.58	1.2832	3.4474	1448.88
Standard deviation	5.80	18.616	0.435	0.421	1278.76
Median	30.0	41.00	1.2000	3.6000	1234.00
Variance	33.69	346.585	0.189	0.178	1635245.6
Minimum	18.00	25.00	0.50	2.70	100.00
Maximum	40.00	86.00	2.10	4.00	3678.00

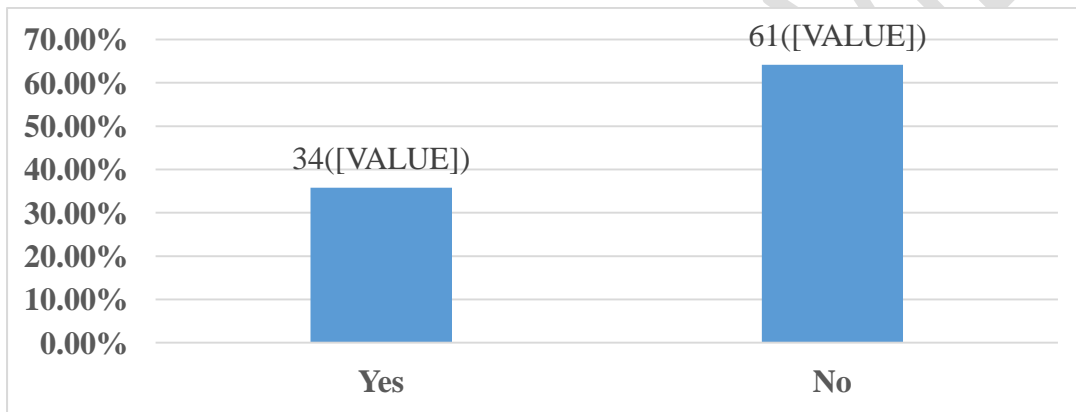


FIGURE 1. Frequency of renal involvement in systemic lupus erythematosus n=95

Table.2 Renal involvement according to age, gender, urine protein and serum albumin n=95

Variables		RENAL INVOLVEMEN		p-value
		Yes	No	
Age groups	18-30 years	26 (27.4%)	28 (29.5%)	0.004
	>30 years	8 (8.4%)	33 (34.7%)	
Gender	Male	11 (11.6%)	26 (27.4%)	0.325
	Female's	23 (24.2%)	35 (36.8%)	
Urine protein	100-2000	15 (15.8%)	41 (43.2%)	0.028
	>2000	19 (20.0%)	20 (21.1%)	

Serum albumin	2.5-3.5	30 (31.6%)	14 (14.7%)	0.001
	>3.5	4 (4.2%)	47 (49.5%)	

DISCUSSION

Lupus Nephritis has never been researched as a separate entity in Pakistan. In Pakistan, there is a scarcity of SLE literature. Rabbani et al [13] described cutaneous signs of lupus patients in Pakistan, while Suleman et al [14] examined the applicability of the American Rheumatology Association categorization to local lupus cases. We think that misreporting of lupus in Pakistani population has led to the mistaken impression that SLE is not a prevalent condition in the country. The real prevalence of SLE, on the other hand, can just be determined by a community-based investigation. It is well known that Arabs Chinese, Indians, and Blacks have a greater frequency of lupus nephritis (54%, 54%, 73% and 78% respectively) in comparison to Caucasians (39%).[15] However, in our study prevalence of renal involvement is 64.2%, which suggests that renal involvement prevalence in our community lies in between Asian and Caucasians. In our study, Malar rash was shown to be less common in people with lupus nephritis. In comparison, in a cross-sectional multicenter research in Colombia, Anay J M et al [17] discovered that patients with nephritis had a greater prevalence of oral ulcers (41 percent vs. 21 percent, $p = 0.01$) and malar rash (77 percent vs. 45 percent, $p=0.001$). Our study also found that renal impairment patients are at a higher risk of dying from SLE, since there were considerably more fatalities in this group, which is in agreement with the predictions of several previous studies. In our study, total mortality rate was 17%, which was greater than in previous studies throughout the world [15]. We consider that the true death rate in our subjects is substantially greater than what our study reflects, as several patients were lost to follow-up, as indicated by a mean follow-up length of lesser than three years. In individuals with biopsy-proven SLE, the male to female ratio was lower as compared to Arabs, Orientals, and Americans [18]. Mean age reported in our study was in line with other reported studies [15]. WHO class 3, class 4, and class 5 (17%, 64% and 5% respectively) were the most common histological types (14 percent) in this study. In addition, we had the highest frequency of WHO histologic class 4 in comparison to Indians, Blacks, Orientals, Arabs, Africans, Europeans, and Americans [15]. The Chinese population has a greater frequency of Grade III renal lesions [11], which may indicate that there is some hereditary component that defines the kind of kidney lesion. However, the increased frequency of Class 3 & 4 can possibly be related to the reality that kidney biopsy was performed in just a subset of patients. Univariate analysis using Fischer's Exact test revealed that individuals with infections and alopecia had a higher death rate. All of those who died were suffering from underlying infections. According to a Chinese research, the majority of deaths in their study were caused by infections. It appears that the higher risk for infection was linked to severe immunosuppressive therapy utilised in classes 4 and 5, which resulted in overwhelming sepsis and bone marrow suppression. It is worth noting that all patients who acquired marrow suppression as a result of immunosuppressive drugs inevitably developed infections. Bone-marrow suppression caused by

immunosuppression was classified as thrombocytopenia, leukopenia, or both, necessitating a dosage decrease of the immunosuppressive agent. Repeated full blood counts revealed the presence of thrombocytopenia and leukopenia in all individuals. The cytotoxicity of immunosuppressive medicines was demonstrated by significantly improved blood images when the respective dosages of AZA and CYC were reduced. Immunosuppressive regimens are now based mostly on western recommendations established from investigations done in western cultures. Unfortunately, no similar research exists for the South Asian nation, which has over 100,000,000 people and is genetically and environmentally distinct from the West. Locally calculated thresholds varied significantly from western numbers [19]. This may need a re-evaluation of contemporary local immunosuppressive regimens, which are now mostly based on Western recommendations. Autoantibodies have been implicated in the development of lupus nephritis, according to research. High-titer antibodies against dsDNA, for instance, have been seen in lupus nephritis, as well as their levels fluctuate with the condition [20]. This generally accepted link has been documented in a variety of lupus patient groups, such as Afro-Caribbeans [16], Caucasians [21], and Asians. DNA-anti dsDNA antibody complexes have been found in studies to have a role in the pathophysiology of lupus nephritis. When the autoantibody profile in lupus nephritis proved by biopsy was compared to other research, ANA was observed to be lower [15], however there was no change in anti dsDNA prevalence [15]. We were unable to discover a link between anti-dsDNA titers and nephritis. Serum complement anomalies seem to correlate with lupus nephritis activity [16]. Persistent C3 complement deficiency has been linked to renal disease development in certain, however not all, patient groups [16]. Exacerbations of lupus nephritis are predicted by declined C3 or C4. High-grade proteinuria has not been identified as a reliable predictor of kidney failure in cases with lupus nephritis [22]. In our study the mean age of the patients was age was 29.11 ± 5.80 years among them 37 (38.9%) were male and 58 (61.1%) were female. In present study mean serum urea level was 48.58 ± 18.61 mg/dL and serum creatinine were 1.28 ± 0.43 mg/dL, serum albumin was 3.44 ± 0.42 mg/dL and urine protein level were 1448.88 ± 1278.76 mg among patients presenting with systemic lupus erythematosus. The results are correlated with most of national and international studies.

CONCLUSION

It is to be concluded that renal involvement is fairly common in patients with systemic lupus erythematosus. Patients with SLE should have kidney biopsy as soon as clinical signs of nephritis are evident in order to accelerate treatment decisions and minimize risk of inflammation-induced irreversible kidney damage. Future prospective, there is a need to conduct randomized studies using large sample size with multiple study centres in Pakistan are needed to confirm the findings of the present study.

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