

Study of Clinical profile of newly diagnosed lupus nephritis in case of systemic lupus erythematosus

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Abstract

Introduction: Lupus Nephritis (LN) affects 25-60% of people with Systemic Lupus Erythematosus (SLE) within the first 5 years of disease onset. We conducted a prospective observational study to look into the demographic and clinical characteristics of newly diagnosed LN patients. **Material and Methods:** Our study included 50 newly diagnosed cases of LN. **Results:** The female-male ratio was 15.67:1. The majority of patients had LN of class IV (69.39 percent). The most common symptoms were alopecia, oral ulcers, and arthritis. All 50 patients were ANA positive, with 54 percent having anti-ds-DNA positivity. **Conclusion:** The most common type of LN in our study was IV. Although extrarenal manifestations, primarily mucocutaneous and musculoskeletal, were present, urine examination should be performed more frequently at the time of LN diagnosis for early diagnosis and treatment.

Keywords: Lupus Nephritis, Systemic lupus erythematosus, renal biopsy, ANA

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Introduction

Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease of unknown aetiology, with a wide range of clinical manifestations caused by the production of autoantibodies, resulting in a complex immunological profile; the outcome is variable, with remissions and flares, and the prognosis varies depending on the severity of the disease. Nonetheless, because of the variety of clinical manifestations, it serves as the prototypical autoimmune disease. The renal disease occurs in up to 25-60% of SLE patients, most frequently within five years of disease onset. It is regarded as one of the strongest predictors of an unfavorable outcome, making it one of the most severe clinical manifestations that eventually affects approximately 50% of patients at some point during their illness. [1,2] The Caucasian population has the lowest prevalence, while Hispanics, Asians, Afro-Caribbeans, and African-Americans have the highest. [3,4] Renal glomeruli are the most involved structure, resulting in lupus nephritis (LN). The pathogenic events that cause histopathological changes in the glomeruli are initiated by immune complex formation and deposition – whether circulating or in situ – in the mesangium, subepithelial, or subendothelial layers. LN defined as per SLEDAI definition [5,6] if any of the four following criteria are met; 1. Urinary casts (Heme-granular or red blood cells casts.) 2. Haematuria (> 5 red blood cells/high power field, excluding stone, infection, and other causes). 3. Proteinuria (>0.5 g/24h, regarding new-onset or recent increase of >0.5g/24h). 4. Pyuria (> 5 white blood cells/high power field, excluding infection). LN classified into six classes by the International Society of Nephrology and Renal Pathology Society (ISN/RPS) to provide a more concise description of various lesions and classes of LN. [7] Not all manifestations are symptomatic, and many are often subclinical for several years before manifesting with life-threatening complications. The diagnostic and monitoring tests available are sensitive, accurate, and relatively inexpensive. The treatment is also well-defined and

reasonably priced. There are very few studies on LN in India, the majority of which are retrospective. Our thesis is an observational prospective study. We investigated the demographic and clinical profiles of LN patients.

Aims and Objectives

1. To investigate the demographic profile of LN patients.
2. To investigate the clinical characteristics of newly diagnosed LN patients. -clinical symptoms and their relationship to the involvement of other systems

Material and Methods

Study design: Observational and prospective study from Aug 2010 to Aug 2012.

Setting: -From August 2010 to August 2012, fifty newly diagnosed LN cases were included in the study. All of these LN patients met the ACR's 1997 revised SLE classification criteria. [8]

For one year, all patients were followed up on at least three times a month, and more frequently if necessary.

Inclusion criteria:

- 1) Patients diagnosed as SLE based on the American College of Rheumatology (ACR) criteria.
- 2) Patients (or their guardians) should give informed consent for the investigations.
- 3) Age >12 yrs.

Exclusion criteria: Patients with 1) Already diagnosed with Lupus Nephritis 2) Overlapping feature of other Glomerulonephritis 3) Pregnancy 4) HIV infection

Consent: All patients or their relatives/guardians provided written informed consent for blood sampling and renal biopsy.

Study procedure: In this study, 50 consecutive subjects who met the inclusion criteria were recruited over a year and then followed up on for another year.

History: During the follow-up, the onset, duration, and progression of all symptoms and clinical manifestations were recorded.

Clinical examination: At each visit, general and systemic examinations were performed.

Investigation and follow up:

Routine investigations: Complete hemogram, Erythrocyte sedimentation rate (ESR), Renal function tests, Liver function tests, Serum

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uric acid, Total protein, albumin, Fasting, and postprandial blood sugar, Lipid profile, HIV, CPK(Creatine phosphokinase) whenever indicated, Thyroid function test, Urine routine, and microscopic examination, 24-hour urinary protein, Chest radiograph-posteroanterior view, ECG,

Special Investigations: ANA by immunofluorescence Anti ds-DNA by indirect immunofluorescence C3 and C4 complement levels (with BNProSpec KIT by nephelometric assay with normal range of C3 – 90- 180 mg/dl and C4- 15- 45 mg/dl) ACLA (anticardiolipin antibody) IgG and IgM ANA blot if necessary ANCA (Anti neutrophil cytoplasmic antibody) Direct and indirect Coomb’s test if required.

USG (Ultrasonography) guided renal biopsy – All newly diagnosed cases of lupus nephritis are subjected to USG guided renal biopsy and are classified into six groups based on the ISN/RPS 2003 classification of LN. Histological criteria were used to determine activity(maximum score,24 points) and chronicity indices (maximum score, 12 points).

Other tests, such as 2D ECHO, USG abdomen and pelvis, computed tomography (CT), magnetic resonance imaging (MRI), and cerebrospinal fluid examination, were performed as needed. Clinical

evaluations and laboratory tests were performed on all patients at the start and at three-month intervals, or more frequently if necessary. In addition, they were evaluated and managed for any complaints or complications that arose between these visits. All patients were followed from the time they were diagnosed with lupus nephritis until one year later.

Management: The patients were investigated and treated in accordance with the protocol for LN. There were no experimental interventions, and the patient was not subjected to any additional financial burden as a result of this study.

Analysis: All data was entered into an Excel spreadsheet, and a descriptive analysis of the demographic and clinical profiles was performed using Mean, Range, and Cumulative Frequency as a percentage.

Results

Demographic profile :Of the 50 newly diagnosed cases of LN, 94 % (n=47) were females, and 6 % (n=3) were males. The female to male ratio was 15.67 :1. Patients ranged in age from 13 to 50 years. The majority of patients were between the ages of 20 and 29. (See Table 1) The average age was 26.18 ± 8.39 years.

Table 1:Age-wise distribution of patients

Age Group (Years)	Number of patients	%
<20	11	22
20-29	27	54
30-39	8	16
>40	4	8
Total	50	100

Class of LN on renal biopsy: Out of 50 newly diagnosed cases of LN,most patients had class IV LN 69.39% (n=34) followed by Class II LN 14.29%(n=7), Class III and IV LN 6.12 % each(n=3) and class VI and class I LN each 2.04 % (n=1). Renal biopsy was not performed in one female patient because she died shortly after admission due to severe disease activity.

Table 2:Class of Lupus Nephritis on Renal Biopsy

Class of Lupus Nephritis	Number of patients	%
I	1	2.04
II	7	14.29
III	3	6.12
IV	34	69.39
V	1	6.12
VI	3	2.04
Total	49	100

Duration of symptoms: Duration of symptoms varied from 1 month to 5 years before being diagnosed with lupus nephritis, mean duration being 12.62 ± 11.95 months.

Symptoms of patients:At the time of diagnosis of Lupus Nephritis, the most common symptoms were Alopecia,Oral Ulcer,Arthralgia, as shown in Table 3

Table 3:Symptoms present at the time of diagnosis of Lupus Nephritis

Symptoms at the time of diagnosis of LN	Number of Patients	%
Fever	33	66
Oral Ulcer	42	84
Arthralgia	44	88
Alopecia	45	90
Photosensitivity	30	60
Discoïd Rash	4	8
Malar Rash	24	48
Raynauld Phenomenon	12	12
Digital Gangrene	2	4
Edema Feet	12	24
Puffiness of Face	15	30
Dyspnea	8	16
Palpitation	9	18
Lymphadenopathy	4	8
Myopathy	7	14

Other system involvement in In patients:Mucocutaneous involvement was most common (100%), followed by musculoskeletal (88%), Gastrointestinal (30%), Cardiovascular

(24%), hematological (22%), hypothyroidism (10%),Respiratory (10%) and neuropsychiatric(8%).

Menstrual abnormality:At the time of diagnosis of LN,31.9 % (n=15) had menstrual abnormalities like amenorrhea, irregular

cycle, menorrhagia, early menopause, and 66% (n=31) had a regular normal menstrual cycle.

Pattern of ANA:All 50 patients were ANA positive out of which most common pattern being homogeneous (60%) followed by Speckled (26%),Nucleolar (6 %),Cytoplasmic (4%), and Centromere (4%)

Antibodies in LN:All 50 patients were ANA positive with above mentioned pattern, out of which 54% (n=27 were ds DNA positive) at the start of study which decreased to 14.89 % after the end of 1-year follow up with treatment.

Discussion

The main feature of this study was that only newly diagnosed cases of LN were included; those who had previously been diagnosed with

Table 4:Demographic profile comparing our study with other studies

Demographic Profile	Dhir V et al[1]	Hsc C Y et al[8]	Our Study
F:M	11.53:1	6.12:1	15.67:1
Age at the time of diagnosis of LN	23.6± 10.5	26	26.18 ± 8.39

The most common histological class was class IV (69.39%),which is similar to the other study, including those in India. Renal biopsy was not done in one patient as she expired soon after diagnosis of SLE because of severe disease activity.

Table 5: Class of LN in various studies

Class of LN	Dhir et al[1]	Faurschou et al[10]	Sharma et al[11]	Our Study
I	0 %	1 %	0 %	2.04 %
II	16.20 %	17 %	8.5 %	14.29 %
III	26.50 %	12 %	17.6 %	6.12 %
IV	44.90 %	58 %	50 %	69.39 %
V	11.80 %	10 %	9 %	6.12 %
VI	0.70 %	2 %	NA	2.04 %

In our study group, the most common symptoms were alopecia or significant hair loss (90 percent), arthralgia (88 percent), and oral ulcer (84 percent). The most common symptoms in Dhir et al's retrospective Indian study were fever (91.30 percent), malar rash (83 percent), and arthralgia (80.3 percent).[1]Satirapoj et al prospective follow-up study had very different baseline clinical characteristics.

LN were excluded from the study. There have only been a few Indian studies of newly diagnosed cases of LN.

In our study, 94 % (n=47) of newly diagnosed cases of LN were female, while 6 % (n=3) were male. The female to male ratio was 15.67:1. The average age at onset of lupus nephritis was 26.18 ± 8.39 years. The majority of patients, 54 % (n=27), were between the ages of 20 and 29, with only 8 % (n=4) being over the age of 40. The M: F ratio indicated a female predominance, but different ratios in different study groups could be due to differences in geographic area, genetic and environmental factors. Table 4 shows that the age at the time of LN diagnosis was comparable to other studies.

Because different studies revealed different baseline clinical characteristics, clinical parameters should not be used to diagnose LN. As a result, in the case of SLE, routine urinary examination is required for early diagnosis of LN and to improve the outcome of LN.

Table 6:Comparing symptoms at the time of diagnosis of LN of our study with other studies

Symptoms	Dhir et al[1]	Satirapoj et al[9]	Our Study
Fever	91.30 %	50 %	66%
Oral Ulcer	45.90 %	45 %	84 %
Arthralgia	80.30 %	65 %	88 %
Alopecia or Significant hair loss	52.90%	30 %	90 %
Photosensitivity	34.60%	60 %	60 %
Discoid Rash	NA	25 %	8 %
Malar Rash	83 %	65 %	48 %
Raynauld Phenomenon	< 1%	20 %	12 %
Digital Gangrene	NA	NA	4 %
Edema Feet	NA	75 %	24 %
Puffiness of Face	NA	NA	30 %
Dyspnea	NA	NA	16 %
Palpitation	NA	NA	18 %
Lymphadenopathy	NA	10 %	8 %
Myopathy	< 1%	NA	14 %

The most common system involvement at the time of diagnosis of LN was mucocutaneous (100%)by musculoskeletal(88%),and gastrointestinal(30%).Comparison with other studies shown in table 7

Table 7:System involved along with LN in different studies

System Involved	Vaidya et al	Satirapoj et al[9]	Our Study
Cardiovascular	11.80 %	0 %	24 %
Respiratory	15.50 %	10 %	10 %
Gastrointestinal	NA	15 %	30 %
Neuropsychiatric	25.50 %	25 %	8 %
Hematologic	NA	55 %	22 %
Mucocutaneous	NA	NA	100 %
Musculoskeletal	NA	65 %	88 %
Hypothyroidism	NA	NA	10 %

In Indian study by Dhir et al (North India)7 ,ANA positivity was 95.3%, anti ds-DNA positivity was 52.80%. As compared to other study ANA positivity was similar to the other study while anti ds

DNA was positive only in 27 % in our study which is quite low as compared to other study as shown in table below which could be due to earlier diagnosis of LN by rheumatologist at our centre and

initiation of earlier treatments. The longer the duration of disease, greater is the possibility of anti ds DNA positivity without treatment. The low C4 level was similar to the other study shown below but Low C3 was different in different study due to different cut off value used for low C3 .(Table 8)ANA,anti-ds DNA,C3,C4 (Marker of disease activities): ANA positivity was 100% in our study, with varying patterns such as centromere (4%),cytoplasmic (4%), homogeneous (60%), nucleolar (6%), and speckled (26 %). In 54% of the patients, the anti-ds DNA was positive. At baseline, our study

found that low C 3 and low C 4 were present in 82.61 % and 74.47 % of participants, respectively. Satirapoj et al found that almost all patients (95.4 %) were ANA positive, with varying patterns such as speckled, nucleolar, homogeneous, and peripheral (52.3 % ,19.3 % ,12.8 % and 1.8 % respectively). 87.5 percent of the people tested positive for anti-ds DNA.[11]Dhir et al conducted an Indian study in which ANA positivity was 95.3 percent and anti-ds-DNA positivity was 52.80 percent.[1]

Table 8:Immunological disease activities in various studies

Serological test	Korbet et al[11]	Dhir et al[1]	Our study
ANA positivity	NA	95.30 %	100 %
Anti-ds-DNA positivity	96.51 %	52.80 %	54 %
Low C3 (< 90 mg/dl)	97.67 %	69.5 %	82.61 %
Low C4 (< 15 mg/dl)	62.79 %	73.50 %	74.47 %

Conclusion

In our study, the most common type of LN was IV. Although extrarenal manifestations, mostly mucocutaneous and musculo-skeletal, were present, at the time of LN diagnosis, urine examination should be done more frequently for early diagnosis and treatment.

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