**ADDIS ABABA UNIVERSITY**

**COLLEGE OF HEALTH SCIENCES**

**SCHOOL OF MEDICINE**

**DEPARTMENT OF INTERNAL MEDICINE**

# Clinical Characteristics and Predictors of Outcome of Lupus nephritis Patients on Follow up at Two Centers in Addis Ababa, Ethiopia from August 1, 2016 up to August 30, 2020

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## Abstract

**Background:** SLE is a multisystem chronic autoimmune disease which commonly involves the kidney and is associated with high mortality and morbidity especially in populations of African descent.

**Objective:** To describe the clinical characteristics, treatment patterns and predictors of outcome in a group of Ethiopia lupus nephritis patients from two centers.

**Patients and Methods:** The records of 97 lupus nephritis patients on follow up from August 1, 2016 up to August 30, 2020 in two centers, Tikur Anbessa specialized hospital and a private practice center (Shebelle Higher Clinic), Addis Ababa, Ethiopia were reviewed to acquire data on clinical characteristics and outcome. All patients fulfilled 2012 SLICC criteria for SLE.

**Result:** There were a total of 89 females and 8 male patients. Mean age at presentation of LN was 27.4 with 80(82.5%) of patients having LN as first presentation of SLE. Nephrotic range proteinuria was present in 27% and impaired kidney function was seen in 51.6% at presentation. Kidney biopsy done for 17 patients showed Class III and class IV as the commonest types. 70(74.5%) patients received immunosuppressive therapy with cyclophosphamide and MMF used in the majority. Favorable outcome was seen in 73(73.7%) after 6 months of therapy. After a median follow up of 41 months, 71.3% of patients had favorable outcome, 8(8.5%) patients had died and 1(1.1%) developed ESRD. Follow up at Tikur Anbessa specialized hospital, renal flare history and absence of response at 6 months were found to be significantly associated with unfavorable outcome.

**Conclusion**: LN, in this study of Ethiopian patients, is mostly diagnosed concomitantly with SLE and it presents at a younger age group and with more degrees of kidney impairment, but has response to treatment comparable to most other series.

**Key words:** Systemic Lupus Erythematosus, Lupus Nephritis, Ethiopia, Africa

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## List of Acronyms

| | |
|---|---|
| Ab | Antibody |
| Alt | Alanine aminotransferases |
| Anti ds-DNA | Anti Double stranded DNA |
| AST | Aspartate aminotransferases |
| ALP | Alkaline phosphatase |
| ANA | Antinuclear antibody |
| BUN | Blood urea nitrogen |
| C3 | Complement 3 |
| C4 | Complement 4 |
| CI | Confidence Interval |
| CNS | Central nervous system |
| CKD-EPI | Chronic Kidney Disease Epidemiology Collaboration |
| Cr | Creatinine |
| CXR | Chest x-ray |
| dL | Deciliter |
| ECG | Electrocardiogram |
| ESRD | End stage renal disease |
| eGFR | Estimated glomerular filtration Rate |
| GFR | Glomerular filtration Rate |
| Gm | Gram |

| | |
|---|---|
| HBsAg | Hepatitis B surface Antigen |
| Hct | Hematocrit |
| HCV | Hepatitis C virus |
| HIV | Human immunodeficiency virus |
| Hgb | Hemoglobin |
| HPF | High power field |
| ISN/RPS | International society of nephrology/Renal pathology society |
| LN | Lupus nephritis |
| MD | Doctor of Medicine |
| MDRD | Modification of diet in renal disease |
| mg | Milligram |
| ml/min | Milliliters per minute |
| MMF | Mycophenolate Mofetil |
| NIH | National Institute of Health |
| NCT | Nerve conduction test |
| OR | Odds ratio |
| RBC | Red blood cell |
| SD | Standard deviation |
| SLE | Systemic lupus erythematosus |
| SLICC | Systemic lupus international collaborating clinics |
| SPSS | Statistical package for social science study |
| US | United States |
| WBC | White blood cell |

# Contents

# 1. Introduction

## 1.1 Background

Systemic lupus erythematosus(SLE) is a chronic inflammatory disorder which can involve any organ but more often involves the kidney[1]. Although its full etiologic mechanisms have not been well stipulated, strong genetic component involving multiple genes and environmental triggers are believed to affect vulnerability and manifestations to this complex disease. [2]

There are marked differences in the burden of SLE worldwide that vary with sex, age, ethnicity and time. Incidence was reported highest in North America and lowest in Africa and Ukraine. Females had higher incidence with the sex ratio ranging from 2:1 to 15:1.And black ethnicity was reported to have higher rates compared to Caucasians. Temporal trends also show a rising pattern in the burden of SLE.[3,4]

Clinically important renal disease occurs in 20-60% of SLE patients, usually occurring in the first few months of diagnosis.[5]It is primarily caused by immune complex mediated glomerular injury, but can involve any part of the renal parenchyma.[6]. Initial presentation ranges from subclinical laboratory derangements to overt nephritis or nephrotic syndrome.[7]. Initial evidences are abnormal urine analysis or kidney function, but kidney biopsy is required for confirmation.[6]

Severity or even the predilection of developing lupus nephritis differs among different regions, races and ethnicities, but it ultimately predicts poor outcome in SLE patients. It is associated with ESRD, poor quality of life and death even with aggressive treatment. Survival rates are worse for patients with renal involvement than those without.[7,8]. Early diagnosis and treatment is key to preserve kidney function and decrease morbidity and mortality.

## 1.2 Statement of the Problem

Patients with SLE have increased risk of mortality and morbidity. This is due to several elements that include increased susceptibility to infection, accelerated atherosclerosis, malignancies, as well as organ damage especially renal injury. LN poses further mortality risk because a significant portion of patients progress to ESRD.[9]

Renal injury, occurring in up to one third of SLE patients, is one of the most crucial predictors of overall outcome. It appears to be more prevalent, even reaching as high as 60%, in certain ethnic groups such as the Asians, African Americans and Hispanics. [9,10]

Depending on several factors, 10 up to 30 % of LN patients develop ESRD during their course of illness. [11,12] In a single center, multiethnic cohort of LN patients with a follow up of 30 years, 19.5% developed ESRD, majority (80%) of which were within 10 years of LN onset. Mortality rate was remarkably high (46.7%) in the ESRD patients with a reduction of life expectancy of around 20 years. Average age at death was 40.3 years. Moreover, outcome was significantly poorer in Afro-Caribbean (Non-white) patients. [13]

In another multicenter, Caucasian predominant cohort of LN patients, the cumulative incidence of ESRD was 10% at 10 years of follow up for patients with LN, compared to 0.5% for patients with SLE patients who never had a diagnosis of LN. The cumulative incidence of death at 10 years of diagnosis of LN was 5.9%.[7]

Data from a US renal database shows 20,974 incident cases of LN associated ESRD in the US over two decades. Mean age at onset was 40 years. 82% of subjects were females and African Americans accounted for 48% of all the cases. More than 4000 patients (19.7%) died over the follow up period.[14]

In the developing world, especially in Africa, the epidemiology and outcome of SLE and LN are not well described. Under-diagnosis and scarcity of data relating to SLE and its complications are more of a culprit rather than its rarity. And there is some reason to believe the prevalence is higher and outcomes are poorer for patients of African descent. [15]

LN reportedly accounts for up to one third of renal biopsy registries in Africa. Renal involvement tends to be more common reaching as high as 44% in native African patients. Outcome also tends to be poorer with a reported five year survival of 54%–93.5% and five year ESRD free survival of 48-84%. Overall mortality ranged from 7.5% to 34.9%, but there are reports as high as 80%.[16,17]

Overall, LN portends a poorer outcome and decreased survival in SLE patients, which tends to be much grimmer in black African patients. And this is partly explained by a delayed or missed diagnosis of the disease. There needs to be an increased awareness and higher index of suspicion

among clinicians. Further studies are needed to ascertain the burden and pattern of the disease before embarking on therapeutic modalities.

Ethiopia, a middle income nation in east Africa, also suffers from a similar paucity of data and under-diagnosis of SLE and its complications. Limited information exists regarding the burden, clinical patterns and outcomes of patients with LN. As far as our knowledge there has not been a study addressing lupus nephritis in Ethiopia. This study, by describing patients with LN, would hope to lay the ground steps in the betterment of diagnosis and care of lupus and LN patients.

# 2. Literature Review

## 2.1 Magnitude of SLE

In a systematic review of worldwide incidence and prevalence of SLE from 2017, the highest values for incidence and prevalence were found in North America, 23.2 per 100, 000 person-years and 241 per 100,000, respectively. Lowest incidences of SLE were reported in Africa and Ukraine (0.3/100 000 person-years), and the lowest prevalence was in Northern Australia, 0 cases in a sample of 847 people. Females were predominantly affected with a female to male ratio reaching as high as 15. Peak age was third to seventh decade for females and fifth to seventh decade in males [3]

In a 4 years review of Medicaid data from the US where the prevalence of SLE was estimated at 143 per 100,000, the incidence in African Americans was considerably higher than in the whites, 31.2/100 000 person-years and 18/100,000 person years respectively. The frequency was 6 times more common in females than males. [10]

Figures from Nottingham, United Kingdom showed an overall prevalence rate of SLE at 24.7 per 100,000. Afro-Caribbean were found to have highest rates, 207/100,000 compared to Asians (48/100,000) and Whites (20.3/100,000). 40 was the mean age at diagnosis and females were primarily affected with a ratio of 12 to 1.[18]

A closer look at analysis of ethnic lines has revealed a higher prevalence of SLE among Black American, Afro-Caribbean and Asian groups than among white populations. As opposed to the high prevalence of SLE in those of African descent reported in US and European surveys, the

incidence and prevalence of SLE on the African continent is reportedly low. This is principally justified by the under reporting and under diagnosis of the disease.[19]

A retrospective case-record based study of SLE patients from a tertiary referral center in South Africa reviewed 226 patients over a period of 10 years. 210 were of black African race, the rest were of Asian, Caucasian and mixed races. Mean age at diagnosis was 34.Female to male ratio was 1.18. The mean age at presentation was higher for males compared to females, 38.9 and 33.7 years respectively.[16]

A prospective follow up of two year hospitalizations in a teaching hospital in Ghana reported of 51 patients who met criteria for LN. Females consisted of 86.5% of the patients at a female to male ratio of 7.5 to 1. Mean age at diagnosis was 31 (SD of 11.7). Mean age for males was 36.5, while it was 30.4 for the females. Duration of admission averaged at 26 days (Range of 1-140). The study estimated the prevalence of SLE at 5.28 per 1000, a significant increment from a prior report of 2.4 per 1000. [20]

One hundred patients with a diagnosis of SLE were described in a review of 15 years of case records from a university hospital in Tunisia. Majority were females (92%). The average age at diagnosis was 32 years and 19 of the patients were above the age of 50. There was an average delay of diagnosis of 13 months (range 1 - 72 months). Eight patients were found to have relatives diagnosed with SLE. [21]

A single year retrospective audit of a rheumatology clinic in Kenya described 13 patients who met the diagnostic criteria for SLE, out of a total of 394 patients on follow up. All of them were female and had a mean age of 34 years. Thirty percent (4/13) had comorbidities that included hypertension, diabetes, and renal failure.[22]

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## 2.2 Magnitude of Lupus Nephritis

LN is one of the most common and serious complications of SLE. About one third of patients end up developing clinically relevant kidney disease during the course of the illness. Patients might have significant pathologic findings without clinical findings and this might undermine the true incidence of LN.[13]

In a review that looked into worldwide patterns of renal biopsy registries, whereby secondary glomerular diseases represented roughly half of those described, LN was consistently found to be the most common cause of secondary glomerular diseases in America, Europe, Middle East, Asia and Australia. A single center retrospective analysis of 30 years of renal biopsy registries (n=1848) in South Africa also showed LN to be the most common of the secondary GN accounting for 31% of all the cases.[23,24]

An international SLE cohort, the SLICC cohort, recruited 1827 patients over a period of 4 years from centers in North America, Europe, and Asia. Females consisted of 90% and mean age at enrollment was 35(SD=13.3). At enrollment mean disease duration was 0.5 years (SD=0.3). Over a mean follow up of 4.6 years, 700(38.3%) of the patients developed LN, majority (80%) of which were diagnosed at entry. Patients with LN were more likely to be men, younger and of non-Caucasian ethnicity.[7]

Medicaid records from 2000 up to 2004 in the US reported of 7,388 LN patients out of a total of 34,399 SLE patients, making the prevalence 30.9 per 100,000 and 0r 21.5%. LN was four times higher than in males and four times more frequent among African Americans (26%) compared to Whites. Prevalence was highest in African-American and Asian women, 75/100,000 and 80/100,000 respectively. The lower figures reported here for African Americans compared to previous surveys of LN, were partly due to the shorter follow up duration and under diagnosis.[10]

In Riyadh, Saudi Arabia, Al Arfaj et al., reviewed 624 cases of SLE in a university hospital spanning a period of 27 years. They identified 299 cases of LN making the incidence 49%. 89% of patients were female making the female to male ratio 8.3 to 1. A higher proportion of males compared to females (55.1 vs. 47.2%) of the SLE patients developed LN. Mean age was 32.6 years (range 10-64 years) and mean age at onset of disease was 23.4 years (range 1-59 years). There were 6 pediatrics patients (2%) during the study period.[25]

Multiple reports have shown that the predilection of developing LN differs among different sex, age groups and ethnicities. This was further explored in a retrospective analysis of 773 SLE patients from the US which included 212 patients with LN at enrollment. Patients with nephritis were more likely to be men and less likely to be of European/American ancestry. Men developed nephritis earlier after diagnosis of lupus than did women. Analysis revealed male sex, non-European/American ethnicity, and younger age at the time of diagnosis of lupus were significantly associated with development of LN.[26]

The PROFILE cohort, a multiethnic and multi-institution group of SLE patients from the US, consisted of 568 patients which were predominantly females with a mean age 40 were followed for a median of 4.5 years. Renal involvement was considerably higher among Hispanic (64.1%) and African-Americans (63.1%) compared to Caucasians (26.9%).[27]

## 2.3 Lupus Nephritis, the African Experience

### 2.3.1 Burden and Clinical Profiles

Systemic lupus erythematosus and its complications have traditionally been taken as a rare phenomenon in Africa and native black Africans, in spite of figures showing increased prevalence and incidence of SLE in African descendants residing in the western world. Recent evidences have shown otherwise and even suggest that the burden is higher and associated with poorer outcome.

In a case review of LN patients spanning three decades from Cape Town, South Africa, 315 cases were described. 90% of patients were females and 78% were of mixed ancestry. Mean age at diagnosis was 31.5. 55% of patients had Class V disease on renal biopsy according to the 2003 ISN/RPS classification of LN. Nephritic syndrome was the most common presenting pattern accounting for 55% of cases. Close to half of patients had hypertension and heavy proteinuria at diagnosis, while 13% of patients had advanced kidney disease at onset.[28]

Another retrospective analysis of native kidney biopsies from Cape Town, South Africa explored 251 patients diagnosed with SLE. At time of biopsy most were below the age of 40 at an average age of 31(SD=11.6). Females accounted for around 85% of the patients. Most of the patients (79%) had mixed ancestry.[29]

In the same Cape Town study, edema and proteinuria were in present in 29% and 50% of patients, respectively at baseline. While majority (90%) had proteinuria at time of biopsy. ANA was positive in 70% of patients. Mean eGFR as calculated by the MDRD formula was found to be 81.4 ml/min (SD=62.5). Most common indication for biopsy was nephrotic range proteinuria. On biopsy, class III and IV LN were the most common ones, found at 20.7% each. Pure class IV accounted for 14.7% of all biopsies.[29]

In Egypt, Mahmoud et al, reported of 135 patients with biopsy proven LN in a decade long retrospective analysis. 129 of them were female and mean age at onset of SLE and LN were 21.7 and 24.3 respectively. Arthritis/Arthralgia occurred in 96% of patient, mucocutaneous lesions in 84.4%, serositis in roughly half of patients. While Neuro-psychiatric symptoms were reported in 29.6% and hematologic in 62.2%, commonest of which was leucopenia.[30]

At onset of LN, 55% were hypertensive. Two third of the patients had hematuria while one third had nephrotic range proteinuria. Classes III and IV were the commonest on biopsy accounting for 33% each. ANA was positive in 98% of cases.[30]

A Moroccan single center study of 114 LN patients also reported majority of females, with a female to male ratio of 7.76. Mean age was 29.6 (SD of 9.8). Most common presenting symptoms were of joint (85%) and skin (74%). Average gap between diagnosis of SLE and LN was 9 months. At presentation, 33.3% of patients had hypertension. Hematuria was seen in 76.3% patients. Nephrotic syndrome was found in 60 patients (52.6%) and renal failure in 68 patients (59.6%). Seventeen (14.9%) patients required acute renal replacement therapy.[31]

Renal biopsy was performed in 96 of the 114 patients, and majority (62%) of those were reported as class IV followed by class III and mixed classes, 10.4% each. [31]

In Senegal, 42 LN cases out of 74 SLE were studied in a 10 year review. Mucocutaneous and joint manifestations, in 92.85% and in 66.66% of cases respectively, were the commonest initial presenting symptoms. Half of them were hypertensive while renal function was impaired in 15 patients (35.71%). 45.2% had nephrotic range proteinuria, while all patients had proteinuria of more than 500 mg/day. Renal biopsy performed for 22 of them. Class V was the commonest followed by classes IV and II. [32]

### 2.3.2 Treatment and outcome

A systematic review of biopsy proven LN cases over a period of 15 years in the continent of Africa reported on the treatment and outcome patients. 16 studies were analyzed from six African countries, most of which were in North Africa. Proliferative classes of LN (class III, IV and mixed class V) were the most common classes identified from the studies.[17]

For induction therapy all studies reported of use of corticosteroids, while 93% of studies also used cyclophosphamide as an induction agent. MMF was used for induction therapy in four studies with a reported frequency of use of 0.4% to 15.6% of all participants. Survival analysis showed five years patient survival of 54-93.5%, while overall mortality ranged from 7.5% to 34.9%. There was one study which reported 80% mortality from Kenya.[17]

A South African report of 105 multiethnic group of patients with LN, where the most common histologic biopsy finding was class V, the induction therapy used in 87 patients was, MMF in 58%, prednisone in 19% and Azathioprine in 1.1%. Maintenance treatment was given to 57 patients, of which 65% received MMF, 25% received prednisone alone, while 11.5 were on cyclophosphamide.[33]

Overall there was a response (complete in 26 and partial in 45) in 71 (81.6%) of the 87 patients to induction therapy (72.2% for cyclophosphamide, 80.4% for MMF and 94.1% for prednisone alone).In the maintenance stage, there was a response (complete in 35 and partial in 29) in 64 (73.6%) of the 87 patients (90% for cyclophosphamide, 68.4% for MMF and 73.7% for prednisone alone) after 12 months of maintenance therapy. Among the non-responders, there was a significant increase in the number of patients with a raised baseline creatinine, positive anti-dsDNA antibodies and a low C3.[33]

In Egypt, where majority of LN patients were given cyclophosphamide for induction (73%) and maintenance (54%) treatment, favorable outcome was registered at the end of the study, for 71% of patients. 54% of patients developed one or more flares during the study period. The overall patient survival rate in this study was 93.5% at five years and 87.5% at 10 years, while the cumulative renal survival, i.e. survival without dialysis, was 88.9% and 87.4% at five and 10 years, respectively. Factors associated with an adverse outcome included male gender, hypertension at

nephritis onset ,serum creatinine ≥1.2 mg/dl, urinary casts, anti-cardiolipin antibodies and class IV nephritis on biopsy.[30]

Meanwhile a study from Senegal reported on 95 LN patients, majority of which had class III was (37.5%) and class IV (31.25%) disease on biopsy. The combination of corticosteroids and immunosuppressive was used in 56.25% of cases. After a follow-up of 6 months, 38.8% were in complete remission, 18.4% were in partial remission, and 42.8% had resistance. Lymphopenia, the presence of anti-native DNA antibodies, nephrotic syndrome, microscopic hematuria, tubular atrophy and interstitial fibrosis were identified as predictors of poor prognosis.[34]

The 5, 10 and 15- year cumulative event-free survival rates were 54, 34 and 27 %, respectively in a study of 66 biopsy proven LN cases from South Africa. While the 5, 10 and 15-year renal survival rates were 63, 52 and 52 %, respectively. Half of the patients reached the composite end point of doubling of serum creatinine, ESRD or death. Hypertension at onset of LN, nephrotic range proteinuria, eGFR of< 60 ml/min and lack of remission following induction therapy were all associated with development of end-stage renal disease.[35]

# 3. Objectives

## 3.1 General objectives

- To describe the clinical characteristics and predictors of outcome of patients diagnosed with lupus nephritis and having follow up at two centers in Addis Ababa, Ethiopia

## 3.2 Specific Objectives

- Assess the magnitude of lupus nephritis
- Describe the clinical and laboratory manifestations of lupus nephritis
- Explore the therapy given to LN patients
- Evaluate outcome of lupus nephritis
- Identify predictors of poor outcome

# 4. Material and Methods

## 4.1 Study Area

Study was conducted at two medical centers in Addis Ababa, Ethiopia; Tikur Anbessa Specialized hospital and Shebelle higher clinic.

Tikur Anbessa Specialized hospital, a governmental, university affiliated teaching tertiary medical hospital located in Addis Ababa, Ethiopia which serves vast majority of rural and urban part of country. The nephrology unit in the internal medicine department of the hospital, hiring four nephrologists, gives both inpatient and outpatient services including hemodialysis services.

Shebelle higher clinic is a private practice center in Addis Ababa, Ethiopia which gives an outpatient based general medicine care in addition to a specialist nephrology clinic run by a nephrologist.

## 4.1. Study Design

The study is a retrospective analysis of cases of LN diagnosed, treated and on follow up at the two centers. Both electronic and chart based records of the patients were reviewed to acquire data of their clinical characteristics, treatments modalities given and their outcomes. Phone contact was used to ascertain the final outcome in those with patients with incomplete records of outcome.

## 4.2 Study Period

Data was collected from April 1, 2020 till September 30, 2020.

## 4.3 Study Population

Study population is all LN patients attending at the two centers, from August 1, 2016 up to August 30, 2020.

### 4.3.1 Inclusion Criteria

- All Patients who fulfill the 2012 SLICC criteria for SLE and have evidence of LN on urine analysis, measures of kidney function or kidney biopsy findings
- Those having follow up for at least 1 month
- Those aged 18 or above

### 4.3.2 Exclusion criteria

- Patients with incomplete medical records

## 4.4 Study Variables

### 4.4.1 Independent variables

- Sociodemographic factors including age, sex and residence place
- Clinical characteristics
- Laboratory and histopathological characteristics
- Treatment modality

### 4.4.2 Dependent Variables

- Renal outcome as defined by remission, nonresponse or ESRD
- Survival at the end of the study

## 4.5 Operational definitions

Systemic lupus Erythematosus – Patient is classified as having SLE if he or she satisfies 4 of the clinical and immunologic criteria used in the SLICC classification criteria, including at least one clinical criterion and one immunologic criterion, or if he or she has biopsy-proven nephritis compatible with SLE in the presence of ANAs or anti-dsDNA antibodies

Lupus nephritis – A patient is who fulfills the above SLE criteria and has

- Positive proteinuria (persistent proteinuria of greater than 0.5 g per day) and/or
- Active urinary sediment ((≥5 RBC/HPF, ≥5 WBC/HPF excluding other causes, Cellular casts) and/or
- Presence of renal failure (increase in serum creatinine of more than 1.5 mg/dL) and/or
- Biopsy Findings Compatible with LN

Hypertension - is defined as blood pressure above or equal to 140/90 mmHg or the use of any antihypertensive medications

Leukopenia – WBC count of <4000/mm3 at least once in the absence of other known causes

Lymphopenia – lymphocyte count of <1,000/mm3 at least once in the absence of other known causes

Thrombocytopenia – Platelet count of <100,000/mm3 at least once in the absence of other known causes

Autoimmune Hemolysis - Evidence of hemolysis, such as reticulocytosis, low hapteglobin, elevated indirect bilirubin, elevated LDH, and positive coomb's test

Delirium - Characterized by 1) change in consciousness or level of arousal with reduced ability to focus, 2) symptom development over hours to <2 days, 3) symptom fluctuation throughout the day, 4) either 4a) acute/subacute change in cognition (e.g., memory deficit or disorientation), or 4b) change in behavior, mood, or affect (e.g., restlessness, reversal of sleep/wake cycle)

Psychosis - defined by delusions and/or hallucinations without insight and absence of delirium

Seizure - Primary generalized seizure or partial/focal seizure

Oral Ulcer - Oral ulcers as observed by a clinician

Non-scarring Alopecia- Non-scarring alopecia observed by a clinician

Subacute cutaneous lupus erythematosus- as observed by a clinician

- Annular or papulosquamous (psoriasiform) cutaneous eruption, usually photodistributed
- If skin biopsy is performed, typical changes must be present (interface vacuolar dermatitis consisting of a perivascular lymphohistiocytic infiltrate, often with dermal mucin noted).

Discoid lupus erythematosus –as observed by a clinician

- Erythematous-violaceous cutaneous lesions with secondary changes of atrophic scarring, dyspigmentation, often follicular hyperkeratosis/plugging (scalp), leading to scarring alopecia on the scalp
- If skin biopsy is performed, typical changes must be present (interface vacuolar dermatitis consisting of a perivascular and/or periappendageal lymphohistiocytic infiltrate. In the scalp, follicular keratin plugs may be seen. In longstanding lesions, mucin deposition may be noted)

Acute cutaneous Lupus - malar rash or generalized maculopapular rash observed by a clinician

- If skin biopsy is performed, typical changes must be present interface vacuolar dermatitis consisting of a perivascular lymphohistiocytic infiltrate, often with dermal mucin noted. Perivascular neutrophilic infiltrate may be present early in the course

Complete remission - is defined as a reduction in the proteinuria to <0.5 grams/24 hours with a return to normal serum creatinine and inactive urinary sediment (≤5 RBC/HPF, ≤5 WBC/HPF, no RBC casts)

Partial remission - a reduction in proteinuria to <3 grams/24 hours if it was in in the nephrotic range or a reduction by more than 50% if it was in the sub-nephrotic range, accompanied by stabilization of the serum creatinine to 25% of the baseline value or an improvement in the serum creatinine (reduction by more than 25%)

Non-response – is defined as increment in creatinine by more than 25% and not meeting criteria for partial or complete remission

Flare – is defined as increase in 24-hour protein to above > 2 grams/day or doubling, if > 3.5 grams /day after response and/or activity increase in urine sediment and/or increase in serum creatinine.

ESRD – Need for chronic dialysis for at least 3 months or transplantation

Favorable outcome – Defined as achievement of complete or partial remission at a defined period of time

Unfavorable outcome – is defined by presence of either death, ESRD or disappearance from follow up

## 4.6 Sample size and Sampling Technique

All patients who fulfill the inclusion criteria and who were diagnosed, treated and on follow up for a period of at least 1 month at the two centers from August 1, 2016 up to August 30, 2020 will be entered into the study.

## 4.7 Data Collection

Data was collected from medical records using a structured questionnaire. The questionnaire was prepared in English language and was adapted from other literatures and previous studies in a way that will address the objectives of this study.

The principal investigator was directly involved in the collection of data from patients' medical records, with supervision from the advisor. Data was checked for completeness and consistency before data entry.

## 4.8 Statistical analysis

Data was entered into SPSS version 21 manually. After data entry, data cleaning was done by running frequencies of each variable to check for accuracy, outliers and consistencies.

The continuous variables will be reported as means and standard deviation or as medians with interquartile range, and the categorical variables will be reported as numbers and percentages. Comparisons for categorical variables and continuous variables was done using a chi-square test and an independent sample t-test respectively. Association will be considered to be statistically significant when the p value is below 0.05. Variables which are found to be significant in univariate analysis will be run in to multivariate logistic regression model.

## 5. Ethical Consideration

Ethical approval was obtained from the ethical review committee of the department of internal medicine and the institutional review board and research and publication committee of the medical faculty of Addis Ababa University. All data was collected anonymously and was kept confidential. Collected data was only accessed by the investigators and had been kept with the utmost confidentiality.

## 6. Results

### Sociodemographic status

The study included a total of 97 patients. 67(69%) of them had follow up at Tikur Anbessa specialized hospital while 30(31%) had follow up at the private practice center. There were 89 females (92%) and 8 males (8.2%) with a sex ratio of 11:1. Mean age at initial presentation of LN was 27.4. Majority of the patients were from Addis Ababa (55%) and Oromia region (27%). The baseline demographic characteristics are depicted in table 1.

Table 1: Baseline sociodemographic status of 97 LN patients

| **Variable** | | Frequency (%) |
|---|---|---|
| **Gender** | Male | 8(8.2) |
| | Female | 89(91.8) |
| **Place** | Tikur Anbessa Specialized Hospital | 67(69.1) |
| | Private practice center | 30(30.9) |
| **Region** | Addis Ababa | 53(54.6) |
| | Oromia | 26(26.8) |
| | Amhara | 9(9.3) |
| | SNNPR | 6(6.2) |
| | Tigray | 1(1) |
| | Harar | 1(1) |
| | Somalia | 1(1) |

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## Clinical and Laboratory Characteristics

80(82.5%) patients had lupus nephritis at initial diagnosis of SLE, while the other 17 (17.5%) had a mean latency period of 6 months (range 1- 96 months) before developing nephritis. At initial presentation 52(53.6%) had body swelling evident on examination and 45(42.6%) were hypertensive. Baseline clinical and laboratory parameters are shown in Table 2.

Table 2: Baseline Clinical features of LN patients

| **Characteristics (n=97)** | **Value (Mean ± SD or %)** |
|---|---|
| Age at initial presentation (years) | 27.4 ± 9.5 |
| Gap between SLE and LN (months) | 6 ± 18.8 |
| Simultaneous diagnosis of SLE and LN (%) | 82.5 |
| Edema present (%) | 53.6 |
| Hypertension present (%) | 42.6 |
| Skin manifestations (%) | 52.6 |
| Oral Ulcers (%) | 10.3 |
| Hair loss (%) | 22.7 |
| Arthritis/Arthralgia (%) | 56.7 |
| Pericardial effusion (%) | 28.9 |
| Pleural Effusion (%) | 53.6 |
| CNS manifestations (%) | 10.3 |
| Anemia (%) | 78.4 |
| Thrombocytopenia (%) | 22.7 |
| Leucopenia (%) | 32 |
| Lymphopenia (n=64); (%) | 45.3 |
| Hematuria (%) | 71.1 |
| ≥3500mg 24 hour urine protein (%) | 27.3 |
| Cr ≥1.5 mg/dl (%) | 50.5 |
| CKD-EPI eGFR < 60 ml/min (%) | 51.6 |

SD: Standard deviation

Of the extra-renal manifestations, constitutional symptoms were present in 38(39.2%) patients, cutaneous manifestations in 51(52.6%) and joint involvement in 55(56.7%). Oral ulcers were found in 10 (10.3%) patients, while pleural and pericardial effusion were found in 52(53.6%) and 28(28.9%) patients respectively. CNS manifestations were evident in 10(10.3%) patients: seizure was seen in 5, transverse myelitis in 2, while delirium, movement disorders and optic neuritis were each seen in one patient. Hematologic involvement was seen in 85(87.6%) out of 89 patients who had documented CBC determinations. Anemia was present in 78.4%, leukopenia in 32% lymphopenia in 45.3% and thrombocytopenia in 22.7%. Mean hemoglobin was 10.11(SD =2.38)) mg/dl while the mean ESR was 87(SD=30) mm/hr.

At the initial presentation of lupus nephritis 69(71.1%) had hematuria and 21(27.3%) had nephrotic range proteinuria. Mean serum creatinine was 1.84 mg/dl (SD=1.5) with 49(50.5 %) patients having a value above or equal to 1.5 mg/dl. Four patients had required hemodialysis at initial presentation. Of the 95 patients that had ANA antibody determination, 87(91.6%) were found to be positive. Antids-DNA antibody was positive in 48(82.8%) out of 58 patients. Only 14 patients had complement level determinations, out of which 6(50%) and 9(64.3%) had low c3 and c4 levels respectively. Baseline laboratory features are shown in Table 3.

Kidney biopsies were done for 17(17.5%) patients. All were described based on the 2004 International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification. 12 were done at initial presentation of LN, while the other 5 were done during the course illness for indications of rising serum creatinine or urine protein. Biopsy findings were class III in 6(35.3%), class IV in 4(23.5%, class V in 3(17.6%), class VI in 2(11.8%) and Classes I and II seen in 1(5.9%) patient each. One of the patients with Class III has a mixed histology of class V and III.

Table 3: Baseline Laboratory Characteristics of LN patients

| **Variable (n=97)** | **Value (Mean ± SD or %)** |
|---|---|
| Hg, mg/dl | 10.11 ± 2.38 |
| WBC count, x $10^{3/}mm^3$ | 1.34 ± .91 |
| Platelet count x $10^{3/}mm^3$ | 247.4 ± 152.2 |
| ESR, mm/hour | 87 ± 30 |
| Serum Albumin, mg/dl (n=34) | 2.7 ± 0.76 |
| Creatinine, mg/dl | 1.84 ±1.54 |
| CKD-EPI eGFR | 69.76 ± 42.81 |
| Positive ANA (n=95); (%) | 91.6 |
| Positive Anti-dsDNA (n=58); (%) | 82.8 |
| Low C4 (n=12); (%) | 50 |
| Low C3 (n=14); (%) | 64.3 |
| Antiphospholipid Ab (n=5); (%) | 40 |
| Kidney Histology (n=17); (%) | |
| Class I | 5.9 |
| Class II | 5.9 |
| Class III | 35.3 |
| Class IV | 23.5 |
| Class V | 17.6 |
| Class VI | 11.8 |
| CKD-EPI eGFR Stages (%) | |
| Stage 1 | 30.9 |
| Stage 2 | 17.5 |
| Stage 3 | 29.9 |
| Stage 4 | 15.5 |
| Stage 5 | 6.2 |

SD: Standard deviation

## Treatment and Outcome

In both medical centers, patients with confirmed or presumed proliferative LN are given pulse steroids with 500-1000 mg IV infusion methylprednisolone or oral prednisolone at 2 mg/kg for 3 days and then steroids are continued with prednisolone of 1 mg/kg/day. For induction phase, cyclophosphamide is given based on the NIH protocol of monthly doses. MMF is started with 500 mg twice daily doses with subsequent escalation while azathioprine is dosed at 50-100 mg daily with similar gradual escalation. Maintenance constitutes similar doses of azathioprine and MMF, or quarterly cyclophosphamide infusions.

For LN with lesser degrees of severity, prednisolone at 1 mg/kg per day is initiated and then tapered within one to three months. All patients are started on oral daily chloroquine of 250 mg. ACE inhibitors drugs are added as needed. In all cases of LN steroids are tapered to 5 mg daily and continued indefinitely as maintenance.

Data on treatment and outcome was available for 94 patients. 70(74.5%) were treated with induction and maintenance regimens, 23(24.5%) with low dose steroid (prednisolone 1 mg/kg/day in combination with chloroquine) and 1(1.1%) with chloroquine only.

A total of 70 patients received induction treatment; 34(48.6%) received steroid pulse followed by cyclophosphamide, 14(20%) received cyclophosphamide only, 18(25.7%) took MMF while 4(5.7%) received azathioprine. All of them received low dose steroid and chloroquine in addition to the immunosuppressive regimen. Table 4 outlines the regimens used and their responses.

Only 59 patients were given maintenance treatment. Out of the 70 that received induction regimens, 3 had died, 3 were lost to follow up, 5 were yet to start maintenance therapy, 5 were not given, (1 had severe infection and 1 was diagnosed with flare while 3 others had no documented reason for failing to receive maintenance regimens). 5 of those patients who received maintenance are yet to reach 12 months for outcome assessment. So of the 54 eligible ones, 24(44.4%) were maintained with MMF, 21(38.9%) with quarterly cyclophosphamide while azathioprine was used for 9(16.7%) patients.

Data on outcome after 6 months of treatment was available for 94 patients. 73(77.3%) had remission, complete in 38(40.4%) and partial in 35 (37.2%). 3(3.2%) had died while 13 (13.8%) had no response. Of the 70 that took induction regimens 51(72.8%) had a favorable outcome

(complete or partial remission). It was observed in 39(81.2%) with cyclophosphamide, 9(50%) with MMF and 3(75%) with azathioprine.

Median follow up for the study was 41 months with a range of 1 to 200 months. 14(14.4%) patients were diagnosed with flares during their course of illness. Treatment included MMF in 6, pulse steroid with cyclophosphamide in 4, azathioprine in 3(1 after failure of cyclophosphamide) and 1 treated with oral angiotensin enzyme inhibitors (ACEI) only. 6 of those patients achieved remission subsequently.

94 patients had a documented outcome at the end of the study. 67(71.3%) patients had a favorable one with 52(55.3%) achieving a complete remission and 15(16%) others achieving partial remission. 1(1.1%) patient developed ESRD while 4 others had no response. 8(8.5%) patients had died with causes of death documented as complication of infection in 2, raised intracranial hypertension in 1 while no record of cause could be retrieved for the remaining 5.

Comorbidities were seen in 16(16.4%) patients. The most commonly observed was cardiac disease, with rheumatic heart disease in 3 and congenital heart disease in 2. Thyroid disorders were seen in 4, idiopathic pulmonary hypertension in 2 and type 1 diabetes mellitus in 2 patients. One patient had mixed connective tissue disease with concomitant Sjogren's syndrome and polymyositis. Migraine, chronic hepatitis c infection and bronchial asthma were seen in one patient each.

Infections were the most common complication observed seen during follow up, tuberculosis occurring in 5(5.3%) patients and other severe infections requiring hospitalization or parenteral medications occurring 10(10.6%). Avascular necrosis was evident in 4 and imaging evidenced thromboembolic events were present in 2 patients. Chloroquine induced corneal damage was seen in 4 while 2 female patients required termination of pregnancy for an active disease.

Table 4: Immunosuppressive regimens and their responses in LN patients

| | Induction Treatment | | | | Maintenance treatment | | | |
|---|---|---|---|---|---|---|---|---|
| | Cyclophosphamide | MMF | Azathioprine | Total | Cyclophosphamide | MMF | Azathioprine | Total |
| Response | 39 | 9 | 3 | 51 | 15 | 22 | 8 | 45 |
| % | 81.25 | 50 | 75 | 72.9 | 71.4 | 91.7 | 88.9 | 9 |
| Total | 48 | 18 | 4 | 70 | 21 | 24 | 9 | 54 |

## Factors associated with outcomes

At 6 months of follow up, 73(77.7%) had a favorable outcome, registering either a complete or partial response, while 21(22.3%) had an unfavorable outcome (either of death, no response or disappearance from follow up).

Of the baseline clinical and laboratory characteristics, only presence of nephrotic range proteinuria and longer gap between diagnosis of SLE and LN were found to be significantly associated with unfavorable outcome at 6 months. After adjusting for cofounders on multivariate analysis, only the presence of nephrotic range proteinuria was significantly associated with unfavorable outcome.

For outcome at end of study; follow up at Tikur Anbessa specialized hospital, non-response at 6 months and flare history were found to be significantly associated with unfavorable outcome at p value of 0.05 in both univariate and multivariate analysis. Tables 5 and 6 depict predictive factors for final outcome.

Table 5: Clinical characteristics and association with final outcome after univariate analysis

| **Variables, n=94** | **Final outcome** | | **p value** |
|---|---|---|---|
| | **Favorable** | **Unfavorable** | |
| | **n=67 (%)** | **n=27 (%)** | |
| Age, mean (years) | 28 | 25 | 0.19 |
| Gap between SLE and LN, mean, (months) | 7 | 4 | 0.45 |
| Follow up, Tikur Anbessa specialized hospital | 43(64.2) | 24(88.9) | 0.02 |

| | | | |
|---|---|---|---|
| Female | 63 (94%) | 23 (85.2) | 0.16 |
| Response at 6 month | 59 (88.1% | 14 (51.9) | <0.01 |
| Hypertension present | 29 (43.3%) | 10 (37.0) | 0.58 |
| Renal flare present | 6 (9.0%) | 8 (29.6) | 0.02 |
| Anemia | 53 (79.1%) | 20 (74.1) | 0.59 |
| Leukopenia | 20 (29.9%) | 10 (37.0) | 0.45 |
| ANA positive | 59 (90.8%) | 25 (92.6) | 0.67 |
| Anti dsDNA positive | 38 (86.4) | 8 (66.7) | 0.11 |
| Cr ≥1.5 mg/dl | 33 (49.3%) | 15 (55.6) | 0.58 |
| Nephrotic range Proteinuria | 13 (24.1%) | 8 (36.4%) | 0.28 |
| Creatinine baseline, mean, (mg/dl) | 1.80 | 2.00 | 0.58 |
| GFR via CKD EPI, mean (ml/min) | 73.74 | 60.88 | 0.15 |
| Serum albumin, mean (mg/dl) | 2.70 | 2.72 | 0.94 |

Table 6: Outcome and associated factors after bivariate analysis

| **Outcome** | **Variables** | **Adjusted OR(95% CI)** | **p value** |
|---|---|---|---|
| **6 month outcome** | Nephrotic range proteinuria | 3.69 (1.19-11.43) | 0.024 |
| | Gap between SLE and LN | 1.04 (0.96-1.13) | 0.305 |
| **Final outcome** | Follow up at Tikur Anbessa specialized Hospital | 4.35 (1.02-18.54) | 0.046 |
| | Response at 6 months | 0.07 (0.02-0.28) | 0.001 |
| | Absence of Flare | 0.15(0.03-0.76) | 0.003 |

## 7. Discussion

This study reports on the clinical characteristics, treatment patterns and outcomes of 97 cases of lupus nephritis from two centers in Addis Ababa, Ethiopia, making it the first of its nature. All patients had fulfilled the SLICC criteria for SLE and a chart based inquiry was used to reveal clinical and laboratory data.

A total of 89 females and 8 male patients were included in the study. Females were predominant with a sex ratio of 11.1 to 1. Mean age was 27.4 (SD =9.5), which was higher for females, 28, compared to males, 24. The sex ratio is comparable to most LN series including in non-native Africans. [7,10,25,28–31] Meanwhile, the age range in this study reveals a younger population in line with other African cohorts with 66% of patients aged below 30, which contrasts to the mean age of 35 in the international SLICC cohort, and a Medicaid record from the US showing only 28% of LN patients below 30. [7,10,25,30,31]

LN occurs in up to two thirds of SLE patients usually in the first few months of disease course. Seligman et al., in a multiethnic retrospective cohort from US, reported 57% of patients had LN at initial diagnosis of SLE. Other studies from Africa had values ranging from 34.8[30]upto 75%[31]with a mean latency period of 1 to 16 months. In this study 82.5% of patients had concomitant diagnosis SLE and LN, which is a relatively a greater proportion, hinting at a delayed presentation and/or diagnosis.

Commonest extra renal manifestation was hematologic, occurring in 87.6%, followed by mucocutaneous (60.8%) and joint (56.7%). The latter two were the predominant ones reported in two studies from Egypt (84% and 96% respectively)[30] and Senegal(93% and 67% respectively)[32]. Anemia was evident in 78.4% with a mean Hg of 10.4 which was comparable to studies in Saudi Arabia (76%), Morocco (91%) and Senegal (100% with mean Hg of 9.4) [25,31,32]

Nephrotic range proteinuria at first presentation found in 27.3% of patients in this LN study which was comparable to studies in Egypt (28.1%) and Saudi Arabia (20.7%); while being significantly lower than those from Senegal (45.2%) and Cape Town, South Africa(45%)[25,28,30,32]. Impaired kidney function was pronounced in this study, with 51.6% of patients having eGFR below 60 ml/min at presentation. This is considerably higher than the 13.4% from the SLICC international cohort, or 31.4% in a South African study. Prevalence of hypertension (42.6%) was also higher

than studies from Morocco (33.6) and South Africa (31%), but comparable to an Egyptian (54.6%) one[30,31,33].

Positivity rates of ANA and antids-DNA were seen in 91.6 and 48.6% in this study respectively. Al Arfaj et al. reported ANA in 99.3% and anti-dsDNA in 81.6% out of 299 patients[25]. Low complement levels have been reported in 60- 80% of patients in multiple studies. In the current study low c4 and low c3 were seen 50 and 64% of patient respectively.

Kidney biopsies were done for 17 patents only in the current study, most (69%) having a proliferative nephritis, class III in 35.3% and class IV 23.5%. In most studies, the commonest histological class, accounting for 40 to 70%, was class IV[33]. In the study by Brijlal et al., class IV accounted for 55% of 315 cases of LN[28]. Studies from Morocco and South Africa also reported a majority of class IV in ranges of 20.7% to 62.5%. Notably, the two class VI reports in the study were from biopsies taken during the course of illness and not at initial presentation.[29,31].

70 of the 94 patients in the current study received induction immunosuppressive regimens. A systemic review by Ameh et al. which explored treatment modalities in Africa revealed that cyclophosphamide had been used in 93% of patients while MMF was used in 0.4 to 15.6% of patients[17]**.**

In this study, cyclophosphamide was used in the majority (68.6%) and had a response rate of 81.2% which was comparable to a South African study in which response was seen in 72.2%. While MMF, used in 25.7% of patients, had a response rate of 50% as compared to 81% in the same South African study[33] Remission rates for MMF have been reported as 52 and 82.6% in **s**tudies by Ginzler et al. and Lu et al. respectively. [36,37]Maintenance regimens with cyclophosphamide and MMF achieved response rates of 71.4 and 91.7% respectively, which are comparable to the South Africans with rates of 90% and 68.4% respectively.[33]

Overall the rate of favorable outcome after 6 months of treatment was 77.7% in this study. In the subgroup of patients who took induction regimens, complete or partial remission was achieved in 72.9%. This was comparable to 81.6% from Mody et al., and higher than a Senegalese study of 95 patients with a rate of 57.2% after induction[33].

At the end of a follow up, 71.3% had a response, while 1.1% had developed ESRD and 8.5% have died. In the subset of 70 patients who received induction/maintenance regimens, 68.6% had a favorable outcome, 1% developed ESRD and 10% had died. Response rate is comparable to studies from Saudi Arabia (75.6%), South Africa (73.6%), and considerably higher than one from Morocco (45.5%). [25,31,33]

Rate of ESRD (1.1%) was lower in this study compared to 9 to 20% reported in the studies from South Africa and Saudi Arabia. Similarly those studies reported higher rates of death than in this study, ranging from 12.6% up to 16%[30,31], while others from Saudi Arabiya and South Africa had comparable rates[25,33]. The lower event rates could partly be explained by a survivor bias, with patients with favorable outcome more likely to appear for follow up and have complete records.

Most studies had identified male gender, hypertension at onset of nephritis, lower eGFR at onset of nephritis, lymphopenia, nephrotic range proteinuria, presence of ANA antibodies and lack of remission following induction therapy as predictors of adverse outcomes in LN[30,34,35]. In the current study, follow up at Tikur Anbessa specialized hospital, history of renal flare and an absence of response at 6 months were found to be significantly associated with unfavorable outcomes. The difference in outcome between the two centers is most likely to be due to a better follow up at the private practice with the same nephrologists operating at the two sites. Additionally, patients at the private practice, requiring admission, especially for severe disease are usually referred to the public one, with a possible referral bias.

## 8. Conclusion

This study demonstrates that LN, in Ethiopian patients, mostly diagnosed concomitantly with SLE and presents at a relatively younger age group and with a higher degree of impairment of kidney function. The response rates to standard treatments are comparable to the ones from most literatures.

## 9. Recommendation

While under-diagnoses and under-reporting have accounted for the perceived rarity of SLE and LN, they ought to be given more attention by all stakeholders as the treatment responses have been encouraging. Clinicians should be adept at diagnosing SLE and LN with proper referral and management. Additionally further studies including prospective ones are required to illuminate the whole spectrum of SLE and LN in Ethiopian patients.

## 10. Limitation of the study

As the study was retrospective and chart based, many patients had to be excluded due to incomplete records. Diagnosis of LN was mostly clinical as kidney biopsies were limited to only a few patients for reasons associated with cost and availability. Additionally there might be a bias towards patients with better outcome as they were more likely to attend follow up and have more complete records

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## 12. Annex

## Annex 1: Declaration

I, the undersigned, declare that this postgraduate thesis is my original work, has not been presented for a degree in this or any other university and that all sources of material used for the thesis have been duly acknowledged.

Postgraduate Candidate: Seife Fekade (MD, Internal Medicine Resident)

Signature: _____

Date: _____

This thesis has been submitted with my approval as advisor:

Advisor: Yewondwossen Tadesse (MD, Internist and Consultant Nephrologist)

Signature: _____

Date: _____

Place: Addis Ababa, Ethiopia

## Annex 2: Questionnaire

### 1. Sociodemographic Status

| No | Variables | Response |
|---|---|---|
| 1.1 | Age | _____ years |
| 1.2 | Sex | 1. Male 2. Female |
| 1.3 | Employed | 1. Yes 2. No |
| 1.4 | Religion | 1. Muslim<br>2. Protestant<br>3. Orthodox<br>4. Catholic<br>5. Other specify_____ |
| 1.5 | Region | 1. Oromo 6. Gambella<br>2. Amhara 7. Benishangul Gumuz<br>3. Tigray 8. Harar<br>4. Afar 9. Addis Ababa<br>5. Somalia 10. Other_____ |

## 2. Baseline Clinical and Biological Features

**2.1 Chief Complaint_____**

**2.2 Blood Pressure**

| | |
|---|---|
| BP ≥ 140/90 | A. Yes B. No C. Not documented |

**2.3 Constitutional symptoms**

| | |
|---|---|
| Fever | A. Yes B. No C. Not documented |
| Fatigue | A. Yes B. No C. Not documented |
| Weight Loss | A. Yes B. No C. Not documented |

**2.4 Skin Manifestation**

| Variable | Historical | If Yes, Physical Finding Description |
|---|---|---|
| Rash | A. Yes B. No | |
| Oral Ulcer | A. Yes B. No | |
| Hair loss | A. Yes B. No | |

**2.5 Serosal Features**

| Variable | | Response |
|---|---|---|
| Historical Chest Pain or Cough | | A.Yes B. No C. Not Documented |
| Pleural Effusion | Signs of pleural effusion | A.Yes B. No C. Not Documented |
| | CXR/Chest Us/ Chest CT evidence | A.Yes B. No C. Not Documented |

| | | |
|---|---|---|
| Pericarditis | Signs of Pericarditis | A.Yes B. No C. Not Documented |
| | ECG/Echocardiography evidence | A.Yes B. No C. Not Documented |

Additional findings on Echo_____

Additional findings on Chest x-ray or Chest CT if any_____

**2.5 Nervous System**

| Variable | Response |
|---|---|
| Change in consciousness/arousal | A.Yes B. No C. Not Documented |
| Memory deficit | A.Yes B. No C. Not Documented |
| Disorientation | A.Yes B. No C. Not Documented |
| Change in behavior | A.Yes B. No C. Not Documented |
| Change in mood or affect | A.Yes B. No C. Not Documented |
| Hallucinations | A. Yes B. No C. Not Documented |
| Delusions | A.Yes B. No C. Not Documented |
| Abnormal body movement | A.Yes B. No C. Not Documented |

Brain MRI or/and CT findings if any _____

NCT findings if any_____

**2.6 Joint manifestations**

| Variable | Response |
|---|---|
| Historical Joint pain and swelling | A.Yes B. No C. Not Documented |
| Signs of Joint Tenderness and swelling | A.Yes B. No C. Not Documented |

## 2.7 Renal Manifestations

### 2.7.1 Clinical Values

| Variable | | Response |
|---|---|---|
| History | Leg/facial swelling | A.Yes B. No C. Not Documented |
| | Urine amount change | A.Yes B. No C. Not Documented |
| | Urine color change | A.Yes B. No C. Not Documented |
| | Flank pain | A.Yes B. No C. Not Documented |
| Physical | Leg and/or Facial swelling | A.Yes B. No C. Not Documented |

### 2.7.2 Laboratory Values

| Variable | | Finding | Normal value | Remark |
|---|---|---|---|---|
| Urine Analysis | Albumin | | | |
| | Blood | | | |
| | Cellular cast | | | |
| | Granular Cast | | | |
| | WBC/hpf | | | |
| | RBC/hpf | | | |
| | 24 Hour Urine Protein (Gm) | | | |
| RFT | Creatinine | | | |
| | BUN | | | |
| Electrolyte | Sodium | | | |
| | Potassium | | | |
| | chloride | | | |
| Kidney Biopsy finding | | | | |

## 2.8 Hematology and Serology

### 2.8.1 Hematology Features

| Variable | | Finding | Normal value | Remark |
|---|---|---|---|---|
| WBC | | | | |
| Lymphocyte | | | | |
| Hemoglobin | | | | |
| Platelet | | | | |
| ESR | | | | |
| Hemolytic anemia | LDH | | | |
| | Total Bilirubin | | | |
| | Coombs test | | | |

### 2.8.3 Serology profile

| | Value | Normal | Remark |
|---|---|---|---|
| ANA | | | |
| Anti DsDNA | | | |
| HbsAg | | | |
| Anti HCV | | | |
| HIV Ab | | | |
| C3 | | | |
| C4 | | | |
| Antiphospholipid Ab | | | |

## 2.9 Gastrointestinal System

### 2.9.1 Clinical Features

| Variable | Response |
|---|---|

| | |
|---|---|
| Ascites | A.Yes B. No C. Not Documented |
| Hepatomegaly | A.Yes B. No C. Not Documented |
| Splenomegaly | A.Yes B. No C. Not Documented |

### 2.9.2 Laboratory Values

| Variable | Finding | Normal values | Remark |
|---|---|---|---|
| Alt | | | |
| Ast | | | |
| Alkaline phosphatase | | | |
| Albumin | | | |
| Total protein | | | |
| Total Bilirubin | | | |

### 2.10 Comorbidity documented if any

_____

## 3. Diagnosis and Treatment

## 3.1 Diagnosis

**3.1.1 Age at SLE diagnosis**_____ years

**3.1.2 LN Diagnosis at onset of SLE** A. Yes B. No

**3.1.3** If **No to Question 3.1.2, Age at LN diagnosis**_____ Years

## 3.2 Treatment

| Stage | Medication | Dose | Duration | Remark |
|---|---|---|---|---|
| induction | Cyclophosphamide | | | |
| | MMF | | | |
| | Azathioprine | | | |
| | Methylprednisolone | | | |
| | Prednisolone | | | |
| Maintenance | Cyclophosphamide | | | |
| | MMF | | | |
| | Azathioprine | | | |
| | Prednisolone | | | |
| Chloroquine phosphate | | | | |

**Remark**_____

_____

_____

_____

## 4. Follow Up

**4.1 Required acute need for dialysis** A. Yes B. No

**4.2 Outcome at end of follow up**

1. Remission
2. ESRD
3. Death

   Cause_____

   Months after diagnosis of LN_____
4. Lost to follow up

**4.3 Total duration of follow up _____** months

**4.4 Flare History** A. Yes B. No

**4.4.1 If Yes, Treatment given_____**

**4.5 Follow up data**

| | Baseline | 6 months after induction | 12 months after induction | End of follow up |
|---|---|---|---|---|
| Cr | | | | |
| Urine RBC | | | | |
| Urine cellular casts | | | | |
| 24 hour Urine protein | | | | |
| Outcome | | | | |

**4.6 Complications Documented**

A. Infection B. Malignancy C. Others_____