



ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

Clinical Characteristics and Predictors of Outcome of SLE patients admitted to Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia

Proposal by: Dr Robel Engida (final year internal medicine resident)

Advisor: Dr. Birhanu Demelash (M.D. Consultant Internist and Rheumatologist)

ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCES, SCHOOL OF MEDICINE
DEPARTMENT OF INTERNAL MEDICINE

Addis Ababa, Ethiopia
February 2024

ADDIS ABABA UNIVERSITY

**COLLEGE OF HEALTH SCIENCES, SCHOOL OF MEDICINE
DEPARTMENT OF INTERNAL MEDICINE**

A research proposal Submitted to the Department of Internal Medicine for the fulfillment of specialty certificate for Internal Medicine

Research title	Clinical Characteristics and Predictors of Outcome of SLE patients admitted to Tikur Anbessa specialized hospital, A two year retrospective chart review
Study Area	Tikur Anbessa specialized hospital
Study Period	From October 2023 up to February 2024
Principal Investigator	Robel Engida Zemedagegnehu (MD) Email: robelengida@gmail.com Phone: +251912-608800
Advisor	Dr. Birhanu Demelash (M.D. Consultant Internist and Rheumatologist)

Addis Ababa, Ethiopia
February 2024

List of Acronyms

AAU Addis Ababa University

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

EULAR/ACR The European Alliance of Associations for Rheumatology (EULAR; formerly known as European League Against Rheumatism)/American College of Rheumatology (ACR)

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

ICU Intensive care unit

ISN/RPS International society of nephrology/Renal pathology society

LN Lupus nephritis

LUMINA (Lupus in Minorities: Nature vs. Nurture) cohort, are the outcome of the interplay between genetic and non-genetic (environmental, socioeconomic-demographic, cultural, and behavioral) variables.

MD Doctor of Medicine

MDRD Modification of diet in renal disease

mg Milligram

ml/min Milliliters per minute

NIH National Institute of Health

NCT Nerve conduction test

OR Odds ratio

OI Opportunistic Infection

RBC Red blood cell SD Standard deviation

SLE Systemic lupus erythematosus

SLEDAI Systemic Lupus Erythematosus Disease Activity Index

SLICC Systemic lupus international collaborating clinics

SPSS Statistical package for social science study

TASH Tikur Anbessa specialized hospital

US United States

WBC White blood cell

ACKNOWLEDGMENT

I would like to extend my sincere gratitude to my adviser, Dr. Birhanu Demelash for the significant contributions he has made for this research. Being able to work with and learn from him was an honor and has greatly influenced me to select this specialty as my desired subject of study. I also want to thank the Department of Rheumatology for their tireless work improving the care of what was until recently, an obscure and neglected group of diseases in this country.

I would like to thank Addis Ababa University, college of health sciences, department of internal Medicine, for offering me the chance to conduct this study and then funding the whole study.

Summery

Introduction: Systemic lupus erythematosus (SLE) is a multi-system connective tissue disorder characterized by the presence of multiple antibodies directed against components of cell nuclei driven by defective clearance of antigens through apoptosis.(1,2) Even though the exact etiology and pathogenesis of SLE is not clearly understood, the clinical manifestations are either directly or indirectly mediated by antibody formation and the creation of immune complexes (IC). The characteristics of the antibody, such as, quantity, its binding site, affinity, charge, and ability to activate complement or other mediators of inflammation. In the glomerulus, for example, the binding sites of different antibodies on the glomerular capillary wall lead to different manifestations.(3,4)

Objective: The objective of this study is to describe the characteristics and poor prognostic factors in SLE patients admitted to Tikur Anbesa Specialized Hospital, Addis Ababa, Ethiopia.

Method: This will be a retrospective study of all patients with SLE admitted to the department of internal medicine at Tikur Anbessa Hospital, in Ethiopia during a 2-year period between October 2021 and December 2023.

Result: The findings of the study will be summarized and presented in percentage, tables and figures.

Conclusion: Finally, the finding will be concluded with main finding.

Funding Sources: College of Health Sciences, Addis Ababa University. A total of 25, 000 ETH BIRR is allocated and the research will be finalized by the end of November 2023.

Contents

1. Introduction.....	9
2. Literature Review.....	10
2.1 Magnitude of SLE.....	10
2.2 SLE in the African Experience.....	11
2.3 Hospitalization and Outcomes in SLE.....	12
3. Objectives.....	13
3.1 The general objective.....	13
3.2 Specific objectives.....	13
4. Methodology.....	13
4.1 Study area and Study period.....	13
4.2 Study Design.....	14
4.3 Population.....	14
4.3.1 Source population.....	14
4.3.2 Study population.....	14
4.4 Eligibility Criteria.....	14
4.4.1 Inclusion Criteria.....	14
4.4.2 Exclusion Criteria.....	14
4.5 Sampling size and Sampling Technique.....	14
4.6 Data collection.....	15
4.7 Study Variables.....	15
4.7.1 Independent Variables.....	15
4.7.2 Dependent Variables.....	15
4.8 Operational Definitions.....	15
4.9 Data quality control.....	16
4.10 Data processing and analysis.....	16
5. Ethical clearance.....	17
6. Dissemination of result.....	17
7. Results.....	18
Table 1. Sociodemographic Characteristics of hospitalized SLE patients.....	18
Table 2. Details of Clinical features before or during Admission.....	19
Table 3. Serologic and Laboratory.....	20
Table 4. Comorbidities in Admitted Patients.....	21
Table 5. Medications Table.....	7. Primary Diagnosis on Admission
Table 6. Reasons for Admission.....	21
Table 8. Final Outcomes.....	21

9. Discussion..... 22

10. Limitations of the study.....24

12. References..... 24

Automatic citation updates are disabled. To see the bibliography, click Refresh in the Zotero tab.....24

13. Annexes..... 24

 13.1 Annex 1: Declaration.....24

 13.2: Questionnaire..... 25

1. Introduction

Systemic lupus erythematosus (SLE) is a multi-system connective tissue disorder characterized by the presence of multiple antibodies directed against components of cell nuclei driven by defective clearance of antigens through apoptosis.(1,2) Even though the exact etiology and pathogenesis of SLE is not clearly understood, the clinical manifestations are either directly or indirectly mediated by antibody formation and the creation of immune complexes (IC). The characteristics of the antibody, such as, quantity, its binding site, affinity, charge, and ability to activate complement or other mediators of inflammation. In the glomerulus, for example, the binding sites of different antibodies on the glomerular capillary wall lead to different manifestations.(3,4)

SLE is a worldwide disease that has a profound predilection for affecting women of childbearing age. The ratio of females to males is from 7:1-15:1 from different studies.(5–7) The reported prevalence of systemic lupus erythematosus (SLE) in US adult population is 20 to 200 cases per 100,000((5,6,8,9). The prevalence is highest in African-American women.(5,6) The prevalence in Black females is estimated to be at least two times higher than Caucasians.(10) SLE begins earlier in the reproductive years of black females and tends to be more active and severe, with increased burden of renal disease and likely progression toward End stage renal disease(ESRD).(11–13) Low socioeconomic status also contributing to these findings. In men with SLE there tends to be higher frequencies of renal disease, skin manifestations, serositis, neurologic, hematologic and cardiovascular involvement with hypertension and vasculitis.(14) Most studies also suggest poorer prognosis in male patients with SLE.(14,15) There is a disposition for SLE to be milder in older adults with presentations more in line to drug Induced Lupus.(16)

The mortality and morbidity associated with lupus is substantial, but due to early disease recognition and treatment, increased awareness, more sensitive diagnostic tests, judicious therapy, and early identification of complications improvements have been seen.(17,18) Some of the highest rates of hospital admissions is in SLE patients even when compared to other chronic medical illnesses, as well as higher in-hospital mortality and other OIs.(19,20) Repeated admissions overburden the already overwhelmed capacity for the health care system of poor countries.

It is believed that infectious diseases are more common and autoimmune and allergy diseases are less common in low- and middle-income countries.(21) Though there are limited studies in the African population, SLE and other autoimmune illnesses are more common than was previously believed, and should not be neglected.(22,23) Although under-recognized and under-reported in developing countries, SLE occurs worldwide, even-though there exists substantial age and racial differences.(24) These variations in disease manifestation, according to studies from the LUMINA (Lupus in Minorities: Nature vs. Nurture) cohort, are the outcome of the interplay between genetic and non-genetic (environmental, socioeconomic-demographic, cultural, and behavioral) variables.(25) Patients in developing countries particularly in sub-Saharan countries have poor outcomes due to lack of awareness among the general public and health professionals. (26,27) There are other challenges in caring for patients in sub-Saharan Africa. These include but are not limited to very few number of Rheumatologists, lack of Accurate and Sensitive diagnostic modalities, drugs mostly substandard when achievable and unaffordable when available, and inadequate in-patient support such as intensive care units (ICUs).(23,28)

Data on rheumatic disorders, including SLE, are lacking in Ethiopia. Although there are significant number of patients seen at our Rheumatology clinics there are few studies addressing the burden, clinical

patterns, and outcomes of patients. Ethiopian patients as their African-American counterparts tend to be younger during presentation with earlier and higher incidence of Renal manifestations and higher proportions ESRD than the international SLICC cohort.(29,30) Even though the pattern of systemic involvement is well studied it is affected by environmental, socioeconomic-demographic, cultural, and behavioral variables.(22,25) Studying the patterns of presentation can help us form a better understanding of the disease in our context. It also allows us predict the clinical progression and focus our efforts in mitigating the common short and long term complications by better directing our limited resources. Because SLE patients have repeated admissions, recognizing the trends and predictors of complications and comorbidities can further enhance outcomes.(20,31) Previous studies have indicated in-hospital mortality associated with SLE is three to five higher in Sub-Saharan Africa.(11,32–34) Rooting out the causes for the discrepancies will help address the gaps in diagnosis, management and overall care. Optimizing existing therapeutic modalities and mobilizing our health sector our best tools in fighting this emerging condition. This study is intended as a supportive tool in achieving that goal. From literature-review of accessible sources such as (google scholar, Pubmed, and other online sources) there is a severe limitation of data on SLE epidemiology, thus leading to this study. The results and identified gaps of this study can be used as an input in improving the overall management of SLE both the in-patient and out-patient setups in Ethiopia.

2. Literature Review

2.1 Magnitude of SLE

In a four-year examination of Medicaid data from the US, where the prevalence of SLE was estimated to be 143 per 100,000, African Americans had an incidence that was much greater than that of whites, at 31.2/100,000 person-years compared to 18/100,000 person-years.(35)

The highest values for incidence and prevalence of SLE were discovered in North America, with rates of 23.2 per 100,000 person-years and 241 per 100,000, respectively, in a systematic assessment of the disease's incidence and prevalence from 2017.(24)

In a UK study, incidence during the study period was 4.91/100 000 person-years (95% CI 4.73 to 5.09) and prevalence was 97.04/100 000 in 2012 (95% CI 94.18 to 99.90) (0.097%). SLE was six times more common in women. The incidence peaked in the 50s with incidence and prevalence highest in minorities.(36)

In the LUMINA study Hispanic patients from Texas had the highest rate of activity(damage) accrual (1.72 events per month) followed by the African Americans (1.17 events per month); the Caucasians and Puerto Rican Hispanics had similar rates and lower than for the African Americans and Hispanics from Texas (0.89 and 0.86 events per month, respectively).(25)

A detailed examination of ethnic analyses has shown that Black Americans, Afro-Caribbeans, and Asian communities have greater rates of SLE than do white people. The incidence and prevalence of SLE on the African continent are relatively low, in contrast to the high prevalence of SLE among people of African heritage recorded in US and European studies. This is mostly explained by the disease's underreporting and underdiagnosis.(37)

In a review of 52 male lupus patients it was found an increased incidence of thrombocytopenia and renal disease but other differences were minor if present at all. The early peak in the age of onset of disease similar to that found among female SLE patients.(14)

In the Michigan Lupus Epidemiology and Surveillance Program Incidence and prevalence were 5.5 per 100,000 persons and 72.8 per 100,000 persons. Among females, the incidence was 9.3 per 100,000 persons and the prevalence was 128.7 per 100,000 persons. The prevalence of SLE was 10-fold higher in females than in males, and 2.3-fold higher in Black people than in White people. Compared to white SLE patients (18.8% and 4.5%, respectively), black SLE patients showed greater rates of renal disease and end-stage renal disease (ESRD), at 40.5% and 15.3%, respectively. Compared to White patients with renal disease (mean 34 and SD 14.9 years versus 41.9 and 21.3 years), Black patients with renal disease received their SLE diagnosis at a younger age.(10)

2.2 SLE in the African Experience

In the United States to Africa lupus prevalence gradient, two unique cohorts of individuals of African heritage. There are unique cultural and ancestral links between the Gullah of South Carolina and the people of Bo, Sierra Leone. It was demonstrated that the overall prevalence of autoantibodies is similar in controls from the groups.(22)

Overall mortality was high(42%) in a South African study that looked at clinical features and outcome of lupus myocarditis. Treatments included were corticosteroids (96%) and cyclophosphamide (75%) and 14% of patients required additional immunosuppression. Improvement was seen in LVEF with treatment($p=0.023\%$). Patients that dies had longer duration of SLE.(38)

In another south african study Arthritis, nephritis and neuropsychiatric disease had a cumulative frequency of 70.4, 43.8 and 15.9% of patients, respectively. The estimated 5 yr survival rate was approximately. 65%. Renal failure(16.4%) and infection(32.7%) were the two most frequent causes of mortality.(27)

A case review of 315 LN patients from Cape Town, South Africa, spanning three decades, was conducted. 78% of patients had mixed ancestry, and 90% of patients were female. According to the 2003 ISN/RPS classification of LN, 55% of patients had Class V illness on renal biopsy, with a mean age at diagnosis of 31.5. The majority of patients (55% of cases) presented with nephritic syndrome. At diagnosis, over 50% of patients had hypertension and significant proteinuria, and 13% of patients had advanced renal disease.(39)

Sabary et al. in Egypt compared the use of high dose intravenous cyclophosphamide (1 g/dose monthly for 6 months) and low dose intravenous cyclophosphamide (500 mg/dose fortnightly for 3 months), followed by treatment with azathioprine in each arm, and reported rates of remission and similar rates of infection in both groups.(40)

A retrospective study of SLE patients seen in a rheumatology clinic over a 6-year period in Nigeria. Polyarthralgia/polyarthritis(87%),m Fever(50%), Hair loss(45%), Discoid rashes,(43.9%), Weight loss(42.4%), Mouth/pharyngeal ulcer (33%) and Fatigue (27.3%) were the commonest manifestations.

Significant positivity of extractable nuclear antigen (71.4%) in those tested was seen as well as anti-Sm (63.6%) and anti-RNP (66.7%). A very high titre of anti-nuclear antibody was positive, with 63% of individuals tested exhibiting positivity at titers of 1:640 and above. (26)

The majority of the 114 LN patients in a Moroccan single-center research were female, with a female to male ratio of 7.76. a 29.6-year-old median (SD of 9.8). Joint (85%) and skin (74%) symptoms were the two most frequent ones to appear. An average of 9 months passed between the diagnosis of SLE and LN. 33.3% of patients had hypertension at the time of presentation. In 76.3% of patients, hematuria was seen. Renal failure was identified in 68 cases (59.6%) and nephrotic syndrome in 60 patients (52.6%). 17 patients (14.9%) needed immediate renal replacement treatment.(41)

A study that reported on the clinical characteristics, treatment patterns and outcomes of 97 cases of lupus nephritis from two centers in Addis Ababa, Ethiopia, showed Females were predominant with a sex ratio of 11.1 to 1. Hematologic manifestations occurred most frequently (87.6%), followed by mucocutaneous manifestations (60.8%), and joint manifestations (56.7%). Cyclophosphamide was used in the majority (68.6%) and had a response rate of 81.2%, while MMF, used in 25.7% of patients, had a response rate of 50%. Overall, the rate of favorable outcome after 6 months of treatment was 77.7% in this study. (29)

2.3 Hospitalization and Outcomes in SLE

A danish study that looked at a total of 101 of the 155 SLE patients (65%) had one or more hospitalization during the study period. Leading causes of admission were complications to SLE or its treatment, but infections were also common. Mean duration of hospital stay was 6.4 ± 10.5 days, and SLE Disease Activity Index 2000 (SLEDAI-2K) on admission was the main risk for prolonged hospital stay.(42)

A retrospective study from Singapore from 348 episodes of hospitalization of 223 individuals found the cause of admission was clinical flare of SLE (58%), infection (37%) and thromboembolic disease (8%). Readmission occurred in 35.8% and was associated with: active nephritis (HR 2.53, $P < 0.01$), flare of lupus (HR 2.0, $P < 0.01$). Individuals with multiple reasons for admission had a longer duration of stay. There were 11 deaths (3.2% of admissions). The deaths were due to infection in nine cases (four with concurrent active SLE). The main predictors of death were. previous multiple admissions (OR 12.4, $P < 0.01$), the presence of infection (OR 7.3, $P < 0.01$) and younger age (OR 0.93 per increase of one year, $P < 0.03$). (34)

In an analysis of the US Nationwide Inpatient Sample, encompassing a cohort of 76,961 hospitalizations over a five-year period from 1998 to 2002, it was observed that 11% of these admissions were attributable to systemic lupus erythematosus (SLE) or exacerbations of the disease. The mortality rate among hospitalized patients was 3.1%, with 2,454 deaths recorded. Notably, 50% of these fatalities occurred within the first seven days of admission. Furthermore, a disparity in mortality outcomes was evident, favoring patients belonging to higher income brackets and those covered by private insurance plans. (32)

In a Tunisian study, that assessed 128 admissions, the most common cause of Admission was Active SLE in 43%. Other causes of admission include infection(9.4%), associated Autoimmune

disease(6.25%), Adverse drug reaction(3.1%) and Thromboembolism(1.25%). 3% of admissions ended up in death.(19)

From 125 episodes of hospitalization of 79 patients with SLE that was seen in a Malaysian study, the cause of admission was flare of SLE (80.8%), infection (23.2%), renal biopsy (22.4%) and others (4%). There was only one admission for thromboembolism. Patients with both flare of SLE and infection have the longest median length of stay of 11 days, requiring more intensive care therapy ($P < 0.01$). Readmission occurred in 31.4% and was associated with admission for other reasons during the first admission. There were six deaths (4.8% of admissions). The deaths were due to infection in three patients, active SLE in two and acute myocardial infarction in one. The deaths have a higher cumulative prednisolone dose than the survivals ($P < 0.01$). The only predictor of death was high Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index score ($P < 0.05$). (33)

A study from Ghana that looked at admission patterns of 51 patients in which 86.5% were female showed the cause of admission was clinical flare of SLE in 86.3% and infection in 56.9%. There were 22 deaths (43.8% of admissions) which were mainly due to infection and renal (43)

3. Objectives

3.1 The general objective of this study is to describe the characteristics and poor prognostic factors in SLE patients admitted to Tikur Anbesa Specialized Hospital, Ethiopia.

3.2 Specific objectives of this study are:

- To characterize demographics of Admissions with SLE
- Understand causes of Admission
- Characterize predictors of Mortality and poor outcomes

4. Methodology

4.1 Study area and Study period

The study will be done in Tikur Anbesa Specialized Hospital (TASH) in Addis Ababa, the capital city of Ethiopia. TASH is the largest tertiary hospital in Ethiopia, offering diagnosis and treatment for approximately 370,000–400,000 patients per year. The study will be mainly done at Rheumatology, Renal wards, and ICU but other wards such as Obg wards may be used if patients have a complicated/protracted course. Other inpatient setups may be included if patients that fulfill the inclusion criteria are found. The study will be conducted over two years between October 2021 and December 2023.

4.2 Study Design

This will be a retrospective study of all patients with SLE(as defined by the 2019 EULAR/ACR criteria) admitted to the department of internal medicine at Tikur Anbessa Hospital, in Ethiopia during a 2-year period between October 2021 and December 2023. Data will be collected on patients admitted during the two-year period to describe the characteristics, out-come, the incidence and risk factors for hospitalization in SLE. To gather information on the patients' clinical features, therapies used, and outcomes, both computerized and paper records will be examined. When a patient's outcome record is lacking, the ultimate outcome will be determined via phone contact.

4.3 Population

4.3.1 Source population

Adult patients with possible/probable or definite SLE who visited Tikur Anbessa Specialized Hospital in the past 02 years.

4.3.2 Study population

Adult patients with definite SLE and were admitted to TASH in the past 02 years.

4.4 Eligibility Criteria

4.4.1 Inclusion Criteria

All hospitalizations for all adult (age > 18 yrs) patients with SLE
Patients diagnosed as ANA-negative Lupus by a qualified Rheumatologist.

4.4.2 Exclusion Criteria

Patients that don't fulfill the 2019 EULAR/ACR diagnostic criteria for Definite Lupus
Those whose charts were not retrievable.

4.5 Sampling size and Sampling Technique

The trial will enroll all patients who meet the inclusion criteria and who were identified, treated, and had follow-up at one of the two facilities between October 2021 and December 2023.

4.6 Data collection

A systematic questionnaire will be used to gather information from medical records. The questionnaire was created in English and modified from other works of literature and earlier research in order to satisfy the study's objectives. The principal investigator will be 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.

4.7 Study Variables

4.7.1 Independent Variables

Socio-Demographic factors (Age, Sex, residence)
Age at Diagnosis
Clinical characteristics
Cause of Hospitalization
Laboratory Results and Histopathology
Treatment Modality

4.7.2 Dependent Variables

Length of Hospital stay
Frequency of Re-admissions
ICU admission
Death

4.8 Operational Definitions

Systemic Lupus Erythematosus- Patients are classified as having SLE with a score of 10 or more points according to the 2019 EULAR/ACR criteria, or patients diagnosed as ANA-negative Lupus by a qualified Rheumatologist.

Lupus Nephritis- An inflammation which affects the nephrons within the kidneys as a result of the complication of SLE. The patient should fulfill the diagnosis of KDIGO criteria. These includes proteinuria of 0.5 g/d and above, serum creatinine of 1.5 mg/dl and above or evidence of decreased or decreasing eGFR, active urinary sediment ($\geq 5\%$ RBC/HPF, $\geq 5\%$ WBC/HPF cellular casts) and biopsy-proven LN.

Hypertension- Blood pressure above or equal to 140/90 mmHg or using of antihypertensive medications on regular follow-up.

Leucopenia- WBC count of $< 4000/\text{mm}^3$ in the absence of other causes (at least once ruled out other causes).

Thrombocytopenia- Platelet count of $< 100,000/\text{mm}^3$ at least once ruled out other causes.

Acute kidney injury (AKI)- Defined as an abrupt decline in renal function, clinically manifesting during the LN diagnosis or after that based on increase in serum creatinine of $\geq 0.3\text{mg/dl}$ or $\geq 50\%$ within 48h or urine output of $< 0.5\text{ml/kg/hours}$ for $> 6\text{h}$ over the course of hours to weeks.

Autoimmune Hemolysis - Evidence of hemolysis, such as reticulocytosis, low haptoglobin, 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

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.

Mild/moderate SLE flare- 1) increase of SLEDAI by ≥ 3 points; and/or 2) new/worse skin, stomatitis, serositis, arthritis, fever; and/or 3) increase in PGA by ≥ 1.0 ; and/or 4) treatment intensification: increase in prednisone $< 0.5\text{ mg/kg}$ or added NSAIDs or hydroxychloroquine

Severe SLE flare: 1) increase of SLEDAI by > 12 ; and/or 2) new/worse CNS involvement, vasculitis, glomerulonephritis, myositis, platelet counts $< 60,000/\text{mm}^3$, hemolytic anemia (hemoglobin $< 70\text{ g/L}$), requiring doubling of prednisone dose or dose $> 0.5\text{ mg/kg}$; and/or 3) need for hospitalization due to SLE; and/or 4) any manifestation requiring prednisone $> 0.5\text{ mg/kg}$ or new immunosuppressive therapy; and/or 4) increase in PGA to > 2.5 .

4.9 Data quality control

Data will be collected by well-trained data collector and investigator after patient selection. The data collector will be trained prior to data collection about objective of the study, methods of data collection, importance, and confidentiality. Collected data will be evaluated regularly for completeness and consistency by the investigator and supervisor.

4.10 Data processing and analysis

Data will be checked for completeness edited, coded and entered into Epi data version 3.1 and exported to SPSS version 25.0 statistical software for cleaning and analysis. Numeric presentation of normal distribution to assess patters in the data and to decision about the most.

suitable way to describe the data will be achieved by making use of mean, variation, and standard deviation.

Social demographic differences will be summarized, and comparisons will be drawn between groups. Two-sided Student's t test and Pearson's chi-square tests will be performed to assess differences in means and proportions, respectively. Multivariate logistic regression analyses for dichotomous outcome will be performed to determine which risk factors predict death and disability. Tables, graphs, and figures will be used to present results. A p value of less than 0.05 will be considered statistically significant.

5. Ethical clearance

Ethical approval will be obtained from Department of Internal Medicine, College of Health Science Addis Ababa University. All data and information collected during this research will be confidential. Since this is a chart review, consent will not be taken.

6. Dissemination of result

Finding of the research will be presented on thesis defense of yearly post graduate study of TASH, AAU. Research findings will be communicated to TASH, AAU research dissemination office and to health sector staff and other organization working rheumatology. Efforts will be made to incorporate the results on seminars, workshops, and meetings and to publish on a scientific journal.

7. Results

There was a total of 57 episodes of admissions from 51 patients in the study period, of which 55 (91%) were females. Females constituted the majority of the patients, 91% (n=55). The mean age of the patients was 31.23 (SD10.03) years, with a range of 14 to 59 years. The mean disease duration was 2.51 (SD2.606) years, ranging from 0 to 10 years. The mean age at symptom onset was 29.02 (SD10.99) years, ranging from 11 to 59 years.

Table 1. Sociodemographic Characteristics of hospitalized SLE patients

Variable	mean \pm SD, median (range) or N(%)	
Age	31.23 \pm 10.03	29(14,59)
Gender(female)	55(91%)	
Disease Duration	2.51 \pm 2.606	2(0-10)
Age at symptom onset	29.02 \pm 10.99	25(11,59)

7% of the patients (n=4) were found to be leukopenic. This is slightly lower than the reported prevalence of leukopenia in SLE patients, which ranges from 22% to 42%. 54% of the patients (n=31) were found to have lymphopenia on admission which is within the reported prevalence range of 20% to 81% in SLE patients. 74% and 39% of the patients were found to have anemia and thrombocytopenia respectively. This is higher than the reported prevalence of Anemia and (44,45)

The baseline clinical features showed that 33% (n=19) had fever, 88% (n=50) had fatigue, 42% (n=24) had weight loss, 58% (n=33) had rash, 39% (n=22) had oral ulcers, 44% (n=25) had photosensitivity, 16% (n=9) had Raynaud's phenomenon, and 54% (n=31) had hair loss. Historical chest pain or cough was reported by 54% (n=31) and evidence of pleural effusion was found in 47% (n=27). Evidence of pericarditis was found in 12% (n=7). Changes in consciousness/arousal were reported by 21% (n=12), memory deficit by 14% (n=8) and abnormal body movements in 14% (n=8). Historical joint pain and swelling were reported by 75% (n=43) but signs of joint tenderness and swelling were only documented in 56% (n=32) during followup.

Table 2. Details of Clinical features before or during Admission

Clinical features during presentation	Number	(%)
Fever	19	33%
Fatigue	50	88%
Weight Loss	24	42%
Documented Rash	33	58%
Documented Oral Ulcer	22	39%
Photosensitivity	25	44%
Raynaud's Phenomenon	9	16%
Hair loss	31	54%
Historical Chest Pain or Cough	31	54%
Pleural Effusion	27	47%
Pericarditis	7	12%
Change in consciousness/arousal	12	21%
Memory deficit	8	14%
Disorientation	8	14%
Change in Behavior	10	18%
Change in mood or affect	13	23%
Hallucinations	4	7%
Delusions	3	5%
Abnormal body mov't	8	14%
Historical Joint pain and swelling	43	75%
Documented Joint Tenderness and Swelling	32	56%
Flank pain	6	11%
Leg and/or Facial swelling (Edema)	30	53%
Documented Ascites	17	30%
Hepatomegaly	7	12%
Splenomegaly	5	9%

Serologic studies showed that 78.9% (n=45) were ANA positive, 31.5% (n=18) were Anti-DsDNA positive, 28.07% (n=16) had low C3, and 17.5% (n=10) had low C4. APL Ab was found in 5.26% (n=3) of the patients although a significant portion of patients don't have serologic studies other than quantitative ANA. See. Table 3. Testing all patients with serologic was limited due to cost constraints and absence of cost-efficient diagnostic laboratories specialized in carrying out such tests at the current time. The time delay that occurs in sending samples abroad for serologic tests also limits such studies in admitted and critical patients.

Table 3. Serologic and Laboratory

Serology	Positive (%)	Negative (%)	Missing (%)
ANA	45(78.9%)	0(0%)	12(21.02%)
Anti- DsDNA	18(31.5%)	5(8.77%)	34(59.64%)
C3(low)	16(28.07%)	5(8.77%)	36(63.16%)
C4(low)	10(17.5%)	10(17.5%)	37(64.91%)
APL Ab	3(5.26%)	5(8.77%)	49(85.96%)
Laboratory features			
Variable mean \pm SD, median (range)			
WBC count	7.94 \pm 4.369	6.84(2-23)	0(0%)
Absolute Lym. Count	1.23 \pm 1.13	0.9(0-6)	0(0%)
Hgb	10.53 \pm 2.801	10(7-19)	0(0%)
Platelet	205.54 \pm 133.971	195(2-592)	0(0%)
24-hr urine protein	2.64 \pm 3.35gm	1.2(0-16)	7(12.2%)
Cr	1.52 \pm 1.493	0.8(0-6)	0(0%)
Urea	54.06 \pm 40.917	42(7-149)	5(9%)
Na	135.18 \pm 4.56	135(122-144)	3(5%)
K	4.36 \pm 0.702	4.3(3-7)	2(4%)
Cl	104.61 \pm 5.166	105(91-115)	3(5%)
ESR	78.89 \pm 49.933	85(5-180)	11(19%)
LDH	371.24 \pm 166.149	328(176-770)	32(56%)
ALT	56.9 \pm 85.584	27(4-489)	2(4%)
AST	52.51 \pm 84.835	24(5-448)	4(7%)
ALP	124 \pm 106.752	92(23-697)	4(7%)
Alb	2.53 \pm 0.9	2.7(1-4)	24(42%)
Total Protein	5.53 \pm 1.774	5.9(0-8)	37(65%)
Total Bilirubin	0.63 \pm 0.657	0.4(0-4)	20(35%)

Hypertension (HTN) as the most prevalent comorbidity (16%), followed by Pregnancy (11%), and Deep Vein Thrombosis (DVT, 7%). This aligns with a study by Luo and Kuo¹ which found cardiovascular diseases, including HTN, to be common in SLE patients. (46) However, our study reports a lower prevalence of Diabetes Mellitus (DM, 5%) and Tuberculosis (TB, 5%) compared to other studies. (47,48)

Renal flare was the most common reason for admission, affecting 29.82% (n=17) of the patients. This is consistent with previous studies that have identified renal involvement as a significant clinical manifestation in SLE (33,43) Serositis and Neuropsychiatric SLE (NPSLE) were the next most common reasons, affecting 10.53% (n=6) and 12.28% (n=7) of the patients respectively. (19,33,38) Gastrointestinal (GI) sepsis was also a notable reason for admission, affecting 10.53% (n=6) of the patients. It's worth noting that the prevalence of serositis and NPSLE in our study is slightly higher than what has been reported in previous African studies.(1,2) This discrepancy could be due to differences in the patient populations or diagnostic criteria used across different setups. (27,49) A significant proportion of admissions, 36.8%, were due to other less common reasons. These include Complicated Deliveries (Flare, Preeclampsia and APS on LWHM). Deep Vein Thrombosis (DVT), Autoimmune Hepatitis (AIH)

and Others. See Table 7. Each of these conditions affected less than 5% of the patients.

46% of patients were on Chloroquine and Prednisolone although not all patients on one drug were not necessarily on the other. Although, 43.75% of patients who were not on chloroquine were admitted in their first year of diagnosis or diagnosis were settled while inpatient.

Table 4. Comorbidities in Admitted Patients

	Frequency	Percent (%)
HTN	9	15.8%
DVT	4	7.0%
Pregnancy	6	10.5%
Others	23	40.4%

Table 5. Medications Table

On Chloroquine	26	46%
On Prednisolone	26	46%
Prednisolone dose	7.65±12.56	

7. Primary Diagnosis on Admission

Renal flare	17	29.8%
Serositis	6	10.5%
NPSLE	7	12.3%
GI sepsis	6	10.5%
Complicated Delivery	4	7.0%
DVT	4	7.0%
Bleeding	3	5.3%
Pneumonia	3	5.3%
Meningitis	1	1.8%
Cellulitis	2	3.5%
Phlebitis	1	1.8%
Deep Abscess	1	1.8%
Tracheostomy stenosis	1	1.8%
AIH	1	1.8%

Table 6. Reasons for Admission

	Frequency	Percent
Flare	34	59.6%
Concurrent Flare and Infection	2	3.5%
Infection	12	21.1%
Other	9	15.8%

Table 8. Final Outcomes

Variable mean ± SD, median (range) or N(%)		
Length of Stay	18.96±15.699	15(2-82)
Total No. of Admissions	1.39±0.65	1(1-3)
Admission place		
ICU/CICU	Frequency	Percent
Ward	7	10.5
Total	50	87.7
Outcome	57	100
Against	2	4%
Died	4	7%
Improved	51	89%
Total	57	100%

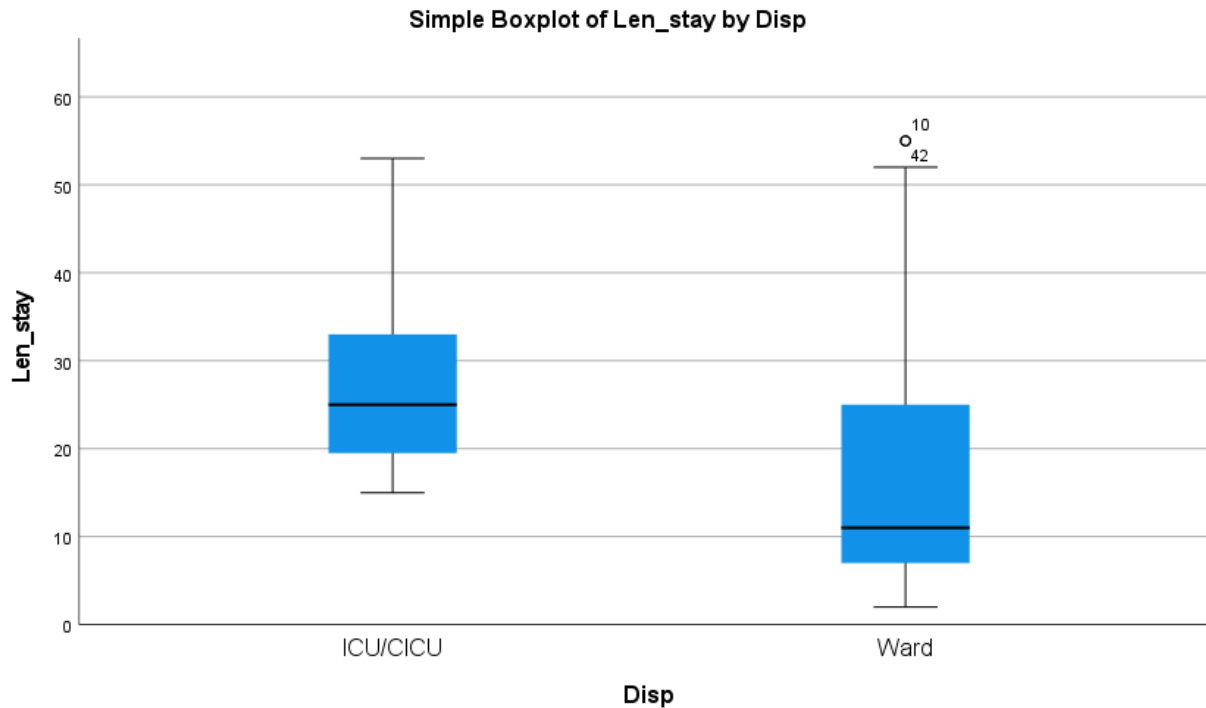


Figure 1 Length of stay for ICU and Ward patients

9. Discussion

From extensive Chart and Electronic medical record review 57 data for admissions spanning 02 years were collected and analyzed. The average number of admissions per patient was 1.39 (SD \pm 0.65), with a range from 1 to 3. Although 17 patients had more than one admission, only the data for 6 readmissions were found. The difficulty in obtaining the data lies in poor chart keeping and admissions to other hospitals and Private setups making data collection hard and expensive. The mean length of stay was 18.96 days (SD \pm 15.699).

Renal flare was the most common reason for admission, affecting 29.82% (n=17) of the patients. This is consistent with previous studies that have identified renal involvement as a significant clinical manifestation in SLE (33,43) Serositis and Neuropsychiatric SLE (NPSLE) were the next most common reasons, affecting 10.53% (n=6) and 12.28% (n=7) of the patients respectively. (19,33,38) Gastrointestinal (GI) sepsis was also a notable reason for admission, affecting 10.53% (n=6) of the patients. It's worth noting that the prevalence of serositis and NPSLE in our study is slightly higher than what has been reported in previous African studies. (1,2) This discrepancy could be due to differences in the patient populations or diagnostic criteria used across different setups. (1,2) A significant proportion of admissions, 36.8%, were due to other less common reasons. These include Complicated Deliveries (Flare, Preeclampsia and APS on LWHM). Deep Vein Thrombosis (DVT), Autoimmune Hepatitis (AIH) and Others. See Table 7. Each of these conditions affected less than 5% of the patients.

In terms of admission location, most patients (87.7%) were admitted to the ward, while a smaller proportion (10.5%) required care in the ICU/CICU. Of 7 patients admitted to the ICU/CICU 4 had flare 2 had infection and 1 had purpural sepsis. Of the patients who died only one did in the wards. The others 3 died in the ICU.

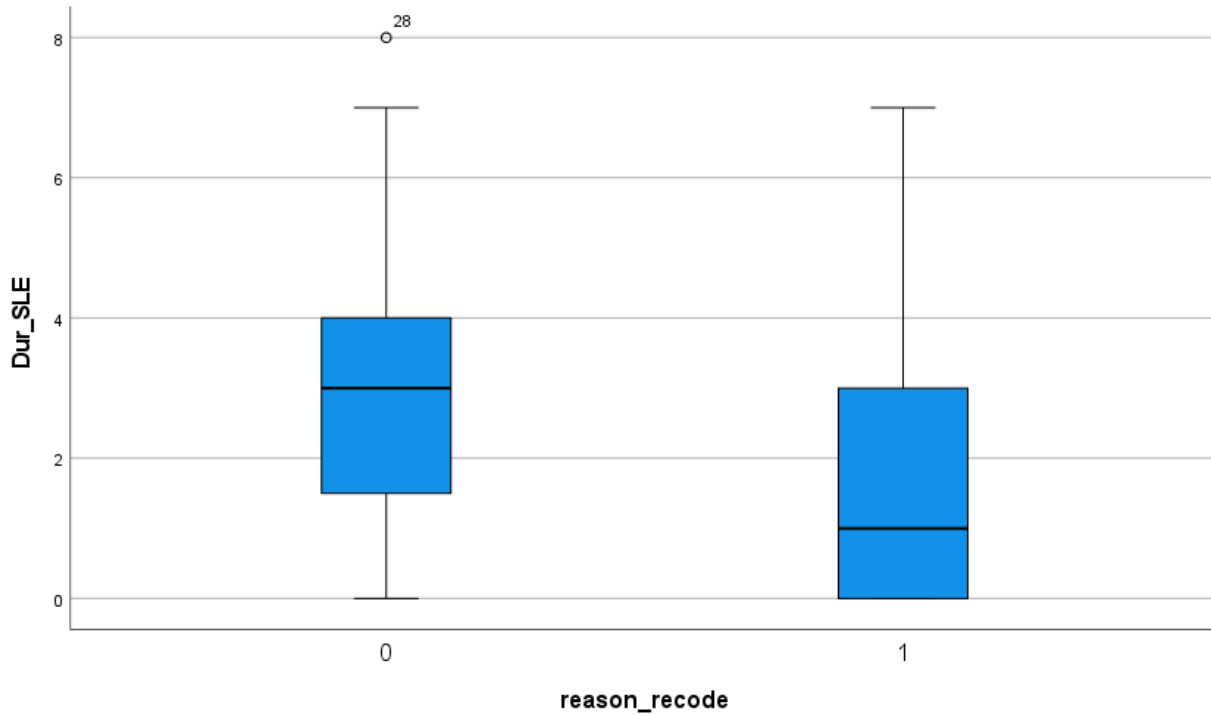


Figure 2 Flare vs. SLE Duration 0- No flare on Admission, 1- Flare on admission.

The outcomes were predominantly positive, with 89% of patients showing improvement on discharge.

The mortality rate is lower than the 42% reported in Ghana (1) but is higher or comparable to other studies done in south Africa and Egypt. (1,2)

		Length of Stay				
		Unstandardized Coefficients		Standardized Coefficients		
Model		B	Std. Error	Beta	t	Sig.
1	(Constant)	23.722	7.122		3.331	.003
	ALT	.236	.067	.811	3.492	.002
	AST	.155	.054	1.033	2.883	.008
	ALP	.058	.030	.560	1.972	.061
	Alb	-6.919	2.392	-.448	-2.893	.008
	Disposition(ICU)	14.994	5.893	.394	2.544	.018

a. Dependent Variable: Length of stay

Linear regression for Length of stay analysis showed, LFT and Albumin at admission are associated with a longer of stay. Admission for Renal flare was not associated with increased length of stay as in other studies. (1,2) ICU admission was not associated with increased length of stay but was significantly associated with death.

10. Limitations of the study

Even-though this is the first study to look at the pattern and predictors of admission in SLE patients it was retrospective, which has its own limitations in forwarding conclusions. The data collection was difficult due to a significant number of missing charts and poor registration of cases on the ward/ICU HMIS record tables. This is also a single center study. Even though attempts were made to trace patients' records admitted to other hospitals, it was difficult and expensive to do. The initial proposal was to do Multivariate logistic regression on the outcomes, but this was not possible in the end due to the low number of deaths in the study period. It's also important to note that these results should be interpreted with caution, as the relationships observed may not be causal. Other unmeasured factors could be influencing the length of stay. Therefore, these findings should be used as a guide for further research rather than definitive evidence. Due to the low number of readmissions, it was also not possible to study the protective effect of Flare from repeat Readmissions for flare.

11. Conclusion

Hospitalization of patients with SLE is often long and complicated and involve frequent readmission. The outcome is often worse for individuals with multiple problems at the time of admission. Renal flares are associated with the most number of admissions. Readmissions are also common due to the multisystem nature of the disease. Furrher studies are of this kind are needed to better understand the pattern and causes of worse outcomes of the disease.

12. References

1. I B, W K, Re V, B M, U G, WI N, et al. Impaired uptake of apoptotic cells into tingible body macrophages in germinal centers of patients with systemic lupus erythematosus. *Arthritis Rheum* [Internet]. 2002 Jan [cited 2022 Aug 5];46(1). Available from: <https://pubmed.ncbi.nlm.nih.gov/11817590/>
2. Yung S, Chan TM. Mechanisms of Kidney Injury in Lupus Nephritis – the Role of Anti-dsDNA Antibodies. *Front Immunol* [Internet]. 2015 [cited 2022 Aug 5];6. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4569852/>
3. D’Andrea DM, Coupaye-Gerard B, Kleyman TR, Foster MH, Madaio MP. Lupus autoantibodies interact directly with distinct glomerular and vascular cell surface antigens. *Kidney Int*. 1996 May;49(5):1214–21.
4. Vlahakos DV, Foster MH, Adams S, Katz M, Ucci AA, Barrett KJ, et al. Anti-DNA antibodies form immune deposits at distinct glomerular and vascular sites. *Kidney Int*. 1992 Jun;41(6):1690–700.
5. Izmirly PM, Parton H, Wang L, McCune WJ, Lim SS, Drenkard C, et al. Prevalence of Systemic Lupus Erythematosus in the United States: Estimates From a Meta-Analysis of the Centers for Disease Control and Prevention National Lupus Registries. *Arthritis Rheumatol* Hoboken NJ. 2021 Jun;73(6):991–6.
6. Pons-Estel GJ, Alarcón GS, Scofield L, Reinlib L, Cooper GS. Understanding the epidemiology and progression of systemic lupus erythematosus. *Semin Arthritis Rheum*. 2010 Feb;39(4):257–68.
7. Petri M. Epidemiology of systemic lupus erythematosus. *Best Pract Res Clin Rheumatol*. 2002 Dec 1;16(5):847–58.
8. Chakravarty EF, Bush TM, Manzi S, Clarke AE, Ward MM. Prevalence of adult systemic lupus erythematosus in California and Pennsylvania in 2000: estimates obtained using hospitalization data. *Arthritis Rheum*. 2007 Jun;56(6):2092–4.
9. Stojan G, Petri M. Epidemiology of systemic lupus erythematosus: an update. *Curr Opin Rheumatol*. 2018 Mar;30(2):144–50.
10. Somers EC, Marder W, Cagnoli P, Lewis EE, DeGuire P, Gordon C, et al. Population-based incidence and prevalence of systemic lupus erythematosus: the Michigan Lupus Epidemiology and Surveillance program. *Arthritis Rheumatol* Hoboken NJ. 2014 Feb;66(2):369–78.
11. Tiffin N, Hodkinson B, Okpechi I. Lupus in Africa: can we dispel the myths and face the challenges? *Lupus*. 2014;23(1):102–11.
12. Fernández M, Alarcón GS, Calvo-Alén J, Andrade R, McGwin G, Vilá LM, et al. A multiethnic, multicenter cohort of patients with systemic lupus erythematosus (SLE) as a model for the study of ethnic disparities in SLE. *Arthritis Rheum*. 2007 May 15;57(4):576–84.
13. Bastian HM, Roseman JM, McGwin G, Alarcón GS, Friedman AW, Fessler BJ, et al. Systemic lupus erythematosus in three ethnic groups. XII. Risk factors for lupus nephritis after diagnosis. *Lupus*. 2002;11(3):152–60.
14. Lu LJ, Wallace DJ, Ishimori ML, Scofield RH, Weisman MH. Review: Male systemic lupus erythematosus: a review of sex disparities in this disease. *Lupus*. 2010 Feb;19(2):119–29.
15. Kaufman LD, Gomez-Reino JJ, Heinicke MH, Gorevic PD. Male lupus: retrospective analysis of the clinical and laboratory features of 52 patients, with a review of the literature. *Semin Arthritis Rheum*. 1989 Feb;18(3):189–97.
16. Cervera R, Khamashta MA, Font J, Sebastiani GD, Gil A, Lavilla P, et al. Systemic lupus erythematosus: clinical and immunologic patterns of disease expression in a cohort of 1,000 patients. The European Working Party on Systemic Lupus Erythematosus. *Medicine (Baltimore)*. 1993 Mar;72(2):113–24.

17. Trager J, Ward MM. Mortality and causes of death in systemic lupus erythematosus. *Curr Opin Rheumatol*. 2001 Sep;13(5):345–51.
18. Urowitz MB, Gladman DD, Tom BDM, Ibañez D, Farewell VT. Changing patterns in mortality and disease outcomes for patients with systemic lupus erythematosus. *J Rheumatol*. 2008 Nov;35(11):2152–8.
19. Jallouli M, Hriz H, Cherif Y, Marzouk S, Snoussi M, Frikha F, et al. Causes and outcome of hospitalisations in Tunisian patients with systemic lupus erythematosus. *Lupus Sci Med*. 2014 Jun 5;1(1):e000017.
20. Tektonidou MG, Wang Z, Dasgupta A, Ward MM. Burden of Serious Infections in Adults With Systemic Lupus Erythematosus: A National Population-Based Study, 1996-2011. *Arthritis Care Res*. 2015 Aug;67(8):1078–85.
21. Greenwood BM, Herrick EM, Voller A. Can Parasitic Infection Suppress Autoimmune Disease? *Proc R Soc Med*. 1970 Jan 1;63(1):19–20.
22. Gilkeson G, James J, Kamen D, Knackstedt T, Maggi D, Meyer A, et al. The United States to Africa lupus prevalence gradient revisited. *Lupus*. 2011 Oct;20(10):1095–103.
23. Vento S, Cainelli F. Commentary: Systemic Lupus Erythematosus in Native sub-Saharan Africans: A Systematic Review and Meta-Analysis. *Front Med [Internet]*. 2020 [cited 2022 Aug 1];7. Available from: <https://www.frontiersin.org/articles/10.3389/fmed.2020.00202>
24. Danchenko N, Satia JA, Anthony MS. Epidemiology of systemic lupus erythematosus: a comparison of worldwide disease burden. *Lupus*. 2006 May 1;15(5):308–18.
25. Uribe AG, McGwin G, Reveille JD, Alarcón GS. What have we learned from a 10-year experience with the lumina (Lupus in Minorities; Nature vs. nurture) cohort? Where are we heading? *Autoimmun Rev*. 2004 Jun 1;3(4):321–9.
26. Adelowo OO, Oguntona SA. Pattern of systemic lupus erythematosus among Nigerians. *Clin Rheumatol*. 2009 Jun 1;28(6):699–703.
27. Wadee S, Tikly M, Hopley M. Causes and predictors of death in South Africans with systemic lupus erythematosus. *Rheumatology*. 2007 Sep 1;46(9):1487–91.
28. Heaton TB, Crookston B, Pierce H, Amoateng AY. Social inequality and children’s health in Africa: a cross sectional study. *Int J Equity Health*. 2016 Jun 14;15(1):92.
29. Fekade S. 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 [Internet] [Thesis]. Addis Abeba University; 2020 [cited 2022 Aug 11]. Available from: <http://etd.aau.edu.et/handle/123456789/25061>
30. Hailu GMT, Hussen SU, Getachew S, Berha AB. Management practice and treatment outcomes of adult patients with Lupus Nephritis at the Renal Clinic of St. Paul’s Hospital Millennium Medical College, Addis Ababa, Ethiopia. *BMC Nephrol*. 2022 Jun 17;23(1):214.
31. Duffy KN, Duffy CM, Gladman DD. Infection and disease activity in systemic lupus erythematosus: a review of hospitalized patients. *J Rheumatol*. 1991 Aug 1;18(8):1180–4.
32. Krishnan E. Hospitalization and mortality of patients with systemic lupus erythematosus. *J Rheumatol*. 2006 Sep 1;33(9):1770–4.
33. Teh CL, Chan GYL, Lee J. Systemic lupus erythematosus in a tertiary, east Malaysian hospital: admission, readmission and death. *Int J Rheum Dis*. 2008 Apr;11(1):24–9.
34. Edwards CJ, Lian TY, Badsha H, Teh CL, Arden N, Chng HH. Hospitalization of individuals with systemic lupus erythematosus: characteristics and predictors of outcome. *Lupus*. 2003 Sep 1;12(9):672–6.
35. Feldman CH, Hiraki LT, Liu J, Fischer MA, Solomon DH, Alarcón GS, et al. Epidemiology and sociodemographics of systemic lupus erythematosus and lupus nephritis among US adults with Medicaid coverage, 2000-2004. *Arthritis Rheum*. 2013 Mar;65(3):753–63.

36. Rees F, Doherty M, Grainge M, Davenport G, Lanyon P, Zhang W. The incidence and prevalence of systemic lupus erythematosus in the UK, 1999-2012. *Ann Rheum Dis*. 2016 Jan;75(1):136–41.
37. Tazi Mezalek Z, Bono W. Challenges for lupus management in emerging countries. *Presse Médicale*. 2014 Jun 1;43(6, Part 2):e209–20.
38. Toit RD, Herbst PG, Rensburg A van, Plessis LM du, Reuter H, Doubell AF. Clinical features and outcome of lupus myocarditis in the Western Cape, South Africa: Lupus [Internet]. 2016 May 25 [cited 2022 Aug 5]; Available from: <https://journals.sagepub.com/doi/abs/10.1177/0961203316651741>
39. Brijlal U, Bates WD, Moosa MR. Lupus nephritis in the Western Cape, a high prevalence area: an experience over three decades. *Lupus*. 2017 Oct 1;26(11):1228–34.
40. Sabry A, Abo-Zenah H, Medhat T, Sheashaa H, Mahmoud K, El-Huseini A. A comparative study of two intensified pulse cyclophosphamide remission-inducing regimens for diffuse proliferative lupus nephritis: an Egyptian experience. *Int Urol Nephrol*. 2009 Mar 1;41(1):153–61.
41. Features and outcomes of lupus nephritis in Morocco: analysis of 114 patients [Internet]. [cited 2022 Aug 12]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3839844/>
42. Busch RW, Kay SD, Voss A. Hospitalizations among Danish SLE patients: a prospective study on incidence, causes of admission and risk factors in a population-based cohort. *Lupus*. 2018 Jan 1;27(1):165–71.
43. Dzifa D, Boima V, Yorke E, Yawson A, Ganu V, Mate-Kole C. Predictors and outcome of systemic lupus erythematosus (SLE) admission rates in a large teaching hospital in sub-Saharan Africa. *Lupus*. 2018 Feb 1;27(2):336–42.
44. Kandane-Rathnayake R, Louthrenoo W, Golder V, Luo SF, Wu YJJ, Lateef A, et al. Independent associations of lymphopenia and neutropenia in patients with systemic lupus erythematosus: a longitudinal, multinational study. *Rheumatology*. 2021 Nov 1;60(11):5185–93.
45. Hepburn AL, Narat S, Mason JC. The management of peripheral blood cytopenias in systemic lupus erythematosus. *Rheumatology*. 2010 Dec 1;49(12):2243–54.
46. Luo SF, Kuo CF. 171 Comorbidities in patients with systemic lupus erythematosus prior to and following diagnosis: case-control study. *Lupus Sci Med* [Internet]. 2017 Mar 1 [cited 2024 Mar 9];4(Suppl 1). Available from: https://lupus.bmj.com/content/4/Suppl_1/A80.3
47. MD CS. *Rheumatology Advisor*. 2016 [cited 2024 Mar 9]. Increased Disease Comorbidity in SLE is Age, Gender Specific. Available from: <https://www.rheumatologyadvisor.com/home/topics/systemic-lupus-erythematosus/increased-disease-comorbidity-in-sle-is-age-gender-specific/>
48. High risk of depression, anxiety, and an unfavorable complex comorbidity profile is associated with SLE: a nationwide patient-level study | *Arthritis Research & Therapy* | Full Text [Internet]. [cited 2024 Mar 9]. Available from: <https://arthritis-research.biomedcentral.com/articles/10.1186/s13075-022-02799-6>
49. Kotb HA, Khalad S, Moghazy A. Hospitalization and outcome of systemic lupus erythematosus patients admitted to the Rheumatology ward of Kasr Al-Ainy University Hospital. *Egypt Rheumatol*. 2023 Jun 1;45(3):235–9.

13. Annexes

13.1 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: _____

13.2: Questionnaire

1. Socio-demographic Characteristics

No	Variables	Response
1.1	Age	_____
1.2	Sex	1. Male 2. Female
1.3	Employed	1. Yes 2. No
1.4	Religion	1. Muslim 2. Protestant 3. Orthodox 4. Catholic 5. Unspecified
1.5	Region	1. Oromia 6. Gambella 2. Amhara 7. Benishangul Gumuz 3. Tigray 8. Harar 4. Afar 9. Addis Ababa 5. Somalia 10. Other _____

1. Baseline Characteristics

1.1 Chief Complaint _____

1.2 Blood Pressure

BP \geq 140/90	A. Yes	B. No	C. Not documented
------------------	--------	-------	-------------------

1.3 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

1.4 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	

1.5 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 _____

2.4 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_____

2.5 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

2.6 Renal Manifestations

2.6.1 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

2.6.2 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				

2.7 Hematology and Serology

2.7.1 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			

2.8 Gastrointestinal System

2.8.1 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

2.8.2 Laboratory Values

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

2.9 Comorbidity documented if any

3. Admission and Outcomes

3.1 Diagnosis at Admission

3.1.1 Age at SLE diagnosis _____ Years.

3.1.2 Age at Admission _____ Year.

3.1.3 No. of Admission _____

3.1.4 Reason for Hospitalization

SLE, Type of flare	
Infection, Type of infection	
Adverse drug reaction, Types	
Pregnancy and labor	
Miscellaneous	

3.1.5 Disposition _____

3.1.6 Reason for ICU admission/Transfer (if any)

3.2 Length of stay

3.3 Outcome, and Causes of Outcome

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100

Baseline Characteristics

மேலே உள்ள பக்கங்களில் உள்ள வினாக்களுக்குரிய பதில்களைக் கொடுக்கவும்.

3. Admission and Outcomes

3.1 Diagnosis at Admission

3.1.1 Age at SLE diagnosis _____ Years.

3.1.2 Age at Admission _____ Year.

3.1.3 No. of Admission _____

3.1.4 Reason for Hospitalization

SLE, Type of flare	
Infection, Type of infection	
Adverse drug reaction, Types	
Pregnancy and labor	
Miscellaneous	

3.1.5 Disposition _____

3.1.6 Reason for ICU admission/Transfer (if any)

3.2 Length of stay

3.3 Outcomes
