UNIVERSITY OF NAIROBI

ASSESSMENT OF DISEASE ACTIVITY AND HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AT KENYATTA NATIONAL HOSPITAL

BY
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A thesis submitted in part fulfilment of the degree of Master of Medicine, Internal Medicine

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DECLARATION

This dissertation is my original work and has been presented as a prerequisite for a Master's degree to the Department of Clinical Medicine and Therapeutics, University of Nairobi, Kenya. It has not been presented for any degree to any other university.

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LIST OF ACRONYMS AND ABBREVIATIONS

ACR	American College of Rheumatology
ANA	Anti-Nuclear Antibodies
Anti-ds DNA	Anti Double Stranded Deoxyribonucleic acid
CBC	Complete Blood Count
HRQoL	Health Related Quality of Life
HCQ	Hydroxychloroquine
KNH	Kenyatta National Hospital
LUPUSQoL	Lupus Quality of Life
MMF	Mycophenolate Mofetil
RNA	Ribonucleic Acid
PI	Principal investigator
SLE	Systemic Lupus Erythematosus
SLEDAI	Systemic Lupus Erythematosus Disease Activity Index
cSLEDAI	Clinical Systemic Lupus Erythematosus Disease Activity Index
SLICC	Systemic Lupus International Collaborating Clinics
SDI	Systemic Lupus International Collaborating Clinics Damage Index
SF - 36	Short Form (36) Health Survey
QoL	Quality of Life
UoN	University of Nairobi

ABSTRACT

Background

Systemic lupus erythematosus (SLE) is an autoimmune disorder characterised by inflammation in different organ systems. Disease activity varies from remissions to exacerbations and progression. Assessment of physical health alone is insufficient to evaluate the impact of the disease. Health-related quality of life (HRQoL) represents the patients' subjective perception of living with the disease and how it affects their physical, emotional and social functions. The aim of this study was to assess the impact of disease activity on HRQoL in SLE patients

Methods

This was a cross-sectional descriptive study conducted at Kenyatta National Hospital rheumatology and renal outpatient clinics. Ninety patients were assessed for eligibility, 62 patients fulfilling ≥4 Systemic Lupus International Collaborating Clinics Criteria (SLICC) 2012 for classification of SLE were consecutively recruited. Twenty-seven patients with overlap syndromes (SLE/RA, SLE/polmyositis/dermatomyosistis/undifferentiated rheumatic disease) were excluded.

Disease activity was assessed by the clinical Systemic Lupus Erythematosus Disease Activity Index 2000 (cSLEDAI-2K). The HRQoL was evaluated using self-administered LupusQoL with scores ranging from 0 (worst) to 100 (best). History of drugs used was corroborated with patients' medical records. Continuous variables were summarised as means±SD and categorical variables expressed as percentages. HRQoL was correlated with age, disease duration and disease activity using Pearson's correlation coefficients. A p value of ≤ 0.05 was considered to be significant. All tests were performed on SPSS version 23.

Results

The study group comprised 60 female and 2 male patients, mean age 34.7±11.8 years. The median disease duration was 36 months, ranging from 1-324 months. Mean cSLEDAI score was 7±5.2 and median disease activity score was 7. Renal disease occurred in 53.2%.

All domains of LupusQoL were impaired. The mean scores (out of 100) of the 8 domains of LupusQoL were: physical health 58.2±28.2, pain 60.2±29.8, planning 65.9±29, intimate relationships 50±38.2, burden to others 50.9±34.7, emotional health 62.3±26.2, body image 51±30 and fatigue 65.4±28.7. SLEDAI scores were inversely correlated with scores of physical

health (p=0.043), pain (p=0.027), burden to others (p=0.004), body image (p=0.007) and general health (p=0.026). The patients with renal disease had significantly lower QoL compared to other patients (p=0.037) and the pain (p=0.009), intimate relationships (p=0.04) and body image (p=0.01) were most affected. Age and disease duration were positively correlated with QoL. Disease duration (p=0.01), was associated with a better QoL in the pain (p=0.01), emotional health (p=0.02) and body image (p=0.007) domains.

Conclusion

Our study showed a low HRQoL in those with active disease. Young age, a recent diagnosis of lupus and presence of renal disease were associated with a poorer QoL. There was marked variation in the drug prescription and limited use of immunosuppressant drugs.

Key words: SLE, Disease activity, Health related quality of life, cSLEDAI-2K, LUPUSQoL

CHAPTER ONE: INTRODUCTION

1.1 Systemic Lupus Erythematosus

Systemic lupus erythematosus (SLE) is a chronic, autoimmune inflammatory disease. It is characterised by a highly variable clinical presentation that ranges from mild cutaneous involvement to life threatening multi-organ failure. It has an unpredictable chronic course, with alternating periods of quiescence and exacerbations of disease activity. SLE predominantly affects young women causing significant morbidity and mortality (1).

Disease activity measures the potentially reversible manifestations of the inflammatory process. However, assessment of physical health is insufficient to account for the impact of the disease. Complementary to disease activity, organ damage and health related quality of life (HRQoL) are necessary in the holistic management of patients (2).

1.2 Assessment of disease activity in SLE

Disease activity refers to the manifestations of the underlying inflammatory process at a point in time in terms of magnitude and severity. Disease severity refers to the type and level of organ dysfunction and its consequences and is described as mild, moderate or severe. Damage refers to the degree of irreversible organ dysfunction. Global disease activity measurements in SLE patients is important for clinical estimation and adjustment of therapy. Increased disease activity leads to an escalated probability of organ damage, increased use of steroids and immunosuppression drugs, and mortality (3). SLE because of its protean manifestations, it has no clinical or laboratory aberration in isolation that would reliably be used as a gold standard in assessing disease activity. Moreover no standard method is available to define response to therapy. There are multiple disease activity indices developed and validated over the years, namely the British ISLEs Lupus Assessment Group (BILAG), European Consensus Lupus Activity Measure (ECLAM) and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) each with their strengths and weaknesses (4). SLEDAI was developed as a model of complete disease activity by experienced clinicians. Thus, it is a summative representation of expert opinion. It has subsequently been validated in different centres and proven to be a reliable, reproducible and sensitive measure of disease activity (5). The clinical SLEDAI-2K (cSLEDAI-2K) eliminates the immunologic variables thus making it cheaper to administer in a

resource constrained setting. The choice of cSLEDAI — 2K as a measure of disease activity in this study is based on its validity and practicability in clinical settings (6).

1.3 Health related quality of life in SLE

Health as defined by the World Health Organisation is ' a state of complete physical, mental and social wellbeing and not merely the absence of disease or infirmity' (7). Health is a subjective assessment of greatest importance to the patient but without obvious disease correlates. Quality of life serves as the patients' subjective perception of living with the disease. Health related quality of life (HRQoL) is a multidimensional concept that provides the patients' self evaluation of how the disease affects their physical, social and psychological wellbeing.

QoL can be assessed using generic tools (WHOQoL, Short Form-36 [SF-36) or disease specific tools. LUPUSQoL measures specific HRQoL in adults with SLE (8). Cross-sectional and longitudinal studies utilising LUPUSQoL have demonstrated a low QoL. Some of the factors contributing to this include disease activity, organ damage accrual and psychosocial factors (9).

SLE disease activity and damage scores are poor surrogates of HRQoL because results linking these measures and QoL are non-uniform (10, 11). High disease activity negatively affects the patients' quality of life (12). In a previous study of quality of life in Kenyan SLE patients, Odhiambo (13) described a low QoL. In addition, multiple studies have been done assessing individual organ systems. The purpose of this study was to perform an assessment of the disease activity in patients attending the rheumatology clinic at the Kenyatta National Hospital. Moreover, this assessment will form the baseline reference for future follow up. It would also serve as an audit of the adequacy of care provided at the clinic while providing the patients perspective regarding their own treatment.

CHAPTER TWO: LITERATURE REVIEW

2.1 Epidemiology of Systemic Lupus Erythematosus

SLE has a global distribution affecting all races, gender and age groups. Geographical and regional variations have been observed in the prevalence of SLE. Globally the incidence of SLE is highest in North America with an estimated prevalence of 241/100 000 people and lowest in Africa at 0.3/100 000 (1). The incidence ranges from 0.9 - 3.1/100 000 in the Asia - Pacific region (14). In the United Kingdom, the incidence is estimated to be 4.91/100 000 person - years (15).

SLE is predominantly a female condition. Females have the highest prevalence of SLE across all the regions and races (16). The prevalence of SLE is high among the black and Hispanic women with Caucasian and Asian women having the lowest rates of SLE (1).

In Africa, the real incidence or prevalence of SLE remains unclear due to few studies conducted in the region and limitations in diagnosis. However, based on the existing studies in the region, SLE is not a rare disease as earlier presumed. Progressively, an upward trend in the frequency of SLE in indigenous populations of East, Central and South African has been reported (17). The number of SLE patients in Kenya has been on the rise over successive years with an increasing prevalence and incidence (18). The prevalence of SLE in Kenya is estimated to be 1.56% (17).

2.2 Pathogenesis of Systemic Lupus Erythematosus

SLE is the prototypical autoimmune disorder. It is defined by diverse clinical phenotypes and the presence of antibodies to nuclear components. The underlying pathophysiological processes are complex due to the varying severity and longevity of inflammation, and the diverse composition of inflammatory infiltrates. The exact aetiology remains unknown; however, genetic, epigenetic, hormonal factors and environmental factors are instrumental in development of the immunologic abnormalities leading to disease pathogenesis (19).

Genetically, about 50 gene loci with polymorphisms have been identified in genome wide studies as predisposing to SLE. Specifically, the Major Histocompatibility Complex has been linked with development of autoimmunity (20). Further observations have shown a 15 - 47% concordance rate among identical twins and an elevated risk in first degree relatives as compared

to the general populace (21). There is also a 29-fold risk among siblings and among those with anti-nuclear anti bodies (22).

Epigenetics are heritable or acquired modifications of DNA without change in the DNA base sequence. These alterations occur via DNA hypo-methylation, histone modification, or microRNA changes during cell division. Epigenetic changes illustrate the importance of adaptivity and the environment. These changes are reversible and amenable to pharmacologic interventions (23).

Hormones such as testosterone, dehydroepiandesterone, progesterone and pituitary hormones play an immune-regulatory role. Particularly, a high endogenous oestrogen concentration, low androgen values and exogenous oestrogen increase the susceptibility to SLE. Androgens, prolactin and oestrogen correlate with disease activity (24). A reduction in hormone production is associated with reduced disease activity while periods of hormonal changes also cause SLE flares and fluctuations of disease activity.

Immune activation among SLE patients occurs as a result of hyper-activated T and B lymphocytes cells, and abnormal phagocytic functions and immunoregulation. Hyper-activation of the B cells may be caused by a raised concentration of Interleukin 6 and Interleukin 10 resulting in an increase in immunoglobulin producing B cells. The hyper-activation of the T cells results from early abnormal events making the T cell function more like the B cells and production of immunoglobulin. Abnormal phagocytic cells have impaired immune complex processing resulting in apoptosis of phagocytic cells. This further results in poor clearance of immune complexes due to defective complement proteins (C2, C4, C1Q) on the cell surfaces and suppression of T lymphocytes and NK cells activity on activated B and T cell lymphocytes hence a dysregulated idiotypic control of antibody production (19).

Antibody formation and creation of immune complexes are however known to have a direct or indirect mediation to the clinical manifestations. The characteristics of the antibodies, nature of the antigen, the rate at which immunoglobulin receptors on monocytes and macrophages clear immune complexes in the liver and spleen and the ability of the immune complexes to be

solubilised by complement and bound by complement receptor on red blood cells determine the pathogenic nature of the immune complexes (19, 25)

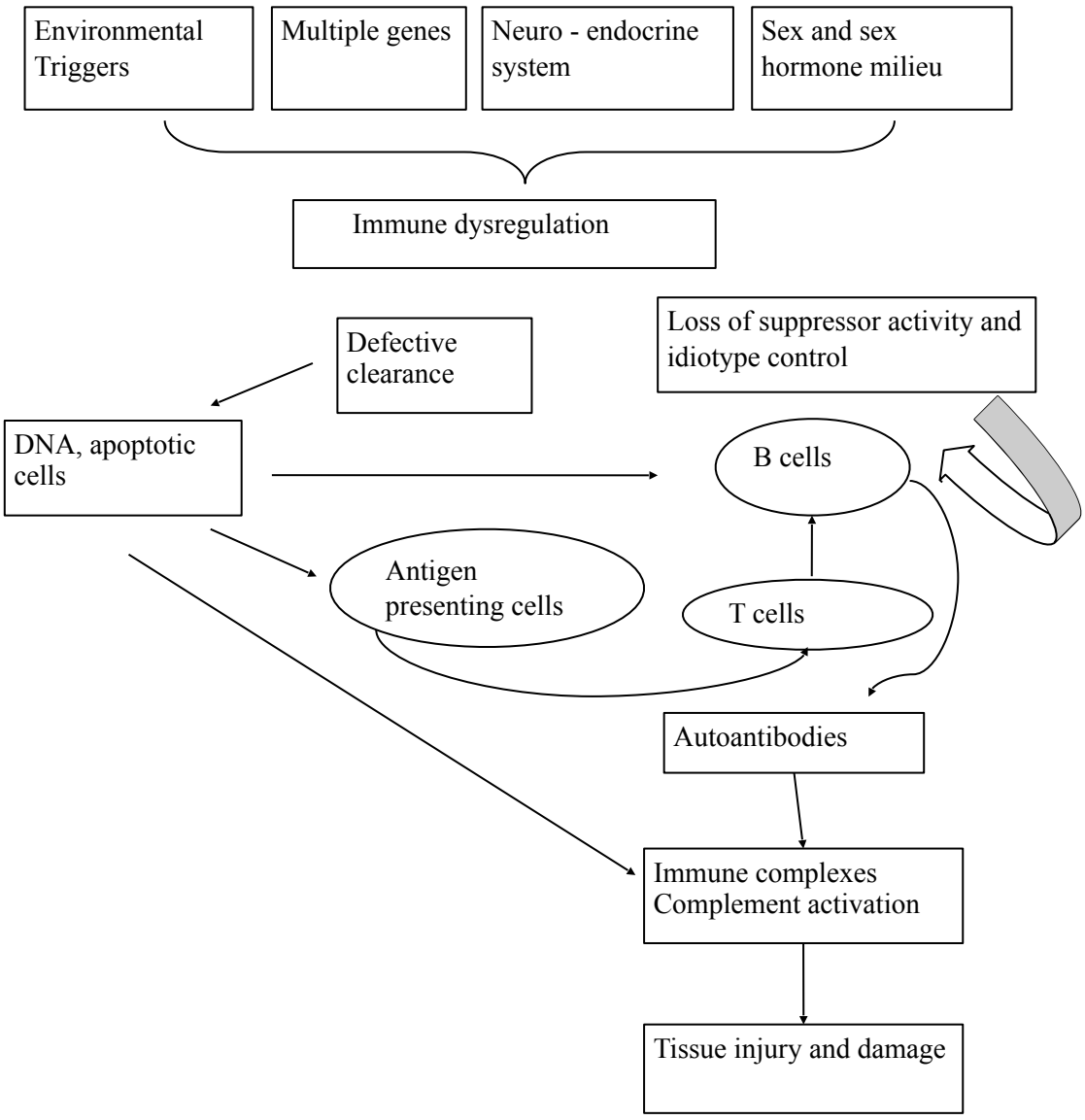


Figure 1: Pathogenesis Of Sle (Adopted From C. Mok And Lau) (26)

The environmental factors related to SLE include chemical and physical factors such as tobacco, hydrazine, hair dyes, drugs (phenytoin, procainamide , etc.) and ultraviolet rays; dietary factors such as high saturated fat intake; infectious agents such as endotoxins and retroviruses and environmental and hormonal oestrogen such as hormone replacement therapy and prenatal exposure to oestrogen (33).

2. 3 Diagnosis of SLE

The diagnosis of lupus is requires both clinical and laboratory findings. Due the absence of SLE diagnostic criteria, SLE classification criteria are used. Classification as having SLE by the 2012 Systemic Lupus International Collaborative Criteria requires that:

a) The patient satisfies four of the seventeen criteria including at least one clinical criterion and one of the six immunologic criteria **or**

b) The patient has biopsy-proven nephritis compatible with SLE and ANA or anti-dsDNA antibodies (Appendix II)(27)

Table 1: Classification Criteria For SLE

SLICC Classification for Systemic Lupus Erythematosus	
Clinical Criteria	**Immunologic Criteria**
1. Acute Cutaneous Lupus	1.ANA
2. Chronic Cutaneous Lupus	2. Anti-Ds DNA
3. Oral or Nasal Ulcers	3. Anti-Smith
4. Non-scarring alopecia	4. Antiphospholipid Antibody
5. Arthritis	5. Low complement (C3,C4)
6. Serositis	6. Direct Coombs' Test
7. Renal	
8. Neurologic	
9. Hemolytic anaemia	
10. Leukopenia	
11. Thrombocytopenia	
Adopted from Petri M et al, Arthritis and Rheumatism, Aug 2012 (27)	

SLICC criteria are cumulative and do not have to be present concurrently.

2.4 Treatment of SLE

Treatment of SLE aims at providing individualised care with the goals of reducing disease activity, avoiding organ damage, reducing the effect of medications and promoting quality long-term survival while actively involving the patient in management of the disease (28, 29).

Treatment depends on the clinical manifestations, patient preferences, disease severity and comorbidities. It requires an integrated approach to care involving a multi-disciplinary team of rheumatologist, cardiologist, nephrologist and nurses, among others. Standard treatment guidelines by the British Society for Rheumatism and the European League Against Rheumatism recommend non-pharmacological treatment and pharmacological therapies to achieve optimal management of SLE (29).

2.4.1 Pharmacological management of SLE

The focus of the pharmacological management of SLE is to reduce disease activity and severity, reduce organ involvement and address specific symptoms and disease manifestations. This management is highly individualised with patient preferences considered when selecting therapy (30). Despite the patient-specific treatment, some of the treatment therapies are general. Hydroxychloroquinolone is an anti-malarial drugs that all patients, regardless of their disease stage receive unless contra-indicated. This drug reduces the flare rates, thrombotic events, organ damage accrual, and mortality and relieves the constitutional symptoms and musculoskeletal manifestations (29). Additional treatment is tailored to specific clinical manifestations, disease activity and severity and comorbidities. The predominant disease manifestation is treated with the assumption that the less concerning manifestation will come under control.

Table 2: Treatment Of Systemic Lupus Erythematosus

<table>
<tr><td rowspan="10">Adjunct

Sun protection
Vaccination
Exercise
Body weight
Blood pressure
Lipids
Glucose
Anti platelets
Anti coagulants</td><td colspan="2">Mild</td><td colspan="2">Moderate</td><td colspan="2">Severe</td><td rowspan="10">Target Remission
SLEDAI=0
HCQ
No GC
Or
Low disease activity
SLEDAI≤4
HCQ
Pred ≤7.5mg/ day
Immunosuppressives (in stable doses and well tolerated)</td></tr>
<tr><td>1st line</td><td>Refractory</td><td>1st line</td><td>Refractory</td><td>1st line</td><td>Refractory</td></tr>
<tr><td colspan="6">HCQ</td></tr>
<tr><td colspan="2">GC PO/IM</td><td colspan="4">GC PO/IV</td></tr>
<tr><td></td><td colspan="2">MTX / AZA</td><td colspan="3"></td></tr>
<tr><td colspan="3"></td><td>BEL</td><td colspan="2"></td></tr>
<tr><td colspan="3"></td><td colspan="2">CNI</td><td></td></tr>
<tr><td colspan="3"></td><td colspan="2">MMF</td><td></td></tr>
<tr><td colspan="5"></td><td>CYC</td></tr>
<tr><td colspan="5"></td><td>RTX</td></tr>
</table>

Mild: constitutional symptoms / mild arthritis / rash ≤ 9% / platelets 50-100x10^3; SLEDAI ≤ 6

Moderate: RA-like arthritis / rash ≥ 9% / cutaneous vasculitis / platelets 20-50x10^3 / SLEDAI 7-12

Severe: major organ threatening disease (nephritis, cerebritis, myelitis, pneumonitis, mesenteric vasculitis, thrombocytopenia with platelets < 20x10^3 , SLEDAI > 12

(AZA, azathioprine; BEL, belimumab; CNI, calcineurin inhibitor; CYC, cyclophosphamide; GC, glucocorticoids; HCQ, hydrocxychloroquine; IM, intramuscular; MMF, mycophenolate mofetil; MTX, methotrexate; Pred, prednisone; PO, per oral; RTX, Rituximab; SLEDAI, systemic lupus erythematosus disease activity index). (Adopted from 2019 update of EULAR recommendations)(29)

2.4.2 Non-pharmacological management of SLE

The non-pharmacological interventions include:

a) Sun protection: SLE manifestations have been shown to be accelerated by exposure to ultraviolet light. Thus, SLE patients should use sunscreens that protect them from ultra violet rays and avoid photosensitive medications (31).

b) Exercise: SLE patients need light exercise to build their muscle mass which is lost during periods of inactivity or as a result of acute illness (32).

c) Nutrition: A conventional balanced diet is recommended for SLE patients due to limited evidence on the effect of diet on SLE patients. However, specific diets can be tailored for SLE patients with comorbidities, on specific treatments such as glucocorticoids which enhance appetite or specific food allergies. Nutrition management should consider supplements of vitamins, in cases of shortage such as vitamin D, which is partly due to poor exposure to sunlight(32).

d) Effective management of comorbidities: Screening and management of common comorbidities should be instituted in all SLE patients. Regular monitoring of the patients for atherosclerosis, pulmonary hypertension, osteoporosis and anti-Phospholipid syndrome should be encouraged during routine check-up (33).

e) Cessation of smoking: In SLE patients, smoking affects efficacy of hydroxychloroquine (45) and increases the risk for cardiovascular diseases and organ damage (34).

f) Immunisation: Immunosuppressant's such as glucocorticoids weakens the immune system and thus patients should be vaccinated against common vaccine-preventable diseases such as pneumonia, influenza, hepatitis B and HPV (29).

g) Pregnancy avoidance: SLE patients should be discouraged from getting pregnant during the active stages of the disease. High disease activity is associated with an increased risk of miscarriage (35).

h) Avoidance of therapies that accelerate SLE disease activity such as sulphonamides and some anti-microbial or those that cause drug induced lupus such as hydralazine. Additionally, radiation therapy should be avoided due to the associated increased risk of toxicity.

2.5 Assessment of disease activity

Active disease is a continuum. Disease activity measures potentially reversible manifestations of the underlying inflammatory disease process. Given the pleiotropic nature of the disease, the assessment of disease activity is not easy. There are formal and informal ways of assessing disease activity. The informal way relies on the clinical impression of the attending practitioner. Patients will be stratified as having mild, moderate or severe disease. Formal assessment of disease activity relies on several different instruments which have been developed to fully quantify disease activity. These disease activity indices convert clinical manifestations and laboratory abnormalities into numerals. The disease activity indices were developed primarily for research purposes but have been incorporated into clinical practice. They have been validated and compared to each other. The most common indices in clinical use are the British ISLEs Lupus Assessment Group (BILAG), European Consensus Lupus Activity Measure (ECLAM), Systemic Lupus Activity Measure (SLAM) and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) (4). These are all global indices which assesses overall disease activity. The clinical features present in each organ are assigned a numerical value which is then totalled to provide a summative score for disease activity. The disadvantage with this scoring system is its inability to distinguish between symptoms that are improving and those that are worsening over

time. Some indices perform better as static indices, others as transitional indices while some may be more feasible than others in clinical research (36).

Fewer flares means less organ damage. On average, patients experience 1.8 flares annually (37). Baseline predictors of SLE flares include renal, neurologic, or vascular involvement, increased anti ds DNA levels, low C3 levels and serum immune factor levels (37). Symptoms that may be indicative of a flare include: increased lethargy/fatigue, increased arthralgia, exacerbation of rash, recurrent episodes of non-healing atrophic ulcers and alopecia.

2.5.1 Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and the modified versions

SLEDAI is a global disease index activity that was developed at the University of Toronto in Canada in 1985. It was formulated as a consensus of rheumatology experts as a clinical index for measuring disease activity in the preceding 10 days (38). In 2002, it was updated to SLEDAI 2K that incorporates the presence of some persisting disease activity features using a time frame of the last 10 - 30 days (5).

SLEDAI evaluates 24 clinical and laboratory parameters that are weighted differently. The scale divides the 24 attributes into 9 domains, called organ systems: Central nervous system, vascular, renal, musculoskeletal, serosal, dermal, immunologic, constitutional and haematological. The variables are scored, if present and attributed to active lupus. The disease manifestations attributable to SLE are weighted with values ranging from 1 to 8 and the scores are then totalled. Life threatening events such as cerebral manifestations and vasculitis have the highest score (score 8). Disease activity in theory may range from 0 - 105 but in practice rarely exceeds the 40 mark. The scores are interpreted as mild disease activity (0-5), moderate disease activity (6-12) and over 12 represents severe disease activity.

A score reduction is defined as the disappearance of a scored parameter and requires the complete resolution of a disease manifestation or laboratory test abnormality. There are differing opinions as to what constitutes a clinically meaningful score reduction but improvement is generally regarded as a 3-to 7 point reduction in the total score. Outcomes based on SLEDAI scores can be further categorised as: SLE flare up, increase in SLEDAI of more than 3;

improvement, reduction in SLEDAI of more than 3; persistently active disease, change in SLEDAI of more than or less than 3 and remission, a SLEDAI score of 0 (39).

There are several limitations to using SLEDAI to assess disease activity. One, SLEDAI does not measure partial improvement of an individual parameter. Secondly, it cannot measure worsening of an existing abnormality. Thirdly, some items are weighted 'unfairly'. For instance, thrombocytopenia is scored as 1 while rash is scored as 2 points. Fourth, as a composite score, it cannot distinguish patients with multiple mild manifestations from those with fewer, more severe manifestations. Moreover, improvement in one organ may be offset by a new disease manifestation in another organ e.g. arthritis contributes 4 points to the total score. However the arthritis may improve with treatment but if the same patient develops proteinuria, which is scored as 4 points so the net is 0, although the patient has new onset nephritis (40).

2.5.2 SLEDAI 2000 (SLEDAI-2K)

SLEDAI-2K assesses global disease activity and was introduced in 2002. It was modified from the original SLEDAI to include persistent disease activity in the variables (mucosal ulcers, rash, proteinuria, and alopecia). It has been validated against the original SLEDAI with a high correlation between both indices ($r = 0.97$, $P = < 0.0001$) (5).

SLE disease activity when assessed by SLEDAI-2K, strongly predicts organ damage accumulation and mortality (5). SLEDAI-2K has been validated for both clinical and research purposes. Its fundamental properties that have led to widespread clinical use include: easy to administer, simplified scoring and practicability in the clinical set-up.

SLEDAI-2K (30day) was formulated as an extension of the SLEDAI-2K and was found to be identical to the original SLEDAI (10 day version) (41).

2.5.3 Clinical SLEDAI and Mexican SLEDAI

Clinical SLEDAI index (cSLEDAI) was derived from SLEDAI-2K by omitting the immunologic variables. MEX-SLEDAI was developed by Mexican researchers to diminish the cost of laboratory tests in SLEDAI. The omission of anti-ds DNA and complement levels reduces costs, particularly when dealing with disadvantaged populations. Both indices have been shown to have convergent validity and high correlation with SLEDAI-2K (6). The cSLEDAI-2K

has a higher sensitivity (86%) and correlation (r = 0.924) compared to MEX-SLEDAI. MEX-SLEDAI has not been validated for use in non-Hispanic populations.

Furthermore, recent literature showed a lack of consistency between complement levels and the occurrence of disease flares; complement levels are impacted by various factors like genetic polymorphisms, variability in synthesis, autoantibodies which may activate complement regardless of disease activity (42). The choice of cSLEDAI in this study was due to its wide use across different cultures, ease of administration and practicability in the clinical setting.

2.5.4 Safety Of Estrogens in Lupus National Study (SELENA-SLEDAI)

This index was developed for a National Institute Health multi-centre study of oestrogen/ progesterone use in women with SLE. The clinical and laboratory parameters of SLEDAI were scored whether they were objective or subjective. It has not been validated with other indices (43).

2.5.5 British ISLEs Lupus Assessment Group (BILAG)

BILAG is a comprehensive organ based transitional index that rates nine organ systems with scores and utilises the principle of intention to treat. The individual organ manifestations are assessed as either non-existent, better, worse or new as compared to disease activity in the prior month. The original BILAG was published in 1988 and later updated in 2004 (BILAG-2004). The revised index had two added systems i.e. ophthalmic and abdominal while vasculitis was removed (44, 45).

The BILAG-2004 index scores each domain into by a letter score of A to E based on a detailed set of rules. Grade A represents severe disease activity which requires immunosuppressive drugs and/prednisone dose of more than 20 mg per day or high dose anticoagulation. Grade B refers to moderate disease activity which requires a reduced dose of steroids, topical steroids, topical immunosuppressive agents, anti malarials or NSAIDs. Grade C is categorised as mild stable disease while Grade D implies no disease activity but the system may have previously been affected. Grade E indicates that there is no current or previous disease activity.

BILAG 2004 index score strength lies in its ability to incorporate changes in disease activity over time. It also shows sensitivity to minor changes and can distinguish between disease

activity and severity. Furthermore, it portrays disease activity in individual systems 'at a glance' rather than combining them into a global score (46).

BILAG is limited in use by its very comprehensive nature and is time consuming to administer. Additionally, it is not anchored to baseline values rather, the values are compared to the prior month. Moreover, it has a ceiling on worsening (46).

2.5.6 European Consensus Lupus Activity measure (ECLAM)

ECLAM is a global activity score which evaluates disease activity within one month (47). It comprises of 34 weighted clinical and serological items but excludes the autoantibody testing. It has 12 domains (10 organ systems plus Erythrocyte Sedimentation Rate [ESR) and complement levels). 4 of the domains are further subdivided. This index, in contrast to others, was derived from the study of 704 actual SLE patients. Disease activity is scored from 0 to 17.5.

The ECLAM global score is unable to detect changes in severity over time.

2.5.7 Systemic Lupus Activity Measure (SLAM)

SLAM was developed in 1988 and reviewed in 1991 (SLAM-R) as a global activity score that estimates disease activity in the last month. The development of this index relied on domain sampling theory. The factors to be scored were selected to represent the most common manifestations. It contains 9 non-weighted clinical and 7 laboratory manifestations. Disease activity ranges from 0 - 84 and is based on 32 variables. Each variable is scored from 0-3 and based on severity. A score of >6 is considered to be clinically relevant as it is associated with a greater than 50% possibility of initiating treatment. SLAM-R can assess both disease activity and severity (48).

However SLAM-R is less than optimal when compared to SLEDAI because of its subjective nature. The scoring is dependent on the patient's report of their symptoms without objective documentation e.g. fatigue (subjective feeling of extra ordinary tiredness). Moreover, it lacks to the ability to discriminate between mild and severe organ disease activity.

2.5.8 Visual Analogue Scale

Another simple index used is the Visual Analogue Scale (VAS) that consists of a line of 10 cm along which the patient or physician draws a perpendicular mark, reflecting their assessment of overall disease activity. The patient VAS gives an overall impression of how patients experience the effects of disease and includes subjective symptoms like fatigue, myalgia, arthralgia and abdominal pain. The physician VAS is a reflection of how active the attending doctor considers the disease state to be, especially with regard to the need for intervention. In many ways, the physician VAS resembles the old case summary note describing whether patients are doing well, unchanged or poorly .

Composite responder indices are largely used in clinical trials. The FDA recommends that improvement in disease activity should be not accompanied by worsening, that a change in disease activity index should be statistically significant, clinically meaningful, and prospectively defined, and that the change in scores on a disease activity index should be measured between the outset and the end of the trial analysis. They include the SLE Responder Index (SRI) and BILAG Based Combined Lupus Assessment (BICLA). In SRI, SLEDAI is the driver of efficacy while in BICLA; BILAG is the driver of efficacy. The SRI can demonstrate incomplete but clinically significant > 50% improvement in disease activity over 30 days in patients with lupus. BICLA requires an improvement in BILAG-2004 in A and B scores, no new BILAG B score, no worsening of the total SLEDAI-2K score from the baseline, no significant deterioration (not > 10% worsening) in the 100 mm Visual Analogue Scale and no treatment failure (49-51).

2.6 Assessment of Damage in SLE

With improved survival in SLE patients, there is need to develop a system that measures the less crude outcomes of the disease. Since the inflammatory process of SLE can result in specific organ damage, the Systemic Lupus International Collaborating Centre Clinics (SLICC) Working group/American College of Rheumatology has developed the SLICC Damage Index (SDI)(52).

Organ damage which is mostly irreversible is common among patients with SLE due to multi system involvement. Damage is only considered as 'damage' after a patient having or experienced it for a period of not less than six months according to the SDI criteria. All the 41 items that constitute the SDI are clearly defined (53). SDI measures cumulative chronic damage

resulting from disease activity and /or treatment of SLE. It assesses 41 different health problems in at least 12 body systems, (maximal score per organ system in brackets): ocular [2], neuropsychiatric [6], renal [3], pulmonary [5], cardiovascular [6], peripheral vascular [4], gastrointestinal [7], musculoskeletal [7] and skin [3]. Damage scores are also given for premature gonadal failure [1], diabetes mellitus [1] and malignancy [1]. SDI has a total score of 0 - 47, with the damage associated with higher scores. Maximum SDI score can theoretically reach 47, but this is unlikely to be compatible with life.

Organ damage to renal and cardiovascular, musculoskeletal and neuropsychiatric, systems occurs during an uncontrolled acute or chronic phase of the disease as well as a result of some medications such as corticosteroids. Organ damage is higher in the early disease stages with SLE patients exhibiting increasing damage with time ranging from 10-30%, 20 - 40% and 40 - 50% in one, five and ten years respectively (54). Early organ damage has been associated with reduced ten year survival (55). However, patients in a Canadian study assessed over different calendar periods found no change in rate of organ damage accrual when comparing populations from 1978-1988 and from 1988-1999 (56).

Extensive individual organ assessment has been done in SLE patients in KNH. An evaluation of cardiovascular risk factors demonstrated a 28% prevalence of carotid atherosclerosis in SLE patients (57). When compared with expected rates based on Framingham models, patients with SLE have a substantial and significant increase in coronary heart disease (CHD) and stroke. They have a 7.5% greater risk of CHD, 17% greater risk of death due to CHD and 7.9 times greater risk of stroke (58). Echocardiographic abnormalities in SLE patients at KNH were found in 88% of patients with 69% having mitral valve dysfunction and 22% had pulmonary hypertension (59). Haematological abnormalities were described in 75% of patients assessed at the same institution at a later study and disease duration of less than one year was found to be significantly associated with anaemia (60).

Up to 60% of SLE patients have renal manifestations. Progressively, (17%) of lupus nephritis deteriorates to end stage renal disease. There is a disproportionate racial bias in renal disease with Blacks and Hispanics being affected more than other patients (61, 62)

Organ damage portends a poor disease prognosis (63). The factors that increase organ damage include: old age at diagnosis, African American race, significant disease activity and involvement of organs such as central nervous system, extended disease duration, lower socio economic status, severe Raynaud's, long term use of steroids and anti-Phospholipid antibody positivity (54).

Since organ damage is to be distinguished from disease activity in SLE, the relevant feature must be present continuously for at least 6 months.

2.7 Disease activity and Quality of life

SLE quality of life is assessed using a disease specific questionnaire, LUPUSQoL. This questionnaire developed and validated in the United Kingdom in 2007 (8). Concurrent validity was assessed by comparing domain scores of LUPUSQoL with the Medical Outcome Study Short Form - 36 (SF - 36) and it was found to have a good correlation (r 0.71 - 0.79) when compared with other comparable domains of SF - 36. A review of Recent studies done in the UK, US and Spain found that the LUPUSQoL has discriminant validity in that it functions relatively independently as an outcome measure in SLE (64).

Existing studies comparing disease activity and quality of life are equivocal. The early studies conducted in developed countries revealed no correlation between quality of life and disease activity (65). There are very few studies done assessing disease activity and health related quality of life in Africa. This is due to diagnostic challenges, access to healthcare and the cost of treatment (66). Most of the studies have been done in North African countries (Egypt, Tunisia) and South Africa. These patient populations are not entirely native African. All these studies report challenges in assessing disease activity at the time of diagnosis. In the retrospective study done in Tunisia, high disease activity was noted at the time of diagnosis (67). Substantial inverse associations between general health, pain and social functions domains in QoL and high disease activity were reported in SLE patients in Egypt (68). In South Africa, disease activity rather disease damage was found to correlate with functional disability and HRQoL (69).

A higher disease activity negatively affects the patients' quality of life (12). The high disease activity impacts the psychological, physical, and environmental domains of QoL (70). A

persistence of the disease is also associated low HRQoL among patients with high cumulative disease activity experiencing a significant drop in pain and general health sub-scores. In addition, both pre-existing and new co-morbidities and organ damage have a negative association with HRQoL (71). Depression and fibromyalgia portend a poorer HRQoL (70). In Kenya, old age was found to positively correlate with physical health (r = 0.306, p=0.02), burden to others (r = 0.272, p=0.03), emotional health (r = 0.315, p=0.01) and fatigue (r= 0.268, p=0.04) (13). However age and duration of disease have not been consistently correlated with quality of life (12, 72). Socio-economic status has a positive association with SLE patients' quality of life. Patients with higher socio-economic status (SES) have a proportionally better quality of life than those with low SES (73).

2.8 Prognosis and survival of SLE patients

The prognosis and survival of patients with SLE has improved over the decades from a 5 year survival rate of <50% in the 1950s to approximately >90% in the 1990s (16). The decline, however, has been slowing partly due to organ damage (74). The mortality rate in SLE is still three fold greater than the general populace mainly contributed by a 6 - 40% death rate as a result of cardiovascular diseases and infection (75). The involvement of organs such as renal especially in childhood-onset SLE is associated with increased damage and mortality ranging from 21 - 65% at diagnosis to between 53-61% over a 20-year period (14). The survival rate is favourably associated with lymphopenia at diagnosis time while it is unfavourably associated with male gender, an initial high SLEDAI score, cyclophosphamide treatment and organ damage (16).

Conversely, SLE patients are living longer due to early disease recognition and treatment. This longevity is compounded by increased morbidity leading to disability, poor quality of life, high health costs and inability to work. Consequently, there are considerable direct and indirect costs to the patient and society (66, 76).

CHAPTER THREE: STUDY JUSTIFICATION

SLE is a common autoimmune disease in patients seen at the Rheumatology clinic. SLE remains a clinical syndrome with a diverse phenotype that is also variable over time in each patient; identification of patients with high disease activity is imperative for implementing cost-effective, evidence based treatment measures. Emphasis should be placed on continuous risk assessment of the patients, in practice, with the goal of implementing appropriate measures to prevent organ damage. Disease activity has been shown to predict patient outcome and mortality (77). In a British cohort study, a one point increase in the adjusted mean total of the BILAG score, observed over a 12 month period, was associated with a 15% increased risk of mortality (corresponding to a reduced survival time) and an 8% increased risk of new organ damage (37).

SLEDAI-2K is a global disease activity index that has been widely used and demonstrated validity when used by investigators from different countries. The intention of this study was to describe the level of disease activity and quality of life among SLE patients in Kenyatta National hospital. Secondly, it aimed to standardise and improve documentation of disease activity in SLE patients in the hospital. Thirdly, it could inform the establishment of a framework for identification and management of SLE patients with high disease activity.

3.1 Research Question

What is the level of disease control, quality of life and the treatment characteristics of patients with Systemic Lupus Erythematosus at Kenyatta National Hospital?

3.2.1 Broad Objective

To determine the disease activity, its impact on quality of life and the drugs used in management of patients with SLE.

3.2.2 Primary Objectives

1. To determine disease activity in patients with SLE using the SLEDAI 2K index.

2. To determine the quality of life in SLE patients using LUPUSQoL questionnaire.

3.2.3 Secondary Objectives

1. To correlate the SLE disease activity with quality of life scores in the study subjects

2. To document the current drug therapy

CHAPTER FOUR: METHODOLOGY

4.1 Study Design

This was a cross sectional, descriptive hospital based study

4.2 Study Setting

This study was carried out at the Rheumatology and Renal Outpatient Clinics in Kenyatta National Hospital (KNH). KNH is a tertiary urban hospital. It is the largest national referral hospital in Kenya and also serves as the teaching hospital for the University of Nairobi. It is situated in Nairobi, the capital city of Kenya. It has a bed capacity of 1800 and over 6000 members of staff. The rheumatology clinic is the only tertiary referral centre for rheumatologic diseases in Kenya. It runs every Thursday from 2-5 pm and is covered by consultant rheumatologists and residents from departments of Internal Medicine and Paediatrics. The average number of patients seen per clinic is 50-60 patients. These patients have diverse rheumatologic conditions including: SLE, rheumatoid arthritis, systemic sclerosis, osteoarthritis among others. The number of SLE patients per clinic visit ranges from 5-10. The renal clinic runs every Friday morning and is covered by nephrologists and fellows from the nephrology program. The clinic has 80-100 patients booked per visit, with multiple renal disorders: chronic kidney disease, hypertensive and diabetic nephropathy, glomerulonephritis, etc. The renal clinic does not have separate clinics for the various diseases seen.

4.3 Study Population

The SLE patients who satisfied the SLICC 2012 criteria and were on follow up at the rheumatology and/or renal clinic at KNH.

4.4.1 Inclusion Criteria

i). The time of SLE diagnosis was defined as the point in time when the patient cumulatively fulfilled at least four of SLICC criteria.

ii). Patients who were older than 18 years.

iii). Patients who consented to participate in the study.

4.4.2 Exclusion Criteria

Patients with overlap syndromes were excluded. These are patients with rheumatic disease with systemic symptoms that overlap two or more specific, recognised entities and cannot be definitively diagnosed. These include: Mixed connective tissue disorder (lupus — scleroderma — polymyositis — rheumatoid arthritis), Rheumatoid arthritis — lupus overlap, Lupus - systemic sclerosis overlap, undifferentiated systemic rheumatic disease.

4.5 Sample Size Estimation

All SLE patients attending the rheumatology/renal clinic were eligible for inclusion in the study. According to data from KNH hospital records, an estimated 70 patients were on follow up at KNH rheumatology clinic between June to December 2017. A representative sample was drawn from the population during the study.

Yamane (1967) provides a simplified formula to calculate sample sizes. Assuming a 95% confidence level, p=.5

n-is the sample size

N-is the population size

e-is the level of precision

$$n = \frac{N}{1 + N(e)^2}$$

$$n = \frac{70}{1 + 70(0.05)^2}$$

n= 60

4.6 Sampling Method

Consecutive sampling was utilised until the desired sample size was achieved. Participant recruitment was done by the principal investigator (PI). The PI visited the rheumatology clinic in KNH clinic 17 every week on Thursdays between two to five pm and the renal clinic on Fridays

from 8am and reviewed files of patients on follow up for SLE. All patients with SLE attending the clinics and satisfied the inclusion criteria were eligible to participate in the study.

4.7 Data collection

4.7.1 Clinical Methods

The sequence of data collection was as follows:

1. Once consent was obtained, a structured screening pro-forma was administered by the PI (Appendix I)

2. The patients who fulfilled the inclusion criteria were recruited to the study. The patients' file was reviewed to extract information pertaining to demographic details, current therapy, duration of illness and documented evidence of organ damage.

3. The PI conducted a comprehensive physical examination which included a general medical examination with evaluation of skin, scalp, presence of scars, ulcerations, oral thrush, pallor, jaundice, cyanosis, oedema and peripheral lymphadenopathy and a targeted systemic exam (respiratory, cardiovascular, abdominal, musculoskeletal and neurologic). An ECG was done once the clinical exam was complete. The clinical aspect of the SLEDAI-2K was then completed with corroboration of findings with the consultant rheumatologist.

4. The patients were provided with the LUPUSQoL questionnaire which was preferentially self-administered. If the education level or the clinical status of the patient prevented the patient from completing the form, the PI filled the form. This was done by reading out the questions and the patient provided their response. The questions were repeated as necessary without providing any clarifications which would direct the response. Only 5 patients required help to fill the questionnaire. The average time taken to complete the LUPUSQoL was 15 minutes.

5. The PI used aseptic technique to draw blood samples (complete blood count, urea, Creatinine, electrolytes, Creatinine kinase) for evaluation. Patients were provided with a sample bottle and advised on how to collect a clean catch sample of urine for urinalysis.

Thereafter, patients had retinal photography done at the diabetic outpatient clinic (fundus photography room) and the images were reviewed by the ophthalmologist.

4.7.2 Laboratory Methods

For the complete blood count, 2 ml was drawn into a sterile EDTA vacutainer. For urea, creatinine, electrolytes, creatinine phosphokinase, 4 ml of blood was put into a sterile red top vacutainer. All blood samples were delivered to the laboratory within 2 hours to avoid degenerative changes. The patient was adequately instructed on how to collect a mid-stream urine sample for urinalysis. (The initial flow of the urine was to be voided in to the toilet. The midstream sample must be collected into the specimen bottle taking care not to touch the inside of the bottle to avoid contamination. This is known as the midstream specimen. Once there was enough urine in the collection pot, voiding was completed in to the toilet).

Urine was analysed using the dipstick method and microscopy. For the dipstick, the manufacturer's strip was dipped into urine ensuring all coloured reagent blocks were covered in urine. The strip was then tapped along the edge of the container to remove excess urine. Once the relevant time indicated on reagent strip instructions had elapsed, the strip was held against the container comparing the standardised chart with the sample strip. Urine microscopy was done on a sample that had been centrifuged.

Creatinine phosphokinase was assessed by an enzymatic rate method that determines CK activity in serum. In the reaction CK catalyses the transfer of a phosphate group from the creatinine phosphate substrate to adenosine diphosphate (ADP). The subsequent formation of adenosine triphosphate was measured through the use of two coupled reactions catalysed by hexokinase and glucose-6-phosphate dehydrogenase which results in production of nicotinamide adenine dinucleotide. The system monitored the rate of change in absorbance at 340nm over a fixed time interval.

The blood samples were analysed using standard laboratory techniques and automated analysers at the KNH laboratory.

4.7.3 Quality Assurance

The standard operating procedures in all aspects of this study were adhered to at all times and the recommended procedure for specimen collection was adhered to. This included proper phlebotomy site cleaning and use of appropriate vacutainers. There was proper labelling of specimens to minimise pre-analytical sources of error.

Specimens were run in the KNH laboratory and the manufacturer's guidelines were strictly adhered to. The CBC was analysed by the CELL-DYN analyser which is calibrated according to the manufacturer and Kenya Bureau of Standards. Urea, creatinine and electrolytes were analysed by a fully automated analyser (biolis 50i superior machine). The KNH laboratory runs daily internal quality control on all tests and has an external quality control programme provided by the Riqas® company.

4.8 Study Variables

4.8.1 Independent Variables

Age - was recorded as number of years documented in the file or reported as from date of birth

Sex - categorised as Male or Female

Level of education —recorded as highest level of education the patient has attained

Current treatment — was defined as drugs used and dosage. Drugs were classified as glucocorticoids, immunosuppressants and immunomodulators.

SLE diagnosis — was defined as months or years from the date SLICC criteria were fulfilled.

Disease duration-was recorded as the time interval from SLE diagnosis until the last follow up

4.8.2 Outcome Variables

1. Disease activity

Disease activity was scored using the SLEDAI 2K index. This was calculated as a continuous variable and further categorised into three groups i.e. Mild disease activity (SLEDAI Score of 0-5), moderate disease activity (SLEDAI score of 6-12) and severe disease activity (SLEDAI

score of >13). The assessment of the clinical components of the SLEDAI was done by the PI and reviewed by the consultant rheumatologist.

Table 3: Assessment Of Disease Activity

Descriptor	Assessment	Definition
Seizure	Assessed clinically	Recent onset, exclude metabolic, infectious or drug causes
Psychosis	Assessed clinically	Altered ability to function in normal activity due to disturbance in the perception of reality. Include hallucinations, incoherence, marked loose associations, impoverished thought content, marked illogical thinking, bizarre, disorganised, or catatonic behaviour. Exclude uraemia and drug causes
Organic brain syndrome	Assessed clinically	Altered mental function with impaired orientation, memory, or other intellectual function, with rapid onset and fluctuating clinical features, inability to sustain attention to environment, plus at least 2 of the following: perceptual disturbance, incoherent speech, insomnia or daytime drowsiness, or increased or decreased psychomotor activity. Exclude metabolic, infectious or drug causes.
Visual disturbance	Assessed by Fundoscopy	Retinal changes of SLE. Include cytoid bodies, retinal haemorrhages, serous exudates or haemorrhages in the choroid, or optic neuritis. Exclude hypertension, infection or drug causes
Cranial nerve disorder	Assessed clinically	New onset of sensory or motor neuropathy involving cranial nerves
Lupus headache	Assessed clinically	Severe, persistent headache: may be migrainous but must be non-responsive to narcotic analgesia
CVA	Assessed clinically	New onset cerebrovascular accident(s). Exclude arteriosclerosis
Vasculitis	Assessed clinically	Ulceration, gangrene, tender finger nodules, periungual infarction, splinter haemorrhages, or biopsy or angiogram proof of vasculitis
Arthritis	Assessed clinically	> 2 joints with pain and signs of inflammation (i.e., tenderness, swelling or effusion).
Myositis	Creatinine phosphokinase levels	Proximal muscle aching/weakness, associated with elevated creatinine phosphokinase/aldolase or electromyogram changes or a biopsy showing myositis
Urinary casts	Urine microscopy	Heme-granular or red cell casts
Hematuria	Urine microscopy	> 5 red blood cells/high power field. Exclude stone or other cause
Proteinuria	Urine microscopy	> 0.5 g /24 hr.
Pyuria	Urine microscopy	> 5 white blood cells / high power field. Exclude infection.
Rash	Assessed clinically	Inflammatory type rash
Alopecia	Assessed clinically	Abnormal, patchy or diffuse loss of hair
Mucosal ulcers	Assessed clinically	Oral or nasal ulcerations

Pleurisy	Assessed clinically	Pleuritic chest pain with pleural rub or effusion. Or pleural thickening
Pericarditis	Assessed clinically, ECG/ ECHO confirmation	Pericardial pain with at least one of the following: rub, effusion, electrocardiographic confirmation or echocardiographic confirmation
Low complement	complement levels by ELISA	Decrease in CH50, C3 OR C4 below lower limit of normal for testing laboratory
Increased DNA binding	Farr assay by ELISA	Increased DNA binding by Farr assay above the normal range for testing laboratory
Fever		> 38^0C. Exclude infectious cause.
Thrombocytopenia	Complete blood count (CBC)	< 100,000 platelets/x 10^9, exclude drug causes
Leukopenia	CBC	< 3,000 white blood cells / x 10^9, exclude drug causes
Adopted from: Gladman DD, Ibañez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. J Rheumatol. 2002 Feb;29(2):288–91.		

The SLEDAI score was calculated based on the clinical and laboratory manifestations present at the time of the visit or in the preceding 30 days.

2. Quality of life

The LUPUSQoL questionnaire has 8 domains namely physical health, emotional health, body image, pain, planning, fatigue, intimate relationship and burden to others. The score ranges from 0 (worst HRQoL) to 100 (best HRQoL). Higher scores indicate better QoL. The mean raw domain score was divided by 4 and then multiplied by 100. The result represented the transformed score for that domain. Transformed domain scores were obtainable when at least 50% of the items were answered. The mean raw domain score was then calculated by totalling the item response scores of the answered items. A non-applicable response was treated as unanswered and the domain score was calculated.

4.9 Ethical Considerations

Approval to conduct the study was given by the KNH/UON Institutional Research and Ethics Committee (P833/12/2018). Eligible patients were enrolled into the study after an explanation of the study was given and subsequent informed consent form duly signed. Patient confidentiality was maintained at all times. There was no discrimination of any patients who declined to enrol for the study. Patient usual care was not interrupted and where possible, was facilitated by the principal investigator. There was minimal risk to the patients. Only blood

samples intended for the study were drawn, and thereafter discarded after analysis according to KNH and Lancet laboratory standard operating procedures. Results were communicated to the patient and attached to the file. Patients who needed therapeutic intervention were called by the PI and booked for review at the rheumatology clinic. A copy of this results will be provided to the relevant KNH management i.e rheumatology and renal units.

The data collection instruments had minimum possible subject identifiers. Only serial numbers were entered into the questionnaire and specimen labels. Data was entered into a password protected data base under the custody of the principal investigator. The statistician was provided with de-identified data. Confidentiality was strictly adhered to and all costs pertaining to this study were borne by the principal investigator.

4.10 Data Management

4.10.1 Data collection, entry and validation

Only data relevant to the study was collected by the principal investigator with strict adherence to the research protocol. Data was collected on a paper based form and checked for accuracy and completion by the PI. Data was entered into a password protected electronic Microsoft access database handled by the statistician. After completion of data entry, entries in the database were compared with the hard copies to ensure accuracy. Inconsistencies in the data were detected by use of simple frequencies and correlations and those identified were rectified before data analysis commenced.

4.10.2 Data handling

The data collected was kept confidential and only available to the PI, statistician and the PI's supervisors. Data capture forms were kept in a sturdy box file accessible only to the PI and were locked at day's end. Data forms are stored securely and will be availed should the department of Clinical Medicine require them. Only de-identified data was provided to the statistician for analysis.

4.10.3 Data Analysis

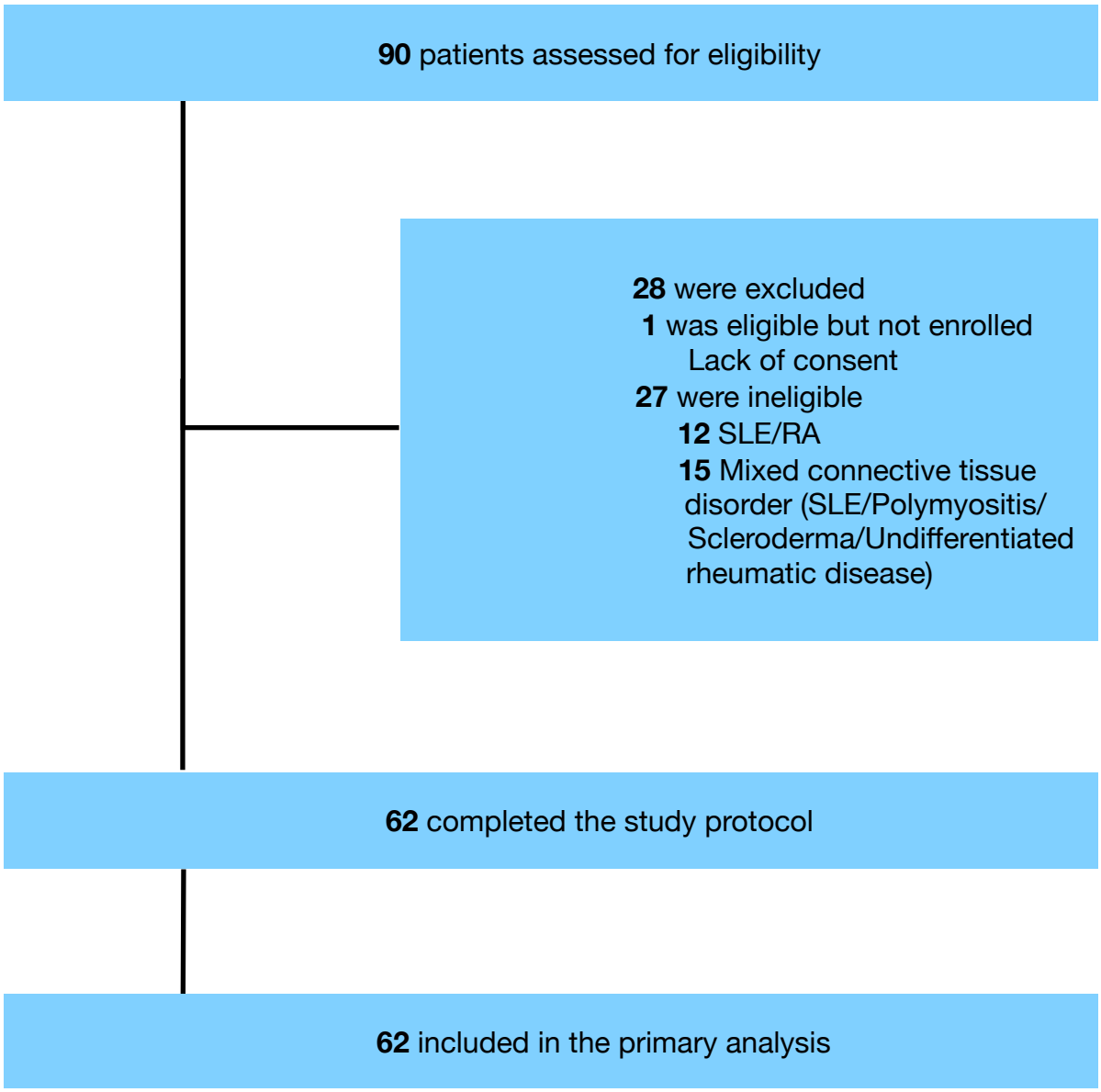
Statistical analysis was done using SPSS version 23 (SPSS Inc., Chicago, IL, USA). Analysis included descriptive statistics such as mean, median and standard deviation for continuous

variables and frequency distributions for categorical variables with their corresponding 95% confidence intervals. Comparisons for continuous data were made using the t-test and of categorical data using chi-square. Prevalence of study variables (disease activity and quality of life) were calculated as the proportion of patients having the variable divided by the total number of patients. A p value of ≤ 0.05 was considered to be significant. The data was presented in the form of tables, charts and graphs.

CHAPTER FIVE: RESULTS

This was a prospective/cross sectional study conducted at Kenyatta national hospital in the period May to July 2019. A total of 90 patients were assessed, 62 respondents who satisfied at least four of the SLICC 2012 criteria and were on follow up at the rheumatology clinic (56) and renal clinic (6) in KNH were recruited and interviewed. One patient declined to provide consent to have their blood samples drawn.

Figure 2: Flow Of Patients



5.1 Demographic and social characteristics of patients

A total of 62 valid questionnaires were collected, giving a response rate of 100%. Majority of the respondents were female (60/96.8%) and only 2 were male. As shown in the table below, the mean age of all respondents was 34.7 years (SD±11.8 years) and age range was 17-61 years. Mean age for female patients was 34.4 years (SD±11.9 years). Of the male respondents; one was aged 40 years and the other 46 years. Amongst all respondents, 36 (58.1%) were married and 27 (43.6%) had attained tertiary level of education (Table 4).

Table 4: Socio-Demographic Characteristics Of The Study Population

Variable	Frequency n=62 (percentage)
Age in years	
17	4 (6.5)
18 – 30	23 (37.1)
31 – 40	15 (24.2)
41 – 50	14 (22.6)
>50	6 (9.6)
Gender	
Female	60 (96.8)
Male	2 (3.2)
Marital Status	
Married	36 (58.1)
Single	26 (41.9)
Level of education	
Primary complete (0-8 years)	5 (8.1)
Primary incomplete	10 (16.1)
Secondary incomplete	6 (9.6)
Secondary complete (9-12 years)	14 (22.6)
Tertiary (>12 years)	27 (43.6)
Residence	
Nairobi	28 (45.2)
Others	34 (54.8)
Employment Status	
Formal employment	17 (27.4)
Self employed	15 (24.2)
Unemployed	30 (48.4)

5.2 Disease history and medication

All 62 respondents provided information on disease history and the drugs prescribed for their condition. This information was corroborated with the patients' hospital records. The median disease duration was 36 months with the shortest follow up being 1 month and the longest was 324 months. Nine (14.5%) of the respondents were not on any medication at the time of interview. Only 2 respondents were on hydroxychloroquine mono-therapy. The other patients were on various drug combinations; HCQ and steroids were prescribed to 77.4% of patients in conjunction with other immunosuppressant drugs. The most frequently prescribed drug combination was hydroxychloroquine, steroid and azathioprine with 13 patients (21%) (table 5). The median dose of steroids was 11.2 mg (Range=2.5 – 60 mg). There was no patient on biologic disease modifying drugs.

Table 5: Duration Of Illness And Medications Used By Patients

Variable	Frequency n =62(%)
Duration of illness	
<1 year	20 (32.3)
1 – 5 years	24 (38.7)
>5 years	18 (29.0)
Combination Therapies	
Not on any medication	9 (14.5)
HCQ+Steroid+Azathioprine	13 (21.0)
HCQ+Steroid	8 (12.9)
HCQ+MMF+Steroids+ACEi/ARBs	8 (12.9)
HCQ+MMF+Steroids	5 (8.1)
HCQ+Steroid+Azathioprine+ACEi/ARBs	3 (4.8)
HCQ+Steroid+ACEi/ARBs	2 (3.2)
HCQ only	2 (3.2)
HCQ+Lef+Steroids+ACEi/ARB	1 (1.6)
HCQ+Lef+Steroids+Azathioprine	1 (1.6)
HCQ+cyclophosphamide+steroid	1 (1.6)
HCQ+MMF	1 (1.6)
HCQ+MMF+steroids+Azathioprine	1 (1.6)
MMF+steroid+ACEi/ARBs	1 (1.6)
MMF+steroid	1 (1.6)
Steroid+Azathioprine+ACEi/ARBs	1 (1.6)
Steroid+Azathioprine	1 (1.6)
Steroid+Cyclosporin	1 (1.6)
HCQ+Methotrexate+steroids	1 (1.6)
HCQ+methotrexate+steroid+ACEi/ARBs	1 (1.6)

5.3 Disease activity

Disease activity was assessed using cSLEDAI-2K, a validated disease activity index that has 24 clinical and laboratory variables that are weighed differently. The score has 9 domains corresponding to different organ systems (central nervous system, vascular, renal, musculoskeletal, serosal, dermal, immunologic, constitutional and haematological). The disease manifestations are weighted with values ranging from 1-8 and the scores are then totalled. The maximum disease activity score is 105 and remission is 0. The scores were divided into three categories: mild disease activity (0-5), moderate disease activity (6-12) and more than 12 was severe disease activity. Low disease activity/remission on therapy is defined by SLEDAI score ≤ 3 on antimalarials or SLEDAI score ≤ 4 on glucocorticoids ≤ 7.5 mg.

The mean disease activity score was 7 (SD ± 5.2) and the median disease activity was 7 (range 0-18). Half of the patients in the study had moderate to severe disease activity. There were 8 patients in remission on therapy.

SLEDAI-2K	**Frequency n=62 (%)**
Disease Activity Score	
Mild	31 (50.0)
Moderate	15 (24.2)
Severe	16 (25.8)
Low disease activity	8 (12.9)

There were no patients presenting with seizures, psychosis, cranial nerve disorders, lupus headache, or cerebrovascular accident at the time of assessment. Complement levels and quantitative DNA levels were not done for majority of patients. There were 13 patients with visual abnormalities [optic atrophy-2], [glaucoma-2], [age-related macular degeneration-3] and [hydroxychloroquine toxicity-6]. None of the retinal changes were indicative of active disease. Among the 62 respondents, 33 (53.2%) had renal involvement with 31 having proteinuria (Six patients were recruited from the renal clinic). The patients with renal disease were all female and had a mean age of 33.2 years (SD±12.6 years). Of the 33 patients, only 10 patients had biopsy proven nephritis, seven were newly diagnosed while the remaining 16 had been on follow up for more than 18 months. The median estimated glomerular filtration rate was 69.4. Fifteen (24.2%)

respondents had myositis while 33.8% (21) had haematological abnormalities (leukopenia and/ or thrombocytopenia) (Table 6)

Table 6: Clinical And Laboratory Characteristics (Sledai-2K)

Descriptor	**Score**	**Frequency n=62 (%)**
Proteinuria	4	31 (50.0)
Hematuria	4	19 (30.6)
Leukopenia	1	17(27.4)
Myositis	4	15 (24.2)
Alopecia	2	9 (14.5)
Pleurisy	2	9 (14.5)
Arthritis	4	7 (11.3)
Thrombocytopenia	1	7 (11.3)
Increased DNA binding	2	5 (8.1)
Rash	2	5 (8.1)
Pyuria	4	4 (6.5)
Vasculitis	8	3 (4.8)
Mucosal ulcers	2	3 (4.8)
Low complement	2	3 (4.8)
Fever	1	2 (3.2)
Rash	4	1
Psychosis	8	1
Urinary casts	4	1
Organic brain disorder	8	1

5.4 Quality of life

Health related quality of life was assessed by the disease-specific LUPUSQoL which has eight domains and a score range of 0 (worst)-100 (best). The questionnaire was self-administered.

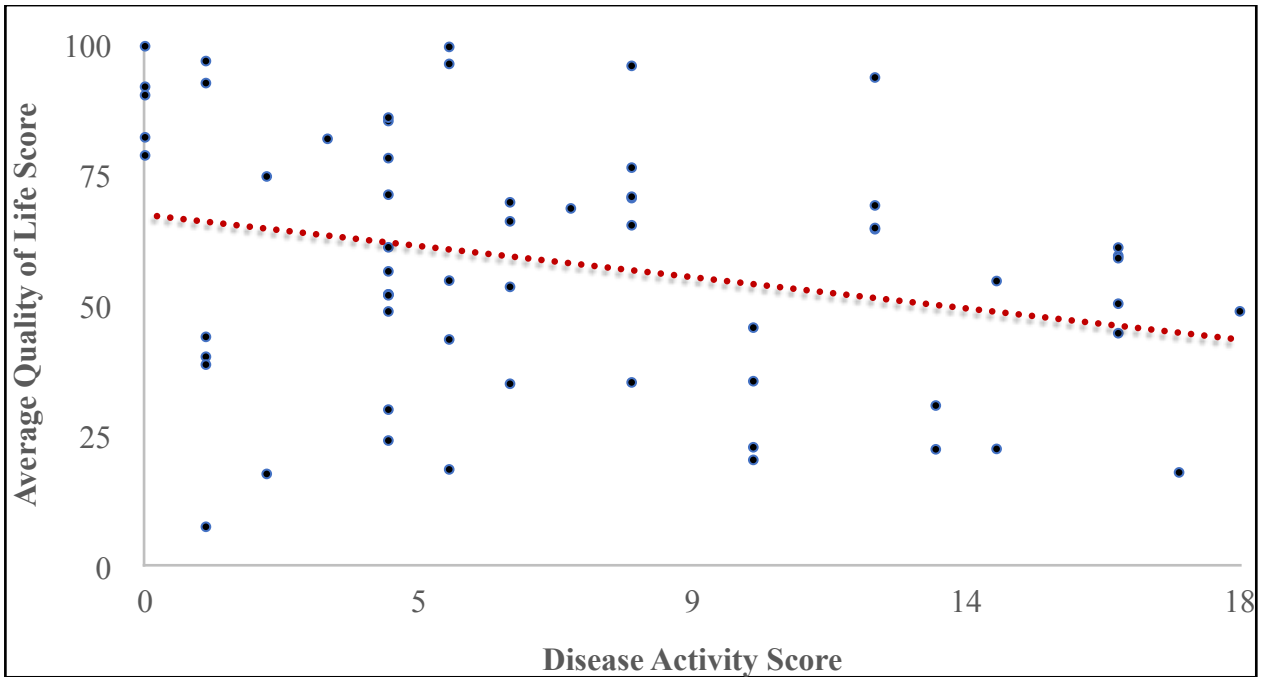
The mean LUPUSQoL score was 56% (S.D 24.4, p=0.026). (Table 7.) All domains of LUPUSQoL were impaired especially the domains of intimate relationships, burden to others and body image. The mean QoL scores amongst the three groups of disease activity were lowest in patients with severe disease activity and highest in patients with mild disease activity. The patients with renal abnormalities had significantly lower QoL compared to other patients (r=-0.36, p=0.037) and the pain (p=0.009), intimate relationships (p=0.04) and body image (p=0.01) were most affected.

Table 7: Average Quality Of Life (Mean Lupusqol Scores)

LupusQoL domains mean±SD (range)	**SLE patients (n=62)**	
	Mean (SD)	Range
Physical health	58.2 (28.2)	6.3 – 100
Pain	60.2 (29.8)	8.3 – 100
Planning	65.9 (29.0)	0 – 100
Intimate relationship	50 (38.2)	0 – 100
Burden to others	50.9 (34.7)	0 – 100
Emotional health	62.3 (26.2)	4.2 – 100
Body image	51.0 (30.1)	0 – 100
Fatigue	65.4 (28.7)	6.3 – 100
Average quality of life score	56.0 (24.4)	7.6 - 99.6

Pearson correlation coefficients were done to correlate the LUPUSQoL scores with disease activity scores, age and disease duration. Disease activity scores showed significant negative correlation with the average QoL with the physical health, pain, burden to others and body image being the worst affected domains. However the planning, intimate relationships, emotional health and fatigue domains did not show any correlation with disease activity scores (table 8, 9).

Figure 3: Correlation Between Average Quality Of Life And Disease Activity For All Respondents'



There was a significant negative relationship between disease activity and quality of life for all the respondents (r =-0.28, p = 0.025)

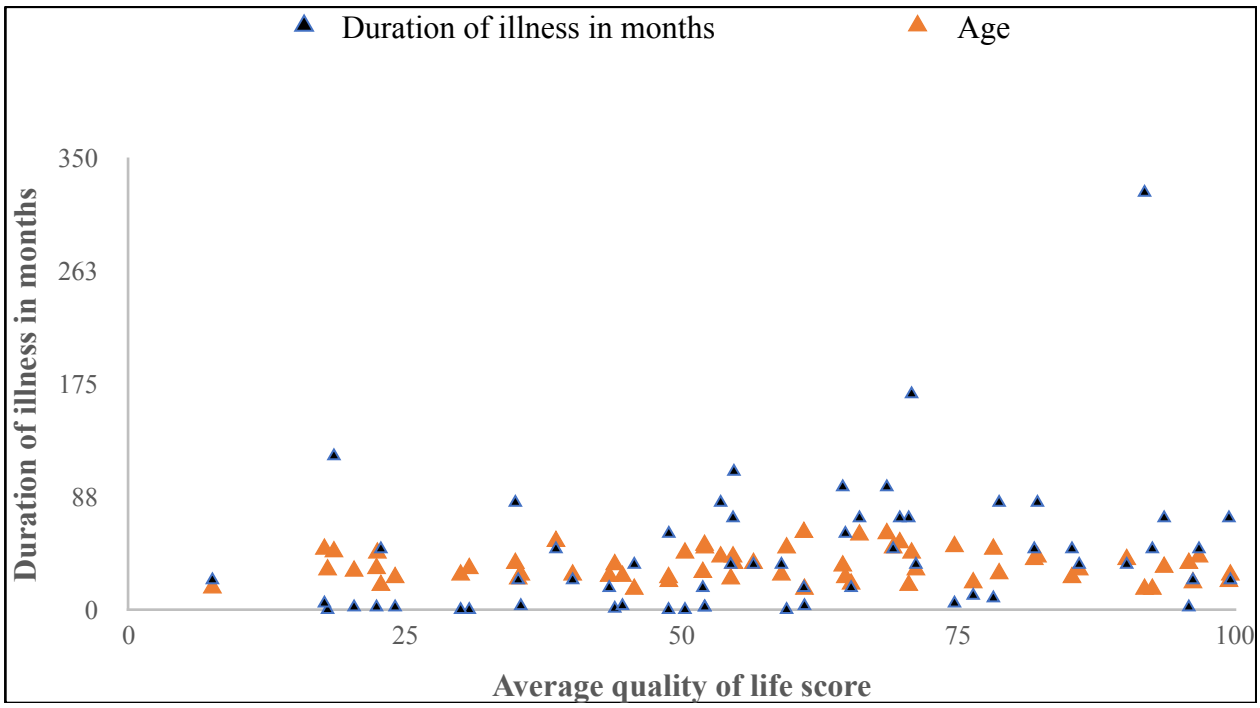
Table 8: Pearson Correlation Between Individual Quality Of Life Domains And Disease Activity Score (Sledai 2K) (n=62)

LupusQoL domains	**SLE patients (n=62)**	
	SLEDAI (r)	**p-value**
Physical health	-0.26	0.043*
Pain	-0.28	0.027*
Planning	-0.15	0.255
Intimate relationship	-0.22	0.092
Burden to others	-0.36	0.004*
Emotional health	-0.079	0.540
Body image	-0.34	0.007*
Fatigue	-0.08	0.532
Average quality of life	-0.28	0.026

r= Pearson's correlation co-efficient, * p value <0.05

Age and disease duration were positively correlated with mean QoL scores. Pain, emotional health and body image domains improved with longer disease duration (table 10,11). However, age did not show any significant statistical correlation with any of the LupusQoL domains.

Figure 4: Correlation Between Quality Of Life, Age And Disease Duration



The average quality of life score was positively correlated with duration of illness (r=0.31, p=0.01)

Table 9: Pearson Correlation (r) Between Disease Duration And Mean Lupusqol Scores

LupusQoL domains	Pearson Co-efficient r	P-value
Physical health	0.24	0.06
Pain	0.32	0.01*
Planning	0.22	0.07
Intimate relationship	0.25	0.05*
Burden to others	0.13	0.31
Emotional health	0.28	0.02*
Body image	0.34	0.007*
Fatigue	0.23	0.08

*p value < 0.05

CHAPTER SIX: DISCUSSION

This study is the first prospective study in SLE patients at KNH, exclusively focusing on disease activity. Previously, multiple studies have been done evaluating specific aspects of disease activity. The study utilised cSLEDAI-2K and LUPUSQoL questionnaires to assess disease activity and quality of life respectively.

As expected, majority of the correspondents were female (96.8%). The mean age of the study population was 34.7 years (SD±11.8 years) and the median age was 32.5 years. This is in keeping with other epidemiological studies which have shown SLE to be a disease with a female preponderance and affecting young adults (1).

More than half of the patients had active disease as the median disease activity score was 7. This score is lower compared to other studies done in Africa to assess disease activity. The most recent study done in Egypt using SLEDAI-2K revealed a mean disease activity score of 17±11 (78). An earlier retrospective study done in Tunisia, found the mean SLEDAI at diagnosis to be 12.7 (67). Our study omitted ds DNA and complement levels thus the total SLEDAI score was lower. These countries have different socio-cultural practices and their population has Arab and Southern European ancestry which differs from the ethnic composition of the Kenyan population. Comparable studies done in other resource constrained settings have reported equivalent results. A study done in India found 69% (n=73) of their patients to have moderate to severe disease (79). In the Western world, the Hopkins Lupus Cohort which was a longitudinal study of patients with SLE for more than 28 years, African Americans (38.9%) tended to have a higher disease activity score and a more aggressive chronic course. This pattern was also observed in the Lupus in minorities: nature versus nurture (LUMINA) cohort that also had multiple ethnicities (n=554)(80-82). Persons having African ancestry are prone to having a more aggressive disease course. The high disease activity can be attributed to a cumulative effect of multiple barriers including delays in diagnosis, lack of access to specialists and prohibitive cost of treatment and regular follow up. Diagnostic delays are affected by the heterogeneous nature of the disease, the lack of immunological assays in most laboratories, long lag period before referral to a specialist which all add up to cause organ damage and severe disease (66).

Kidney disease had a significant contribution to the high disease activity. Renal disease was defined by abnormal urinalysis with or without elevated plasma creatinine. The prevalence of renal dysfunction was 53%. This is consistent with other studies that have demonstrated racial disparity in lupus nephritis (LN) (83). Patients of African descent have more aggressive disease (83). Lupus nephritis requires a biopsy for definitive diagnosis. Only 10 patients had biopsy proven nephritis. The renal histopathology findings were mainly proliferative LN (class III and IV). This is similar to the findings of a systematic review of lupus nephritis in Africa which showed that proliferative LN is the most prevalent subtype (62). Most of the patients with renal disease were asymptomatic. This delay in diagnosis could be attributed to lack of finances to pay for laboratory investigations and fragmentation of care and follow up of patients. Most of the patients were on follow up at the rheumatology clinic while others (6) attend the renal clinic. These two clinics are not integrated and there are no local protocols to be followed. Thus, patients are managed with varying therapeutic options depending on whether they visit the rheumatologist or the nephrologist.

SLE strongly influences the health status of patients. LUPUSQoL is a disease specific questionnaire that targets outcomes in lupus. Quality of life is critical in providing the patients perspective regarding their disease and how it impacts their physical and psychological wellbeing. This study demonstrated a global poor quality of life with the average QoL mean score being 56%. Progressive decline in QoL was noted with worsening disease activity (p = 0.025). The results of this study confirm the discriminant validity of LupusQoL in defining outcomes in lupus. As a disease specific measure, it was able to reliably distinguish between patients with varying degrees of disease severity. Similarly, in Egyptian patients, the overall QoL was poor and an inverse relationship existed between disease activity and QoL. Their scores in the LupusQoL domains were comparable to the ones obtained in our study except for intimate relationships and body image where they scored significantly higher. The overall quality of life in SLE as reported in other studies has been reduced albeit with different domains affected (70). In developed societies, ethnicity impacts HRQoL with African Americans having greater impairment compared to Caucasians (84). This impairment is further worsened by the greater vulnerability of Blacks to severe disease.

In 2013, the first study done on quality of life in SLE patients in KNH, QoL was correlated with age. This study demonstrated an overall low HRQoL, mean LupusQoL score of 55%. Although the current study demonstrated a marginal improvement in most domains (except for burden to others which worsened), the overall quality of life remains unvaried. The poor quality of life in patients with lupus at KNH contrasts sharply with the better quality of life in patients with rheumatoid arthritis in the same institution. In spite of the patients with rheumatoid arthritis having poor disease control, they have a better HRQoL (85). We can only postulate as to the reason why this is so could be due to older age of patients with rheumatoid arthritis and better social support.

The present study similarly showed a positive correlation between age and HRQoL. However this did not translate to any statistically significant correlation unlike previously where physical health, burden to others and body image were found to improve with age. It is worthwhile to note that the patient demographics for both studies were not identical. The foregoing study had included participants with a lower age limit (14) while the present study had a higher age limit. On the other hand, disease duration had no impact on the HRQoL. This contrasts with the current study which delineated a positive correlation between disease duration and the pain, emotional health and body image domains. Quality of life has been shown to improve with age. With passage of time, patients find it easier to accept their disease and the impact it has. Thus they are able to develop coping strategies. However, other studies have shown contradictory results regarding the effect of age and disease duration (9, 12, 79, 80).

Table 10: Review Of Quality Of Life In Previously Reported Series

LupusQoL domain Mean ±SD	**2013 (Kenya) n=62**	**2019 (Kenya) n=62**	**2019 (Egypt) n=94**
Physical health	54.0±23.3	58.2±28.2	60.4±23.7
Pain	56.6±29.6	60.2±29.8	63.6±14.1
Planning	63.7±29.3	65.9±29.0	71.9±13.6
Intimate relationship	41.1±38.4	50±38.2	73.3±19.6
Burden to others	58.9±31.2	50.9±34.7	58.8±19.8
Emotional health	61.3±26.5	62.3±26.2	60±15.5
Body image	47.1±24.2	51.0±30.1	59.3±23.7
Fatigue	57.5±30.0	65.4±28.7	66.2±16.0
Average LupusQoL	55	56	64.75

The most impaired domains were intimate relationships (50%), burden to others (50.9%) and body image (51%). Further, when correlated with disease activity, physical health (p=0.043), pain (p=0.027), burden to others (p=0.004) body image (p=0.007) and general health were the most affected. These domains had questions with regard with to sexual activity, being burdensome to family and friends and the physical appearance relating with weight loss/gain and lupus related skin rash. The domains that were least impaired were planning (65.9%) and fatigue (65.4%). Planning domain entailed questions with regard to ability to plan and attend to social events while fatigue domain inquired whether the patients had impaired concentration, early morning exhaustion and lethargy.

Lupus disproportionately affects women. Patients' demographics consisted mainly of young adult females with varying physical, social and psychological needs. Aesthetic concerns in this age group are a major factor. The changes in physical appearance (weight gain/loss, Cushing facies) can elicit low self esteem compared to healthy women of a similar age. Moreover, sexual intimacy is impaired by pain and lack of confidence to engage with their partners. More than half of the patients were unemployed and this dependence of family and/friends to cater for their financial needs created an undue imposition on their support system.

The findings of the current study are in tandem with similar findings done in resource constrained settings. A study in India revealed a negative correlation between high disease activity and disease the physical and psychological aspects of lupus while the social and environmental aspects were not affected (79). In South Africa, high disease activity negatively impacted functional ability and health related quality of life (86). However, the relationship between disease activity and HRQoL in SLE is not uniform. A lack of correlation between disease activity and HRQoL is present in other settings (72). This can be attributed to different patient characteristics, different instruments of assessment, the diverse nature of the disease and the periodicity of symptoms. Patients with renal disease also scored lower in the average QoL compared to patients with non-renal disease. This pattern was also observed in the Egyptian patients and in a systematic review (78, 87). In conclusion, high disease activity portends a worse QoL. It is thus necessary to incorporate measures that provide patient reported outcomes in routine clinical practice to better evaluate the impact of disease on the overall health status.

Regarding the medications used by patients, there was significant heterogeneity noted in the prescriptions given to patients. This is due to multiple factors. The patients are evaluated by doctors of different cadres during their clinic visits. The patients attend the rheumatology clinic and some overlap with the renal clinic. These clinics happen on different days. There is no integrated lupus/renal clinic. These clinics are staffed by specialists consultants and residents from Internal Medicine at different levels of training. There are no local institutional guidelines or any international guidelines adopted for use in our set-up. Although hydroxychloroquine is one of the cornerstone drugs in management of lupus, only 77% of patients had it prescribed. This percentage remains unchanged compared to another study done in KNH in 2016 (60). This discrepancy was attributed to in part by the cost of the medication which reported to be expensive by the patients, drug allergies and other unclear reasons. The median dose of steroids was 11.2 mg (range 2.5 mg – 60 mg) which is higher than the dose needed to achieve remission for patients without renal abnormalities, cardio-pulmonary involvement or fever. This is based on the recommendations from the low lupus disease activity score (LLDAS) which defines inactive lupus as: 1) SLEDAI-2K score ≤ 4 with no activity in major organ systems (renal, neurological, cardiovascular, pulmonary, vasculitis, fever); 2) a current prednisone (or

equivalent) dose of ≤ 7.5 mg daily (88). On the other hand, complete remission (absence of clinical activity, without use of glucocorticoid or immunosuppressive drugs) in SLE is rare. The consensus panel, DORIS (definition of remission in SLE) recommended low disease activity to be defined as SLEDAI ≤ 3 on antimalarials or SLEDAI ≤ 4 with glucocorticoid ≤ 7.5 mg of prednisone and immunosuppressant drugs as tolerated (77). Only 8 patients with mild disease were found to have remission on therapy. The immunosuppression background necessary to achieve remission in lupus nephritis includes induction and maintenance phase with the preferred agents being mycophenolate mofetil (MMF) and cyclosporine (CYC) (41). Only 33% of patients with renal disease were on MMF and most of them were on a suboptimal daily dose. The access to cost effective medication was impeded by high cost of drugs. The cost of biologics was too prohibitive. Additionally, it was also observed that some of the patients who attend renal clinic are not on follow up with the rheumatologist. Renal clinic also has higher patient numbers with diverse kidney diseases. There is no separate clinic for patients with lupus nephritis, hence they are reviewed like other patients with chronic kidney disease.

While cSLEDAI has the advantage of being easy to administer and score, it is limited by its inability to differentiate between partial improvement and worsening of active manifestation. This creates a ceiling effect. The SLEDAI-2K scoring system assigns the same numerical scoring to proteinuria regardless of severity or whether the proteinuria is new, recurrent or persistent. This in part explains the high disease activity demonstrated by patients with renal abnormalities (proteinuria, haematuria, and urinary casts). It would be imperative to perform a quantitative protein analysis to better define remission. Another drawback of the global scoring system is that the aggregate score cannot distinguish between those with multiple mild manifestations from those with fewer but severe manifestations (52). Given that most of the patients demonstrating renal involvement were asymptomatic, early diagnosis and detection of renal abnormalities is thus necessary to avert progression to CKD and improve longterm morbidity and mortality.

CONCLUSION

Most of the patients in the study had moderate to severe disease as assessed by SLEDAI-2K. Those with severe disease had renal involvement and majority of them had been on longterm follow up. Thus, they require periodic review of their treatment options.

This study demonstrated a reduced HRQoL as assessed by LupusQoL. The health status of patients was impaired across all the domains of the LupusQoL. HRQoL was negatively associated with young age, a recent diagnosis of lupus, active disease and presence of renal involvement. HRQoL is an important measure of outcome in assessment of the impact of disease and should be incorporated in routine clinical care.

There was a lack of consistency noted in the drug prescription patterns. There is need to adopt international treatment guidelines and integrate rheumatology and renal clinics to reduce the discrepancies in the prescriptions.

STRENGTHS

This is the first study that evaluates disease activity with a large sample size. Previous studies assessed individual components of disease activity without providing a global score. This study provides a baseline survey which can be used in future to follow up patients or be part of a longitudinal study to assess improvement or decline in health status.

The study also included assessment of the health related quality of life. This is one of the measures of patient-reported outcomes which can be used to guide therapy.

LIMITATIONS

- SLEDAI-2K is inherently limited by the dichotomous nature of the scoring system which disregards the severity of the abnormalities thus creating a ceiling effect. The score assigns the same numerical weight which makes it insensitive to any partial improvement or worsening of active manifestations (thrombocytopenia of $100x10^3$ is scored the same as platelet count of $10x10^3$)
- SLEDAI-2K is also unable to differentiate proteinuria due to active nephritis or glomerular damage. The SLEDAI-2K does not provide for continuous scoring thus categorising all

patients with their varying levels of renal manifestations as having the same severity. Patients with lupus nephritis on longterm follow up require quantitative urine studies to better define whether they were in remission or not.

- Cross-sectional nature of the study could not account for the periodic variation of the disease and cannot establish the temporal relationship between SLE/myositis overlap.
- This was a single centre study and the findings and outcomes may not be generalisable.

RECOMMENDATIONS

- The institution should develop a form for assessing disease activity at every visit. This is especially important for those patients having high disease activity and renal impairment. A complete blood count and a quantitative urinalysis may suffice to identify the patients with active lupus.
- Measures of patient reported outcomes like quality of life should be incorporated into routine clinical practice.
- Establishment of a patient support program to include educational materials, group therapy to enable patients cope with their disease.
- There is need to integrate the rheumatology clinic with the renal clinic to standardise care and harmonise the follow up of patients.
- National/Institutional guidelines should be developed in line with international best practice guidelines and adopted to minimise the discrepancies and variation in therapy for patients on follow up at KNH.
- The records' filling system should be improved and International Statistical Classification of Diseases and Health Problems (ICD) coding to be done for patients' on follow up in the clinic to improve access to files.
- The laboratory should provide a comprehensive urinalysis report, including urine microscopy.
- Routine screening for retinopathy should be done.

APPENDIXES

Appendix I: Study Questionnaire

Study Date: ……Study Number: ……Hospital Number…….
Consent Given: Yes No: Slicc Criteria : Yes No
Sex: Male Female Age: Duration Of Disease:

Occupation: Residence:

Marital Status: Single Married Divorced Separated

Drug	History of usage		If Yes, Total Daily Dose (Mg)	SLEDAI-2K Score				LUPUSQoL Score	
	YES	NO		CLINICAL		LAB		Physical health	
NSAIDS					Seizure	Myositis		Pain	
HCQ					Psychosis	Urinary casts		Planning	
Methotrexate					Organic brain syndrome	Hematuria		Intimate relationship	
Leflunomide					Visual disturbance	Proteinuria		Burden to others	
Mycophenolate Mofetil					Cranial nerve disorder	Pyuria		Emotional health	
Cyclosporine					Lupus headache	Low complement		Body image	
Azathioprine					CVA	Increased DNA binding		Fatigue	
Steroids					Vasculitis	Fever			
Biologic agents					Arthritis	Thrombocytopenia			
Anticonvulsants					Seizure	Leukopenia			
Heart failure meds					Rash	eGFR			
Other drugs					Alopecia	Renal biopsy			
					Mucosal ulcers				
					Pleurisy				

Appendix II: The 2012 Slicc Criteria For Classification Of SLE

Classify a patient as having SLE if a) The patient satisfies four of the criteria including at least one clinical criterion and one immunologic criterion or b) The patient has biopsy-proven nephritis compatible with SLE and with ANA or anti-dsDNA antibodies	
CLINICAL CRITERIA	
1. Acute Cutaneous Lupus	Lupus malar rash (do not count if malar discoid), Bullous lupus, Toxic epidermal necrolysis variant of SLE, Maculopapular lupus rash. Photosensitive lupus rash (in the absence of dermatomyositis). Subacute cutaneous lupus (nonindurated psoriaform and/or annular polycyclic lesions that resolve without scarring, occasionally with post-inflammatory dyspigmentation or telengectasias)
2. Chronic Cutaneous Lupus	Classical discoid rash-localised (above the neck) or generalized (above and below the neck). Hypertrophic (verrucous) lupus. Lupus panniculitis (profundus). Mucosal lupus. Lupus erythematosus tumidus, Chillblains lupus, Discoid Lupus- lichen overlap.
3. Oral ulcers	Palate, Buccal, Tongue or Nasal ulcers (in the absence of other causes, such as vasculitis, Behcets, infection(herpes), IBD, reactive arthritis, and acidic foods
4. Non-scarring alopecia	Diffuse thinning of hair or hair fragility with visible broken hairs (in the absence of other causes such as alopecia areata, drugs, iron deficiency and androgenic alopecia
5. Synovitis involving > 2 joints	Characterized by swelling and effusion or tenderness in 2 or more joints and thirty minute or more of morning stiffeness
6. Serositis	Typical pleurisy for more than 1 day or pleural effusions or pleural rub. Typical pericardial rub pain (pain with recumbency improved by sitting forward) for more than 1 day or pericardial effusion Or pericardial rub or pericariditis by ECG (in the absence of other causes, such as infection, uremia, and Dressier's pericarditis
7. Renal manifestations	Urine protein/creatinine (or 24 hr urine protein) representing 500mg of protein in 24 hrs or red blood cell casts
8. Neurological manifestations	Seizures, psychosis, Mononeuritis multiplex (in the absence of other known causes such as primary vasculitis), myelitis, peripheral or cranial neuropathy (in the absence of other known causes such as primary vasculitis, infection, diabetes mellitus), acute confusional state (in the absence of other known causes, including toxic-metabolic, uremia, drugs)
9. Hemolytic anaemia	
10. Leukopenia/ Lymphopenia	Leukopenia < 4000mm3 at least once (in the absence of other known causes such as Felty's drugs, and portal hypertension) Lymphopenia < 1000mm3 at least once (in the absence of other known causes such as corticosteroids, drugs and infection)
11. Thrombocytopenia	< 100 000mm3 at least once (in the absence of other known causes such as drugs, portal hypertension and TTP
IMMUNOLOGICAL CRITERIA	
1. ANA	Above the reference range of the laboratory
2. Anti-dsDNA	Above the reference range of the laboratory, except ELISA: twice above the laboratory reference range
3. Anti -Sm	
4. Anti Phospholipid Antibody	Lupus anticoagulant, False positive RPR, Medium or high titre anticardiolipin (IgA, IgG or IgM) and beta 2 glycoprotein I(IgA, IgG or IgM)
5. Low Complement	Low C3, C4 or CH50

6. Direct Coomb's Test	In the absence of hemolytic anemia
Criteria are cumulative and need not be present concurrently Petri M, Orbai AM, Alarcon GS, Gordon C, Merill JT, Fortin FR et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics Classification for systemic lupus erythematosus. Athritis Rheum 2012.	

Appendix III: Sledai-2K License Agreement

UHN Toronto Western Hospital

UNIVERSITY OF TORONTO LUPUS CLINIC
Centre for Prognosis Studies in the Rheumatic Diseases
Room 1-410B East Wing, 399 Bathurst Street
Toronto, Ontario, Canada, M5T 2S8

October 30th, 2019

Carlo Rodriguez
Managing Editor
The Journal of Rheumatology
365 Bloor St. E., Ste. 901
Toronto M4W 3L4 ON Canada

Re: Gladman DD, Ibanez D, Urowitz, MB. Systemic lupus erythematosus disease activity index 2000. J Rheumatol 2002;29:288-291. Table 2

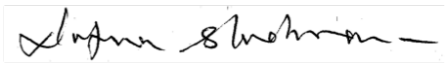
Dear Carlo:

This letter is to confirm that as authors of the above paper we give permission to reproduce the questionnaire portion (SLEDAI2K) of this manuscript to Nyambane Eunice, with the University of Nairobi-Kenya.

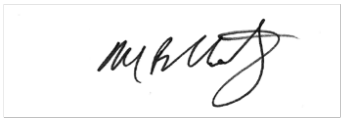
With this permission is the understanding that no modifications will be made to the instrument without further approval of the authors.

Thank you.

Yours sincerely,



Dafna D. Gladman, MD, FRCPC



Murray B. Urowitz, MD, FRCPCP

Appendix IV: Sledai-2K Disease Activity Index

SLEDAI 2K		
	Descriptor	Definition
Weight SCORE		
8	Seizure	Recent onset, exclude metabolic, infectious or drug causes
8	Psychosis	Altered ability to function in normal activity due to disturbance in the perception of reality. Include hallucinations, incoherence, marked loose associations, impoverished thought content, marked illogical thinking, bizarre, disorganized, or catatonic behavior. Exclude uremia and drug causes
8	Organic brain syndrome	Altered mental function with impaired orientation, memory, or other intellectual function, with rapid onset and fluctuating clinical features, inability to sustain attention to environment, plus at least 2 of the following: perceptual disturbance, incoherent speech, insomnia or daytime drowsiness, or increased or decreased psychomotor activity. Exclude metabolic, infectious or drug causes.
8	Visual disturbance	Retinal changes of SLE. Include cytoid bodies, retinal hemorrhages, serous exudates or hemorrhages in the choroid, or optic neuritis. Exclude hypertension, infection or drug causes
8	Cranial nerve disorder	New onset of sensory or motor neuropathy involving cranial nerves
8	Lupus headache	Severe, persistent headache: may be migranious but must be non responsive to narcotic analgesia
8	CVA	New onset cerebrovascular accident(s). Exclude arteriosclerosis
8	Vasculitis	Ulceration, gangrene, tender finger nodules, periungual infarction, splinter hemorrhages, or biopsy or angiogram proof of vasculitis
4	Arthritis	> 2 joints with pain and signs of inflammation (i.e. tenderness, swelling or effusion).
4	Myositis	Proximal muscle aching/weakness, associated with elevated creatinine phosphokinase/aldolase or electromyogram changes or a biopsy showing myositis
4	Urinary casts	Heme-granular or red cell casts
4	Hematuria	> 5 red blood cells/ high power field. Exclude stone or other cause
4	Proteinuria	> 0.5 g /24 hr
4	Pyuria	> 5 white blood cells / high power field. Exclude infection.
2	Rash	Inflammatory type rash
2	Alopecia	Abnormal, patchy or diffuse lose of hair
2	Mucosal ulcers	Oral or nasal ulcerations
2	Pleurisy	Pleuritic chest pain with pleural rub or effusion. Or pleural thickening

2	Pericarditis	Pericardial pain with at least one of the following: rub, effusion, electrocardiographic confirmation or echocardiographic confirmation
2	Low complement	Decrease in CH50, C3 OR C4 below lower limit of normal for testing laboratory
2	Increased DNA binding	Increased DNA binding by Farr assay above the normal range for testing laboratory
1	Fever	> 38^0C. Exclude infectious cause.
1	Thrombocytopenia	< 100000 platelets/x 10^9, exclude drug causes
1	Leukopenia	< 3000 white blood cells/x 10^9, exclude drug causes
TOTAL SCORE		
Gladman DD, Ibañez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. J Rheumatol. 2002 Feb;29(2):288–91.		

Appendix V: Participant Information And Consent Form

Title of Study: Assessment of disease activity in patients with Systemic lupus erythematosus at Kenyatta National Hospital

Principal Investigator/and or institutional affiliation

Dr. Nyambane Eunice

Department of Clinical Medicine and Therapeutics

University of Nairobi

P. O. Box 30197

Nairobi, Kenya

Co-Investigators and Institutional affiliation

1. Dr. L. Achieng'

Department of Clinical Medicine and Therapeutics

University of Nairobi

P. O. Box 30197

Nairobi, Kenya

2. Dr. E. Genga

Department of Clinical Medicine and Therapeutics

University of Nairobi

P. O. Box 30197

Nairobi, Kenya

3. Prof. C. F. Otieno

Associate Professor

Department of Clinical Medicine and Therapeutics

University of Nairobi

P. O. Box 30197

Nairobi, Kenya

Introduction

I would like to tell you about a study being conducted by the above listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, possible risks and benefits, your rights as a volunteer, and anything else about the research. When I have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent'. Once you understand and agree to be in the study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in a medical research: i) Your decision to participate is entirely voluntary ii) You may withdraw from the study at any time without necessarily giving a reason for your withdrawal iii) Refusal to participate in the research will not affect the services you are entitled to in this heath facility or other facilities. I will give you a copy of this form for your records.

May I continue? YES NO

This study has been approved by the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee protocol number…….

WHAT IS THIS STUDY ABOUT?

The researchers listed above are interviewing individuals who have SLE (systemic lupus erythematosus) to determine the disease activity in patients with SLE on follow up at the KNH Rheumatology clinic. SLE is characterised by periods of active disease (flares) and remission. Disease activity is important in establishing potentially reversible impairments which are amenable to therapy. This will help to determine whether your disease is adequately controlled on medical therapy. I will also be evaluating how the disease affects your quality of life. Participants will also have the choice to undergo blood tests (complete blood count, kidney function tests, creatinine phosphokinase) and a urine test. There will be approximately 60 participants in this study randomly chosen. We are asking for your consent to consider participating in this study.

WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH STUDY?

If you agree to participate in this study, the following things will happen:

You will be interviewed by a trained interviewer in a private area where you will feel comfortable answering questions. The interview will last approximately 20 minutes. The interview will cover information such as your personal bio-data i.e. age, gender, marital status, level of education. Your name and hospital number will not be included in this information to protect your privacy. Information regarding your disease (SLE) will be obtained and verified from your medical records. Details on quality of life will be inquired from you.

After the interview is complete you will have a vein-puncture for withdrawal of about 6 ml (equivalent to a teaspoon) of blood for tests. These tests will enable me determine your complete blood count, urea, creatinine and creatinine phosphokinase. You will also provide a urine sample for urinalysis.

We will ask for a telephone number where we can contact you if necessary. If you agree to provide your contact information, it will only be used by the people working for this study and will never be shared with others. The reason we may need to contact you include if we find any abnormalities on your laboratory tests that requires urgent medical attention.

ARE THERE ANY RISKS, HARMS, DISCOMFORTS ASSOCIATED WITH THIS STUDY?

Medical research has the potential to introduce psychological, social, emotional and physical risks. Effort should always be put in place to minimise the risks. One potential risk of being in the study is loss of privacy. We will keep everything you tell us confidential as possible. We will use a code number to identify you in a password-protected computer database and will keep all of our paper records in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely secure, so it still possible that someone could find out you were in this study and could find out information about you.

Moreover, answering questions in the study may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview or any question asked during the interview.

It may be embarrassing for you to have a physical examination conducted. We will do everything we can to ensure that this is done in a private room. Additionally, all study staff and interviewers are professionals with special training in these examinations/interviews.

You may feel some discomfort when we draw some blood and you may have a small bruise or swelling in your arm. In case of an injury, illness or complications related to this study, contact the study staff right away at the number provided at the end of this document. The study staff will treat you for minor conditions or refer you when necessary.

ARE THERE ANY BENEFITS TO BEING IN THIS STUDY?

You may benefit by receiving free testing (Complete blood count, creatinine, creatinine phosphokinase, urinalysis). We will refer you to a hospital for care and support where necessary. Also, the information you provide will help us better understand how well we are managing SLE.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

The study will not cost you anything. All the costs pertaining to the investigations will be borne by the investigators.

WILL YOU GET A REFUND FOR ANY MONEY SPENT AS PART OF THIS STUDY?

If the study will not be done on the same day, the participant will be given some allowance to facilitate their return trip.

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your rights as a research participant you may contact the Secretary/ Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102, email uonknh_erc@uonbi.ac.ke.

The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to participate in this research is voluntary. You are free to decline participation in the study and you can withdraw at any time without injustice or loss of any benefits.

CONSENT FORM

Participant's statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counsellor. I have had my questions answered in a language that I understand. The risks and benefits of this study is voluntary and that I may choose to withdraw at any time. I freely agree to participate in this research study. I understand that all efforts will be made to keep information regarding my personal identity confidential. By signing this consent form, I have not given up any legal rights that I have as a participant in a research study.

I agree to participate in this research study:	**Yes**	**No**
I agree to have blood sample preserved for later study:	Yes	No
I agree to provide contact information for follow up:	Yes	No

Participant printed name:……

Participant signature/thumb print……..... Date……

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher's Name……Date……

Signature……

Role in the study……..(i.e. study staff who explained informed consent form)

For more information, contact Dr. Eunice Nyambane, Tel: 0720176330 at University of Nairobi, Department of Clinical Medicine and therapeutics, from 8:00am to 5:00pm.

Witness printed name *(If witness is necessary. A witness is a person mutually acceptable to both the researcher and participant).*

Name ……

Signature/thumb print…….Date……

Appendix VI: Maelezo Ya Washirika Na Fomu Ya Ruhusa

Jina la utafiti: Uchunguzi wa udhihirisho wa ugonjwa wa SLE

Mtafiti Mkuu/ ushirikiano wa taasisi:

Dr. Eunice Nyambane

Chuo Kikuu cha Nairobi

P.O. Box 30197, GPO, Nairobi , Kenya

Simu: 0720176330

Wachunguzi wa ushirikiano / ushirika wa taasisi:

Dr. Loise Achieng'

Chuo Kikuu cha Nairobi

P.O. Box 30197, GPO, Nairobi , Kenya

Dr. Eugene Genga

Chuo Kikuu cha Nairobi

P.O. Box 30197, GPO, Nairobi , Kenya

Prof. C. F. Otieno

Chuo Kikuu cha Nairobi

P.O. Box 30197, GPO, Nairobi , Kenya

Utangulizi

Ningependa kukueleza kuhusu utafiti utakaofanywa na watafiti waliotajwa hapo juu. Madhumuni ya fomu hii ya idhini ni kukupa taarifa unayohitaji ili kukusaidia kuamua kama utashiriki katika utafiti huu. Jiskie huru kuuliza maswali yoyote kuhusu madhumuni ya utafiti, kitakochotokea ikiwa utashiriki katika utafiti, hatari na faida iwezekanayo, haki zako kama kujitolea, na kitu kingine chochote kuhusu utafiti au fomu hii ambayo hauelewi.

Nitakapo jibu maswali yako yote kwa kuridhika kwako, unaweza kuamua kushiriki katika utafiti huu au la. Utaratibu huu unaitwa 'kibali cha habari'. Ukishaelewa na kukubali kushiriki katika utafiti, nitaomba uandikishe jina lako na utie saini kwenye fomu hii. Unapaswa kuelewa kanuni za jumla ambazo zinatumika kwa washiriki wote katika utafiti wa matibabu: i) Uamuzi wako wa kushiriki ni kwa hiari yako ii) Unaweza kujiondoa kwenye utafiti wakati wowote bila ya kutoa sababu ya kujiondoa iii) Kukataa kushiriki katika utafiti haita athiri huduma unazopata kwenye kituo hiki cha afya au vituo vingine. Tutakupa nakala ya fomu hii kwa rekodi zako.

Naweza kuendela? NDIO/LA

Utafiti huu una kibali ya Hospitali ya Taifa ya Kenyatta-Chuo Kikuu cha Nairobi Kamati za Utafiti na Maadili, Nambari:…….

UTAFITI HUU UNAHUSU NINI?

Watafiti waliotajwa hapo juu watahojiana na watu ambao wana ugonjwa wa 'Systemic Lupus Erythematosus' (SLE). SLE ni ugonjwa ambao una vipindi vya kulipuka au kutulia. Kusudi la mahojiano ni kuelewa udhihirisho wa ugonjwa wa SLE ambao una uwezekano wa kubadilishwa kwa matumizi ya dawa. Utatolewa mililita 6 za damu(kijiko kidogo) tupeleke kupima kwa maabara pamoja na kutoa kipimo cha mkojo. Pia utajaza fomu ya maswali ya ubora wa maisha. Kutakuwa na washiriki takriban 60 katika utafiti huu. Tunaomba ridhaa yako kufikiria kushiriki katika utafiti huu.

NI NINI KITAKACHOTOKEA IKIWA UNAAMUA KUWA KATIKA UTAFITI HUU?

Ikiwa unakubali kushiriki katika somo hili, mambo yafuatayo yatatokea:

Utashughulikiwa na mhojiwa mwenye ujuzi, katika eneo la kibinafsi ambapo utajibu maswali. Mahojiano yataendelea kwa dakika 20. Mahijiano yatakuwa kwa mada kama habari kuhusu umri, jinisa, hali ya ndoa na kiwango cha elimu. Jina lako na nambari ya hospitali hazitajumuishwa katika habari hii kwa faragha yako. Taarifa juu ya utambuzii wako wa ugonjwa wa SLE na matibabu yake utaulizwa kisha kuthibitishwa kwenye kumbukumbu zako za matibabu.

Baada ya mahojiano kumalizika, tutafanya uchunguzi wa kimwili.Uamauzi utahifadhiwa katika hatua zote za utaratibu huu.

Tutaomba nambari yako ya simu ambapo tunaweza kuwasiliana na wewe ikiwa ni lazima. Ikiwa unakubaliana kutoa maelezo yako ya mawasiliano, itatumiwa na watu wanaofanya kazi kwa ajili ya utafiti huu na kamwe hawatashirikiwa na wengine. Sababu ambazo tunaweza kuwasiliana na wewe ni kukupa matokeo ya utafiti huu na kukutaja kwa daktari wako kwa matibabu zaidi ikiwa ni lazima kulingana na matokeo.

JE, KUNA HATARI YOYOTE, MADHARA, NA USUMBUFU UNAOHUSIANA NA UTAFITI HUU?

Utafiti wa matibabu unaweza kuanzisha hatari za kisaikologia, kijamii, kihisia na kimwili. Jitihada zinapaswa kuwekwa daima ili kupunguza hatari. Hatari moja ya kuwa katika utafiti ni kupoteza faragha. Tutaweka kila kitu unachotuambia kama siri iwezekanvyo. Tutatumia nambari ya utafit ili kukutambua kwenye databana la kompyuta iliyohifadhiwa na neno siri na kuhifadhi kumbukumbu zote za karatasi kwenye baraza la mawaziri lililofungwa. Hata hivyo, hakuna mfumo wa kulinda siri yako unaweza kuwa salama kabisa, kwa hivyo bado inawezekana kwamba mtu anaweza kujua wewe ulikuwa katika utafiti huu na anaweza kupata maelezo kuhusu wewe.

Pia, kujibu maswali katika mahojianoo inaweza kuwa wasiwasi kwako. Ikiwa kuna maswali yoyote hautaki kujibu, unaweza kuruka. Una haki ya kukataa mahojiano au maswali yoyote yaliyoulizwa wakati wa mahojiano.

Inaweza kuwa aibu kwako uchunguzi wa kimwili unaofanywa. Tutafanya kila kitu kuhakikisha kuwa hii inafanyika katika chumba cha faragha. Zaidi ya hayo, wafanyakazi wote wa utafiti na wahojiwa ni wataalamu wenye mafunzo maalum katika mtihani/mahojiano haya.

Unaweza kujiskia uchungu utakapotolewa damu na huenda ukawa na uvimbe kidogo katika ngozi. Ikiwa kuna jeraha, magonjwa au matatizo yanayohusiana na utafiti huu, wasiliana na wafanyakazi wa utafiti huu mara moja kwa idadi iliyotolewamwishoni mwa hati hii. Wafanyakazi watafanya kwa hali ndogo au kukuelekeza utakapo pata matibabu zaidi.

JE, KUNA FAIDA YOYOTE KUWA KATIKA UTAFITI HUU?

Unaweza kufaidhika kwa kupata vipimo vya damu damu kwa bure. Tutakupeleka kwenye hospitali kwa ajili ya utunzaji na msaada ikiwa inahitajika. Pia, maelezo unayotoa yatatusaidia kuboresha uamuzi wa kliniki na huduma ya mgonjwa katika kitengo hiki. Taarifa hii italeta mchango kwa sayansi na itasaidia kutoa miongozo ya kliniki ya mtaalamu juu ya uchunguzi wa ugonjwa wa SLE.

KUSHIRIKI KATIKA UTAFITI HUU UNADAI GHARAMA YOYOTE

Hautalipa chochote kushirii kwa utafiti huu. Gharama zote zinazohusiana na utafiti huu zitalipiwa na wachunguzi.

JE, UTAPATA REJESHEWA PESA YOYOTE ITAKAYOTUMIKA KWA SEHEMU YA UTAFITI HUU?

Ikiwa utafiti hautafanywa siku hiyo, washiriki watapewa posho ili kuwezesha safari yao ya kurudi.

JE, KAMA UTAKUWA NA MASWALI BAADAYE?

Ikiwa una maswali zaidi au wasiwasi juu ya ushiriki katika utafiti huu, tafadhali piga simu au tuma ujumbe wa maandishi kwa wafanyakazi wa kujifunza kwa idadi iliyotolewa chini ya ukurasa huu.

Kwa habari zaidi juu ya haki zako kama mshiriki wa utafiti unaweza kuwasiliana na katibu /mwenyekiti, Kenyatta National Hospital-Chuo Kikuu cha Nairobi, kamati ya maadili na utafiti kwa nambari: 2726300 Ext: 44102, barua pepe: uonknh_erc@uonbi.ac.ke.

Watafiti watalipia malipo yako kwa idadi hizi ikiwa ni wito kwa ajili ya mawasiliano yanayohusiana na utafiti.

JE, NI UCHAGUZI GANI NYINGINE UNAYO?

Uamuzi wako wa kushiriki katika utafiti ni wa hiari. Wewe una uhuru wa kupinga kushiriki katika utafiti na unawezea kujiondoa kwenye utafiti wakati wowote bila udhalimu au kupoteza faida yoyote.

FORM YA KIBALI (TAARIFA YA IDHINI)

Taarifa ya mshiriki

Nimesoma fomu hiii ya idhini au nilisomewa habari. Nimekuwa na fursa ya kujadili utafiti huu na mtafiti. Nimekuwa na maswali , akajibu kwa lugha ambayo nianyoelewa. Hatari na faida zimeelezewa kwangu. Ninaelewa kuwa ushirki wangu katika utafiti huu ni hiari na kwamba ninaweza kuchagua kujiondoa wakati wowote. Ninakubali kwa hiari kushiriki katika utafiti huu.

Ninaelewa kuwa jitihada zote zitafanywa ili kuweka habari kuhusu siri ya utambulisho wangu binafsi.

Kwa kutia saini fomu hii ya kibali, sijaacha haki yoyoteya kisheria ambayo mimi nishiriki katika utafiti.

Nakubali kushiriki katika utafiti huu: NDIO/LA

Nakubaliana kutoa maelezo ya mawasiliano kwa kufuatiliwa: NDIO/LA

Jina la kuchapishwa la mshiriki:……

Saini ya mshiriki/ Saini ya kidole……Tarehe……

Taarifa ya mtafiti

Mimi, aliyechaguliwa, nimemweleza kikamilifu maelezo muhimu ya utafiti huu kwa mshiriki aliyechaguliwa hapo juu na kuamini kwamba mshiriki ameelewa na ametoa kibali chake kwa hiari.

Jina la mtafiti……Tarehe…….

Sahihi……..

Jukumu katika utafiti……(mtafiti ambaye alieleza fomu ya kibali cha habari)

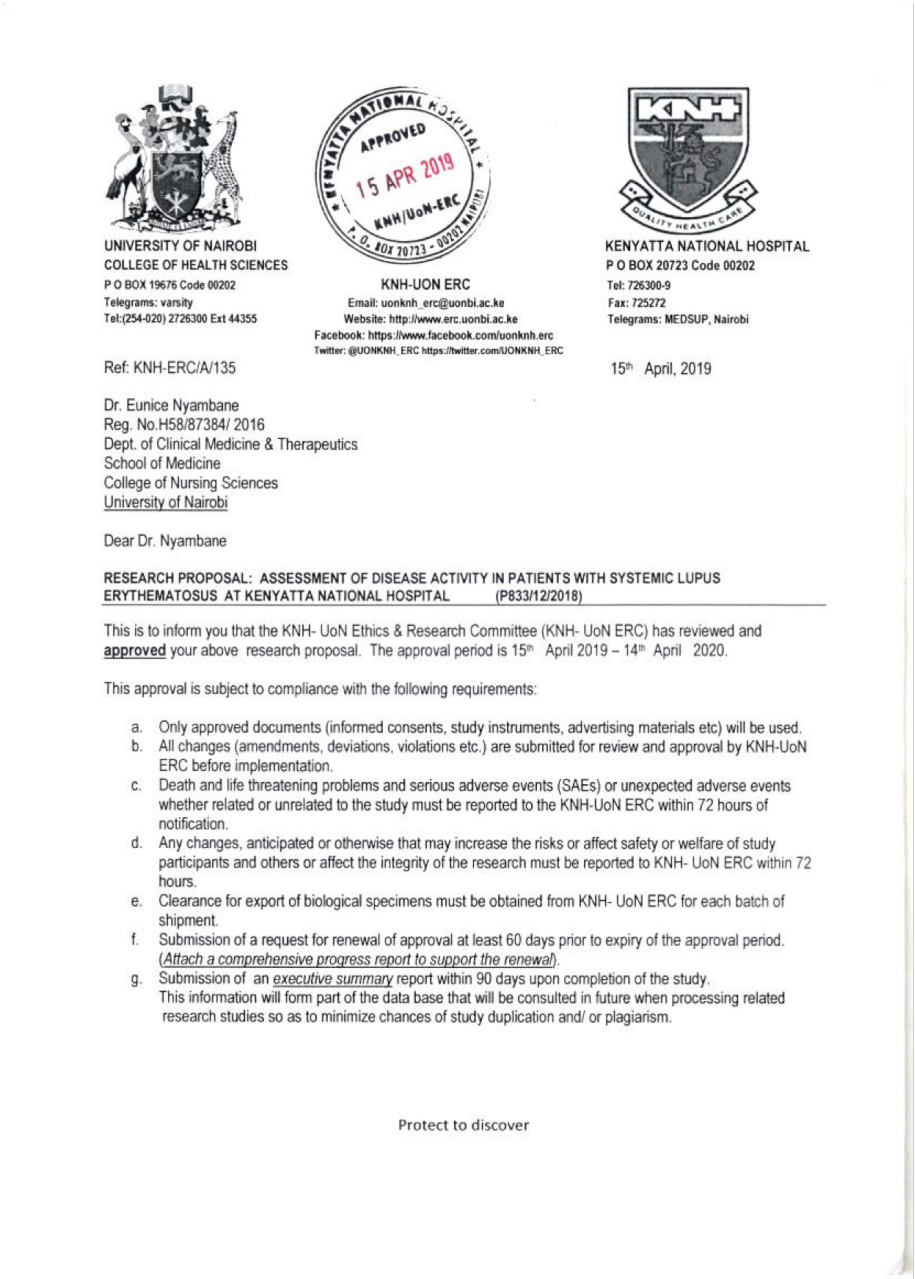
Kwa maelezo zaidi wasiliana na Dr. Eunice Nyambane, simu: 0720176330 katika chuo kikuu cha Nairobi, kutoka 8:00 asubuhi hadi saa 5:00 jioni.

Jina la kuchapishwa la shahidi (ikiwa shahidi ni muhimu, shahidi ni mtu anayekubaliana na mtafiti na mshiriki)

Jina…….....

Sahihi……..Tarehe…….
.

Appendix VII: Knh-Uon Ethics Review Committee Approval



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Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

APPROVED 15 APR 2019 KNH/UoN-ERC

Ref: KNH-ERC/A/135

15th April, 2019

Dr. Eunice Nyambane
Reg. No.H58/87384/ 2016
Dept. of Clinical Medicine & Therapeutics
School of Medicine
College of Nursing Sciences
University of Nairobi

Dear Dr. Nyambane

RESEARCH PROPOSAL: ASSESSMENT OF DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AT KENYATTA NATIONAL HOSPITAL (P833/12/2018)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 15th April 2019 – 14th April 2020.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Protect to discover

Appendix VIII: Lupusqol License Agreement

10.5 For the purposes of the Contracts (Rights of Third Parties) Act 1999 the Contract is not intended to, and does not, give any third party any right to enforce any of its provisions save that UCLan may enforce its rights under the Contract.

11. **Governing Law and Jurisdiction**

11.1 This Agreement shall be subject to the laws of England and the Licensee submits to the exclusive jurisdiction of the English Courts PROVIDED THAT the Licensor may bring proceedings of any nature in any other jurisdiction or jurisdictions, whether concurrently or not, and the Licensee agrees to submit to such jurisdiction or jurisdictions.

LICENSOR	**LICENSEE**
By: RWS Life Sciences	By: _____
Name: Amanda Rosett	Name: Nyambane Eunice_____
Title: Lead Licensing Coordinator	Title: ___Dr_____
Signature: _____	Signature: Eunice _____
Date: _____	Date: _____21/10/2019_____

Amanda Rosett Digitally signed by Amanda Rosett Date: 2019.10.22 08:56:38 -04'00'

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Appendix IX: Lupusqol Questionnaire

LupusQoL Questionnaire	
The following questionnaire is designed to find out how SLE affects your life. **Read** each statement and then tick the response, which is **closest to how you feel**. Please try to answer all the questions as honestly as you can.	
How often over the last 4 weeks	
1. Because of my Lupus I need help to do heavy physical jobs such as digging the garden, painting and/or decorating, moving furniture	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
2. Because of my Lupus I need help to do moderate physical jobs such as vacuuming, ironing, shopping, cleaning the bathroom	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
3. Because of my Lupus I need help to do light physical jobs such as cooking/preparing meals, opening jars, dusting, combing my hair or attending to personal hygiene	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
4. Because of my Lupus I am unable to perform everyday tasks such as my job, childcare, housework as well as I would like to	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
5. Because of my Lupus I have difficulty climbing stairs	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
6. Because of my Lupus I have lost some independence and am reliant on others	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
7. I have to do things at a slower pace because of my Lupus	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
8. Because of my Lupus my sleep pattern is disturbed	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
9. I am prevented from performing activities the way I would like to because of pain due to Lupus	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never

LupusQoL Questionnaire *(continued)*	
How often over the last 4 weeks	
10. Because of my Lupus, the pain I experience interferes with the quality of my sleep	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
11. The pain due to my Lupus is so severe that it limits my mobility	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
12. Because of my Lupus I avoid planning to attend events in the future	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
13. Because of the unpredictability of my Lupus I am unable to organise my life efficiently	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
14. My Lupus varies from day to day which makes it difficult for me to commit myself to social arrangements	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
15. Because of the pain I experience due to Lupus I am less interested in a sexual relationship	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never ☐793 Not applicable
16. Because of my Lupus I am not interested in sex	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never ☐793 Not applicable
17. I am concerned that my Lupus is stressful for those who are close to me	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
18. Because of my Lupus I am concerned that I cause worry to those who are close to me	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never

LupusQoL Questionnaire *(continued)*	
How often over the last 4 weeks	
19. Because of my Lupus I feel that I am a burden to my friends and/or family	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
Over the past 4 weeks I have found my Lupus makes me	
20. Resentful	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
21. So fed up nothing can cheer me up	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
22. Sad	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
23. Anxious	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
24. Worried	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
25. Lacking in self-confidence	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
How often over the past 4 weeks	
26. My physical appearance due to Lupus interferes with my enjoyment of life	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never

LupusQoL Questionnaire *(continued)*

How often over the past 4 weeks	
27. Because of my Lupus, my appearance (e.g., rash, weight gain/loss) makes me avoid social situations	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never ☐793 Not applicable
28. Lupus related skin rashes make me feel less attractive	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never ☐793 Not applicable
29. The hair loss I have experienced because of my Lupus makes me feel less attractive	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never ☐793 Not applicable
30. The weight gain I have experienced because of my Lupus treatment makes me feel less attractive	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never ☐793 Not applicable
31. Because of my Lupus I cannot concentrate for long periods of time	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
32. Because of my Lupus I feel worn out and sluggish	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
33. Because of my Lupus I need to have early nights	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never
34. Because of my Lupus I am often exhausted in the morning	☐1 All of the time ☐2 Most of the time ☐3 A good bit of the time ☐4 Occasionally ☐5 Never

Please check that you have answered each question
Thank you, for completing this questionnaire

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