Assessment of disease activity and health-related quality of life in patients with systemic lupus erythematosus at Kenyatta National Hospital

Nyambane E[1], Genga EK[1], Achieng L[1], Otieno FCF[1]

Department of Clinical Medicine and Therapeutics, School of Medicine, College of Health Sciences, University of Nairobi, P. O. Box 19676-00202, Nairobi, Kenya

Corresponding author:
Dr. Eunice Nyambane .
Email: nyambanen@gmail.com

Abstract

Objective: To determine disease activity in Systemic Lupus Erythematosus (SLE) patients and correlate it with quality of life.

Design: Cross-sectional descriptive study.

Methods: SLE patients fulfilling SLICC 2012 criteria for SLE were included in this cross-sectional study. Disease activity was measured using the clinical Systematic Lupus Erythematosus Disease Activity Index (SLEDAI-2K). Quality of life was assessed using the self-administered LupusQoL.

Results: The study group had 62 patients (60 females and 2 males) with a mean age of 34±11.8 years, and the mean duration of follow up was 36 months. The mean cSLEDAI-2K score was 7±5.2, and the median disease activity score was 7. All the domains of LupusQoL were impaired. Higher disease activity scores were associated with lower QoL scores in the domains of physical health, pain, burden to others, body image and general health. Patients with renal disease had significantly lower QoL compared to other patients, and the pain, intimate relationships and body image were most affected. Age and disease duration had a positive correlation with QoL. Disease duration (p=0.01), was associated with a better QoL in the pain, emotional health and body image domains.

Conclusion: This study is showing a low HRQoL in those with active disease mainly in the young age group. A recent diagnosis of lupus and the presence of renal disease was associated with a more reduced quality of life.

Key words: SLE, Disease activity, Health-Related Quality of Life, cSLEDAI-2K, LUPUSQoL

Introduction

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disorder characterised by inflammation in different organ systems. It has 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. 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[2].

SLE disease activity and damage scores are poor surrogates of HRQoL because results linking these measures and QoL are non-uniform[3,4]. High disease activity negatively affects the patients' quality of life[5]. In Kenya, a low QoL in SLE patients' has been described[6]. Besides, multiple studies have been done assessing individual organ systems[7,8]. The purpose of this study was to assess the impact of disease activity on HRQoL in SLE patients attending the rheumatology clinic at the Kenyatta National Hospital. It would also serve as an audit of the adequacy of care provided at the clinic while providing the patients perspective regarding their treatment.

Materials and methods

Patient selection: This was a cross-sectional descriptive study conducted at Kenyatta National Hospital rheumatology and renal outpatient clinics. The institutional ethics review committee approved the study. Informed

consent was obtained before enrolment. Ninety patients were reviewed, and 62 patients who fulfilled the Systemic Lupus International Collaborating Clinics 2012 classification criteria for SLE were consecutively recruited. One patient refused to consent, and 28 with overlap syndromes were excluded.

Data collection: Data collected included demographic characteristics (age, gender, marital status, education level, employment status) and disease duration. Disease activity was evaluated using the clinical Systemic Lupus Erythematosus Disease Activity Index 2000 (cSLEDAI). The disease-specific LupusQoL assessed the health-related quality of life. The treatment characteristics: type of drugs used (use of glucocorticoids, use of immunomodulators and immunosuppressants, e.g., hydroxychloroquine, azathioprine, biologics) and daily dosage were corroborated with the patients' medical records.

Instruments: Disease activity was evaluated by clinical SLEDAI, which omits complement and ds DNA. SLEDAI-2K is a valid, widely used index with excellent cross-cultural compatibility[9]. The cSLEDAI has been validated against the SLEDAI-2K and shown a high correlation (r=0.924)[10]. The omission of the immunological variables makes it cheaper to administer in a resource-constrained setting like Kenya.

Disease activity was scored by 22 clinical and laboratory parameters instead of the original 24 variables. The descriptors were scored if they were present at the time of the interview or in the preceding 30 days. cSLEDAI is an ordinal scale that gives a composite score ranging from 0-105. Patients scoring 0-5 were classified as having mild disease, those scoring between 6-12 were categorised as moderate, and those with scores higher than 12 were defined as having severe disease.

The health status was assessed using the disease-specific LupusQoL©, which was self-administered[11]. LupusQoL contains 34 items in 8 domains. Each item was scored with a Likert type scale to grade the patients' response with 1 (all the time), 2 (most of the time), 3 (a good bit of the time), 4 (occasionally), and 5 (never). The eight domains are physical health (8 items), pain (3 items), planning (3 items), intimate relationships (2 items), the burden to others (3 items), emotional health (6 items), body image (5 items) and fatigue (4 items). The response from the items was calculated per domain, and the mean domain score was then obtained by dividing the total score by the number of items in that domain. The mean raw domain was divided by 4 then multiplied by 100 to obtain the transformed domain score. Scores range from 0 (worst) to 100 (best). Higher scores indicate better quality of life.

Data analysis: Descriptive statistics were used to summarise the data on socio-demographic and patient characteristics. Categorical data were summarised as numbers and percentages, while continuous data were summarised as mean and standard deviation/medians and interquartile ranges, as appropriate. Pearson correlation coefficients were done to compare LupusQoL scores with disease activity, age, and disease duration. A p-value of ≤0.05 was considered to be significant. All analyses were performed on the Statistical Package for Social Sciences (SPSS) software version 23 (SPSS©, Chicago, IL, USA).

Results

The 62 patients included in the study were 60 females and 2 males. There were 56 patients from the rheumatology clinic and six from the renal clinic. The mean age was 34±11.7 years, range 17-61 years. Amongst all respondents, 36 (58.1%) were married, 27 (43.6%) had attained a tertiary level of education, and 32 (51.6%) were employed. The median disease duration was 36 (50%) months, range 1-324 months. The socio-demographic characteristics are as shown in Table 1.

Table 1: Socio-demographic characteristics of the patient population

Variable mean±SD or n (%)	SLE patients (n=62)
Age (years), mean (SD)	34±11.8
Gender, female, *n* (%)	60(96.8)
Marital status	
Married	36 (58.1)
Single	26 (41.9)
Level of education, n (%)	
Primary (0-8 years)	15(24.2)
Secondary (9-12 years)	20(32.2)
Tertiary (>12 years)	27(43.6)
Employment status	
Employed	32(51.6)
Unemployed	30(48.4)
Disease duration, n (years)	
<1 year	20(32.3)
1-5 years	24(38.7)
≥5 years	18(29.0)
Treatment characteristics	
Use of glucocorticoids	49(79.0)
Use of HCQ	48(77.4)
Use of AZA	20(32.2)
Use of Mycophenolate	17(27.4)
Other immunosuppressants	6(0.09)

The other immunosuppressants drugs used were cyclophosphamide, cyclosporin, leflunomide, and methotrexate. HCQ; hydroxychloroquine, AZA; azathioprine

Nine (14.5%) of the respondents were not on any medication at the time of the interview. Only two patients were on hydroxychloroquine monotherapy. HCQ and steroids were prescribed to 77.4% of patients in conjunction with other immunosuppressants. The median dose of steroids used was 11.2 mg (range 2.5-60mg). There was no patient on biologic disease-modifying drugs.

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 eight patients in remission on therapy (Table 2).

Table 2: Disease activity score

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)

(Max disease activity score=105, remission=0, low disease activity score ≤3 [HCQ], ≤4 [steroids])

No patients presented with seizures, psychosis, cranial nerve disorders, lupus headache, or cerebrovascular accident at the time of assessment. 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(50%) having proteinuria. The other clinical characteristics are shown in Table 3.

Table 3: Clinical and laboratory characteristics of SLEDAI-2K

Descriptor	Score	Frequency n=62 (%)
Proteinuria	4	31 (50.0)
Haematuria	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)
Rash	2	5 (8.1)
Pyuria	4	4 (6.5)
Vasculitis	8	3 (4.8)
Mucosal ulcers	2	3 (4.8)
Fever	1	2 (3.2)
Rash	4	1
Psychosis	8	1
Urinary casts	4	1
Organic brain disorder	8	1

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.

The mean LupusQoL score was 56%±24.4. All the domains of LupusQoL were impaired, especially the domains of intimate relationships, the burden to others, and body image (Table 4). 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 (Table 5). 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 4: Average quality of life (Mean LupusQoL)

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
The average quality of life score	56.0 (24.4)	7.6-99.6

Table 5: The mean LupusQoL scores amongst different groups of disease activity

LupusQoL domain	Disease activity		
	Mild (0-5)	Moderate (6 – 12)	Severe (>12)
	Mean (SD)	Mean (SD)	Mean (SD)
Physical health	63.3 (28.1)	55.2 (31.8)	51.4 (24.4)
Pain	64.5 (30.4)	62.2 (27.1)	50.0 (30.6)
Planning	69.1 (30.0)	63.3 (29.3)	62.0 (27.9)
Intimate relationship	55.2 (38.7)	49.2 (39.7)	40.6 (36.4)
Burden to others	60.9 (34.3)	47.8 (36.3)	34.4 (28.4)
Emotional health	63.0 (30.9)	59.2 (23.0)	63.8 (19.5)
Body image	59.8 (30.9)	45 (26.8)	39.7 (27.8)
Fatigue	66.3 (28.4)	61.3 (29.8)	67.2 (29.6)

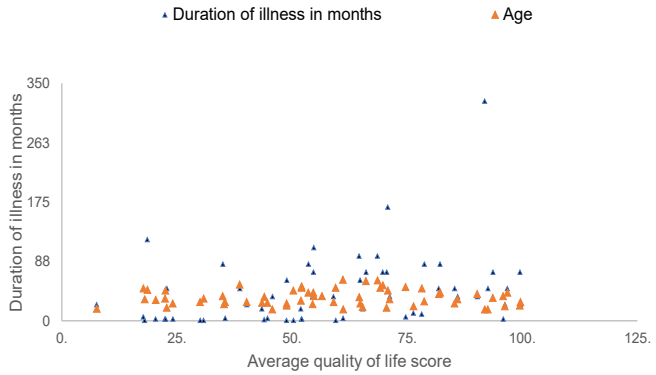
Pearson correlation coefficients were done to correlate the LUPUSQoL scores with disease activity scores, age, and disease duration. Disease activity scores showed a significant negative correlation with the average QoL with the physical health, pain, burden to others, and body image being the worst affected domains. However, the planning, intimate relationships, emotional health, and fatigue domains did not show any correlation with disease activity scores (Table 6).

Table 6: Pearson correlation between the individual quality of life domains and SLEDAI score

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
The average quality of life	-0.28	0.026

r=Pearson's correlation coefficient, *p-value ≤0.05
Age and disease duration correlated positively with mean QoL scores (Figure 1).

Figure 1: Correlation between quality of life, age and disease duration



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

Pain, emotional health, and body image domains improved with longer disease duration (Table 7). However, age did not show any significant statistical correlation with any of the LupusQoL domains.

Table 7: Pearson correlation (r) between disease duration and mean LupusQoL score

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

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. This study sought to evaluate the impact disease activity has on health-related quality of life in patients with SLE.

More than half of the patients had active disease as the median disease activity score was 7. The high disease activity can be attributed to a cumulative effect of multiple barriers, including delays in diagnosis, lack of access to specialists, and the 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, the long lag period before referral to a specialist, which all add up to cause organ damage and severe disease. However, this score is lower than what has been reported in other African countries[12,13]. Our study omitted ds DNA and complement levels; thus, the total SLEDAI score was lower. These countries also have different population diversity and socio-cultural practices. Persons having African ancestry are prone to having a more aggressive disease course. Similarly, 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 has been seen in the Lupus in the minorities: nature versus nurture (LUMINA) cohort that also had multiple ethnicities (n=554)[14-16].

Kidney disease had a significant contribution to the high disease activity. The prevalence of renal dysfunction was 53%. Most of the patients with renal disease were asymptomatic. This delay in diagnosis could be attributed

to a 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. This study demonstrated a poor global quality of life, with the average QoL mean score being 56%. 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 distinguish between patients with varying degrees of disease severity reliably. These results are similar to other studies that have shown that the overall quality of life in SLE is reduced, albeit with different domains affected[17]. Some studies have reported that ethnicity impacts HRQoL with African Americans having more significant impairment compared to Caucasians[18]. This impairment is further worsened by the greater vulnerability of Blacks to severe disease.

In 2013, the first study done on the quality of life in SLE patients in KNH demonstrated an overall low HRQoL, mean LupusQoL score of 55%[6]. 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 a better quality of life in patients with rheumatoid arthritis in the same institution. Despite the patients with rheumatoid arthritis having poor disease control, they have a better HRQoL[19]. We can only postulate as to the reason why this is so could be due to the older age of patients with rheumatoid arthritis and better social support. The current study 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. Over time, patients find it easier to accept their disease and the impact it has. Thus they can develop coping strategies. However, other studies have shown contradictory results regarding the effect of age and disease duration[5,20].

Progressive decline in QoL was noted with worsening disease activity. These findings conform to what has been reported elsewhere. Among Egyptian patients, the overall QoL was weak, 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. Similarly, in India, a negative correlation existed between high disease activity and the physical and psychological aspects of lupus, while the social and environmental aspects were not affected[21]. In South Africa, high disease activity negatively impacted functional ability and health-related quality of life[22]. 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[23]. The lack of correlation 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 the non-renal disease. This pattern was also observed in Egyptian patients and a systematic review[13,24].

Regarding the medications used by patients, there was significant heterogeneity noted in the prescriptions given to patients. The varied prescription patterns are due to multiple factors. Doctors of different cadres evaluate the patients 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 the management of lupus, only 77% of patients had it prescribed. This percentage remains unchanged compared to another study done in KNH in 2016[7]. 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 11.2mg (range 2.5mg – 60mg), which is higher than the dose needed to achieve remission for patients without renal abnormalities, cardio-pulmonary involvement, or fever[25,26].

The cross-sectional nature of the study was a limitation. It did not account for the periodic nature of the disease. SLEDAI-2K is also 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.

In conclusion, high disease activity portends a worse QoL. Young age, renal disease, and a shorter disease duration adversely affect the HRQoL. It is thus necessary to incorporate measures that provide patient-reported outcomes in routine clinical practice to evaluate better the impact of the disease on the overall health status.

Conflict of interest: None to declare.

References

1. Rees F, Doherty M, Grainge MJ, Lanyon P, Zhang W. The worldwide incidence and prevalence of systemic lupus erythematosus: a systematic review of epidemiological studies. *Rheumatology*. 2017; **56**:1945-61.
2. Olesińska M, Saletra A. Quality of life in systemic lupus erythematosus and its measurement. *Rheumatologia*. 2018; **56**(1):45-54.
3. Gladman DD, Urowitz MB, Ong A, Gough J, MacKinnon A. Lack of correlation among the three outcomes describing SLE: disease activity, damage, and quality of life. *Clin Exper Rheumatol*. 1996; **14**:305-308.
4. Jolly M, Utset TO. Can disease specific measures for systemic lupus erythematosus predict patients health related quality of life? *Lupus*. 2004; **13**:924-926.
5. Chaigne B, Chizzolini C, Perneger T, Trendelenburg M, Huynh-Do U, Dayer E, *et al.* Impact of disease activity on health-related quality of life in systemic lupus erythematosus - a cross-sectional analysis of the Swiss Systemic Lupus Erythematosus Cohort Study (SSCS). *BMC Immunol*. 2017; **18**(1):17.
6. Odhiambo J, Oyoo GO, Amayo E. An evaluation of quality of life in ambulatory patients with systemic lupus erythematosus attending rheumatology clinic in Kenyatta National Hospital. *Afr J Rheumatol.* 2014; **2**(1): 18-22.
7. Njoroge JW, Oyoo GO, Kitonyi G, Barasa A, Odhiambo A. Haematological parameters in systemic lupus erythematosus patients at Kenyatta National Hospital, Nairobi. *Afr J Rheumatol*. 2016; **4**(2): 57-62.
8. Conteh S, Ogola EN, Oyoo GO, Gitura BM, Achieng L. Echocardiographic abnormalities in systemic lupus erythematosus patients at Kenyatta National Hospital. *Afr J Rheumatol*. 2016; **4**(1): 9-13.
9. Gladman DD, Ibañez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. *J Rheumatol*. 2002; **29**:288-291.
10. Uribe AG, Vilá LM, McGwin G, Sanchez ML, Reveille JD, Alarcón GS. The Systemic Lupus Activity Measure-revised, the Mexican Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), and a modified SLEDAI-2K are adequate instruments to measure disease activity in systemic lupus erythematosus. *J Rheumatol*. 2004; **31**:1934-40.
11. McElhone K, Abbott J, Shelmerdine J, Bruce IN, Ahmad Y, Gordon C, *et al*. Development and validation of a disease-specific health-related quality of life measure, the LupusQol, for adults with systemic lupus erythematosus. *Arthritis & Rheumatism*. 2007; **57**:972-979.
12. Khanfir MS, Houman MH, Cherif E, Hamzaoui A, Souissi S, Ghorbel IB, *et al*. TULUP (TUnisian LUPus): A multicentric study of systemic lupus erythematosus in Tunisia. *Intern J Rheumatic Dis*. 2013; **16**:539-546.
13. Gaballah NM, El-Najjar AR. Clinical characteristics and health related quality of life (HRQoL) in Egyptian patients with systemic lupus erythematosus. *Egyptian Rheumatologist*. 2019; **41**:117-121.
14. González LA, Toloza SM, McGwin G, Alarcón GS. Ethnicity in systemic lupus erythematosus (SLE): its influence on susceptibility and outcomes. *Lupus*. 2013; **22**:1214-24.
15. Giannakou I, Chatzidionysiou K, Magder LS, Györi N, van Vollenhoven R, Petri MA. Predictors of persistent disease activity and long quiescence in systemic lupus erythematosus: results from the Hopkins Lupus Cohort. *Lupus Sci Med.* 2018; **5**(1):000287-93.
16. Peschken CA, Wang Y, Abrahamowicz M, Pope J, Silverman E, Sayani A, *et al*. Persistent disease activity remains a burden for patients with systemic lupus erythematosus. *J Rheumatol.* 2019; **46**:166-175.
17. Etchegaray-Morales I, Méndez-Martínez S, Jiménez-Hernández C, Mendoza-Pinto C, Alonso-García NE, Montiel-Jarquín A, *et al*. Factors Associated with Health-Related Quality of Life in Mexican Lupus Patients Using the LupusQol. *PLOS One*. 2017; **12**(1):e0170209.
18. Kiani AN, Strand V, Fang H, Jaranilla J, Petri M. Predictors of self-reported health-related quality of life in systemic lupus erythematosus. *Rheumatology*. 2013; **52**(9):1651-57.
19. Oyoo GO. An Evaluation of health related quality of life in patients with rheumatoid arthritis. *East Afr Orthop J*. 2011; **5**:40-45.
20. McElhone K, Abbott J, Teh LS. A review of health related quality of life in systemic lupus erythematosus. *Lupus*. 2006; **15**:633-463.
21. Khanna S, Pal H, Pandey RM, Handa R. The relationship between disease activity and quality of life in systemic lupus erythematosus. *Rheumatology.* (Oxford, England). 2004; **43**:1536-40.

22. Phuti A, Schneider M, Makan K, Tikly M, Hodkinson B. Living with systemic lupus erythematosus in South Africa: a bitter pill to swallow. *Health Quality Life Outcomes*. 2019; **17**(1):65-70.
23. McElhone K, Castelino M, Abbott J, Bruce IN, Ahmad Y, Shelmerdine J, *et al*. The LupusQoL and associations with demographics and clinical measurements in patients with systemic lupus erythematosus. *J Rheumatol*. 2010; **37**:2273-79.
24. Jolly M, Toloza S, Goker B, Clarke AE, Navarra SV, Wallace D, *et al*. Disease-specific quality of life in patients with lupus nephritis. *Lupus*. 2018; **27**:257-264.
25. van Vollenhoven RF, Mosca M, Bertsias G, Isenberg D, Kuhn A, Lerstrøm K, *et al*. Treat-to-target in systemic lupus erythematosus: recommendations from an international task force. *Annals Rheumatic Dis.* 2014; **73**:958-967.
26. Franklyn K, Lau CS, Navarra SV, Louthrenoo W, Lateef A, Hamijoyo L, *et al*. Definition and initial validation of a Lupus Low Disease Activity State (LLDAS). *Annals Rheumatic Dis.* 2016; **75**:1615-21.