

## Original article

### Impact of pediatric systemic lupus erythematosus on the health-related quality of life

**Background:** Pediatric SLE (pSLE) patients suffer from enhanced morbidity and hence poor health related quality of life (HRQOL), and this is expected to be more pronounced in developing countries. **Objective:** We sought to objectively evaluate the impact of pSLE on the health-related quality of life (HRQOL) in relation to disease activity and organ involvement aiming to aid strategies of improving quality of life (QOL) of those patients and their families. **Methods:** This is a cross-sectional analytical study. We enrolled 60 subjects with pSLE from the Pediatric Allergy, Immunology and Rheumatology Unit, Children's Hospital, Ain Shams University, Cairo. They were subjected to HRQOL assessment using the SLE specific QOL (SLEQOL) scales which encompass 40 items comprising physical functioning, activities, symptoms, treatment, mood, and self-image. The higher the total score the worst is the HRQOL of the patient. We also used the SMILEY scoring questionnaire, which consists of 26 items for children with SLE up to 18 years of age, in assessment of the patients' QOL. **Results:** The patients' ages ranged between 12-18 years (mean  $\pm$  SD = 12.2  $\pm$  1.9 years); 57 were females and 3 were males. All domains of the SLEQOL were significantly altered in patients evaluated during disease activity. The SMILEY scores, as well, were significantly affected by disease activity and correlated positively to the total SLEQOL score results. Most of our series (59 out of 60) had lupus nephritis, 31 (51.7%) had lupus arthritis, 12 (20.0%) had lupus carditis, and 5 (8.3%) had lupus cerebritis. The SLEQOL score in patients with lupus nephritis and arthritis were comparable (142.86  $\pm$  33.74 and 143.1  $\pm$  33.34 respectively). The scores were worse in lupus cerebritis and carditis (158.6  $\pm$  49.9 and 152.75  $\pm$  39.98, respectively). **Conclusion:** We observed a significant impact of pSLE on the HRQOL especially during disease activity. Patients with lupus cerebritis and carditis had the worst QOL status and this might be related to the physical impairment and/or intensity of immunosuppressive medications. Wider-scale prospectively designed studies would better validate our conclusions. HRQOL assessment should be implemented in the care of pSLE patients on regular basis.

Keywords: health-related quality of life, pediatric SLE, SMILEY score.

**Elham M. Hossny,  
Azza M. Youssef\*,  
Nesrine M. Radwan,  
Mohamed T. Al-  
Ashkar\*\*.**

Pediatric Allergy,  
Immunology and  
Rheumatology Unit,  
\*Pediatric Psychiatry  
Unit, Department of  
Pediatrics, \*\*Resident,  
Children's Hospital, Ain  
Shams University, Cairo,  
Egypt.

**Correspondence:**  
Mohamed Tarek  
Ramadan Al-Ashkar,  
Resident, Children's  
Hospital, Ain Shams  
University, Cairo 11566,  
Egypt.  
Email: Mohamedtarek  
803@yahoo.com

## INTRODUCTION

Pediatric systemic lupus erythematosus is an autoimmune disease which predominantly affects females.<sup>1</sup> The incidence of pSLE varies between 0.3 and 0.9/100,000 per year. Children tend to have a more severe disease than adults at the onset.<sup>2</sup>

Health related quality of life (HRQOL) is defined as the perception that individuals have of their position in life, in the context of the culture and system of values in which they live and in relation to their objectives, expectations, standards, and concerns. HRQOL can change according to the environment and the experiences, as well as in response to certain diseases.<sup>3</sup> Different questionnaires have been developed to assess HRQOL. Validated Arabic version of SLEQOL is a developed generic instrument, based on the adult

version, which provides the opportunity to address a child's HRQOL, regardless of the disease.<sup>4,5</sup>

The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) is used to measure the activity of pSLE. Its score ranges from 0 to 104, with higher scores indicating more pronounced inflammatory changes. Sometimes, a SLEDAI score  $<5$  is considered a measure of sufficient control.<sup>6</sup>

We sought to evaluate the impact of pediatric SLE on the health-related quality of life in relation to disease activity and specific organ involvement. The ultimate objective is to aid strategies that could help those patients and their families lead a normal life.

## METHODS

This analytical cross-sectional study was conducted on a group of patients with pSLE enrolled from the Pediatric Allergy, Immunology and Rheumatology Unit, Children's Hospital, Ain Shams University during the period from December 2019 to May 2020. The patients were enrolled consecutively after excluding those with other chronic illnesses or major social problems as in single parent's setting. The study gained approval from the local ethics committee of the Department of Pediatrics, Ain Shams University (Approval no. FWA00017585). Informed consent was obtained from the parents or caregivers prior to enrollment.

The HRQOL of all subjects was evaluated using two engines: the SLE quality of life (SLEQOL) and SMILEY questionnaires:

**The SLEQOL scales** encompass 40 items comprising physical functioning (6 items), activities (9 items), symptoms (8 items), treatment (4 items), mood (4 items), and self-image (9 items).<sup>7</sup> It utilizes a recall period of one week and response options/scale. A 7-point response scale is involved (subsections have different anchors, including "not difficult at all" to "extremely difficult," "not at all" to "extremely troubled," and "not at all" to "extremely often"). The patient's score is derived from the sum of all responses across the domains; alternatively, a summary score can be obtained by taking the mean of each of the 6 subsections. This scoring system places greater emphasis on domains with a greater number of items. Scores range from 40–280, with higher values corresponding to worse QOL.<sup>7</sup>

**The SMILEY questionnaire** consists of 26 items for children with SLE up to 18 years of age. It has the following domains: effect on self, limitations, social and burden of SLE. The answers in the form of a five faces scale. A higher percentage score designates better HRQOL. The answers in the form of a five faces scale, which will contain two extreme poles and a neutral option connected with intermediate answer options. Assign each response a point value, from 1 to 5. Common values for the options start with "Very sad face" at 1 point and "very happy face" at 5. A higher percentage score designates better HRQOL.<sup>8</sup>

The results of both methods were analyzed in relation to the patients' clinical data obtained by detailed history and examination, SLE disease activity index (SLEDAI) recent reference,<sup>9</sup> and treatment received.

## Statistical analysis

We used an IBM SPSS software package version 25.0. Qualitative data were described using number and percent. Quantitative data were described using median (minimum and maximum) for non-parametric data and mean, standard deviation for parametric data after testing normality using Kolmogorov-Smirnov test. Student T Test was used to assess the statistical significance of the difference between two study group means. ANOVA test was used to assess the difference between more than two study group means. Post Hoc Test was used for comparisons of all possible pairs of group means. Correlation analysis (Pearson's method) was used to assess the strength of association between two quantitative variables. Significance was judged at the (0.05) level.

## RESULTS

The patients' ages ranged between 12-18 years with a mean  $\pm$  SD of  $12.2 \pm 1.9$  years. They were 57 female and only 3 males and there was no difference in the SLEQOL score in male and female being  $138.44 \pm 30.67$  and  $138.45 \pm 35.33$ , respectively. However, the limited number of males would not permit accurate interpretation.

Our results reveal a significant negative effect of pSLE disease activity on all domains of the HRQOL according to the SLEQOL assessment (Table 1). Among our series, 59 (98.3%) patients had lupus nephritis, 31(51.7%) had lupus arthritis, 12 (20.0%) had lupus carditis, and 5 (8.3%) had lupus cerebritis. Those who had lupus nephritis (LN) were further classified based on the renal biopsy histopathological findings into 31(53%) with class II, 19 (33%) with class III, and 9 (11%) class IV LN. Patients with lupus nephritis had a collective score of  $142.86 \pm 33.74$ . The mean score in class II LN was  $128.7 \pm 29.4$ ; in class III it was  $148.76 \pm 25.83$ , and it was  $173.89 \pm 39.8$  in class IV LN. The total SLEQOL score was worst in patients with LN class IV as compared to classes II or III (Figure 1). Patients with lupus arthritis had score  $143.1 \pm 33.34$ , those with lupus carditis had a mean score of  $152.75 \pm 39.98$ , and patients with lupus cerebritis had a mean score of  $158.6 \pm 49.9$ . SLEQOL scores of patients with lupus cerebritis and carditis were higher than those with lupus arthritis or nephritis denoting a worse QOL. The type of immunotherapy used, whether cyclophosphamide or mycophenolate mofetil, did not significantly influence the SLEQOL scores of different domains of HRQOL (Table 2).

A significant effect of disease activity on the SMILEY score was observed. pSLE patients in

activity had higher SMILEY scores than those in remission (Figure 2). Moreover, the SMILEY score results correlated positively to the SLEQOL total score of the studied sample (Figure 3). The

SMILEY scores did not vary according to the class of lupus nephritis or immunosuppressive modality used.

**Table 1.** Variation of SLEQOL score results according to disease activity

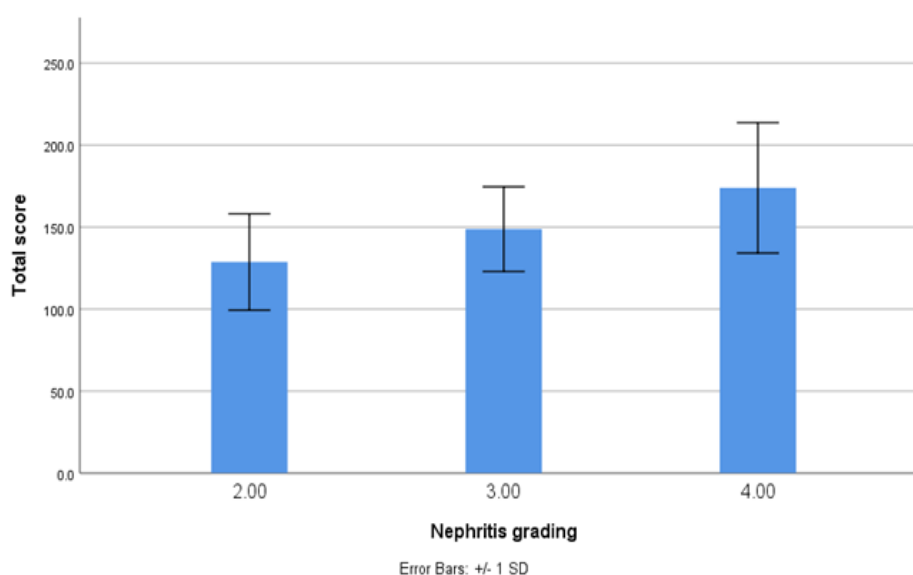
Variables	Disease status		t	p-Value
	Remission (n=48)	Activity (n=12)		
	Mean $\pm$ SD	Mean $\pm$ SD		
Social achievement	7.4 $\pm$ 2.41	9.25 $\pm$ 2.22	-2.417	<b>0.019*</b>
Emotional component	64.13 $\pm$ 11.72	83.5 $\pm$ 15.79	-4.765	<b>&lt;0.001*</b>
Learning Problems	14.54 $\pm$ 6.13	21.42 $\pm$ 4.74	-3.618	<b>0.001*</b>
Physical Activity	46.83 $\pm$ 15.34	66.67 $\pm$ 16.13	-3.967	<b>&lt;0.001*</b>
Total score	132.92 $\pm$ 26.65	180.83 $\pm$ 31.7	-5.363	<b>&lt;0.001*</b>

\* Significant; n= number; SD: standard deviation

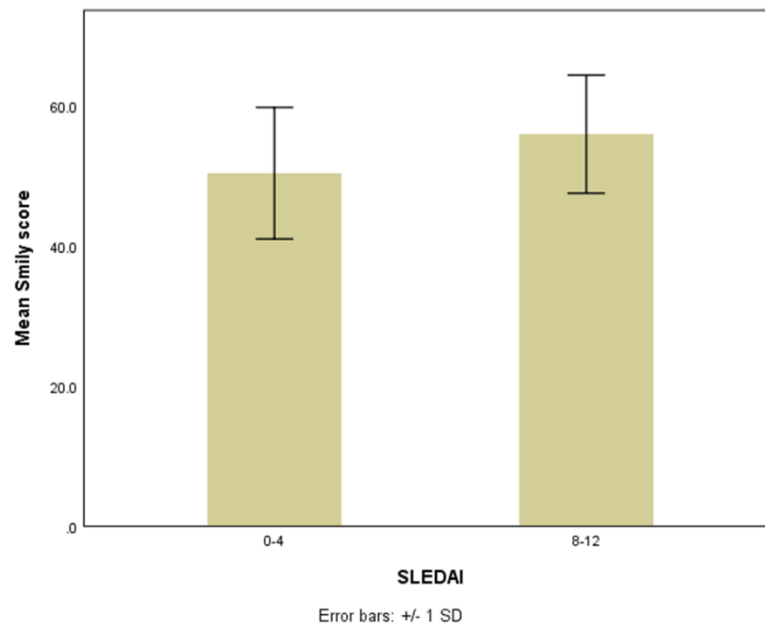
**Table 2.** Variation of SLEQOL score results according to type of immunosuppressive

Variables	Cyclophosphamide (n=11)	Mycophenolate (n=20)	t	p-value
	Mean $\pm$ SD	Mean $\pm$ SD		
Social achievement	8.2 $\pm$ 1.9	8.8 $\pm$ 1.9	-0.794	0.434
Emotional Problems	64.4 $\pm$ 16.5	72.5 $\pm$ 13.7	-1.465	0.154
Learning Problems	19.8 $\pm$ 6.1	16.9 $\pm$ 5.6	1.346	0.189
Physical Activity	55.5 $\pm$ 15.3	56.7 $\pm$ 17.6	-0.189	0.851
Total score	147.8 $\pm$ 30.5	154.8 $\pm$ 32.0	-0.586	0.562

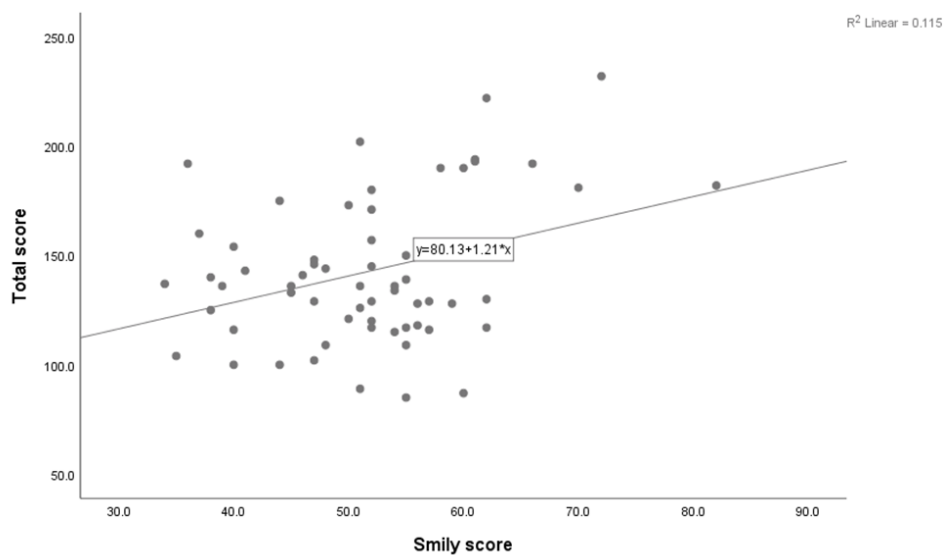
\* Significant; n= number; SD: standard deviation



**Figure 1.** Variation of SLEQOL total score according to the class of lupus nephritis.



**Figure 2.** Influence of lupus activity as judged by SLEDAI indices on SMILEY scores of the SLE patient.



**Figure 3.** Positive correlation between the smiley scores and total score of SLEQOL.

## DISCUSSION

We report a significant impact on all the domains of SLEQOL scores. pSLE did affect behavior and social achievements ( $p = 0.019$ ), emotional domain ( $p < 0.001$ ), learning functions ( $p$ -value:  $0.001$ ), and physical activity ( $p < 0.001$ ). The SLEQOL score was worse in those with active disease, and the quantitative SLEDAI score significantly affected the total SLEQOL score ( $p = 0.001$ ).

According to the SMILEY score, pSLE disease activity does alter the QOL. This differs from the observations of Moorthy et al<sup>10</sup> who reported that the pediatric patients with SLE demonstrated no significant changes on HRQOL over time according

to the SMILEY score. Another study reported a moderate correlation between the child and parent reports of SLE activity on social Life and self domains.<sup>11</sup>

Our findings conform with the results reported by Ruperto and colleagues<sup>12</sup> from 297 pediatric SLE patients. They used the Child Health Questionnaire (CHQ) and found that the SLEDAI score was significantly correlated with both the physical summary score and psychosocial summary score. Another relevant study was conducted on 40 adult SLE patients and 40 age and sex matched controls, in Sohag University, Egypt. They used the SF-36 and SLEQOL questionnaires. They found significant negative correlation between the SF36

score and the SLEDAI. But with the SLEQOL score, there was positive correlation to SLEDAI.<sup>13</sup> Several other studies reported positive correlation between the SLEQOL global score and SLEDAI score of SLE patients.<sup>14,15</sup> Earlier, Khanna et al<sup>16</sup> found in their study on 73 adult SLE patients, a significant negative correlation between physical and psychological aspects of QOL and SLEDAI. On the other hand, Leong and his coworkers<sup>7</sup> found a poor correlation between SLEQOL score and the SLE disease activity as measured by SLEDAI.

In our series, a statistically significant correlation was elicited between quantitative SLEDAI and the SMILEY score; a finding that was previously observed in a relevant study.<sup>17</sup> It was reported that, by using the SMILEY questionnaires, there was moderate correlation between the child and parent reports in the effect on social life and the burden of SLE, while a strong correlation was noted between the SMILEY total score and effect on self.<sup>18</sup>

In our study there was no correlation between SLEQOL and duration of illness ( $p = 0.166$ ). It is expected that the narrow age group of our sample limited the variation in disease duration and hence its impact on QOL. This goes in agreement with a multi-center study on 467 children with SLE using the SMILEY score<sup>19</sup> as well as several adult studies.<sup>16,20</sup> On the contrary, Brahem et al<sup>15</sup> reported that the SLEQOL global score was correlated with longer disease duration ( $p=0.05$ ). Our findings are indeed limited by the sample size.

We found no significant influence for residency on social achievement, emotional affection, learning problems, or physical activity domains ( $p > 0.05$ ) according to SLEQOL scoring in our sample suggesting comparable long-term outcomes between urban and rural residents. The same was observed by Pons-Estel and colleagues<sup>21</sup> from their study on 1426 SLE Latin American patients who constitute the GLADEL cohort (a multinational, inception longitudinal study). Once SLE patients are diagnosed, and irrespective of their residential place, they are likely to be monitored and treated by physicians with experience in the disease.<sup>22</sup> However, the opposite was reported from a study on 80 pSLE patients in which rural residents had higher activity scores, lower physical function, and more depressive symptoms.<sup>23</sup> In our study, residency showed a significant impact on the SMILEY scores with a  $p$ -value of 0.022. A larger sample size would be more decisive in this issue.

Our results showed that SLE children with organ affection whether nephritis, carditis, cerebritis, or arthritis had bad impact on HRQOL according to

both the SLEQOL and SMILEY scores. The alterations in HRQOL were more pronounced in cases suffering from lupus cerebritis and carditis. This comes in line with a relevant study on 467 children with SLE in which lupus nephritis and cerebritis were associated with greater damage and more impaired HQOL.<sup>19</sup> The same was reported in a cross-sectional study conducted on 218 pediatric and 1,715 adult patients<sup>24</sup> and in an earlier study that noted that renal damage had a negative impact on the patients' HRQL and was associated with general health, physical health, and family life components.<sup>12</sup> Nevertheless, an adult study did not observe an association between irreversible renal damage, and changes in QOL.<sup>25</sup>

The influence of immunosuppressives on QOL was not impressive among our series. The SLE patients receiving cyclophosphamide had higher HRQOL scores ( $147.82 \pm 30.5$ ) than those without ( $141.31 \pm 34.4$ ) but the difference did not reach statistical significance according to the SLEQOL ( $p = 0.565$ ) and SMILEY scores ( $p = 0.516$ ). However, it significantly affected the learning problems' domain according to SLEQOL ( $p = 0.025$ ). This finding is supported by a publication that reported no difference between the National Institutes of Health (NIH) protocol, characterized by a high dose of cyclophosphamide, and the Euro-Lupus protocol, characterized by a low-dose cyclophosphamide as far as the HRQOL was concerned.<sup>26</sup> Concerning mycophenolate mofetil, patients on such a therapy had higher scores ( $p$ -value=0.045). This was especially evident in social achievement. Mycophenolate as a treatment showed no significant impact on SMILEY score results. In general, cyclophosphamide and mycophenolate had comparable effects according to SLEQOL scores ( $p = 0.562$ ). A previous investigation, on the contrary, found that patients on mycophenolate mofetil plus prednisone had better HRQOL than those on CYC and prednisone.<sup>27</sup> A study conducted in Peru reported that the intake of immune suppressive drugs in general had a worse outcome on QOL because of their effect on patient activity and general condition.<sup>28</sup>

The main strength of our study is that the patients were evaluated using two major scores assessing the HRQOL; the SLEQOL and the SMILEY scores which are well-characterized SLE-specific generic scores, and their Arabic translation was well validated. Also, substantial efforts were made to eliminate confounding variables. Although disease-specific (SLEQOL) instrument was superior in the assessment of HRQOL in our pSLE patients, the SMILEY score proved to be a brief,

easy-to-understand, valid and reliable tool for assessing pediatric SLE-specific HRQOL. It may help physicians understand the impact of the treatment on their patients' daily lives. SLEQOL may provide more sensitive information over time according to disease status. This assumption needs prospective studies to validate.

The main limitations of our study are the small sample size, and the cross-sectional study design which limits the interpretation of the influence of disease status over time. Also, the consecutive manner of enrollment did not allow for even distribution of the sample according to some variables such as the type of organ involvement.

In conclusion, organ involvement in pSLE does have a significant impact on many domains of the HRQOL and that the SLEQOL and SMILEY scores could spot much of this impact. pSLE patients with lupus cerebritis and carditis had a worse HRQOL score than those with lupus nephritis and arthritis. We recommend assessment of HRQOL as an important part of providing care to pSLE patients and it should be implemented in regular follow up visits. Wider-scale, multicenter and prospectively designed studies are needed to better assess the impact of the disease activity, severity, and therapeutic modalities on the HRQOL of our patients. Involvement of a control group may help providing comparative analysis and reference values to aid further research.

## REFERENCES

1. **NAZRI, SKSM, WONG KK, HAMID WZW.** Pediatric systemic lupus erythematosus. Retrospective analysis of clinico-laboratory parameters and their association with Systemic Lupus Erythematosus Disease Activity Index score. *Saudi Med J* 2018;39(6):627–31.
2. **AYGÜN E, KELESOĞLU FM, DOĞDU G, ERSOY A, BASBUG D, AKÇA D, ET AL.** Antinuclear antibody testing in a Turkish pediatrics clinic: is it always necessary? *Pan Afr Med J* 2019;32:181.
3. **DIDSBURY MS, KIM S, MEDWAY MM, TONG A, MCTAGGART SJ, WALKER AM, ET AL.** Socio-economic status and quality of life in children with chronic disease: A systematic review. *J Paediatr Child Health* 2016;52(12):1062-9 .
4. **RAVENS-SIEBERER U, ERHART M, RAJMIL L, HERDMAN M, AUQUIER P, BRUIL J, ET AL.** European KIDSCREEN Group. Reliability, construct and criterion validity of the KIDSCREEN-10 score: a short measure for children and adolescents' well-being and health-related quality of life. *Qual Life Res* 2010;19(10):1487-500.
5. **RAVENS-SIEBERER U, WILLE N, BADIA X, BONSEL G, BURSTRÖM K, GAVRINI G, ET AL.** Feasibility, reliability, and validity of the EQ-5D-Y: results from a multinational study. *Qual Life Res* 2010;19(6):887-97.
6. **BRUNNER HI, SILVERMAN ED, TO T, BOMBARDIER G, FELDMAN BM.** Risk factors for damage in childhood-onset systemic lupus erythematosus: cumulative disease activity and medication use predict disease damage. *Arthritis Rheum* 2002;46(2):436-44 .
7. **LEONG KP, KONG KO, THONG BY, KOH ET, LIAN TY, TEH CL, ET AL.** Development and preliminary validation of a systemic lupus erythematosus-specific quality-of-life instrument (SLEQOL). *Rheumatology (Oxford)* 2005; 44(10):1267-76.
8. **MOORTHY LN, PETERSON MG, BARATELLI M, HARRISON MJ, ONEL KB, CHALOM EC, ET AL.** Multicenter validation of a new quality of life measure in pediatric lupus. *Arthritis Rheum* 2007;57(7):1165-73.
9. **PUGÈS M, BISCAY P, BARNETCHE T, TRUCHETET MÉ, RICHEZ C, SENESCHAL J, ET AL.** Immunogenicity and impact on disease activity of influenza and pneumococcal vaccines in systemic lupus erythematosus: a systematic literature review and meta-analysis. *Rheumatology (Oxford)* 2016; 55(9):1664-72.
10. **MOORTHY LN, PETERSON MG, HASSETT AL, BARATELLI M, CHALOM EC, HASHKES PJ, ET AL.** Relationship between health-related quality of life and SLE activity and damage in children over time. *Lupus*. 2009;18(7):622-9.
11. **MOORTHY LN, SAAD-MAGALHÃES C, SATO JO, LEN CA, VASCO MB, APPENZELLER S, ET AL.** Validation of the Portuguese Simple Measure of Impact of Lupus Erythematosus in Youngsters (SMILEY) in Brazil. *Lupus* 2013;22(2):190-7.
12. **RUPERTO N, BURATTI S, DUARTE-SALAZAR C, PISTORIO A, REIFF A, BERNSTEIN B, ET AL.** Health-related quality of life in juvenile-onset systemic lupus erythematosus and its relationship to disease activity and damage. *Arthritis Rheum* 2004;51(3):458-64 .
13. **AHMED AM, ISMAIL MA, ELBAYED SA , ALI RH.** Quality of Life in Patients with Systemic Lupus Erythematosus. *Sohag Med J* 2018;22(3):125-31.
14. **FREIRE EA, BRUSCATO A, LEITE DR, SOUSA TT, GICONELLI RM.** Translation into Brazilian Portuguese, cultural adaptation and validation of the systemic lupus erythematosus quality of life questionnaire (SLEQOL). *Acta Reumatol Port* 2010;35(3):334-9
15. **BRAHEM M, ARDHAOU M, ARFA S, HACHFI H, REJEB BB, SARRAJ R, ET AL.** AB0337 assessment of health-related quality of life in systemic lupus erythematosus using the SLEQOL (systemic lupus erythematosus-specific quality of life questionnaire). *Ann Rheum Dis* 2021;80:1193-4.
16. **KHANNA S, PAL H, PANDEY RM, HANDA R.** The relationship between disease activity and quality of life in systemic lupus erythematosus. *Rheumatology (Oxford)* 2004;43(12):1536-40.

17. **HERSH A.** Measures of health-related quality of life in pediatric systemic lupus erythematosus: Childhood Health Assessment Questionnaire (C-HAQ), Child Health Questionnaire (CHQ), Pediatric Quality of Life Inventory Generic Core Module (PedsQL-GC), Pediatric Quality of Life Inventory Rheumatology Module (PedsQL-RM), and simple measure of impact of lupus erythematosus in youngsters (SMILEY). *Arthritis Care Res (Hoboken)* 2011;63(Suppl 11):S446-53.
18. **PUNZALAN JM, CANONIGO BB, CABANSAG MRF, FLORES DS, GALUTIRA PJT, BERNAL CB, ET AL.** A cross-cultural validation of a quality of life measure using the simple measure of the impact of lupus erythematosus in youngster (SMILEY©) among Filipino pediatric lupus patients. *Open Urol Nephrol J* 2016;9:60-6.
19. **MOORTHY LN, BALDINO ME, KURRA V, PUWAR D, LLANOS A, PETERSON MG, ET AL.** Relationship between health-related quality of life, disease activity and disease damage in a prospective international multicenter cohort of childhood onset systemic lupus erythematosus patients. *Lupus* 2017;26(3):255-65.
20. **JOLLY M, PICKARD SA, MIKOLAITIS RA, ROBBY RA, SEQUEIRA W, BLOCK JA.** LupusQoL-US benchmarks for US patients with systemic lupus erythematosus. *J Rheumatol* 2010;37(9):1828-33.
21. **PONS-ESTEL GJ, SAURIT V, ALARCÓN GS, HACHUEL L, BOGGIO G, WOJDYLA D, ET AL.** The impact of rural residency on the expression and outcome of systemic lupus erythematosus: data from a multiethnic Latin American cohort. *Lupus* 2012;21(13):1397-404.
22. **GERGIANAKI I, FANOURIAKIS A, ADAMICHOU G, SPYROU G, MIHALOPOULOS N, KAZADZIS S, ET AL.** Is systemic lupus erythematosus different in urban versus rural living environment? Data from the Cretan Lupus Epidemiology and Surveillance Registry. *Lupus* 2019;28(1):104-13.
23. **ABDUL-SATTAR AB, ABOU EL MAGD S.** Association of perceived neighborhood characteristics, socioeconomic status and rural residency with health outcomes in Egyptian patients with systemic lupus erythematosus: one center study. *Int J Rheum Dis* 2017;20(12):2045-52.
24. **LEVY DM, KAMPHUIS S.** Systemic lupus erythematosus in children and adolescents. *Pediatr Clin North Am* 2012;59(2):345-64.
25. **CLARKE AE, PANOPALIS P, PETRI M, MANZI S, ISENBERG DA, GORDON C, ET AL.** SLE patients with renal damage incur higher health care costs. *Rheumatology (Oxford)* 2008;47(3):329-33.
26. **DALEBOUDT GM, BERGER SP, BROADBENT E, KAPTEIN AA.** Health-related quality of life in patients with systemic lupus erythematosus and proliferative lupus nephritis. *Psychol Health Med* 2011;16(4):393-404.
27. **TSE KC, TANG CS, LIO WI, LAM MF, CHAN TM.** Quality of life comparison between corticosteroid and mycophenolate mofetil and corticosteroid and oral cyclophosphamide in the treatment of severe lupus nephritis. *Lupus* 2006;15(6):371-9.
28. **ELERA-FITZCARRALD C, FUENTES A, GONZÁLEZ LA, BURGOS PI, ALARCÓN GS, UGARTE-GIL MF.** Factors affecting quality of life in patients with systemic lupus erythematosus: important considerations and potential interventions. *Expert Rev Clin Immunol* 2018;14(11):915-31.