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Quality Of Life in Female Patients with Systemic Sclerosis

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ABSTRACT

Background: Autoimmune diseases, such as systemic sclerosis (SSc), affect the entire body. As the most noticeable aspect of the disease. SSc is characterized by a gradual fibrosis process that results in organ failure and significant damage to many organs such as the skin and joints. It is one of the most common causes of organ malfunction, disability, and even death.

Objective: This study aimed to analyse the quality of life in Egyptian female SSc patients and their associated risk variables.

Patients and Methods: During the course of this cross-sectional study, 21 patients from the Rheumatology and Rehabilitation Department of the Faculty of Medicine, Zagazig University Hospitals, were surveyed. The Systemic Sclerosis Quality of Life Questionnaire (SScQoL) and the modified Rodnan skin score (mRSS) were used to evaluate SSc patients' quality of life and disease activity (SAQ).

Results: There was statistically significant relation between studied SSC patients' quality of life (SScQoL) and deformity (p=0.022), muscle wasting (p=0.027), dyspnea (p=0.023) and nausea and vomiting (p=0.038). Also, there was a statistically significant relation between SScQoL high score and type of medication especially cyclophosphamide and biologic treatment. There was a statistically significant higher Systemic Sclerosis Quality of life Score of Systemic Sclerosis patients and positive anti scleroderma. There was statistically significant and direct correlation between SScQol score and scleroderma assessment questionnaire (SAQ).

Conclusion: Patients with SSc have plenty of other symptoms that point to a lowered quality of life. In our studied population, nausea, vomiting, dyspnea, deformity and muscle wasting were the most prominent features.

Keywords: SSC, SScQoL, SAQ, QoL.

INTRODUCTION

Autoimmune diseases, such as systemic sclerosis (SSc), affect the entire body. As the most noticeable aspect of the disease. SSc is characterized by a gradual fibrosis process that results in organ failure and significant damage to many organs such as the skin and joints. A female to male ratio of 4:1 to 1:1 is common, with the proportion varying with age and ethnicity [(1)]. SSc is a multifaceted disease that is associated with significant morbidity and death. SSc patients' health-related quality of life (HRQoL) suffers greatly compared to the general population and patients with other rheumatic diseases or chronic disorders because of the disease's severe and systemic nature [(2)]. Because of its long-term and multisystem nature, SSc has a significant impact on patient's capacity to participate in both professional and social activities. In addition, the costs of treating these diseases and the resulting loss of productivity could have a significant financial impact [(3)].

Patients with SSc are frequently plagued by pain, which impairs their ability to do daily tasks and has a negative impact on their overall health and well-being. Joint pain is the most common cause of discomfort. Finger ulcers, joint contractures, synovitis, gastrointestinal problems, and Raynaud's phenomenon are among the other causes of pain [(4)]. In addition to physical, psychological, and social aspects, fatigue is a prevalent concern in persons with arthritis, and it can be a substantial cause of pain and disability in those with SSc [(5)].

Systemic sclerosis is incurable and has no therapy options. Patients' well-being can be improved by reducing symptoms and disabilities, reducing tolerance to treatment, or reducing risks associated with co-morbid conditions and their concomitant diseases [(6)].

Our study's goal was to assess the health and well-being of Egyptian female SSc patients, as well as any and all potential risk factors.

PATIENTS AND METHODS

21 patients from the Rheumatology and Rehabilitation Department of the Faculty of Medicine, Zagazig University Hospitals were included in a cross-sectional study. Women with SSc were identified by the American College of Rheumatology's (ACR) criteria for SSc who were at least 18 years old.

Exclusion criteria: Patients with other rheumatologic diseases, malignancy, endocrinal disease, infectious diseases (hepatitis or Tuberculosis) and patients who were exposed to any chemical agents or organ solvents as silica.

Ethical approval:

Zagazig University's Faculty of Medicine's Institutional Review Board ("IRB") gave its approval for this study. Every patient signed an informed written consent for acceptance of the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

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Clinical assessments:

All patients were subjected to full history taking with special stress on age at study visit, sex, disease duration and disease subtype. All patients were clinically examined with stress on general examination, joint examination, skin examination, musculoskeletal examination for muscle atrophy and wasting.

1. ***The Modified Rodnan's skin score (MRSS):***

Skin thickness is measured by the MRSS, which is utilized in clinical trials of systemic sclerosis as a primary or secondary outcome measure. Skin tightness was measured using a 0–3 scale in 17 places of the body. As a result, the highest possible score was 51. Additionally, a visual analogue scale (VAS) was utilized to assess the change in skin involvement over the past month [(7)].

2. ***The Scleroderma Assessment Questionnaire (SAQ):***

An assessment questionnaire for patients with Systemic Scleroderma (SAQ) is used to examine their disease condition. Among the questions are four linked to vascular dysfunction, six to respiratory dysfunction, five to digestive dysfunction, and eight to musculoskeletal dysfunction? The total number of items is 23. The scores ranged from 0 to 3. The Index of Disease Status (IDS) was calculated by dividing the overall score for the full questionnaire by the number of questions. As a result, the SAQ is a useful tool for assessing the extent of organ system dysfunction in patients with SSc [(8)].

3. ***The Systemic Sclerosis Quality of Life Questionnaire (SScQoL):***

Reay [(11)] created the SScQoL and had it translated into six different languages. Because it is founded on the idea that people are motivated by their wants and that life's quality is determined by how well they can meet those needs, it measures how a sickness affects a person's overall health and happiness. To assess quality of life, patients use the SScQoL, a self-report questionnaire composed of 29 questions on four main topics: emotions, physical adaptability, impact on others, and impact on one's own identity. It takes about 5 minutes for the patient to complete and gives quantitative data that allow accurate evaluation of the impact of SSc on an individual patient or groups of people with the disease. [(12)].

In our study SAQ and SScQoL were translated, back translated, revised by experts and tested for our patients.

Stages of Arabic translation:

1) ***Initial translation:*** The forward translation was the initial step. There were some differences in the original or in the translation process between the two translations, so we compared and analyzed them. Translators who are fluent in both the target language and the source language generate two separate translations [(9)].
2) ***Synthesis of the translations:*** Translator 1 and Translator 2 worked together to produce a single translation based on the original questionnaire as well as the translations by the first and second translators (T1-2) [(9)].
3) **Back translation:** Translators then translated the questionnaire from the T1-2 version into the original language, completely unaware of the original form. To ensure that the translated version reflected the same item content as the original version, this validation process was carried out. It guarantees that the translations are consistent [(10)].
4) **Revision & final version:** Preliminary field testing will be conducted on the questionnaire once it has undergone several revisions. A pilot study was conducted on 10% of the sample size to test the viability of the questionnaire, as well as the clarity of the tool, and to estimate the time needed to fill it out. The surveys were found to be clear and relevant in the pilot study results.

Laboratory assessments:

For each subject, we collected 2 blood samples, one on K3-EDTAvacutainer tube to measure hemoglobin concentration using Sysmex XN-2000 auto-analyzer (Siemens diagnostic, Germany) and to measure erythrocyte sedimentation rate (ESR) using Vision B analyzer (YHLO Biotech diagnostic ,china). The other blood sample was collected on plain tube to separate serum for measurement of C-reactive protein (CRP), transaminases (ALT and AST), fasting serum glucose, creatinine, and serum urea nitrogen on Cobasc702/8000 (Roche diagnostic, Germany) using dedicated reagents. Serum was also used to measure ANA titer and pattern using indirect immunofluorescence technique on NOVA Lite Human epithelial cell 2 (Hep2 kit) (Inova Diagnostics, San Diego, USA) and anti-topoisomerase (Anti-scl70) using sandwich Enzyme-Linked Immunosorbent Assay (ELISA) (Bioassay Technology Laboratory, Shanghai, China), Cat.No#E0505Hu both according to manufacturer instructions.

Statistical Methods

SPSS IBM Corp. released in 2015 was used for all data collection, tabulation, and statistical analysis (Version 23.0 of the IBM SPSS Statistics software for Windows. Armonk, New York, IBM). To compare two sets of non-normally distributed variables, the Mann Whitney U test was employed. More than two groups of non-normally distributed variables were compared using the Kruskall Wallis test. Coefficients of Spearman's correlation were used to examine the correlation between various study variables. All the tests were two-sided. Statistical significance was defined as a p-value equals or lower than 0.05, while statistical insignificance was defined as a p-value higher than 0.05 (NS).

RESULTS

Table (1) showed that the mean age of SSc patients was 41.1 ± 11.4. They were further characterized as 19 patients with diffuse SSc and 2 patients with limited subtype. Most of the patients were from rural areas 16 (76.2%). Mean of mRSS was 27 ± 8.1, SScQoL was 20.2 ± 6.5 and SAQ was 1.17 (0.26-2.48). About half of patients had homogenous ANA pattern 11(52.4%) and about 76% of them were anti Scl 70 positive.

Table (1): Basic characteristics of Systemic Sclerosis (SSc) patients

Variables	
Age (years)	41.1±11.4
Residence	
Rural	16 (76.2)
Urban	5 (23.8)
Duration (years)	3 (0.5-8)
<5	16 (76.2)
≥5	5 (23.8)
Disease subtype	
Diffuse scleroderma	19 (90.5)
Limited scleroderma	2 (9.5)
Weight (kg)	64.7 ± 15.9
Height (cm^2)	160 ± 6
BMI (kg/m^2)	25.3 ± 6.4
Number of swollen joints (NSJ)	4 (0-10)
Number tender joint	6 (0-12)
Modified Rodnan score (mRSS)	27 ± 8.1
SScQOL	20.2 ± 6.5
The scleroderma assessment questionnaire (SAQ)	1.17 (0.26-2.48)
FBS (mg/dl)	98±20.1
ESR (mm/hr)	50 ±11.2
CRP (mg/L)	12 ±3
Blood urea nitrogen (BUN) (mg/dl)	9 ± 2.1
S. creatinine (mg/dl)	0.8 ±0.1
AST (U/L)	23 ±3.8
ALT (U/L)	21.7 ±4.9
S. albumin (g/L)	3.7 ± 0.47
Hb (g/dL)	12.3 ± 1.46
ANA Pattern	
Homogenous	11 (52.4)
Nuclear	4 (19.0)
Speakled	6 (28.6)
ANA titer fold	
1.00	6 (28.6)
2.00	8 (38.1)
3.00	3 (14.3)
4.00	3 (14.3)
5.00	1 (4.8)
Anti-scleroderma 70	16 (76.2)

Data express: Mean ±SD, median (range), n(%) **BMI**: body mass index, **ESR**= erythrocyte sedimentation rate, **CRP**= C reactive protein, **AST**= aspartate transaminase**, ALT**= alanine transaminase, **ANA**= antinuclear antibody, **SSCQOL**=Systemic Sclerosis Quality of Life, **FBS**= fasting blood sugar, **HB**= hemoglobin, **NSJ**= number of swollen joints.

Table (2) showed that the most common clinical manifestations in SSc patients were myalgia and Raynaud's phenomenon, while about 81% of them had epigastric pain, ILD and swelling.

Table (2): Clinical presentation and medication of systemic sclerosis patients

Variable	n	%
DM	3	14.3%
HTN	7	33.3%
Myalgia	21	100.0%
Monoarthritis	2	9.5
Oligoarthritis	3	14.3
polyarthritis	9	42.9
Swelling	17	81.0%
Deformity	16	76.2%
Muscle wasting	12	57.1%
LL.edema	9	42.9%
Renal crisis	3	14.3%
dyspnea	18	85.7%
Interstitial Lung Disease	17	81.0%
Pulmonary hypertension	4	19.0%
Cardiac involvement	1	4.8%
Nausea, Vomiting	16	76.2%
Dysphagia	16	76.2%
Epigastric pain	17	81.0%
Constipation	16	76.2%
Stool incompetence	0	0.0%
Diarrhea	11	52.4%
Raynaud's phenomenon	21	100.0%
ulcer	10	47.6%
pitting	9	42.9%
Telangiectasia	9	42.9%
Calcini	6	28.6%
puffing	17	81.0%
Gangrene	1	4.8%
NSAIDs	13	61.9%
corticosteroids	8	38.1%
MTX	6	28.6%
cyclophosphamide	13	61.9%
biological	6	28.6%
Immuran	16	76.2%
Mofetil	10	47.6%

Table (3) showed that there was statistically significant relation between studied SSc patients' quality of life (SScQoL) and deformity (p=0.022), muscle wasting (p=0.027), dyspnea (p=0.023) and nausea and vomiting (p=0.038). These clinical manifestation were associated with high systemic sclerosis quality of life Score. Also, there was statistically significant relation between SScQoL high score and type of medication especially cyclophosphamide and biologic treatment.

Table (3): Comparison of systemic sclerosis quality of life score of systemic sclerosis patients regard clinical manifestation and treatment

Clinical data	Systemic Sclerosis Quality of life Score		U	p
	Yes	No		
Myalgia	22 (4-27)		-	-
DM	26 (14-27)	21.5 (4-27)	0.76	0.45
HTN	25 (4-27)	19.5 (9-27)	1.46	0.14
LL.edema	26 (13-27)	19.5 (4-27)	1.78	0.074
Swelling	22 (9-27)	19.5 (4-27)	0.58	0.56
Deformity	24 (13-27)	18 (4-21)	2.3	**0.022***
Wasting	24.5 (14-27)	18 (4-27)	2.2	**0.027***
Renal crisis	26 (14-27)	21.5 (4-27)	0.76	0.45
Neurological	-	22 (4-27)	-	-
Dyspnea	23 (13-27)	9 (4-18)	2.27	**0.023***
Interstitial Lung Disease	22 (13-27)	16.5 (4-27)	0.72	0.47
Pulmonary hypertension	24.5 (14-27)	21 (4-27)	0.99	0.32
Cardiac Involvement	27 (27-27)	21.5 (4-27)	1.4	0.16
Nausea, Vomiting	23 (14-27)	13 (4-26)	2.07	**0.038***
Dysphagia	23 (9-27)	18 (4-26)	1.28	0.2
Epigastric pain	22 (9-27)	15.5 (4-26)	1.44	0.15
Constipation	22 (9-27)	18 (4-27)	0.49	0.62
Diarrhea	21 (9-27)	22 (4-27)	0.21	0.83
Stool Incontinence	-	22 (4-27)		
ulcer	24.5 (9-27)	21 (4-26)	0.96	0.34
pitting	24 (9-27)	21.5 (4-26)	0.68	0.49
Telengectisia	22 (9-27)	21.5 (4-26)	0.53	0.59
Calcinosis	24 (4-27)	21 (9-27)	1.06	0.29
Puffing	22 (9-27)	18 (4-24)	1.3	0.19
Gangrene	27 (27-27)	21.5 (4-27)	1.4	0.16
Raynaud's phenomenon	22 (4-27)		-	-
NSAIDs	21 (4-27)	23 (14-27)	0.69	0.49
Corticosteroids	23 (14-27)	21 (4-27)	0.69	0.49
MTX	22.5 (4-27)	22 (9-27)	0.23	0.81
Cyclophosphamide	25 (14-27)	17 (4-22)	2.9	**0.004***
Biological	25 (22-27)	18 (4-27)	2.19	**0.028***
Imuran	23 (13-27)	18 (4-27)	1.3	0.2
Mofetil	22 (9-27)	21 (4-27)	0.28	0.78

U=Mann-Whitney U test of sig, (NS) insignificant p>0.05, *significant p<0.05

Table (4) showed statistically significant higher systemic sclerosis quality of life score of systemic sclerosis patients and positive anti scleroderma 70 **(P=0.004**).

Table (4): Comparison of SScQoL in SSc patients regarding basic characteristics

	Median (range)	u/ KW	p
Residence			
Rural	21.5 (4-27)	0.12	0.901
Urban	22 (14-26)		
Disease duration.			
<5	22.5 (9-27)	0.706	0.48
≥5	22 (4-27)		
Disease subtybe			
Diffuse scleroderma	22 (9-27)	1.6	0.104
Limited scleroderma	11 (4-18)		
ANA Pattern			
Homogenous	24 (14-27)	1.1	0.57
Nuclear	17.5 (9-27)		
Speakled	21.5 (4-26)		
ANA titer fold			
1.00	20.5 (9-27)		
2.00	21 (14-26)		
3.00	25 (24-27)	2. 7	0.6
4.00	22 (4-26)		
5.00	18 (18-18)		
Anti-Scleroderma 70			
Positive	22 (4-27)	**2.9**	**0.004***
Negative	14 (9-27)		

U=Mann-Whitney U test of sig, KW= Kruskall Wallis test of sig, (NS) insignificant p>0.05.

Table (5) showed that there was statistical significance and direct correlation between SScQol score and scleroderma assessment questionnaire (SAQ) **(P= 0.001)**.

Table (5): Correlation between SScQoL and, age duration of disease, NSJ, number tender joint modified Rodnan score, (SAQ),HB, FBS, ESR, CRP, BUN, S. creatinine, AST, ALT, S albumin (n.21):

	Systemic Sclerosis Quality of life Score	
	r	p
Age per years	-0.11	0.65
Duration per years	0.005	0.984
NSJ	-0.033	0.888
Number tender joint	0.158	0.495
Modified Rodnan score (mRss)	0.371	0.098
the scleroderma assessment questionnaire (SAQ)	**0.659****	**0.001**
HB	- 0.259	0.256
FBS	0.332	0.142
ESR	0.432	0.051
CRP	0.407	0.067
BUN	0.289	0.203
s. creatinine	0.142	0.538
AST	-0.008	0.973
ALT	0.312	0.169
s. albumin	-0.162	0.508

(r) Correlation coefficient insignificant p > 0.05,

DISCUSSION

The fibro-proliferative changes in the microvasculature caused by SSc lead to an excessive buildup of collagen fibers in the skin and other internal organs. SSc is an autoimmune disease [13]. Patients with chronic or severe diseases are known to have a diminished quality of life (QoL), which is a multidimensional subject that can measure both the impact of sickness and the success of therapy [14]. Patients with SSc and their associated risk factors were the primary focus of our investigation.

Our study showed that the most common clinical manifestations in SSc patients were myalgia and Raynaud's phenomenon, while about 81% of patients had epigastric pain, ILD and swelling. Also, **Alian *et al.*** [15] in their study showed that Raynaud's phenomenon, arthritis/arthralgia and gastrointestinal symptoms were identified to be the most common conditions in the patients studied. However, these manifestation were not associated with low quality of life in our studied population according to SSc quality of life score (SScQoL). However, as other studies have shown, they may cause issues for those who have SSc. In contrast with our results **Pauling *et al.*** [16] in their study revealed that the most common symptom is Raynaud's phenomenon in SSc that decrease HRQoL. Also, previous study of **Lumetti *et al.*** [17] have shown that internal organ involvement, particularly in the lungs, makes it difficult to do ordinary duties and may also restrict social functioning in Raynaud's sufferers.

On the other hand, **van Leeuwen *et al.*** [18] in their multivariable analysis found that contrary to expectations, the existence of ILD had no effect on HRQoL over time. It is possible that this is due to the fact that not all SSc-ILD patients suffer symptoms that are directly linked to ILD.

Regarding SScQoL, there were significant statistical association between GIT symptoms especially nausea and vomiting (p=0.038) and SScQoL high score and consequently quality of life in patients with these manifestations was worse than others without. In agreement with our results, **Alian *et al.*** [15] discovered an important link between total QoL ratings and visceral involvements, notably GIT involvement and pericardial effusion.

Also, **van Leeuwen *et al.*** [18] noted that HRQoL-related to SSc is adversely affected by extensive GI involvement. However, **Laeubli *et al.*** [19] stated that the overall burden of GIT symptoms in SSc patients on quality of life was mild. These variations may be due to different tools used in assessment of QoL.

As regards our study results, we found that there was statistically significant association between studied SSc patients' quality of life (SScQoL) and deformity (p=0.022) and also muscle wasting (p=0.027). Other studies of **Poole *et al.*** [20] on patients with SSc hand deformity, referred to as a "tight glove," who have trouble doing fine motor skills due to painful finger cracks and ulcers. They found that they suffer in their quality of life.

As regards the medications used in treatment of patients with scleroderma, unfortunately we found in our study that patients who received cyclophosphamide (CYC) were associated with low quality of life according to SScQoL score. On the other hand **Khana *et al.*** [21] in their study showed that a significant improvement in HAQ DI, general health, energy, and emotional and mental well-being was seen with CYC treatment against placebo. Cyc's side-effect profile and its use in individuals with more severe organ dysfunction may explain this discrepancy.

Our study revealed that there was no significant clinical association between disease duration and quality of life in SSc patients. However, **Müller *et al.*** [22] reported that patients with a longer course of disease have a better quality of life, according to their findings. Possible explanation is that lesser disease severity is linked to prolonged length of illness.

According to the type of scleroderma, we found in our results that there was no significant association between disease subtype and Qol of patients. On the other hand **Iudici *et al.*** [23] in their studies revealed that HR-QoL is impaired in both limited cutaneous SSc (lcSSc) and diffuse cutaneous SSc (dcSSc) but more in dcSSc patients.

Concerning the influence of the disease severity on the patient`s quality of life, our study found that there was a statistical significance and direct correlation between SScQol score and scleroderma assessment questionnaire (SAQ) (P= 0.001). Similar to our results, the study of **Xiaofei *et al.*** [24] revealed that SSc patients with particular organ involvement had higher scores, which indicates that the disease is worsening. Also, **Sierakowska *et al.*** [25] highlighted that SSc patients' Qol may be adversely affected by emotional problems due to the severity of their sickness. Finally, we can assume that the SScQoL was able to better capture the disease-specific aspects influencing quality of life in SSc patients in different demographics than other quality of life assessments. Because of this, it is an effective clinical and research tool.

Because of the rarity of SSc as a rheumatologic condition, our sample size was modest. Therefore, no conclusions can be drawn about the overall SSc population based on these findings, because of this. Another drawback is that participants' selection bias may be present due to their attendance at a medical institution.

CONCLUSION

A lower quality of life (QoL) is present in many SSc patients. People in our study had a high prevalence of symptoms such as vomiting, dyspnea, deformity and muscular loss. In light of the fact that there is no effective treatment or cure for SSc, it is critical that physicians, psychologists, physical and occupational

therapists, and social workers work together to identify the main manifestations affecting SSc patients' quality of life and develop a strategy for treating them.

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REFERENCES

1. **Bielecka O, Fransen J, Avouac J *et al.* (2017):** Update of EULAR recommendations for the treatment of systemic sclerosis, Annals of the Rheumatic Diseases, 76: 1327–1339.
2. **Park E, Strand V, Oh Y *et al.* (2019):** Health-related quality of life in systemic sclerosis compared with other rheumatic diseases: a cross-sectional study. Arthritis Research & Therapy, 21 (1): 1-10.
3. **Guillevin L, Hirschi M, Trautinger F *et al.* (2013):** Functional impairment of systemic scleroderma patients with digital ulcerations: results from the DUO Registry. Clin Exp Rheumatol., 31 (76):71-80.
4. **Ostojic P, Jankovic K, Djurovic N *et al.* (2019):** Common causes of pain in systemic sclerosis: Frequency, severity, and relationship to disease status, depression, and quality of life. Pain Management Nursing, 20: 331–336.
5. **Sierakowska M, Sierakowski S, Sierakowska J *et al.* (2018):** Pain, fatigue and functional disability are associated with higher educational needs in systemic sclerosis: A cross-sectional study. Rheumatology International, 38 (8): 1471–1478.
6. **Sierakowska M, Rudzik T (2017):** Nursing care for people with rheumatic diseases. In D. Talarska& D. Zozulińska-Ziółkiewicz (Eds.), Nursing Internship. Pp: 335–373.
7. **Rodnan G, Steen V, Medsger T (1982):** D-Penicillamine therapy in progressive systemic sclerosis (scleroderma): a retrospective analysis. Ann Intern Med., 97 (5): 652-9.
8. **Ostojić P, Damjanov N (2006):** The Scleroderma Assessment Questionnaire (SAQ). Z Rheumatol., 65: 168–75.
9. **Epstein J, Santo R, Guillemin F (2015):** A Review of Guidelines for Cross-Cultural Adaptation of Questionnaires Could Not Bring Out a Consensus. J Clin Epidemiol., 68: 435–441.
10. **Beaton D, Bombardier C, Guillemin F *et al.* (2000):** Guidelines for the process of cross-cultural adaptation of self-report measures. Spine, 25: 3186-3191.
11. **Reay N (2008):** The quality of life in patients with diffuse and limited systemic sclerosis [Monograph: University of Leeds]. Nurse Researcher,15 (3): 26 - 31.
12. **Ndosi M, Alcacer-Pitarch B, Allanore Y *et al.* (2018):** Common measure of quality of life for people with systemic sclerosis across seven European countries: a cross-sectional study. Ann Rheum Dis., 77: 1032-1038.
13. **McFarlane I, Bhamra M, Kreps A *et al.* (2018)**: Gastrointestinal manifestations of systemic sclerosis. Rheumatology, 8 (1): 235-39.
14. **Preis E, Franz K, Siegert E *et al.* (2018):** The impact of malnutrition on quality of life in patients with systemic sclerosis. Eur J Clin Nutr., 72: 504–510.
15. **Alian S, Sherby N, Sarhan S (2021):** Cultural adaptation and validation of the Systemic Sclerosis Quality of Life questionnaire into Arabic language. Clin Rheumatol., 40: 1409–1416.
16. **Pauling J, Saketkoo L, Matucci-Cerinic M *et al.* (2019):** The patient experience of Raynaud's phenomenon in systemic sclerosis. Rheumatology, 58: 18–26.
17. **Lumetti F, Barone L, Alfieri C *et al.* (2015):** Quality of life and functional disability in patients with interstitial lung disease related to Systemic Sclerosis. Acta Bio Medica, 86 (2): 142–148.
18. **van Leeuwen M, Ciaffi J, Liem S *et al.* (2021):** Health-related quality of life in patients with systemic sclerosis: evolution over time and main determinants. Rheumatology, 60: 3646–3655.
19. **Laeubli J, Dobrota R, Maurer B *et al.* (2020):** Impaired micronutrients and prealbumin in patients with established and very early systemic sclerosis. Clin Exp Rheumatol., 38 (125): 120-126.
20. **Poole J, Macintyre N, Deboer H (2013):** Evidence-based management of hand and mouth disability in a woman living with diffuse systemic sclerosis (scleroderma). Physiotherapy Canada, 65 (4): 317–320.
21. **Khanna D, Yan X, Tashkin D *et al.* (2007):** Impact of oral cyclophosphamide on health-related quality of life in patients with active scleroderma lung disease: Results from the scleroderma lung study. British J of Rheumatology, 56: 1371-76.
22. **Müller H, Rehberger P, Günther C *et al.* (2012):** Determinants of disability, quality of life and depression in dermatological patients with systemic scleroderma. British J of Rheumatology, 166: 343-353.
23. **Iudici M, Cuomo G, Vettori S *et al.* (2013):** Quality of life as measured by the short-form 36 (SF-36) questionnaire in patients with early systemic sclerosis and undifferentiated connective tissue disease. Health and Quality of Life Outcomes, 11: 23-28.
24. **Xiaofei M, Qiuning S (2014):** Evaluations and analyses of quality of life in 90 patients with systemic sclerosis by health assessment questionnaire-disability index. Zhonghua Yi Xue Za Zhi., 94 (44): 3471-74.
25. **Sierakowska M, Doroszkiewicz H, Sierakowska J *et al.* (2019):** Factors associated with quality of life in systemic sclerosis: a cross-sectional study. Qual Life Res., 28: 3347–3354.