Dermatology Practical & Conceptual

Family and Quality of Life Challenges in Mycosis Fungoides Patients: A Case-Control Study from Shiraz, Southern Iran

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ABSTRACT

Introduction: The quality of life (QoL) of patients suffering from cutaneous malignancies like cutaneous T-cell lymphoma (CTCL) and their family caregivers is widely affected by the disease and its treatment.

Objectives: This study aimed to evaluate the impact of the disease and its treatment on patients with MF and their families through self-administered questionnaires in our referral center in Shiraz.

Methods: Patients with mycosis fungoides, the most common variant of CTCL, and one of their family members participated in this study by filling out the questionnaires on Dermatology Life Quality Index (DLQI) and Family Dermatology Life Quality Index (FDLQI). The World Health Organization Quality of Life Brief Version (WHOQOL-BREF) was also completed by patients and healthy controls.

Results: A total of 113 cases, 91 patients' relatives, and 129 healthy controls participated in this study. The mean DLQI total score was 8.00 ± 6.41. WHOQOL-BREF and/or their subdomains were ameliorated with advanced stage, active disease, increasing MSWAT score, early disease, the head/neck location, as well as interferon and gemcitabine. "Symptoms and feelings" and "leisure" dimensions of DLQI were the most affected, while regarding WHOQOL-BREF, the disease significantly impacted the "psychological", "environmental" and "general health" aspects ($P<0.001$, $P=0.045$, and $P<0.001$, respectively). Given the sociodemographic characteristics of the study participants, patients with a higher level of education suffered more ($P=0.035$).

The FDLQI score was 8.44 ± 6.93, not affected by sex, relationship, or caregivers' education level. Family QoL deteriorated over the course of the disease (P=0.020), head/neck lesions (P= 0.003), less than 12 months duration (P=0.029), and interferon (P=0.034).

Conclusions: Due to the distress that patients and caregivers experience during the first year of diagnosis, head/neck lesions, and specific treatment, appropriate measures to prevent unrealistic expectations and better coping mechanisms are recommended.

Introduction

Mycosis fungoides (MF), the most common type of cutaneous t-cell lymphoma (CTCL), is a chronic disease with a recurrent nature which primarily emerges as erythematous patches and plaques, with a minority of patients developing tumors, ulceration, and even systemic involvement and death [1]. This rare disease had an estimated incidence of 3.7 cases per million persons per year in the United States in 2016 [2].

There are multiple strategies for MF treatment, including systemic and local skin-directed therapies [3]. Unfortunately, MF remains a relatively incurable disease; planning for the most effective yet tolerable treatment strategy could potentially improve the patient's quality of life (QoL).

Patients with CTCL perceive their condition as enduring and persistent, exhibiting a somewhat pessimistic emotional reaction towards their illness [4]. Demierre et al. indicated that CTCL (80% of the study population were MF) somehow affects the QoL of patients; almost 72.7% of cases were depressed, and about 39% felt ashamed [5].

Therefore, an assessment of the quality of life of these patients can contribute to better management of their disease and mood, enhancing their psychological well-being, with the ultimate aim of improving overall quality of life through treatment [6]. Moreover, assessing the QoL can help physicians make better decisions about treatment strategies [7, 8].

Aside from the patients themselves, their family members also feel the strain and burden of chronic and malignant disease as caregivers. Basra et al. in their study on the impact of skin diseases on family members concluded that these diseases can significantly impair the health-related QoL of the patient's family in many ways, and asking them about this impact is greatly appreciated [9].

Given the significance of the subject and the paucity of published articles, this study aimed to evaluate the impact of the disease and its treatment on patients with MF and their families through self-administered questionnaires in our referral center in Shiraz.

Materials and Methods

Study Design and Setup

In this cross-sectional study, patients with MF were recruited from the outpatient MF clinic affiliated with Shiraz University of Medical Sciences, a referral clinic in southern Iran, between February 2022 and January 2023. All consecutive patients with histologically confirmed MF (hematoxylin & eosin and immunohistochemistry staining) were enrolled according to the inclusion and exclusion criteria and their willingness to participate in the study. The diagnosis of new and early MF was done according to the ISCL (International Society of Cutaneous Lymphoma) algorithm. One of the first-degree relatives accompanying the patient was considered the family member. Also, normal healthy individuals participated in this study as a control group.

Inclusion and Exclusion Criteria

We studied patients aged over 18, with diagnosis made more than one month earlier and able to read or understand Farsi to complete the questionnaires. Caregivers or family members (parent, sibling, spouse, or offspring) willing to participate in the study were also recruited. Normal healthy age, sex, and education-matched population aged over 18 without any skin disease were considered as the control group.

Measures

We collected demographics including age, sex, education, marital status, duration of the disease (since the diagnosis was confirmed), course of the disease, severity of disease based on Modified Severity-Weighted Assessment Tool (mSWAT) score, stage (TNM staging), and treatment modality according to each patient's medical record.

Questionnaires

We used three questionnaires: the Persian version of Dermatology Life Quality Index (DLQI), the Family Dermatology Life Quality Index (FDLQI), and the World Health Organization Quality of Life Brief Version (WHOQOL-BREF)

(ll patients completed the three questionnaires, while the healthy control group completed only the WHOQOL-BREF questionnaire.

The DLQI questionnaire contains 10 questions grouped into six subscales, "symptoms and feelings", "daily activities", "leisure", "work and school", "personal relationships", and "treatment" [10]. Each question is scored from 0 (not at all) to 3 (very). The sum of these subscales yields the total score, which is categorized into "no effect" (score: 0-1), "small effect" (score: 2-5), "moderate effect" (score: 6-10), "very large effect" (score: 11-20), and "extremely large effect" (score: 21-30). Dermatology-specific quality of life was assessed using the DLQI questionnaire, translated into Persian by Aghaei et al. [11].

The FDLQI questionnaire consists of 10 questions each scored from 0 (not at all) to 3 (very much), and a higher total score indicates a larger effect of the disease on family QoL. The internal consistency of this test was measured as Cronbach's alpha = 0.88, and the reliability was measured as interclass correlation coefficient = 0.94 [12, 13]. The FDLQI was administered in its Persian version, which has been validated by Safizadeh et al. [13].

The WHOQOL-BREF questionnaire consists of 26 items, scored from 1 (very bad) to 5 (very good). A higher total score means a better quality of life. It is also divided into four domains of quality of life, including "physical" (seven items), "psychological" (six items), "social" (three items), and "environmental" (eight items) [14]. The internal consistency of this questionnaire was examined using Cronbach's alpha, resulting in a value of 0.896. The internal reliability of all domains was found to be 0.70 [15, 16]. The Persian version of the WHOQOL-BREF questionnaire, validated by Nejat et al. [17], was used to assess quality of life.

Statistical Analysis

Statistical analysis was performed using SPSS software, version 24. We report mean and standard deviation (SD) for quantitative variables, and relative frequency for qualitative variables. The difference significance assessed using an independent two-sample T, one-way ANOVA, and Pearson correlation tests were used to analyze the quantitative variables. Chi-squared test was performed for qualitative variables. Statistical significance was set at $P<0.05$.

Ethical Consideration

The Ethics Committee of Shiraz University of Medical Sciences approved this study (approval code IR.SUMS.MED.REC.1403.035). Verbal and written consent were obtained from the participants after informing them about the study protocol.

Results

The sociodemographic and clinical characteristics of the study participants (113 cases, 91 patients' relatives, and 129 healthy controls) are shown in Tables 1 and 2, respectively.

Table 1. Demographic Data of the Study Participants

Parameters	Participants		P-value	Caregiver (n=91)
	Case (n=113)	Control (n=129)		
Sex, n (%)				
Male	42 (37.2)	51 (39.5)	0.654	51 (56.0)
Female	71 (62.8)	78 (60.5)		40 (43.1)
Age (y), mean ± SD (range)	43.85 ± 14.20 (18-80)	42.13 ± 13.19 (22-81)	0.338	44.73 ± 12.75 (17-77)
Marital status, n (%)				
Unmarried	25 (22.1)	31 (24.0)	0.937	-
Married	88 (77.9)	98 (76.0)		-
Educational status, n (%)				
Illiterate	4 (3.5)	3 (2.3)	0.366	0
High school	24 (21.2)	24 (18.6)		11 (12.1)
Diploma	30 (26.6)	32 (24.8)		32 (35.2)
Bachelor	34 (30.1)	46 (35.7)		27 (29.6)
MS and higher	10 (8.9)	24 (18.6)		14 (15.4)
Not Known	11(9.7)	0		7(7.7)

SD, standard deviation.

Table 2. Clinical Characteristics of the Patients.

Parameters	Value
Disease duration(m), mean ± SD, (range)	52.49 ± 38.58 (2 – 168)
Course of disease, n (%)	
Active progressive	20 (17.7)
Partial remission	59 (52.2)
Complete remission	28 (24.8)
Recurrence	6 (5.3)
Stage, n (%)	
1-A	21 (18.6)
1-B	60 (53.1)
2-A	22 (19.5)
2-B & 3-A	10 (8.8)
mSWAT mean ± SD, (range)**	36.57 ± 29.96 (3 – 174)
Lesion location	
Groin lesion, n (%)	
Yes	49 (43.4)
No	64 (56.6)
Head&neck lesion, n (%)	
Yes	22 (19.5)
No	91 (80.5)
Treatment	
Topical treatment, n (%)	
Yes	103 (91.1)
No	10 (8.9)
Phototherapy, n (%)	
Yes	78 (69.0)
No	35 (31.0)
Acitretin, n (%)	
Yes	40 (35.4)
No	73 (64.6)
Methotrexate, n (%)	
Yes	15 (13.3)
No	98 (86.7)
Interferon, n (%)	
Yes	23 (20.4)
No	90 (79.6)
Gemcitabine monotherapy, n (%)	
Yes	4 (3.5)
No	109 (96.5)

The enrollment of participants is shown in Figure 1. Of the 113 patients with MF diagnosis, 71 (62.8%) were female and 42 (37.2%) were male; in the healthy control group, 78 (60.5%) were female and 51 (39.5%) were male. Both groups were matched in terms of sociodemographic variables, including sex, age, marital status, and educational status. As shown in Table 2, more than half of the patients had stage IB disease. None of the participants suffered from Sezary syndrome or visceral involvement.

DLQI

The mean DLQI total score was 8.00 ± 6.41, with a range of 0 to 25 in our patients, and more than half of the patients experienced moderate, very large, or extremely large effects of the disease on their lives (Figure 2). Analysis revealed that DLQI was significantly ameliorated with advanced stage of disease, i.e., active disease, increasing MSWAT score, and also the location of the lesion, with significantly higher impact of head/neck lesion on patients' QoL (Table 3).

Different treatment modalities did not significantly affect the total DLQI score except for better QoL in patients receiving topical therapy. Regarding the subscales, interferon significantly affected "leisure", and the personal relationship index of DLQI (P=0.045, P=0.037), and gemcitabine also deteriorated the patients' "symptoms and feelings" (P= 0.046).

Based on the DLQI subscales, "symptoms and feelings" and "leisure" dimensions of DLQI were the most impacted by MSWAT, disease stage, course of the disease, and location of the lesion (Table 3).

Interestingly, the DLQI total score and its dimensions were not affected by age, disease duration, educational level, or marital status (P>0.05).

Although we also analyzed the effect of disease duration by dividing less and more than 12 months from the time of diagnosis, results indicated no significant difference in the DLQI score in either group.

FDLQI

The FDLQI score was 8.44 ± 6.93 with a range of 0–24 in patients' relatives. Our results revealed a significant negative correlation between FDLQI score and disease duration, (P=0.008). Family QoL deteriorated over the course of disease and for head/neck lesions (P=0.020, P=0.003, respectively). Similar to the DLQI score, FDLQI indicated that interferon statistically significantly influenced the patients' family QoL (P=0.034) (Table 4). Data analysis revealed no significant relationship between the sex, family relationship, and educational level of the caregivers and the FDLQI score.

We also analyzed the FDLQI score, with less than and more than 12 months of caregiving, which indicated significant deteriorated Qol with early disease (P=0.029).

As shown in Figure 3, the areas most affected in caregivers were extra-expenditure, burden of care, and emotional.

WHOQOL-BREF

WHOQOL-BREF total score demonstrated a significantly higher score, i.e., better quality of life, in the control group in comparison with the MF cases (P=0.001). Although

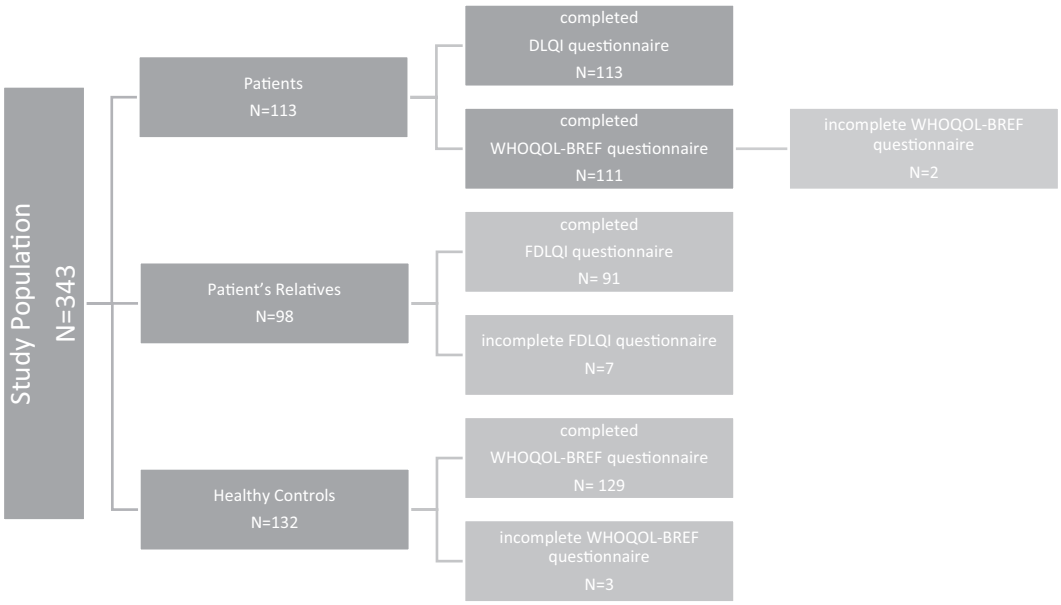

Figure 1. Flow diagram of participants enrolled in the study.

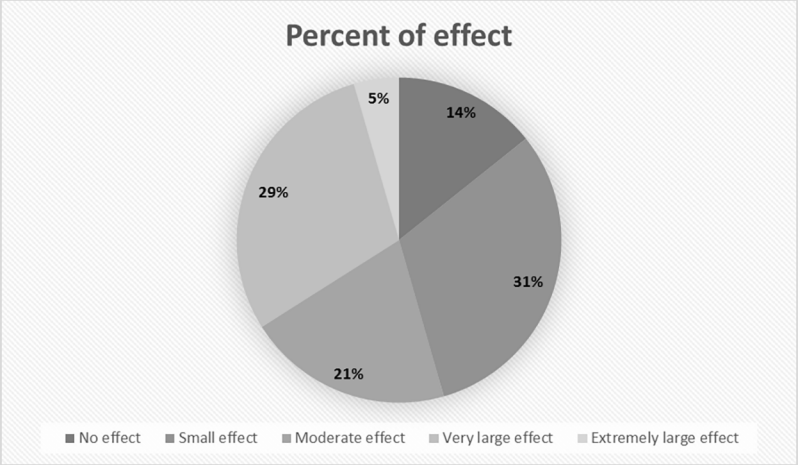

Figure 2. Percentage of DLQI Categorical scale.

WHOQOL-BREF dimension scores revealed that the disease had no impact on the physical and social relationship dimensions of MF patients (P=0.101, P=0.097, respectively), it significantly ameliorated the psychological, environmental, and general health aspect of the cases compared with healthy individuals (P<0.001, P=0.045, and P<0.001, respectively) (Table 5).

Considering the impact of patients' sociodemographic and clinical characteristics, it was demonstrated that educational status significantly impacted the QoL of patients (P=0.035), and that patients with active disease had worse general health QoL (P=0.031). The MSWAT score showed significantly deteriorated physical, psychological, and general health, and the total QoL of patients (r=-0.244, P=0.012, r=-0.256, P=0.008, r=-0.197, P=0.043, r=-0.247, P=0.011, respectively).

Among treatment regimens, topical treatment enhanced the general health perception of patients (P=0.043).

Further analysis of the WHOQOL score of patients under 12 months from diagnosis and those more than 12 months revealed that there was significantly better QoL in those with prolonged duration (P=0.034).

Finally, Table 6 reveals that the total QoL scores measured by all three questionnaire instruments had a significant correlation with each other, demonstrating valid QoL evaluation (P<0.001).

Discussion

According to the present study, the QoL of patients with MF and their families was impaired by this chronic skin cancer. The mean DLQI score, 8.00 ± 6.41 showing moderate effect,

Table 3. Association between DLQI dimension scores and patients' clinical characteristics.

DLQI subscales parameters	Total	Symptoms and feelings	Daily activities	Leisure	Work and school	Personal relationships	Treatment
Disease duration							
Pearson Correlation	-0.105	-0.141	0.069	-0.186*	-0.098	-0.084	-0.004
P-value	0.272	0.137	0.470	0.050	0.306	0.379	0.966
MSWAT							
Pearson Correlation	0.318	0.279	0.187	0.285	0.166	0.306	0.152
P-value	**<0.001**	**0.004**	0.055	**0.003**	0.089	**0.001**	0.119
Disease stage							
1-A	4.71 ± 4.73	1.61 ± 1.77	0.81 ± 0.98	0.76 ± 1.33	0.24 ± 0.43	0.38 ± 0.80	0.90 ± 1.09
1-B	7.77 ± 6.15	2.05 ± 1.51	1.71 ± 1.79	1.43 ± 1.64	0.42 ± 0.60	1.25 ± 1.70	0.89 ± 0.94
2-A	9.50 ± 6.75	2.5 ± 1.50	1.59 ± 1.43	2.0 ± 1.92	0.50 ± 0.80	1.68 ± 2.17	1.23 ± 1.11
2-B & 3-A	11.40 ± 8.2	3.3 ± 2.16	1.90 ± 1.91	2.50 ± 2.54	0.90 ± 0.88	1.70 ± 1.25	1.10 ± 0.88
P-value	**0.022**	**0.043**	0.143	**0.036**	0.067	0.051	0.570
Course of disease							
Active progressive	13.07 ± 7.22	3.67 ± 1.76	2.67 ± 2.13	2.87 ± 2.10	0.87 ± 0.83	1.67 ± 1.83	1.33 ± 1.18
Partial remission	8.0 ± 5.92	2.18 ± 1.57	1.44 ± 1.51	1.66 ± 1.93	0.40 ± 0.60	1.28 ± 1.77	1.04 ± 0.95
Complete remission	6.27 ± 5.99	1.50 ± 1.50	1.27 ± 1.21	1.19 ± 1.63	0.31 ± 0.47	1.04 ± 1.48	0.96 ± 1.0
Recurrence	5.67 ± 4.08	2.0 ± 1.55	1.50 ± 1.64	1.0 ± 1.26	0.33 ± 0.52	0.50 ± 0.84	0.33 ± 0.82
P-value	**0.006**	**<0.001**	**0.039**	**0.038**	0.35	0.469	0.221
Groin lesion							
Yes	7.92 ± 5.87	2.18 ± 1.56	1.43 ± 1.40	1.67 ± 1.95	0.45± 0.61	1.24 ± 1.75	0.94 ± 0.85
No	7.98 ± 6.87	2.19 ± 1.74	1.63 ± 1.78	1.49 ± 1.75	0.46± 0.69	1.14 ± 1.63	1.03 ± 1.09
P-value	0.957	0.983	0.506	0.606	0.928	0.827	0.614
Head/neck lesion							
Yes	11.32 ± 8.0	2.90 ± 2.0	2.09 ± 1.85	2.36 ± 2.17	0.77 ± 0.92	2.00 ± 2.12	1.18 ± 0.94
No	7.13 ± 5.74	2.0 ± 1.52	1.41 ± 1.54	1.38 ± 1.70	0.38 ± 0.55	1.01 ± 1.50	1.05 ± 0.98
P-value	**0.029**	0.059	0.078	**0.023**	0.066	**0.013**	0.316
Topical Treatment							
Yes	7.41 ± 6.07	2.03 ± 1.53	1.44 ± 1.53	1.50 ± 1.80	0.42 ± 0.60	1.09 ± 1.63	0.93 ± 0.97
No	12.0 ± 6.11	3.50 ± 2.14	2.50 ± 2.07	2.25 ± 1.75	0.50 ± 0.53	2.0 ± 1.60	1.25 ± 1.04
P-value	**0.042**	**0.013**	0.069	0.260	0.718	0.131	0.372
Phototherapy							
Yes	7.23 ± 6.01	1.96 ± 1.58	1.49 ± 1.67	1.47 ± 1.82	0.45 ± 0.65	0.95 ± 1.51	0.92 ± 0.97
No	8.48 ± 5.83	2.45 ± 1.65	1.55 ± 1.36	1.65 ± 1.62	0.39 ± 0.50	1.48 ± 1.71	0.97 ± 0.95
P-value	0.330	0.153	0.871	0.636	0.618	0.113	0.809
Acitretin							
Yes	8.47 ± 6.75	2.28 ± 1.59	1.66 ± 1.84	1.72 ± 1.85	0.62 ± 0.79	1.22 ± 1.64	0.96 ± 1.03
No	7.51 ± 5.99	2.08 ± 0.67	1.51 ± 1.48	1.53 ± 0.81	0.34 ± 0.48	1.12 ± 1.66	0.92 ± 0.92
P-value	0.468	0.570	0.660	0.634	0.068	0.786	0.802
MTX							
Yes	9.80 ± 6.07	2.53 ± 1.46	2.20 ± 1.52	2.20 ± 2.18	0.27 ± 0.46	1.33 ± 1.76	1.27 ± 1.10
No	7.47 ± 6.20	2.08 ± 1.67	1.44 ± 1.59	1.49 ± 1.74	0.46 ± 0.62	1.12 ± 1.63	0.88 ± 0.92
P-value	0.179	0.323	0.089	0.162	0.263	0.648	0.144

Table 3. Association between DLQI dimension scores and patients' clinical characteristics. *(continued)*

DLQI subscales parameters	Total	Symptoms and feelings	Daily activities	Leisure	Work and school	Personal relationships	Treatment
Interferon							
Yes	9.65 ± 5.42	2.57 ± 1.31	1.52 ± 1.38	2.26 ± 1.94	0.52 ± 0.51	1.78 ± 2.0	1.0 ± 0.85
No	7.28 ± 6.35	2.02 ± 1.71	1.56 ± 1.66	1.40 ± 1.75	0.40 ± 0.63	0.98 ± 1.50	0.91 ± 0.98
P-value	0.106	0.164	0.917	**0.045**	0.404	**0.037**	0.706
Gemcitabine monotherapy							
Yes	11.75 ± 6.60	3.75 ± 1.71	2.50 ± 1.29	2.0 ± 1.83	0.75 ± 0.50	1.75 ± 2.06	1.00 ± 0.82
No	7.64 ± 6.18	2.08 ± 1.62	1.51 ± 1.60	1.57 ± 1.82	0.42 ± 0.60	1.13 ± 1.64	0.93 ± 0.96
P-value	0.196	**0.046**	0.227	0.648	0.279	0.462	0.887

Table 4. Association between FDLQI and Patients' Clinical Data.

Parameters	FDLQI Total (mean ± SD)	Pearson correlation	P-value
Disease duration	-	-0.265	**0.008**
MSWAT	-	0.160	0.126
Disease stage			0.494
1-A	7.43 ± 6.74	-	
1-B	8.34 ± 7.04	-	
2-A	9.48 ± 7.96	-	
2-B & 3-A	8.33 ± 2.78	-	
Course of disease			**0.020**
Active	14.38 ± 10.21	-	
Partial remission	9.14 ± 6.7	-	
Complete remission	6.14 ± 6.29	-	
Recurrence	8.40 ± 7.92	-	
Groin lesion			0.725
Yes	9.06 ± 6.20	-	
No	8.55 ± 8.19	-	
Head/neck lesion			**0.003**
Yes	12.95 ± 7.82	-	
No	7.66 ± 6.73	-	
Interferon			**0.034**
Yes	11.14 ± 7.19	-	
No	7.59 ± 6.65	-	

was in agreement with mean DLQI scores of 6.3 ±6.7, and 12±8 reported by a study describing a diverse population of patients with MF [18] and 5.83±4.92 by an Austrian multicenter study [19].

Overall, the key findings indicated that advanced stage disease, active uncontrolled disease, a higher mSWAT, lesion on the head/neck, higher educational level, and treatment involving interferon or gemcitabine monotherapy negatively affected QoL across various domains. The domains most significantly impacted included "leisure" and "feelings and symptoms" as measured by the DLQI subscales, along with "general health," "environmental," and "psychological" perceptions evaluated through the WHOQOL-BREF scoring system. An interesting finding was that patients with longer disease duration and those receiving topical treatments reported a better QoL.

In contrast to earlier research by Molloy, Sampogna, and Chalaka, this study revealed that the extent of QoL impairment experienced by patients was not significantly affected by sex or sociodemographic factors [6, 20, 21]. This observation aligns with a study conducted on 121 Greek

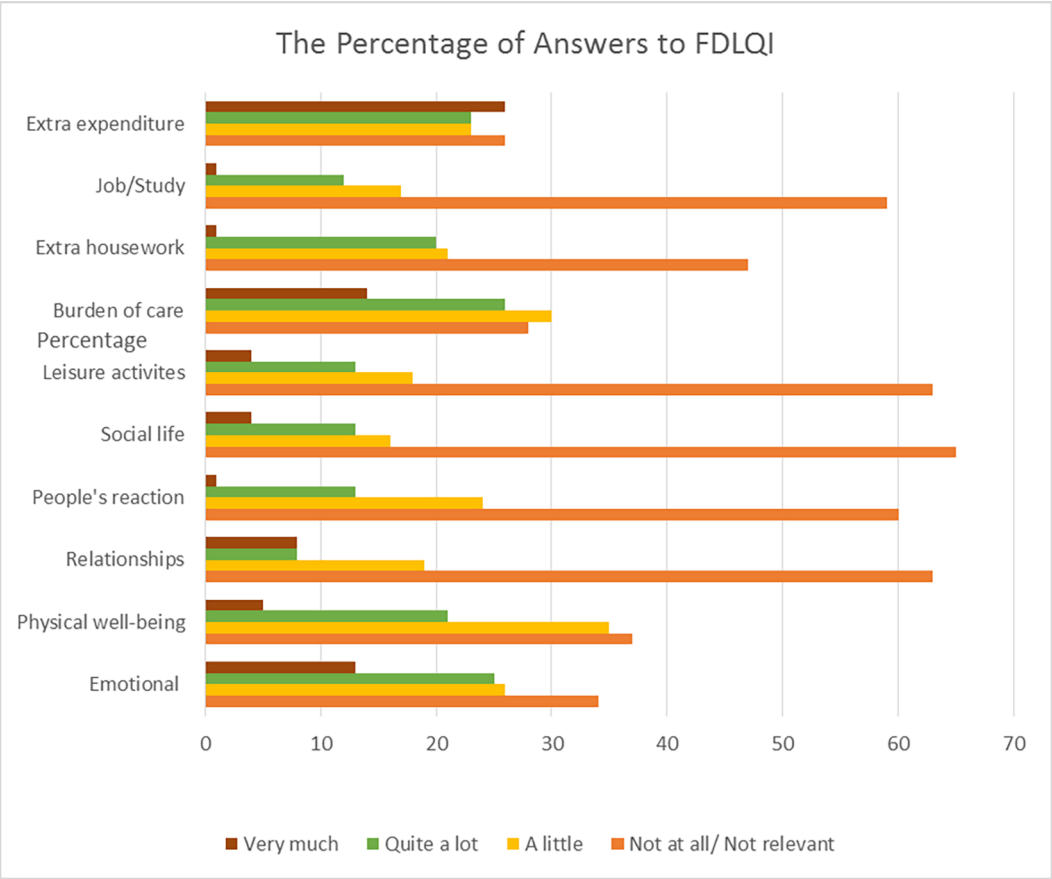

Figure 3. Percentage of answers to each individual item of FDLQI by family caregivers.

Table 5. Association between WHOQOL-BREF Dimension Scores between Case and Control groups.

	Case (mean ± SD)	Control (mean ± SD)	p-value
WHOQOL Total	90.02 ± 15.34	96.16 ± 13.78	**0.001**
WHOQOL Physical	59.27 ± 23.37	63.42 ± 16.61	0.110
WHOQOL Psychological	60.66 ± 16.72	70.80 ± 14.42	**<0.001**
WHOQOL Social relationship	62.99 ± 18.96	66.93 ± 17.83	0.099
WHOQOL Environmental	63.69 ± 16.17	68.14 ± 15.94	**0.045**
WHOQOL General health	60.62 ± 17.93	69.67 ± 18.41	**<0.001**

Table 6. Correlation between the Total Scores Obtained from DLQI, FDLQI, and WHOQOL-BREF Questionnaires.

		FDLQI Total	WHOQOL Total	DLQI Total
DLQI Total	Pearson correlation	0.595	-0.462	
	p-value	**<0.001**	**<0.001**	
WHOQOL Total	Pearson correlation	-0.460		-0.462
	p-value	**<0.001**		**<0.001**
FDLQI Total	Pearson correlation		-0.460	0.595
	p-value		**<0.001**	**<0.001**

MF patients [22] and findings from two studies involving 300 Iranian patients [23, 24]. This might be partially attributed to cultural practices, such as specific clothing choices (hijab) among Iranian women that obscure skin diseases and disfigurements.

Further analysis indicated that patients with head/neck lesions faced greater challenges, emphasizing the detrimental effects of facial lesions and alopecia, thus underscoring the need for timely and possibly more intensive systemic therapies for these individuals. Interestingly, despite 43.4%

of patients exhibiting groin lesions, their QoL was comparable to patients with lesions in other body areas, suggesting that sexual embarrassment might not be as pronounced in this study compared to the findings of Shinohara et al. [25].

Moreover, a related study conducted in Isfahan from 2017 to 2019 utilizing the SF-36 questionnaire noted that advanced disease stages, longer duration, and lesions in sun-exposed areas correlated with lower QoL [24]. Our finding that patients with longer disease duration reported a better QoL deviates from this study while aligning with recent observations by Ottevanger [26] and could reflect a coping mechanism developed over time in response to living with a chronic disease, evolving their perception of illness. Notably, patients with higher educational backgrounds experienced poorer QoL, which diverges from findings from Nourmohammadpour et al. on a smaller cohort of patients [23] and from the study by Porkert [27]. This discrepancy might be related to increased access to information regarding the disease, heightened awareness about its seriousness, and growing concerns regarding its progression.

Although we expected the treatment response to be linked to an improved QoL, notably interferon and gemcitabine worsened QoL scores despite objective disease response. Interferon therapy negatively influenced the leisure and personal relationships domain of DLQI as many patients experienced flu-like symptoms of fever, chills, fatigue, and arthralgia with an injection every other day lasting for 48 hours. This situation became particularly distressing during the COVID-19 pandemic, as many symptoms were mistakenly attributed to coronavirus disease. Interestingly, our findings indicated that the use of topical treatments, especially topical corticosteroids provided at our center, led to a notable improvement in QoL. Patients who utilized these treatments experienced a reduction in symptoms such as redness, scaling, roughness, and itchiness, resulting in significantly improved total DLQI and symptoms and feeling domain scores.

Additionally, FDLQI score averaged 8.44 ± 6.93, with a range of 0–24 for relatives of affected patients, with extra expenditures being particularly bothersome and highlighting the need for financial support. The study unveiled a notably worse FDLQI score in cases involving newly identified active disease and in those located in the head/neck area. This aligns with earlier qualitative research involving seven patients with erythrodermic MF, highlighting the shocking and upsetting nature of the diagnosis for both patients and their families [28]. Comparisons with other studies, such as the one by Bin Saif et al. involving vitiligo patients' families (n=129), which reported a mean FDLQI of 10.3 [29], and a study by Sampogna on families of epidermolysis bullosa patients which yielded a mean score of 9.8 [30], suggest that the deteriorating impact on family members of MF patients is similarly significant.

Furthermore, when assessed using the WHOQOL-BREF tool, changes in QoL among our patients were less favorable compared to healthy individuals; they exhibited worse scores in psychological, environmental, and general health aspects. It has been noted that patients with MF generally have a reduced QoL compared to those with Hodgkin and non-Hodgkin lymphoma, with skin manifestations contributing significantly to these diminished scores [24].

Certain domains within our study remained unaffected, including "daily activities" (except in those suffering from active uncontrolled disease), "work and school", and "treatment" in DLQI, as well as "physical" and "social relationship" dimensions in WHOQOL-BREF. This indicates that our patients experienced intense distress primarily in the emotional and psychological domains, which should be considered within MF management guidelines.

Conclusion

This study uniquely examined the impact of MF and its treatments on specific QoL domains, providing a more granular understanding of the patient experience. Furthermore, we extended our analysis to include the QoL of family caregivers, offering a more comprehensive perspective.

The intricate relationship between treatment, QoL, and psychological well-being underlines the need for holistic approaches in addressing the complexities encountered in MF patients' care.

Consistent with our findings and prior research, we advocate for the routine assessment of QoL in MF patients, both before and after initiating any therapy that may impact their daily lives and those of their families. Given the significant distress experienced upon diagnosis, particularly in the first year, interventions aimed at managing expectations and enhancing coping strategies are crucial.

Our findings also highlight the negative impact of a patient's illness on the QoL of their family caregivers, underscoring the need for future research into effective support strategies for these individuals. Finally, the development of a validated, standardized, and disease-specific QoL instrument for CTCL and MF would facilitate more robust comparisons across studies.

Limitations

The present study included all patients referring to our clinic, not just the newly diagnosed ones, and although it had the benefit of considering the effect of treatment on patient's QoL, some of the participants were in partial or complete remission. Another limitation was our decision not to use cancer-related questionnaires as an instrument; by using DLQI and WHOQOL-BREF, we focused only on cutaneous symptoms, not considering cancer-related ones. This was because we

usually do not use the term "cancer" or "lymphoma" when communicating with our patients, especially in early-stage disease, due to the negative impact these terms have on the patients and their families. The influence of selection bias of non-responders may also be a limitation in the current study.

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