Original Article

Clinical Profile and Quality of Life in Patients with Resistant to Treatment Vitiligo Lesions in Iran: Vitiligo Patients need Medico-psycho-social Assistance

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Abstract

Background: Vitiligo is a common chronic disease associated with physical effects, psychological impacts, and impaired quality of life (QoL). Lesions in acral areas are resistant to treatments. Since these areas are exposed and visible, they have a profound effect on patients' self-confidence. Despite the high prevalence of these conditions, information in this field, especially for Iranian patients, is scarce.
Objectives: To study the clinical profile of patients with vitiligo lesions in the acral areas, assess the burden of QoL impairment, and investigate the association between patient's characteristics and their QoL outcomes
Methods: A total of 84 patients with non-segmental vitiligo who had involvement in resistant treatment areas were recruited in this study. Clinical characteristics and disease outcomes, with a special emphasis on the quality of life (QoL), were investigated using the Dermatology Life Quality Index (DLQI) questionnaire. Furthermore, the extent of the disease was calculated by utilizing the Vitiligo Area Scoring Index (VASI). Descriptive and comparative analyses were conducted using SPSS software (version 29).
Results: The most common comorbidity observed among the patients was various types of immune diseases. The mean total score of DLQI was 8.1, indicating a moderate effect of the disease on the patient's life since the score falls within the range of 6-10. The Kruskal-Wallis non-parametric test illustrated a significant difference in QoL among different age groups (P=0.020). The results indicated a positive, direct, and significant relationship between the extent of the disease and DLQI (r=0.269,;P=0.013). Nonetheless, the relationship between the engagement of the genital area in married patients and difficulties in sexual relations was not found to be statistically significant at α=0.05.
Conclusion: The involvement of end-extremities based on existing studies is a frequent occurrence in vitiligo. These affected areas hold considerable significance in terms of the patient's quality of life (QoL) due to their prominent visibility and resistance to available treatments. Considering the high prevalence of psychological consequences, diversity in skin phototypes, and social acceptance, regional studies are necessary for more efficient and responsive medical management integrated with psychosocial assistance.

Keywords: DLQI, Iran, Quality of life, Resistant to treatment lesion, Vitiligo

1. Background

Vitiligo is a common skin disease with a prevalence ranging from 0.5%-2% (1). In this condition, the skin turns white due to the loss of melanocytes. Studies have demonstrated differences in the clinical course of the disease based on gender, age, and ethnicity. One study indicated that the face was the most frequently affected area, followed by the acral areas and extremities (2). Conducting further research in Iran on clinical patterns and the impact of the disease on quality of life (QoL) is essential to develop clinical and social support.

The understanding and acceptance of vitiligo in different cultures may vary significantly (3), profoundly affecting social and family relationships. A study has revealed that patients with different skin phototypes experience varying disease-related burdens and stress (4). A survey conducted on 1000000 Iranians estimated the prevalence of vitiligo at 0.6% (5). Another study in Iran found that vitiligo patients experience significantly higher anxiety and hopelessness levels than healthy individuals (6).

Psychosocial comorbidities in vitiligo have a high prevalence, reaching nearly 90% (7).

Meanwhile, lesions in acral areas (hands and feet) and bony prominences, such as knees and elbows, are resistant to conventional treatments (8). People with treatment-resistant vitiligo lesions, who have sought a cure for a long time and experienced weak improvement responses, naturally suffer more. This study adds more clarification on the prevalence of these complications, their severity, and their correlation with different factors. The stress resulting from the social stigma of vitiligo and the impaired quality of life may exacerbate the disease (9). Naturally, a number of patients may hide their disease due to the stigma. Since the conditions of patients vary across various ethnicities and cultures, this study can demonstrate how and to what extent social health policymakers, NGOs, and charity institutions should focus on supporting vitiligo patients, especially those with treatment-resistant cases, to improve efficiency, equity, responsiveness, and humanitarian assistance.

2. Objectives

To study the clinical profile of patients with acral area involvement

To assess the burden of Quality of Life (QoL) impairment and investigate the dependencies that patients' characteristics have on their QoL outcomes.

3. Methods

This analytical observational study was conducted on 84 patients who were referred to the Skin and Stem Cell Research Center Clinic over a two-year period. The inclusion criteria encompassed patients with non-segmental vitiligo and treatment-resistant areas, particularly acral regions. On the contrary, patients with segmental vitiligo, those lacking treatment-resistant areas, and individuals with incomplete medical records were excluded. A statistical power analysis was conducted to ascertain the suitable sample size for the study, taking into account the anticipated effect size, significance level, and desired power.

Based on findings from similar countries, the expected prevalence of impairment in the quality of life is estimated to be 90% ([10]). To achieve a study power of 80%, a confidence level of 95%, and a precision of 10%, the estimated sample size was initially determined to be 82. Nonetheless, we increased the sample size to 84. From patients referred to the Clinic of Skin and Stem Cell Research Center of Tehran University of Medical Sciences, 84 Non-segmental vitiligo patients with involvement in resistant to treatment areas, such as acral and bony prominences, were recruited and evaluated during a 24-month period from 2018 to early 2021. After obtaining general information, a detailed medical history was taken, and a meticulous physical examination was performed. Different variables relevant to the clinical course, location of involvement, and extent of depigmentation were investigated.

The assessment of quality of life in vitiligo patients is routinely measured using the Dermatology Life Quality Index (DLQI) questionnaire, a recognized and reliable tool ([11]). The DLQI comprises 10 questions addressing various life aspects, including disease symptoms, emotional distress, daily activities, such as shopping and home care, clothing choices, social and leisure engagements, sports participation, work or study-related matters, as well as relationships and sexual well-being. Each question is rated on a 4-point scale from 0-3, and the total DLQI score ranges from 0-30. A high DLQI score indicates a significant impact of the disease on patients' quality of life. The instructions for this questionnaire establish five impact rate categories: 0-1 (no effect at all), 2-5 (small effect), 6-10 (moderate effect), 11-20 (very large effect), and 21-30 (extremely large effect

on the patient's life). To evaluate the effects of vitiligo on the quality of life, the Persian version of the DLQI questionnaire was utilized. The validity and reliability of this version had been previously assessed ([12]).

Using the Vitiligo Area Scoring Index (VASI)([13]), the extent of the total body engagement was calculated at 0%-100%. This is the most commonly used method and widely cited tool that uses the rule of 1% of the palm in the vitiligo extent assessment ([14], [15]). The degree of depigmentation is graded on a scale from 0-5, representing various levels of involvement: 0: No depigmentation, 1: depigmentation involving 1%-10% of the area, 2: depigmentation involving 11%-25%, 3: depigmentation involving 26%-50%, 4: depigmentation involving 51%-90%, and 5: depigmentation involving 91%-100% of the area.

All participants signed written informed consent before participating in the study. Data analysis was performed using SPSS software (version 29). A descriptive analysis was conducted to estimate the central tendency and dispersion of various variables and DLQI. To assess the correlation and perform a comparative analysis based on the ranking of DLQI, contingency tests, such as the Chi-Square test, were administered. The level of significance was set at 0.05.

4. Results

All participants included in the study were adults aged 18 years or older with non-segmental vitiligo. Among the selected cases, 49 (58.3%) subjects were female, while 35 (41.7%) cases were male. Out of the total participants, 42 (50%) patients were married, and an equivalent number of cases were single. During the initial visit, the mean age score was 34.38 years, with a median of 32.78. The age range spanned 45 years, from a minimum of 18 years to a maximum of 63. Detailed statistical information is presented in Table 1, which provides a classification of various variables. The average duration of the disease was 13.90 years, with a standard deviation of 8.896. The duration ranged from less than one year to a maximum of 37 years. Among the 84 patients, all reported their first observed sign of the disease as skin whitening.

4.1. Areas of onset and progression of the disease

Figure 1 shows tissue and areas of involvement in patients. All the patients had loss of skin color while premature whitening of hair and mucus membrane loss of color had the next scores.

To investigate the distribution patterns of vitiligo, we divided the entire body surface into 38 routine localization commonly associated with vitiligo involvement. As depicted in Figure 2, the initial sites of disease onset were frequently observed on the dorsal surface of the hand, eyelids,

Table 1. DLQI in different groups of variables

| Variable	Group	Frequency	No effect at all	small	moderate	very large	extremely large	Total in raw
All patients		No	7	33	16	27	1	84
		%	8%	39%	19%	32%	1%	100%
Age group	**<25**	No	1	8	4	2	0	15
		% in raw	7%	53%	27%	13%	0%	100%
	25-35	No	2	10	7	16	1	36
		% in raw	6%	28%	19%	44%	3%	100%
	35-45	No	3	9	2	7	0	21
		% in raw	14%	43%	10%	33%	0%	100%
	>45	No	1	6	3	2	0	12
		% in raw	8%	50%	25%	17%	0%	100%
Gender	**Female**	No	2	21	8	17	1	49
		% in raw	4%	43%	16%	35%	2%	100%
	Male	No	5	12	8	10	0	35
		% in raw	14%	34%	23%	29%	0%	100%
Marital status	**Single**	No	3	17	8	13	1	42
		% in raw	7%	41%	19%	31%	2%	100%
	Married	No	4	16	8	14	0	42
		% in raw	10%	38%	19%	33%	0%	100%
Education level	**Under the diploma**	No	1	6	1	0	0	8
		% in raw	13%	75%	13%	0%	0%	100%
	Diploma	No	3	7	7	11	0	28
		% in raw	11%	25%	25%	39%	0%	100%
	Associate Degree	No	0	0	1	1	1	3
		% in raw	0%	0%	33%	33%	33%	100%
	Bachelor	No	2	13	5	6	0	26
		% in raw	8%	50%	19%	23%	0%	100%
	MA	No	1	5	2	6	0	14
		% in raw	7%	36%	14%	43%	0%	100%
	Doctorate or higher	No	0	2	0	3	0	5
		% in raw	0%	40%	0%	60%	0%	100%
VASI score classification	**0%- 10%**	No	7	23	12	17	1	60
		% in raw	12%	38%	20%	28%	2%	100%
	11%- 25%	No	0	9	4	5	0	18
		% in raw	0%	50%	22%	28%	0%	100%
	26%- 50%	No	0	1	0	5	0	6
		% in raw	0%	17%	0%	83%	0%	100%
Genitalia engagement	**No**	No	5	11	5	12	0	33
		% in raw	15%	33%	15%	36%	0%	100%
	Yes	No	2	22	11	15	1	51
		% in raw	6%	67%	33%	45%	2%	100%
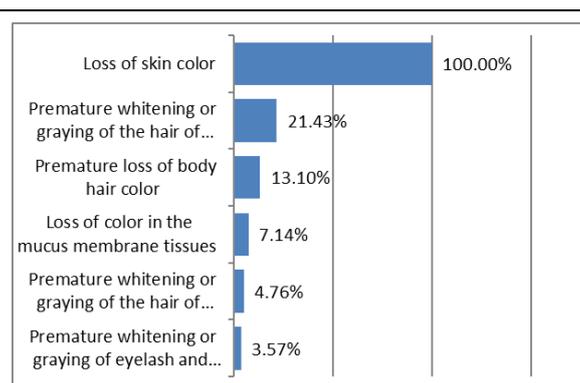
Figure 1. Tissue and areas of involvement in patients

elbows, knees, and lower limbs. In comparison with primary sites of involvement, the distribution observed during the patient's visit demonstrated the highest frequency of engagement on the lower limbs, accounting for 71 (84.52%) cases, followed respectively by the back of the hand, fingers, cubital area, forearm, ankle, and wrist. The highest rates of increase between the onset of disease and at the time of visit were, respectively, feet, hand fingers, ankle, as well as back of hand and wrist.

4.2. Vitiligo Area Scoring Index Score

The VASI Score exhibited a mean value of 9.48, alongside a median of 7.00 and a standard deviation

of 8.225. The observed range extended to 34, varying between a minimum of 1 and a maximum of 35. The categorization of VASI score outcomes was carried out using a well-established classification framework consisting of six standard percentile categories (16), delineating depigmentation levels as follows: no depigmentation, 1-10%, 11-25%, 26-50%, 51-90%, and 91-100% of body involvement. As depicted in Figure 3, a total of 60 patients (71.4%) fell within the 0%-10% category. Furthermore, no patient exhibited more than 50% of vitiligo involvement.
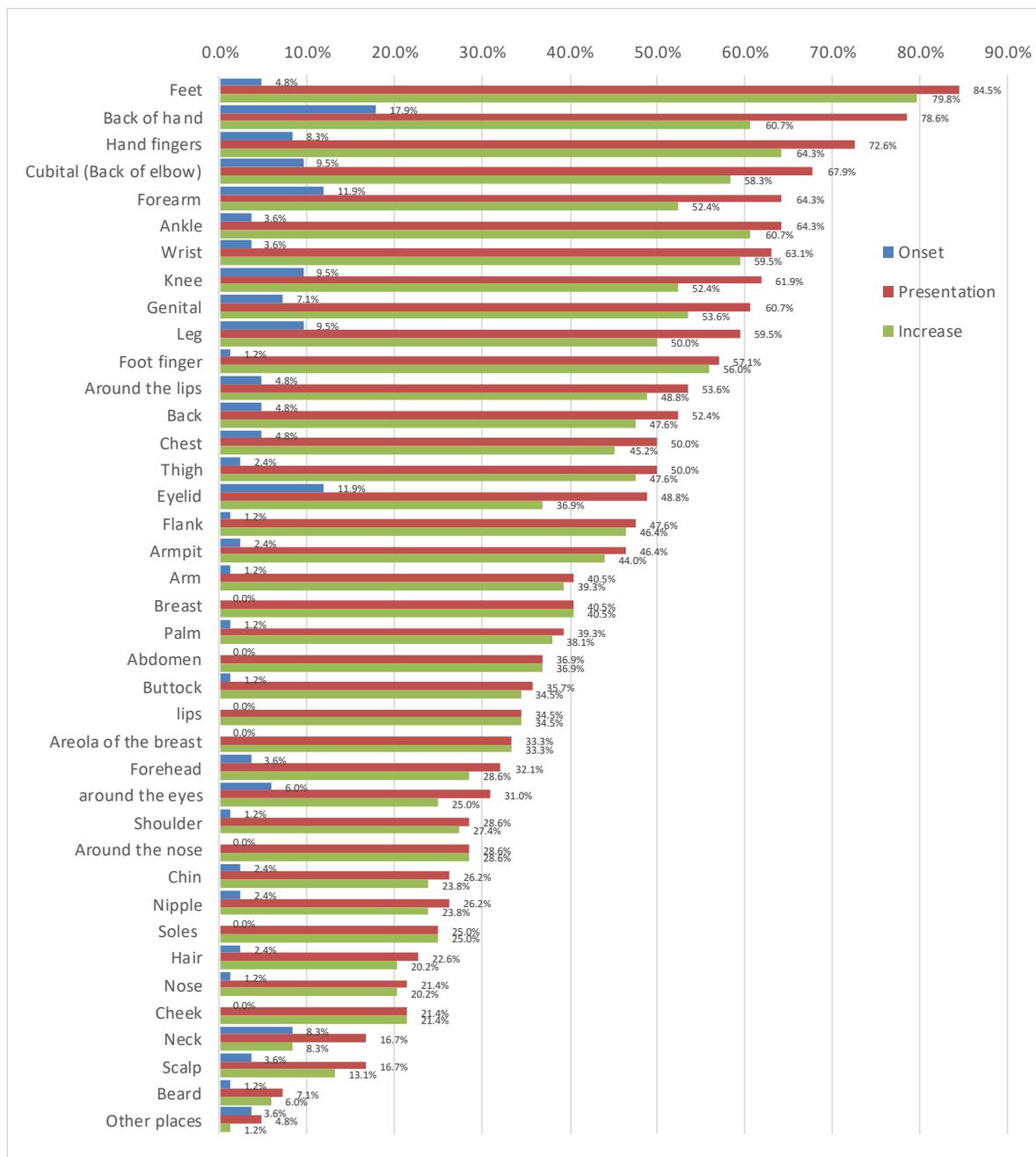
Figure 2. Distribution of involvement of different areas with vitiligo at onset, at the time of visit (presentation), and progress (increase)

4.3. Associated comorbidities

The most frequent condition was the psychological effects of vitiligo. We have elaborated on the psychological consequences in the subsequent sections of this article. Skin allergy, seasonal allergy, iron deficiency anemia, and a history of hypothyroidism are, respectively, the next most frequent comorbidities (Figure 4).

4.4. DLQI and different variables

The data indicate that the mean total score for all patients was 8.1. This score falls within the range of 6-10, indicating a moderate effect of the disease on the patients' lives. The scores obtained from patients are illustrated in Figure 5. Furthermore, Figure 6

presents the outcomes of the data classification into

five DLQI groups. Figure 7 displays the mean scores
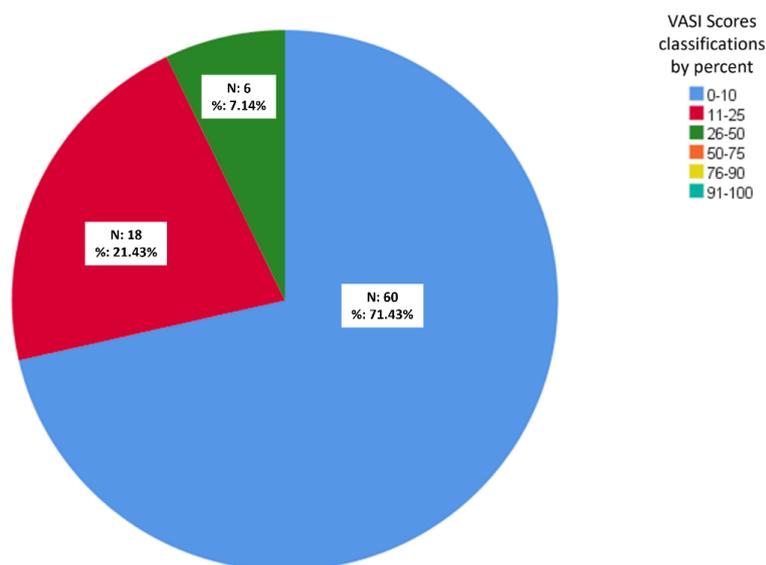
Figure 3. Percentage of patients in VASI Score classifications. There were no patients with a VASI score greater than 50
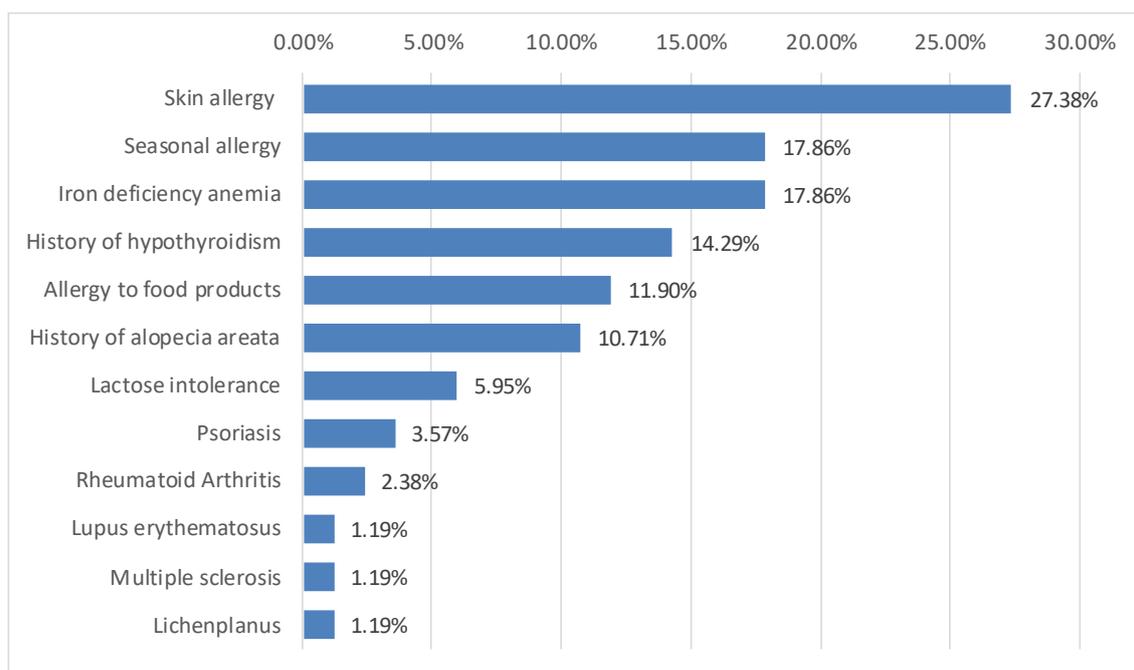
Figure 4. Associated comorbidities in patients

for each of the 10 questions. Notably, such factors as clothing and embarrassment emerged as prominent contributors, while the impact of sexual difficulty was comparatively lower.

4.5. Relationship between DLQI and demographic and clinical variables
4.5.1. Age
As depicted in Table 1, the majority of patients aged under 25 years, within the age range of 35-45, and those aged 45 and above were situated within the category where vitiligo has a minimal impact on their lives. However, the majority of individuals aged 25-35 experienced a very large effect. The Chi-Square test was used to determine the relationship between different age groups and DLQI. The conclusion showed that there is no significant relationship between these two variables (P=0.535). The One-Sample Kolmogorov-Smirnov test of normality indicated that the age of subjects in all DLQI groups followed a normal distribution, except for the group with the moderate effect, where a normal distribution

is not observed (P=0.017). Taking this into consideration, we employed a one-way ANOVA
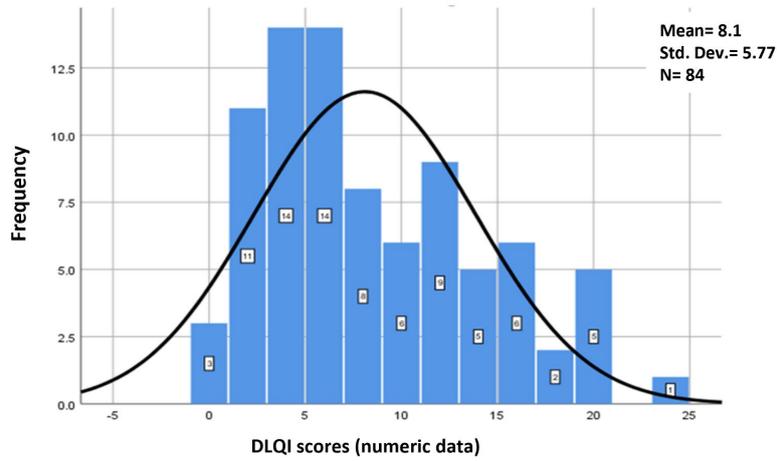
Figure 5. Histogram of Dermatology Life Quality Index (DLQI) in the patients
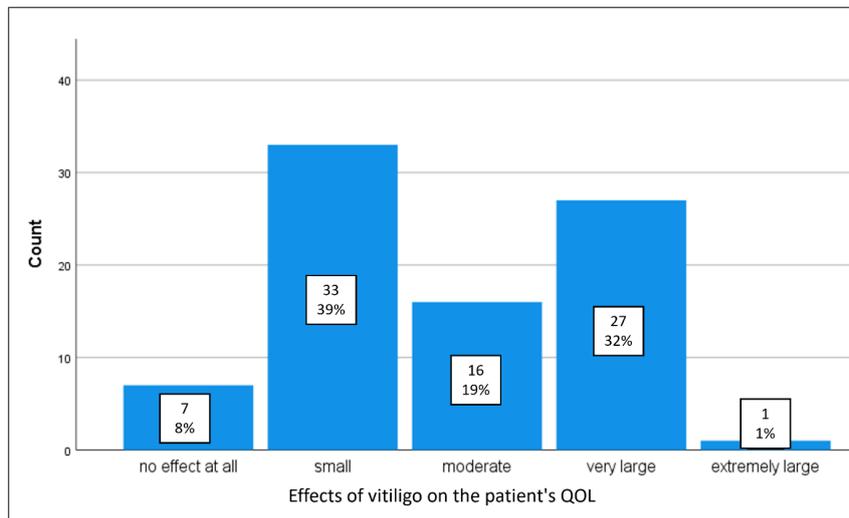
Figure 6. Severity of vitiligo impact on patient's QoL (DLQI ranked in five categories)
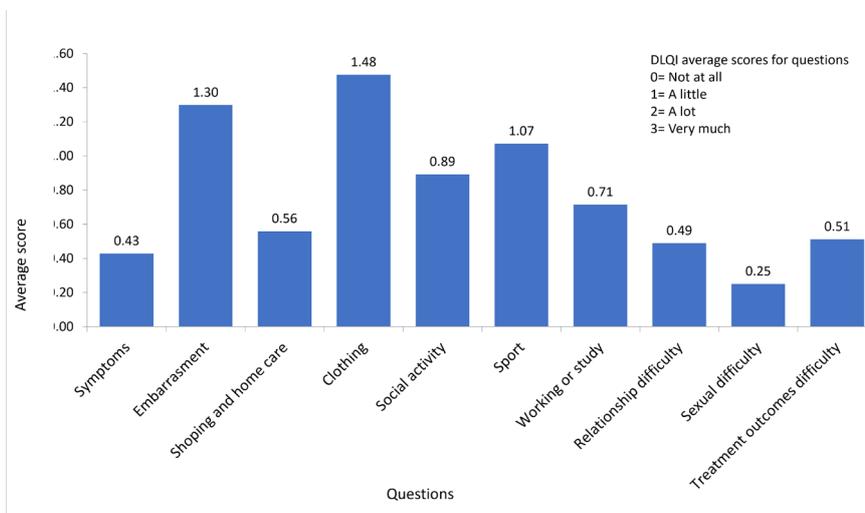

Figure 7. Average Dermatology Life Quality Index (DLQI) scores for each of the 10 DLQI questions

parametric analysis. The results pinpointed that the age of cases in different categories of DLQI did not exhibit significant differences (P=0.903). Nevertheless, a significant difference was observed when the numerical data (scale scores) of the DLQI are analyzed using the Kruskal-Wallis non-parametric test (P=0.020). Among all age categories, the age group of 25-35 demonstrates a higher mean and SEM (standard error of the mean) compared to other groups (10.28, 1.02).

4.5.2. Gender and marital status

Based on Table 1, in both females and males, as well as single and married cases, most patients are in the group with a small effect of vitiligo on their lives. Contingency tests, such as the Chi-Square test, showed no significant difference in DLQI scores between males and females (P=0.362). Moreover, there is no significant difference in mean DLQI score between married and single cases (P=0.876).

4.5.3. Educational level

We stratified educational levels. Most had diplomas (n=28; 34.57%) and bachelor's degrees (n=26; 32.10%). A non-parametric correlation coefficient, such as Kendall's Tau-b, demonstrated a weak and non-significant relationship between educational groups and DLQI categories (r= 0.094; P=0.305). In addition, the result obtained using Kruskal-Wallis yielded a similar outcome (P=0.097). However, what can be inferred from the results is that the mean and median DLQI scores in patients with lower education are lower than in cases with higher education. Although this result is not reported as statistically significant at α= 0.05, if the significance level is increased to 0.1, we can consider this relationship to be significant.

4.5.4. Extent of disease (VASI score)

To investigate the relationship between VASI and DLQI, we employed Spearman's correlation coefficient. We conducted this analysis using the numeric scale scores of these two variables. The results indicate a positive, direct, and significant correlation between these two variables (r=0.269; P=0.013). This implies that individuals with higher VASI scores also exhibit higher DLQI scores.

4.5.5. Duration of disease

The assessment of disease duration for each of the DLQI categories demonstrated that the means are close to each other. The means are 14.7, 11.9, 13.9, 16.0, and 17.0, respectively, for the DLQI groups, including no effect at all, small, moderate, very large, and extremely large effect on patient's quality of life. The One-Sample Kolmogorov-Smirnov Test illustrated that the length of the vitiligo in some DLQI groups has a normal distribution and in others, including the small and very large effects on the

patient's life, does not have a normal distribution. Suppose we use the Kruskal-Wallis non-parametric test (assuming not being normal disease duration distribution). In that case, we come to the conclusion that the duration of the disease in different DLQI groups is not significantly different from each other (P=0.358). According to the above-mentioned reasons, it is appropriate to use One-way ANOVA parametric analysis to investigate if variations of different levels of the length of the disease have a measurable effect on the dependent variable of DLQI groups. The result shows that the length of vitiligo duration in different categories of DLQI does not differ significantly from each other (P=0.362).

4.5.6. Genital area engagement

The relationship between genital area vitiligo and DLQI levels was investigated using the Chi-Square test. The obtained result demonstrated no significant relationship between these two variables (P=0.297).

4.5.7. Genital area engagement and sexual activity

The Chi-square test was employed to investigate the relationship between genital area involvement and sexual problems among married patients. The sexual problem was assessed based on their response to the question, "Over the past week, to what extent has your skin caused any sexual difficulties?" The findings indicate no statistically significant relationship (α=0.05) (P=0.090).

5. Discussion

The results of this study pointed to the moderate effect of vitiligo on the overall quality of life, primarily impacting clothing and causing embarrassment. Comparisons with other studies unveiled variations in the quality of life among diverse populations and cultures. Educational level was identified as correlating with DLQI scores, thereby emphasizing the effect of cultural and social factors on the disease. As illustrated in Figure 2, the most frequent areas of onset and progression were the extremities. At the time of the visit, the highest frequency of involvement was in the feet, back of the hand, hand fingers, cubital (back of elbow), forearm, ankle, wrist, knee, leg, and foot fingers. The results of the present research are relatively similar to the study by R. Speeckaert and N. van Geel in Belgium ([2]). In this study, the most frequently affected areas after the face were the acral areas and extremities. In our study, none of the patients had the onset of vitiligo on the breast, abdomen, lips, around the nose, soles, or cheek.

Our study demonstrated that the mean DLQI score was 8.10, indicating that vitiligo has a moderate effect on the patient's life. This score was similar to the study conducted by A. Abdurrahman A. Gao and Xing-Hua, in which the mean DLQI scores worldwide

ranged from 1.82-15, with an overall average of 8.2 (17). This was also similar to the study by Narumol Silpa-archa et al. In our study, as depicted in Figure 7, the three main effects of vitiligo on the quality of a patient's life were embarrassment, social activities, and clothing choices (18). In agreement with the current research, the study by Dolatshahi et al. on Iranian patients indicated that the mean DLQI score was 8.16 (19).

The quality of life obtained in our study was compared with several other types of research. Based on these comparisons, in European countries, such as France, Estonia, and Germany, the impact of vitiligo on the quality of life was lower. In a French referral center study, the mean DLQI in patients with vitiligo was 7.17 (20). Another study on vitiligo patients of the Dutch-speaking Belgian population (Flanders) showed a mean DLQI of 4.95 (21). The total mean DLQI score in vitiligo was 4.7 in the Estonian sample (22). This difference can be ascribed to various reasons, including the darker skin color in Iranian people and vitiligo skin lesions that create a higher color difference. Moreover, this discrepancy can be attributed to differences in culture and social acceptance. On the other hand, based on an assessment in Saudi Arabia, the mean DLQI for all vitiligo patients in the Qassim province was 14.72 (SD +/-5.173). This means that quality of life impairment among Saudi patients is higher and has a significant difference compared to Iranian patients, possibly due to the difference in skin phototype, which depends on the amount of melanin pigment in the skin of the populations of the two countries (23).

Based on our study, the DLQI scores for patients in different grading, including no effect, small, moderate, very large, and extremely large effect on the quality of life, had ratios respectively, 8.33%, 39.29%, 19.05%, 32.14%, and 1.19%, while these scores based on a study in north-east India conducted by LN Sangma, et al. were respectively 5%, 19%, 38%, 38% and 0% of patients (24). This signifies a shift to higher impairment in QoL in the recent study. The mean DLQI score for this study was 9.08, which is higher compared to our study. In the present study, in the age range of 25-35, most people were in a very large effect (44.3%). This recent result was similar to the review conducted by A. Amer et al., in which they observed the highest mean DLQI in the age range of 20-29 (17). Based on the results, patients with higher VASI have higher DLQI. A similar result has been shown by Mustafa A. Hammam et al.(25). With $\alpha=0.1$, it can be concluded that there is a significant relationship between genital area engagement and impairment in sexual activity. This result has similarities to the study by Borimnejad et al., in which female patients experienced impairment in sexual activity (26).

5.1.Limitations

In this study, we have selected our research participants from individuals with non-segmental vitiligo who have involvement in the acral region. These areas are usually resistant to treatment, and this aspect should be considered when generalizing the results. Nonetheless, as mentioned in this article, studies indicate that most vitiligo patients have lesions in their extremities.

6. Conclusion

According to other studies, the involvement of extremities is a frequent occurrence in vitiligo. These affected regions hold significance for the quality of life due to their visibility and resistance to treatment. It is crucial to pay attention to psychological aspects, especially in those who have lesions resistant to treatment. Quality of life impairment in Iranian vitiligo patients moderately affects them. Attention to the psychosocial status of vitiligo patients is of great importance. Impairment in the quality of life depends on the affected area of the body, the extent of the disease, and the natural color of the skin, which differs among various races and regions. Patients may need psychological counseling and care for depression. Therefore, to ensure more effective treatment and responsive healthcare with improved quality of life, an integrated medico-psycho-social service approach is needed. Improving NGO charity societies to construct a safe, supportive community would be helpful.

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