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Prediction of Quality of Life Using Dermatology Life Quality Index in Iranian Patients with Neurofibromatosis Type 1

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Abstract

Background: Neurofibromatosis type 1 (NF1), a genetic condition most commonly characterized by the presence of dermal neurofibromas and café au lait macules, has a significant impact upon the Quality of Life (QoL). The purpose of this study is to predict the QoL with Dermatology Life Quality Index (DLQI) in Iranian patients with neurofibromatosis type 1.

Methods: This cross-sectional study was conducted on 223 patients with neurofibromatosis type 1 using available sampling. Data collection tools were demographic information form, SF-36 and DLQI questionnaires. Quality of life was predicted by DLQI. Linear and multiple regression tests were utilized to analyze the data.

Results: Predicting the quality of life by dermatology quality of life showed that the physical function by the variable "work and school" and treatment, role limitations due to physical health by the variable of work and school, the role limitations due to emotional problems by the variable of treatment, emotional well-being by the variable of interpersonal relationships, pain by the variable of symptoms and feelings, daily activities, and personal relationships were predictable. Finally, social function, general health and fatigue cannot be predicted by any variable.

Conclusion: The results of this study indicated that the quality of dermatology life is able to predict some aspects of quality of life. These findings can be used to provide better health services to this group of patients and improve their quality of life.

Keywords: Dermatology, Neurofibromatosis type 1, Quality of life

Introduction

Neurofibromatosis type 1 (NF1), also known as von Recklinghausen's disease, is an autosomal dominant neurological skin disease that occurs equally in different sexes, races, and ethnicities (1). NF1 is the most common type of neurofibromatosis occurring in approximately one out of every 3,500 births (2,3). The first symptoms of this disease are skin lesions in the form of café au lait spots (4-6). Internal neurofibromas may affect vital organs, inhibit their activity, and be potentially malignant. External neurofibromas might be aesthetically deforming and associated with significant stigma for affected individuals (7). The clinical manifestations are variable, unpredictable and potentially life threatening. The resulting deformity and social isolation is a cause of psychological distress in these patients (8). Depression is common in NF patients. Previous studies have shown a significant prevalence of depression and psychiatric disorders in NF adults compared to the general population (9). Various physical, cognitive and social complications of NF significantly reduce the Quality of Life (QoL) (10). NF has the most severe negative impact on patients' lives through severe complications and negative cosmetic effects. Although NF-related complications and death occur due to complications of the disease and involvement of various organs, patients' perception of physical deformity has been reported as the most important treatment problem (11). Chronic skin diseases, which have a significant impact on a person's mental image, affect mental health and can reduce self-confidence and thus reduce QoL (12). NF patients have a negative image of their body, which leads to low self-confidence and psychological anxiety (13). Although skin diseases are not life-threatening and do not interfere with daily activities, they, like other diseases, influence QoL, especially when the symptoms of the disease appear in visible areas of the body such as hands and face (14). Since results of studies represented that skin manifestations of NF have the greatest impact on QoL (15,16), the aim of the present study was to predict general QoL using Dermatology Life Quality Index (DLQI).

Materials and Methods

This cross-sectional study was performed on the Iranian population of patients with NF1 in 2020. Participants were selected using non-random convenience sampling. A total of 223 patients with NF1 who met the inclusion criteria participated in the present study. Inclusion criteria included patients with NF1, Iranian nationality, aged 18 years and over, no other chronic diseases (such as multiple sclerosis, cancer), no known underlying mental diseases, non-use of psychotic drugs, and the ability to read and write. Considering the rarity of NF and the unavailability of patients with the coordination of Neurofibromatosis Association of Iran, the questionnaires were designed online. Participants completed the questionnaire online through a secure website. Patients' responses were collected anonymously and confidentially. Data collection tools consisted of a demographic information collection form including questions on age, sex, education, occupation, ethnicity, *etc*., and two questionnaires to determine the quality of life, *i.e.*, DLQI and SF-36 questionnaire. DLQI was designed by Kodra *et al* (17). It comprises 10 questions regarding the symptoms and feelings, daily activities, work or school, leisure, personal relationships, and treatment of patients over the past week. Each question is assigned 4 options: Very much (score 3), much (score 2), a little (score 1), and at all (score 0). The DLQI score ranges from 0 (no effect on quality of life) to 30 (very high effect on quality of life). In the DLQI, scores are classified as follows: 0 to 1, no effect; 2 to 5, small effect; 6 to 10, moderate effect; 11 to 20, very large effect; 21 to 30, extremely large effect (18). Considering the two-item nature of the DLQI dimensions, inter-item correlation (ACI) was used to assess reliability and the reliability results were as follows: symptoms and feelings (0.22), daily activities (0.41), leisure (0.73), work and school (0.58), personal relationships (0.52). SF-36 questionnaire was developed by Ware and Sherbourne (19). It consists of 36 terms and 8 domains: Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role Emotional (RE), and Mental Health (MH). The possible score range is 0 to 100, with a higher score representing better QoL (20). The reliability of different dimensions of SF-36 was within 0.76 to 0.83.

Data analysis

Simple linear regression was utilized to predict general QoL variables. Also, the variables, which were significant in simple linear regression, were simultaneously examined in multiple linear regression using the standard model. Multicollinearity and the independence between the residuals were evaluated using Variance Inflation Factor (VIF) and Durbin-Watson, respectively. $p<0.05$ was considered as the significance level in all the tests. Data analysis was performed using SPSS 25 (IBM Corp., Armonk, New York, USA).

The present study was approved by the Ethics Committee of Golestan University of Medical Sciences (IR.GOUMS.REC.1398.366). Informed consent form was obtained from all the participants regarding participation in the research after stating the purpose, nature, and methodology of the study. Participants were assured that their information would be kept confidential.

Results

Out of 223 patients studied, 159 patients (66.3%) were female with a mean age of 33.11±7.53 years and a confidence interval of 32.11-34.10 years (Table 1).

The mean DLQI score in this study was 9.24 out of 30, which indicates the average impact of the disease on DLQI. The mean DLQI score was assessed in 6 dimensions of symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. The results showed that the highest and the lowest mean scores were related to the symptoms and feelings (2.38), treatment (0.4) dimensions, respectively (Table 2). The mean scores of SF-36 dimensions are also shown in table 3.

DLQI was used to investigate SF-36 dimensions in the multiple linear regression model and results indicated that the PF dimension of SF-36 can be predicted by the two dimensions of DLQI, *i.e.*, work and school (B=-0.626 and p=0.027) and treatment (B=-1.232, p=0.012). In other words, if there is one-score reduction in "work and school" and treatment dimensions of DLQI (increasing score in all dimensions of DLQI is associated with a decrease in skin quality), the SF score will be reduced by 0.626 and 1.232, respectively (any decrease in scores of all dimensions of SF-36, except for BP, is associated

Table 1. Demographic information of the patients

Variables	N (%)	Total
Age (years)		
18-35 (young adulthood)	149 (66)	223 (100)
36-55 (middle age)	71 (31)	
≥56 older adulthood	3 (1.34)	
Sex		
Female	159 (66.3)	223 (100)
Male	64 (26.7)	
Marital status		
Single	158 (70.5)	223 (100)
Married	57 (25.4)	
Divorced	8 (3.6)	
Job		
Jobless	71 (31.7)	223 (100)
Self-employment	49 (21.9)	
Employee	38 (17)	
Worker	16 (7.1)	
Housewife	45 (20.1)	
Retired	4 (1.8)	
Education		
Primary	10 (0.44)	223 (100)
Middle and High school	75 (33)	
Associate	29 (13)	
BSc	78 (34)	
MSc	31 (13)	

Table 2. Dimensions of the DLQI Life questionnaire in the neurofibromatosis patients

Dimensions of DLQI questionnaire	Mean±SD	CI
Symptoms and feelings	2.38±1.51	2.17 to 2.59
Daily activities	2.11±1.71	1.87 to 2.35
Leisure	2.26±2.0	2.05 to2.67
Work and School	0.70±1.41	0.50 to 0.90
Personal relationships	1.28±1.60	1.05 to 1.50
Treatment	0.40±0.75	0.29 to 0.50
Total	9.24±6.88	8.28 to 10.21

Table 3. Dimension of SF-36 questionnaire in the neurofibromatosis patients

Dimensions of SF-36 questionnaire	Mean±SD	CI (95)
Physical functioning	23.95±5.45	23.21 to 24.69
Role limitations due to physical health	6.62±1.50	6.41 to 6.82
Role limitations due to emotional problems	4.65±1.22	4.48 to 4.81
Social function	5.72±1.29	5.55 to 5.90
Pain	5.68±2.32	5.36 to 5.99
Emotional well-being	18.82±2.79	18.44 to19.20
Energy/Fatigue	14.23±2.31	13.92 to 14.54
General health	16.80±2.43	16.47 to17.13

with a decrease in general QoL).

The emotional role and physical role problems due to health issues can be predicted by the work/school variable (B=0.251 and p=0.001). In other words, if there is one-score reduction in the work and school dimension, the score of role limitation due to health problems of SF-36 is reduced by 0.251. The RE dimension can be predicted by the treatment dimension (B=-0.364 and p=0.004). In other words, if there is one-score reduction in the treatment dimension of DLQI, RE score will be reduced by 0.364.

No variable was significant in simple linear regression in the SF dimension of SF-36. Therefore, the multiple linear regression model was not applicable for this dimension. The results of simple linear regression showed no significant difference in the symptoms and feelings (B=0.054 and p=0.349), daily activities (B=-0.017 and p=0.726), leisure (B=0.014 and p=0.719), work and school (B=-0.055, and p=0.410), personal relationships (B=-0.079 and p=0.114), and treatment (B=0.114 and p=0.306) dimensions. Thus, no variable was entered into multiple regression model.

The MH dimension can be predicted by the dimension of personal relationships (B= -0.336 and p=0.019). In other words, if there is one-score increase in the dimension of personal relationships, MH score will decrease by 0.336.

Also, no variable remained in the model with regard to GH dimension of SF-36, while the dimension of symptoms and feelings was significant in linear regression (B=0.251 and p=0.022).

BP dimension of SF-36 can be predicted by three variables of symptoms and feelings (B=0.709 and p=<0.001), personal relationships (B=0.288 and p=0.008), and daily activities dimension (B= -0.331, p=0.024). In other words, if there is one-score increase in the dimensions of symptoms and feelings and personal relationships, BP score of SF-36 will increase by 0.709 and 0.288, respectively, and the same score was reduced by 0.331 with one score increase in the daily activities dimension.

Finally, no variable was included in the multiple linear regression model with regard to vitality. The results of linear regression were as follows: symptoms and feelings (B=-0.093, p=0.347), daily activities, (B= 0.029, p=0.729), leisure (p=0.968, B=0.003, work and school (B=-0.130 and p=0.247), personal relationships (B=0.111 and p=0.198) and treatment (p=0.435, B=0.150) (Table 4).

Discussion

The results of the present study showed that the patients had a moderate DLQI score. With regard to SF-36 score, NF patients had low average QoL score in various SF-36 dimensions. In a systematic review study, Sanagoo *et al* reported a decrease in QoL score in NF patients, regardless of the type of instrument used compared to the general population. Results represented impaired QoL in all the SF-36 subscales. Results showed impaired QoL in all the DLQI subscales. These results indicate that NF imposes significant pressure on patients and affects all aspects

Table 4. Linear and multiple regression models of SF-36 and DLQI questionnaire

Linear regression	Simple (raw)			Multiple (modified)		
Dimensions	B	p	CI 95٪	B	p	٪CI 95
10.8%=R^2 (physical functioning)						
Symptoms and feelings	-0.722	0.002	-1.180 to -0.264			
Daily activities	-0.199	0.316	-0.589 to 0.191		-	
Leisure	-0.369	0.020	-0.679 to -0.059			
Work and school	-0.840	0.001	-1.332 to -0.347	-0.624	0.027	-1.176 to -0.071
Personal relationships	-0.483	0.019	-0.885 to -0.081			
Treatment	-1.752	<0.001	-2.631 to -0.874	-1.232	0.012	-2.280 to - 0.184
16.%=R^2 (role limitations due to physical health)						
Symptoms and feelings	-0.269	<0.001	-0.397 to -0.142			
Daily activities	-0.165	0.003	-0.274 to -0.057		-	
Leisure	-0.201	<0.001	-0.286 to -0.116			
Work and school	-0.355	<0.001	-0.491 to- 0.219	-0.251	0.001	-0.404 to -0.098
Personal relationships	-0.179	0.002	-0.292 to -0.066			
Treatment	-0.513	<0.001	-0.762 to -0.265		-	
16.7%=R^2 (role limitations due to emotional problems)						
Symptoms and feelings	-0.269	<0.001	-0.373 to -0.166		-	
Daily activities	-0.210	<0.001	-0.297 to -0.123		-	
Leisure	-0.155	<0.001	-0.225 to -0.084		-	
Work and school	-0.166	0.006	-0.285 to- 0.047		-	
Personal relationships	-0.206	<0.001	-0.297 to -0.115		-	
Treatment	-0.542	<0.001	-0.742 to -0.343	-0.364	0.004	-0.609 to -0.120
Social function R^2 (*)						
Symptoms and feelings	0.054	0.349	-0.059 to 0.167		-	
Daily activities	-0.017	0.726	-0.112 to 0.078		-	
Leisure	0.014	0.719	-0.062 to 0.090		-	
Work and school	-0.055	0.410	-0.185 to 0.076		-	
Personal relationships	0.079	0.114	-0.019 to 0.177		-	
Treatment	0.114	0.306	-0.105 to 0.334		-	
R^2=%10.7 (emotional well-being)						
Symptoms and feelings	-0.445	0.004	-0.690 to -0.220		-	
Daily activities	-0.412	<0.001	-0.608 to -0.216		-	
Leisure	-0.285	<0.001	-0.444 to -0.126		-	
Work and school	-0.298	0.028	-0.564 to -0.032		-	
Personal relationships	-0.402	<0.001	-0.607 to -0.197	-0.336	0.019	-0.616 to -0.056
Treatment	-0.556	0.020	-1.022 to -0.098		-	
***=R^2 (general health)**						
Symptoms and feelings	0.251	0.022	0.037 to 0.464			
Daily activities	0.028	0.764	-0.153 to 0.208			
Leisure	0.132	0.073	- 0.012 to 0.276			
Work and school	-0.022	0.862	-0.268 to 0.224			

Contd. table 4.

Personal relationships	0.056	0.557	-0.132 to 0.244			
Treatment	-0.184	0.388	-0.603 to -0.235			
20.1%=R^2 (pain)						
Symptoms and feelings	0.695	<0.001	0.486 to 0.904	0.709	<0.001	0.425 to 0.992
Daily activities	0.265	0.006	0.078 to 0.453	-0.331	0.024	-0.617 to -0.045
Leisure	0.320	<0.001	0.172 to 0.467		-	
Work and school	0.400	0.002	0.155 to 0.646		-	
Personal relationships	0.310	0.002	0.116 to 0.505	0.288	0.008	0.499 to 0.077
Treatment	0.780	<0.001	0.348 to 1.211		-	
Energy/fatigue R^2 (*)						
Symptoms and feelings	-0.093	0.347	-0.288 to 0.102		-	
Daily activities	0.029	0.729	-0.135 to 0.192		-	
Leisure	0.003	0.968	-0.129 to -0.134		-	
Work and school	-0.130	0.247	-0.350 to 0.091		-	
Personal relationships	0.111	0.198	-0.058 to 0.281		-	
Treatment	0.150	0.435	-0.229 to 0.530		-	

R^2 (*)= Variables in a multiple regression model were not significant.

of their lives. In addition, the present study showed a significant relationship between a reduction in QoL with physical, cognitive, and social complications (21).

In a systematic review study, Vranceanu *et al* reported the results of 8 studies on QoL of NF adults. This study revealed reduction in QoL score in SF-36 dimensions, including PF, RP, BP, GH, VT, SF, RE, and MH) as compared to the general population. Consequently, NF is associated with a decrease in QoL in physical, mental, and social dimensions (18). The present study also indicated that the degree of visibility and severity of symptoms predict a decrease in DLQI score in NF patients (22). Another systematic study showed that children and adolescents with NF have a lower QoL score in some SF-36 dimensions as compared to the general population. These subscales in patients aged 7-16 years included motor, cognitive, and emotional performance (19). The results of various studies showed that impairment in all SF-36 sub-scales, including RP, BP, MH, SF, and GH in NF patients have a negative impact on their QoL and these patients experience a reduced QoL in all these dimensions (23,24). A study investigated some of the concerns of NF1 patients using a qualitative approach in 2016 and the results showed that patients and their families were more worried about physical functioning, pain, appearance, and deformity, social stigma, and anxiety (20). Another study was carried out using semi-structured interviews and results represented that NF1 confers a wide range of severity and imposes a heavy burden on patients and affects all aspects of life (1).

DLQI was used in children and adults and results showed that the DLQI score was lower in adults than in children, which may be due to the fact that neurofibromas typically occur in adulthood and cause skin problems and reduce QoL (25).

Crawford *et al* carried out a qualitative study on the effect of NF1 on the health of adult patients. The results showed that NF affects patients' lives in 5 ways, including the burden of physical problems, learning difficulties, and concerns regarding the risk of transmission of NF to children, unpredictable progression of the disease, and pain (14). Another study showed a correlation between pain score

and decreased QoL (6). In a cross-sectional study, Wolkenstein P *et al* investigated the relationship between DLQI score and disease severity in NF patients. The results showed that with increasing disease severity, QoL is impaired in three dimensions of feelings, symptoms, and function. Comparison of general quality of life in these patients also show impairment in different dimensions of QoL (16). Garwood *et al* reported that pain can be a predictor of physical functioning in NF patients (26). Kodra *et al* indicated that NF affected the emotional-psychological aspects of life than symptoms and function (17).

Rastogi showed that skin problems can interfere with education. In this study, symptoms and feelings were more affected than other dimensions. Feelings of embarrassment and lack of attractiveness caused patients to avoid society (27). Providing information about QoL to physicians may help them to achieve a better understanding of damage incurred to the patients' life as well as improving the appropriateness of treatment decisions. One of the limitations of the present study includes the limitation of access to samples. Since the questionnaires were designed online and participants completed the questionnaires online through a valid website, those that did not have access to the Internet, computers, and smart phones may not have been included in the study. Obviously, if a database is created, patients can be better identified.

Conclusion

The results of the present study showed that NF has a negative impact on various aspects of QoL. The present study investigated and predicted the general quality of life using DLQI, and the results indicated that patients have moderate DLQI score and impaired dermatology life quality had a negative effect on the dimensions of general quality of life, except VT, SF, and GH dimensions. The findings of the present study can be used to plan for the promotion of the health status of this group of genetic patients who are not currently supported by any government organization.

Ethical Approval

The present study was approved by Ethics Committee of Golestan University of Medical Sciences (IR.GOUMS.REC.1398.366).

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Conflict of Interest

We declare that we have no conflicts of interest.

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