Quality of life in patients with autoimmune bullous disorders: a cross-sectional study

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Background and Aim: Autoimmune Bullous Diseases (AIBDs) are characterized by blistering skin and mucous membrane lesions. This study evaluated the quality of life and associated factors in patients with AIBDs.

Methods: In this cross-sectional study, we included all clinically- and laboratory-confirmed AIBD patients older than 16 years who sought care at the Dermatology and Hair Clinic of Sina Hospital (Tabriz, Iran) from March to September 2020. We collected the demographic characteristics, disease profile, Autoimmune Bullous Disease Quality of Life (ABQOL) score, and Autoimmune Bullous Skin Disorder Intensity Score (ABSIS). The recorded data were analyzed using SPSS v16 software.

Results: One hundred patients (44 men and 46 women) with a mean age of 52 ± 2 years participated in this study. Among them, 76 had pemphigus vulgaris, 18 had bullous pemphigoid, and 6 had pemphigus foliaceous. A median score of six was recorded for the ABQOL, and a median score of one was recorded for the ABSIS scale. The relationship between quality of life and disease severity was statistically significant ($P = 0.001$). Also, a weak but statistically significant association was observed between the quality of life and patients' age ($P = 0.049$).

Conclusion: We demonstrated that increased disease severity significantly impairs AIBD patients' quality of life. On this account, patients with severe AIBDs require more social, psychological, and financial support.

Keywords: autoimmune bullous diseases, pemphigus, quality of life, severity of illness, vesiculobullous

INTRODUCTION

Autoimmune Bullous Diseases (AIBDs) are a group of life-threatening diseases that clinically manifest with blisters on the skin and mucous membranes [1]. Pemphigus, bullous pemphigoid, epidermolysis bullosa acquisita (EBA), linear IgA bullous dermatosis (LABD), dermatitis herpetiformis, and pemphigoid gestationis are different AIBDs, divided based on the location of the blisters into the intraepidermal and subepidermal categories [2].

Intraepidermal blistering diseases result from autoantibodies forming against the protein structure of the desmosome; the destruction of the intercellular structure causes keratinocyte cells to separate from each other and form intraepidermal blisters that can be easily ruptured [3,4]. In subepidermal blistering diseases, autoantibodies are produced against the structure of the junctions between the dermis and epidermis, causing blisters in the subepidermal areas of the skin [5]. An exact diagnosis of an AIBD facilitates proper treatment and better outcomes [6]. The diagnostic approach is based on clinical suspicion, and the subtype is determined by histopathological analysis, direct/indirect immunofluorescence (DIF/IIF), ELISA, or evaluation of the target antigens' molecular weight [7-10].

The daily life and psychological well-being of an individual can be affected by an AIBD [11]. Several previous studies have demonstrated that the quality of life is severely impaired among AIBD patients [12,13]. Researchers and clinicians around the world use various tools to assess the AIBD patients' conditions and quality of life, including the Autoimmune Bullous Disease Quality of Life (ABQOL) scale, which specifically examines the quality of life in AIBD patients, and Dermatology Life Quality Index (DLQI), which measures the quality of life in patients suffering from a skin disease [14,15].

To manage the clinical symptoms, improve the quality of life, and stabilize AIBD patients, systemic corticosteroids are often administered as the first line of treatment [16]. In patients who are resistant to treatment or where corticosteroids are contraindicated, immunosuppressive agents, such as azathioprine, mycophenolate mofetil, cyclophosphamide, mycophenolic acid, dapsone, methotrexate, sulfonamides, tetracycline, anti-CD20 and anti-IgE monoclonal antibodies, intravenous immunoglobulin (IVIG), and plasma exchange are used to manage the symptoms [17]. However, treatment with corticosteroids and immunosuppressive drugs might also affect the quality of life or result in serious side effects associated with mortality. Therefore, close monitoring of mental well-being and quality of life is essential in these patients. This study aimed to assess the quality of life in patients with AIBDs, with an eye to help improve the management of these patients.

METHODS
Study Design

During this cross-sectional study, all patients older than 16 years with an AIBD seeking care at the Dermatology and Hair Clinic of Sina Hospital (Tabriz, Iran) from March to September 2020, whose diagnosis was confirmed by a dermatologist according to the clinical manifestations, laboratory findings, histopathology, and immunofluorescence study were included. The exclusion criteria were not wishing to participate, incomplete recorded data, lack of definitive diagnosis, and mental retardation. The eligible patients were asked to complete three following questionnaires:

1. Demographic information and details of the AIBD
2. The Autoimmune Bullous Disease Quality of Life (ABQOL) questionnaire for quality of life [14]
3. The Autoimmune Bullous Skin Disorder Intensity Score (ABSIS) for disease severity [18]

Age, gender, marital status, type of disease, duration of disease, history of recent hospitalization, duration of disease diagnosis, duration of disease control, drug history, underlying diseases, and patient status were recorded using a researcher-made questionnaire.

The ABQOL questionnaire includes 17 multidimensional questions, each with a score of zero to three, summing up to a total score range of zero to 51. This questionnaire was completed by the patient. The Persian version of the ABQOL questionnaire, validated by Teimourpour *et al.*, with a Cronbach's alpha coefficient value of 0.855, was used in this study [19]. The ABSIS tool measures the severity of the disease with a maximum score of 206. In this system, the severity of the disease is based on skin involvement, consisting of the percentage of skin involvement based on body surface area (BSA) as well as the quality of skin lesions, and oral involvement, based on the presence and severity of the lesions in 11 different areas of the mouth. The severity of these lesions is evaluated based on the amount of pain and bleeding while eating and drinking.

Ethical Considerations

Written consent was obtained from all participants, and all information was confidential. Participation in this study was optional, and the patients could

withdraw at any time. The Ethics Committee of Tabriz University of Medical Sciences approved the study protocol in compliance with the Helsinki Declaration (IR.TBZMED.REC.1399.690).

Statistical Analysis

The obtained data were analyzed using SPSS v16 software. The study results were reported using descriptive statistics (mean ± SD and percentage). Quantitative and qualitative analyses were performed using the t-test and chi-squared test, respectively. A P-value less than 0.05 was considered statistically significant.

RESULTS

Of the 100 patients who entered the study, 56 were women, and 44 were men. The mean age of the participants was 52 ± 2 years. Ninety-four patients were married, and six were single. The patients had a mean of 6.79 ± 0.57 years of education. The mean disease duration was 26.09 ± 2.97 months, and the mean duration from onset of symptoms to disease diagnosis was 69.49 ± 10.66 days. The participants had a mean of 1.71 ± 0.15 hospitalizations in their medical history. They were under treatment with prednisolone and azathioprine for a mean duration of 24 ± 3.13 months, and the disease was controlled for a mean duration of 6.43 ± 1.41 months. The patients' disease information, including hospitalization status, type of disease, and disease activity, are presented in Table 1.

The results of the patients' responses to the ABQOL questionnaire regarding the quality of life are summarized in Table 2. On a scale of 0 to 51, a median score of 6 (minimum: 0, maximum: 18) was noted. The skin involvement, determined based on BSA, had a median of 0% (minimum skin involvement: 0%, and maximum skin involvement 18%). On a scale of 0 to 11, oral involvement had a median of 0 (minimum 0 and maximum 4). Difficulty in eating, which was scored from 0 to 45 according to the problems in eating, had a median of 0, ranging from 0 to 19.5 among the patients. Likewise, ABSIS had a median score of one, ranging from 0 to 81.75.

The association between the quality of life (ABQOL) and disease severity (ABSIS) was significant ($P = 0.001$). The association between ABQOL and patients' age was also significant

Table 1. Demographic characteristics and disease information of the patients

	Number of patients (n)
Gender	
Female	56
Male	44
Medical history	
Diabetes Mellitus	25
Hypertension	16
Hyperlipidemia	7
Ischemic heart disease	5
Stroke	1
Psychiatric disorders	2
Others (Hepatic, renal, etc.)	5
Drug history	
Azathioprine	46
Prednisolone	85
Cellcept	11
Rituximab	1
Hospitalization status	
Hospitalized	1
Outpatient	99
Type of disease	
Pemphigus vulgaris	76
Pemphigus foliaceous	6
Bullous pemphigoid	18
Status of disease activity	
Active, new-onset	-
Active, recurrent	4
Partial remission following treatment	34
Complete remission following reduction therapy	5
Complete remission following minimal therapy	47
Complete remission without treatment	10

($P = 0.049$). The association of patients' quality of life with their gender and their type of disease was not statistically significant ($P = 0.095$ and 0.153, respectively).

DISCUSSION

Bullous lesions significantly affect the quality of life; treatment with corticosteroids and immunosuppressive drugs can also affect the quality of life in AIBD patients. Therefore, considering the quality of life and mental health is as crucial as the clinical condition of these patients. In this study, quality of life and disease severity were evaluated in patients with AIBDs, and quality of life was linked with disease severity and age.

In our study, pemphigus vulgaris was the most prevalent AIBD (76%), followed by bullous

Table 2. A summary of the responses to the Autoimmune Bullous Disease Quality of Life (ABQOL) questionnaire

Item	n (%)	Item	n (%)
Burn, sting, or pain in the skin		Never (0)	67 (67%)
All the time (3)	0 (0%)	Depressed or angry because of the disease	
Sometimes (2)	4 (4%)	All the time (3)	2 (2%)
Occasionally (1)	22 (24%)	Sometimes (2)	18 (18%)
Never (0)	74 (74%)	Occasionally (1)	48 (48%)
Itching		Never (0)	32 (32%)
All the time (3)	0 (0%)	Anxious because of the disease	
Sometimes (2)	3 (3%)	All the time (3)	1 (1%)
Occasionally (1)	24 (24%)	Sometimes (2)	14 (14%)
Never (0)	73 (73%)	Occasionally (1)	57 (57%)
The need to change clothes		Never (0)	28 (28%)
All the time (3)	1 (1%)	Worry that friends and family find the condition tiresome	
Sometimes (2)	4 (4%)	All the time (3)	0 (0%)
Occasionally (1)	22 (22%)	Sometimes (2)	3 (3%)
Never (0)	73 (73%)	Occasionally (1)	32 (32%)
Slow healing of the skin		Never (0)	65 (65%)
All the time (3)	0 (0%)	Sexual difficulties with partner	
Sometimes (2)	1 (1%)	All the time (3)	0 (0%)
Occasionally (1)	5 (5%)	Sometimes (2)	0 (0%)
Never (0)	83 (83%)	Occasionally (1)	15 (15%)
Difficulty bathing or showering		Never (0)	85 (85%)
All the time (3)	0 (0%)	Effect of disease on relationship with friends or beloved ones	
Sometimes (2)	0 (0%)	Had to end relationship/cannot have a relationship (3)	0 (0%)
Occasionally (1)	10 (10%)	Relationships are very difficult (2)	2 (2%)
Never (0)	90 (90%)	Relationships are a little difficult (1)	36 (36%)
Painful erosions in the mouth		Relationships are not affected (0)	62 (62%)
All the time (3)	3 (3%)	Effect of disease on social life	
Sometimes (2)	8 (8%)	Cannot socialize (3)	1 (1%)
Occasionally (1)	29 (29%)	Can attend some social events (2)	11 (11%)
Never (0)	60 (60%)	Can attend most social events (1)	38 (38%)
Easy bleeding in gums		Social life is not affected (0)	50 (50%)
All the time (3)	0 (0%)	Effect of disease on work or study	
Sometimes (2)	2 (2%)	Unable to work or study (3)	12 (12%)
Occasionally (1)	18 (18%)	Work or study with difficulty (2)	13 (13%)
Never (0)	80 (80%)	Work or study is harder than before (1)	18 (18%)
Avoid eating favorite food or drink		Work or study are not affected (0)	57 (57%)
All the time (3)	10 (10%)	Unable to find or keep a job	
Sometimes (2)	18 (18%)	Unable to find a job (3)	12 (12%)
Occasionally (1)	37 (37%)	Constantly changing jobs (2)	2 (2%)
Never (0)	35 (35%)	Keeping job with difficulty (1)	16 (16%)
Embarrassed because of the disease		Keeping job without difficulty (0)	70 (70%)
All the time (3)	1 (1%)		
Sometimes (2)	5 (5%)		
Occasionally (1)	27 (27%)		

pemphigoid (18%) and pemphigus foliaceous (6%), which is consistent with previous studies [20,21]. In addition, a median score of 6 was recorded from the responses to the ABQOL questionnaire, which is also consistent with previous studies [22]. Terrab *et al.* conducted a study to evaluate the quality of life among pemphigus patients and compare it with the healthy population [23]. They used the Short Form-36 (SF-36) tool, and the results showed a significant difference between the patients and the healthy group. The pemphigus patients had significantly lower mean scores in all aspects other than "physical pain" and "alteration in the general health status." Facial involvement had the most significant effect on

the patients' physical and emotional states, and the extent of the lesion was highly correlated with the total scores of patients with pemphigus. Also, 70% of pemphigus patients expressed great embarrassment about their appearance, 60% reported anxiety about their disease, 63% reported a significant decrease in self-esteem, and 81% expressed concern about their sexual function. In our study, the feeling of embarrassment was reported by 32%, and sexual problems were reported by 15% of patients; likewise, 72% of the patients expressed their feelings of anxiety. Terrab and colleagues blamed social/cultural factors and the misconception that skin conditions are related to poor hygiene or unconventional sexual activity. In another qualitative study conducted in the Netherlands, researchers demonstrated that the quality of life is affected in patients with bullous disease due to itching, pain, difficulty in participation, lack of understanding of others, and the feeling of being different [24].

The current study showed that the quality of life (according to the ABQOL score) is affected by the severity of the disease (based on ABSIS), where a more severe disease results in a higher ABQOL score and a worse quality of life. This finding is similar to the findings of Paradisi *et al.*, who conducted a study to describe the health status, assess the impact of disease on quality of life, and define a clinical set of quality-of-life assessment tools in a large sample of patients with pemphigus [25]. They reported that quality of life was significantly lower in pemphigus patients and was significantly related to the severity of the disease. Other studies have also resulted in similar outcomes [26]. For instance, a comparable study in the Greek population found that the quality of life was influenced by disease severity [22]. Although the association of ABQOL and ABSIS in that study was considered non-significant by a P-value of 0.64, the DLQI was significantly and strongly associated with the ABSIS ($P = 0.006$). The lack of s significant association in the Patsati *et al.* study could be justified by its small sample size.

Kalinska-Bienias and colleagues conducted a study to measure the quality of life in AIBD patients and validate the ABQOL questionnaire [27]. Although the quality of life was less in women, the association between quality of life and gender was not statistically significant. This finding is close to Paradisi *et al.*'s study [25] and similar to our study's findings. In contrast, Tabolli *et al.*, who used the SF-36 and Skindex-29 questionnaires, reported that women had a worse quality of life than men [28]. Tabolli and colleagues explained that nearly half of the women had positive results in the psychological distress assessment, which points out the higher presence of anxiety and depression among women and justifies the inconsistent results. However, according to the cross-sectional entity of the study, it could not be determined whether the quality of life was the cause or the effect of psychological problems. The Tabolli *et al.* study supports our findings on the impact of age on quality of life, where a higher age results in worse quality of life.

This study demonstrated the association between quality of life and disease severity in AIBD patients, benefiting from an acceptable sample size and study duration. However, further studies with more patients could help achieve more precise results. Also, considering the significant effects of AIBDs and their severity on the patients' quality of life, the effectiveness of different support methods should be assessed in future studies. Moreover, similar studies could be conducted with other major skin diseases since most of them result in major alterations in appearance.

CONCLUSION

We conclude that the quality of life (according to the ABQOL score) is significantly related to the disease severity (based on ABSIS) in AIBD patients. Also, unlike the gender and type of disease, the quality of life is significantly associated with patients' age. Therefore, it is necessary to improve these patients' social, psychological, and financial support, especially for those with more severe diseases.

Authors' contributions

Mohadese. Dalvand. MD student developed the original idea, collected the data, abstracted and analyzed data, wrote the manuscript, and is guarantor. Armaghan Ghareh Aghaji Zare, MD and Afsaneh Radmehr, MD and Sara Saniee, MD contributed to the development of the protocol, abstracted data, and prepared the manuscript.

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