ORIGINAL ARTICLE

Characteristics and quality of life in pemphigus patients

Chiaw Ting Tee, MRCP[1], Choon Sian Lee, AdvMDerm[1], Preamala Gunabalasingam, AdvMDerm[2]

[1]Department of Dermatology, Hospital Melaka, Malaysia, [2]Department of Dermatology, Hospital Tuanku Jaafar, Seremban, Malaysia

ABSTRACT

Introduction: Pemphigus is an autoimmune blistering disease affecting the skin and mucus membranes. It is a debilitating skin condition with painful bullae and erosions, which may limit the patient's daily activities. Therefore, measuring the quality of life (QoL) from the perspective of physical, functional, social, and emotional well-being is important to address the disease burden. This study aims to review the demography and assess the impact of disease on QoL in pemphigus patients at the Department of Dermatology, Hospital Melaka.

Materials and methods: This is a single-centre, cross-sectional study on the characteristics and QoL among the pemphigus patients at the Department of Dermatology, Melaka General Hospital, from August 2020 to July 2021. Patients' information was collected, and each patient was assessed objectively on the disease severity physically using the Pemphigus Disease Area Index (PDAI) scoring system. The disease severity was then assessed subjectively, in which each participant was given three questionnaires to answer, namely the Dermatology Life Quality Index (DLQI), Visual Analogue Scale (VAS) for pain and itch, and Autoimmune Bullous Disease Quality of Life (ABQOL).

Results: There were a total of 30 pemphigus patients (13 males, 17 females), with an average age of 54.0 ± 13.6 years. Our study population had low median PDAI score (2.0 ± 4.0) with low median DLQI (3.0 ± 8.0) and ABQOL (11.0 ± 12.0). The median VAS scores for pain (1.0 ± 2.0) and itch (2.0 ± 3.0) were also low. Patients with tertiary educational qualification reported higher median DLQI (10.0 ± 12.0, $p = 0.016$) and ABQOL (21.0 ± 23.0, $p = 0.026$). Significant correlation was neither observed between PDAI and DLQI scores nor observed between PDAI and ABQOL scores. The DLQI and ABQOL scores were not affected by gender, age, ethnicity, and duration of illness.

Conclusion: Most of the patients in our study cohort had low DLQI and ABQOL scores, with mild clinical severity, as evidenced by low PDAI and VAS scores for both pain and itch. Disease severity had no correlation with QoL in our study. However, educational level showed significant influence on the QoL.

KEYWORDS:
Pemphigus, quality of life, characteristics, demography

INTRODUCTION

The word 'pemphigus' is derived from the Greek word pemphix meaning blister or bubble. Pemphigus is an autoimmune intraepithelial blistering disease affecting the skin and mucous membranes and potentially life threatening. It is mediated by circulating autoantibodies directed against antigens on the keratinocyte cell surfaces, causing loss of adhesion between keratinocytes and subsequently giving rise to blister formation and painful erosions on the skin and mucous membrane. The two major subtypes are pemphigus vulgaris (PV) and pemphigus foliaceous (PF). PV accounts for approximately 70% of pemphigus cases.[1] It is also considered the most severe form of the disease. Other subtypes of the pemphigus group are paraneoplastic pemphigus, drug-induced pemphigus, and Ig A pemphigus.

Pemphigus usually occurs in adults, with an average age of 40–60 years for PV and nonendemic PF. However, it may occur at any age. In some countries of the Middle East and Brazil, disease onset is earlier. A Brazilian study estimated that 17.7% of cases occur before the age of 30 years.[2] The incidence of PV worldwide varies from 0.1 to 0.5 cases per 100,000 population per year. In most countries, PV is more prevalent than PF. For example, PV accounts for 73% of cases of pemphigus in France. In Japan, the ratio of PV to PF is 2:1.[3] The male to female ratio for PV and PF appears to be equivalent or close to equivalent. However, there are studies showing imbalance in the gender distribution. Male to female PF patient ratio is 1:4 in Tunisia and 19:1 in an endemic location in Colombia.[4-5]

Pemphigus can be debilitating, particularly if the affected areas are of high visibility. Bullae and erosions secondary to the rupture of bullae may be painful and therefore limit the patient's daily activities, especially during the active stage. Based on the consensus statement by the International Pemphigus Committee in 2008, complete remission is defined as the absence of new or established lesions for at least 2 months, whereas partial remission is defined as the presence of transient new lesions that heal within 1 week.[6]

This severe debilitating disease has strong negative impact on the patients, both physically and psychosocially. Measuring the quality of life (QoL) is important in assessing the disease burden. The QoL encompasses the physical, functional, social, and emotional well-being of a person.[7] The World Health Organization (WHO) defines QoL as individuals' perception of their position in life in the context of the culture

This article was accepted: 25 April 2022
Corresponding Author: Chiaw Ting Tee
Email: teechiawting@hotmail.com

and value systems in which they live, and in relation to their goals, expectations, standards, and concerns.[8] Contributing factors to QoL include physical discomfort, time spent on treatment, staining of sheets, clothes with skin scales or blood, and the visible nature of skin diseases, which often brings negative reactions from the public, leading to low self-esteem.[9]

Several studies have been done worldwide on QoL in pemphigus patients. A study done in Korea revealed that pemphigus significantly impaired the QoL and significantly correlated with clinical severity.[7] An Egyptian study, as well as a local study at Selayang Hospital, Malaysia, showed that pemphigus decreased the patients' QoL.[10-11] The median PDAI score for Selayang cohort done in 2015 was 4 and median ABQOL score was 20.[11] To date, there are not many studies done on the QoL in pemphigus patients in Malaysia. The aim of this study was to review the demography and assess the impact of disease on QoL in pemphigus patients who were under the follow-up at the Department of Dermatology in Hospital Melaka. We expected to see the correlation of disease severity with the QoL in this study. Patients' satisfaction is crucial in pemphigus disease management. Clinicians evaluate patient clinically, but patients view their own disease in different manner. Better understanding of patients' needs and improving the QoL will lead to better management of the disease.[10]

MATERIALS AND METHODS

This was a cross-sectional study of pemphigus patients conducted at the Department of Dermatology, Melaka General Hospital, in which patients were observed at a single time point during the course of the disease. Universal sampling method was adopted, in which all pemphigus patients attending Dermatology clinic, Melaka General Hospital, from August 2020 to July 2021, were included. Inclusion criteria were patients who were 18 years old and above; who were diagnosed to have pemphigus clinically, confirmed with skin biopsy histopathology and direct immunofluorescence study; who were able to provide written informed consent; who could understand either English language or Bahasa Malaysia. Patients who were deemed mentally incapable of giving consent and patients with other concurrent dermatoses were excluded from this study.

The demographic data and disease profile of the participants were collected. Pemphigus severity was evaluated by two investigators, one dermatologist and one dermatology trainee, using the Pemphigus Disease Area Index (PDAI) score. Both the investigators discussed and decided on the PDAI score during the assessment. This aimed to reduce the inter-rater variability. The PDAI scoring system was developed by the International Pemphigus Committee. It has three components relating to the skin, scalp, and mucous membranes. Skin and mucous membranes were further subdivided into 12 anatomical sites, while scalp to four quadrants. Each site was reviewed, and a score was assigned according to the number of erosions, blisters, or new erythema. The total activity score for PDAI ranges from 0 to 250. The scores of PDAI were classified into mild (0–8), moderate (9–24), and severe (≥25).[12] PDAI had the highest validity and is recommended for use in pemphigus vulgaris.[13] This scoring system is recognised to be more reproducible than the Autoimmune Bullous Skin Disorder Intensity Score (ABSIS).[7]

Each participant was given three questionnaires: the Dermatology Life Quality Index (DLQI), Autoimmune Bullous Disease Quality of Life (ABQOL), Visual Analogue Scale (VAS) for pain and itch. Patients were assessed using different questionnaires to ensure consistency in their responses. We expected the ABQOL to be correlated highly with the DLQI, as reported in a previous study.[14] In the event, if we found the answers provided by the participants in the questionnaires were not consistent, we would reassess the understanding of the language again, as it was one of the inclusion criteria. However, this did not happen. The other reason of using both DLQI and ABQOL is to compare with other studies, as certain studies used DLQI, such as the Korean study, while some used ABQOL, such as the study done in Selayang Hospital.[7,11]

DLQI is a skin-specific QoL assessment tool. The questionnaire in DLQI evaluates patient from different aspects, which include symptoms and feelings, daily activities, leisure, work or school, personal relationships, and treatment. The maximum DLQI score is 30, and the minimum score is 0. ABQOL questionnaire was developed by an Australian group and has been validated.[15] It is a reliable tool in measuring the impact of autoimmune bullous disease on QoL, in terms of pain, itch, clothes changes, healing, showering, pain in the oral cavity, gingival bleeding, food avoidance, embarrassment, depression, anxiety, friend and family, sexual activity, relationship, social life, work or study, and discrimination. The ABQOL score ranges from 0 to 51. For both DLQI and ABQOL, higher score reflects greater impairment in the patient's QoL. We implemented both English version as well as the validated Bahasa Malaysia version of the DLQI and ABQOL in this study.

Visual Analogue Scale (VAS) for pain and itch assessment is a psychometric response scale to measure subjective pain and itch perception. The validated VAS is a 10-cm line with number 0 (no pain or no itch) to number 10 (extremely painful or worst imaginable itch). Patient was asked to indicate his/her perceived pain or itch by marking the score on the scale. Pain and itch were assessed in ABQOL, from the aspects of frequency: never, occasionally, sometimes, or all the time. Meanwhile, VAS assessed the intensity of pain and itch.

DLQI and ABQOL were analysed against variables, such as gender, age group, ethnicity, educational level, pemphigus subtypes, comorbidities, employment, marital status, disease severity (mild if PDAI ≤ 8, moderate or severe if PDAI > 8), disease duration (<6 months or ≥6 months), disease activity (active; partial remission; complete remission), and treatment with corticosteroid only or with adjuvant immunosuppressant. Data were analysed using SPSS statistics software version 23.0. Categorical variables were described using frequencies and percentages. Numerical variables were described using mean ± standard deviation or median ± interquartile range. Correlation between

Table I: Effects of gender, age group, ethnicity, educational level, pemphigus subtypes, disease duration, comorbidities, PDAI, treatment, employment, and marital status on DLQI and ABQOL

	DLQI		ABQOL	
Variables (n)	**Median ± IQR**	**p-value**	**Median ± IQR**	**p-value**
Gender				
Male (13)	3.0 ± 12	0.145	12.0 ± 11	0.257
Female (17)	2.0 ± 8		8.0 ± 14	
Age				
≤55 years old (14)	3.0 ± 8	0.834	13.0 ± 15	0.269
>55 years old (16)	2.0 ± 9		7.0 ± 12	
Ethnicity				
Malay (22)	3.5 ± 9	0.266*	11.5 ± 15	0.410*
Chinese (5)	1.0 ± 6		11.0 ± 9	
Indian (2)	6.0 ± 0		24.5 ± 0	
Portuguese (1)	0.0 ± 0		9.0 ± 0	
Education				
Primary/Secondary (21)	1.0 ± 6	0.016	9.0 ± 10	0.026
Tertiary (9)	10.0 ± 12		21.0 ± 23	
Pemphigus subtypes				
P. vulgaris (20)	1.5 ± 4	0.152*	11.0 ± 10	0.804*
P. foliaceous (9)	8.0 ± 15		16.0 ± 17	
P. erythematosus (1)	7.0 ± 0		8.0 ± 0	
PDAI				
≤8 (26)	2.5 ± 7	0.295	11.0 ± 12	0.691
>8 (4)	7.5 ± 7		11.5 ± 24	
Comorbidities				
With (28)	2.5 ± 8	0.502	11.0 ± 14	0.405
Without (2)	5.5 ± 0		15.5 ± 0	
Treatment				
CS only (3)	3.0 ± 0	0.780	15.0 ± 0	0.835
CS with adjuvant Immunosuppressant (27)	3.0 ± 9		11.0 ± 15	
Employment				
Working (11)	4.0 ± 6	0.778	14.0 ± 12	0.262
Unemployed/Retired (19)	3.0 ± 9		8.0 ± 12	
Disease activity				
Active disease (11)	5.0 ± 7	0.187*	11.0 ± 9	0.449*
Partial remission (15)	2.0 ± 10		15.0 ± 17	
Complete remission (4)	1.0 ± 3		8.0 ± 9	
Disease duration				
<6 months (3)	4.0 ± 0	0.862	7.0 ± 0	0.467
≥6 months (27)	3.0 ± 7		11.0 ± 11	
Marital status				
Single/Divorce/Widow/Widower (7)	3.0 ± 7	0.767	12.0 ± 23	0.712
Married (23)	3.0 ± 9		11.0 ± 11	

p-values generated using Mann–Whitney test, except for * generated using Kruskal–Wallis test
CS = Corticosteroid

categorical and numerical variables was analysed using Mann–Whitney test and Kruskal–Wallis test, while correlation between two numerical variables was analysed using Spearman correlation. Statistical significance was taken at p<0.05

RESULTS

There were a total of 30 pemphigus patients (13 males, 17 females), with an average age of 54.0 ± 13.6 years, presented to the Department of Dermatology, Hospital Melaka, from August 2020 to July 2021. Majority of patients were Malays (22/73.3%), followed by Chinese (5/16.7%), Indians (2/6.7%), and 1 Portuguese. This is consistent with the racial distribution in Melaka, Malaysia. Twenty patients had pemphigus vulgaris (PV), while nine patients had pemphigus foliaceous (PF) and one patient had pemphigus erythematosus. The ratio of PV to PF was almost 2:1. There were 10 pemphigus patients presented with mucocutaneous involvement, 16 with cutaneous involvement only, and 4 with mucosal involvement only. Oral cavity was the commonest site of mucosal involvement.

The mainstay of treatment for pemphigus patients is systemic corticosteroids. All 30 patients in our study received either intravenous hydrocortisone or oral prednisolone. Twenty-seven of them had adjuvant immunosuppressant (Table I). Azathioprine is the commonest steroid sparing immunosuppressant, which was used in pemphigus patients in our study. The demography and clinical characteristics of the study population are summarised in Table II.

Overall, our study population had low PDAI score (2.0 ± 4.0) with low DLQI (3.0 ± 8.0) and ABQOL (11.0 ± 12.0). The VAS scores for pain (1.0 ± 2.0) and itch (2.0 ± 3.0) were also low. We observed significant difference in the DLQI and ABQOL scores among patients with different educational levels. Those patients who have tertiary educational qualification

Table II: Characteristics of the study population, n = 30

Patient characteristics	Mean ± SD or n (%)
Age (years)	54.0 ± 13.6
Gender	
Male	13 (43.3)
Female	17 (56.7)
Ethnicity	
Malay	22 (73.3)
Chinese	5 (16.7)
Indian	2 (6.7)
Portuguese	1 (3.3)
Subtype	
Pemphigus vulgaris	20 (66.7)
Pemphigus foliaceous	9 (30.0)
Pemphigus erythematosus	1 (3.3)
Site of disease involvement	
Cutaneous only	16 (53.3)
Mucocutaneous	10 (33.3)
Mucosal only	4 (13.3)
Mucosal involvement	
Oral/lips	9 (30.0)
Ear, nose, throat	7 (23.3)
Genital	2 (6.7)
Conjunctival	0 (0.0)
Treatment modalities	
Corticosteroid	30 (100.0)
Azathioprine	26 (86.7)
Intravenous immunoglobulin	11 (36.7)
Methotrexate	6 (20.0)
Rituximab	4 (13.3)
Cyclophosphamide	3 (10.0)

Table III: Pemphigus Disease Area Index (PDAI), Dermatology Life Quality Index (DLQI), Visual Analogue Scale (VAS) for pain and itch, and Autoimmune Bullous Disease Quality of Life (ABQOL) scores

Variables	Median ± IQR
PDAI	2.0 ± 4.0
DLQI	3.0 ± 8.0
VAS pain	1.0 ± 2.0
VAS itch	2.0 ± 3.0
ABQOL	11.0 ± 12.0

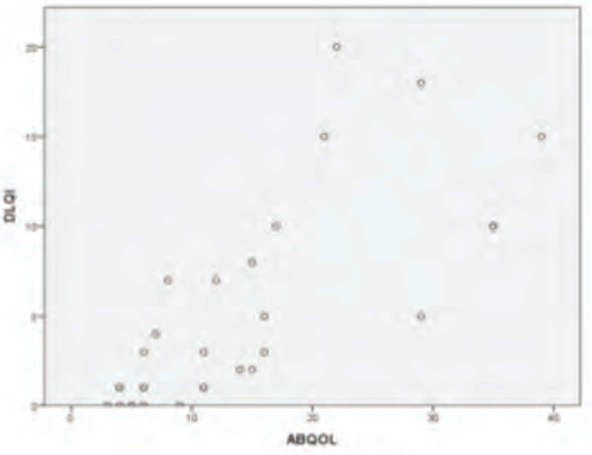

Fig. 1: Correlation between DLQI and ABQOL generated using Spearman correlation.

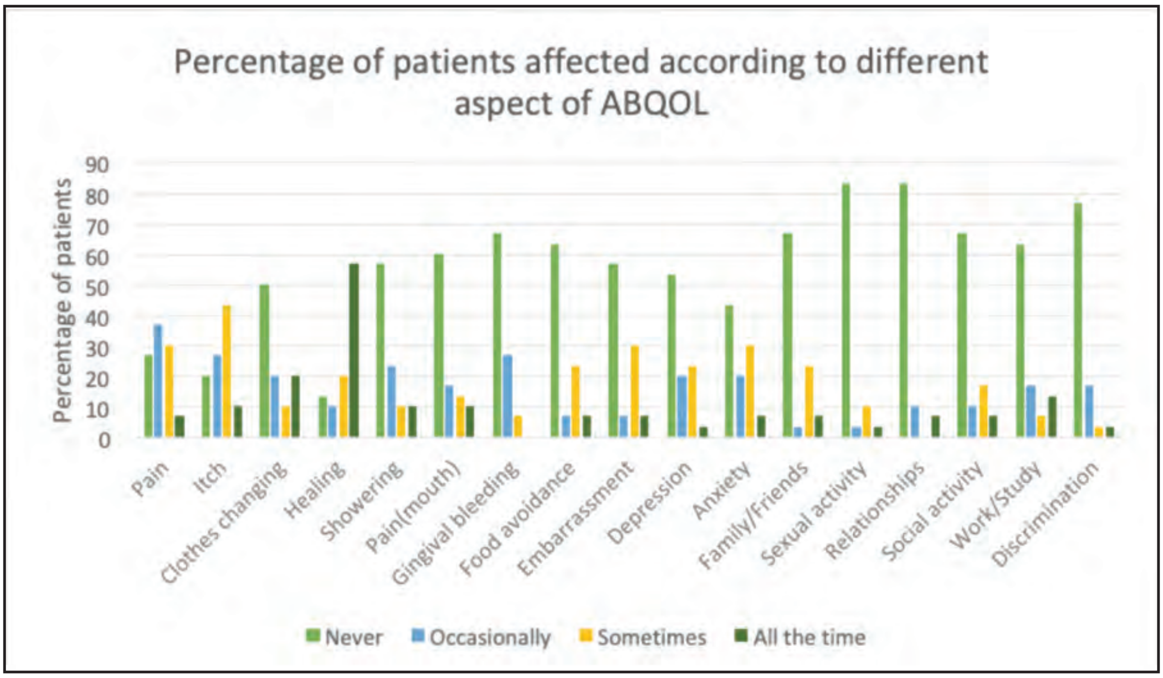

Fig. 2: Percentage of affected patients according to different aspects of ABQOL.

tend to report higher DLQI (10.0 ± 12.0, $p = 0.016$) and ABQOL (21.0 ± 23.0, $p = 0.026$) compared to the group of patients who have either primary or secondary education level (Table I).

There were no significant differences in the DLQI and ABQOL scores among patients with differences in gender, age, ethnicity, pemphigus subtypes, disease severity, disease activity, duration of illness, and marital and employment status. This study revealed that there was no significant difference in QoL between patients with or without comorbidities. In addition, the use of adjuvant immunosuppressive agents did not significantly affect the QoL of pemphigus patient in our study cohort. We noticed that the working group of pemphigus patients reported higher DLQI and ABQOL, compared to the unemployed or retired group. However, this was not statistically significant.

DLQI was found to correlate positively with ABQOL ($r = 0.84$, $p < 0.001$) in our study (Figure 1). There was no correlation observed between disease severity and QoL in our study cohort, as there was neither significant correlation between PDAI and DLQI scores ($r = 0.24$, $p = 0.202$) nor PDAI and ABQOL scores ($r = 0.18$, $p = 0.355$).

Majority of the patients were affected by the symptoms of pain (73.3%) and itch (80.0%), occasionally, sometimes, or all the time. However, the median VAS scores for pain (1.0 ± 2.0) and itch (2.0 ± 3.0) were low (Table III). Fifty percent of patients encountered difficulty in changing clothes and 43.4% in showering. About one-third of patients (36.7%) were unable to enjoy food, 33.3% had gingival bleed, and 40.0% experienced mouth pain. From the psychosocial aspects, 43.0% of the patients felt embarrassed, 46.7% were depressed, and 56.7% were anxious about their condition. One-third of the patients (33.3%) claimed their social life was affected, and 36.7% had difficulty in carrying out their work or study. However, only small number of patients (16.7%) reported relationship and sexual difficulties (Figure 2).

DISCUSSION

In general, most of our study population had mild disease, with low PDAI scores. The results may be different if this was done in the group with more patients of moderate and severe disease. Pemphigus patients often presented with highly active disease for a short period of time, and they were treated with corticosteroid, which is effective and fast-acting, to control the disease. Most of the patients in our cohort had their disease controlled by the time they were enrolled in our study. Twenty-seven patients (90%) had disease duration of 6 months or more during data collection. There were 26 patients (86.7%) presented with PDAI scores of 8 or less. Disease duration of less than 6 months had clinical stages of baseline and flare, where clinical states were expected to be most severe. According to a local study done in Hospital Sultanah Aminah, Johor Bahru, only 5.2% were in severe stages, amongst patients with disease duration of more than 6 months.[14] Therefore, our finding may be different if we collect the data at the peak of the disease activity for each patient. As reported in a Singapore study, oral cavity was the commonest site of mucosal involvement in our study cohort.[16]

There were various studies that reported average DLQI score of 10 in pemphigus patients.[7,17-18] However, our study cohort showed low DLQI scores in general, with the median score of 3. This can be attributed to the mild disease during presentation. ABQOL was found to correlate positively with the DLQI ($r = 0.837$, $p < 0.001$) in our study, which is similar to that reported in a previous study.[14] Overall, our study population had lower ABQOL scores, with median of 11, compared to median ABQOL score of 20 in Selayang study.[11]

Again, this can be attributed to the mild disease severity during the study. Since most of our study population had the disease for 6 months or more, they have better coping and adaptation abilities to their condition following sufficient understanding of the clinical implications of the disease. This may lead to low scores in both DLQI and ABQOL.

A Korean study showed that the DLQI score strongly correlated with the clinical severity of the disease ($r = 0.71$, $p < 0.0001$), while a local study in Malaysia reported moderate correlation between ABQOL and PDAI ($r = 0.47$, $p < 0.001$).[7,14] However, a Polish study found poor correlation between ABQOL and disease severity ($r = 0.38$).[19] Our study showed no correlation between disease severity and both ABQOL and DLQI.

Furthermore, QoL could be affected by other factors such as patient demographic characteristics. This study analysed other factors that may influence the DLQI and ABQOL scores. Interestingly, we found that educational level was one of the factors that had significant effect on the QoL. Patients who had lower educational level tend to report lower score in DLQI as well as ABQOL, and vice versa. This could be accounted by the fact that patients with lower educational level tend to endure, accept, and adapt to the presence of illnesses, while higher levels of educational attainment were associated with better self-assessed health and physical functioning. The higher educated group reported a greater sense of control over their health.[20]

Even though there was no significant difference in DLQI and ABQOL in terms of employment status, we noticed that the working group of patients reported higher DLQI and ABQOL scores. This was consistent with a previous study, which reported that disturbance in work performances negatively affected QoL.[21] An Egyptian study revealed a significant increase in DLQI scores in pemphigus patients who was single compared to married patients.[10] However, in our study, these two groups of patients had almost the same median scores for both DLQI and ABQOL.

In terms of ABQOL, sexual activity (83.3%), interpersonal relationships (83.3%), and discrimination at workplace or school (76.7%) were the three highest aspects with the score of zero reported. This was similar with the study done in Hospital Sultanah Aminah, Johor Bahru, Malaysia. Since sexual issue is not comfortably discussed as well as due to the preservation of public appearance in the local culture, these questions had lower scores.[14]

LIMITATION

This study is limited by its cross-sectional design at a single time point during the course of the disease and small sample size.

CONCLUSION

There were 30 pemphigus patients presented to Melaka General Hospital from August 2020 to July 2021. Most of them had low DLQI and ABQOL scores with mild clinical severity, as evidenced by low PDAI and low VAS scores for both pain and itch. Disease severity had no correlation with QoL in our study. However, the educational level showed significant influence on the QoL.

ACKNOWLEDGEMENT

The authors would like to thank the director of Hospital Melaka for a grant in conducting this research.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

REFERENCES

1. Vanessa Ngan, StaffWriter, 2003. Updated by DermNet NZ Editor-in-Chief, Adjunct Prof. Amanda Oakley, Dermatologist, January 2019. [cited Jan 2022] Available from: https://dermnetnz.org/topics/pemphigus-vulgaris.
2. Celere BS, Vernal S, Brochado MJF, Segura-Munoz SI, Roselino AM. Geographical foci and epidemiological changes of pemphigus vulgaris in four decades in Southeastern Brazil. Int J Dermatol 2017; 56: 1494-6.
3. Adriana Maria Porro, Camila Arai Seque, Maria Carolina Corsi Ferreira, Milvia Maria Simoes e Silva Enokihara. Pemphigus vulgaris. An Bras Dermatol 2019 May-Jun; 94(3): 264-78.
4. Bastuji-Garin S, Souissi R, Blum L, Turki H, Nouira R, Jomaa B, et al. Comparative epidemiology of pemphigus in Tunisia and France: Unusual incidence of pemphigus foliaceus in young Tunisian women. J Invest Dermatol 1995 Feb; 104(2): 302-5.
5. Abreu-Velez AM, Hashimoto T, Bollag WB, Tobon Arroyave S, Abreu-Velez CE, Londono ML, et al. A unique form of endemic pemphigus in northern Colombia. J Am Acad Dermatol 2003; 49(4): 599.
6. Murrell DF, Dick S, Ahmed AR, Sirois D, Zillikens D, Werth VP, et al. Consensus statement on definitions of disease, end points, and therapeutic response for pemphigus. Journal of the American Academy of Dermatology 2008 June; 58(6): 1043-6.
7. Jae Yong Sung, Mi Ryung Roh, Soo-Chan Kim. Quality of life assessment in Korean patients with pemphigus. Ann Dermatol 2015; 27(5): 492-8.
8. WHOQOL: Measuring Quality of Life [cited Jan 2022]. Available from: https://www.who.int/tools/whoqol.
9. Pemphigus and Quality of Life [cited Jan 2022]. Available from: https://plasticsurgerykey.com/pemphigus-and-quality-of-life/.
10. Morsy H, Abdel-Motaleb AA, Soliman AMA. Quality-of-life assessment in pemphigus vulgaris in Upper Egypt using the Dermatology Life Quality Index and SF-36 questionnaires. Egyptian Journal of Dermatology and Venereology 2016; 36: 1-3.
11. Ng HW, Khairul SMA, Ng FY, Rohna R, Yue YC, Ang WS, et al. Quality of Life in Pemphigus Vulgaris patients in Selayang Hospital. E-poster 17 [cited Jan 2022]. Available from: http://www.dermatology.org.my/pdf/eposters%2017.pdf.
12. Shimizu T, Takebayashi T, Sato Y, Niizeki H, Aoyama Y, Kitajima Y, et al. Grading criteria for disease severity by pemphigus disease area index. The Journal of Dermatology 2014; 41: 96973.
13. Rahbar Z, Daneshpazhooh M, Mirshams-Shahshahani M, Nafiseh Esmaili N, Heidari K, Aghazadeh N, et al. Pemphigus disease activity measurements. Pemphigus disease area index, autoimmune bullous skin disorder intensity score, and pemphigus vulgaris activity score. JAMA Dermatol 2014; 150(3): 266-72.
14. Yap EWY, Tey KE, Supramaniam P, Murrell D, Choon SE. Validation of the Malay version of Autoimmune Bullous Disease Quality of Life (ABQOL) questionnaire. Malaysian Journal of Dermatology 2020; 44: 2-8.
15. Sebaratnam DF, Hanna AM, Chee SN, Frew JW, Venugopal SS, Daniel BS, et al. Development of a quality-of-life instrument for

autoimmune bullous disease: The Autoimmune Bullous Disease Quality of Life questionnaire. JAMA Dermatol 2013; 149: 1186-91.

16. Valencia L, Tay YK, Teo R. Pemphigus: A Singapore perspective. Malaysian Journal of Dermatology 2016 Dec; 37: 28-34.
17. Mayrshofer F, Hertl M. Significant decrease in quality of life in patients with pemphigus vulgaris. Results from the German Bullous Skin Disease (BSD) Study Group. J Disch Dermatol Ges 2005; 3: 431-5.
18. Ghodsi SZ, Chams-Davatchi C, Daneshpazhooh M, Valikhani M, Esmaili N. Quality of life and psychological status of patients with pemphigus vulgaris using Dermatology Life Quality Index and General Health Questionnaires. J Dermatol 2012; 39: 141-4.
19. Kalinska-Bienias A, Jakubowska B, Kowalewski C, Murrell DF, Wozniak K. Measuring of quality of life in autoimmune blistering disorders in Poland. Validation of disease-specific Autoimmune Bullous Disease Quality of Life (ABQOL) and the Treatment Autoimmune Bullous Disease Quality of Life (TABQOL) questionnaires. Adv in Medical Sciences 2017; 62: 92-6.
20. Ross CE, Wu CL. The links between education and health. American Sociological Review 1995; 60: 719-45.
21. Heelan K, Hitzig SL, Knowles S, Drucker AM, Mittmann N, Walsh S, et al. Loss of work productivity and quality of life in patients with autoimmune bullous dermatoses. J Cutan Med Surg 2015; 19: 546-54.