RESEARCH PAPER

AUTOIMMUNE BULLOUS DISEASES IN SRI LANKA: EXPLORING PATIENT CHARACTERISTICS, QUALITY OF LIFE, AND SOCIO-DEMOGRAPHIC INFLUENCES AT THE NATIONAL HOSPITAL

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ABSTRACT
The autoimmune bullous diseases (AIBD) are a group of clinical conditions characterized by erosions and bullae of the skin and mucous membranes, which can be prolonging to serious concerns for patients in their activities of daily living (ADL) and adversely affect their quality of life. Descriptive cross - sectional study design was conducted in dermatology clinic at National Hospital Colombo. 121 participants more than 18 years old were included. Non-probability, consecutive sampling technique was used to collect the study sample. Interviewer-administered questionnaire included with dermatological quality of life index was used as study instrument. Most prevalent bullous disorder is pemphigus vulgaris (N=81:66.9%). Extremely larger effect was created on the quality of life of significant majority of the study participants due to the disease condition (N=80 ;66.1%). Highest effect on quality of life after treatments was created on PV patients (t=17.08: p<0.001). Majority of participants represented extensive disease severity scores (N=99:81.8%) at initial presentation. Participants who had significant disease severity at the end of the treatments (N=15:12.4%) showed moderate and large improvement of quality of life. Majority of the study participants had reduced disease severity with treatment (Z>1.96:p<0.001). Majority of the study participants had detected side effects during the first two months following commencement of treatment. 62.8% (N=76) had experienced remission episodes of the disease condition. Age above 50 years (OR=2.75:95%CI=1.26-5.95), Patients with significant initial disease severity (OR=3.82:95%CI=1.39-10.49) and patients who acquire more rapid disease remissions (OR=9.91:95%CI=3.89-25.16) show a significant association with improvement of excellent quality of life. Having oral lesions associated with moderate improvement of Quality of life. 40-60 years age group and female gender are identified as more susceptible factors for AIBD. Among AIBD, highest prevalence is demonstrated by Pemphigus Vulgaris. An extremely larger effect is created on the quality of life of AIBD patients. Quality of life is properly managed by the patients in the higher age group and patients with a higher income. A successful improvement in quality of life is achieved by the patients who initially present with a higher severity and patients who experience early remission. It is clearly demonstrated that it is possible to improve dermatological quality of life by managing the disease condition rationally and methodically. This knowledge should be used to conduct modifications in the health system in order to improve compliance of patients treated for AIBD.

Key words: Dermatology, Bullous, Quality of life

INTRODUCTION

Autoimmune bullous diseases (AIBD) encompass a group of rare yet debilitating conditions characterized by skin and mucous membrane blistering, resulting from the production of autoantibodies targeting critical components of the skin's structural framework. These conditions can be categorized into two main groups based on where the blistering occurs: intraepidermal and subepidermal bullous diseases. Prominent classifications of AIBD include pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid, linear immunoglobulin A dermatosis, dermatitis herpetiformis, and epidermolysis bullosa acquisita. The clinical manifestations of AIBD are diverse and largely dependent on the specific autoantibodies involved. Timely diagnosis and prompt referral for treatment are pivotal to mitigate complications and enhance patient outcomes.

Notably, AIBD, though rare, is a global concern, with cases reported worldwide and varying regional prevalence. Unfortunately, comprehensive data regarding the disease burden of AIBD in many countries remain limited. However, a few studies have reported annual incidence rates of AIBD, with rates as high as 20.4 per million in some regions. Recent studies have indicated an increasing incidence of AIBD in certain areas, emphasizing the need for a better understanding of these conditions.

The impact of AIBD extends beyond the physical realm and significantly affects the quality of life (QoL) of those afflicted. AIBD patients often grapple with negative emotional domains, medication dependence, fatigue, and pain, all of which impede their QoL. These dermatological conditions can lead to disfigurement, particularly visible skin lesions, severely impacting self-confidence and social interactions, further limiting QoL.

The most common symptoms of AIBD, such as pain, itching, disfigurement, and side effects from treatment, further contribute to the disease burden. Regrettably, there is a dearth of research exploring and measuring QoL in AIBD patients, and the psychological effects often remain invisible to clinicians unless specifically sought out.

METHODS

A descriptive cross-sectional design was employed at the National Hospital in Colombo, Sri Lanka. Data collection took place between March 1, 2018, and September 25, 2020, with specific data gathering conducted from July 21, 2020, to September 30, 2020. The study population consisted of adult AIBD patients, be over 18 years of age, diagnosed within the past three years. Exclusion criteria encompassed patients with communication difficulties, including deaf, blind, or mentally retarded individuals, and those unable to respond due to acute illness or disability.

Interviewer-administered questionnaire collected socio-demographic data, disease details, and a Dermatology Life Quality Index (DLQI) questionnaire for the assessment of quality of life. Severity scoring indexes, such as the Autoimmune Bullous Skin Disorder Intensity Score (ABSIS), were calculated to assess inter-individual changes in disease severity. Quality of life was assessed using the DLQI questionnaire, with grades indicating the extent of the impact on quality of life.

RESULTS

Age of the study participants ranged from 22years to 80 years (mean=51.79; SD=12.15). Majority of the study participants represented the 41-50 years age group (N=47; 38.8%). Majority of the study participants were females. Significant majority of the study participants possessed a Sinhala Buddhist cultural background. Majority of them were married study participants. There were three types of bullous disorders detected among study participants. Most prevalent bullous disorder is pemphigus vulgaris(n=81:66.9). Other two disorders were reported in same percentage.

Table 1: Distribution of quality-of-life statements

	Very Much	A lot	A little	Not at all
	Before & after treatment			
Over the last week, how itchy, sore, painful or stinging has your skin been?	113(93.4) 8(6.6)	1(0.8) 30(24.8)	7(5.8) 3(2.5)	- 80(66.1)
Over the last week, how embarrassed or self-conscious have you been because of your skin?	113(93.4) 17(14.0)	1(0.8) 26(21.5)	7(5.8) 32(26.4)	- 46(38.1)
Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden?	112(92.6) 17(14.0)	2(1.7) 23(19.0)	7(5.8) 28(23.1)	- 53(43.8)
Over the last week, how much has your skin influenced the clothes you wear?	112(92.6) 16(13.2)	2(1.7) 33(27.3)	7(5.8) 29(24.0)	- 43(35.5)
Over the last week, how much has your skin affected any social or leisure activities?	111(91.7) 16(13.2)	5(4.1) 33(27.3)	5(4.1) 28(23.1)	- 44(36.4)
Over the last week, how much has your skin made it difficult for you to do any sport?	7(5.8) -	1(0.8) -	- 6(5.0)	113(93.4) 115(95.0)
Over the last week, has your skin prevented you from working or studying?	105(86.8) 16(13.2)	3(2.5) 35(28.9)	5(4.1) 16(13.2)	8(6.6) 54(44.6)
Over the last week, how much has your skin created problems with your partner or any of your close friends or relatives?	108(89.3) 10(8.3)	6(5.0) 31(25.6)	7(5.8) 43(35.5)	- 37(30.6)
Over the last week, how much has your skin caused any sexual difficulties?	108(89.3) 10(8.3)	6(5.0) 30(24.8)	7(5.8) 38(31.4)	- 43(35.5)
Over the last week, how much of a problem has the treatment for your skin been, for example by making your home messy, or by taking up time?	- -	- -	71(58.7) 29(24.0)	50(41.3) 92(76.0)

It was observed that, at the beginning of the disease, patients commonly experienced painful, itchy, and sore sensations, but the majority of them were able to recover from these symptoms over time. Additionally, improvements in self-consciousness and reduced embarrassment were noted among the patients. Barriers faced in social situations due to the disease gradually diminished, and challenges related to clothing and sports activities were minimized with time. An overall improvement in the mental well-being of the participants following treatment procedures was observed. However, the study also identified some impact on the quality of life due to the treatment procedures. Nevertheless, an improvement in the quality of life was commonly observed among the study participants in all aspects. (Table 1).

Table 2: Distribution of quality of life among participants.

	Before		After	
	Frequency	**Percentage**	**Frequency**	**Percentage**
Extremely large effect on patient's life	109	90.1	13	10.7
Very large effect on patient's life	5	4.1	28	23.1
Moderate effect on patient's life	7	5.8	80	66.1
Total	**121**	**100.0**	**121**	**100.0**

It was observed that, before commencing treatment an extremely larger effect was created on the quality of life of significant majority of the study participants due to the disease condition (N=80 ;66.1%) (Table 2)

Table 3: Distribution of Quality-of-life improvement among participants

	Frequency(N)	**Percentage (%)**
Large improvement	46	38.0
Moderate improvement	44	36.4
Low/No improvement	31	25.6
Total	**121**	**100.0**

When the improvement of quality of life among study participants was considered, study findings demonstrate a larger improvement among majority of the study participants. But 6.6% (n=8) of participants did not experience any improvement in their quality of life. However, significant majority of the study participants had experienced some improvement in their quality-of-life following treatment (Table 3).

Table 4: Distribution of disease severity among study participants

	Frequency(N)	Percentage (%)	Frequency(N)	Percentage (%)
	Before		**After**	
No/Moderate	7	5.8	88	72.7
Severe	15	12.4	18	14.9
Extensive	99	81.8	15	12.4
Total	**121**	**100.0**	**121**	**100.0**

Increased body weight was also noted as a considerable side effect. Most common co-morbidity identified among study participants was Diabetes Mellitus. Majority of the study participants did not show any co-morbidities (Table 5).

Table 5: Distribution of side effects and treatment modalities among study participants

	Frequency (N)	Percentage (%)
Side effects		
DM worsening	24	19.8
Weight gain	22	18.2
Secondary infection	7	5.8
DM	19	15.7
Cytopenia with cyclophosphamide.	8	6.6
GORD	24	19.8
Sepsis	1	0.8
Osteopenia/osteoporosis	8	6.6
No side effects	16	13.2
Treatment modalities among study participants		
DCP Pulse Monthly	78	64.4
DP Monthly	54	44.6
Oral Prednisolone	110	90.9
Interval Pulse	84	69.4
Oral Cyclophosphamide	79	65.2
Oral MMF	46	38.1
Plasma paresis	6	4.9
Rituximab	2	1.6
IVIG	7	5.7
Oral Azathioprine	10	8.2
Oral doxycycline	12	9.9
Interstitial steroid	5	4.1
Osteoporosis prophylaxis	112	92.6

ABSIS scores ranged from 13.5 to 117. Majority of the participants represented extensive severity scores before treatment but significant improvement of ABSIS score was noted with treatment. (Table 4) When side effects of medical treatment were considered, worsening of Diabetes Mellitus and experiencing GORD were identified as major side effects.

When treatment modalities relevant to study participants were considered, majority of the participants were treated with oral Prednisolone. Dexamethasone pulse monthly, Interval pulse and oral Cyclophosphamide were other common treatment strategies. Osteoporosis prophylaxis was applied for preventing adverse event following treatment.

When diagnosing the disease condition, study participants were included into a range from 18 years to 80 years (Mean=50.76 years: SD=12.63 Years). Highest number of diagnosed study participants were included into the 40 – 60 years age group. Most commonly used diagnosis methods were skin biopsy and DIF method. Majority of the study participants had detected side effects during the first two months following commencement of treatment. Number of study participants who did not experience any side effect during the treatment period was 14.04% (n=17). Among the study participants 62.8% (N=76) had experienced remission episodes of the disease condition. Majority of them had experienced remission episodes in a period of 4-5 months.(Table 5).

Table 6: Socio demographic associated factors for good adherence to treatment

	Excellent Adherence	Poor Adherence	OR	95%CI
Age				
>50 years	45	10	1.44	0.59-3.45
<50 years	50	16		
Gender				
Male	39	16	0.43	0.18-1.06
Female	56	10		
Income				
<Rs.50,000.00	71	22	0.54	0.17-1.72
>Rs.50,000.00	24	4		
Employment				
Employee	48	11	1.39	0.58-3.34
Unemployed	47	15		
Education				
Up to O/L	55	20	0.41	0.15-1.12
A/L & Above	40	6		

When factors related to the treatment adherence are considered, it was observed that a contributary effect could be generated towards excellent treatment adherence with age above 50 years, female gender, obtaining a

relatively higher income, having and occupation and possessing a higher educational level. However, adequate statistical evidence to conclude these contributary effects as significant associations is not generated through the study participants (Table 6).

Table 7: Associated factors for Quality of Life improvement.

	Large and Moderate Improvement	Less and No Improvement	OR	95%CI
Age				
>50 years	41	14	2.75	1.26-5.95
<50 years	34	32		
Gender				
Male	30	25	0.56	0.26-1.18
Female	45	21		
Income				
< Rs. 50,000.00	53	40	0.36	0.13-0.97
>Rs. 50,000.00	22	6		
Employment				
Employee	38	21	1.22	0.58-2.52
Unemployed	37	25		
Education				
Up to O/L	47	28	1.07	0.57-2.29
A/L & Above	28	18		
Associated Comorbidities				
Yes	30	13	1.69	0.76-3.73
No	45	33		
Initial Disease Severity				
Significant	68	33	3.82	1.39-10.49
Moderate	7	13		
Adherence to treatment				
Excellent	62	33	1.87	0.78-4.51
Poor Adherence	13	13		
Remission				
Within 6 months	48	7	9.91	3.89-25.16
After 6 months	27	39		
Oral Lesions Before				
Yes	30	58	0.55	0.24-1.24
No	16	17		
Oral Lesions After				
Yes	24	-	4.41	3.05-6.36
No	22	75		
Total	**75**	**46**		

When improvement of quality of life among participants is considered, socio-demographic factors such as age above 50 years and obtaining a relatively higher income show a significant association with improvement of excellent quality of life.

When the disease condition is considered, study findings demonstrate that significant quality of life improvements are achieved by patients with significant disease severity before commencing treatment and patients who acquire more rapid disease remissions.

Although patients who excellently adhere to treatment methods indicate a contribution towards improvement of quality of life, it is not elicited as a significant association. Participants who had significant disease severity at the end of the treatments showed moderate and large improvement of quality of life. Having oral lesions associated with moderate improvement of Quality of life. (Table7)

DISCUSSION

The study's findings highlight significant differences in the prevalence of Autoimmune Bullous Diseases (AIBD) and associated conditions among patients in Sri Lanka when compared to global data. The research included AIBD patients ranging from 18 to 80 years of age, with a concentration in the 40-60 years age group. Certain factors, like unemployment among females, were associated with a higher likelihood of AIBD diagnosis.

While adherence to treatment methods was reasonably high, a majority of participants experienced medication-related side effects, with worsening diabetes mellitus being the most common. This was primarily due to the frequent use of corticosteroids, which elevate blood sugar levels. Many patients presented with higher disease severity at diagnosis, significantly impacting their quality of life, likely due to the stress induced by these factors. Notably, the study revealed a higher propensity for AIBD among middle-aged and older patients, who are already at a higher risk for developing diabetes. This underscores the importance of comprehensive health education, focusing on both diabetes management and gastroesophageal reflux disease (GORD) prevention.

The study also identified several factors associated with treatment adherence, such as gender, age, employment status, income level, and education level. Special attention is warranted for patients with these challenging adherence factors.

Patients with comorbidities, higher initial disease severity, and early remissions experienced substantial improvements in their quality of life through treatment, indicating effective patient management strategies. Healthcare stakeholders should prioritize the continued enhancement of these successful approaches.

According to the study findings, highest prevalence is noted with PV. But, according to Bernard et al, highest prevalence was identified with BP [38]. According to Alpsoy et al, in European countries, both PV and BP persist for a longer period with recurrence.

According to the present study findings, mean age of ABD is 51.79 years and majority of the study participants represent the 41-60 years age group. Observation of recurrence among majority of the study participants was not noted during the study. On the other hand, due to receiving treatment and different geographical location of present study participants, there are challenges of comparing with the studies done by Phillippe and Alpsoy [39].

Mariana et al, who analysed dermatological quality of life among university hospital patients in Brazil demonstrated that, their daily activities, recreational activities, work related activities and family relationships are significantly affected due to AIBD. Studies done by Sebartnem et al in 2012[40], Finlay et al in 1994, Nijsten et al in 2006 and the present study findings demonstrate that quality of life is considerably affected by AIBD. Also, above mentioned studies reveal that effects created on quality of life do not differ according to the type of AIBD. Present study findings also confirm this situation and present study findings further demonstrate that improvement of DQLI with treatment methods is higher in PV and relatively less in PF. Lewis et al demonstrates that work related quality of life is reduced among patients with higher disease severity and patients with low treatment adherence [41]. But, according to the studies done by Chee and Mural in 2011[42] and Reilly et al in 2004[43], improvement in dermatological associated quality of life is less with higher disease severity. But they have not compared their findings with treatment duration as an association.

But in current study same patients were reviewed twice with regard to severity of bullous disease and DQLI at initial status and present level. According to the present study findings, patients with increased age, patients with higher disease severity before commencing treatment and patients who experience early remissions achieve proper management of their disease condition. It is possible to expect that sociocultural differences study populations and differences of study settings could have affected these gathered study findings.

The research was conducted in a single setting in Sri Lanka's main city, making it easier to recruit the required sample due to high patient numbers. However, the sample's homogeneity and the use of consecutive sampling introduced potential sample bias, challenging the applicability of findings to other settings. To enhance external validity in future studies, planning larger sample sizes, diverse participant selection from different settings, and utilizing randomized sampling techniques are emphasized, although financial and time constraints in postgraduate research make this challenging. The study tool used to measure quality of life lacked specific validation for Sri Lanka, affecting the internal validity of the findings, especially considering the sociocultural variations in the concept of quality of life. Additionally, information bias was expected due to recall issues when collecting past data relevant to the quality of life questionnaire, highlighting a limitation in the study's internal validity

In conclusion, this study identifies the 40-60 years age group and female

gender as more susceptible factors for Autoimmune Bullous Diseases (AIBD), with Pemphigus Vulgaris being the most prevalent form. AIBD significantly impacts the quality of life of patients, particularly those in the higher age group and with a higher income. Successful quality of life improvement is seen in patients with higher initial severity and those experiencing early remissions. The study underscores the importance of a rational and methodical approach to disease management to enhance dermatological quality of life. The findings also highlight the need to address challenges and capitalize on strengths in patient management to improve AIBD treatment compliance. Multisectoral treatment approaches should be planned to mitigate side-effects, further emphasizing the significance of comprehensive and coordinated care for AIBD patients.

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