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Original Research Article

Quality of Life in Patients with Autoimmune Bullous Disease (AIBD)

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Abstract

Background: Background: AIBD is a chronic dermatological condition of autoimmune origin, affecting skin and mucous membrane. Systemic corticosteroids are mainstay of treatment. Use of newer biologic Rituximab has been introduced in the last decade. Comprehensive studies reporting quality of life, factors affecting it are few in India.

Methods and Materials: Prospective observational study in paitents with AIBD, followed up at 1 and 3 months. Data on demographics, disease characteristics, treatment, and treatment costs were collected. QOL was assessed and data were summarized using descriptive statistics and compared using chi-squared and t-tests.

Results: Of the 47 patients recruited, 66% were females, mean age (SD) of participants being 46.6 (±11.1) years. Median (IQR) duration of AIBD was 0.83 (0.46-1.50) years. The baseline DLQI was 10 with 44.7% patients having a poor QoL (DLQI ≥11). The mean change in DLQI over 3 months was 8.67 (±2.83), which was statistically significant. Significant predictors of poor QoL was adjuvant treatment [OR 55.00, 95% C.I. (4.30-703.43) p=0.002].

Conclusion: Patients had moderate severity of disease and poor QoL at baseline. They received rational treatment and there was an improvement in the DLQI score. There was a high economic burden due to hospital and drug costs. We recommend that health insurance coverage should be increased to help these patients.

Keywords: AIBD; Autoimmune bullous disease/ Pemphigus/ Bullous pemphigoid/drug therapy; Administration, Corticosteroids, Rituximab, Quality of life, Health Care Costs, Drug Costs, Quality of Life.

INTRODUCTION

Autoimmune blistering diseases are group of conditions characterized by blisters in the skin with or without mucosal involvement. The prevalence of AIBD varies worldwide, mostly seen in Ashkenazi Jews, Southeast Asians and elderly. Based on site of bullae formation, they are grouped as 'Pemphigus' group where intraepidermal blisters are seen and 'Pemphigoid' group which have sub epidermal bullae. Pathophysiology involves auto antibodies that target components of the epidermis or dermoepidermal junction (DEJ). Blisters are formed due to inflammatory cascade that follows antigen-antibody reaction.[1]

The symptom of fluid filled blisters, itching, burning sensation and pain vary from one person to another. The severity of the disease depends on the site of blistering and presence of a secondary infection. AIBD runs a chronic course, but can be controlled with regular/ proper treatment and monitoring. Mainstay of treatment are corticosteroids, Azathioprine, Mycophenolate mofetil are a second-line treatment. [2-3] Other treatment options are Rituximab (anti-CD20 monoclonal antibody) intravenous immunoglobulins, immunoadsorption, Cyclophosphamide, Dapsone or Methotrexate. Both Corticosteroids and Rituximab have shown considerable disease control. [4] Most patients with a dermatological condition suffer from social stigma because of the physical appearance, and AIBD is no exception. The disfiguring nature, of the disease negatively affect self-confidence and limit social capacity. AIBD impacts all of life-personal life, mental health, professional performance, financial burden, and disruption in social activity, leading overall decrease in quality of life.

MATERIAL AND METHODS

The study was done by the Department of Pharmacology in collaboration with the Department of Dermatology at St John's Medical College Hospital, Bangalore. The patients in our study belonged to varied socioeconomic strata and came from different geographical regions. The present study was conducted among the outpatients and inpatients with AIBD, coming to the Department of Dermatology. Institutional Ethics Committee (IEC) approval was obtained for the conduct of the study [IEC Study Ref No: 967 / 2018]. We conducted the study for 21 months. Patients were recruited from January 2019 to June 2020. There were 2 follow ups at 1 month and 3 months from the time of recruitment. One of the primary objectives of our study was to evaluate the quality of life using DLQI. A study conducted by Patsatsi A et al (2017) had the median DLQI score of 7.0(2.0-28.0) at baseline, 5.0(0.0-18.0) at 4 weeks and 9.0(0.0-22.0) after 12 weeks[5]. Using this DLQI score, we obtained a minimum sample size of 36. Taking into account a dropout rate of 30% the final sample size to be taken was 47 patients. The secondary objective of our study was to assess clinical outcomes (remission/relapse). All registered patients with Dermatologist confirmed diagnosis of AIBD, Age >18 years, both males and females were included in the study. Patients in whom the three month follow up is not possible or Patients with severe cognitive impairment were excluded from the study.

The informed consent form (ICF) was designed to obtain voluntary, informed consent from all the patients participating in the study. The Case Record Form (CRF) was designed to capture demographic characteristics, treatment data, quality of life and costs of treatment. Recruitment began from January 2019. After which the patients were followed up at 1 month and 3 months via telephonic conversation. During the designated follow-ups at 1 month and 3 months, data on change in QOL, hospitalizations, relapses, remission, change in treatment were recorded. We summarized the baseline and demographic data of patients using descriptive statistics. Continuous variables were summarized using mean (±SD) or median with Interquartile range (IQR). All continuous variables were checked for normality. Parametric data were analysed using Independent sample t-test and non-parametric data were analyzed using Mann Whitney U test. Categorical variables were analyzed using Chi-squared tests. Change in QoL, was analysed using repeated measures Wilcoxon tests. Univariate and multivariate logistic regression statistics were employed to determine the factors affecting patients' poor QoL. In analyses, a p value of <0.05 was considered significant for all tests. All data were entered into the EpiInfo software (version

7), and statistical analyses were performed using commercially available software (SPSS version 20).

RESULTS

A total of 47 patients with AIBD were recruited. Of the 47 patients, 45 (96%) completed the first follow up and 42 (89%) completed the 2nd follow up. Five (10%) patients were considered lost to follow up by the end of the study.Among the study population had 31 (66%) were females and 16 (34%) were males with a male to female ratio of 1:5. The mean age of the patients was 46.6 (SD 11.1). The patients' demographic characteristics and distribution by percentage are given in Table no. 1

Table 1: Demographic profile at baseline

Variables		**Total Sample (N=47) N(%)**
Age (mean± SD)		46.6± 11.1
Gender	Female	31 (66.0%)
	Male	16 (34.0%)
Domicile	Rural	19 (40.4%)
	Urban	28 (59.6%)
Marital Status	Married	40 (85.1%)
	Unmarried	7 (14.9%)
Median monthly family income (in Indian rupees)		12000.00 (7500.00-30000.00)
Non vegetarian diet		42 (89.4%)
Substance abuse	Smoking	10 (21.3%)
	Alcohol	11 (23.4%)
	Tobacco chewing	8 (17.0%)
Education	Illiterate	17 (36.2%)
	Primary/middle/high school	22 (46.8%)
	Diploma/graduate/professional	8 (17.0%)
Occupation	Unemployed	16 (34.0%)
	Elementary/ Agriculture/ Fisheries	15 (31.9%)
	Sales-workers/ Clerks/ Technicians	11 (23.4%)
	Professionals/ Managers	5 (10.6%)
No: of Family members (mean± SD)		4.7± 1.4

The median duration of AIBD was 0.83 years (IQR 0.46-1.50) and the mean age at diagnosis of AIBD was 45 (SD 11.9) years. In 5 (10.6%) patients, the duration of disease was more than 5 years. 22 (46.8%) patients had at least one co-morbidity, diabetes mellitus being the most frequent at 27.7%, followed by hypertension 25.5%, coronary artery disease, asthma and thyroid disorders 4.3% each and vitamin B12 deficiency and chronic fungal infection (tinea) seen in 2.1 % patients respectively .

The commonest type of AIBD among the patients was Pemphigus vulgaris at 87.2%. Bullous pemphigoid was present in 8.5% patients, IgA bullous disease and Pemphigus follicaeous in 2.1% each. Multiple areas were involved in most patients. Oral Mucosa affected in 74.5% patients, chest/ breast in 53.2% patients, abdomen and back 42.6%, followed by Lower Limb (Flexor aspect) in 38.3% and Upper Limb (Flexor aspect) in 36.2% patients. Scalp was affected in 34% patients, Head & Neck in 21.3% patients and Genitals in 10.6% patients. 65.9% patients presented at the hospital with complaints of blisters, 8.5% with itching. 25.5% patients came for routine therapy.

Severity of the disease was measured using the ABSIS (Autoimmune bullous skin disorder intensity score) and OMS (oral

mucosal score). 23.3% patients had severe AIBD at baseline. 25 (53.2%) of the patients were reported to have an aggravation of the condition. The median ABSIS score of the study population was 2.50 (IQR 1.50-8.50). The median OMS score of the study population was 3.00 (IQR 3.00-5.00). Both score indicate moderate severity of disease.

The quality of life of patients with AIBD was assessed using the DLQI score, with the study population showing a mean score of 10.64 (SD 3.24). 44.7% patients had a DLQI score of more than 11 at baseline indicating a poor quality of life. Details of the clinical characteristics of the population are given in Table no. 2

Table 2: Baseline clinical characteristics of the study subjects

Variables		**Total Sample (N=47) N(%)**
Age at diagnosis (years) (mean± SD)		45.03 ± 11.92
Duration of AIBD (years)	Median, IQR	0.83 (0.46-1.50)
	>5 years	42 (89.4%)
	< 5 years	5 (10.6%)
Duration of treatment of AIBD (years) (median, IQR)		0.50 (0.29-0.83)
Hospital site	In-patient	40 (85.1%)
	Out-patient	7 (14.9%)
Mean no. of days of admission (mean ± SD)		3.7± 0.84
Co-morbidities	Total	22 (46.8%)
	Diabetes Mellitus	13 (27.7%)
	Hypertension	12 (25.5%)
	Coronary Artery Disease	2 (4.3%)
	Thyroid disorders	3 (6.4%)
	Asthma	2 (4.3%)
	Neurological disorder	11 (2.1%)
	Chronic nutritional deficiency	1(2.1%)
	Fungal infection	1(2.1%)
Type of AIBD	Pemphigus Vulgaris	41 (87.2%)
	Bullous Pemphigoid	4 (8.5%)
	Pemphigus Folliacious	1 (2.1%)
	IgA disease	1 (2.1%)
Areas affected	Lower limbs	26 (55.3%)
	Upper limbs	29 (61.7%)
	Chest/ breasts	25 (53.19%)
	Scalp	16 (34.04%)
	Genitals	5 (1.06%)
	Oral mucosa	34 (72.34%)
	Abdomen &back	20 (42.5%)
Presenting complaints	Blisters	31 (65.95%)
	Itching	4 (8.51%)
	Routine pulse/ rituximab therapy	12(25.53%)
OMS score	Median (IQR)	3.00 (3.00-5.00)
ABSIS score	Median (IQR)	2.50 (1.50-8.50)
DLQI score at baseline	Mean	10.63+/- 3.2
	<11	24 (51.06%)
	≥11	23 (48.93%)

DLQI is a self-explanatory, validated questionnaire which is used to assess the quality of life of patients with dermatological diseases. The questionnaire contains 10 questions with a final score ranging from 0 to 30. A score > 11 is taken as an indication of poor quality of life. At baseline, the median DLQI score was 10 (IQR 8-13), with 21 (44.7%) patients having a poor quality of life (DLQI ≥ 11). Among the 45 patients who completed first follow up, the median DLQI score was 10 (IQR 8 -12) with 12 (26.7%) patients having a poor quality of life. Out of the 42 patients who completed second follow up, the median DLQI score was 8 (IQR 7 -11) with 10 (23.8%) patients having a poor quality of life.(Figure 1)

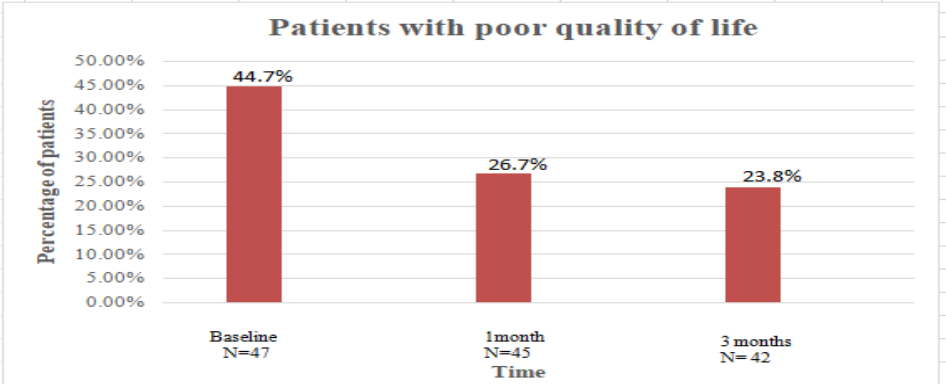

Figure 1: Proportion of patients having a poor quality of life (DLQI ≥11)

There was no change in DLQI score at first follow up. At 2nd follow up there was a difference of -2 (IQR -1, -2) in the median DLQI score from baseline. A repeated measures analysis with Wilcoxon test found this change in DLQI scores to be statistically significant. The median DLQI scores are given in Table no.8 and the statistical test details in Table no. 3.

Table 3: Analysis of change in DLQI scores from baseline, at 1 month and 3 month follow up- Wilcoxon Test

Time point	DLQI			Wilcoxon Test	
	Mean (SD)	Median (IQR)	Range	V-value	P-value
1 Month	9.69 (2.72)	10.00 (4.00)	5.00 - 15.00	231.0	0.004
3 Months	8.67 (2.83)	8.00 (4.00)	0.00 - 13.00		
Absolute Change	-1.05 (2.37)	0.00 (2.75)	-10.00 - 3.00		

40 (85.1%) patients reported having anxiety of having treatment ADRs. The mean no. of physicians seen in the past 2 years by patients was 1.68 (SD 0.91). 87.2% Patients had a regular follow up of at least one visit in a month. 37 (78.7%) patients visited the hospital with attendants or relatives, of which 21 (56.8%) were employed, which added to the economic and social burden of the disease. 13 (41.9%) patients complained of missing work due to AIBD with mean no. of work days lost being 13.15 (SD 10.8) days. 7 (14.9%) patients continued work irrespective of severe disease. (Table no. 4)

Table 4: Parameters affecting Quality of Life of patients with AIBD (a measure of Intangible costs)

Variables		Total Sample (N=47) N(%)
Fear of ADRs		40 (85.1%)
No. of physicians seen in past 2 years (median, IQR)		1 (1 -2)
Regular follow-up		87.2%
Bystanders	Presence of bystanders	37 (78.7%)
	Employed	21 (56.8%)
	Unemployed	16 (43.2%)
Patients who missed work due to AIBD		13 (41.9%)
Average no. of missed days of work (mean ± SD)		13.15 ±10.8
Patients who worked in spite of severe disease		7 (14.9%)

The study population was categorized into those with good quality of life [DLQI<11, n=26 (55.3%)] and those with poor quality of life [DLQI≥11, n= 21 (44.7%)]. Demographic variables were compared between these two groups using chi-squared tests and t-tests to determine the factors affecting quality of life. Duration of disease in years, baseline ABSIS Score, baseline OMS Score, duration of continuous treatment in years, use of adjuvant treatment, presence of tiredness, DLQI at baseline and disease status were found to influence quality of life negatively and were statistically significant (p value <0.05). (Table 5)

Table 5: Comparison of demographic, clinical and treatment factors affecting Quality of life at baseline

Factors		Good QoL DLQI<11 n = 26)	Poor QoL DLQI≥11 (n = 21)	p value
Age		45.42 ± 8.98	48.10 ± 13.38	0.44
Age at diagnosis		43.02 ± 9.11	47.52 ± 14.54	0.139
Gender	Female	17 (54.8%)	14 (45.2%)	0.927
Domicile	Urban	17 (60.7%)	11 (39.3%)	0.366
No of family members	Mean ± SD	4.81 ± 1.23	4.67 ± 1.62	0.744
Hospital site	In-patient	24 (60.0%)	16 (40.0%)	0.217
Higher Socio-economic status		19 (54.3%)	16 (45.7%)	0.647
Monthly family income (mean, SD)		27000.00 ± 24519.38	18476.19 ± 15085.16	0.452
Duration of AIBD (mean, SD)		2.71 ± 3.40	0.80 ± 0.88	0.004
ABSIS Score		3.58 ± 3.61	6.92 ± 5.25	0.028
OMS Score		3.06 ± 1.98	5.50 ± 2.71	0.028
Pemphigus Vulgaris		25 (61.0%)	16 (39.0%)	0.150
Areas affected	Oral Mucosa	21 (60.0%)	14 (40.0%)	0.270
	Upper Limb Flexor	9 (52.9%)	8 (47.1%)	0.805
	Lower Limb Flexor	8 (44.4%)	10 (55.6%)	0.237
Polypharmacy (>6 drugs)		25 (56.8%)	19 (43.2%)	0.579
Adjuvant Treatment		17 (73.9%)	6 (26.1%)	0.012
Tiredness		5 (29.4%)	12 (70.6%)	0.007
DLQI (Baseline		8.27 ± 2.05	13.57 ± 1.60	<0.001
In Flare at baseline		10 (40.0%)	15 (60.0%)	0.024

Univariate regression analysis was done to find the predictors for poor quality of life in AIBD patients. The variables selected were Duration of disease in years, baseline ABSIS Score, baseline OMS Score, duration of continuous treatment in years, use of adjuvant treatment, tiredness (ADR), DLQI at baseline and disease status. (Table no. 6). Following this a multivariate logistic regression was done, with those variables having a p value <0.2. This analysis showed adjuvant treatment to be significant predictor of poor quality of life [OR 55.00 (4.30-703.43, p=0.002)]. A small sample size could be a reason for a the wide odds ratio and CI.

Table 6: Predictors of poor quality of life at baseline (N=26)

Variable	Unadjusted odds ratio (OR) Univariate	p value	Unadjusted odds ratio (OR) multivariate	p value
Age Years	0.98 (0.90-1.08)	0.720		
Duration of AIBD	1.55 (0.69-3.46)	0.288	-	
ABSIS Score	0.72 (0.50-1.02)	0.065	-	
OMS Score	0.65 (0.42-1.00)	0.052	-	
Adjuvant Treatment	55.00 (4.30-703.43)	0.002	59.31 (3.40-1034.48)	0.005
Flare	11.00 (1.06-14.09)	0.045	-	

DISCUSSION

In our study, the mean age of the participants was 46.62 (SD±11.1) years. Study done by Mini et al (2019) reported a similar results - 40–59 years.[6] A study conducted in Korea (2014), reported a higher mean age of 69.15 (SD± 15.7) years [7]. The mean age of onset in our study was 43 years (SD ± 9.11). Studies in the western population show a later age of onset between 53- 73 years (Baican et al, 2010) [8]. Our study had a female preponderance (M: F ratio 1:5) with 66% patients being females. Other studies showing similar results were done by Kiran et al (2018) [9] - female preponderance of 60.7% and Davatchi et al (2005) with 59.9% (Kiran et al)[10].

The median duration of disease in our study was 0.83 (IQR 0.46-1.50) years with 10.6% patients having had the disease for > 5 years. A study from Eastern India gave a mean duration of 0.68 years [11]. Longer duration of disease and severity adversely affects QoL in patients with AIBD. In our study disease duration of >5years was not significant predictor of poor QoL, can be attributed to smaller sample size (n=47), 40% patients having stable disease at baseline and treatment being effective in these patients.

Quality of life was assessed in our study using the Dermatology Life Quality Index (DLQI). The median (IQR) DLQI score 10 (8.5 -13), with 44.7% patients having a DLQI score ≥11 indicating poor quality of life (QoL). This was similar to the study by Jae Yong et al (2015) with a mean DLQI of 10.2±8.8. But a study by Kiran et al found patients with higher DLQI 13.75 ± 0.30 mostly because patients were treatment naïve. Few other studies found mean DLQI scores between 9 to 13. In our study the mean DLQI score reduced from 10 to 8 at 3 months. There was a mean difference in DLQI score by -1.05 from baseline to 3 months. The main factors affecting the QoL at baseline were; the severity of the disease, Duration of continuous treatment, and disease status.

AIBD is a complex disease which affects the patient physically, emotionally, socially and financially. Therefore, the management should be comprehensive. Screening for co-morbidities, triggers like viral infections, should become a part of routine practice. The treatment should be aimed at reduction of severity, control of lesions and minimizing the adverse effects

caused by the treatment. Assessment of QoL mirrors treatment response of the patient and can be a guiding tool for planning effective treatment strategies, therefore must be encouraged for routine use.

To the best of our knowledge, this study is the first comprehensive study evaluating the patterns of drug use, costs incurred by the patients and factors associated with quality of life among patients with AIBD in India. The study had a sample size of 47 (calculated based on change in DLQI from other studies), which was adequately powered to detect a DLQI change in 1 month, and the lost-to-follow up rate of 10% was lower than the expected 30%. Being a tertiary care hospital, we had a fair representation of patients from different sections of the society. We managed to include a good representation of patients from both the rural and urban areas, and from the out-patient and inpatient wards and also patients with varying types and severity of AIBD.

CONCLUSION

Our study evaluated the factors affecting the quality of life among patients with AIBD in a tertiary care hospital in India. The baseline quality of life scores in our study was comparable to other studies done in India. As treatment progressed, there was significant improvement in the quality of life of the patients.

In our study, patients were found to have a physical, psychosocial and financial burden and it increased by the presence of co-morbidities, frequent relapses or flares. Management strategies for AIBD should take into account the quality of life of the patients, and improvement in the same should be an aim of treatment along with decreasing the disease severity. In our study we used DLQI questionnaire to measure Qol, a more specific questionnaire would have been the ABQOL questionnaire.

In conclusion, our study though an important one in generating treatment and Qol data among patients with AIBD in South India, was limited by short duration of the study and relatively small number of patients. The findings from our study may be used to design larger studies, preferably, multi centre studies with larger sample size, to generate more meaningful information about burden of disease, trigger factors, management strategy, and determination of factors affecting quality of life in AIBD patients.

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