

**Original Article**

**AN ANALYSIS OF PRESCRIPTION PATTERN, ADHERENCE TO PHARMACOTHERAPY AND QUALITY OF LIFE IN PEMPHIGUS VULGARIS PATIENTS**

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**ABSTRACT**

**Objective:** Pemphigus Vulgaris [PV] is a chronic autoimmune disease. Corticosteroids and Immunosuppressants are the main line of treatment. The aim of this study was to evaluate the prescription pattern and patient adherence behavior with therapy. We determined the association between patient adherence and quality of life in patients with pemphigus vulgaris.

**Methods:** A prospective observational study was conducted from February 2020 to May 2021. The age and sex of patients who were diagnosed with PV within 1 mo period and confirmative histopathological findings in Biopsy were included in the study. A total of 35 patients were analyzed and patients were reviewed for medication adherence and quality of life by using MMAS-8 and WHOQOL respectively, monthly till 3 mo after initiation of therapy. Statistical analysis was done by using Epi Info version 7.1.5.

**Results:** Out of 140 prescriptions, vitamin C and zinc were the most common drug prescribed in 129 prescriptions followed by prednisolone prescribed in 128 prescriptions. The average number of drugs per encounter was 8.67. 97.56 % of drugs were prescribed by generic names. No significant improvement was seen in the adherence behavior of patients from 1st follow-up to 3<sup>rd</sup> follow-up. It was observed that physical, psychological, and environmental domains have significant associations with medication adherence in all 3 follow-up visits.

**Conclusion:** It was concluded that Polypharmacy and inappropriate use of medicines may decrease the adherence behavior of patients to the therapy. Low adherence to pharmacotherapy affects the quality of life in PV patients. This study is beneficial for raising awareness about treatment adherence and also encouraging the development of appropriate interventions.

**Keywords:** PV, Prescription pattern, Medication adherence, Quality of life

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**INTRODUCTION**

Pemphigus Vulgaris [PV] is a chronic and life-threatening autoimmune disease. The existence of antibodies against the desmoglein protein [dsg1 and dsg3], which are found in the skin and mucosa epithelial cells. Acantholysis is caused by the development of antibodies against these proteins. The mucocutaneous lesions are characterized by thin-walled, flaccid and easily ruptured bulla and erosions of the skin and mucous membranes [1]. The scalp, face, axillae, and oral cavity are the most usually affected sites, as they are where the PV antigen is most abundant.

It is a rare condition [0.1-0.5 cases per 100,000 people per year] with symptoms appearing in the fifth or sixth decade of life. PV affects both men and women equally and has a strong genetic and environmental association [1, 2].

Systemic corticosteroids, particularly prednisolone, are the drug of choice for the treatment of PV disease. Although corticosteroids may cause rapid resolution of lesions, they alone are not effective as well as safe in PV patients for prolonged periods of time. Thus, concomitant drugs like azathioprine, cyclophosphamide, cyclosporin, dapsone, tetracyclines and immunoglobulins are advocated to reduce the high dose of steroids for longer duration.

Irrational usage of medication is a serious issue in modern medicine. Unnecessary prescription of drugs leads to adverse drug reactions [ADRs] and ineffective treatment [3]. The study of prescription patterns is important to monitor prescribing practices and assess drugs for efficacy, safety, convenience, and cost.

Patients' adherence behavior may be affected by long-term conditions, ADRs, lack of awareness and importance of adherence to therapy, multiple doses, and lack of knowledge about their

medications etc. According to a 2003 World Health Organization [WHO] report, the average patient adherence to long-term therapy for chronic diseases in developed countries is only 50%, while it is even lower in developing countries [4].

Adherence is necessary for the effectiveness of therapy to any condition and quality of life [QoL] has become an important outcome metric to assess the effectiveness of given therapy in PV patients. Disease progression and mortality are seen with PV if individuals are not treated adequately.

Previously, no research for this rare condition has been evaluated, and that is why it is the reason for conducting research on this topic.

The aim of this study was to evaluate prescription patterns and the patient's adherence to therapy. Periodic prescription auditing in the form of drug utilization studies is an important technique to enhance therapeutic efficacy, reduce side effects, lower treatment costs, and provide meaningful feedback to clinicians. This will also improve patient's trust in their physician and therapy. We also wanted to assess whether there is any significant association between treatment adherence and treatment effectiveness by using the WHOQOL scale.

**MATERIALS AND METHODS**

This prospective observational study was conducted at the Department of Dermatology and Venereology of a tertiary care teaching hospital from February 2020 to May 2021. A total of 18 mo of study duration. Either the age and sex of patients who were diagnosed with PV within 1 mo of period and confirmative histopathological findings in Biopsy were enrolled in the study. Old cases of PV or patients who were already taking treatment of pemphigus vulgaris in any form of therapy were excluded from

study. The study was started after initial approval from the Institutional Ethics Committee [IEC] (IEC/4502/2020) and prior permission obtained from the Head of the Department of Dermatology. Patients were provided with the patient information sheet and written informed consent was taken before enrolling all patients in the study. Patients were reviewed for their follow-up visit monthly till 3 mo after initiation of therapy for PV.

Thirty-five patients were analyzed during the study period. The sample size was calculated using the formula given below:

$$\text{Sample size } [n] = Z^2Pq/d^2$$

Where n = sample size, Z = value for a level of confidence of 95% [Z value is 1.96], P = expected prevalence [P = 0.04], q= 1-P [0.96], and d = precision [if 5%, d = 0.05].

$$n = [1.96]^2 \times 0.04 \times 0.96 \div [0.05]^2 = 59$$

Since in this study, only new cases of PV were included, the minimum sample size came out to be 30 only.

The patient's demographic profile, clinical details and treatment details were collected from the Patient's case notes and treatment sheets and by interviewing patients and mentioned in Case record form [CRF]. The CRF included details like patient initials, age, gender, weight, education, occupation and address details, clinical presentation of PV, sites of lesions and duration of lesions. Other necessary information about past history, family history, comorbid conditions and other autoimmune diseases and systemic therapy, topical therapy and concomitant drugs prescribed to patients of PV.

In each follow-up visit, detailed drug history and Adverse Drug Reactions [ADRs] were asked. Questionnaires were asked of patients to evaluate adherence to pharmacotherapy and quality of life in PV patients during each follow-up visit till 3 mo after initiating the therapy. A total of 3 follow-ups were included.

Patients' adherence to the treatment was assessed by an investigator with the help of Morisky's 8-item Medication Adherence Questionnaire [MMAS] by interviewing them in vernacular language [5].

The patient's quality of life was assessed by an investigator with the help of the WHO Quality of Life-BREF scale [WHO-QoL BREF]. Patients were interviewed in vernacular language for the questionnaire [6].

Adverse drug reaction was recorded in ADR reporting form version 1.3. Causality assessment was done using World Health Organization [WHO] causality assessment criteria [7].

#### STATISTICAL ANALYSIS

Demographic details of patients were presented using Microsoft Excel Office 2019. Other data [clinical profile and treatment profile] was also analyzed using Microsoft Excel Office 2019. For association between two independent variables chi-square test was used. Kruskal Wallis test was used to analyze non-parametric data. Statistical analysis was done by using Epi Info version 7.1.5.

#### RESULTS

The Mean age of thirty-five patients was 46.51±13.35. 25.71 percent of patients were enrolled from the 41-50 age group, followed by the 51-60 age group. 60% of females participated in this study compared to males, which was 40 %. Out of thirty-five patients, a total of 24 patients have been educated. Twenty-six patients were unemployed, while only nine patients were earning members of their families.

Twelve patients visited the Department of Skin and Venereology within 10-15 d of the onset of symptoms. Ten patients visited the department 25-30 d after the onset of symptoms. Eight and five patients visited the department at 2-7 d and 20-25 d of the onset of symptoms, respectively.

Out of 35 patients, 20 patients presented with only skin lesions of PV. Different sites of skin lesions were present on the face, upper and lower limbs, abdomen, neck, axilla, back, scalp, etc. Nine patients presented with skin and mucous membrane lesions. Only six patients presented with mucus membrane lesions. The oral cavity, buccal mucosa, and soft palate were involved in mucous membrane lesions. A total of twelve patients were associated with co-morbid conditions [fig. 1].

**Table 1: Drugs used in the treatment of pemphigus vulgaris**

S. No.	Group	Name of drugs	Number of prescriptions N=140 [%]
1.	Steroids	Prednisolone	128 [91.42%]
		Dexamethasone	12 [8.57%]
2.	Immuno-suppressants	Azathioprine	59 [42.14%]
		Cyclophosphamide	22 [15.71%]
		Dapsone	24 [17.14%]
3.	Antibiotics	Augmentin	12 [8.57%]
		Doxycycline	38 [27.14%]
4.	Non-antibiotics Antimicrobials	Fluconazole	22 [15.71%]
		Metronidazole	8 [5.71%]
5.	Antacids	Famotidine	116 [82.85%]
		Ranitidine	14 [10%]
		Omeprazole	7 [5%]
6.	Antihistaminics	Levocetirizine	36 [25.71%]
		CPM	13 [9.29%]
7.	Bisphosphonates	Alendronate	93 [66.43%]
8.	Vitamins and minerals	MVBC+folic acid	121 [86.42%]
		Vit. C+zinc	129 [92.14%]
		Calcitriol	124 [88.57%]
		Framycetin	102 [72.85%]
9.	Topical therapy	Clotrimazole	72 [51.42%]
		Betamethasone	15 [10.71%]
		Mucopain	17 [12.14%]
		Neomycin	4 [2.85%]
		Triamcinolone	4 [2.92%]

As shown in table 2, the average number of drugs per encounter was 8.67. 97.56 % of drugs were prescribed by generic names and 67.65% of drugs were prescribed from the essential drugs list of medicines [EML 2021]. 21.68% of encounters were prescribed with antimicrobial drugs [table 2].

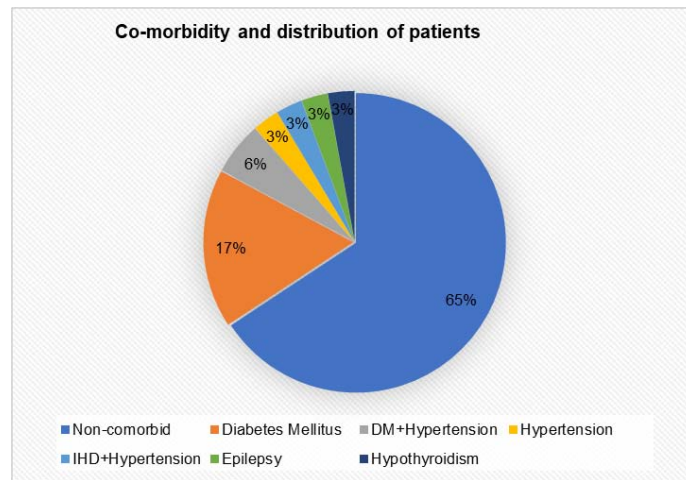


Fig. 1: Patients are categorized based on their co-morbid conditions; all the patients with PV were treated with systemic and topical therapy mentioned in below table 1

Table 2: Analysis of prescriptions according to WHO core indicators

S. No.	WHO core indicators	Number or percentage
1.	Average number of drugs per encounter	8.67
2.	Percentage of drug prescribed by generic name	97.56%
3.	Percentage of encounters with an antimicrobial prescribed	21.68%
4.	Percentage of encounters with an injection prescribed	3.87%
5.	Percentage of drugs prescribed from essential drugs list of medicines [2021]	67.65%

Table 3: Treatment adherence behaviour at 1, 2 and 3 mo of treatment based on morisky medication adherence scale [MMAS-8]

Adherence behaviour	No. of patients at 1 <sup>st</sup> mo [%]	No. of patients at 2 <sup>nd</sup> mo [%]	No. of patients at 3 <sup>rd</sup> mo [%]	Test of significance
Low adherence [<6]	25 [71.43%]	22 [62.86%]	18 [51.43%]	X <sup>2</sup> = 2.988
Medium adherence [6-7]	10 [28.57%]	13 [37.14%]	17 [48.57%]	df= 2
High adherence [8]	0	0	0	p= 0.22

X<sup>2</sup>= Chi-square value, df= degree of freedom, significant P=<0.05

According to the results shown in table 3, the P-value of the chi-square table does not show any significant improvement in medication adherence behavior of patients from 1<sup>st</sup> to 3<sup>rd</sup> follow-up visits.

According to the WHOQOL score, the mean [SD] of physical, psychological, social and environmental domains were 42.62[5.46], 38.51[10.37], 38.97[11.80] and 46.02[9.66] at the 1<sup>st</sup> follow-up visit.

While at the end of 3<sup>rd</sup> follow-up visit, the mean [SD] were 53[7.93], 49.82 [11.50], 41.2 [11.2] and 53.44 [9.66] in physical, psychological, social and environmental domains, respectively [table 4].

Table 4: Different domains scores at 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> mo of therapy

Domains of QOL score	1 <sup>st</sup> mo mean±SD	2 <sup>nd</sup> mo mean±SD	3 <sup>rd</sup> mo mean±SD
Domain-1 physical	42.62±5.46	45.85±8.16	53±7.93
Domain-2 psychological	38.51±10.37	44.31±10.41	49.82±11.50
Domain-3 social	38.97±11.80	39.14±11.63	41.2±11.24
Domain-4 environmental	46.02±9.66	49.2±10.85	53.44±9.66

We observed that the physical domain, psychological domain, and environmental domain have significant associations with medication adherence in all 3 follow-up visits. A P-value of different domains and Kruskal Wallis test values are shown in table 5.

Table 5: Association between medication adherence and quality of life

Variable <sup>b</sup>	Quality of life domains							
	Physical domain		Psychological domain		Social domain		Environmental domain	
	H	P-value	H	P-value	H	P-value	H	P-value
F <sup>u</sup> p visit-1	10.171	.038	9.302	.054	4.393	.355*	9.723	.045
F <sup>u</sup> p visit-2	11.981	.017	13.652	.008	8.792	.067*	12.605	.013
F <sup>u</sup> p visit-3	11.319	.023	10.587	.032	7.328	.120*	15.025	.005

H=Kruskal Wallis test value, b= Grouping variable [Adherence score], Significant P-value =<0.05 [\*=>0.05], F<sup>u</sup>p= Follow up

Only two adverse drug reactions were reported. One reaction was thrombocytopenia due to the tablet azathioprine and other was steroid-induced hyperglycemia. Both reactions were probably associated with suspected medications as per the WHO causality assessment scale. Both reactions were non-serious and both patients recovered from the events.

## DISCUSSION

This study observed that the most common age group of newly diagnosed patients was 41-50 y of age followed by 51-60 y of age. In Hicham T. *et al.*'s study, the incidence peak was observed in the fifth decade of life [8]. Other studies reported a similar result of the onset of PV in the fourth and fifth decades of life [9,10]. Studies have found a female preponderance with female-to-male ratios of 1.16: 1 in India [11] and 1.2: 1 in France [12]. This study also has an observation of a female-to-male ratio of 3:2. Education helps to gain knowledge about the risks and benefits of medications that are used to treat PV. In this study, literate patients (24) were more common compared to illiterate patients (11).

In the present study, twenty patients presented with only skin lesions followed by mucocutaneous lesions [9] and only 6 patients had lesions over the mucous membrane. In contrast, other studies reported the mucocutaneous type of lesion in PV was commonly presented by their patients [8, 13].

The study done by Heelan K. and colleagues reported frequently occurring comorbidities of pemphigus, including diabetes, hypertension, hypothyroidism, solid organ malignancy, heart disease, and asthma [14]. The present study observed most frequent co-morbidities in PV patients to be of diabetes mellitus followed by hypertension with diabetes, hypothyroidism, ischemic heart disease, and epilepsy. In the present study, hypothyroidism was seen in one patient, and another patient had a family history of PV. This result supports the theory that more than one autoimmune disease can be present in one patient or within a family.

Out of 140 prescriptions, prednisolone was prescribed in a total of 128 prescriptions. The most common immunosuppressant drug used as adjuvant therapy was azathioprine [59] followed by dapsone [24] and cyclophosphamide [22]. In the study done by Askin O, azathioprine was also prescribed more commonly as adjuvant therapy [15]. The comparison between the observed pattern of drug usage and current recommendations or guidelines for PV therapy will help to conclude whether the prescriptions were well-documented with optimal information.

This study observed 97.56% of drugs to be prescribed with generic names in the study area. The study also observed that 67.65% of drugs are prescribed from the essential drug list of medicines [2021]. Only 21.68% of encounters were prescribed with antimicrobial drugs. We observed that more than 8 numbers of drugs per prescription may decrease patient adherence behavior and also increase the chances of drug-drug interactions and increase adverse drug reactions. The well-documented prescriptions and limited use of drugs are required to prevent or avoid these consequences.

Inadequate adherence to treatment is the primary cause of limitations efficacy of therapeutic medication [16]. Patient's behavior regarding nonadherence to medication will have personal and financial consequences for the patient. Some studies analyze adherence to treatment in chronic diseases in patients with DM, hypertension, COPD, arthritis, liver diseases, chronic renal failure, SLE, etc. No analogous study has been found in patients with PV. Although we observed that the number of patients increased from low to medium adherence, there was no significant difference between the 1<sup>st</sup> and 3<sup>rd</sup> follow-up visits.

In the current study, the Kruskal-Wallis test was used to determine the association between adherence to medication and quality of life. It was found that the p-values of the physical, psychological, and environmental domains were 0.023, 0.032, and 0.005, respectively. This value suggests these domains to have significant associations with adherence to therapy. This significant association is noted with these 3 domains in all follow-up visits. The study done by Khayyat M *et*

*al.* supported our study and reported that adherent patients had significantly better quality of life compared to non-adherent patients [17]. In contrast, the study conducted by Alsaqabi YS did not find any such significant association between medication adherence with any of the domains of quality of life on the WHOQOL-BREF scale [18].

As a result, it was concluded that adherence to treatment positively relates to the effectiveness of pharmacotherapy in PV patients. In the future, this study will help to understand that the effectiveness of therapy also depends on the compliance factor. So, during the treatment of a chronic disease, physicians also to keep in mind the compliance of patients because poor adherence of patients may worsen the disease or its complications as well as have a negative impact on therapy for the particular disease. It's important to note that the study's findings may be limited by the duration of the research.

## CONCLUSION

Findings of this study concluded that overuse of vitamins and other concomitant medicines were noted which have no significant role in treating PV disease. This knowledge will directly or indirectly improve the outcome of disease, the beliefs of patients in doctors and treatment and the quality of life of patients and family. Although there is no significant improvement seen in patient behavior for medication adherence, we observed a significant association between medication adherence and quality of life. So, this study is beneficial for raising awareness about treatment adherence and also encouraging the development of appropriate interventions.

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Nil

## AUTHORS CONTRIBUTIONS

Dr. Ridhdi served as the principal investigator for this study, actively contributing to every stage, from data collection to manuscript writing. The other co-authors played key roles in data analysis and manuscript review.

## CONFLICTS OF INTERESTS

Declared none

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