

## Original Research Article

# Impact of clinical pharmacist intervention in the treatment of pemphigus with rituximab at a tertiary care hospital

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**Received:** 25 June 2024

**Accepted:** 08 August 2024

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## ABSTRACT

**Background:** Pemphigus is an autoimmune bullous disease that causes lesions and blisters over skin and mucous membrane. Treatment involves long-term administration of systemic corticosteroids and/or other immunosuppressive agents. Rituximab is a type of monoclonal antibody target specific cells in the body. PDAI score is used to measure the extent of pemphigus. DLQI questionnaire is used to interpret the quality of life. Aim was to evaluate the impact of clinical pharmacist intervention in the treatment of pemphigus with rituximab.

**Methods:** A prospective interventional study was carried out in dermatology department. 40 patients diagnosed with pemphigus were included in the study. The demographic data, lab parameters, PDAI score and DLQI questionnaire were collected before and after infusion and pharmacist intervention. The data were statistically analyzed using paired t-test.

**Results:** Females represented the majority of the study population. The mean $\pm$ SD of age was found to be 44.57 $\pm$ 12.90. During rituximab administration majority of the patients experienced no adverse events. Notably, hypertension emerged as the most commonly reported adverse effect. Before the intervention, the mean $\pm$ SD for PDAI was found to be 29 $\pm$ 19.78 and DLQI was found to be 9.55 $\pm$ 4.32. After the intervention, the mean $\pm$ SD for PDAI was found to be 24.25 $\pm$ 18.13 and DLQI was found to be 7.925 $\pm$ 3.99. The values are analyzed using paired t-test and have significance with p value <0.0001.

**Conclusions:** Clinical pharmacist intervention regarding treatment, disease and life style modification having a significant improvement in patients with pemphigus.

**Keywords:** Clinical pharmacist, DLQI, PDAI, Pemphigus, Rituximab

## INTRODUCTION

Pemphigus refers to a collection of chronic blistering epithelial diseases characterized by the production of IgG autoantibodies targeting the extracellular domains of cell membrane proteins of keratinocytes. These conditions involve the production of IgG autoantibodies that attack proteins on the surface of skin cells, leading to a loss of adhesion between these cells, a process known as acantholysis.<sup>1</sup> Pemphigus vulgaris (PV) and pemphigus foliaceus (PF) are major types of pemphigus. The distribution of pemphigus vulgaris (PV) and pemphigus foliaceus (PF) varies across different regions. In some countries, like Mali, PF is more common, accounting for

up to 95% of cases. In Europe and north America, PV makes up the majority (65-90%) of pemphigus cases. Regions like south America and north Africa have higher rates of PF, leading to the term “endemic PF”. Paraneoplastic pemphigus (PNP), a rare variant, accounts for about 5% of cases, while IgA pemphigus and pemphigus herpetiformis are even less common, with limited epidemiological data available.<sup>2</sup> In India, the incidence of pemphigus among dermatology outpatient attendees has shown a wide range, from 0.09 to 1.8%. In a clinic-based questionnaire survey conducted in Thrissur district, Kerala, the incidence was determined to be 4.4 per million populations per year. This incidence was higher than reported data from Germany and France but

lower than that observed in Tunisia.<sup>3</sup> Pemphigus has a profound impact on individual's quality of life and public health, yet many aspects of their etiology and management remain unclearly understood. Treatment for these conditions typically involves long-term administration of systemic corticosteroids and/or other immunosuppressive medications, such as intravenous immunoglobulin (IVIg). However, these treatments can lead to considerable morbidity and mortality.<sup>4</sup> Rituximab is a type of monoclonal antibody; it made to target specific cells in the body. It is designed to attach to a protein called CD20 found on the surface of certain B cells, which are a type of white blood cell involved in the immune system.<sup>5</sup> This research is particularly relevant due to previously used corticosteroids and intravenous immunoglobulin in the treatment of pemphigus, has long term adverse effects compared to rituximab. By addressing gaps in the treatment protocol, our study aimed to know the potential role of clinical pharmacist and rituximab treatment in patients affected with pemphigus.

## METHODS

A prospective interventional study was conducted in the department of dermatology at a tertiary care hospital for a period of one year, after obtaining the institutional ethical committee approval (reference number: IHEC/2023/ Appr/Exp/363 and Proposal no.23/352).

After obtaining written informed consent a total of 40 patients were included according to the inclusion criteria like age above 18 years, confirmed diagnosis of pemphigus, receiving rituximab therapy and willing to participate in the study. Remaining patients with diagnosis of pemphigus were excluded.

A specially designed patient data collection form, validated for accuracy and completeness, was utilized to gather relevant patient information. This form included demographics, medical history, laboratory data, and concomitant medication use. Disease severity was assessed using the pemphigus disease area index (PDAI), a validated scoring system based on lesion severity and post-inflammatory changes and quality of life was assessed using dermatology life quality index (DLQI) questionnaire. The study was preceded in two stages, stage 1 was baseline assessment conducted before rituximab infusion, including PDAI score and administration of DLQI questionnaire. Stage 2, in which patient counseling by a clinical pharmacist regarding drug and disease management was provided during rituximab infusion. PDAI score and DLQI questionnaire were reassessed after 2 weeks of initial assessment. Statistical analysis was performed using Graph Pad Prism software. Paired t-test was utilized to assess differences in PDAI and DLQI scores before and after intervention. Normal distribution of data was confirmed, and significance was determined based on p values.

## RESULTS

A comprehensive study was conducted by enrolling 40 patients diagnosed with pemphigus across various age groups. Females represented the majority, comprising 67.5% of the study cohort. The patient distribution analyses revealed a notable concentration of patients were between the age of 40-59 years. Interestingly, within specific age categories, females aged 40-49 years and males aged 18-29 years constituted the largest proportions. The mean age was  $44.57 \pm 12.90$  years. The vast majority of patients (87.5%) reported no significant social habits. Regarding the diagnosis of pemphigus, pemphigus vulgaris emerged as the most prevalent subtype, affecting 87.5% of patients, followed by pemphigus foliaceus (7.5%). This distribution sheds light on the disease landscape within the study population and underscores the predominance of certain pemphigus subtypes. Type 2 diabetes mellitus (32.5%) and systemic hypertension (15%) were present in majority of the patients.

**Table 1: Demographic details, social habits and various characteristics.**

Characteristics	Number	Percentage
<b>Gender</b>		
Female	27	67.5
Male	13	32.5
<b>Age (in year)</b>		
18-29	8	20
30-39	6	15
40-49	11	27.5
50-59	9	22.5
60-69	6	15
<b>Social habits</b>		
Smoker and alcoholic	3	7.5
Non-smoker and non-alcoholic	35	87.5
Ex smoker and ex alcoholic	1	2.5
Ex alcoholic	1	2.5
<b>Diagnosis</b>		
Pemphigus vulgaris	35	87.5
Pemphigus foliaceus	3	7.5
Pemphigus erythematousus	1	2.5
Pemphigus vegetans	1	2.5
<b>Co-morbidities</b>		
Diabetes mellitus	13	32.5
Systemic hypertension	6	15
Others	13	32.5
<b>Adverse effects</b>		
Hypertension	4	10
Hypotension	3	7.5
No adverse effects	29	72.5
Others	8	20

The presence of these comorbidities may impact disease management and outcomes. During rituximab administration, the majority of patients (72.5%)

experienced no adverse events. Notably, hypertension emerged as the most commonly reported adverse effect (10%), highlighting the importance of monitoring and management during therapy (Table 1).

**Table 2: PDAI and DLQI scores.**

Scores	Number of patients (%)		P value
PDAI score	Before	After	
0-15 (moderate)	12 (30)	19 (47.5)	<0.0001
15-45 (significant)	22 (55)	15 (37.5)	
>45 (extensive)	6 (15)	6 (15)	
DLQI score			
0-1 (no effect at all)	0 (0)	1 (2.5)	<0.0001
2-5 (small effect)	6 (15)	12 (30)	
6-10 (moderate effect)	20 (50)	17 (4.5)	
11-20 (very large effect)	14 (35)	10 (25)	
21-30 (extremely large effect)	0 (0)	0 (0)	

The study evaluated disease severity and quality of life outcomes using the pemphigus disease area index (PDAI) score and dermatology life quality index (DLQI) questionnaire respectively before and after pharmacist intervention (Table 2). While evolving PDAI score before pharmacist intervention, 30% of patients exhibited moderate intensity, 55% exhibited significant intensity and 15% exhibited extensive intensity of pemphigus. While in post-intervention, there is a significant shift in the intensity. Nearly 18% of the patients shifted from significant intensity to moderate intensity. This improvement in disease severity, coupled with the statistical significance ( $p<0.0001$ ) observed in PDAI score comparison, underscores the efficacy of the intervention in mitigating disease burden. Similarly, the DLQI questionnaire revealed significant improvements in quality of life after pharmacist intervention. This improvement shows statistically significant ( $p<0.0001$ ), indicating a tangible enhancement in patient well-being following the intervention. Overall, these findings underscore the importance of tailored interventions and holistic patient care in managing this challenging condition.

## DISCUSSION

Pemphigus is an autoimmune bullous disease which causes blisters and erosions over skin and mucous membrane. It affects individuals of almost all age groups, and both the genders. The etiology of pemphigus is not clear yet. Genetic factors may affect first degree relatives which have been reported in few studies.<sup>1</sup> Rituximab has showed good results as compared to corticosteroids which have been previously used to cure pemphigus. Corticosteroids have long term adverse effects and chances of patients attaining complete remission is less;

whereas rituximab mostly has infusion related reactions and fluctuations in blood pressure.<sup>6</sup>

Our study assessed the impact of clinical pharmacist intervention in the treatment of pemphigus with rituximab. During gender wise distribution more female were affected than male. In a similar study, both groups had more female patients. The specification for more female patients affected due to pemphigus was not described, but may involve hormonal influences, genetic variations and/or epigenetic regulation of gene expression.<sup>7</sup>

Most of the patients in our study were affected by pemphigus vulgaris in which female were affected more compare to male, followed by pemphigus foliaceus (7.5%), then pemphigus erythematosus and vegetans (2.5%). Pemphigus vulgaris has affected majority of patients worldwide, and severity of vulgaris is more than other subtypes of pemphigus. In another study the distribution of pemphigus vulgaris observed more in United States, Europe and Japan and affecting majorly female patients.<sup>8,9</sup> The female patients were found to be in the age group of 40-59 years and male patients in 18-29 years. The overall mean $\pm$ SD of age was found to be 44.57 $\pm$ 12.90 in years. Similarly in Europe, United States and Japan pemphigus vulgaris patients were affected between the age group of 50-60 years. In paraneoplastic pemphigus affected age group was found to be 45-70 years.<sup>1,10</sup> Even though the specific reason behind patients falling in this age group is not known, further more studies conducted in Iran and Italy during COVID-19 pandemic found that average age group was 41.8 $\pm$ 9.6 and 68.3 $\pm$ 9.7 who had pemphigus and were under rituximab treatment.<sup>11</sup>

In a similar study male patients were more likely to present with disease onset before age 40 years than females. Males have increased cutaneous involvement and display greater co-expression of anti-Dsg1 and anti-Dsg3 antibodies, while females tend to have mucosal predominance and stronger personal and family histories of autoimmunity. Social habits like alcoholic and smoker were also found during the study. The patients with social habits or without social habits have same distribution of disease. Among patients in our study diabetes mellitus (32.5%) was observed as major co-morbidity. Followed by hypertension (15%), none of the treatment was stopped during rituximab infusion. Even after discharge the same treatment was continued for the patients.

In a comparison study the results showed that corticosteroid increases the intensity of co-morbid diseases whereas rituximab doesn't increase the intensity much.<sup>12</sup> Few adverse effects were observed during infusion. In our study we observed fluctuations in blood pressure (hypertension and hypotension) throat discomfort with cough and right-side chest pain. During fluctuations in blood pressure the infusion was slowed down or stopped then after sometime it was again re-

started. As per the protocol pre-medication were given in order to attain stability. PDAI score shows there was an improvement in the severity of the disease that is 7.5% of the patients shifted from significant extent to moderate extent of pemphigus. 15% have extensive of pemphigus even though these patients remained in same category their scores have reduced significantly after rituximab treatment along with pharmacist intervention. Paired t-test yield a significant change in PDAI score with p value <0.0001.

In another study pemphigus patient with exclusive oral involvement showed improvement in their PDAI score after weeks of follow up treated with rituximab as adjuvant after being non-responders to conventional immunosuppressive therapy.<sup>13</sup> In a related study majority of the patients achieved disease control and partial or complete remission at 6 and 12 months. Only few patients faced relapse and have to take additional infusion of rituximab.<sup>14</sup> DLQI questionnaire score shows significant changes after pharmacist intervention. The significance was proved using paired t-test with p value <0.0001. In a similar study HRQOL was assessed using tools like DLQI and SF-36. The final conclusion derived that rituximab administration in pemphigus patients showed rapid and notable improvement in HRQOL.<sup>15</sup>

To obtain more accurate results we need larger population. Long term study follow-up would be useful to observe long term adverse effects and efficacy of treatment.

## CONCLUSION

Pemphigus is an autoimmune disease which requires constant monitoring in order to achieve remission. Each patient achieves remission in their specific timeline depending upon their habits and lifestyle. Some do have relapse based on severity and the treatment they are undergoing. Corticosteroids and immunosuppressant are widely used to treat pemphigus but it increases the relapse rate and adverse effects. Rituximab is a monoclonal antibody which was used as first line drug or adjuvant therapy for pemphigus.

Our study assessed the disease severity, efficacy of rituximab and quality of life using PDAI and DLQI questionnaires. The pharmacist intervention was provided regarding disease, drug and life style modifications. The combined effect of pharmacist intervention with rituximab shows a better patients' understanding about their health condition and improvement in treatment. It also helps to understand them to continue treatment till they reach complete remission.

## ACKNOWLEDGEMENTS

Authors would like to thank Dr. Reena Rai, HOD of dermatology, PSG Hospitals and all the teaching staff of

department of pharmacy practice, PSG College of Pharmacy, Coimbatore for encouraging this research.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Subadradevi J, Arthi SM. Impact of clinical pharmacist intervention in the treatment of pemphigus with rituximab at a tertiary care hospital. *Int J Res Med Sci* 2024;12:3305-9.