

Serum Prolactin Concentration in Patients with Pemphigus Vulgaris

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Abstract

Background: Pemphigus vulgaris (PV) is an autoimmune bullous disorder characterized clinically by blisters and erosions of the skin and/or mucous membranes. Serum prolactin plays a role in the pathogenesis of pemphigus vulgaris.

Objective: The study aims to observe the serum prolactin concentration in patients with pemphigus vulgaris.

Methods: This cross-sectional study was conducted at the Department of Dermatology & Venereology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, between May 2017 and April 2018. A total of 35 patients were included in the study. A consecutive type of sampling technique was used. The dermatological examination was done to ascertain the extent of involvement of the disease.

Results: Among 35 patients, 31.4% belonged to 30-50 years age group, while 62.9% belonged to >50 years and 5.7% patients belonged to <30 years age group. The mean age was found 42.7±11.8 years with ranged from 19-65 years. The majority of the patients (57.1%) were male, and 42.9% patients were female. It was observed that 30(85.7%) had vesicles, 25(71.4%) had bulla, 35(100%) had erosions and 6(17.1%) had other types of lesions. 28 patients (80.0%) had scalp, 32(91.4%) had extremity, 35(100.0%) had trunk and 31(88.6%) had mucous membrane as the sites of involvement. The mean duration of disease was 9.0±12.7 months with a range from 0.5 to 36 months. It was observed that 9 patients (25.7%) had hyperprolactinemia, while 26 patients (74.3%) had normal levels of prolactin. The mean serum prolactin level was found 28.7±16.7 ng/ml with a range from 1.64 to 51.04 ng/ml.

Conclusion: Since serum prolactin plays a role in the pathogenesis of pemphigus vulgaris, it may offer a novel therapeutic target for treatment of PV. Thus, we may reduce morbidity and mortality rate in PV patients by modifying their serum prolactin levels.

Keywords: Serum prolactin, pemphigus vulgaris, autoimmune disease

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INTRODUCTION

Pemphigus vulgaris is an autoimmune bullous disorder characterized clinically by blisters and erosions of the skin and/or mucous membranes.¹ Thin walled, easily ruptured bullae appear on apparently normal skin and mucous membranes or on erythematous bases. The bullae rupture to form erosions, the denuded areas increase in size and have little/no tendency to heal.² Both mucous membrane and skin are affected by pemphigus vulgaris.² A study done in Bangladesh among the patients with pemphigus diseases reported that the majority of the patients had mucocutaneous involvement (76.50%), while in 56.8% patients, there was only mucosal involvement and 43.2% patients had only skin involvement.³ The primary lesion on the skin is a flaccid blister. These blisters are fragile, rupture easily and, therefore, are not often seen. More likely to be noticed are the painful erosions that are the result of broken blisters. These erosions bleed easily and often become crusted. The lesions are round to oval in shape and range from skin-colored to erythematous. Nikolsky's sign, in which the epidermis is easily detached from the skin, is elicited by applying lateral pressure to a bulla, leading to lateral extension of the blister, and is usually positive.² Sites of predilection include the scalp, face, chest, axillae, groin, and umbilicus.^{2,4} In pemphigus vulgaris inhibition of desmoglein (Dsg) 1 and 3 by autoantibodies results in loss of cell adhesion, binding of pemphigus vulgaris antibody results in activation of a variety of intracellular signaling pathways with phosphorylation of keratinocyte proteins, including activation of EGF receptors and phosphorylation of its downstream substrates [p38 mitogen activated protein kinase (MAPK), Fas apoptotic cascade].⁵ Hence, proper clinical examination and skin biopsy for histopathology and DIF both are important for proper diagnosis. Prolactin (PRL) is a 199 amino acid long polypeptide (23kDa) that acts systemically as a hormone, and locally as a cytokine.⁶ PRL is generated and secreted by the lactotroph cells of the anterior pituitary gland under the inhibition of dopamine. In addition to production by immune cells, prolactin has receptors on monocytes, macrophages, natural killer cells and T and mainly B lymphocytes. Thus, PRL is involved in the activation and differentiation of thymic epithelial cells, thymocytes, lymphocytes, and macrophages. It also operates as part of a neuroendocrine-immune network by stimulating the

release of specific cytokines. This complex network is postulated to link a diverse repertoire of responses to homeostasis disrupting inputs such as stress, infection, metabolic demands, and tumor growth.⁷ The highest serum PRL level was detected in patients with mucocutaneous involvement, followed by those with mucosal involvement, and was the least in those with cutaneous involvement. Though several clinical tools for assessing the severity of pemphigus vulgaris are available, no relevant biochemical marker was commonly recommended for patients with pemphigus vulgaris. Therefore, we proposed this study to observe the serum prolactin concentration in patients with pemphigus vulgaris.

METHODS

This cross-sectional study was conducted at the Department of Dermatology & Venereology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, between May 2017 and April 2018. A total of 35 patients were included for the study according to following inclusion and exclusion criteria:

Inclusion Criteria

1. Diagnosed cases of pemphigus vulgaris patients by expert clinician and /or histopathological and DIF findings of any age and sex; and
2. Patients willing to give informed written consent for the study.

Exclusion Criteria

1. Patients having acute illness (fever, joint pain, abdominal complaints, history of chest pain);
2. Patients having renal, hepatic, endocrinopathies (prolactinoma, hypothyroidism, hyperthyroidism), connective tissue disease (systemic lupus erythematosus, rheumatoid arthritis);
3. Use of drugs that are known to affect level of PRL (i.e., psychotropic drugs, thyroid hormones, glucocorticoids, and estrogens or contraceptives);
4. Pregnant and lactating females and having menstrual abnormalities were also not included in the study; and
5. Patients refused to be included in the study.

A consecutive type of sampling technique was used. Dermatological examination was done to ascertain the extent of involvement of the disease. The data collection sheet was filled accordingly. It took around 20-30 minutes to complete the whole procedure. 5ml blood sample was collected in morning between 8:00

to 10:00 AM in regard to circadian variation, it was preserved under -200C in duplicates until assay for prolactin is done. The serum prolactin (PRL) level was measured routinely by a radioimmunoassay (RIA) technique. Data was collected in pre-designed data collection sheet and data was compiled and analyzed. Data were then presented through tables expressed in frequencies with percentage. Statistical analysis was carried out by using the Statistical Package for the Social Sciences (SPSS) software version 23.0 for windows (SPSS Inc, Chicago, Illinois, USA). Ethical clearance for this study was obtained from the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.

RESULTS

Among 35 patients, 31.4% belonged to 30-50 years age group, while 62.9% belonged to >50 years and 5.7% patients belonged to <30 years age group (Fig. 1). The mean age was found 42.7±11.8 years with ranged from 19-65 years. The majority of the patients (57.1%) were male, and 42.9% patients were female (Fig. 2). Table-I shows distribution of the study patients by pemphigus vulgaris. It was observed that 30(85.7%) had vesicles, 25(71.4%) had bulla, 35(100%) had erosions and 6(17.1%) had other types of lesions. 28 patients (80.0%) had scalp, 32(91.4%) had extremity, 35(100.0%) had trunk and 31(88.6%) had mucous membrane as the sites of involvement. The mean duration of disease was 9.0±12.7 months with a range from 0.5 to 36 months. Table-II shows serum prolactin level of the study patients. It was observed that 9 patients (25.7%) had hyperprolactinemia, while 26 patients (74.3%) had normal levels of prolactin. The mean serum prolactin level was found 28.7±16.7 ng/ml with a range from 1.64 to 51.04 ng/ml.

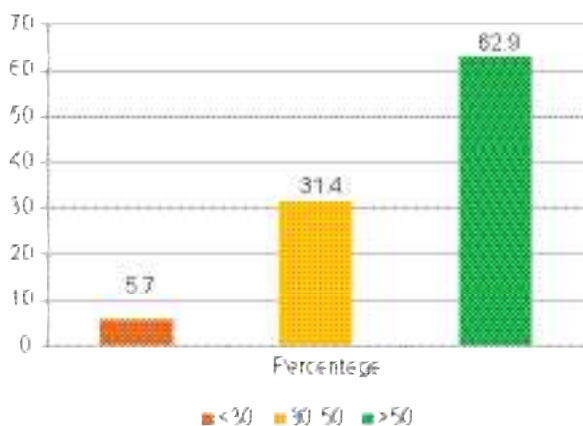


Fig. 1: Bar diagram shows age distribution of the study patients (n=35)

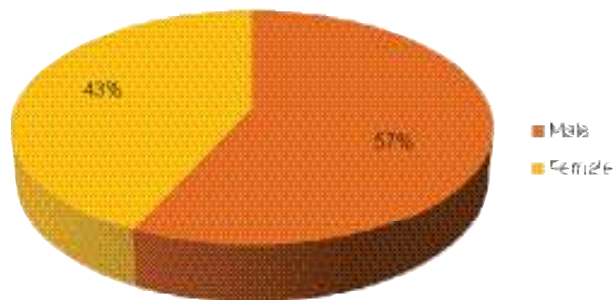


Fig. 2: Pie chart shows sex distribution of the study participants (n=35)

Table-I: Distribution of the study patients by pemphigus Vulgaris (n=35)

Pemphigus vulgaris	Number of patients	Percentage
Types of lesions		
Vesicles	30	85.7
Bulla	25	71.4
Erosion	35	100.0
Other	6	17.1
Site of involvement		
Scalp	28	80.0
Extremity	32	91.4
Trunk	35	100.0
Other (Mucosa)	31	88.6
Duration of disease (month)		
≤12	27	77.1
≥12	8	22.9
Mean ±SDRange(min-max)	9.0±12.7	0.5-36

Table-II: Distribution of the study patients by serum prolactin level (n=35)

Serum Prolactin level (ng/ml)	Number of patients	Percentage
Normal	26	74.3
Hyperprolactinemia	9	25.7
Mean±SD	28.7±16.7	1.64-51.0
Range (min-max)		

DISCUSSION

Pemphigus is a life-threatening autoimmune bullous disease, characterized by blister formation and erosions on the skin and mucous membranes caused by loss of cell-cell adhesion of keratinocytes. In this study the mean age of PV patients was 42.7 ± 11.8 years ranging from 19-65 years. Though it is thought that PV is a disease of 5th and 6th decades of life, this study found a number of PV patients of younger age group also. Fallahzadeh et al.⁸ found mean age of PV patients was 45.91 ± 3.35 years with a range from 20-83 years. Pitoia et al.⁹ also found mean age PV patients was 48.3 ± 11.3 years with a range from 25-65 years. Aghmiyuni et al.¹⁰ found among 116 patients, the mean age of pemphigus vulgaris patients was 42.5 ± 17.53 years with a range from 6 to 88 years. Xiaoling et al.¹¹ found mean age of PV patients was 44.19 ± 21.45 years with a range from 8 to 65 years and the peak age of PV patients was 31-50 years. This suggests that in Asia the onset of the disease is in younger age groups. Men and women aged 31-50 years are under huge work and life stresses, which may lead to high incidence rate in this age group. Regarding gender, male: female ratio was 1.3:1. William et al.¹² showed a male predominance in this study, though usually pemphigus vulgaris is equal between male and female. In Bangladesh, women seek less medical attention for their illness due to cultural, social, religious aspects and may be that is way our study observed a male predominance. Fagheei Aghmiyuni et al.¹⁰ also found male predominance in their study with 54.4% male and 45.6% female. Chmurova et al.¹³ found female: male ratio was 1.4:1. Zhu et al.¹¹ found that ratio of female and male was 1.40:1 in Northeast China. The reason for this difference was not clear. The difference in sex may result from the fact that estrogen exerts different influences on the development and function of the immune system in males and females, in which females may have a greater immune responsiveness to exogenic insults as well as to autoimmunity.¹⁴ In our study, 30(85.7%) had vesicles, 25(71.4%) had bulla, 35(100%) had erosions and 6(17.1%) had other types of lesions. 28(80.0%) patients had scalp, 32(91.4%) had extremity, 35(100.0%) had trunk and 31(88.6%) had mucous membrane as the sites of involvement. The mean duration of disease was 9.0 ± 12.7 months with a range from 0.5 to 36 months. Esmaili et al.¹⁵ found among 155 patients, the mean age of pemphigus vulgaris patients was 41.66 ± 13.29

years with a range from 14 to 70 years. In the present study, 9 patients (25.7%) had hyperprolactinemia. The mean serum prolactin level of PV patients was found 28.7 ± 16.7 ng/ml with a range from 1.64-51.04 ng/ml. Helmy et al.¹⁶ found mean serum PRL level of PV patients was 14.5 ± 12.5 ng/ml with a range from 2.7 to 45.9 ng/ml. In another study, Jacobi et al.¹⁷ found mean prolactin level 17.4 ± 15.1 ng/ml. Lajevardi et al.¹⁸ also found that mean prolactin (PRL) level was 15.60 ± 11.72 ng/ml. Ghandi et al.¹⁹ found mean serum PRL level 15.9 ± 14.1 ng/ml. In this study, mean serum prolactin level was higher than that of previous studies. Study findings showed that five male patients (55.6%) had hyperprolactinemia and four female patients (44.4%) had hyperprolactinemia. No statistical difference was noted in between two groups ($P > 0.05$). Yousefi et al.²⁰ found mean serum prolactin level in male patient was 185.4mIU/L and in female patient was 197.5mIU/L. There was no statistical difference between the two groups. Helmy et al.¹⁶ found mean serum prolactin level in male patient was 12.1 ± 9.3 ng/ml and in female patient was 15.5 ± 13.8 ng/ml. There was no statistical difference between the two groups.

In the present study, a limited number of pemphigus vulgaris patients were included. The cross-sectional design of the study did not allow us to draw any conclusion regarding the cause and effect relationship between pemphigus vulgaris and hyperprolactinemia. The patients enrolled were biased toward having higher disease severity, since the study population was based on a tertiary medical center. It was a single center study, which may not be able to demonstrate the true population of pemphigus vulgaris of the whole country.

CONCLUSION

There is no therapy that would give hope for a complete cure of pemphigus vulgaris. Different worldwide studies suggested that serum prolactin (PRL) level may serve as a useful biological marker for PV disease activity. No such study has been conducted in Bangladeshi population till date to evaluate serum prolactin level in PV patients. Thus, this study will be of great help in treating pemphigus vulgaris patients in urban as well as in rural areas where the vast majority of our people reside. Therefore, serum prolactin plays a role in pathogenesis of pemphigus vulgaris and this will in turn offer a novel therapeutic target for treatment of PV and thus may

reduce morbidity and mortality rate in the PV patients. A prospective multicenter evaluation should be approached. Further studies could be undertaken by including a large number of patients. Case control study should be a better option to find out actual increase in serum prolactin level.

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