# Original Article

# **Thyroid Function Abnormalities Among Pemphigus Vulgaris Patients**

Alam AKMM<sup>1</sup>, Hoq AJMS<sup>2</sup>, Ahmed MI<sup>3</sup>, Ahmed ARS<sup>4</sup>, Snigdha KSR<sup>5</sup>, Hamid MA<sup>6</sup>, Sayem MAS<sup>7</sup>

### **ABSTRACT**

**Background:** It is known that individuals with autoimmune diseases such as pemphigus vulgaris (PV) are at increased risk of developing other autoimmune diseases. However, it is not clearly known whether there is any specific relationship between PV and thyroid autoimmunity.

**Objective:** The study aims to determine the effects of pemphigus vulgaris on the thyroid glands with analyzing the thyroid function tests.

Methods: This cross-sectional, descriptive study was conducted in the Department of Dermatology & Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, between November 2015 and October 2016. A total of 42 patients participated in this study. Pemphigus vulgaris was diagnosed clinically with the help of a panel of experts and confirmed by the investigations e.g., histopathological and DIF examination. Demographic profile, detailed history, and clinical features was recorded in data collection sheet. Then the thyroid function tests – serum TSH,  $\mathrm{FT}_4$  and  $\mathrm{FT}_3$  were measured by chemiluminescent microparticle immunoassay.

**Results:** In the present study, the mean age of the patients was 46.7 $\pm$ 9.9 years. Male: female ratio was 1.1:1. Hypertension was the most commonly observed comorbidity (16.7%), followed by anaemia (11.9%). Seum TSH was abnormal in 9.5% patients, while abnormal serum FT $_4$  was observed in 2.4%, and FT $_3$  in 16.7%. Overall, most of the patients (88.1%) had normal thyroid functions i.e., euthyroid state, 4(9.5%) patients had hypothyroidism and 1(2.4%) had hyperthyroid state.

**Conclusion:** Among pemphigus vulgaris patients, thyroid function tests revealed that serum  $FT_3$  is the most affected by pemphigus vulgaris; nonetheless, serum TSH and  $FT_4$  are also affected in smaller proportion in comparison to  $FT_3$ .

Keywords: Thyroid function test, pemphigus vulgaris, autoimmune disease.

Mugda Med Coll J. 2022; 5(1): 29-33

- 1. Dr. AKM Mahbubul Alam, Assistant Professor, Department of Dermatology and Venereology, Mugda Medical College Hospital, Dhaka-1214.
- Dr. Abu Jafar Md Shahidul Hoq, Assistant Professor, Department of Dermatology and Venereology, Mugda Medical College Hospital, Dhaka-1214.
- 3. Dr. Md Iqbal Ahmed, Assistant Professor, Department of Dermatology and Venereology, Mugda Medical College Hospital, Dhaka-1214.
- 4. Dr. Abu Reza Sayem Ahmed, Assistant Professor, Department of Dermatology and Venereology, Mugda Medical College Hospital, Dhaka-1214.
- Dr. Kaniz Shahali Reza Snigdha, Assistant Professor, Department of Dermatology and Venereology, Mugda Medical College Hospital, Dhaka-1214.
- Dr. Md Abdul Hamid, Assistant Professor, Department of Dermatology and Venereology, Mugda Medical College Hospital, Dhaka-1214.
- 7. Dr. Md Abu Sayed Sayem, Junior Consultant, Department of Dermatology and Venereology, Mugda Medical College Hospital, Dhaka-1214.

Address of correspondence: Dr. Abu Jafar Md Shahidul Hoq, Assistant Professor, Department of Dermatology and Venereology, Mugda Medical College Hospital, Dhaka-1214. Email: drshahidulhoq@gmail.com

#### INTRODUCTION

Pemphigus vulgaris (PV) is a kind of autoimmune bullous illness that has been linked to myasthenia gravis and thymoma in the past. 1 Blisters form on the skin and mucous membranes, and the skin and mucous membranes erode. It nearly always affects persons in their 40s or 50s. Pemphigus vulgaris is characterized by a soft blister filled with clear fluid that develops on healthy or inflamed skin. In many cases, mouth blisters are prevalent, followed by recurrent skin blisters.<sup>2.3</sup> Because of the blisters in his or her mouth, it may be difficult for the individual to eat. Burst blisters on the skin can be painful and interfere with a person's normal activities. Pemphigus vulgaris is still considered of having unknown aetiology. It is thought to be activated when a person with a genetic predisposition to the disease comes into touch with an environmental trigger, such as a chemical or a medicine. Blisters form as a consequence of an accumulation of fluid between the skin cells. Individuals with autoimmune disorders like pemphigus vulgaris are known to be at a higher risk of getting additional autoimmune diseases.3 However, whether there is a link between thyroid autoimmunity and PV has yet to be determined.<sup>2</sup> Thyroid diseases are common in medical practice and are linked to a variety of skin problems.<sup>3,4</sup> Thyroid illnesses have been linked to skin conditions such as melasma, vitiligo, alopecia, Sjogren's syndrome, connective tissue disorders, and bullous diseases.<sup>5</sup> Thyroid disorders and dermatitis herpetiformis are said to be closely linked.<sup>6</sup> Pemphigus vulgaris is associated with autoimmune problems, and a recent study found that people with pemphigus vulgaris had a higher risk of developing autoimmune diseases in their families.<sup>7</sup> The most effective treatment for pemphigus vulgaris is corticosteroid, which is also used to treat people with Hashimoto's thyroiditis.<sup>4,8</sup> Glucocorticoids may lower antithyroid antibody titers and restore thyroid function in these individuals.9 Regardless, the number of research examining thyroid autoimmunity in pemphigus vulgaris patients is still limited;<sup>4,10-12</sup> in our country, such reports are rare. Hence, we proposed this study to observe the results of different thyroid function tests to determine whether pemphigus vulgaris affects the thyroid functions in diseased individuals.

#### **METHODS**

This cross-sectional, descriptive study was conducted at the Department of Dermatology & Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, between November 2015 and October 2016. A total of 42 patients were selected for the purpose of this study from patients with PV fulfilling the inclusion and exclusion criteria.

#### **Inclusion criteria:**

- Patients with PV diagnosed by history, clinical features, histopathological examination and direct immunofluorescence (DIF) assay;
- 2) Patients of both sexes with any age group; and
- 3) Patients who gave consent to participate in the study.

#### **Exclusion criteria:**

- Patients using drugs (Iodine and Iodide containing drugs, Lithium, Interferon-á, Interleukin-2, Dopamine, Levodopa, Amiodarone, Phenytoin, Carbamazepine) that interfere with thyroid functions;
- 2) Unable to answer the criteria question; and
- 3) Exclude those affected with other chronic diseases, like diabetes mellitus, chronic renal failure, chronic thyroiditis, nodular goitre, etc.

Informed written consent was obtained from the participants prior to the commencement of the study. Then the selected patients were biopsied under the supervision and sent to the Department of Pathology of the same institution for histopathological and DIF examination. Pemphigus vulgaris was diagnosed clinically with the help of a panel of experts and confirmed by the investigations. Demographic profile, detailed history, and clinical features was recorded in data collection sheet. Then serum thyroid profiles of the patients were evaluated with analyzing thyroid function tests. Serum thyroid stimulating hormone (TSH), free triiodothyronine (FT<sub>3</sub>), free thyroxine (FT<sub>4</sub>), were measured by using chemiluminescent microparticle immunoassay in Abbott Alinity i Autoanalyzer (made by Abbott Inc., USA), as performed in the Department of Biochemistry and Molecular Biology of the same institution.

All the relevant data were compiled on a data sheet, then statistical analysis was done using Statistical Packages for Social Sciences (SPSS) version 22.0 for windows. The results were presented in tables. Quantitative data were expressed as mean and standard deviation and qualitative data were expressed as frequency and percentage.

The present study was approved by the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.

#### RESULTS

In the present study, 22(52.4%) patients belong to the age range 19-49 years followed by 18(42.9%) patients were in 50-70 years and 2(4.8%) patients within 5-18 years. The age range of the patients was 12 to 62 years. The mean age of the patients was 46.7±9.9 years (Table-I). 52.4% of patients were male and 47.6% were female. Male: Female ratio was 1.1:1. (Table-II). 11.9% of patients had anaemia, jaundice was present in 2.4%, bradycardia in 2.4%, hypertension in 16.7%, and fever in 9.5%, lymphadenopathy in 2.4% and oedema in 7.1% (Table-III). Thyroid function tests of the patients revealed that 4(9.5%) patients had abnormal serum TSH level, while 7(16.7%) patients had abnormal serum FT<sub>3</sub> and 1(2.4%) patient had abnormal serum FT<sub>4</sub> level (Table-IV). Regarding thyroid status, most of the patients (88.1%) had normal thyroid functions i.e., euthyroid state, 4(9.5%) patients had hypothyroidism and 1(2.4%) had hyperthyroid state (Table-V).

**Table I:** *Distribution of the study patients by age* (n=42)

Age in years	Number of patients	Percentage
5-18	2	4.8
19-49	22	52.4
50-70	18	42.9
Mean±SD	46.7±9.9 years	
Range	(12 – 62) years	

**Table II:** Distribution of the study patients by sex (n=42)

Gender	Number of patients	Percentage
Male	22	52.4
Female	20	47.6

**Table III:** Distribution of the study subjects based on clinical features (n=42)

Clinical features	Frequency	Percentage
Anaemia	5	11.9
Jaundice	1	2.4
Bradycardia	1	2.4
Hypertension	7	16.7
Fever	4	9.5
Lymphadenopathy	1	2.4
Oedema		

**Table IV:** Distribution of the study subjects by thyroid function test (n=42)

Thyroid function tests	Frequency	Percentage
Serum TSH		
Normal (0.47-5.01mIU/L)	38	90.5
Abnormal (< 0.47 or >5.01 mIU/L)	4	9.5
Total	42	100.0
Serum FT3		
Normal (2.62-5.70 pmol/L)	35	83.3
Abnormal ( $< 2.62 \text{ or } > 5.70 \text{ pmol/L}$ )	7	16.7
Total	42	100.0
Serum FT4		
Normal (9.14-23.81 pmol/L)	41	97.6
Abnormal (< 9.14 or>23.81 pmol/L)	1	2.4
Total	42	100.0

<b>Table V:</b> Distribution of the study subjects by thyro	id
<i>status (n=42)</i>	

Thyroid status	Frequency	Percentage
Hypothyroid	4	9.5
Hyperthyroid	1	2.4
Euthyroid	37	88.1
Total	42	100.0

#### **DISCUSSION**

Pemphigus vulgaris, or PV for short, is a rare form of autoimmune disease that causes blisters on the skin and the mucous membranes throughout the body. It is commonly observed in people over the age of 40, but it can occur in people of any age and gender. It is generally understood that pemphigus vulgaris occurs due to a combination of both genetic factor and environmental trigger. It is known that individuals with autoimmune diseases such as pemphigus vulgaris, are at increased risk of developing other autoimmune diseases and vice-versa. 10-12

The present study was conducted to observe the effects of pemphigus vulgaris on patients' thyroid glands via evaluation of thyroid function. The mean age of the present study participants was 46.7±9.9 years, with majority being from the age group of 19-49 years. The male: female ratio of our study was 1.1:1, with 52.4% male predominance. In contrast, in some other studies, female predominance was observed.<sup>4,5</sup> Among the participants of the study, 11.9% had anaaemia, 16.7% had hypertension, 9.5% had fever and 7.1% had oedema. Some other minor features were also present in the study. These findings were different compared to other studies, where patients had comorbidities like Cushing syndrome, hypothyroidism, and fungal infection in much higher rates compared tom other comorbidities. 13,14 Thyroid functions of the participants were measured via serum TSH, FT<sub>3</sub> and FT<sub>4</sub> levels. Over 90% of the participants had normal serum TSH levels in the present study, while only 9.5% had deviations from the range values. Serum FT<sub>3</sub> test (i.e., free triiodothyronine) amount in the blood, which is a major hormone produced by the thyroid glands. We observed that 16.7% of the participants had abnormal FT<sub>3</sub> levels, while serum FT4 levels were found abnormal in only 2.4% of the patients.

Pemphigus vulgaris was observed to coexist with many of the autoimmune disorders like myasthenia gravis, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and Graves' disease.  $^{15,16}$  Moreover, evidence suggested that autoimmune thyroid diseases have been linked to pemphigus vulgaris.  $^{10-12}$  In the present study, regarding thyroid status, majority of the patients (88.1%) had euthyroid state, while 4 (9.5%) patients had hypothyroid and only 1 (2.4%) had hyperthyroid states.

There are some limitations of the present study, as it was conducted in a single hospital with small sample size due to time and budget constraints. Hence, the results may not represent the whole community. Moreover, the cross-sectional design hardly establishes any causal relationship.

## **CONCLUSION**

Our data suggest that serum  $FT_3$  is the most affected by pemphigus vulgaris; nonetheless, serum TSH and  $FT_4$  are also affected in smaller proportion in comparison to  $FT_3$  as per thyroid function tests of pemphigus vulgaris patients. We recommend that this study needs to be conducted with a large sample size and with a control group to better understand the effects of pemphigus vulgaris on the thyroid glands of patients.

# **REFERENCES**

- James WD, Berger TG, Elston DM. Andrew's Diseases of the Skin: Clinical Dermatology. 11th ed. London: Saunders Elsevier; 2011. p.448-9.
- Parameswaran A, Attwood K, Sato R, Seiffert-Sinha K, Sinha AA. Identification of a new disease cluster of pemphigus vulgaris with autoimmune thyroid disease, rheumatoid arthritis and type I diabetes. Br J Dermatol. 2015;172(3):729-38.
- Niepomniszcze H, Amad RH. Skin disorders and thyroid diseases. J Endocrinol Invest. 2001;24(8):628-38.
- 4. Pitoia F, Moncet D, Glorio R, Graciela Diaz A, Rodriguez Costa G, Carbia S, et al. Prevalence of thyroid autoimmunity in patients with pemphigus vulgaris. Medicina. 2005;65(4):307-10.
- 5. Kavala M, Kural E, Kocaturk E, Zindanci I, Turkoglu Z, Can B. The evaluation of thyroid diseases in patients with pemphigus vulgaris. ScientificWorldJournal. 2012;2012:146897.
- 6. Diven DG, Gwinup G, Newton RC. The thyroid. Dermatol Clin. 1989;7(3):547-58.
- 7. Firooz A, Mazhar A, Ahmed AR. Prevalence of autoimmune diseases in the family members of

- patients with pemphigus vulgaris. J Am Acad Dermatol. 1994;31(3 Pt 1):434-7.
- 8. McGregor AM. Immunoendocrine interactions and autoimmunity. N Engl J Med. 1990;322(24):1739-41.
- 9. Murray IP. The effect of prednisolone on Hashimoto's thyroiditis. Scott Med J. 1958;3(8):341-5.
- 10. Ansar A, Farshchian M, Farahnaki S, Farshchian M. Thyroid autoimmunity in Iranian patients with pemphigus vulgaris. J Eur Acad Dermatol Venereol. 2009;23(6):719-20.
- 11. Iino Y, Hara H, Suda T, Okada T, Baba S, Suzuki H. Co-existence of pemphigus vulgaris and Hashimoto's thyroiditis. Eur J Dermatol. 2005;15(1):40-2.
- 12. Wolf R, Feuerman EJ. Pemphigus in association with autoimmune thyroid disease. Cutis. 1981;27(4):423-4,431.

- 13. Hsu DY, Brieva J, Sinha AA, Langan SM, Silverberg JI. Comorbidities and inpatient mortality for pemphigus in the U.S.A. Br J Dermatol. 2016;174(6):1290-8.
- 14. Heelan K, Mahar AL, Walsh S, Shear NH. Pemphigus and associated comorbidities: a cross-sectional study. Clin Exp Dermatol. 2015;40(6):593-9
- Patten SF, Dijkstra JW. Associations of pemphigus and autoimmune disease with malignancy or thymoma. Int J Dermatol. 1994;33(12):836-42.
- Bartalena L, Bogazzi F, Chiovato L, Tanda ML, Martino E. Graves' hyperthyroidism and ophthalmopathy associated with pemphigus vulgaris: onset of thyroid autoimmune disease during chronic low-dose glucocorticoid therapy. J Endocrinol Invest. 1997;20(3):155-7.