

Original Research Article

Association of thyroid autoimmunity with psoriasis

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ABSTRACT

Background: Psoriasis is a chronic, relapsing, multifactorial inflammatory disorder of the skin. Psoriasis has been found to be associated with different autoimmune disorders; autoimmune thyroid disorder is one of them. Several studies have suggested an association of thyroid autoimmunity with psoriasis.

Methods: A total of 63 patients with psoriasis and equal number of age and sex matched apparently healthy subjects were included. Psoriasis area and severity index (PASI) score was calculated. Free triiodothyronine (FT3), free thyroxine (FT4), thyroid stimulating hormone (TSH), antithyroglobulin (AbTG), antithyroidperoxidase antibody (AbTPO) and TSH receptor Ab levels were measured in all of the subjects.

Results: The mean age of psoriasis patients was 35.8±16.7 years compared to 35.4±16.9 years in the control group and was found non-significant (p=0.899). Psoriasis group consisted of 63.5% males and 36.5% females, while the control group had 66.7% males and 33.3% females (p=0.709). Majority of psoriasis patients and control subjects were euthyroid (87.3% and 96.8% respectively). Anti TPO antibodies were elevated in 34.9% psoriasis patients compared to 4.8% in control group which was statistically significant (p<0.001). Anti TG Antibodies were elevated in 46.0% psoriasis patients compared to 7.9% in control group and was statistically significant (p<0.001).

Conclusions: This study showed significantly higher frequency of elevated anti TPO antibodies and anti-thyroglobulin (TG) antibodies in psoriasis patients compared to control group. So, there is association between thyroid autoimmunity and psoriasis. However, further large-scale studies are required to expand our knowledge about thyroid autoimmunity and its association with psoriasis.

Keywords: Psoriasis, Thyroid autoimmunity, Anti-thyroid peroxidase antibody, Anti-thyroglobulin antibody, Autoimmune thyroid disease

INTRODUCTION

Psoriasis is a chronic, multifactorial, recurrent inflammatory disorder of the skin. The precise prevalence of psoriasis in our nation is yet to be ascertained. Psoriasis is believed to affect 1-3% of the global population.¹ The overall incidence of psoriasis was 1.02% in a hospital-based study conducted in India.² Chronic plaque psoriasis,

erythrodermic psoriasis, guttate psoriasis, Palmoplantar psoriasis, pustular psoriasis, and inverse psoriasis are among the various forms of psoriasis. Chronic plaque psoriasis is considered the most prevalent among these. It is characterized by well-defined erythematous plaques with dry, silvery white scales that are primarily found on the extensor surfaces of both extremities, elbow, knee, scalp, palm, sole and nails.³ Genetic factors such as

predisposition to specific HLA, such as CW6 and environmental factors like stress, trauma, infection, sunlight and certain medications causes release of DNA by stressed keratinocytes, which results in the activation of cathelicidin LL-37. This causes activation of plasmacytoid dendritic cells which release INF-gamma to activate dermal dendritic cells. These cells activate Naive T cells of lymph nodes and convert them into active T cells of three subtypes: Th1, Th17 and Th22. Th1 releases IL 1, which sustains the inflammatory cascade. Th17 releases IL 17, which induces inflammation and proliferation of keratinocytes. Th22 releases IL 22, which sustains inflammatory cascades. Macrophages and natural killer (NK) cells release cytokines, including gamma INF and TNF alpha, which induce vasodilation and VEGF which induces angiogenesis.⁴ Several studies have found association of psoriasis with many autoimmune diseases, one of them is autoimmune thyroid disease (AITD). Thyroid autoimmunity is defined as loss of tolerance to thyroid proteins in a genetically susceptible individual in conjunction with environmental factors. Antibody-dependent cell-mediated cytotoxicity and the development of autoantibodies to thyroid peroxidase (TPO-Ab) and thyroglobulin (Tg-Ab) are the defining features of autoimmune thyroiditis.⁵ AITD is a thyroid-related inflammatory disease evidenced by thyroid autoantibodies, lymphocytic infiltration of the thyroid parenchyma with or without thyroid dysfunction.⁶ The two primary clinical subtypes of AITD are Graves' disease (GD) and Hashimoto's thyroiditis (HT). GD is characterized by hyperthyroidism and the presence of thyroid-stimulating hormone receptor antibodies (TRAb) in serum, whereas Hashimoto's Thyroiditis is evidenced by hypothyroidism and presence of anti-thyroid peroxidase antibodies (Anti-TPO Ab) or anti thyroglobulin antibodies (Anti TG Ab) in serum.⁷ The T3 and T4 receptors on the epidermis have been identified and proposed to play an important role in keratin synthesis, cell growth, differentiation, and proliferation of keratinocytes.^{8,9} Thyroid hormones bind to T3 and T4 receptors in the epidermis, resulting in the production of epidermal growth factor (EGF). This factor induces keratin synthesis and epidermal hyperplasia.¹⁰ The precise relationship between the pathogenesis of thyroid abnormalities and psoriasis is not yet fully comprehended and numerous inflammatory and non-inflammatory pathways have been proposed. IL 17, a cytokine that is crucial in the pathophysiology of epidermal barrier disruption, keratinocyte hyperproliferation and sustained inflammation in psoriasis, plays an important role in GD and Hashimoto's thyroiditis.¹¹⁻¹³ Additionally, thyroid dysfunction results in an increase in reactive oxygen species (ROS), which in turn affects the immune response, cell differentiation, apoptosis, and cell proliferation, all of which are observed in psoriasis.¹⁴ Signal transducer and activator of transcription (STAT) 4 gene polymorphisms are linked to an elevated risk of developing various autoimmune diseases, such as AITD and.¹⁵ Psoriasis and AITD share certain pathophysiological characteristics including inflammation and Th1-mediated adaptive

immune responses. Additionally, the severity of psoriasis has been demonstrated to be correlated with AITD and thyroid dysfunction in numerous studies.

METHODS

This was conducted as a case-control study. Department of Dermatology and Venereology, BMU. Skin biopsy for Histopathology was done in Dept. of Histopathology, BMU. Serum FT3, FT4, TSH, Anti TPO, Anti Thyroglobulin and anti TSH receptor antibody levels were done in the Department of Biochemistry and Molecular Biology, BMU. The total duration was 12 months, from the acceptance of the protocol in November 2023 until October 2024. Sample size was increased to 63 participants in each group.

Group A

Clinically and/or histopathologically detected psoriasis patients attending in the Department of Dermatology and Venereology, BMU.

Group B

Age and sex matched apparently healthy subjects of psoriasis or staffs of BMU.

Inclusion criteria

Patients diagnosed as psoriasis clinically and/or histopathologically, able to understand instructions and communicate well, age and sex matched apparently healthy subjects, absence of psoriasis, able to give informed written consent were included in study.

Exclusion criteria

Known case of chronic kidney disease, chronic liver disease and malabsorption syndrome, pregnancy, smokers, alcoholics, patients taking drugs like lithium, iodine, steroids, dopamine, anticonvulsant drugs and interferon were excluded.

Data collection technique

This was a case-control study. Steps of data collection were as follows- non-satisfactory. All patients were interviewed by structured questionnaire. A proper diagnostic work up of psoriasis was made by taking detail history and clinical examination. History included duration of disease, course of disease, treatment history, concomitant illnesses, personal habits such as smoking, alcohol, family history of psoriasis, diabetes, and cardiovascular disease.

Biochemical analysis

Venous samples of 8 ml were taken using sterile syringe from antecubital vein after full aseptic condition in the next

morning from subjects after 12 hours of overnight fasting. Samples were collected in EDTA tube and were kept vertically in a rack for 40 mins. Then the blood sample was centrifuged at 1500 rpm for 15 mins. Then 4 microlitres of serum was collected by a micropipette and kept in an aliquot. Serum FT3, FT4, TSH, Anti TPO Ab, Anti TG Ab and TSH receptor Ab were estimated using automated analyzer, SIEMENS Atellica Immunoassay System in the Department of Biochemistry and Molecular Biology, BMU.

Data processing and analysis

Data was collected on proposed data sheets and was recorded in digital formats for analysis. Continuous variables were expressed as mean and standard deviation (SD) whereas categorical variables were summarized using numbers and percentages. The student's t-test or Mann-Whitney U test was used to compare continuous variables for normal distributed data and skewed distributed data respectively. A Statistical analysis was conducted by expert statistician of this institute using SPSS software (version 23). The value of $p < 0.05$ was considered statistically significant.

Ethical consideration

An approval of the study protocol was obtained from the IRB of BMU before the commencement of the study. The eligibility of everyone was assessed, and they were informed about the procedure and the study objectives and that there was no harm to the individuals by inclusion in the study. Individuals were also informed that they could refuse to participate or to withdraw at any time. Everyone was interviewed who willingly took part in the study with consent and individual's confidentiality were strictly maintained.

RESULTS

Table 1 presents the baseline characteristics of the study participants. The mean age was 35.4 ± 16.9 years (range, 7-84 years) in group-A and was 35.4 ± 16.9 years (range, 7-84 years) in group-B, showing no statistically significant difference ($p = 0.899$). Majority of the psoriasis cases as well as controls were male (63.5% in cases and 66.7% control), difference was not significant ($p = 0.709$). Therefore, both case and control groups were sex matched.

Table 2 describes the clinical presentation of the psoriasis patients. The majority (77.8%) had psoriasis for ≤ 5 years, while 22.2% had a duration of > 5 years. All the patients had chronic plaque psoriasis. The majority of patients (73.0%) had a PASI score > 12 , indicating severe psoriasis, and 66.7% had more than 10% of body surface area (BSA) involvement.

Table 3 presents the thyroid function test (TFT) results for the study population. TSH (mIU/l) values FT3 (pmol/l) ($p = 0.088$) and TSH receptor antibody (iu/l) ($p = 0.747$)

levels did not differ significantly between two groups. But anti-TPO antibody (IU/ml) ($p = 0.002$) and anti TG antibody (IU/ml) ($p < 0.001$) were significantly higher in psoriatics than control; whereas FT4 (pmol/l) ($p = 0.035$) was significantly lower in psoriatics than control. TSH levels were found normal for most participants in both groups, though 9.5% of group B had elevated TSH levels compared to 1.6% in group A; difference was not significant ($p = 0.111$). A notable finding was the significantly higher frequency of elevated anti-TPO antibody and TG antibodies in group A (psoriasis patients), with 34.9% having elevated anti-TPO antibodies compared to 4.8% in group B ($p < 0.001$). Similarly, 46.0% of group-A had elevated TG antibodies, while only 7.9% of group-B had elevated anti thyroglobulin antibodies ($p < 0.001$), suggesting a significant relationship between thyroid autoimmunity and psoriasis.

Table 4 shows comparison of thyroid function tests (TFT) and clinical parameters in the case group ($n = 63$). Majority of participants with abnormal TFTs being ≤ 40 years (78.6%) compared to normal TFTs (54.3%) ($p = 0.045$). There was no significant difference in the proportion of males and females ($p = 0.907$). Regarding the duration of illness, the majority of participants with both normal and abnormal TFTs had the disease for ≤ 5 years ($p = 0.278$). Patients with PASI > 12 had more abnormal TFT (82.1%) compared to the normal (65.7%) with no statistical significance ($p = 0.144$).

Table 5 shows comparison of TFT results and clinical parameters in the control group. The age was similar between those with normal and abnormal TFT, with similar proportions of participants ≤ 40 years (63.9% normal versus 66.7% abnormal) and > 40 years (36.1% normal versus 33.3% abnormal) ($p = 0.819$). Gender distribution also showed no significant difference, with 69.4% males in the normal group and 63.0% males in the abnormal group ($p = 0.589$).

Table 6 shows association between anti-TPO antibody levels and clinical parameters in the case group. Regarding age, 75.6% of individuals with normal anti-TPO levels were ≤ 40 years, compared to 45.5% in elevated anti-TPO group ($p = 0.017$). Regarding gender, 58.5% of males and 41.5% of females were in the normal group, while 72.7% of males and 27.3% of females were in the elevated anti-TPO group ($p = 0.265$). Regarding disease duration, 75.6% of patients with ≤ 5 years of illness had normal anti-TPO levels, compared to 72.7% in those with elevated anti-TPO Ab ($p = 0.572$). Disease severity, as measured by the PASI score, showed no significant association with elevated anti-TPO level ($p = 0.577$). However, BSA involvement was nearly significant, with 72.7% of patients with elevated anti-TPO levels having BSA $> 10\%$, compared to 58.5% in those with normal anti-TPO levels ($p = 0.062$).

Table 7 shows the association between TG antibody levels and clinical parameters in the case group. Regarding Age, 73.5% of patients with normal anti TG antibodies were

≤40 years, compared to 55.2% of those with elevated levels (p=0.128). Gender distribution also showed no significant difference, with 67.6% of males and 32.4% of females in the normal group, and 58.6% of males and 41.4% of females in the high TG group (p=0.458). However, a significant relationship was seen between disease duration and high TG antibodies, as 89.7% of

patients with a disease duration ≤5 years had high TG antibodies, compared to 67.6% in the normal group (p=0.036). Disease severity, indicated by PASI score, did not show a significant relationship with elevated TG levels (p=0.299). Similarly, BSA involvement shows 75.9% of patients with high TG levels having BSA >10%, compared to 58.8% in the normal group (p=0.153).

Table 1: Baseline characteristics of the study subjects.

Baseline characteristics	Study group N (%)		P value
	Group A, (n=63)	Group B, (n=63)	
Age (in years)			
<20	11 (17.5)	12 (19.0)	0.986
21-30	16 (25.4)	15 (23.8)	
31-40	14 (22.2)	14 (22.2)	
41-50	13 (20.6)	14 (22.2)	
51-60	5 (7.9)	3 (4.8)	
>60	4 (6.3)	5 (7.9)	
Mean±SD (Range)	35.8±16.7 (7-84)	35.44±16.9 (7-84)	0.899
Sex			
Male	40 (63.5)	42 (66.7)	0.709
Female	23 (36.5)	21 (33.3)	

Table 2: Clinical presentation of psoriasis patients, (n=63).

Clinical parameters	N	Percentage (%)
Duration of illness		
Mean±SD (years)	3.56±1.63	
≤5 years	49	77.8
>5 years	14	22.2
Type of psoriasis		
Plaque psoriasis	63	100.0
PASI score		
Mean±SD	13.37±2.10	
≤12	17	27.0
>12	46	73.0
BSA		
Mean±SD	11.43±1.36	
≤10%	21	33.3
>10%	42	66.7

Table 3: Comparison of TFT between two groups.

TFT	Study group		P value
	Group A, (n=63)	Group B, (n=63)	
TSH (mIU/l) [median (IQR)]	1.74 (1.17-2.87)	2.11 (1.17-2.80)	0.684
Low	2 (3.2%)	1 (1.6%)	0.111
Normal	55 (87.3%)	61 (96.8%)	
Elevated	6 (9.5%)	1 (1.6%)	
FT3 (pmol/l)	4.52±1.03	4.78±0.55	0.088
Low	3 (4.8%)	0 (0.0%)	0.211
Normal	40 (63.5%)	38 (60.3%)	
Elevated	20 (31.7%)	25 (39.7%)	
FT4 (pmol/l)	11.80±2.55	12.62±1.69	0.035
Low	5 (7.9%)	0 (0.0%)	0.058
Normal	58 (92.1%)	63 (100.0%)	
Elevated	0 (0.0%)	0 (0.0%)	

Continued.

TFT	Study group		P value
	Group A, (n=63)	Group B, (n=63)	
Anti-TPO Ab (IU/ml) [median (IQR)]	1.21 (0.64-59.10)	0.71 (0.37-1.38)	0.002
Normal	41 (65.1%)	60 (95.2%)	<0.001
Elevated	22 (34.9%)	3 (4.8%)	
Anti TG Ab (IU/ml) [median (IQR)]	3.67 (0.54-21.84)	1.11 (0.94-1.59)	<0.001
Normal	34 (54.0%)	58 (92.1%)	<0.001
Elevated	29 (46.0%)	5 (7.9%)	
TSH receptor Ab (iu/l)	1.17±0.49	1.15±0.22	0.747
Normal	63 (100.0%)	63 (100.0%)	-
Elevated	0 (0.0%)	0 (0.0%)	
Thyroid status			
Hypothyroidism	3 (4.8%)	1 (1.6%)	1.000
Hyperthyroidism	1 (1.6%)	0 (0.0%)	
Subclinical hypothyroidism	3 (4.8%)	0 (0.0%)	
Subclinical hyperthyroidism	1 (1.6%)	1 (1.6%)	
Euthyroid	55 (87.3%)	61 (96.8%)	

Table 4: Comparison of TFT and clinical parameters in case group.

Clinical parameters	TFT impressions N (%)		P value
	Normal, (n=35)	Abnormal, (n=28)	
Age (in years)			
≤40	19 (54.3)	22 (78.6)	0.045
>40	16 (45.7)	6 (21.4)	
Gender			
Male	22 (62.9)	18 (64.3)	0.907
Female	13 (37.1)	10 (35.7)	
Duration of illness			
≤5 years	29 (82.9)	20 (71.4)	0.278
>5 years	6 (17.1)	8 (28.6)	
PASI score			
≤12	12 (34.3)	5 (17.9)	0.144
>12	23 (65.7)	23 (82.1)	
BSA			
≤10%	16 (45.7)	5 (17.9)	0.020
>10%	19 (54.3)	23(82.1)	
TSH (µIU/mL) [median (IQR)]	1.56 (1.09-2.52)	2.21 (1.21-4.52)	0.067
FT3 (pg/dL)	4.33±0.36	4.76±1.47	0.099
FT4 (ng/dL)	12.04±1.51	11.51±3.45	0.416

Table 5: Comparison of TFT and clinical parameters in control group.

Clinical parameters	TFT impressions		P value
	Normal, (n=36)	Abnormal, (n=27)	
Age (in years)			
≤40	23 (63.9%)	18 (66.7%)	0.819
>40	13 (36.1%)	9 (33.3%)	
Gender			
Male	25 (69.4%)	17 (63.0%)	0.589
Female	11 (30.6%)	10 (37.0%)	
Thyroid hormone			
TSH (µIU/mL) [median (IQR)]	2.12 (1.36-2.80)	1.86 (1.09-2.47)	0.420
FT3 (pg/dL)	4.45±0.37	5.22±0.44	<0.001
FT4 (ng/dL)	12.48±1.70	12.80±1.68	0.463

Table 6: Association between anti-TPO antibody and clinical parameters in case group.

Clinical parameters	Anti-TPO antibody N (%)		P value
	Normal, (n=41)	Elevated, (n=22)	
Age (in years)			
≤40	31 (75.6)	10 (45.5)	0.017
>40	10 (24.4)	12 (54.5)	
Gender			
Male	24 (58.5)	16 (72.7)	0.265
Female	17 (41.5)	6 (27.3)	
Duration of illness			
≤5 years	31 (75.6)	16 (72.7)	0.753
>5 years	10 (24.4)	6 (27.3)	
PASI score			
≤12	12 (29.3)	5 (22.7)	0.577
>12	29 (70.7)	17 (77.3)	
BSA			
≤10%	17 (41.5)	4 (18.2)	0.062
>10%	24 (58.5)	18 (81.8)	

Table 7: Association between TG antibody and clinical parameters in case group.

Clinical parameters	TG antibody N (%)		P value
	Normal, (n=34)	Elevated, (n=29)	
Age (in years)			
≤40	25 (73.5)	16 (55.2)	0.128
>40	9 (26.5)	13 (44.8)	
Gender			
Male	23 (67.6)	17 (58.6)	0.458
Female	11 (32.4)	12 (41.4)	
Duration of illness			
≤5 years	23 (67.6)	26 (89.7)	0.036
>5 years	11 (32.4)	3 (10.3)	
PASI score			
≤12	11 (32.4)	6 (20.7)	0.299
>12	23 (67.6)	23 (79.3)	
BSA			
≤10%	14 (41.2)	7 (24.1)	0.153
>10%	20 (58.8)	22 (75.9)	

DISCUSSION

The aim of this study was to evaluate the correlation between psoriasis and thyroid autoimmunity. The study included 63 patients with psoriasis and an equal number of controls who were matched by age and sex. Psoriasis and autoimmune thyroid disorders share some common pathophysiological features, such as Th1-predominant adaptive immune reaction. Hence, the relationship between autoimmune thyroid disorders and psoriasis has been hypothesised and studied. In recent years, several observational studies regarding the association between psoriasis and AITD were published in succession, but the results of the studies were inconsistent.^{13,16-18} Mean age of Psoriasis patients in this study was 35.8±16.7 years. Psoriasis is documented to be more frequent in the middle-aged population in several.¹⁸⁻²⁰ In our study, there is a male predominance among the Psoriasis patients (63.5%). Male

predominance in psoriasis patients was also reported in previous studies.^{18,20-22} The majority of Psoriasis patients had severe psoriasis, as evidenced by a PASI score of >12 in 73% of patients and a body surface area of >10 in 66.7% of patients. In terms of duration, the majority of psoriatic patients (77.8%) had disease duration of up to five years. Finding of our investigation was in line with the study conducted by Yumnam et al.²³ The results of the TFT were compared between the case and control groups in the present study. The majority of patients with psoriasis as well as control group had normal TSH levels (87.3% and 96.8% respectively, p=0.122). Majority of psoriasis patients and control group had normal FT3 level (63.5% and 60.3% respectively, p=0.165). Similarly, majority of patients with psoriasis and all the healthy controls had normal FT4 levels (92.1% and 100% respectively). The majority of participants were euthyroid (87.3% in psoriasis group and 96.8% in control group). The prevalence of

overt hypothyroidism was 4.8% in psoriasis group and only 1.6% in control group. The results of the TFT were compared between the case and control groups in the present study. The majority of patients with psoriasis as well as control group had normal TSH levels (87.3% and 96.8% respectively, $p=0.111$). Majority of psoriasis patients and control group had normal FT3 level (63.5% and 60.3% respectively, $p=0.211$). Similarly, majority of patients with psoriasis and all the healthy controls had normal FT4 levels (92.1% and 100% respectively, $p=0.058$). TG antibodies were also raised in psoriasis patients compared to control group in the current study (46.0% versus 7.9%, $p<0.001$). Among the psoriasis patients having thyroid dysfunction a significant number of patients had higher PASI score (>12) and higher body surface area (>10) (82.1% and 82.1% respectively). This was consistent with the case-control study conducted by Arican et al which discovered that psoriasis patients with altered thyroid functions had a substantially higher PASI score than euthyroid psoriasis patients.²⁴ Among the psoriasis patients with elevated anti-TPO antibodies, a greater number of patients had a higher PASI score (>12) and body surface area ($>10\%$) (77.3% and 81.8% respectively). The results of our study were in line with those of a study conducted by Yumnam et al.²³ In the same way, psoriasis patients with elevated TG antibodies exhibited a higher PASI score and body surface area (79.3% and 75.9% respectively). Nevertheless, there was no significant difference among psoriasis patients with normal and elevated anti-TG antibodies in terms of age, gender and severity of psoriasis. This result was also relevant with the research conducted by Yumnam et al.²³

CONCLUSION

The present study demonstrated that elevated anti-TPO antibodies and elevated anti thyroglobulin antibodies are more frequent in psoriasis patients compared to healthy controls. So, it may be concluded that there is an association between thyroid autoimmunity and psoriasis.

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Conflict of interest: None declared

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

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