Brief Report

The Association of Thyroid Dysfunction with Chronic Plaque Psoriasis: A Hospital-Based Retrospective Descriptive Observational Study

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Abstract

Background: Associations among thyroid dysfunction, thyroid autoimmunity, and clinical features including age, gender, disease duration, and severity of psoriasis is less studied. **Objectives:** To study frequency of thyroid dysfunction and thyroid autoimmunity and examine association among thyroid dysfunction, thyroid autoimmunity, and clinical features including gender, age, duration, and severity of psoriasis. **Material and Methods:** The medical records of 290 (m:f 2.15:1) patients aged 13–75 years with plaque psoriasis were analyzed for thyroid dysfunction and thyroid autoimmunity. Thyroid dysfunction was defined as 10% variation in any thyroid hormone levels. Thyroid autoimmunity was diagnosed from presence of antithyroid peroxide (anti-TPO) antibodies. **Results:** The majority, 57.9% patients, was aged ≥41 years (Type-2 psoriasis) and duration of disease was <5 years in 58.6% patients. Mild and moderate to severe psoriasis was present in 58.3% and 41.7% patients, respectively. Deranged thyroid functions were present in 29 (10%) patients. Hypothyroidism and hyperthyroidism occurred in 5.4% and 2.7% patients, respectively. Anti-TPO antibodies were observed in 13.5% patients; 11had hypothyroidism. There was no statistically significant difference in gender, age, duration, and severity of psoriasis when compared with patients having normal thyroid function tests. **Conclusion:** The study suggests possible thyroid dysregulation and thyroid autoimmunity in psoriasis but results need careful interpretation and clinical application. Their significance as standalone risk factor for the chronicity, severity, and relapses in psoriasis or whether thyroid hormone replacement or antithyroid drugs become a useful therapeutic option remains tenuous at best for need of more robust evidence. Retrospective, observational, cross-sectional study design, small number of patients, and lack of controls remain major limitations.

Keywords: *Hyperthyroidism, hypothyroidism, plaque psoriasis, thyroid autoimmunity, thyroid dysfunction*

Introduction

Genetic, immunologic and metabolic mechanisms have been implicated in etiopathogenesis of psoriasis that remains largely elusive. Currently, psoriasis is considered a multiorgan systemic disease due to chronic inflammation. Epidermal hyperproliferation is considered secondary to Th1 type of immune reaction and inflammatory milieu in the dermal microenvironment induced by inflammatory cells, elevated TNF-α and other cytokines, chemokines and growth factors.[1] This inflammation is also implicated for enhanced risk of metabolic syndrome or its individual components (obesity, dyslipidemia, atherosclerosis, type-2 diabetes mellitus), cardiovascular disease (hypertension, myocardial infarction, stroke), chronic kidney disease, cancer, Crohn's disease, and depression that significantly impair quality of life in psoriatics.[2-5] The role of various hormones such as thyroid hormones, thyroid stimulating hormone, cortisol, and prolactin in the pathogenesis of psoriasis has been studied previously.[6-8] Thyroid hormone levels have been reported to change during the active phase of psoriasis and psoriasis showed improvement in patients with hyperthyroidism, suggesting a possible role of thyroid hormones in the pathogenesis of psoriasis.[8] The T3 receptors on the skin have been identified and suggested to play a role in keratin synthesis, cell growth, and differentiation and proliferation of keratinocytes.[9-11] T3 and T4 have hyperproliferative effect on the skin via epidermal growth factor which is increased by thyroid hormones.[8,12] Reported resolution of

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psoriasis following surgical thyroidectomy and usefulness of antithyroid drug propyl thiouracil in topical and systemic treatment of psoriasis by some workers further support this hypothesis.[9,13-16] However, how exactly pathophysiology of thyroid abnormalities and psoriasis is interlinked remains less understood and several inflammatory or non-inflammatory pathways have been proposed. Interleukin (IL)-17, one of the important cytokines in the pathophysiology of epidermal barrier disruption, keratinocyte hyperproliferation, and sustained inflammation in psoriasis, also plays an important role in Graves' disease and Hashimoto thyroiditis.[17-19] Similarly, various other chemokines such as CCL2 (monocyte chemo attractant protein-1; MCP1), CCL22 (macrophage-derived chemokine; MDC), CXCL9 (monokine induced by IFN-γ; Mi-g), and CXCL10 [interferon (IFN)-inducible protein-10; IP-10] are expressed both in autoimmune thyroiditis and psoriasis.[20-25] Furthermore, a prolonged clinical course of both psoriatic arthritis and Graves' disease has been attributed to CCL2- and CCL22-meditated shift from a Th1- to Th2-type immune response.[22,24,25] Besides, both psoriasis and autoimmune thyroid disease along with several other autoimmune diseases have been associated with disruption in the nuclear factor-κB (NF-κB) signaling pathway.[26] However, any association between thyroid dysfunction and psoriasis remains unclear and the exact role of thyroid hormones in etiopathogenesis of psoriasis needs elucidation by experimental studies for their antiproliferative effect or that of antithyroid drugs on keratinocytes. Nevertheless, it may be useful to assess thyroid functions in patients with uncontrolled and relapsing psoriasis for a holistic management. We studied the frequency of thyroid dysfunction and thyroid autoimmunity in patients with psoriasis and also examined the associations among thyroid dysfunction, thyroid autoimmunity, and clinical features including age, gender, disease duration, and severity of psoriasis for paucity of relevant data in Indian context.

Material and Methods

The medical records of patients with chronic plaque psoriasispresenting in dermatology clinicbetween Jan 2014 and Dec 2018 were analyzed retrospectively for this hospital-based descriptive observational study. The study was approved by Institutional Ethics Committee (regn no. ECR/490/Inst/HP/2013/RR-16).The demographic profile, duration and evolution of skin disease, detailed medical history and clinical details of psoriasis were recorded. Children aged <12 years, pregnant and lactating women, and patients on antipsoriatic or immunomodulator medications (methotrexate, folic acid, ciclosporin, acitretin, biologicals), or other drugs effecting thyroid metabolism (corticosteroids, anticonvulsants, NSAIDs, furosemide, lithium, amiodarone), or with psoriatic arthritis, palmoplantar psoriasis, pre-existing thyroid disorders on treatment, hypertension, diabetes mellitus, morbid obesity (BMI >30kg/m^2), hepatorenal disease, collagen vascular disorders, or malignancy were excluded.The diagnosis of psoriasis was clinical and the severity of psoriasis was assessed by body surface area (BSA) measured by Wallace rule of nine and psoriasis area severity index (PASI) score as described by Fredriksson and Pettersson.[27] The severity of psoriasis was defined as mild (PASI <6 or BSA 10%), moderate (PASI 6–12 or BSA 11–20%), or severe (PASI >12 or BSA >20), giving precedence to PASI score in case of ambiguity.[28]

After overnight fasting, blood sample (5 ml) was collected between 8am and 10am by antecubital venepuncture for relevant tests performed in institutional central research laboratory. Complete blood counts and serum biochemistry including blood sugar, lipid profile, and hepatorenal function tests were carried out by standard protocols. Thyroid function tests and antithyroid peroxide antibody (Anti-TPO Ab) were measured using chemiluminescent immunoassay (CLIA). Thyroid dysfunction was defined as 10% variation in any thyroid hormone levels (triiodothyronine [T3, normal 6-202 ng/dl], thyroxine [T4, normal 4.4-11.6 ng/dl] and thyroid-stimulating hormone [TSH, normal 0.5–5.4 μIU/ml]). Subclinical hypothyroidism was defined as high TSH and normal T3 and T4 levels and subclinical hyperthyroidism was defined for low TSH and normal T3 and T4 levels along with absence of thyroid-related clinical features. A diagnosis of probable thyroid disease was considered in case of discordant results.The presence of anti-TPO Abs indicated thyroid autoimmunity.

Data analysis

The medical records of six patients were incomplete and were excluded from final analysis. MS Word Excel software was used to tabulate and analyze the data. The continuous data are presented as mean and categorical variables are presented as frequencies and percentages. The Chi-square test and student *t*-test were used for the statistical analysis of the categorical and parametric data, respectively. A $P < 0.05$ calculated at 5% level (95% confidence limit) was considered statistically significant.

Results

Table 1 depicts baseline clinicodemographic features and thyroid function abnormalities of 290 patients comprising 190 (68.3%) men and 92 (31.7%) women (m:f 2.15:1) aged between 13 and 75 years (mean 41.9 years) at presentation. The majority, 168 (57.9%) patients were aged between 41 and 75 years (type-2 psoriasis). The duration of psoriasis varied between1 month and 30 years (mean 5.1 years) and the majority, 170 (58.6%) patients had presented within 5 years. The disease was mild in 169 (58.3%) patients, while 121 (41.7%) patients had moderate to severe psoriasis. Deranged thyroid functions

Table 1: Baseline characteristics of psoriasis patients

Baseline characteristics		Thyroid function *n*=290 (%)
Gender	Males (M)	198 (68.3)
	Females (F)	92 (31.7)
	M: F	2.15:1
Age in years	Range	13-75
	Mean	41.9
	≤20	14 (48.3)
	21-30	49 (16.9)
	31-40	59 (20.3)
	41-50	94 (32.1)
	51-60	48 (16.55)
	>60	26 (8.96)
Duration of psoriasis	Range	1mo-30 years
	Mean	5.11 years
	<5 years	170 (58.6)
	5-10 years	81 (27.9)
	>10 years	39 (13.4)
PASI score (severity)	<6 (mild)	169 (58.3)
	6-12 (moderate)	80 (27.6)
	>12 (severe)	41 (14.1)
BSA (severity)	<10% (mild)	165 (56.9)
	10-20% (moderate)	72 (24.8)
	>20%(severe)	53 (18.3)
Deranged TFT *n*=29 (10%)	SubclinicalHypothyroidism	21 (72.4)
	Subclinical Hyperthyroidism	01 (3.4)
	Probable hypothyroidism	05 (17.2)
	Probable hyperthyroidism	02 (6.9)
Anti TPO antibodies *n*=39 (13.5%)	Euthyroid	28 (71.8)
	Hypothyroidism	11 (28.2)

BSA=Body surface area; PASI=Psoriasis area severity index; TFT=Thyroid function tests; TPO=Thyroid peroxide; mo, month

were present in 29 (10%) patients consistent with subclinical hypothyroidism in 21 (5.4%) and subclinical hyperthyroidism in one (2.7%) patient, respectively. A diagnosis of probable thyroid disease; hypothyroidism in five and hyperthyroidism in two patients was considered because of discordant results.Thirty-nine (13.5%) patients demonstrated elevated anti-TPO Ab levels indicating autoimmune thyroiditis and 11 (28.2%) of them showed serodiagnosis of hypothyroidism.

Comparative clinicoepidemiologic features of patients with normal thyroid function tests and thyroid dysfunction are shown in Table 2. Greater number of males than females (58.6% vs. 41.4%), and patients aged above 41 years than younger ones (55.2% vs. 44.8%), having psoriasis for more than 5 years than 5 years or less (51.7% vs. 48.3%), or moderate to severe psoriasis (both by PASI score and BSA involvement) than mild disease (51.7% vs. 48.3%) showed thyroid dysfunction. However, there was no statistically significant difference in gender, age, duration, and severity of psoriasis when compared with patients having normal thyroid function tests.

Table 3 depicts comparative clinicoepidemiologic features of normal patients and those having thyroid autoimmunity with no statistically significant difference in gender, age, duration, and severity of psoriasis. Men and patients aged above 41 years outnumbered women and younger patients to have autoimmunity (58.6% vs. 41.4%) and (55.2% vs. 44.8%), respectively. However, greater number of patients with thyroid autoimmunity showed mild disease both in terms of PASI score (66.7% vs. 57%) and BSA involved (74.4% vs. 54.2%).

Discussion

The overall clinico-epidemiologic features in our study subjects, majority comprising males, aged above 41 years and having type-2 psoriasis of more than 5-year duration with remissions and relapses corroborates previous reports.[29-32] However, it is possible that exclusion of females, as in most studies, accounts for their number being less in this study. Although no significant association between psoriasis and thyroid disease has been observed in U.S. based National Health and Nutrition Examination Survey data analysis, thyroid abnormalities in psoriasis patients are not uncommon and presence of anti-TPOAb, hypothyroidism and hyperthyroidism were associated with prevalent psoriatic disease, particularly in patients with psoriatic arthritis, in a recent meta-analysis.[33-35] Arican *et al*.[36] observed elevated levels of at least one thyroid hormone and high PASI score in 22% patients in a case-control study. They imputed high PASI score to excessive thyroid hormones because of direct or indirect role played byT3 receptors in keratin synthesis and resultant psoriasis severity. Hyperthyroidism in 4%, hypothyroidism in 3%, and anti-TPO Ab in 9% patients, respectively, were also reported in another study.[37] Recently, Manvi *et al*.[30] reported prevalence of hypothyroidism with elevated anti-TPO Ab, suggestive of autoimmune thyroid dysfunction in their 8.6% patients. However, the prevalence of thyroid autoimmunity has been not found different between psoriatic patients and normal population.[37,38] We also observed deranged thyroid status in 10% patients and majority, 72.4% of them had subclinical hypothyroidism while 28.2% of 39 patients with autoimmunity also had hypothyroidism. Comparatively, hyperthyroidism was noted in fewer patients only. However, the interpretation of these observations remains complex in the absence of any statistically significant difference between various clinicoepidemiologic parameters between psoriatic patients with normal and abnormal thyroid function tests or autoimmunity as was also noted by Borges *et al*.[39] It remains distinctly possible that the pattern of biochemistry indicative of mild hypothyroidism in our majority patients reflects a general trend of its prevalence of 4–10% in general population which is still higher in the elderly particularly affecting up to 20% women aged 60 years and above.[40] We also cannot rule out with impunity a possibility

Table 2: Characteristics of psoriasis patients with abnormal thyroid functions

Baseline characteristics		Thyroid function		
		Normal *n*=261 (%)	Abnormal *n*=29 (%)	*P*
Gender	Males (M)	181 (69.3)	17 (58.6)	0.2397
	Females (F)	80 (30.7)	12 (41.4)	
	M: F	2.26:1	1.42:1	
Age in years	Range	13-75	18-75	
	Mean	43.2	30.3	
	≤40 years	109 (41.8)	13 (44.8)	0.7566
	≥41 years	152 (58.2)	16 (55.2)	
Duration of psoriasis	Range	1mo-30 years	6mo-22 years	
	Mean	5.11 years	5.09 years	
	≤5 years	156 (59.8)	14 (48.3)	0.2337
	>5 years	105 (40.2)	15 (51.7)	
PASI score (severity)	≤6 (mild)	155 (59.4)	14 (48.3)	0.2509
	>6(moderate to severe)	106 (40.6)	15 (51.7)	
BSA	<10% (mild)	150 (57.5)	15 (51.7)	0.5503
	≥10% (moderate to severe)	111 (42.5)	14 (48.3)	

BSA=Body surface area; PASI=Psoriasis area severity index; mo=Month. *P*<0.05 calculated at 5% level (95% confidence limit) was considered statistically significant

Table 3: Characteristics of psoriasis patients with abnormal Anti TPO Ab

Baseline characteristics		Anti-TPO Antibody		
		Normal *n*=251 (%)	Abnormal *n*=39 (%)	*P*
Gender	Males (M)	173 (68.92)	25 (64.10)	0.5498
	Females (F)	78 (31.08)	14 (35.90)	
	M: F	2.22:1	1.79:1	
Age	Range	13-75	16-65	
	Mean	42.2	39.0	
	≤40 years	99 (39.4)	23 (59.0)	0.0213
	≥41 years	152 (60.6)	16 (41.0)	
Duration of psoriasis	Range	1mo-30 years	6mo-30 years	
	Mean	5.06 years	5.39 years	
	≤5 years	144 (57.4)	26 (66.7)	0.2734
	>5 years	107 (42.6)	13 (33.3)	
PASI score (severity)	≤6 (mild)	143 (57.0)	26 (66.7)	0.2539
	>6(moderate to severe)	108 (43.0)	13 (33.3)	
BSA	<10% (mild)	136 (54.2)	29 (74.4)	0.5503
	≥10% (moderate to severe)	115 (45.8)	10 (25.6)	

BSA=Body surface area; PASI=Psoriasis area severity index; mo=Month, TPO=Thyroid peroxide. *P*<0.05 calculated at 5% level (95% confidence limit) was considered statistically significant

of non-thyroid illness (sick euthyroid syndrome) defined as abnormal thyroids function tests usually in patients with acute or chronic systemic illnesses including organic and psychiatric diseases.[41] This seems logical in view of the emerging evidence that favors psoriasis being more of an autoimmune systemic disease of chronic inflammation and multiorgan complications causing significant psychosocial distress. However, whether thyroid hormone replacement, surgical thyroidectomy, or propyl thiouracil becomes a useful therapeutic option in these patients, or these serological changes reflect associated pathology or is just an adaptive response to stress to lower the metabolic rate to the benefit of patient needs further elucidation. The presence of thyroid autoimmunity and normal thyroid function tests in this study observed as elevated serum anti-TPO Ab concentration in 13.5% patients and 71.8% of them with euthyroid status indicating possible subclinical autoimmune thyroiditis also needs careful interpretation. This is important as assay interference by cross-reacting heterophilic (intrinsic) antibodies such as human anti-animal antibodies, auto antibodies to TSH, T4 or T3, or nonspecific antibodies can cause unpredictable results in 0.03–3% of all samples tested for thyroid autoimmunity.[42,43]

Limitations

The hospital-based retrospective, observational, cross-sectional study design, small number of patients especially with psoriatic arthritis, lack of controls, no

screening for concurrent autoimmune or other systemic disorders, anti-thyroid antibodies other than anti-TPO Ab, and no follow-up for thyroid status or therapeutic outcome remain major limitations.

Conclusion

Deranged thyroid status in 10% patients and thyroid autoimmunity in 13.5% patients with subclinical hypothyroidism in majority suggests thyroid dysfunction and autoimmunity in psoriasis patients in this study. However, the significance of thyroid dysfunction as a risk factor for the chronicity, severity, and relapses in psoriasis appears tenuous at best for want of robust evidence. Whether thyroid dysfunction/autoimmunity is a culprit or bystander in the etiopathogenesis and overall systemic inflammatory process in psoriasis or treatment with antithyroid drugs can be an option in psoriasis needs confirmation with well-designed experimental and prospective clinical studies.

Statement of ethics

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2013. All patients were provided treatment and care as per standard guidelines. The authors also certify that they have obtained all appropriate patient consent forms. In the form, the patients or their parents/guardians have given their consent for the patient's images and other clinical information to be reported in the journal. The patient/parents/guardians understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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