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Autoimmune thyroiditis in psoriatic disease

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ABSTRACT

Objectives. To assess autoimmune thyroiditis prevalence in subclinical and clinical psoriatic arthritis (PsA).

Materials and methods. 45 female adult Egyptian patients with psoriatic disease were classified into 3 equal groups: PsA, subclinical PsA, and psoriasis. A full assessment was done including Health Assessment Questionnaire, Psoriasis Area Severity Index (PASI), Leeds Enthesitis Index (LEI), PsA disease activity score (DAPSA), MAdrid Sonographic Enthesitis Index (MASEI), thyroid hormones (TSH, FT4, and FT3), thyroglobulin and thyroid peroxidase antibodies (Tg and TPO Abs), and thyroid ultrasound.

Results. Thyroid abnormalities prevalence was: 33.3% with subclinical hypothyroidism, 80% with positive TPO Ab, and 46.7% with positive Tg Ab in PsA group, 26.7% with subclinical hypothyroidism, 60% with positive TPO Ab, and 33.3% with positive Tg Ab in subclinical PsA group and none in psoriasis group. PsA patients had higher TPO Ab levels compared to psoriasis patients with high statistical significant difference and lower FT3 levels compared to psoriasis patients with statistical significant difference. In subclinical PsA group, MASEI was positively correlated with TPO Ab with high statistical significance and with FT3 and Tg Ab with statistical significance, FT4 was negatively correlated with LEI with high statistical significance, and FT4 was correlated with PASI with statistical significance. In PsA group, TPO Ab was correlated with DAPSA with statistical significance.

Conclusions. Autoimmune thyroiditis is more common in PsA than subclinical PsA patients. PsA patients are advised to be tested for TPO and Tg Abs. Musculoskeletal ultrasound is a screening tool to detect enthesitis in psoriasis patients.

Keywords: psoriatic disease, psoriatic arthritis subclinical psoriatic arthritis, autoimmune thyroiditis, MASEI

List of abbreviations (in alphabetical order):

AITD	– Autoimmune thyroid disease
DAPSA	– Disease Activity score for PSoriatic Arthritis
FT3	– Free tri-iodothyronine
FT4	– Free thyroxine
HAQ	– Health Assessment Questionnaire
LEI	– Leeds Enthesitis Index
MASEI	– MAdrid Sonographic Enthesitis Index
PASI	– Psoriasis Area Severity Index
PsA	– Psoriatic arthritis
Subclinical PsA	– Subclinical psoriatic arthritis
Tg Ab	– Thyroglobulin antibody
Thyroid US	– Thyroid ultrasound
TPO Ab	– Thyroid peroxidase antibody
TSH	– Thyroid stimulating hormone

INTRODUCTION

Psoriasis is a chronic inflammatory multifactorial immune-mediated skin disease with almost a third of psoriasis patients developing psoriatic arthritis (PsA) [1]. PsA is a chronic systemic heterogeneous inflammatory autoimmune disease [2]. It has various musculoskeletal presentations such as peripheral arthritis, axial disease, dactylitis, and enthesitis, together

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with nail affection being a common extra-articular manifestation. Comorbidities include cardiovascular disease, inflammatory bowel disease, and anxiety. Peripheral arthritis is an important feature with diverse presentations [3]. One of the hallmarks of PsA is enthesitis, which is thought to be the main lesion that starts the synovial joint inflammation [4]. Enthesitis leads to a worse quality of life by causing pain, fatigue, and sleep disturbances, affecting the functional status, and overall impairment [5]. It occurs in the axial and peripheral skeleton. It may precede joint symptoms and increase the risk of erosive disease [6].

Preclinical PsA definition and differentiation from psoriasis is challenging as PsA is a broad disease with a wide range of manifestations. It can overlap early with features of osteoarthritis or mechanical overuse, especially in old-age psoriasis patients. Early symptoms of PsA in women include arthralgia, heel pain, fatigue, and stiffness. A worsening in pain, stiffness, fatigue, and physical function may anticipate PsA diagnosis [7]. This makes diagnosis and assessment a challenge. So, imaging has a major importance in the assessment, diagnosis, and follow-up. US is used to visualize abnormal vascularity, and structural abnormalities in soft tissue and bone [8]. US application in patients with psoriasis without musculoskeletal symptoms revealed 30-50% subclinical enthesitis and/or synovitis. Subclinical enthesitis shows higher degrees of power Doppler activity which is a marker of inflammation and angiogenesis [9].

Autoimmune thyroid disease (AITD) or Hashimoto's thyroiditis is one of the commonest autoimmune diseases [10]. Hashimoto's thyroiditis is considered the most frequent cause of hypothyroidism [11]. It is more prevalent in middle-aged females and can deteriorate the quality of life [12]. Antibodies are formed against thyroglobulin (Tg) and thyroid peroxidase (TPO) antigens [13]. In about 90% of patients, thyroid peroxidase antibody (TPO-Ab) is the most prevalent antibody [14]. Antibodies can be positive for a considerable amount of time prior to the onset of thyroid dysfunction indicating the thyroid gland's large functional reserve [15]. AITD can present with musculoskeletal manifestations such as fibromyalgia, chronic fatigue, arthropathy without inflammatory synovitis, and undifferentiated inflammatory seronegative arthropathy which can mimic the early phase of PsA [16]. AITD is a T-helper 1-mediated immune disease. Its main characteristics are thyroid gland lymphocytic infiltration with the secretion of large amounts of interferon-gamma (IFN-γ), tumor necrosis factor-alpha (TNF-α), and chemokines enhancing the autoimmune process [17]. AITD and psoriatic disease association is still debatable. Complications and progression of both diseases can be avoided by early diagnosis and treatment [18]. More studies are required to evaluate the definite role of thyroid hormones and antibodies in psoriasis and PsA, if thyroid dysfunction has a role in psoriasis chronicity and severity, and to determine the pathogenesis of both diseases' association [14]. This study aimed to assess AITD and subclinical and clinical PsA association.

MATERIALS AND METHODS

Forty-five female Egyptian patients ≥18 years-old diagnosed with psoriatic disease were included in this comparative cross-sectional study. The patients were classified into 3 equal groups. The PsA group included patients classified in accordance to CASPAR criteria (ClASsification criteria for Psoriatic ARthritis)[19]. The subclinical PsA and psoriasis groups included patients classified by MAdrid Sonographic Enthesitis Index (MASEI) [20]. Informed consent from the ethical committee was obtained from each patient. Patients were excluded from participating in the study in case of other rheumatological diseases, known non-autoimmune thyroid disease or thyroidectomy, systemic diseases other than diabetes mellitus and hypertension, malignancy, and previous radiotherapy on the neck or mediastinum, drugs that interfere with thyroid function such as amiodarone, lithium, and high-dose steroids, and pregnant females.

The detailed medical history of every patient was reviewed, paying particular attention to the health assessment questionnaire (HAQ)[21] by El Meidany et al., 2003 [22], Arabic translated form, thorough clinical examination with focus on assessment of psoriasis disease activity using Psoriasis Area Severity Index (PASI) [23], enthesitis clinical evaluation using Leeds Enthesitis Index (LEI) [24], PsA disease activity using disease activity score for psoriatic arthritis (DAPSA) [25], and laboratory tests entailed complete blood count (CBC), Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum uric acid level, glycated hemoglobin, thyroid profile including thyroid hormones; thyroid stimulating hormone (TSH), free thyroxine (FT4), and free tri-iodothyronine (FT3), thyroid peroxidase antibody (TPO-Ab), and thyroglobulin antibody (Tg-Ab). Thyroid US was performed with the patient's neck extended in the supine position to assess the thyroid gland's volume, echogenicity, nodules, and vascularity. The evaluation of enthesitis for MASEI was done using a high-resolution US with a linear transducer of 10-12 MHz (LOGIQ 5 pro series, GE medical systems, Germany), total score is 136 with a cut-off value of ≥18.

Statistical analysis

It was done using the Statistical Package for Social Science (IBM SPSS) version 23. Number (percentage) or range, mean ± standard deviations, or median and

TABLE 1. Demographic data of the PsA, subclinical PsA and psoriasis groups

		PsA	Subclinical PsA	Psoriasis	Test value	P-value	Sig.
Age (years)	Range Mean±SD	32 – 64 47.67 ± 10.56	25 – 63 43.53 ± 11.39	23 – 53 38.33 ± 9.39	2.988••	0.061	NS
Psoriasis duration (years)	Range Median(IQR)	2 – 46 15 (4 – 38)	3 – 30 13 (6 – 20)	2 – 30 6 (5 – 13)	3.231≠≠	0.199	NS
PsA duration (years)	Range Median(IQR)	2 – 30 5 (2 – 10)	– –	– –	–	–	–
Hypertension		5 (33.3%)	4 (26.7%)	4 (26.7%)	0.216*	0.897	NS
Diabetes mellitus		4 (26.7%)	3 (20%)	3 (20%)	0.257*	0.879	NS
Body mass index ≥30		11 (73.3%)	10 (66.7%)	7 (46.7%)	2.458*	0.293	NS
Nail psoriasis		10 (66.7%)	8 (53.3%)	6 (40%)	2.143*	0.343	NS
Gastrointestinal affection		3 (20%)	2 (13.3%)	0 (0%)	3.15*	0.207	NS
Eye affection		0 (0%)	0 (0%)	0 (0%)	–	–	–
HAQ	Mild Moderate Severe	2 (13.3%) 9 (60 %) 4 (26.7 %)	15 (100 %) 0 (0 %) 0 (0 %)	15 (100 %) 0 (0 %) 0 (0 %)	36.563*	**<0.001**	**HS**
LEI	Range Median(IQR)	3 – 6 6 (5 – 6)	0 – 6 4 (0 – 5)	0 – 2 0 (0 – 1)	24.989≠≠	**<0.001**	**HS**
DAPSA	Low Moderate High	2 (13.3%) 5 (33.3%) 8 (53.3%)	– – –	– – –	–	–	–
PASI	Mild Moderate Severe	4 (26.7%) 5 (33.3%) 6 (40%)	4 (26.6%) 6 (40%) 5 (33.3%)	5 (33.3%) 6 (40%) 4 (26.7%)	0.671*	0.955	NS

*PsA: Psoriatic arthritis, Subclinical PsA: Subclinical psoriatic arthritis, HAQ: Health Assessment Questionnaire, LEI: Leeds Enthesitis Index, DAPSA: Disease Activity for PsA, PASI: Psoriasis Area Severity Index, SD: Standard deviation, IQR: Interquartile range, Sig.: Significance, P-value ≥ 0.05: Non-significant (NS), P-value < 0.05: Significant (S), P-value < 0.001: Highly significant (HS), %: Percentage, ••: One-Way ANOVA test, ≠≠: Kruskal-Wallis test, *: Chi-square test*

interquartile range were utilized for data presentation. Statistical tests comprised spearman correlation coefficient (r), independent t-test, Mann-Whitney test, Chi-square test, One-Way ANOVA test, and Kruskall-Wallis test.

RESULTS

The demographic data of all patients are presented (Table 1). Patients in the PsA group had higher HAQ scores with a high statistical significant difference in comparison to those in the subclinical PsA and psoriasis groups. Patients in the PsA group had higher LEI when compared to those in the subclinical PsA group with a statistical significant difference and to those in the psoriasis group with a high statistical significant difference. Subclinical PsA patients had higher LEI compared to those with psoriasis with a statistical significant difference.

The subclinical PsA group had psoriasis patients with MASEI ≥18, either with musculoskeletal complaints not fulfilling the entry criterion of CASPAR classification criteria or without musculoskeletal complaints. The psoriasis group had psoriasis patients without musculoskeletal complaints with MASEI <18 (Figure 1).

In all psoriatic disease patients, 20% had subclinical hypothyroidism, 46.67% had TPO-Ab positivity, and 26.67% had Tg-Ab positivity. These percentages were elevated in the PsA group in contrast to the subclinical PsA group. In the PsA group, 33.3% had subclinical hypothyroidism, 80% had TPO-Ab positivity, and 46.7% had Tg-Ab positivity. In the subclinical PsA group, 26.7% had subclinical hypothyroidism, 60% had TPO-Ab positivity, and 33.3% had Tg-Ab positivity. While in the psoriasis group, 100% of patients were within the normal range of serum levels of thyroid hormones with negative thyroid antibodies. PsA patients had higher TPO-Ab levels compared to psoriasis patients with a high statistical significant difference and subclinical PsA patients had higher TPO-Ab levels compared to psoriasis patients with a statistical significant difference. PsA patients had lower FT3 levels compared to psoriasis patients with a statistical significant difference. Features of thyroiditis in the US were present in 26.7% of the PsA patients and 20% of the subclinical PsA patients with none (0%) of the psoriasis patients. Sonographic thyroiditis features included non-homogenous coarse echopattern, multiple fibrous strands, multiple small nodules, and increased vascularity. There was no change in the thyroid gland volume in thyroiditis patients. No sta-

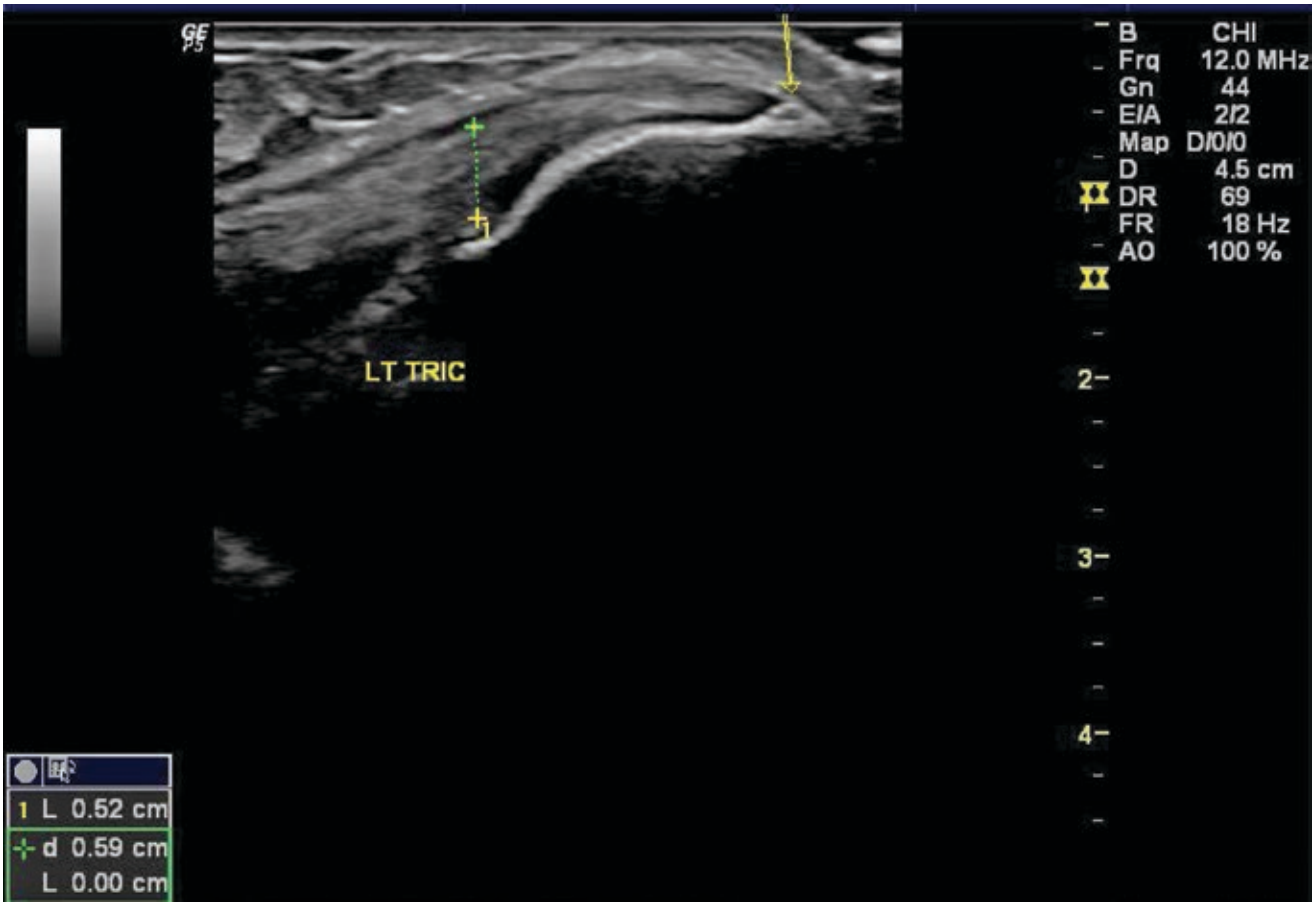

FIGURE 1. Triceps tendon thickening 5.2mm (>4.3mm), hypoechogenicity, and enthesophyte

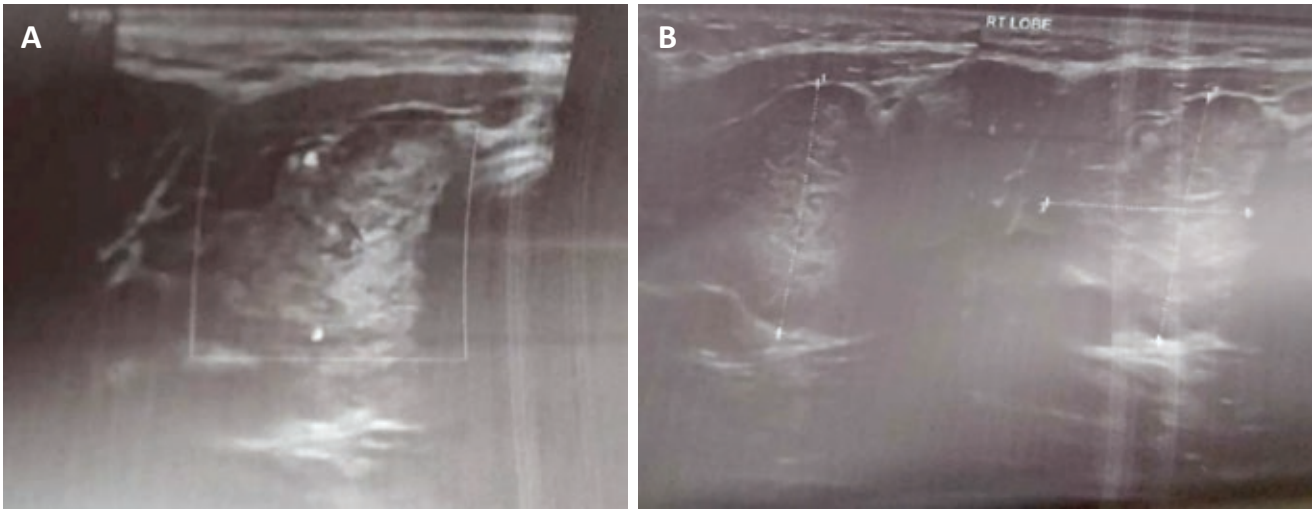

FIGURE 2. (A) & (B) Thyroid US of thyroiditis: thyroid enlargement, coarse echopattern, and nodules

tistical significant difference was detected regarding thyroid US features comparing the 3 groups (Table 2, Figure 2). The correlations of the thyroid profile with other parameters in the 3 groups are demonstrated in (Tables 3-6).

DISCUSSION

Psoriasis is an inflammatory autoimmune chronic disease affecting multiple systems but mainly the skin [26]. Synovioentheseal inflammation will occur eventually in up to 30% of patients with psoriasis [27]. PsA is a chronic inflammatory autoimmune heterogeneous musculoskeletal disease with various presentations involving peripheral arthritis, axial disease, enthesitis, and dactylitis with negative effects on the quality of life [28]. AITD is a common autoimmune disease affecting almost 5% of the population. Hashimoto's thyroiditis is the most common form, with lymphocytic thyroid gland infiltration and antibodies production including TPO and Tg Abs resulting eventually in hypothyroidism [26].

TABLE 2. Comparing the 3 groups regarding thyroid profile

Thyroid Profile		PsA	Subclinical PsA	Psoriasis	Test value	P-value	Sig.
TSH (uIU/ml)	Range Median(IQR)	0.65 – 6.1 2.05 (1.32 – 4.9	0.94 – 6.8 2.85 (1.65 – 5.2)	1.69 – 4.15 3.4 (2.76 – 3.9)	1.587≠≠	0.452	NS
FT3 (pg/ml)	Range Mean±SD	2.01 – 3.33 2.85 ± 0.39	1.96 – 4.2 3.17 ± 0.63	2.8 – 4.1 3.41 ± 0.52	4.388••	**0.019**	**S**
FT4 (ng/dl)	Range Mean±SD	0.96 – 1.63 1.33 ± 0.23	0.98 – 1.61 1.28 ± 0.21	0.98 – 1.53 1.19 ± 0.19	1.722••	0.191	NS
TPO Ab (IU/ml)	Range Median(IQR)	10 – 750 141.84 (119 – 223.4)	10 – 312 154 (24.3 – 213.1)	10 – 90 25 (14.8 – 33.6)	10.472≠≠	**0.005**	**HS**
Tg Ab (IU/ml)	Range Median(IQR)	10 – 389.3 52.1 (10.2 – 206.7)	10 – 337 28.5 (15 – 179)	10 – 51.6 24 (13.7 – 34)	2.455≠≠	0.293	NS
Thyroid US	Normal Thyroiditis	11 (73.3%) 4 (26.7%)	12 (80%) 3 (20%)	15 (100%) 0 (0%)	4.398*	0.111	NS

*PsA: Psoriatic arthritis, Subclinical PsA: Subclinical psoriatic arthritis, TSH: Thyroid stimulating hormone, FT3: Free tri-iodothyronine, FT4: Free thyroxine, TPO Ab: Thyroid peroxidase antibody, Tg Ab: Thyroglobulin antibody, IQR: Interquartile range, SD: Standard deviation, Sig.: Significance, P-value ≥0.05: NS, P-value < 0.05: S, P-value < 0.01: HS, %: Percentage, ≠≠: Kruskal-Wallis test, ••: One-Way ANOVA test, *: Chi-square test.*

TABLE 3. Thyroid profile correlations in the PsA group

PsA group	TSH (uIU/ml)			FT3 (pg/ml)			FT4 (ng/dl			TPO Ab (IU/ml)			Tg Ab (IU/ml)		
	r	P-value	Sig.	r	P-value	Sig.	r	P-value	Sig.	r	P-value	Sig.	r	P-value	Sig.
Age (years)	-0.018	0.95	NS	-0.052	0.854	NS	0.089	0.752	NS	**-0.524***	**0.045**	**S**	-0.115	0.684	NS
Psoriasis duration (years)	-0.052	0.854	NS	-0.211	0.451	NS	0.005	0.985	NS	-0.471	0.076	NS	-0.138	0.623	NS
PsA duration (years)	0.078	0.783	NS	-0.164	0.56	NS	0.164	0.558	NS	-0.481	0.069	NS	-0.147	0.601	NS
LEI	0.406	0.133	NS	0.341	0.213	NS	0.471	0.077	NS	-0.007	0.981	NS	0.164	0.56	NS
ESR (mm/hr)	-0.338	0.218	NS	-0.24	0.389	NS	-0.172	0.541	NS	0.035	0.902	NS	-0.016	0.954	NS
CRP mg/l	-0.246	0.376	NS	-0.122	0.666	NS	0.082	0.771	NS	-0.275	0.321	NS	-0.265	0.339	NS
Serum Uric acid (mg/dl)	**0.721****	**0.002**	**HS**	0.066	0.814	NS	0.404	0.136	NS	0.423	0.116	NS	0.383	0.158	NS
TSH (uIU/ml)	–	–	–	-0.125	0.657	NS	0.193	0.491	NS	0.427	0.112	NS	**0.545***	**0.036**	**S**
FT3 (pg/ml)	-0.125	0.657	NS	–	–	–	**0.58***	**0.024**	**S**	-0.096	0.734	NS	0.372	0.173	NS
FT4 (ng/dl)	0.193	0.491	NS	**0.58***	**0.024**	**S**	–	–	–	-0.175	0.532	NS	0.136	0.628	NS
TPO Ab (IU/ml)	0.427	0.112	NS	-0.096	0.734	NS	-0.175	0.532	NS	–	–	–	0.343	0.211	NS
Tg Ab (IU/ml)	**0.545***	**0.036**	**S**	0.372	0.173	NS	0.136	0.628	NS	0.343	0.211	NS	–	–	–

PsA: Psoriatic arthritis, LEI: Leeds Enthesitis Index, ESR: Erythrocyte Sedimentation Rate, CRP: C-reactive protein, TSH: Thyroid stimulating hormone, FT3: Free tri-iodothyronine, FT4: Free thyroxine, TPO Ab: Thyroid peroxidase antibody, Tg Ab: Thyroglobulin antibody, r: Spearman correlation coefficient, Sig.: Significance, P-value ≥ 0.05: NS, P-value < 0.05: S, P-value < 0.001: HS

In our study, no statistical significant difference was detected between the 3 groups regarding the patient's age, psoriasis duration, prevalence of hypertension, diabetes mellitus, or obesity. Our results agreed with Yumnam et al., 2022 [14], Valduga et al., 2021 [29], and Vastarella et al., 2021 [30] who demonstrated an association between psoriatic disease and autoimmune thyroiditis, while disagreed with Vassilatou et al., 2017 [15] and Khan et al., 2017 [31] who found no association between psoriatic disease and autoimmune thyroiditis. Psoriasis patients have twice the chance to develop another autoimmune disease [14]. Many theories have been postulated to explain this association. Both diseases are common autoimmune inflammatory diseases that share many characteristics such as a long asymptomatic period before the starting of symptoms, an elevated comorbidity risk most likely metabolic syndrome, and several complications affecting the health and quality of life of patients, as well as many risk factors besides genetic predisposition sharing in both diseases such as dietary, lifestyle, and environmental factors [32]. Both diseases are Th-1 cell-mediated immune diseases [30]. Thyroid hormones may have a role in psoria-

TABLE 4. Thyroid profile correlations in the PsA group

PsA group		TSH (uIU/ml) Median (IQR)	Test value	P-value	Sig.	FT3 (pg/ml) Mean ± SD	Test value	P-value	Sig.	FT4 (ng/dl) Mean ± SD	Test value	P-value	Sig.	TPO Ab (IU/ml) Median (IQR	Test value	P-value	Sig.	Tg Ab (IU/ml) Median (IQR	Test value	P-value	Sig.
HAQ	Mild Moderate Severe	1.56(1.32–1.8) 2.03(1.07–3.03) 5.71(3.78–6)	5.947 ≠≠	0.051	NS	2.83±0.04 2.9±0.38 2.75±0.55	0.183 ••	0.835	NS	1.37±0.06 1.3±0.25 1.36±0.26	0.11 ••	**0.896**	NS	10(10–10) 136(21.5–200) 161(141.02–267.08)	5.047 ≠≠	0.08	NS	10.7(10.2–11.2) 52.1(10–206.7) 142(87.9–193.3)	2.045 ≠≠	0.36	NS
DAPSA	Low Moderate High	1.56(1.32–1.8) 2.03(1.93–2.48) 4.4(1.5–5.71	2.375 ≠≠	0.305	NS	2.83±0.04 2.83±0.47 2.87±0.42	0.016 ••	0.984	NS	1.37±0.06 1.3±0.28 1.33±0.24	0.05 ••	0.952	NS	10(10–10) 136(121–178.48) 201.78(141.02-297.31)	**6.853** **≠≠**	**0.032**	**S**	10.7(10.2–11.2) 19.1(10–52.1) 152.1(87.9-224.15)	3.661 ≠≠	0.16	NS
PASI	Mild Moderate Severe	2.05(1.93–4.9) 2.14(1.32–3.03) 3.97(1.34–6)	0.623 ≠≠	0.733	NS	2.86±0.5 2.73±0.37 3.03±0.24	0.692 ••	0.519	NS	1.21±0.24 1.27±0.2 1.55±0.08	3.714 ••	0.056	NS	223.4(178.48–240.62) 71.25(10–136) 160.18(129.6–190.08)	4.702 ≠≠	0.095	NS	52.1(36.8–139) 15.15(10.2–214) 152.1(77.5–200.4)	0.431 ≠≠	0.806	NS
Thyroid US	Normal Thyroiditis	1.93(1.07–2.48) 5.21(4.4–5.71)	**-2.35** **≠**	**0.019**	**S**	2.89±0.34 2.76±0.54	0.555 •	0.589	NS	1.34±0.2 1.28±0.33	0.449 •	0.661	NS	136(21.5–178.48) 297.31(210.39–552)	**-2.613** **≠**	**0.009**	**HS**	19.1(10–145) 224.15(172.85–315.45)	**-2.358** **≠**	**0.018**	**S**

PsA: Psoriatic arthritis, HAQ: Health Assessment Questionnaire, DAPSA: Disease Activity for PsA, PASI: Psoriasis Area Severity Index, TSH: Thyroid stimulating hormone, FT3: Free tri-iodothyronine, FT4: Free thyroxine, TPO Ab: Thyroid peroxidase antibody, Tg Ab: Thyroglobulin antibody, IQR: Interquartile range, SD: Standard deviation, Sig.: Significance, P-value ≥ 0.05: NS, P-value < 0.05: S, P-value < 0.001: HS, ≠≠: Kruskal-Wallis test, ≠: Mann-Whitney test, ••: One-Way ANOVA test, •: Independent t-test

sis pathogenesis by many factors. Skin has receptors for thyroid hormones on which thyroid hormones have hyperproliferative effects through epidermal growth factor that increases epidermal hyperplasia and keratin synthesis. Psoriasis disease severity is demonstrated in some studies to be correlated with TSH level and is improved with antithyroid therapy [32].

Compared to psoriasis, PsA patients have a higher risk of hypothyroidism, hyperthyroidism, and AITD. This may be illustrated by the increased systemic inflammation denoted by the elevated levels of IL-6, IL-1 receptor, IL-1 receptor antagonist, soluble IL-2 receptor, vascular endothelial growth factor, high-sensitive CRP, CD16+ proinflammatory monocytes, and osteoprotegerin in patients with PsA in contrast to patients with psoriasis and the general population [14,30]. Patients with PsA and AITD had more peripheral polyarticular involvement indicating that thyroid evaluation could be included in PsA patients' assessment, especially females with peripheral polyarticular affection [30].

In the PsA group, a statistical significant negative correlation was detected between TPO-Ab level and the patient's age while in the subclinical PsA group, a statistical significant positive correlation was detected between TPO-Ab level and the patient's age. In the subclinical PsA group, a high statistical significant positive correlation was detected between TPO-Ab level and the psoriasis duration. Vassilatou et al., 2017[15] and Borges et al., 2018[33], demonstrated that there was no association between AITD and neither psoriatic patient's age, age at disease onset, or psoriatic disease duration. Alidrisi et al., 2019[34], demonstrated a significant correlation between psoriasis onset at age >40 and higher TPO-Ab level (42.1%) while there were no correlations found between the patient's age and the thyroid antibodies. Fallahi et al., 2017[35], found an increase in thyroid abnormalities in PsA patients with long-standing disease.

In the subclinical PsA group, a high statistical significant negative correlation was demonstrated between FT4 and LEI, a high statistical significant positive correlation was demonstrated between TPO-Ab and MASEI, and statistical significant positive correlations between each of FT3 and Tg-Ab and MASEI. Higher MASEI scores as in subclinical PsA are associated with more enthesitis which reflects more inflammation and are associated with more peripheral and radiographic damage. AITD is more frequent in psoriatic disease due to increased inflammation [30].

There were statistical significant correlations between TPO-Ab and DAPSA score and between FT4 and PASI in the PsA group. This agrees with Vastarella et al., 2021[30], who demonstrated an increased frequency of AITD in PsA with peripheral

TABLE 5. Thyroid profile correlations in the subclinical PsA group

Subclinical PsA group	TSH (uIU/ml)			FT3 (pg/ml)			FT4 (ng/dl			TPO Ab (IU/ml)			Tg Ab (IU/ml)		
	r	P-value	Sig.	r	P-value	Sig.	r	P-value	Sig.	r	P-value	Sig.	r	P-value	Sig.
Age (years)	0.168	0.549	NS	-0.046	0.869	NS	-0.209	0.454	NS	**0.631***	**0.012**	S	0.382	0.159	NS
Psoriasis duration (years)	0.086	0.761	NS	-0.163	0.562	NS	-0.05	0.859	NS	**0.71****	**0.003**	HS	0.129	0.647	NS
MASEI	0.348	0.204	NS	**0.609***	**0.016**	**S**	-0.045	0.874	NS	**0.698****	**0.004**	HS	**0.547***	**0.035**	**S**
LEI	-0.308	0.264	NS	-0.19	0.497	NS	-0.704**	0.003	HS	0.174	0.536	NS	-0.201	0.471	NS
ESR (mm/hr)	-0.03	0.914	NS	0.093	0.742	NS	-0.356	0.192	NS	**0.626***	**0.013**	S	0.316	0.251	NS
CRP mg/l	-0.021	0.94	NS	0.307	0.265	NS	-0.301	0.276	NS	0.129	0.648	NS	0.368	0.177	NS
Serum Uric acid (mg/dl)	-0.048	0.864	NS	0.138	0.624	NS	0.344	0.209	NS	-0.356	0.193	NS	-0.054	0.849	NS
TSH (uIU/ml)	–	–	–	0.425	0.114	NS	0.488	0.065	NS	0.4	0.14	NS	**0.689****	**0.004**	**HS**
FT3 (pg/ml)	0.425	0.114	NS	–	–	–	0.279	0.314	NS	0.286	0.302	NS	0.432	0.108	NS
FT4 (ng/dl)	0.488	0.065	NS	0.279	0.314	NS	–	–	–	0	1	NS	0.277	0.317	NS
TPO Ab (IU/ml)	0.4	0.14	NS	0.286	0.302	NS	0	1	NS	–	–	–	0.386	0.156	NS
Tg Ab (IU/ml)	**0.689****	**0.004**	**HS**	0.432	0.108	NS	0.277	0.317	NS	0.386	0.156	NS	–	–	–

Subclinical PsA: Subclinical psoriatic arthritis, MASEI: MAdrid Sonographic Enthesitis Index, LEI: Leeds Enthesitis Index, ESR: Erythrocyte Sedimentation Rate, CRP: C-reactive protein, TSH: Thyroid stimulating hormone, FT3: Free tri-iodothyronine, FT4: Free thyroxine, TPO Ab: Thyroid peroxidase antibody, Tg Ab: Thyroglobulin antibody, r: Spearman correlation coefficient, Sig.: Significance, P-value ≥ 0.05: NS, P-value < 0.05: S, P-value < 0.001: HS

TABLE 6. Thyroid profile correlations in the psoriasis group

Psoriasis group	TSH (uIU/ml)			FT3 (pg/ml)			FT4 (ng/dl			TPO Ab (IU/ml)			Tg Ab (IU/ml)		
	r	P-value	Sig.	r	P-value	Sig.	r	P-value	Sig.	r	P-value	Sig.	r	P-value	Sig.
Age (years)	-0.087	0.758	NS	-0.224	0.422	NS	-0.031	0.912	NS	0.179	0.523	NS	0.03	0.914	NS
Psoriasis duration (years)	0.217	0.438	NS	-0.288	0.298	NS	-0.002	0.995	NS	0.016	0.954	NS	0.346	0.206	NS
MASEI	-0.074	0.792	NS	-0.144	0.608	NS	0.152	0.588	NS	-0.198	0.48	NS	0.041	0.883	NS
LEI	0.012	0.966	NS	-0.35	0.201	NS	-0.067	0.812	NS	-0.098	0.729	NS	-0.14	0.618	NS
ESR (mm/hr)	-0.084	0.765	NS	-0.089	0.752	NS	0.043	0.879	NS	0.203	0.467	NS	-0.139	0.622	NS
CRP mg/l	0.36	0.188	NS	0.131	0.643	NS	0.162	0.564	NS	-0.167	0.553	NS	**0.657****	**0.008**	**HS**
Serum Uric acid (mg/dl)	-0.293	0.289	NS	-0.278	0.316	NS	-0.094	0.739	NS	-0.327	0.234	NS	-0.147	0.602	NS
TSH (uIU/ml)	–	–	–	-0.209	0.456	NS	0.315	0.253	NS	0.143	0.611	NS	0.175	0.532	NS
FT3 (pg/ml)	-0.209	0.456	NS	–	–	–	-0.132	0.638	NS	-0.126	0.655	NS	0.298	0.281	NS
FT4 (ng/dl)	0.315	0.253	NS	-0.132	0.638	NS	–	–	–	-0.131	0.642	NS	0.126	0.654	NS
TPO Ab (IU/ml)	0.143	0.611	NS	-0.126	0.655	NS	-0.131	0.642	NS	–	–	–	0.039	0.889	NS
Tg Ab (IU/ml)	0.175	0.532	NS	0.298	0.281	NS	0.126	0.654	NS	0.039	0.889	NS	–	–	–

Subclinical PsA: Subclinical psoriatic arthritis, MASEI: MAdrid Sonographic Enthesitis Index, LEI: Leeds Enthesitis Index, ESR: Erythrocyte Sedimentation Rate, CRP: C-reactive protein, TSH: Thyroid stimulating hormone, FT3: Free tri-iodothyronine, FT4: Free thyroxine, TPO Ab: Thyroid peroxidase antibody, Tg Ab: Thyroglobulin antibody, r: Spearman correlation coefficient, Sig.: Significance, P-value ≥ 0.05: NS, P-value < 0.05: S, P-value < 0.001: HS

polyarticular disease with more swollen joints and functional impairment. Yumnam et al., 2022 [14], showed 17.1% of psoriasis patients have increased TPO-Ab levels with less severe disease. Vassilatou et al., 2017 [15] and Borges et al., 2018 [33], showed no association between AITD and severity of psoriatic disease.

A statistical significant positive correlation was detected between TPO-Ab and ESR in the subclinical PsA group and a high statistical significant positive

correlation was detected between Tg-Ab and CRP in the psoriasis group. AITD is more prevalent in psoriatic disease due to increased inflammation represented by increased levels of inflammatory mediators such as IL-6, CRP, IL-1 receptor, IL-1 receptor antagonist, and soluble IL-2 receptor [30].

In the PsA group, a high statistical significant positive correlation was found between TSH and serum uric acid. This disagrees with Jat et al., 2019 [36] who demonstrated no significant correlations between thyroid hormones in various thyroid disorders and serum uric acid levels. Helmy, 2020 [37], found a statistical significant negative correlation between TSH and serum uric acid and a statistical significant positive correlation between each of FT4 and FT3 and serum uric acid. The effect of hypothyroidism on purine metabolism results in increasing serum uric acid levels. Hypothyroidism also results in a reduction in renal perfusion and glomerular filtration rate [37].

The study's limitations included the limited number of patients including females only. We recommend future larger-scale longitudinal studies involving both genders. Musculoskeletal ultrasound can be used to screen for subclinical synovitis and enthesitis in psoriasis patients to screen for subclinical PsA. Assessment of psoriatic disease patients by thyroid antibodies and thyroid stimulating hormone is needed to diagnose autoimmune thyroid disease in these patients and to reduce the risk of comorbidities, especially cardiovascular diseases.

CONCLUSION

Musculoskeletal ultrasound is a screening tool to detect enthesitis in psoriasis patients. It also can help in diagnosing psoriasis patients with musculoskeletal complaints not fulfilling the entry criterion for CASPAR criteria whether they have subclinical PsA or fibromyalgia. Autoimmune thyroiditis is increased in psoriatic disease. The percentage of thyroglobulin and thyroid peroxidase antibodies' positivity is higher in PsA patients than in subclinical PsA and higher in subclinical PsA than psoriasis.

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REFERENCES

1. Bragazzi NL, Bridgewood C, Watad A, Damiani G, Kong JD, McGonagle D. Harnessing Big Data, Smart and Digital Technologies and Artificial Intelligence for Preventing, Early Intercepting, Managing, and Treating Psoriatic Arthritis: Insights From a Systematic Review of the Literature. *Front Immunol.* 2022 Mar 10;13:847312. doi: 10.3389/fimmu.2022.847312.
2. Cigolini C, Fattorini F, Gentileschi S, Terenzi R, Carli L. Psoriatic arthritis: one year in review 2022. *Clin Exp Rheumatol.* 2022 Sep;40(9):1611-1619. doi: 10.55563/clinexprheumatol/x3sfxe.
3. Hackett S, Coates LC. Outcome measures in psoriatic arthritis: Where next? *Musculoskeletal Care.* 2022 Nov;20 Suppl 1(Suppl 1):S22-S31. doi: 10.1002/msc.1692.
4. Polachek A, Cook R, Chandran V, Gladman DD, Eder L. The association between sonographic enthesitis and radiographic damage in psoriatic arthritis. *Arthritis Res Ther.* 2017 Aug 15;19(1):189. doi: 10.1186/s13075-017-1399-5.
5. Dulovic D, Rancic N, Bozic K, Stamatovic R, Mijuskovic Z, Pesic J, et al. Assessment of enthesitis in patients with psoriasis: relationships with clinical features, screening questionnaires results, and quality of life- An ultrasound study. *Vojnosanitetski pregled*. 2021;78(12):1249-1256. doi: 10.2298/VSP191014041D.
6. Kaeley GS, Kaler JK. Peripheral Enthesitis in Spondyloarthritis: Lessons from Targeted Treatments. *Drugs*. 2020;80(14):1419-1441. doi: 10.1007/s40265-020-01352-6.
7. Eder L, Polachek A, Rosen CF, Chandran V, Cook R, Gladman DD. The Development of Psoriatic Arthritis in Patients With Psoriasis Is Preceded by a Period of Nonspecific Musculoskeletal Symptoms: A Prospective Cohort Study. *Arthritis Rheumatol.* 2017;69(3):622-629. doi: 10.1002/art.39973.
8. Mathew AJ, Østergaard M, Eder L. Imaging in psoriatic arthritis: Status and recent advances. *Best Pract Res Clin Rheumatol.* 2021;35(2):101690. doi: 10.1016/j.berh.2021.101690.
9. Savage L, Tinazzi I, Zabotti A, Laws PM, Wittmann M, McGonagle D. Defining Pre-Clinical Psoriatic Arthritis in an Integrated Dermato-Rheumatology Environment. *J Clin Med.* 2020;9(10):3262. doi: 10.3390/jcm9103262.
10. Ralli M, Angeletti D, Fiore M, D'Aguanno V, Lambiase A, Artico M, et al. Hashimoto's thyroiditis: An update on pathogenic mechanisms, diagnostic protocols, therapeutic strategies, and potential malignant transformation. *Autoimmun Rev.* 2020;19(10):102649. doi: 10.1016/j.autrev.2020.102649.
11. Gerenova J, Manolova I, Stanilova S. Serum levels of Interleukin 23 and Interleukin 17 in Hashimoto's thyroiditis. A*cta Endocrinol.* 2019;5(1):74-79. doi: 10.4183/aeb.2019.74.
12. Sarandi E, Kruger Krasagakis S, Tsoukalas D, Rudofsky G, Tsatsakis A. A Clinical Trial for the Identification of Metabolic Biomarkers in Hashimoto's Thyroiditis and in Psoriasis: Study Protocol. *Pathophysiology*. 2021;28(2):291-306. doi: 10.3390/pathophysiology28020019.
13. Du J, Ma C, Wang R, Lin L, Gao L, Chen S, et al. Relationship between Different Psoriasis Types and Thyroid Dysfunction: A Retrospective Analysis. *Scanning*. 2021;2021(1834556). doi: 10.1155/2021/1834556.
14. Yumnam D, Kansal NK, Kant R. Association of Psoriasis with Thyroid Disorders: A Hospital-Based, Cross-Sectional Study. *Cureus*. 2022;14(3):e22987. doi: 10.7759/cureus.22987.
15. Vassilatou E, Papadavid E, Papastamatakis P, Alexakos D, Koumaki D, Katsimbri P, et al. No association of psoriasis with autoimmune thyroiditis. *J Eur Acad Dermatol Venereol.* 2017;31(1):102-106. doi: 10.1111/jdv.13767.
16. Perez-Chada LM, Haberman RH, Chandran V, Rosen CF, Ritchlin C, Eder L, et al. Consensus terminology for preclinical phases of psoriatic arthritis for use in research studies: results from a Delphi consensus study. *Nat Rev Rheumatol.* 2021;17(4):238–243. doi: 10.1038/s41584-021-00578-2.
17. Fallahi P, Ferrari SM, Elia G, Ragusa F, Paparo SR, Caruso C, et al. Myo-inositol in autoimmune thyroiditis, and hypothyroidism. *Rev Endocr Metabolic Disord.* 2018;19(4):349–354. doi: 10.1007/s11154-018-9477-9.
18. Abd Mallick Y. Frequency of thyroid disorders in patients with chronic plaque psoriasis and psoriatic arthritis. *Journal of Pakistan Association of Dermatologists*. 2019;29(2):182-187.

19. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H; CASPAR Study Group. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. *Arthritis Rheum.* 2006;54(8):2665-73. doi: 10.1002/art.21972.
20. De Miguel E, Cobo T, Muñoz-Fernández S, Naredo E, Usón J, Acebes JC, et al. Validity of enthesis ultrasound assessment in spondyloarthropathy. *Ann Rheum Dis.* 2009;68(2):169-174. doi: 10.1136/ard.2007.084251.
21. Bruce B, Fries JF. The Stanford Health Assessment Questionnaire: dimensions and practical applications. *Health Qual Life Outcomes.* 2003;1(20). doi: 10.1186/1477-7525-1-20.
22. El Meidany YM, El Gaafary MM, Ahmed I. Cross-cultural adaptation and validation of an Arabic Health Assessment Questionnaire for use in rheumatoid arthritis patients. *Joint Bone Spine.* 2003;70(3):195-202. doi: 10.1016/s1297-319x(03)00004-6.
23. Feldman SR, Krueger GG. Psoriasis assessment tools in clinical trials. *Ann Rheum Dis.* 2005; 64(Suppl 2):65–68. doi: 10.1136/ard.2004.031237.
24. Healy PJ, Helliwell PS. Measuring clinical enthesitis in psoriatic arthritis: assessment of existing measures and development of an instrument specific to psoriatic arthritis. *Arthritis Rheum.* 2008;59(5):686-691. doi: 10.1002/art.23568.
25. Schoels M, Aletaha D, Funovits J, Kavanaugh A, Baker D, Smolen JS. Application of the DAREA/DAPSA score for assessment of disease activity in psoriatic arthritis. *Ann Rheum Dis*. 2010;69(8):1441-7. doi: 10.1136/ard.2009.122259.
26. Cira CI, Carsote M, Nistor C, Pecta A, Pecta RC, Sandru F. Conundrum for Psoriasis and Thyroid Involvement. *Int J Mol Sci.* 2023;24(5):4894. doi: 10.3390/ijms24054894.
27. Karmacharya P, Wright K, Achenbach SJ, Crowson CS, Ogdie A, Bekele D, et al. Time to transition from psoriasis to psoriatic arthritis: A population-based study. Semin Arthritis Rheum. 2022;52:151949. doi: 10.1016/j.semarthrit.2021.12.013.
28. Leung YY, Orbai AM, De Wit M, Balanescu A, Dernis E, Soubrier M, et al. Comparing the Patient-Reported Physical Function Outcome Measures in a Real-Life International Cohort of Patients With Psoriatic Arthritis. *Arthritis Care Res.* 2021;73(4):593-602. doi: 10.1002/acr.24139.
29. Valduga JAG, Rebeiko LB, Skare TL. Prevalence of Hashimoto's thyroiditis in psoriasis patients. *Rev Assoc Med Bras* (1992). 2021;67(1):52-57. doi: 10.1590/1806-9282.67.01.20200274.
30. Vastarella M, Megna M, Lupoli GA, Napolitano M, Gallo L, Balato A, et al. Is there any association between psoriasis, psoriatic arthritis, and thyroid autoimmunity? *Australas J Dermatol.* 2021;62(2):207-11. doi: 10.1111/ajd.13484.
31. Khan SR, Bano A, Wakkee M, Korevaar TIM, Franco OH, Nijsten TE, et al. The association of autoimmune thyroid disease (AITD) with psoriatic disease: a prospective cohort study, systematic review, and meta-analysis. *Eur J Endocrinol*. 2017;177(4):347–359. doi: 10.1530/EJE-17-0397.
32. Sweta K, Freeda MM, Lenin M. The putative role of thyroid hormones and vitamin D on severity and quality of life in psoriasis. *Int J App Basic Med Res.* 2020;10(3):173-177. doi: 10.4103/ijabmr.IJABMR_437_19.
33. Borges AS, Valejo Coelho MM, Brasileiro A. A possible association between psoriasis and thyroid dysfunction. *Eur J Dermatol.* 2018;28(5):715-6. doi: 10.1684/ejd.2018.3374.
34. Alidrisi HA, Al Hamdi K, Mansour AA. Is There Any Association Between Psoriasis and Hashimoto's Thyroiditis? *Cureus*. 2019;11(3):e4269. doi: 10.7759/cureus.4269.
35. Fallahi P, Ferrari SM, Ruffilli I, Elia G, Miccoli M, Sedie AD, et al. Increased incidence of autoimmune thyroid disorders in patients with psoriatic arthritis: a longitudinal follow-up study. *Immunol Res.* 2017;65(3):681-686. doi: 10.1007/s12026-017-8900-8.
36. Jat A, Khare A, Patel N. A study of relationship of hyperuricemia in hypothyroid patients. *Int J Med Res Rev.* 2019;7(1):19-3. doi: 10.17511/ijmrr.2019.i01.04.
37. Helmy MY. Correlation between Uric Acid and Thyroid Hormones in Patients with Thyroid Disorders, A Case Control Study. *Egypt J Hosp Med.* 2020;81(2):1499-1505. doi: 10.21608/EJHM.2020.115312.