

Hypothyroidism in patients with rheumatoid arthritis and its relation to disease activity

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Background and objective

The relationship between thyroid disease and rheumatic disorders has been the subject of considerable debate. Thyroid abnormal function and/or autoimmune thyroid disease were observed in patients with rheumatoid arthritis (RA), which could be attributed to the natural feature of autoimmune diseases and their tendency to overlap. Consideration of the fact that autoimmunity plays a role in the pathogenesis of both RA and hypothyroidism has raised the need to study the frequency of hypothyroidism and thyroid antibodies in RA patients and their relation to disease activity.

Patients and methods

One hundred and fifty RA patients and 50 control participants were included in this study. RA patients were subjected to a full assessment of medical and rheumatological history, and examination as well as routine lab tests. Patients and controls underwent thyroid function testing including thyroid antibodies. Patients' disease activity was determined using the Modified Disease Activity Score and their functional status was assessed using the Modified Health Assessment Questionnaire.

Results

The most common thyroid dysfunction was hypothyroidism, which was found in 36 (24%) RA patients, followed by subclinical hypothyroidism in six (4%) patients, whereas subclinical hyperthyroidism was present in two (1.3%) patients. Autoimmune thyroid disease was present in 10 (6.6%) patients and absent in the controls. There was a significant positive correlation between thyroid stimulating hormone levels and RA disease activity parameters.

Conclusion

Hypothyroidism was the most common thyroid disorder associated with RA, present in 24%, with a significant association with RA disease activity parameters.

Keywords:

autoimmune thyroid disease, hypothyroidism, rheumatoid arthritis, rheumatoid arthritis disease activity

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Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune systemic inflammatory multisystem disease of unknown cause that may affect many tissues and organs, but principally attacks synovial joints, primarily affecting the peripheral joints in a symmetrical pattern [1]. The pathology of the disease process often leads to destruction of articular cartilage [2].

RA affects ~1% of the adult general population. Constitutional symptoms including fatigue, malaise, and morning stiffness are frequently experienced [1]. Although the cause of RA is unknown, autoimmunity plays a pivotal role in both its chronicity and its progression through the high level of cytokines, especially the tumor necrosis factor α (TNF- α) [2].

Thyroid dysfunction may be broadly classified as hypothyroidism and hyperthyroidism. The most common cause of thyroid disorders worldwide is iodine deficiency, leading to goiter formation and hypothyroidism. However, in noniodine deficiency

areas, the cause of hypothyroidism is either autoimmune (Hashimoto's thyroiditis), with a prevalence of 1–2%, and it is 10 times more common in women than in men [3], or hypothyroidism associated with the destructive treatment for thyrotoxicosis [4].

The relationship between thyroid dysfunction and RA has been a subject of debate, where several surveys suggested a relation between Hashimoto's thyroiditis and RA [5]. Other studies showed that abnormal or changing thyroid status may precipitate or exacerbate musculoskeletal disease, especially when common features and symptoms for hypothyroidism such as fatigue, malaise, dyslipidemia, and increased weight could be masked by the original RA symptoms [6].

Moreover, thyroid dysfunction was observed at least three times more often in women with RA than women with similar demographic features with noninflammatory rheumatic diseases such as osteoarthritis and fibromyalgia [7]. This was also confirmed in a more recent study in which thyroid abnormal function and/

or autoimmune thyroid disease (AITD) was observed in 6–33.8% of patients with RA, which can be attributed to the natural feature of autoimmune diseases and their tendency to overlap [8]. Frequent association with autoimmune diseases of other organs such as systemic lupus erythematosus [9], Sjogren's syndrome, scleroderma [10], and vasculitis [11] was observed.

Considering that autoimmunity plays a role in the pathogenesis of both RA and hypothyroidism through TNF- α , with the noticeable improvement in hypothyroidism in RA patients with anti-TNF- α treatment [2], this raised the need to study hypothyroidism and thyroid antibodies in RA patients and their relation to disease activity.

Aim of the work

To investigate the association of hypothyroidism and thyroid autoantibodies with RA and study their correlation with RA disease activity.

Patients and methods

Patients and controls

(1) The patient group included 150 adult RA Egyptian patients who presented to the outpatient clinics and were inpatients of the Rheumatology and Rehabilitation and Internal Medicine Departments of Ain Shams University Hospitals in the period from January 2012 to December 2012. These patients were either newly diagnosed according to the 2010 American College of Rheumatology (ACR)/EULAR RA classification criteria [12] or had been diagnosed previously according to the ACR revised criteria of RA 1987 [13].

Exclusion criteria were as follows:

- (a) Patients on medication known to cause thyroid dysfunction (e.g. lithium, interferon alpha, etc.).
 - (b) Evidence of malignancy.
 - (c) Concurrent infection.
 - (d) Any collagen disease other than RA.
 - (e) Pregnant women.
 - (f) Chronic liver or renal diseases.
 - (g) Diabetic patients.
 - (h) Patients who had undergone thyroidectomy.
- (2) The control group included 50 healthy individuals age and sex matched with the patient group.

Methods

The nature of our study was explained to all participants and a verbal consent was obtained. All patients were subjected to the following:

Assessment of medical and rheumatological history

Medical and rheumatological history was assessed with a special focus on symptoms of thyroid problems (e.g. palpitation, cold intolerance, weight gain, RA disease duration, morning stiffness, tender joints, swollen joints, etc.).

General and rheumatological examination

Careful general and musculoskeletal examination, thyroid gland examination, and calculation of BMI (weight in kg divided by the patient's height in m²; ≥ 25 was considered abnormal) were performed. Waist circumference [an abnormal waist circumference was defined according to the International Diabetes Federation (IDF) for men as a circumference ≥ 94 cm and for women as ≥ 80 cm (<http://www.idf.org/metabolic-syndrome>) was measured. Medical treatment with methotrexate and/or prednisone was recorded including their current doses.

Assessment of disease activity was performed using the Modified Disease Activity Score (MDAS28) including 28 tender and swollen joint count scores, erythrocyte sedimentation rate (ESR), and the patient's subjective assessment (SA) of RA disease activity in the last 7 days recorded on a scale between 0 and 10, where 0 indicated 'no activity' and 10 indicated 'highest activity possible'. MDAS28 is calculated using the following formula [14]:

$$DAS28 = 0.56 \times \sqrt{TEN28} + 0.28 \times \sqrt{SW28} + 0.70 \times \ln(ESR) + 0.014 \times SA$$

The activity score of patients is graded as follows:

- (1) A score of ≤ 2.6 was considered to indicate remission.
- (2) > 2.6 and ≤ 3.2 as low activity.
- (3) > 3.2 and ≤ 5.1 as moderate activity.
- (4) > 5.1 as high activity [15].

Rheumatoid arthritis functional status was assessed using the Modified Stanford Health Assessment Questionnaire

A questionnaire composed of eight questions on dressing, arising from bed, eating (or drinking), walking, self-hygiene, reaching objects, hand grip, and outside activities was used. One of four responses is recorded for each item: score 0 (without any difficulty), score 1 (with some difficulty), score 2 (with much difficulty), and score 3 (when unable to do). The mean of the total scores is the patient's score [16].

Laboratory investigations

Routine laboratory investigations were performed including the following:

1. Complete blood count using a Coulter JS (California, USA) cell counter.
2. The ESR in the first hour, estimated using the Westergren method.
3. Quantitative C-reactive protein (CRP) titer assessed using the immunoturbidimetric method.
4. Kidney function tests (serum creatinine, blood urea nitrogen) were performed using the calorimetric method.
5. Liver enzymes (ALT, AST) were assessed using the kinetic method.
6. Fasting blood sugar and 2 h postprandial were determined.
7. The lipid profile including total cholesterol, serum triglycerides, low-density lipoprotein (LDL), and high-density lipoprotein was assessed.
8. Immunological assessment was performed for the rheumatoid factor (RF/IgM) that was measured using a Biotec (San Diego, USA, Genway Biotech) RA factor latex agglutination slide for the qualitative and semiquantitative determination of RF in the serum.
9. Anti-cyclic-citrullinated peptide antibodies were assessed using an enzyme-linked immunosorbent assay. The cut-off value for the anti-cyclic-citrullinated peptide antibody was 5 U/ml [17].

Assessment of thyroid function was performed using the following:

1. Thyroid stimulating hormone (TSH) was measured using immunometric assays (IMMULITE 2000 Third Generation; Diagnostic Products Corporation, Los Angeles, California, USA).
2. Free serum triiodothyronin (FT3) level was determined using IMMULITE 2000 FT3, competitive, analog-based immunoassay for quantitative estimation of FT3 in serum on an IMMULITE 2000 system.
3. Free serum thyroxin level (FT4) was measured using IMMULITE 2000 FT4, solid-phase chemiluminescent competitive immunoassay method for the quantitative determination of FT4 in serum on an IMMULITE 2000 system. Reference values were 0.27–4.2 IU/ml for TSH, 2.57–4.43 pg/ml for FT3, and 0.93–1.71 ng/dl for FT4 [9].

Clinical hypothyroidism and hyperthyroidism

Clinical hypothyroidism and hyperthyroidism were defined on the basis of the criteria of thyroid abnormalities as defined by the Dutch National Healthcare Consensus Committee [9]:

Subclinical hypothyroidism: it was indicated by increased serum TSH in the presence of a normal serum FT4 level.

Clinical hypothyroidism: it was indicated by increased serum TSH with decreased serum FT4 level, at which stage most patients have symptoms and benefit from treatment.

Subclinical hyperthyroidism: it was indicated by normal serum FT4 and FT3 levels, with TSH levels below the normal range, usually undetectable.

Clinical hyperthyroidism: it was indicated by increased serum FT4 and FT3 levels, with TSH levels suppressed below the normal range, usually undetectable.

Antithyroglobulin (anti-TG) antibodies and antithyroid peroxidase (anti-TPO) antibodies were assayed using an enzyme-linked immunosorbent assay method (Calbiotech Inc. California, USA). The reference values were less than 100 IU/ml for anti-TG antibodies and less than 50 IU/ml for anti-TPO [9].

The diagnosis of AITD was made on the basis of the presence of antithyroid antibodies (presence of increased anti-TPO antibodies levels) in patients with concomitant thyroid dysfunction and/or goiter. However, AITD was suspected if the values of anti-TPO antibodies were close to the reference range with increased levels of anti-TG [9].

Thyroid ultrasound was performed routinely at the Radiology Unit to indicate the need for a thyroid biopsy. However, biopsy was not performed as ultrasound did not show any indications such as cold nodules.

A thyroid scan was performed for the patients who showed subclinical hyperthyroidism (two patients and one control) using ^{99m}Tc radionuclid (g-rays emitters) and a gamma camera.

Statistical analyses

All data were collected, tabulated, and statistically analyzed.

Analysis of data was carried out by an IBM computer using statistical program for social science (SPSS) (software and services, North California, USA) version 18 as follows:

- (1) Description of quantitative variables as mean, SD, and range.
- (2) Description of qualitative variables as number and percentage.
- (3) The χ^2 -test was used to compare groups in terms of qualitative variables.
- (4) The Fisher exact test was used instead of χ^2 -test if one of the compared items (cell on excel) is less than digit 5.
- (5) An unpaired *t*-test was used to compare two groups in terms of quantitative variable.

- (6) *P* value more than 0.05 was considered insignificant, *P* value more than 0.05 was considered significant, and *P* value less than 0.001 was considered highly significant [18].
- (7) Relationships between parameters were analyzed using the Pearson correlation coefficients (*r*).

Results

This study included 150 adult RA patients; 135 (90%) were women and 15 (10%) were men, and their ages ranged from 35 to 62 years (mean 45.2 ± 7.8 years), and a disease duration of 1–15 years (mean 7.7 ± 4.3 years). The study also included 50 age-matched and sex-matched controls; 45 (90%) were women and five (10%) were men, and their ages ranged from 38 to 60 years (mean 43.7 ± 9.3 years).

Table 1 shows the descriptive data of patients and controls, with insignificant differences between both groups in age, sex, BMI, and waist circumference.

Cold intolerance was present in 15 (10%) patients, fatigue was present in 10 (6.6%), and palpitation in 12 (8%). Only three (6%) patients complained of palpitation. Clinical thyroid examination of patients indicated that 14 (9.3%) patients had multinodular goiter, 18 patients (12%) had diffuse goiter, and only two control participants (4%) had diffuse goiter.

In terms of the disease activity of rheumatoid arthritis patients:

- (1) 15 (10%) were in remission, $DAS \leq 2.6$.
- (2) 45 (30%) had low disease activity, $DAS < 2.6$ and ≤ 3.2 .
- (3) 60 (40%) had moderate disease activity, $DAS > 3.2$ and ≤ 5.1 .
- (4) 30 (20%) had high disease activity, $DAS > 5.1$.

The Modified Health Assessment Questionnaire (MHAQ) score ranged from 4 to 15, with a mean value of 5.25 ± 3.7 .

Laboratory data and thyroid function tests of patients and controls

There were highly significant differences between both groups in ESR ($P < 0.00$), CRP ($P < 0.00$), and LDL ($P < 0.00$), as well as significant differences in the levels of TSH ($P < 0.05$), anti-TPO antibodies ($P < 0.05$), and anti-Tg antibodies ($P < 0.05$) (Table 2).

Of the 150 RA patients studied, laboratory thyroid abnormalities were present in 44 (29.3%) patients versus four (8%) control participants (Table 3).

- (1) Hypothyroidism was the most common disorder found in 36 (24%) patients versus one (2%) control participant.

Table 1 Descriptive and demographic data of rheumatoid arthritis patients and the control group

Variables	Patients (N = 150)	Controls (N = 50)	<i>t</i> / χ^2 / <i>f</i>	<i>P</i>	S
Age (years)	35–62 (45.2 ± 7.8)	38–60 (43.7 ± 9.3)	0.677	>0.05	NS
Sex	135 F 15 M	45 F 5 M	0.87a 0.26b	>0.05 >0.05	NSNS
BMI (kg/m ²)	32.98–41.91 (35.82 ± 5.05)	30.82–35.78 (33.10 ± 3.75)	1.84	>0.05	NS
waist circumference (cm)	89.74–125.81 (112.8 ± 19.2)	85.91–120.7 (105.3 ± 11.7)	0.609	>0.05	NS

F, female; *f*, Fisher's exact test; M, male; S, significance; *t*, Student's *t*-test.; ^a χ^2 -Test.; ^bFisher's exact test.

Table 2 Comparisons between patients and controls in laboratory and thyroid function data

Laboratory data	Patients (N = 150)	Controls (N = 50)	<i>T</i>	<i>P</i>	Significance
ESR (mm/1st h)	55.3 ± 30.1	12.8 ± 4.7	7.641	0.00	HS
CRP (mg/l)	27.3 ± 22.1	8.7 ± 7.8	4.347	0.00	HS
Fasting blood sugar (mg/dl)	115.3 ± 32.2	98.7 ± 32.4	1.990	>0.05	NS
Postprandial blood sugar (mg/dl)	163.4 ± 52.3	142.1 ± 56.4	1.517	>0.05	NS
Creatinine (mg/dl)	0.812 ± 0.291	0.795 ± 0.103	0.253	>0.05	NS
TG (mg/dl)	138.3 ± 33.4	128.4 ± 50.7	0.893	>0.05	NS
Cholesterol (mg/dl)	194.7 ± 25.7	181.3 ± 26.7	1.980	>0.05	NS
LDL (mg/dl)	122.2 ± 15.3	101.2 ± 20.3	4.525	0.00	HS
HDL (mg/dl)	49.3 ± 29.1	52.1 ± 27.2	0.382	>0.05	NS
TSH (IU/ml)	3.95 ± 7.07	2.22 ± 2.17	2.13	<0.05	S
Free T3 (pg/ml)	3.14 ± 0.72	3.34 ± 0.77	1.034	>0.05	NS
Free T4 (ng/dl)	1.73 ± 0.72	1.45 ± 0.69	1.538	>0.05	NS
Anti-TPO antibodies (IU/ml)	85.69 ± 106.83	43.16 ± 132.23	2.15	<0.05	S
Anti-Tg (thyreoglobulin) antibodies (IU/ml)	58.2 ± 83.9	24.19 ± 36.74	2.23	<0.05	S

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HDL, high-density lipoprotein; HS, highly significant; LDL, low-density lipoprotein; S, significant; TPO, thyroid peroxidase; TG, thyreoglobulin; TSH, thyroid stimulating hormone.

- (2) Subclinical hypothyroidism was found in six (4%) patients versus two (4%) control participants.
- (3) Subclinical hyperthyroidism was found in two (1.3%) patients versus one (2%) control participant.
- (4) None of the patients or the controls had hyperthyroidism.

Classification of rheumatoid arthritis hypothyroid patients ($n = 36$) according to their activity state

On classifying one (0.06%) patient was found to be in an inactive state, four (2.6%) in a mild activity state, 25 (16.6%) in a moderate activity state, and six (4%) in a severe activity state.

According to the (laboratory thyroid functions) [9], patients were subdivided into two groups: 114 (76%) patients were either normal or had a subclinical thyroid

state (group A), whereas 36 (24%) patients were in a hypothyroid state (group B).

On comparing the demographic data between 114 (76%) patients with normal or subclinical thyroid disorders (group A) and 36 (24%) patients in a hypothyroid state (group B), there were significant differences in disease duration ($P < 0.05$), BMI ($P < 0.00$), waist circumference ($P < 0.00$), disease activity ($P < 0.05$), and MHAQ ($P < 0.05$). In addition, there were significant laboratory differences in ESR ($P < 0.05$), levels of cholesterol ($P < 0.05$), TG ($P < 0.05$), LDL ($P < 0.05$), anti-TPO ($P < 0.05$), and anti-Tg ($P < 0.05$) antibodies. Highly significant differences were present in TSH ($P < 0.001$), FT3 ($P < 0.001$), and FT4 ($P < 0.001$).

Current prednisone used (daily dose) and methotrexate (weekly dose) were higher in group B than in group A, with a significant difference ($P < 0.05$) (Table 4).

Anti-TPO antibodies were present in 14 (9.3%) RA patients, whereas anti-Tg antibodies were present in five (3.3%) RA patients compared with three (6%) and one (2%) control participants, respectively, with no statistical difference ($P > 0.05$) between both groups.

Accordingly, AITD was considered positive in 10 (6.6%) patients who showed hypothyroidism together

Table 3 Frequency of thyroid abnormalities among rheumatoid arthritis patients and controls

Variables	Patients ($N = 150$) [N (%)]	Controls ($N = 50$) [N (%)]	f	P	Significance
Subclinical hypothyroidism	6 (4)	2 (4)	1.23	>0.05	NS
Subclinical hyperthyroidism	2 (1.3)	1 (2)	1.26	>0.05	NS
Hypothyroidism	36 (24)	1 (2)	0.31	<0.001	HS

f , Fisher's exact test; HS, highly significant.

Table 4 Comparison between demographic and laboratory data of rheumatoid arthritis patients (group A) and rheumatoid arthritis patients with hypothyroidism (group B)

Variables	Group A ($N = 114$) (76%)	Group B ($N = 36$) (24%)	$t/\chi^2/f$	P	Significance
Age (years)	38–60 (40 ± 5.6)	32–50 (38.3 ± 9.7)	0.588	0.561	NS
Sex [N (%)]					
Male	10 (10.5)	5 (13.88)	1.00b	>0.05	NS
Female	104 (91.22)	31 (86.11)	0.567	>0.05	NS
Disease duration (years)	3.2 ± 5.3	9.8 ± 4.3	2.990	<0.05	S
BMI (kg/m^2)	30.4 ± 2.1	38.3 ± 3.8	9.966a	0.00	HS
Waist circumference (cm)	92.4 ± 9.8	115.2 ± 5.7	5.818	0.00	HS
MDAS28	4.3 ± 1.2	6.9 ± 1.9	0.042	<0.05	S
MHAQ	3.89 ± 0.71	11.98 ± 4.38	2.41	<0.05	S
ESR (mm/1st h)	35.7 ± 9.4	52.1 ± 10.2	3.967	0.0005	HS
CRP (mg/l)	23.3 ± 12.3	25.2 ± 10.8	0.367	>0.05	NS
Serum creatinine (mg/dl)	0.73 ± 0.5	0.81 ± 0.4	0.38	>0.05	NS
Cholesterol (mg/dl)	30/114 (26.3%)	21/36 (58.33%)	0.181a	<0.05	S
TG (mg/dl)	25/114 (21.9%)	15/36 (41.66%)	0.344a	<0.05	S
LDL (mg/dl)	40/114 (35.08%)	26/36 (72.22%)	0.189a	<0.05	S
Prednisone (mg/day)	5–10 (3.2 ± 1.8)	5–20 (7.8 ± 9.2)	2.343	<0.05	S
Methotrexate (mg/week)	10–12.5 (8.5 ± 1.2)	12.5 ± 25 (12.7 ± 6.5)	3.049	0.005	S
TSH (IU/ml)	1.56 ± 1.5	18.2 ± 7.3	10.615	0.000	HS
Free T3 (pg/ml)	3.31 ± 0.6	2.3 ± 0.4	4.155	0.0003	HS
Free T4 (ng/dl)	1.52 ± 0.3	0.8 ± 0.5	4.731	0.0001	HS
Anti-TPO antibodies	68.69 ± 108.33	120.18 ± 122.23	2.15	<0.05	S
Anti-Tg antibodies	47.2 ± 73.98	54.19 ± 46.74	2.23	<0.05	S

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HS, highly significant; LDL, low-density lipoprotein; MDAS, Modified Disease Activity Score; MHAQ, Modified Health Assessment Questionnaire; S, significant; TPO, thyroid peroxidase; TG, thyroglobulin; TSH, thyroid stimulating hormone.; ^a χ^2 -Test.; ^bFisher's exact test.

Table 5 Correlations of levels of thyroid stimulating hormone and free T3 with disease duration, activity score, BMI, cholesterol, thyreoglobulin levels, and drug intake in rheumatoid arthritis patients

Variables	TSH (IU/ml)		Free T3 (pg/ml)	
	<i>r</i>	<i>P</i> value	<i>r</i>	<i>P</i> value
Disease duration	0.256	0.12	-0.31	0.54
ESR	0.783	0.02*	-0.763	0.01*
MDAS28	0.888	0.01*	-0.874	0.01*
MHAQ	0.854	0.014*	-0.798	0.034*
BMI (kg/m ²)	0.754	0.032*	-0.781	0.031*
Waist circumference (cm)	0.839	0.019*	-0.801	0.024*
Cholesterol (mg/dl)	0.251	0.335	-0.244	0.302
TG (mg/dl)	0.677	0.049*	-0.705	0.036*
LDL (mg/dl)	0.211	0.301	-0.302	0.554
Prednisone (mg/dl)	0.315	0.423	-0.112	0.56
Methotrexate (mg/week)	0.7454	0.035*	-0.844	0.012*

ESR, erythrocyte sedimentation rate; LDL, low-density lipoprotein; MDAS, Modified Disease Activity Score; MHAQ, Modified Health Assessment Questionnaire; TG, thyreoglobulin; TSH, thyroid stimulating hormone; **P* < 0.05 (significant)

with positive anti-TPO antibodies that was not observed in any of the controls.

On correlating between TSH levels and the RA disease activity parameters, there were significant positive correlations with (ESR, MDAS28, MHAQ, and dose of methotrexate) [$r = 0.783$ ($P < 0.02$), $r = 0.888$ ($P < 0.01$), $r = 0.854$ ($P < 0.01$), and $r = 0.7454$ ($P < 0.03$), respectively].

Significant positive correlations were also found between TSH levels and BMI, waist circumference, and TG [$r = 0.75$ ($P < 0.32$), $r = 0.83$ ($P < 0.019$), and $r = 0.67$ ($P < 0.049$), respectively].

However, the levels of FT3 showed significant negative correlations with the RA disease activity parameters: ESR ($r = -0.76$, $P < 0.01$), MDAS28 ($r = -0.87$, $P < 0.01$), MHAQ ($r = 0.79$, $P < 0.03$), and dose of methotrexate ($r = -0.084$, $P < 0.012$) as well as significant negative correlations between FT3 levels and BMI ($r = -0.78$, $P < 0.031$), waist circumference ($r = -0.80$, $P < 0.024$), and TG ($r = -0.70$, $P < 0.036$) (Table 5).

Discussion

The coexistence of thyroid dysfunction/thyroiditis and RA has been a subject of debate [19]. Some workers have suggested that hypothyroidism might exacerbate rheumatoid disease with a destructive arthropathy affecting mainly the proximal interphalangeal joints [20,21], associated with fatigue, anemia, and myalgia, all attributed to the inflammatory state of RA [22].

This study was designed to investigate the association of hypothyroidism and thyroid autoantibodies with RA and to study their correlation with RA disease

activity. The study included 150 adult RA patients, 135 (90%) women and 15 (10%) men.

Thyroid abnormalities were present in 44 (29.3%) RA patients and four (8%) control participants, which is not in agreement with the study of Shiroky *et al.* [7], who found that 29 (30%) RA patients had evidence of thyroid dysfunction compared with 10 (11%) of their controls, although another Egyptian study has reported less frequent thyroid dysfunction (8.3%) [11].

Hypothyroidism was the most common disorder in our study, found in 36 (24%) patients, similar to other authors who showed that clinical hypothyroidism was the most common thyroid disorder associated with RA [9,11,23,24].

Clinical hypothyroidism was observed three times more often in RA female patients than in women of the general population [9,25]. In our study, 31 (20%) female RA patients compared with five (4%) men had hypothyroidism.

Anti-TPO and anti-Tg antibodies were present in 14 and five of our RA patients (9.3 and 3.3%, respectively), with insignificant differences from the controls ($P > 0.05$). These results are almost in agreement with the results of Mousa *et al.* [11], who found positive anti-TPO and anti-Tg antibodies in 10 and 6% of Egyptian RA patients. However, our data were different from those of other populations, where these antibodies were present in 15.9 and 12.3% of Turkish RA patients [26]. Also, a higher percentage of thyroid antibodies was recorded in Polish RA patients (15 and 12%, respectively) [9] as well as in Colombian RA patients (37.8 and 20.8%) [27]. These variations in the percentage of antithyroid antibodies can be attributed to ethnic and environmental differences of the studied populations.

Fewer studies have studied the relationship of the AITD with RA disease activity [22].

AITD was considered positive in 10 (6.6%) RA patients, which was almost in agreement with the results of other studies that found a prevalence of AITD in 9.8% of their studied RA patients; however, others have found a higher prevalence of 16% in their RA patients [9].

Common etiological factors for RA and hypothyroidism have been discussed such as the use of salicylates and many other NSAIDs or corticosteroids in treating RA, which have been shown to alter thyroid gland function [7,22,28]. Therefore, the pathogenesis of thyroid disease in patients with RA may have a common pathway and it was speculated that thyroid

disorders are the result of the antithyroid activity of one of the antibodies produced in RA [29]. Moreover, a genetic predisposition determined by a certain Human Leucocyte Antigen (HLA) type, most often HLA-DR, is one possible explanation for the presence of two or more autoimmune diseases in one individual [30]. More explanations have been suggested when anti-TNF- α treatment improved thyroid function in hypothyroid patients with RA [2], also provided evidence that inflammatory cytokines may play a pathogenic role in thyroid dysfunction [31].

Our results showed positive significant correlations between serum levels of TSH and RA activity parameters (ESR, MDAS28, MHAQ, and dose of methotrexate), indicating that higher levels of TSH are associated with higher grades of RA disease activity. Also, we found negative significant correlations between serum levels of FT3 and RA activity parameters (ESR, MDAS28, MHAQ, and dose of methotrexate), indicating that lower levels of FT3 are linked to higher grades of RA disease activity.

Some authors found that hypothyroidism correlated with the number of swollen joints in RA patients [9], whereas others found higher levels of CRP in RA patients with hypothyroidism [11], which is in contrast to our results. However, other studies could not find a correlation between hypothyroidism and RA disease activity state [22,32] and concluded that thyroid hormonal defects were related to the disease duration and not the disease activity, although it is inconsistent with our results; this could be because of the short mean duration of our RA (7.7 ± 4.3 years) compared with theirs.

Conclusion

Thyroid dysfunction and AITD are common in RA patients, with hypothyroidism being the most common disorder prevalent in 24% of patients. TSH and FT3 have shown an evident correlation with RA disease activity as well as clinical and laboratory disease parameters.

Recommendations

- (1) Thyroid function and antithyroid antibodies tests should be performed as part of the biochemical and immunological profile in RA patients.
- (2) Treatment of both clinical and subclinical hypothyroidism should be considered in RA patients.
- (3) Clinical follow-up is needed to clarify the effect of thyroid dysfunction treatment on RA activity and vice versa.

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Conflicts of interest

None declared.

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