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Evaluating thyroid disorders in patients with rheumatoid arthritis:a cross-sectional study

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Abstract

Introduction:*The prevalence of autoimmune thyroid disease (AITD) in RA varies considerably; and there is no recommendation for routine population screening for thyroid diseases in RA. In this study, we assessed the prevalence of thyroid disorders in RA patients referred to the Razi Hospital, Rasht, Iran.*

Patients and Methods: *This was ananalytical cross-sectional study.The prevalence of thyroid abnormalities in 224 patients diagnosed with RA was evaluated according to ACR criteria who referred to the Razi hospital rheumatology clinic during 2008-2010, Rasht, Iran. All patients were checked for free T4, free T3, Thyroid-stimulating hormone (TSH), Anti-thyroid peroxidase (Anti-TPO) and Anti-Thyroglobulin.*

Results: *Generally, 224 patients were included in the study and 87.1% were female;the mean age was 49.05±13.53 years (CI: 18-80). Sixty-four patients (28.6%) had thyroid disorders.There was no significant relationship between the existence of thyroid disorder and age, familial history of thyroid or RA diseases (P>0.05) but there was a significant relationship between the existence of thyroid disorder and gender (P<0.001) and it was more in women. In the clinical examination results,the existence of nodule was a significant predictor of thyroid dysfunction (OR: 1.12, CI: 0.6-0.98; P<0.001).*

Conclusion:*Our study confirmed an increase in the prevalence of thyroid dysfunction in patients with RA associated with a low prevalence of hormonal alterations. The most thyroid dysfunction was hypothyroidism.*

Keywords:*Rheumatoid Arthritis, Thyroid Dysfunction, Hypothyroidism*

I. Introduction

Thyroid dysfunction has been reported in 6% to 33.8% of patients with rheumatoid arthritis (RA) (1-4).Clinical manifestation of these diseases is oftenproceeded by the presence of organ-specificantibodies that might

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occur in serum evena few years before symptom onset and makinga diagnosis. However, it is not a reliable earlysymptom of the disease because the antibodiesare also found in low concentrations in healthyindividuals(2). Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease of unknown etiology. It is characterized by symmetrical polyarthritis and the progressive destruction of articular cartilage and bone, primarily affecting the peripheral joints in a symmetrical pattern (5). This leads to increasing disability and is associated with several co-morbidities (6). It is the commonest inflammatory arthropathy worldwide with a gender predilection towards women. The prevalence of RA in the adult general population is approximately 1% (6, 7). Associated autoimmune diseases, such as thyroid and coeliac diseases, have been previously described, mainly in rheumatoid arthritis (8, 9). However, the risk of thyroid dysfunction in RA patients has not yet been fully established(3).

The worldwide prevalence of autoimmune thyroid disease (AITD) in RA varies considerably, ranging from 0.5% (10) to 27%(11). Most internists do not recommend routine population screening for thyroid diseases. It is thought that individuals from risk groups (of thyroid diseases development) should be screened i.e. women with family history of thyroid diseases, with previous thyroid dysfunction, with symptoms suggestive of hyperthyroidism or hypothyroidism, with abnormalities in physical examination of the thyroid gland, type 1 diabetes and a history of other autoimmune diseases(12).Although thepathogenic mechanism in RA is still undefined, autoimmunityplays a crucial role in both its chronicityand its progression as evidenced by the high level ofcytokines found, especially tumor necrosis factor a(TNF-a)(5, 13).In this study, we assessed the prevalence of thyroid disorders in RA patients referred to the Razi Hospital, Rasht, Iran.

II. Patients and Methods

This was ananalytical cross-sectional study in which the prevalence of thyroid abnormalities in diagnosed RA patients was evaluated according to the 1987American College of Rheumatology (ACR) criteria who referred to the Razi hospital rheumatology clinic during May2008and January2010, Rasht, Iran.

The sample size was calculated with an anticipated prevalence of thyroid dysfunction among rheumatoid arthritis and an absolute error of 5% with a 30% prevalence and 95% confidence level(14).

$$n = \frac{z^2_{(1-\frac{\alpha}{2})} P(1-P)}{d^2}$$

Inclusion criteria:

Patients,30 years and older, with RA that was done according to ACR criteria (15) and underwent rheumatologists' visit.

Exclusion criteria:

- Patients with a history of pregnancy
- Surgical removal of the thyroid gland

- Sepsis and serious underlying diseases
- Patients on oral contraceptives
- Taking drugs that cause thyroid disorder,
- Any malignancy on radiotherapy and damage to the thyroid
- Taking oral contraceptives

At the inclusion visit, complete thyroid examinations focused on thyroid function performed for all patients participating in the study**.** Demographic data and the type of thyroid dysfunction (Autoimmune clinical hypothyroidism, Autoimmune subclinical hypothyroidism,Goiter, Multinodular goiter, Nodule) base on results of clinical examination and thyroid testswere recorded.Under spastic conditions, 5 ml of blood collected from the medial cubital vein for thyroid laboratory tests.Samples of blood were taken after 10-12 hours of fasting. Thyroid tests were performed at the Razi hospital laboratory in Rasht.

Thyroid function evaluation

All patients checked for free T4 with ECLIA method (normal range: 0.8-2 ng/dl), free T3 with ECLIA method (normal range: 1.8-4.4 ng/dl), Thyroid-stimulating hormone (TSH) with IRMA method (normal range: 0.3-5.5 IU/ml), Anti-thyroid peroxidase (Anti-TPO) with ECLIA method (<34: negative and >34: positive) and Anti-Thyroglobulin with ECLIA method (<115: negative and >115: positive). After reporting the results of thyroid function tests, patients referred to endocrinologists for more evaluation and possible treatment.

Ethics

All patients filled informed consent for enrollment and all the steps of the study were performed according to Guilan University of Medical Sciences' ethical committee.

Statistics

The RA and thyroid dysfunction related data compared using Pearson's Chi-square test for dichotomous variables and using the Mann–Whitney U test for continuous variables. Logistic regression analysis was used to calculate the odds ratio (OR) with 95% confidence interval (CI) for thyroid disorders as risk factors. A p-value below 0.05 was considered statistically significant. For all analyses, SPSS 13.0 for Windows (SPSS, Inc., Chicago, Illinois, USA) was used.

III. Results

The main characteristics of our population are shown in table 1. In this study, 224 patients with RA were evaluated, 195 of which were women (87.1%). The mean age of participants was 49.05±13.53 years old (CI: 18-80).

Table 1. Demographic data of patients with RA enrolled in the study

Characteristics		Frequency	Percent
Gender	Male	29	12.9
	Female	195	87.1
Age group (years)	≤39	51	22.8
	40-60	130	58
	≥61	43	19.2
Familial history of RA		68	30.4
Familial history of thyroid disorder		44	19.6

Sixty-four patients (28.6%) had thyroid disorders. Characteristics of RA patients with thyroid disorder are shown in Table2. There was no significant difference between age, gender and familial history of RA with thyroid disorder ($P>0.05$) but there was a significant relationship between thyroid disorder and familial history of thyroid disease ($P<0.02$).

Table2.Characteristics of RA patients with thyroid disorders

Characteristics		
Gender N (%)	Male	3 (4.7)
	Female	61 (95.3)
Age (Mean± S.D) years	49.64±12.29	

Familial history of RA N (%)	16	(23.5)
Familial History of thyroid disorder N (%)	19	(43.2)
Type of thyroid disorder		
Autoimmune clinical hypothyroidism	27	(12.1)
Autoimmune subclinical hypothyroidism	4	(1.8)
Goiter	3	(1.8)
Multinodular goiter	3	(1.3)
Nodule	2	(0.8)
Thyroid examination		
Goiter	13	(5.8)
Nodule	12	(5.4)
Multinodular goiter	9	(4)
Normal	190	(84.8)

There was no significant relationship between thyroid disorder and age, family history of thyroid diseases and RA (P> 0.05);however there was a significant relationship between thyroid disorder and gender (P <0.001) and it was more observed in women (Table 3). In clinical examination results, nodules were significant predictives of thyroid dysfunction (OR: 1.12, CI: 0.6-0.98; P <0.001).

Table3. Prevalence of hypothyroid status in rheumatoid arthritis (RA) patients

Thyroid function	Sex	N(%)	P* value
Euthyroid	Men	27(93.71)	-
	Women	155(79.5)	-
Hypothyroidism	Men	3(10.3)	0.074

	Women	24(12.3)	0.045
Goiter	Men	1 (3.4)	0.2
	Women	5(2.5)	0.41
Subclinical Hypothyroidism	Men	0(0)	-
	Women	4(2.05)	0.34
Other	Men	0(0)	-
	Women	2(1.02)	0.56

*chi square test

IV. Discussion

In our study, 64 patients (28.6%) had thyroid dysfunction and most of them were hypothyroidism. In clinical examination results, the nodule was a significant predictor of thyroid dysfunction. There was no significant relationship between thyroid disorder and age, familial history of thyroid and RA diseases;however, there was a significant relationship between thyroid disorder and gender and it was observed more in women. It proves that thyroid abnormalities are sex-related, albeit the number of studied males was relatively small in our investigation.

An association between autoimmune thyroid disease, with or without evidences of thyroid dysfunction, and systemic rheumatic diseases such as Sjo¨gren's syndrome, rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), or scleroderma has been described (16).Positive thyroid autoantibodies, anti-thyroperoxidase (TPOAb) and/or anti-thyroglobulin antibodies (TgAb), have been detected in about11% of RA patients(9), with a wide difference in mostseries, ranging from 2 (17) to 16% (18). In a series of58 multicase UK families with RA, 6% of the patientshad thyroid disease, and 5% of the men and 15% ofthe women had TPOAb. In a controlled series of 101RA patients from Greece (9), 12.9% had TPOAb,compared to 8.6% of controls; similar results havebeen found in Norway and Quebec (19, 20). El-Sherifet al. (21) have reported an increase in thyroiddisorders in patients with RA and/or SLE. Buchananet al. (22) demonstrated a statistically significantassociation between Hashimoto's thyroiditis and RA. Moreover, Silman et al. (1) reported a highfrequency of Hashimoto's thyroiditis and thyroidautoantibodies not only in patients with RA but alsoin their families.

Decades ago, signs of hypothyroidism had been reported in 12–30% of patients with arthritis; therefore, it seems likely that the prevalence rates of hypothyroidism are increased in patients with inflammatory arthritis (23). Indeed, we observed an increased prevalence of hypothyroidism in patients with inflammatory arthritis when compared to controls. These results emphasize the tendency of autoimmune disorders to cluster. Explanations for the

coexistence of autoimmune disorders involve immunological disturbances (in B and T lymphocytes), a tendency to react abnormally in the presence of an antigen or genetic susceptibility (24). The cause of hypothyroidism in RA patients may be due to the anti-thyroid activity of one of the antibodies produced (25). A genetic factor such as human leukocyte antigen (HLA) type, most often HLADR, is one possible explanation for the presence of two or more autoimmune diseases in one individual (26). It is also suggested that anti-TNFa treatment improves thyroid function in hypothyroid patients with RA,5 and there is evidence that shows inflammatory cytokines may play a pathogenic role in thyroid dysfunction (27).The most common cause of thyroid dysfunction is autoimmunity, but in patients with RA, there is some discrepancy between the presence of these autoantibodies and hormonal function (28, 29).The worldwide prevalence of autoimmune thyroid disorder has been reported between 0.5% to 27%(30). In a cohort, 22.9% of the patients were positive for TgAband 37.1% of the patients had TPOAb, but only 2.8%of the patients had clinical hypothyroidism and theywere treated with L-thyroxine for hypothyroidism(29).This may be related to the presence of subclinicalthyroiditis or the interactions between FT4 or antithyroidantibodies with other serum factors, such asRF(31). One of the limitations of our study was the lack of information on the prevalence of thyroid disorders in the population for comparison with rheumatoid arthritis patients.

V. Conclusion

In our study, the prevalence of thyroid disorders in patients with rheumatoid arthritis was 28.6%. Autoimmune hypothyroidism was the most common thyroid dysfunction (12.1%). The Nodule was a significant predictor of thyroid dysfunction. There was no significant difference between age, gender and familial history of RA with thyroid disorder but there was a significant relationship between thyroid disorder and familial history of thyroid disease. Screening tests for thyroid disorders in patients with rheumatoid arthritis are recommended.

Conflict of interest

There was no conflict of interest.

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