

## Thyroid disorders in rheumatoid arthritis and osteoarthritis

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### ABSTRACT

**Objective:** Auto immune disorders such as rheumatoid arthritis (RA) and thyroid disorders are caused by a reaction of the immune system against self antigens and there is a tendency for more than one syndrome in a patient. Our objective was to determine the prevalence of thyroid disorders in patients with RA and compare it with that in osteoarthritis (OA) patients, as well as determination of characteristics of RA patients with thyroid disorders.

**Methodology:** Subjects were 80 patients with RA and 80 age and sex matched patients with osteoarthritis. All participants were examined for thyroid disorders by physical examination and thyroid function tests. Criteria of disease activity in RA patients were recorded.

**Results:** Clinical hypothyroidism was observed in 13 (16.3%) of RA patients, which was not significantly different from controls ( $p=0.3$ ). Existence of antithyroid peroxidase antibody (Anti TPO Ab) was lower in RA patients (20% vs. 36.3%) ( $p=0.02$ ) and thyroid nodules were more prevalent in RA patients (17.5% vs. 7.5%) ( $p=0.1$ ). There were two RA patients with subclinical hyperthyroidism. No significant difference was found in patients' age, seropositivity and disease activity in RA patients with or without thyroid disorders ( $p<0.05$ ).

**Conclusions:** Patients with RA and OA did not have any significant difference in thyroid dysfunction. RA patients did not have any particular characteristic pointing to a requirement for assessment of thyroid disorders, too. Because of its importance in cardiovascular disorders, monitoring of thyroid function in all patients with RA is recommended.

**KEY WORDS:** Thyroid diseases, Thyroid nodule, Rheumatoid arthritis, Osteoarthritis, Hypothyroidism.

Pak J Med Sci April - June 2011 (Part-II) Vol. 27 No. 3 595-598

### How to cite this article:

Mobini M, Kashi Z, Thyroid disorders in rheumatoid arthritis and osteoarthritis. Pak J Med Sci 2011;27(3):595-598

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- \* Received for Publication: July 4, 2010
- \* Revision Received: December 18, 2010
- \* Revision Accepted: April 26, 2011

### INTRODUCTION

One important feature of autoimmune disease is that more than one autoimmune diseases can be present in one patient.<sup>1</sup> Chronic autoimmune thyroiditis frequently overlaps with autoimmune rheumatic disease.<sup>2</sup> A possible explanation of the presence of two or more autoimmune diseases in one individual is microchimerism, the presence of a small number of fetal cells in the mother as well as maternal cells in the fetus<sup>3</sup>, or there may be a common genetic link between them.<sup>4</sup> In some studies thyroid abnormal function tests and / or autoimmune thyroid disorders were observed in 6-33/8% patients with rheumatoid arthritis (RA).<sup>2</sup>

Table-I: Comparison of thyroid disorders in rheumatoid arthritis (RA) and osteoarthritis (OA) patients.

Type of thyroid disorder	RA, n (%)	OA, n (%)	P value
Thyroid disorders	28 (35%)	36 (45%)	0.19
Family history of thyroid disorders	18 (22.5%)	22 (27.5%)	0.4
Past history of thyroid disorders	15 (18.8%)	8 (10%)	0.1
Thyroid nodule	15 (18.8%)	9 (11.3%)	0.1
Sub clinical hyperthyroidism	2(2.5%)	0	0.1
Clinical hypothyroidism	13 (16.3%)	9 (11/3%)	0.3
Sub clinical hypothyroidism	5 (6.3%)	10 (12.5%)	0.1
Anti TPO*	16 (20%)	29 (36.3%)	0.02

\*Antithyroid peroxidase antibodies.

An accelerated progression of atherosclerosis may contribute to the increased mortality due to cardiovascular disease reported in RA.<sup>5</sup> Clinical hypothyroidism was associated with a fourfold higher risk of CVD in comparison with euthyroid female RA patients independently of the traditional risk factors.<sup>6</sup> Thyrotoxicosis is an important but under recognized cause of osteoporosis.<sup>7-8</sup> Recently, TSH deficiency, rather than thyroid hormone excess, has been suggested as the underlying cause.<sup>7</sup> Thyroid disorders in RA patients are often asymptomatic.<sup>2</sup>

The aim of this study was to determine whether thyroid disorders are more prevalent in RA patients compared to the age and sex matched OA patients and whether there are some indicators for screening RA patients at risk for thyroid disorders.

## METHODOLOGY

In this study 80 RA patients were compared with 80 age and sex matched osteoarthritis patients (OA) regarding thyroid disorders in a case-control study. RA was diagnosed according to the 1987 criteria by American College of Rheumatology.<sup>9</sup> OA was diagnosed according to history and physical examination. All of the patients were examined by a rheumatologist.

Exclusion criteria for both groups was usage of >20 mg/day prednisolone, anti convulsion therapy, estrogen, Amiodarone, lithium, Androgens and Immunosuppressive. The patients were enrolled from January to September 2009.

In RA patients, at the inclusion visit, demographic, clinical and laboratory findings and RF (rheumatoid factors) and anti CCP (Antibodies to cyclic citrullinated peptides) were recorded. In sex and age matched OA patients demographic data were recorded, too.

Then participants were referred to an endocrinologist for evaluation of thyroid disorders including history and physical examination, thyroid function tests and anti TPO. (Biomeriexn, Roche, Germany).

The endocrinologist was blinded to type of disease. We considered TSH less than normal range (0.27-4.7 mIU/ml) with normal T4 (66-140 nmol/L) and T3 (1.2-2.1 nmol/L) as subclinical hyperthyroidism and with increased T4 and T3 as clinical hyperthyroidism. Patients with TSH more than normal range and normal T4 were considered subclinical hypothyroid and with TSH more than normal range and low T4 as clinical hyperthyroid. Anti Tpo of more than 34 IU/ml was considered positive.

For data analysis, we used X<sup>2</sup> test and compared means. P value < 0.05 was considered statistically significant. For data analysis, SPSS 16 was used. The study was approved by ethics committee of Mazandaran University of Medical Sciences.

## RESULTS

In this study 80 (76 female /4 male) patients with RA were compared with 80 age and sex matched patients with OA. The mean age in RA patients was 51/4 ±12 and in OA patients was 52/3 ± 11, (P= 0.2). The characteristics of thyroid disorders in our patients are recorded in Table-I. This study showed that the prevalence of thyroid disorders was not significantly different in RA and OA patients (35%

Table-II: Comparison of rheumatoid arthritis (RA) patients with and without thyroid disorders.

Characteristics of patients with RA	RA with thyroid disorders (n=28)	RA without thyroid disorders (n=52)	P value
Age (mean± SD)	48.3± 12	53± 12	0.1
ESR (mean± SD)	25/4± 22	22/9± 12	0.5
RF * (%)	33%	41%	0.49
Anti CCP** (%)	14%	24%	0.8
Mean of tender joint count (n)	3.2±2.3	2.8±2.1	0.4
Mean of swollen joint cont	1.03±1.6	0.9±1.5	0.8

\* Rheumatoid factor.

\*\*Antibodies to cyclic citrullinated peptides.

vs. 45%,  $p=0.19$ ). Sub clinical hypo and hyper thyroidism were found in 6.3% and 2.5% while clinical hypothyroidism was found in 16.3% of RA patients.

There was no significant difference between patients with RA and OA in thyroid disorders except for thyroid presence of nodules in RA patients and anti TPO in OA patients. We found two patients with sub clinical hyperthyroidism in RA patients.

RA patients with and without thyroid disorders were also compared. There was no significant difference in seropositivity or disease activity (tender or swollen joint and ESR) in the two subgroups, but patients with thyroid disorder were younger (Table-II).

## DISCUSSION

Rheumatoid arthritis (RA) and thyroid disorders are associated with an enhanced risk of cardiovascular disorders (CVD) and osteoporosis.<sup>5,7,8</sup> In this study, we have shown that prevalence of thyroid disorders in RA patients is same as controls.

Abnormal thyroid functions and / or autoimmune thyroid disease were reported in 6- 33/8% patients with rheumatoid arthritis.<sup>1,2,6,10</sup> Some of these studies have shown higher prevalence of thyroid disorders in RA patients<sup>6,10,11</sup>, but there are studies that did not have these differences.<sup>2</sup> Clinical and sub clinical hypothyroidism in RA patients were shown in 2.8-24% and 1.7-10.7%<sup>1,6,10-13,14</sup> and our findings are 16.3% and 6.3%. It may be because of increased thyroid disorders after iodine supplementation in Iran.<sup>15-17</sup> In this study, prevalence of sub clinical hypothyroidism in RA patients and controls were 6.3% vs 12.5% ( $p=0.1$ ).

This finding might be explained by the pyramid hypothesis. According to this hypothesis, sub clinical hypothyroidism will develop into clinically

manifest hypothyroidism in approximately one quarter of the cases. Autoimmune disease such as RA may accelerate this progression of sub clinical disease into a clinical disease.<sup>6,18</sup> There are two other studies in Iran about prevalence of thyroid disorders in RA patients. Haghighi's study showed that RA patients have more abnormal thyroid function than control group<sup>1</sup>, but in this study, RA patients were older than their controls. In Zaieni's study, 18.8% of RA patients were hypothyroid<sup>19</sup> but this study did not have a control group.

Subclinical hyperthyroidism was seen in 2.5% in RA patients while there was none in controls. In other studies prevalence of hyper thyroidism (clinical and sub clinical) was shown as 1.3-5% in RA patients.<sup>1,2,11,12</sup> Presence of anti TPO Ab in RA was shown in 5-37% of patients. This prevalence in some populations was more common in RA patients<sup>11,14</sup> but in other studies was more prevalent in controls.<sup>2,12</sup> In this study anti TPO antibody significantly was more common in controls (36.3% vs. 20%,  $p=0.02$ ). It may be because of anti inflammatory and immunosuppressive therapy in patients with RA, which lead to lower prevalence of anti TPO in these patients. It was shown that Anti thyroglobin (ATG) Ab is more common in RA and anti TPO is more common in systemic lupus erythematosus.<sup>12</sup> Presence of anti TPO does not correlate with the occurrence of thyroid hormone functional disorders in RA patients.<sup>2</sup>

Thyroid nodules in RA patients were more common but difference was not significant (18.8% vs 11.3%  $p=0.1$ ). In one study in Tehran in 2002, prevalence of thyroid nodules was 5.9% in general population. In another study in Iranian patients with RA, prevalence of thyroid nodules was 9.4%.<sup>19</sup> This may be from usage of drugs such as methotrexate and TNF inhibitors that can make nodules or rheumatoid nodules.<sup>20,21</sup>

Table-III: Some studies about thyroid disorders in rheumatoid arthritis (RA).

Author, Year, (n)	Clinical hypothyroidism		Subclinical hypothyroidism		Antithyroid peroxidaseAb		Subclinical hyperthyroidism	
	RA	Control	RA	Control	RA	Control	RA	Control
El-Sherif <sup>12</sup> , 2004, (n=20)			10%		5%	10%	5%	
Al-Awadhi <sup>11</sup> , 2008, (n=177)	10.2%	1.4%	10.2%	10.7%	12.4%	3.1%	4.5%	0.2%
Rateman <sup>6</sup> , 2007, (n=358)	6.8%	2.7%	2.5%	18%				
Przygodzka <sup>2</sup> , 2009, (n=100)	16%	9%			15%	18%	2%	0
Haggighi <sup>1</sup> , 2009, (n=75)	8%	0	10.7%	0	25%	6.25%		
Zaieni <sup>16</sup> , 2009, (n=224)	18.8%				17.7%*			
Mobini, 2009, (n=80)	16.3%	11.3%	6.3%	12.5%	20%	36.3%	2.5%	0

\*Antithyroid peroxidase antibody and thyroglobin antibody.

We examined RA patients for probable findings that may be suggestive for simultaneous thyroid disorders (Table-III), but we did not find any significant difference between RA patients with or without it. In Ratterman's study<sup>6</sup> there was no significant difference in RA patients with or without thyroid disorders. Factors such as shorter duration of arthritis<sup>22</sup> and lower disease activity of RA<sup>2</sup> were suggested for evaluation of thyroid disorders in these patients, but anti-thyroid antibodies do not seem to identify any peculiar RA phenotype.<sup>14</sup>

Monitoring of thyroid function is of particular importance since as the course of thyroid disease in RA patients is often asymptomatic.<sup>2</sup> In this study we have shown that clinical hypothyroidism is not significantly more common in RA than OA patients; probably OA patients have some metabolic disorders such as hypothyroidism.<sup>23</sup>

Keeping in view of the importance of thyroid disorders in RA patients we suggest that thyroid examination and thyroid function tests should be done in all such patients. Prevalence of thyroid disorders in patients with RA was found to be unrelated to their age, RA factor status and disease activity in this study. We suggest more studies should be done with a larger group of RA patients comparing them with a control group.

#### ACKNOWLEDGMENTS

This work was supported by a grant from Mazandaran University of Medical Sciences Sari, Iran. This research was a student thesis of Nazanin Ravanbakhsh to receive MD degree in faculty of Medicine, Mazandaran University of Medical Sciences Sari, Iran.

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