Journal of Advances in Medical and Pharmaceutical Sciences
7(1): 1-6, 2016, Article no.JAMPS.24689
ISSN: 2394-1111

SCIENCEDOMAIN *international*
www.sciencedomain.org

Relationship between Autoimmune Thyroid Disorders and Rheumatoid Arthritis

Rawdha Tekaya[1], Aicha Ben Tekaya[1*], Hana Sahli[1], Ines Mahmoud[1], Olfa Saidane[1] and Leila Abdelmoula[1]

[1]Department of Rheumatology, Charles Nicolle Hospital, Tunis, Tunisia.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMPS/2016/24689
Editor(s):
(1) Palmiro Poltronieri, National Research Council of Italy, CNR-ISPA, Italy and Institute of Sciences of Food Productions, Operative Unit in Lecce, Italy.
Reviewers:
(1) Carlos A. Canas, Universidad Icesi, Cali, Colombia.
(2) Shamala Moodley, Mangosuthu University of Technology, South Africa.
Complete Peer review History: http://sciencedomain.org/review-history/13683

Original Research Article

Received 29th January 2016
Accepted 3rd March 2016
Published 14th March 2016

ABSTRACT

Objectives: The aims of this study were to assess the prevalence of thyroid abnormalities in rheumatoid arthritis (RA) patients and to determine the characteristics of rheumatoid patients with thyroid disorders.
Methods: We conducted a prospective study over a six months period. Patients with RA were examined for thyroid disorders by clinical examination, biological tests and ultrasound exams. The characteristics of the rheumatic disease were recorded.
Results: Fifty five patients (41 women and 14 men) were enrolled into study. Mean age was 55.5±10 years, rheumatoid factor was positive in 89.1%, and 63.6% of them had an active RA (DAS28>5.1). Thyroid abnormalities were detected in 40% of the patients (n=22). The mean abnormality seen was asymptomatic nodules without biological dysfunction. There were no differences between RA patients with and without thyroid abnormalities in all characteristics of the rheumatic disease. Patients with RA have a high prevalence of thyroid abnormalities but this does not interfere with the characteristics of the articular disease.
Conclusion: Screening of thyroid disease should be done, as well as osteoporosis and cardiovascular risk factors, which are elevated in RA and are associated with some thyroid diseases.

**Corresponding author: E-mail: aichabentekaya@gmail.com;*

Keywords: Rheumatoid arthritis; thyroid diseases; autoimmune disease; thyroid nodule; dysthyroidism; thyroid antibodies.

1. INTRODUCTION

Thyroid abnormalities frequently overlap with autoimmune rheumatic disease. This hormonal dysfunction has been described in patients with rheumatoid arthritis (RA) with a prevalence which ranges from 6% to 33.8% [1,2]. Usually, in the initial phase, the thyroid disorder is asymptomatic. This association can be explained by a genetic predisposition determined by the affiliation to some HLA haplotypes [3] and may mislead the diagnosis. Moreover, thyroid diseases or dysfunctions may cause a variety of rheumatic manifestations.

Our objective was to determine the prevalence of thyroid abnormalities in RA patients and to compare the RA patients with and without thyroid disorders in order to study the characteristics of RA with thyroid disorders.

2. PATIENTS AND METHODS

Over a period of six months, patients admitted in the Clinical Department of Rheumatology with the diagnosis of RA, according to the 2010 American College of Rheumatology/European League against Rheumatism criteria [4] were studied. Informed consent was obtained from all subjects, and the study was approved by the Hospital's local Ethics Committee. For all the patients, the following examinations were performed:

1. Clinical examination including medical history, physical examination including musculoskeletal system assessment. Activity of RA was evaluated using the Disease Activity Score (DAS 28) with 4 parameters (tenderness joints, swelling joints, global score and erythrocyte sedimentation rate).
2. Laboratory tests used to:

   - Specify the immunological profile of RA: antinuclear antibodies (ANA), Rheumatoid Factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies,
   - Evaluate RA activity: erythrocyte sedimentation rate (ESR), C-reactive protein (CRP),
   - Test function thyroid (FT4 and TSH).

3. Thyroid ultrasound was routinely performed for all the patients.
4. Autoimmune thyroid disease was diagnosed on the presence of antithyroid antibodies (antithyroglobulin (AntiTG) and antithyroid peroxidase antibodies (antiTPO))

Thyroid disorder was defined by any abnormality in the clinical examination of the thyroid gland and/or in the biological tests and/or in the ultrasound exam.

For data analysis, SPSS 11.5 was used and p value<0.05 was considered statically significant.

3. RESULTS

In this study, fifty five patients with RA were evaluated. Forty one were women and fourteen were men. The mean age of the patients was 55.5±10.5 (range 31 to 79 years). The mean duration of RA was 9,5±8,5 (range 0 to 30 years). The principal characteristics of the RA are recorded in Table 1. RF was detected in 89.1% of the patients. Anti CCP antibodies were detected in 18.2% of the patients. The mean disease activity score (DAS 28) was 5.59±1.64 with a high activity of the RA in 35 cases (63.6%). Systemic manifestations of the RA were noted in the majority of the patients: Sjögren's Syndrome in 18.2%, ocular sicca syndrome in 30.9% and buccal sicca syndrome in 25.5% of the patients. This study showed that thyroid abnormality, as defined previously, was detected in 40% of the patients (n=22). Clinical symptoms were noted in 5 cases, as specified in Table 2. Clinical examination revealed abnormalities in three patients (nodule in one case and multinodular goiter in two cases). Biological disorders were noted in 6 cases as hyperthyroidism in 3 and hypothyroidism in 3. Ultrasound exam revealed abnormalities in 18 cases. The characteristics of thyroid disorders in our patients are recorded in Table 2.

Anti-TG and anti-TPO were done in 18 cases and were positive in only one case. There was no significant difference between RA patients with and without thyroid abnormalities in the age of onset of the RA (p=0.903), the disease duration (p=0.445), the gender (p=0.1), the positivity of RF (p=0.158), the presence of anti-CCP antibodies (p=1), the erosive character

(p=0.475), the disease activity (p=0.378) nor the association with Sjögren's Syndrome (p=1), but the patients with biological abnormalities had more anti-CCP antibodies than the patients without (p=0,066). These results are summarized in Table 3.

Table 1. Characteristics of patients with rheumatoid arthritis

Characteristic	Result
Age of onset (years) mean (SD)	45.7(±11.5)
Mean disease duration (years) mean (SD)	9,5(±8,5)
Rheumatoid factor >0 (%)	89.1
Antinuclear antibodies >0 (%)	16.4
Anti CCP antibody >0 (%)	18.2
Erosive disease (%)	81.8

Anti-CCP: Anti-cyclic citrullinated peptide

4. DISCUSSION

It has been demonstrated in many studies that in RA patients, thyroid dysfunction is three times more frequent than in the general population [4-10]. A Portuguese study including 109 women with RA and 149 controls demonstrated that the prevalence of thyroid abnormalities was 12.8% in RA patients versus 4.6% in controls [11]. In a prospective study, 30% of women with RA had evidence of thyroid dysfunction compared with 11% of controls and this excess is due to either hypothyroidism or Hashimoto's thyroiditis [6]. Przygodzka et al. had noted in a controlled study this high prevalence but without statistically significant difference: 16% in RA patients and 9% in the control group [7]. However, this high prevalence of thyroid disease was not always confirmed in RA patients [8]. In our study, the prevalence of thyroid dysfunction in RA patients is higher compared to the prevalence in general population such as noted in the Wickham study [5]. Indeed, that study showed the prevalence of subclinical hypothyroidism (normal T4, raised TSH) to be around 7.5% in females (range 5–10%, age >18 yr). The results of a recent meta-analysis showed that the prevalence of thyroid autoantibody positivity in patients with RA was higher than that in healthy controls, suggesting that thyroid autoimmunity is more prevalent in patients with RA than in the control population [12].

Table 2. Thyroid abnormalities in RA patients

	N	%	
Clinical symptoms	5	9,1	- Hyperthyroidism: 3 cases - Hypothyroidism: 1 case - Compressive goiter with dyspnea: 1 case
Clinical exam abnormality	3	5,5	- Nodule: 1 case - Multinodular goiter : 2 cases
Biological abnormality	6	10,9	- Hyperthyroidism: 3 cases - Hypothyroidism: 3 cases
Ultrasound abnormality	18	32,7	- Nodule: 10 cases - Multinodular goiter: 8 cases

N: Number of patients

Table 3. Comparison of the RA patients with and without thyroid disorders

Characteristics of RA patients	With thyroid disorder (n=22)	Without thyroid disorder (n=33)	p
Mean age	56,6±9	54,7±11	0,51
Mean disease duration	22±8	33±8	0,44
Disease activity			0,37
- Low	1	5	
- Moderate	7	7	
- High	14	21	
Presence of RF	81,8% (n=18)	93,9% (n=31)	0,15
Presence of anti CCP antibodies	18,1% (n=4)	18,1% (n=6)	1
Presence of antinuclear antibodies	13,6% (n=3)	18,1% (n=6)	0,65
Erosive character	77,2% (n=17)	84,8% (n=28)	0,48

RA: Rheumatoid arthritis, N: Number, RF: Rheumatoid factor, CCP: Anti-cyclic citrullinated peptide

The association between RA and thyroid diseases might be the result of a genetic predisposition to autoimmunity [4,13]. This predisposition explain the high prevalence of thyroid diseases in other systemic disorders such as systemic lupus erythematosus [8,9] and primary Sjögren's Syndrome [10]. It had been also seen an overexpression of endemic goiter in RA patients [14]. A possible explanation of the presence of more than one autoimmune disease in one individual is microchimerism [15]. The polymorphism of the protein tyrosine phosphatase 22 gene was studied in Tunisian population with autoimmune thyroid diseases and RA. The data showed no implication of this polymorphism in the thyroid or the rheumatic diseases [16].

The second objective of this paper was to study the effect of thyroid abnormality on the articular disease. We find that the presence of thyroid abnormalities had no influence on the characteristics of the RA but that biological abnormalities were associated with a parameter of severity of the RA which is the presence of anti-CCP antibodies. Some authors studied the relationship between RA activity and thyroid disease and found no links between the thyroid diseases and the RA activity [17-21]. Shiroky et al. [6] did not found any significant difference in age, RF status, antinuclear antibodies status between women with and without thyroid disorders although there was a tendency to have a shorter duration of arthritis. This was confirmed in our study as there were no significant differences in the DAS28 between the RA patients with and without thyroid abnormalities. In contrast, Przygodzka et al. [7] showed that the RA patients with thyroid disorders had a lower disease activity assessed using the DAS 28 and the CRP, and less RF prevalence than RA patients without thyroid disorders. In our study, the mean activity score of RA was globally high and a score of DAS28 >5.1 was found in almost two-thirds of the patients.

RA patients disability evaluated by Health Assessment Questionnary (HAQ) was reported to be worse in patients with RA with concomitant thyroid diseases [22] but this finding was not confirmed in Przygodzka et al. study [7].

The main abnormality seen was asymptomatic nodules which does not agree with the data of the literature, saying that the common thyroid dysfunction was subclinical hypothyroidism present in 9.4 to 21% of patients with RA [7,9,20-25].

Attention should be draw to the fact that only 5 of the 22 patients with thyroid abnormalities had clinical manifestations suggesting the thyroid abnormality. This could be in part explained by a predominance of RA clinical manifestations which probably masked the symptoms of the thyroid dysfunction [18,20,26].

We should include the thyroid exam in systematic clinical examination of our RA patients to find a possible asymptomatic thyroid disease for multiples reasons. First, the thyroid dysfunction and particularly the chronic autoimmune thyroiditis may cause rheumatic manifestations with an incompletely established pathogenesis [27]. Second, the thyroid diseases may cause osteoporosis which is often present in RA. Finally, some thyroid disorders and especially hypothyroidism are associated with higher risk of cardiovascular diseases and may increase this risk in RA patients independently of the traditional risk factors [28]. Increased prevalence of antithyroid antibodies in RA patients with low hormonal alterations had been seen [29]. Our study does not confirm this finding, with only one positive in a symptomatic patient on 18 tested. Although we have no control group, it seems that prevalence of thyroid abnormalities in RA patients is high, motivating us for screening these patients for thyroid dysfunction.

5. CONCLUSION

Screening of thyroid disease should be done which is elevated in RA and is associated with some thyroid diseases. However, the influence of the thyroid abnormality on the RA is not clear, larger studies should be done before concluding.

COMPLIANCE WITH ETHICAL STANDARDS

This cross-sectional study enrolled patients (humans) who were admitted to the rheumatology outpatient in Charles Nicolle Hospital, Tunisia. The study was approved by the Hospital local Ethics Committee, and informed consent was obtained from all subjects.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Roitt IM, Doniach D, Cambell PN, Hudson RV. Autoantibodies in Hashimoto's disease (lymphadenoid goitre). Lancet 1956;271: 820-821.
2. Caron P , Lassoued S, Dromer C, Oksman F, Fournie A. Prevalence of thyroid abnormalities in patients with rheumatoid arthritis. Thyroidology. 1992;4:99-102.
3. Staykova ND. Rheumatoid arthritis and thyroid abnormalities. Folia Med. 2007; 49:5-12.
4. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, et al. Rheumatoid arthritis classification criteria: An American College of Rheumatology/ European League Against Rheumatism collaborative initiative. Arthritis Rheum. 2010;62:2569-2581.
5. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, et al. The spectrum of thyroid disease in the community: The Whickham survey. Clin Endocrinol. 1997;7:41-93.
6. Shiroky JB, Cohen M, Ballachey ML, Neville C. Thyroid dysfunction in rheumatoid arthritis: A controlled prospective survey. Ann Rheum Dis. 1993; 52:454-456.
7. Przygodzka M, Filipowicz-Sosnowska A. Prevalence of thyroid diseases and antithyroid antibodies in women with rheumatoid arthritis. Pol Arch Med Wewn. 2009;119:39-43.
8. Chan ATY, Al-Saffar Z, Bucknall RC. Thyroid disease in systemic lupus erythematosus and rheumatoid arthritis. Rheumatology. 2001;40:353-354.
9. El-Sherif WT, El Gendi SS, Ashmawy MM, Ahmed HM, Salama MM. Thyroid disorders and autoantibodies in systemic lupus erythematosus and rheumatoid arthritis patients. Egypt J Immunol. 2004; 11:81-90.
10. D'Arbonneau F, Ansart S, Le Berre R, Dueymes M, Youinou P, Pennec YL. Thyroid dysfunction in primary Sjögren's syndrome: A long-term followup study. Arthritis and Rheum. 2003;49:804-809.
11. Vaz C, Ventura S, Medina JL, Lopes-Vaz A. Dysthyroïdie et polyarthrite rhumatoïde. Rev Rhum. 2006;73:1185.
12. Pan XF, Gu JQ, Shan ZY. Increased risk of thyroid autoimmunity in rheumatoid arthritis: A systematic review and meta-analysis. Endocrine. 2015;50:79-86.
13. Lazúrová I, Jochmanová I, Benhatchi K, Sotak S. Autoimmune thyroid disease and rheumatoid arthritis: Relationship and the role of genetics. Immunol Res. 2014;60: 193-200.
14. Wahlberg P, Nyman D, Carlsson SA. 25 year fillow up of the Aland thyroid study of 1956. Thyroid status and incidence of rheumatoid arthritis. Acta Endocrinol. 1983;251:47-52.
15. Mobini M, Kashi Z. Thyroid disorders in rheumatoid arthritis and osteoarthritis. Pak J Med Sci. 2011;27:595-598.
16. Chabchoub G, Teixiera EP, Maalej A, Ben Hamad M, Bahloul Z, Cornelis F, et al. The R620W polymorphism of the protein tyrosine phosphatase 22 gene in autoimmune thyroid diseases and rheumatoid arthritis in the Tunisian population. Ann Hum Biol. 2009;36:342-349.
17. Silman AJ, Ollier WE, Bubel MA. Autoimmune thyroid disease and thyroid autoantibodies in rheumatoid arthritis patients and their families. Br J Rheum. 1989;28:18-21.
18. Bianchi G, Marchesini G, Zoli M, Falasconi MC, Iervese T, Vecchi F. Thyroid involvement in chronic inflammatory rheumatological disorders. Clin Rheum. 1994;13:479-84.
19. Deighton CM, Fay A, Walker DJ. Rheumatoid arthritis in thyroid disease positive and negative same- sexed sibships. Br J Rheum. 1992;31:13-17.
20. Andonopoulos AP, Siambi V, Makri M, Christofidou M, Markou C, Vagenakis AG. Thyroid function and immune profile in rheumatoid arthritis. A controlled study. Clin Rheum. 1996;15:599-603.
21. Dołęga B. Evaluation of thyroid gland function in patients with rheumatoid arthritis. Rheumatologia. 1996;24:616-618.
22. Magnus JH, Birketvedt T, Haga HJ. A prospective evaluation of antithyroid antibody prevalence in 100 patients with rheumatoid arthritis. Scan J Rheumatol. 1995;24:180-182.
23. Del Puente A, Savastano S, Lupoli G, Esposito A, Lupoli G. High prevalence of thyroid autoantibodies in newly diagnosed rheumatoid arthritis patients. Clin Exp Rheumatol. 2003;21:137.
24. Marasini B, Massarotti M. Rheumatoid arthritis and thyroid disease. Clin Exp Rheumatol. 2004;22:265.

25. Dessein PH, Joffe BI, Stanwix AE. Subclinical hypothyroidism is associated with insulin resistance in rheumatoid arthritis. Thyroid. 2004;14:443-446.
26. Vanderpump MPJ , Tunbridge WM, French JM, Appleton D, Bates D, Clark F, et al. The incidence of thyroid disorders in the community: A twenty-year follow up of the hickham survey. Clin Endocrinol. 1995; 43:55-68.
27. Punzi L, Betterle C. Chronic autoimmune thyroiditis and rheumatic manifestations. J Bone Spine. 2004;71:275-83.
28. Raterman HG, van Halm VP, Voskuyl AE, Simsek S, Dijkmans BA, Nurmohamed MT. Rheumatoid arthritis is associated with a high prevalence of hypothyroidism that amplifies its cardiovascular risk. Ann Rheum Dis. 2008;67:229-232.
29. Alzeni F, Doria A, Ghirardello A, Turiel M, Batticciotto A, Carrabba M, et al. Anti-thyroid antibodies and thyroid dysfunction in rheumatoid arthritis: Prevalence and clinical value. Autoimmunity. 2008;41: 111-115.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/13683