

THE ASSOCIATION OF AUTOIMMUNE THYROIDITIS WITH RHEUMATOID ARTHRITIS

Wisal Salman Abd Mohsen

Department of Biotechnology, College of Science, Baghdad University.

Abstract

There has been controversy over the possible association of antithyroid with RA (Thyroiditis with Rheumatoid Arthritis). We have therefore compared the prevalence thyroid antibody anti thyroglobuline (anti-TG) and abnormal thyroid stimulating hormone (TSH) levels in 57 RA patients with 20 aged matched control. 9 (16%) of the RA patients had thyroid Ab whereas no one of control had thyroid Ab ($p < 0.01$). RA patients had TSH levels between (6-25 mU/L), while all control group had TSH levels within normal range ($p < 0.01$). These results suggests that RA is associated with RA have minor hypothyroidism.

Keywords: Rheumatoid arthritis, Thyroiditis, Hypothyroidism, Thyroglobulin antibodies.

Introduction

An association between autoimmune thyroiditis and RA Thyroiditis with Rheumatoid Arthritis has long been detected, the data mostly derived from new studies.) Hypothyroidism or thyrotoxicosis may produce a variety of musculoskeletal symptoms, drug treatment of thyrotoxicosis is occasionally followed by rheumatological sequelae (1,2,3) and lastly there may be an association between organ-specific autoimmune thyroid diseases and non-organ-specific rheumatological disorders [4]. Recognized associations with thyroiditis include Sjogren's syndrome [5] and giant cell arteritis [6,7] possible relationship between rheumatoid arthritis and Hashimoto's thyroiditis. Other autoimmune diseases such as myasthenia gravis also occur more frequently in subjects with rheumatoid arthritis.(8) A common autoimmune pathogenesis or a strong genetic association between these diseases and the expression of certain types of major histocompatibility complex have been hypothesized. The association between RA and endocrine autoimmunity, in particular type 1 diabetes mellitus (T1DM) or thyroid autoimmunity has been reported in adults (9-14). The aim of this study is to find if there is an association between the two diseases.

Materials and Methods

Patients

Serum was obtained from 57 randomly selected patients with RA [11 male, 46 female; mean age (\pm SD), 40 (\pm 10)] and compared with 20 age- and sex-matched controls derived from hospital staff. All patients with RA fulfilled the criteria for the diagnosis of RA (1) with family history of RA. The patients were admitted to Monther Mustafa, Al-Fanar Clinical Laboratories and Rheumatology Department in Baghdad Teaching Hospital. All samples of patients and control were clotted at room temperature, centrifuged at 3000 rpm. for 45 min. and the sera stored at -20°C until used in the assay.

Anti thyroglobulin Antibody(anti-TG) :

were assayed by ELISA method Biomeghrib(Tunisia) diagnostics that is based on double antibody sandwich technique, Table (1) show cut off values of anti-TG.

*Table (1)
Normal values of anti-TG.*

	Anti-TG (IU/ml)
Normal	<100
Border line	100-150
Elevated	>150

Results

Age Distribution: In our study, the mean age of clinically autoimmune thyroiditis in RA patients was 56 years Fig. (1).

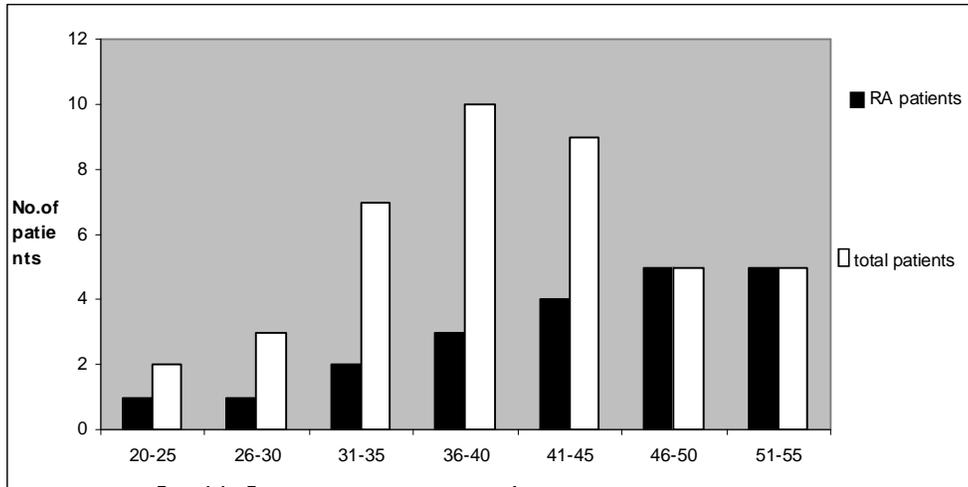


Fig. (1) : Age distribution pattern of RA patients with Anti-TG Ab.

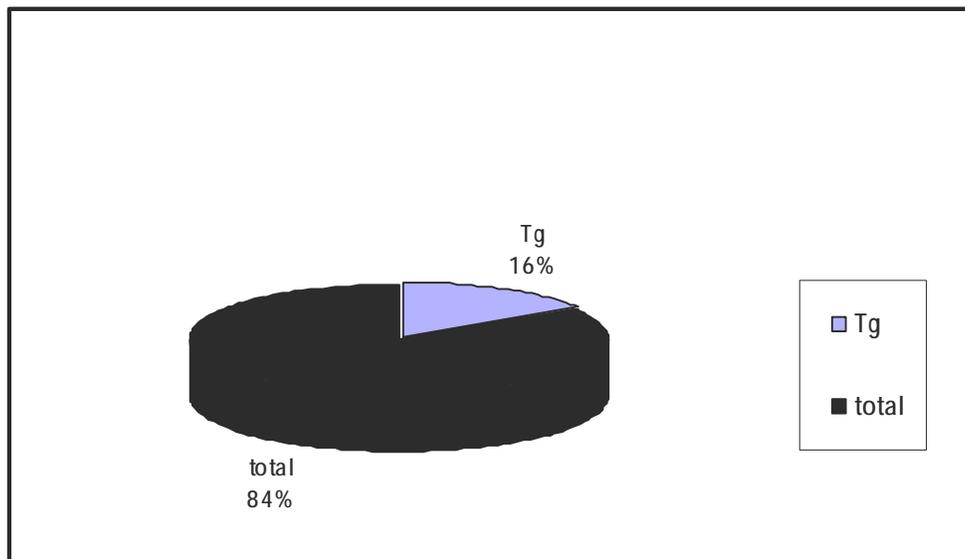


Fig. (2) : Distribution of anti-TG in RA patients.

Anti-TG Antibody:

The distribution of anti-TG amongst patients is shown in (Fig. (2)). Overall, 9 (16%) of the RA patients had anti-TG whereas no healthy subject had a positive results for anti-TG antibody ($p < 0.01$). 20% of (51-55)

had anti-TG, 40% of (56-60) had anti-TG and 21% of (36-40) had anti-TG one of them had low titer of anti-TG and this goes with TSH levels two of them had high levels and one of them had 6.1U/L, 18% of (31-35) had anti-TG and moderate levels of TSH (6.5) U/L.

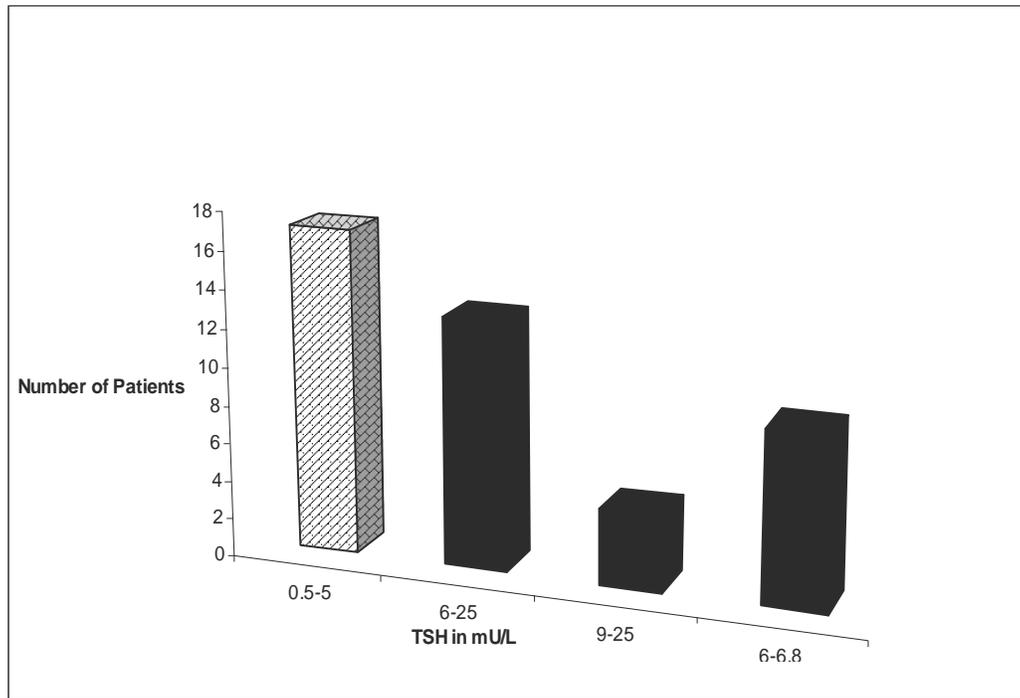


Fig. (3) : TSH level in mudl/L in RA patients and normal.

Table (2) shows that 4(7%) of total patients were with high TSH level, 4(7%) of total patients were with moderate TSH levels (6.1-6.7) and 9(15.7) were with low levels of TSH. Two of age groups (56-60) and (36-40) had high levels of TSH and high titers of anti-TG.

TSH levels:

None of the patients or controls had TSH values in the hyperthyroid range. Only three of control group have a moderate levels of TSH, while RA patients had levels (6-25 mU/L) Fig. (3). 17 (29.8%) of the RA patients had TSH levels above the upper limit of the normal reference range (0.5-5mU/L).

Table (2)
Age groups with TG+ve pts. and abnormal TSH.

Age Group	Total No.	RA pts.(TG+ve)	Abnormal TSH
20-25	5	0	0
26-30	5	1	1
31-35	11	2	3
36-40	14	3	5
41-45	6	0	2
46-50	8	0	2
51-55	5	1	1
56-60	5	2	3
total	57	9	17

Discussion

Our data showed significantly increased prevalence of subclinical hypothyroidism and thyroid autoimmunity. The mean age incidence of clinically hypothyroidism was 56 years. In RA, the mean age of Chan et.al.(15) was 60.5 yrs. 40% of (56-60) had thyroid Ab, these results strengthen the hypothesis of slow universal progression (16) of autoimmune process. This model suggests a 'disease pyramid' in autoimmune thyroiditis, in which patients progress from mild thyroiditis to clinical disease over time. The half-time for progression from mild thyroiditis to clinical disease is estimated to be 80 years (17). SLE may accelerate progression up this disease pyramid. 15.7% of RA patients have thyroid Ab, whereas 29.8% of the presented with subclinical hypothyroidism. These results might suggest that thyroid function in RA could also be impaired without an associated autoimmune thyroiditis or reflecting another type of thyroid autoimmunity (18). RA commonly shows high association with autoimmune thyroid disease.(18-21) In agreement with (21) that found 20% of RA patients have autoimmunity.

In conclusion, our data indicate that there is a higher prevalence of thyroid disorder. In order to minimize the risk of delayed and/or undiagnosed thyroid disease, this seems to suggest the need for careful monitoring of possible associated autoimmunity.

Acknowledgement

I would like to thank Mr. Immad Omran and Mr. Ibrahim in Monther Mustafa Laboratories and Mr. Mohammad Jasim in Al-Bashaier Laboratory and Abdulzahraa in Educational Laboratories for helping me in working ELISA and having serum samples from their laboratories.

References

- [1] D.L. Kasper, E. Braunwald, S., H. Fauci, S.L. Longo, and D.L. Jameson; Harrison's, Principles of Internal Medicine vol:5. International Edition Mc Graw-Hill Health Professions Division(2005).
- [2] T.G. Parslow, D.P. Stite, A.I. Terr, J. BJohn ; Immunology 10th ed, a Lange Medical Book, Mc Graw-Hill companies, 2001.
- [3] D.P. Stite, J.B. Stobo and W.Wells: Basic and Clinical Immunology 6th ed. Appelton & Lange, 1987.
- [4] V.Kyle and B.L. Hazleman ; The thyroid. Clin.Rheum Dis 1981 ;7:711-22.
- [5] K. Whaley, J.Webb and B.A. McAvoy, et.al.; Sjogren's syndrome: 2. Clinical associations and immunological phenomena. Q J Med 1973;42:513-48.
- [6] R.D. Thomas and D.N. Croft.; Thyrotoxicosis and giant cell arteritis. Br.Med.J. 1974; 2:408-9.
- [7] G.R. Dent and O.M. Edwards. Autoimmune thyroid disease and the polymyalgia rheumatic giant cell arteritis syndrome. Clin Endocrinol.1978;9:215-19.
- [8] "Article Hypothyroidism after Sunitinib Treatment 664 7 November 2006 Annals of Internal Medicine Volume 145 • Number 9 www.annals.org.
- [9] P.Caron, S. Lassoued, D.Romer, F. Coksma and A. Fournei; Prevalence of thyroid abnormalities in patients with rheumatoid arthritis. Thyroidology 1992; 4: 99-102.
- [10] A.P.Andonopoulos, V.Siambi, M.Makri, M.Christofidou and A.G. Vagenakis: Thyroid function and immune profile in rheumatoid arthritis. A controlled study. Clin Rheumatol 1996; 15: 599-603.
- [11] M. Pietropolo, M.Peakman and S.L.Pietropolo et al.; Combined analysis of GADA65 and ICA512 (IA-2) autoantibodies in organ and non-organ-specific autoimmune diseases confers high specificity for insulin dependent diabetes mellitus. J.Autoimmune 1988; 11: 1-10.
- [12] E. Yamato, H. Ikegami and Y.Kawaguchi et.al; Insulin-dependent diabetes mellitus associated with autoimmune thyroiditis and rheumatoid arthritis. Am. J. Med Sci 1997; 313: 64-6.
- [13] H.Yoshida, T.Inoue, Y.Hakamata et al.; Slowly progressive IDDM with rheumatoid arthritis and Hashimoto disease in high elderly. Nippon Ronen Igakkai Zasshi 1998; 35:571-6.

- [14] A.Linos, J.W. Worthington, P. J. Palumbo, O. Fallon, L.T. Kurland: Occurrence of Hashimoto's thyroiditis and diabetes mellitus in patients with rheumatoid arthritis. *J Chron Dis* 1980; 33: 73-7.
- [15] Chan A.T.Y., Al-Safar Z. and Buchnall R.C.: Thyroid disease in Systemic Lupus Erythematosus and Rheumatoid Arthritis. *Rheum*. 2001; 40:353-354.
- [16] Dayan CM. The natural history of autoimmune thyroiditis : how normal is autoimmunity. *Proc R. Coll. Physicians Edin*. 1996; 26 : 419-33.
- [17] Steel NR, Weightman DR, Taylor JJ, Kendall-Taylor P. Blocking activity to action of thyroid stimulating hormone in serum from patients with primary hypothyroidism. *Br. Med J* 1984; 288:1559-62.
- [18] Walker DJ, Griffiths M, Griffiths ID. Occurrence of autoimmune diseases and autoantibodies in multicase rheumatoid arthritis families. *Ann Rheum Dis* 1986; 45:23-33.
- [19] Caron P, Lassoued S, Dromer C, Oksman F, Fournei A. Prevalence of thyroid abnormalities in patients with rheumatoid arthritis. *Thyroidology* 1992;4:99-102. [Medline]
- [20] Andonopoulos AP, Siambi V, Makri M, Christofidou M, Vagenakis AG. Thyroid function and immune profile in rheumatoid arthritis. A controlled study. *Clin Rheumatol* 1996;15:599-603. [Medline]
- [21] Gonçalves, Fabrícia Torres MD; Feibelmann, Taciana Carla Maia MD, MSc; Ranza, Roberto MD, MSc; Daud, Mariana Salomão MD; Taliberti, Ben Hur Braga MD, PhD; Pinto, Rogério de Melo Costa PhD; Jorge, Paulo Tannús MD, PhD: Autoimmune Thyroiditis and Rheumatoid Arthritis: Is There Really an Association? *The Endocrinologist* : January / February 2009- Volume 19 - Issue 1 - pp 31-34.

الخلاصة

هناك جدل حول احتمالية ترافق التهاب الغدة الدرقية المناعي مع داء الروماتزم الرثوي. لذا فقد تمت مقارنة وجود احد أضداد الدرقية الشايروكلوبولين ومستويات الهرمون المحفز للدرقية في (57) من مرضى الروماتزم الرثوي مع مجموعة سيطرة لأشخاص طبيعيين ، ووجد 9 (%16) من المرضى ($p < 0.01$) في حين لا يوجد هذا الضد في اي من افراد مجموعة السيطرة وكانت مستويات الهرمون المحفز للدرقية بين (6-25 mU/L) من مرضى الروماتزم الرثوي ولم تكن هناك مستويات اعلى من الطبيعي في اي من افراد مجموعة السيطرة ($p < 0.01$). وهذه النتائج تشير الى وجود علاقة بين داء الروماتزم الرثوي و التهاب الغدة الدرقية المناعي، وهذا يعني ان للعديد من مرضى الروماتزم الرثوي نقصان طفيف في افراز الغدة الدرقية.