

Thyroid Dysfunctions among Jordanian Patients with Rheumatoid Arthritis and Systemic Lupus Erythematosus: A Hospital-Based Study

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ABSTRACT

Objective: To determine the frequency of thyroid dysfunction among Jordanian patients with Systemic Lupus Erythematosus and Rheumatoid Arthritis.

Method: This study was conducted in collaboration between Rheumatology and Endocrine clinics at King Hussein Medical Center in the period between January 2010 and July 2010. One hundred and twenty-two patients were studied; 80 patients with Systemic Lupus Erythematosus and 42 patients with Rheumatoid Arthritis were screened for thyroid diseases (clinical or subclinical hyper/hypothyroidism) regardless of their symptoms. The results were compared with 304 apparently healthy controls.

Result: A total number of 122 patients, female to male ratio 7.7:1 and a mean age (SD) of 37.1±13.5 years, were included in the study. Twenty-six patients were found to have thyroid function abnormalities. The frequency of thyroid disease was 21.3%. The mean age in the control group was 49.4 years. The frequency of thyroid dysfunction in the control was 6.6%. Subclinical hypothyroidism was seen in 5% of healthy controls, 13.7% of Systemic Lupus Erythematosus and 7.1% of Rheumatoid Arthritis patients. The majority of cases of subclinical hypothyroidism with Systemic Lupus Erythematosus and all cases with Rheumatoid Arthritis were females. Overt hypothyroidism was seen in 0.9% of controls, 8.7% of Systemic Lupus Erythematosus and 4.7% of Rheumatoid Arthritis patients. Biochemical hyperthyroidism was seen in 0.3% of controls, 2.5% of Systemic Lupus Erythematosus and 2.3% of Rheumatoid Arthritis patients, all of whom were female.

Conclusion: Patients with rheumatologic disorders have high frequency rate of thyroid dysfunction. These dysfunctions are often subclinical in nature with female predominance. Screening should be regularly conducted in all patients with rheumatologic diseases for proper early detection and management.

Key words: Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), Thyroid disease

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Introduction

Rheumatologic disorders like Systemic lupus

erythematosus (SLE) and Rheumatoid Arthritis (RA) are autoimmune multi-systemic diseases that can affect any organ system in the body.

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These disorders are commonly encountered in our outpatient practice and constitute a health challenge to the Jordanian community.

Autoimmune thyroid disorders are commonly associated with autoimmune diseases such as scleroderma, Primary Sjogren's Syndrome, RA and SLE.⁽¹⁻⁶⁾ The pathogenesis of thyroid disease seen in rheumatic diseases is probably due to the activity of one of the thyroid auto-antibodies produced in these diseases.⁽⁷⁻⁸⁾ However, the frequency of thyroid disorders differs from population to population.⁽⁹⁻¹²⁾

Many studies around the world have shown an increased frequency of autoimmune thyroid diseases in SLE.^(5,13-16) It is still controversial whether both hypothyroidism and hyperthyroidism are more common^(5,13) or this finding is restricted to hypothyroidism alone.⁽⁶⁾ In fact there is disagreement as to whether SLE is a risk factor for the development of thyroid disease or just a coincidental finding as young middle aged female adults are at risk for both SLE and autoimmune thyroid disorders.⁽¹⁷⁾

Reports from Jordan on the frequency of thyroid disease in healthy Jordanians are scarce and it is assumed to be similar to that found in other studies.⁽¹⁸⁾ Only one study have looked into the association of thyroid diseases and autoimmune disorders in Jordan,⁽¹⁹⁾ compared to detailed reports from other neighboring countries.⁽²⁰⁻²²⁾

Therefore, this study was designed to assess the frequency of abnormal thyroid determine in Jordanian patients with SLE and RA and to compare results with those from healthy Jordanian controls.

Methods

Patients

Eighty patients (73 female, 7 male) with SLE and forty two (35 female, 7 male) consecutive ambulatory patients with RA from Rheumatology clinic at King Hussein Medical Center fulfilling the American College of Rheumatology criteria for RA⁽²³⁾ and SLE⁽²⁴⁾ were evaluated by rheumatologist and endocrinologist for thyroid disease (clinical or sub clinical hyper/hypothyroidism) regardless of their symptoms. All patients regardless of their rheumatologic clinical status were included in this study. Informed consents were obtained from all

participants and the study was approved by the ethical committee of KHMC.

Controls:

A group of 304 subjects, 174 (57.2%) females, and 130 (42.8%) males, were used as a control group. Controls data were obtained with permission from Radaideh *et al.*⁽¹⁸⁾ This group was not known to have previous rheumatic, endocrine or any other disease that may affect thyroid function. The mean age of the control was 49.4 years (age range was 30-80 years).

Thyroid function tests:

Venous blood samples were collected from the patients. Serum was separated and tested immediately on same day.

Serum free thyroxin (FT4), free triiodothyronine (FT3) and thyroid stimulating hormone (TSH) were measured and determined by enzyme-linked immunosorbent assay (ELISA) method (Abbott Lab, USA) and compared with the normal reference range in our laboratory, serum FT4 (normal range: 0.93-1.71 ng/dl, serum FT3 (normal range: 2.0-4.4 pg/ml) and serum TSH (0.27-4.20 uIU/ml).

Subjects were classified into four groups and the following guidelines for detection of abnormal thyroid function were considered (a) normal when both FT4 and TSH were within the normal range; (b) subclinical hypothyroid when TSH >4.20 uIU/ml and FT4 was within the normal range; (c) overt hypothyroidism when TSH >4.2 uIU/ml and FT4 <0.93 ng/dl; (d) biochemical hyperthyroidism (clinical or subclinical) when TSH<0.27 uIU/ml and FT4 >1.71 ng/dl.

Statistical Analysis:

SPSS version 10 was used for statistical analysis; a p value <0.05 was considered as significant. Chi-square was used to determine significance among the study variables with a p value <0.05 was considered as significant.

Results

Demographic Data: (Table I).

The majority of patients included in this study were predominantly females. The mean age of control group is 49.4; in RA is 44.6± 14.6 (age range 19-75) yrs and in SLE patients 33.4± 11.3 (age range 18-65) yrs.

Table I: Demographic data of the different study groups

	Controls	RA	SLE
Total participants	304	42	80
Male	42.7%	6.6%	8.7%
Female	57.3%	83.4%	91.3%
F/M	1.3/1	5/1	10.4/1
Age, Years	49.4±14.2	44.6±14.6	30.4±11.3

Table II: Frequency of abnormal thyroid function tests in all groups

Type of thyroid dysfunction	Controls			SLE			RA		
	Females N:(174)	Males N:(130)	Total N:(304)	Females N:(73)	Males N:(7)	Total N:(80)	Females N:(35)	Males N:(7)	Total N:(42)
Subclinical hypothyroid	9 (5.2%)	6 (4.6%)	15 (4.9%)	10 (13.7%)	1 (14.3%)	11 (13.7%)	3 (8.6%)	0	3 (7.1%)
Overt hypothyroid	2 (1.1%)	1 (0.8%)	3 (0.9%)	7 (9.6%)	0	7 (8.7%)	2 (5.7%)	0	2 (4.7%)
Biochemical hyperthyroid	1 (0.57%)	0	1 (0.3%)	2 (2.7%)	0	2 (2.5%)	1 (2.8%)	0	1 (2.3%)
Total	12* (6.9%)	7** (5.4%)	19*** (6.25%)	19* (26%)	1** (14.3%)	20*** (25%)	6* (17.1%)	0**	6*** (14.3%)

*F. control vs. F. SLE and RA -Chi square=14.62, p value =0.0067

**M. control vs. M. SLE and RA-Chi square=1.44, p value=0.48

***Total group vs. total SLE and RA-Chi square=24.2, p value=0.0000542

Twenty six patients were found to have thyroid function abnormalities; 25 patients were female and only one patient was male. The overall frequency of thyroid dysfunction was 21.3%. The frequency of abnormal thyroid function in the different groups is shown in Table II.

We observed 20 (25.0%) SLE patients with abnormal thyroid function: 18 (22.4%) with hypothyroidism (clinical or subclinical) and two (2.5%) with hyperthyroidism (clinical or subclinical). In contrast, only 6 (14.1%) RA patients found to have thyroid disease: five (11.8%) with hypothyroidism and one (2.3%) with hyperthyroidism.

Subclinical hypothyroidism was seen in 15 (4.9%) of controls, three (7.1%) RA and 11 (13.7%) SLE patients. The frequency of subclinical hypothyroidism in RA and SLE were higher than in the control group ($p=0.015$; C.I=1.16-4.67), (1.1-5.68). SLE patients were having a significantly higher rate of subclinical hypothyroidism ($p=0.005$, C.I=1.25-7.0) than controls, but no significant difference between RA and SLE patients ($p=0.21$).

The frequency of subclinical hypothyroidism in females was higher than in males in control subjects (5.2% vs. 4.6%), significantly higher in RA (8.6% vs. 0%) and (13.7% vs. 14.3%) in SLE patients. Also the frequency of subclinical hypothyroidism in females with RA and SLE were significantly higher than in female controls.

Clinical hypothyroidism was more frequent among SLE (8.7%) and RA (4.7%) patients than healthy controls (0.9%). Again this condition was higher in females with SLE and RA than females in control group. Biochemical hyperthyroidism (clinical or subclinical) was seen in 2 (2.5%) of SLE (T3= 9.68, 5.6 pg/ml), 1 (2.3%) of RA (T3= 6.3 pg/ml) vs. only one subject in control group (0.3%) (Table II).

In total, the frequency of thyroid dysfunction was seen in 25% SLE, 14.3% RA and 6.25% of healthy controls (Table II). The difference between SLE, RA and control group was statistically significant (Chi square=24.25, $p=0.0000542$) (see Table III). Again, females had higher frequency of thyroid dysfunction than males, in SLE (26.1% vs. 14.3%; $p=0.3$) and in RA (17.1% vs. 0%; $p=0.5$).

Discussion

Symptoms of thyroid disease can be confused with those of connective tissue diseases, especially SLE and RA. SLE is a multi-systemic disease and the clinical complaints investigated in this study, despite the possibility of being characteristic of hyper or hypothyroidism may also be a manifestation of SLE.^(14,16) Some studies have shown that the overall frequency of autoimmune thyroid disease did not differ among SLE patients and control. However, SLE patients had more frequent subclinical

Table III: Frequency of total thyroid dysfunction for whole group of rheumatologic diseases vs. control according to gender

		Control	Rheumatological disease	P value Disease vs. Control
Male	No.	130	14	0.56
	Thyroid Dysfunction No.(%)	7(5.4%)	1(7.1%)	
Female	No..	174	108	0.0000852
	Thyroid Dysfunction n.(%)*	12(6.9%)	25(23.2%)	
P value M vs. F		0.59	0.15	

Table IV: Comparison of frequency of thyroid dysfunction in some Arab and western countries

	RA				SLE			
	Pt no.	Total thyroid dysfunction No.(%)	Hypo-Thyroid No.(%)	Hyper-Thyroid No.(%)	Pt no.	Total thyroid dysfunction No. (%)	Hypo-Thyroid No. (%)	Hyper-Thyroid No. (%)
Current study	42	6(14.3)	5(11.9)	1(2.3)	80	20(25)	18(22.5)	2(2.5)
El-Sherif <i>et al.</i> ⁽²¹⁾ 2004	20	4(20)	2(10)	2(10)	20	6(30)	4(20)	2(10)
AL-Awadhi <i>et al.</i> ⁽²²⁾ , 2008	177	44(24.9)	36(20.4)	8(4.5)	60	16(26.6)	13(21.6)	3(5)
Shiroky, <i>et al.</i> ⁽³¹⁾ , 1993	91	29(30)	–	–	–	–	–	–
Kumar, <i>et al.</i> ⁽²⁹⁾ , 2012	–	–	–	–	100	36(36)	26(26)	2(2)
Pyne <i>et al.</i> ⁽¹⁶⁾ , 2002	–	–	–	–	300	–	17(5.7)	5(1.7)
Takehasi <i>et al.</i> ⁽³⁰⁾ , 2006	–	–	–	–	100	17(17)	13(13)	2(2) (subclinical)

hypothyroidism,^(5,25) this was further confirmed by our study (see Table II). This highlights the importance of identifying thyroid dysfunction in connective tissue diseases and be treated accordingly.

The frequency of thyroid abnormalities in our study are considerably lower than those reported from other populations, and this condition could be related to variable factors such as difference of age, ethnic origin and small sample size in comparison with other studies.⁽⁹⁻¹²⁾

In this study, the frequency of hypothyroidism (clinical or subclinical) was higher in autoimmune rheumatologic disorders than in healthy general population. Females constitute the vast majority of cases in both SLE and RA. Subclinical hypothyroidism was more common than clinical hypothyroidism in SLE (13.7% vs. 8.7%) and RA (7.1% vs. 4.7%). This is in contrast to the study reported by Porkodi *et al.*⁽²⁶⁾ where majority of the cases had clinical hypothyroidism (60% vs. 20%).

Some reports have showed an association of autoimmune thyroid disease in active SLE⁽²⁷⁾ that fluctuates according to SLE activity.⁽²⁸⁾ Other studies reported that a number of patients with subclinical hypothyroidism may progress to clinical hypothyroidism.⁽¹⁰⁾ Many factors are

claimed to play a role in this progression including female gender, advanced age and presence of thyroid antibodies.⁽⁹⁾

Arnaout *et al.*⁽¹⁹⁾ from Jordan looked into the frequency of thyroid disease in various Connective Tissue Diseases (CTD); he showed a lower frequency of thyroid dysfunction in CTD (3.5%) compared with our data of that showed an overall frequency of thyroid disease (21.3%). The explanation might be due to selection as we selected patients with any stage of disease activity while the activity of disease in their study was stated.

When comparing our results with national and international studies (Table IV), we found two studies were conducted in Egypt⁽²¹⁾ and Kuwait;⁽²²⁾ results of these studies were consistent with our results. In contrast to a study conducted by Kumar *et al.*⁽²⁹⁾ who found a frequency of thyroid dysfunction in SLE of (36%); much higher than our findings (25%). While other studies reported lower frequency of hypothyroidism in SLE patients from UK⁽¹⁶⁾ and from Brazil⁽³⁰⁾ (5.7%, 13% respectively). Shiroky *et al.*⁽³¹⁾ found a higher frequency of thyroid dysfunction in RA patients from Canada (30%) when compared with our study. It seems that genetic and environmental factors would play a

role in this difference between our results and European and other Western countries.

Limitations

Definite conclusion may not be possible to be drawn from this study because of small sample size, limited number of rheumatologic diseases studied, female predominance in rheumatological group and the control group was older than studied group.

Conclusion

Thyroid dysfunction, particularly hypothyroidism is common among patients with autoimmune diseases in Jordan and often is subclinical in nature. Screening for thyroid function should be regularly performed in all patients with rheumatologic diseases for proper early detection and management. Larger cross sectional samples including testing of thyroid auto-antibodies are warranted to confirm the present observations.

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