Kufa Medical Journal | Vol. 20, No. 1, 2024

Original article | DOI: https://doi.org/10.36330/kmj.v20i1.14270

p-ISSN: 1993-517X

e-ISSN: 2709-4464

Prevalence of Hashimoto's Thyroiditis among Rheumatoid Arthritis Patients

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ABSTRACT

Background: *Rheumatoid arthritis is an inflammatory illness that affects the entire body but its cause is unknown. There has been a considerable debate about the relation between thyroid gland and Rheumatoid arthritis.* ***Aim of the study:*** *To determine the frequency of Hashimoto's thyroiditis in patients with Rheumatoid Arthritis and determine whether patients with Rheumatoid arthritis are at higher risk of Hashimoto's thyroiditis.* ***Patients and methods:*** *This study is a cross-sectional observational study done in the governorate of Najaf from September 2022 to February 2023 involving 140 participants diagnosed with Rheumatoid arthritis, determined by rheumatologist doctors in line with ACR/EULAR 2010 Criteria and serological testing. Patients including 16 males and 124 females, ranging between the ages of 20 and 60. All participants underwent complete clinical and laboratory assessments. The data were collected during the direct patient interview and the information from the questionnaire, verbal approval has been received from the study participant.* ***Results:*** *The frequency of Hashimoto's disease in the selected patients of rheumatoid arthritis (N=140), was 45 (32.14%), While euthyroidism (Rheumatoid arthritis patients without Hashimoto's) was 95(67.9%). Hashimoto's disease included subclinical 9 (6.4%) and overt Hashimoto's thyroiditis 36(25.7%).* ***Conclusions:*** *HT is frequent among patients with RA. Therefore, there is a need of screening of thyroid hormone dysfunction as well as presence of Anti-TPO antibodies as markers of HT in RA patients particularly in young patients, females, and those with high disease activity. The association was a significance among RA patients with HT and ACCP, BMI, and ESR.*

Keywords: Rheumatoid arthritis, Hypothyroidism, Hashimoto's.

Article Information

Received: November 30, 2023; Revised: May 17, 2024; Online: June, 2024

INTRODUCTION

Rheumatoid arthritis (RA) is a polyarticular symmetric illness that has an impact on a number of joints on both sides of the body. Pain as well as swelling, mainly in the hands and feet joints, are the most typical signs of RA. The most swollen joints are the wrists, metacarpophalangeal, metatarsophalangeal, and proximal interphalangeal (1).

One of the most important aspects of disease management is its focus on early detection and treatment (2). The increased occurrence of thyroid dysfunction in RA patients has been reported (3). Depending on the study population, geographic area, and definition of Autoimmune thyroid disease (AITD), the prevalence of AITD among RA patients has ranged from 3 to 30% (4).

A variety of studies have shown that hypothyroidism and its prevalent symptoms of discomfort, weariness, weight gain, and dyslipidemia can be easily missed in the early stages of rheumatoid arthritis since they are so similar to the initial signs of the disease (5).

AITD is an autoimmune attack on the thyroid gland caused by immune system dysfunction. It affects more people than any other autoimmune disorder (6). The etiology is complex, that involves genetic, environmental, and dietary variables . The most common form of AITD is Hashimoto's thyroiditis (HT) (7).

Women and the elderly are particularly at risk for developing hypothyroidism in RA patients (8). The exact mechanism through which RA and AITD are linked remains unknown, numerous studies have shown autoimmunity as a key player in the development of both conditions. Some genes, including STAT4, HLA-DRB1, and the vitamin D receptor, were also found to have important roles in the progression of both disorders (9). Further, environmental risk factors, including as infection and smoking, play important roles in the development of both RA and AITD (3)

The question of whether there are other links between RA and AITD, such as AITD having a causal effect on the onset of RA or sharing environmental triggers, remains unanswered. To better understand the nature of the link between RA and AITD, it may be helpful to evaluate the risk of acquiring AITD at different points in time for patients with RA (10). Several studies have linked hypothyroidism to a worsening of rheumatoid arthritis, particularly the destructive arthropathy that mostly affects the proximal interphalangeal joints(5).

The purpose of this study is to investigate the prevalence of HT among patients with RA.

PATIENTS AND METHODS

Participants in this research were Iraqi patients with RA who attended the Rheumatology department in Al-Sadr Medical City in Najaf.

The Study Design

It is a cross-sectional observational study.

Subjects

This research was carried out on a total of 140 participants diagnosed with RA, determined by rheumatologist doctors in line with ACR/ EULAR 2010 criteria and serological testing. The patients including 16 males and 124 females, ranging the ages of 20 and 60. Patients were asked about their name, gender, age, and any other items. Prior to the start of the study, the ethical committee of the Faculty of Medicine, University of Kufa, provided its permission. Individuals' informed agreement was also gained.

Exclusion criteria

Participants who have other rheumatologically diseases, prior thyroidectom, pregnant women, Evidence of malignancy, patients have chronic liver or renal diseases, or hyperthyroidism were excluded.

Data collection:

For data collection a questionnaire was designed to record the subject’s information.

Instruments

The equipment utilized in this study include gel serum tubes 5 & 10 ml, disposable sterile syringes, 5 &10 ml, disposable pipette tips, Eppendorf tubes, 1.5 & 2 ml, disposable ESR tubes, and disposable gloves. The instruments utilized in this study were a centrifuge, deep freeze, incubator, ELISA, Refrigerator, micro pipettes with different sizes.

Methods

The sample collected of venous blood was from five to ten ml. The blood sample was divided in half: 2 mL was placed in a disposable ESR tube for the Westergren method of measuring ESR, and 3–7 mL was placed in a sterile gel tube for further analysis. After the blood was drawn in its whole, it was left undisturbed at room temperature to clot within an average of about 10-20 minutes. Centrifugation at 3,000 to 3,000 rpm for 20 minutes was used to dislodge the clot. The sample needs to be centrifuged once more if precipitates form during the reservation. Each patient's sample was separated into three parts and stored in an Eppendorf tube at temperatures ranging from minus 20 to minus 45 ºC. Determination of Anti-CCP antibodies, anti-thyroid peroxidase (Ab-TPO) autoantibodies, Thyroid-stimulating hormone (TSH), and T4 in RA patients by ELISA kit.

STATISTICAL ANALYSIS

The SPSS program, version 26, was utilized to analyze the data. Descriptive statistics was done through calculation of frequency, percentage, mean, and standard error of mean of sociodemographic characteristics of study sample presented by tables. After testing the normality of data, inferential statistics were by application of independent T test and ANOVA to differentiate means of rheumatoid and autoimmune thyroiditis markers in addition to testing correlation and regression relationship of some numerical parameters. Chi square and Fishers exact probability tests were applied for categorical association. statistical significance was regarded as having a P value that must be equal to or less than 0.05.

RESULTS

Table 1 Show thyroid dysfunction definitions (Ralli et al., 2020).

Table 2 shows Frequency of Hashimoto's disease in the selected patients of rheumatoid arthritis (N=140), was 45 (32.14%), While euthyroidism, RA patients without HT, was 95(67.9%). HT disease included subclinical 9 (6.4%) and overt 36(25.7%).

Table 3 shows 36 (25.7%) patients had TSH levels >4 µIU/mL and FT4<0.8 ng/dl with elevated Anti-TPO (> 50 IU/mL); therefore, they were classified as having overt HT and 9 (6.4%) patients with TSH levels >4µIU/mL and normal FT4, with elevated Anti-TPO (> 35) as subclinical HA. There were no significant differences in regard to age, gender, residency, and duration of RA disease, between euthyroid patients and HT, (P-value >0.05). While Family history of RA and Treatment response have significant differences among three groups (euthyroid, overt HT and subclinical HT), (P-value <0.05). Family history of RA have (P-value=0.032) was more in euthyroid RA patients compared to RA patients with HT. Treatment response have (P-value=0.018), poor response was more in overt HT and subclinical HT compared to euthyroid RA patients the percent (55.6%,55.6%,30.5%) respectively.

Table 1: Thyroid dysfunction definitions.

Thyroid dysfunction	TSH (µIU/L)	Free T4 (ng/dl)	Anti-TPO (IU / ml)
Euthyroidism	0.3– 4 (normal)	(0.8–1.8)(normal)	< 50 (normal)
Subclinical HT	>4 (increased)	(0.8-1.8) (normal)	> 50 (increase)
Overt HT	>4 (increased)	<0.8 (decreased)	> 50 (increase)

Table 2: Number and percent of thyroid dysfunction among selected group (140).

Thyroid dysfunction	No.	(%).
Euthyroidism	95	67.9
Subclinical HT	9	6.4
Overt HT	36	25.7
Total	140	100

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Table 3: Comparison of socio and clinical characteristics between euthyroid patients and Hashimoto's patients.

Patient's characteristics			Study sample (N=140)			Total	P-value
			Subclinical HT; n=9	Overt HT n=36	Euthyroid n=95		
Age groups (Year)	≤ 40	(%)	2 (22.2%)	14 (38.9%)	26 (27.4%	42 30.0%	.382
	>40	(%)	7 (77.8%)	22 (61.1%)	69 (72.6%)	98 70.0%	
		Total	9 (100.0%)	36 (100.0%)	95 (100.0%)	140(100.0)	
Gender	Female	(%)	8 (88.9%)	35 (97.2%)	81 (85.3%)	124(88.6%)	.158
	Male	(%)	1 (11.1%)	1 (2.8%)	14 (14.7%)	16 (11.4%)	
		Total	9 (100.0%)	36(100.0%)	95(100.0%)	140(100.0%)	
Residency	Urban	(%)	7 (77.8%)	30 (83.3%)	74 (77.9%)	111(79.3%)	.785
	Rural	(%)	2 (22.2%)	6 (16.7%)	21 (22.1%)	29 (20.7%)	
		Total	9(100.0%)	36(100.0%)	95(100.0%)	140(100.0%)	
Marital status	Married	(%)	9 (100.0%)	35 (97.2%)	89 (93.7%)	133 (95.0%)	.550
	Single	(%)	0 (0.0%)	1(2.8%)	6 (6.3%)	7 (5.0%)	
		Total	9(100.0%)	36(100.0%)	95(100.0%)	140(100.0%)	
Occupation	Unemployed	(%)	8 (88.9%)	33 (91.7%)	88 (92.6%)	129 (92.1%)	.609
	Employed	(%)	1 (11.1%)	3 (8.3%)	4 (4.2%)	8 (5.7%)	
	Students	(%)	0 (0.0%)	0 (0.0%)	3 (3.2%)	3 (2.1%)	
		Total	9 (100.0%)	36(100.0%)	95 (100.0%	140 (100.0%)	
Duration of RA (Months)	≤ 12	(%)	3 (33.3%)	9 (25.0%)	35 (36.8%)	47 (33.6%)	.440
	> 12	(%)	6 (66.7%)	27 (75.0%)	60 (63.2%)	93 (66.4%)	

		Total	9 (100.0%)	36(100.0%)	95 (100.0%	140(100.0%)	
Family history of RA	Yes	(%)	2 (22.2%)	2 (5.6%)	25 (26.3%)	29(20.7%)	.032
	No		7 (77.8%)	34 (94.4%)	70(73.7%)	111(79.3%)	
		Total	9(100.0%)	36(100.0%)	95(100.0%)	140(100.0%)	
Family history of HT	Yes	(%)	0 (0.0%)	2 (5.6%)	6 (6.3%)	8 (5.7%)	.737
	No	(%)	9 (100.0%)	34 (94.4%)	89 (93.7%)	132 (94.3%)	
		Total	9 (100.0%)	36(100.0%)	95(100.0%)	140(100.0%)	
Treatment response	Good	(%)	4 (44.4%)	16 (44.4%)	66 (69.5%)	86 (61.4%)	.018
	Poor	(%)	5 (55.6%)	20 (55.6%)	29 (30.5%)	54 (38.6%)	
		Total	9 (100.0%)	36 (100.0%	95 (100.0%	140 (100.0%)	

Table 4 show that there was a higher mean concentration of ESR among patients with overt HT (38.05±.2.46 mm/h) and subclinical (43.88±6.39 mm/h), when compared to the mean concentration of the Euthyroid RA patients (30.33±1.96 mm/h); i. e., there was a significant difference (P-value = 0.019) among RA patients with HT and euthyroid RA patients regarding to the concentration of ESR. There was a higher mean concentration of Anti-CCP, Anti-TPO, TSH among patients with HT (overt and subclinical) in compared to euthyroid patients. The mean concentration of Anti-CCP, Anti-TPO, TSH in overt HT was (73.78±5.38 U/ml, 142.98±10.29 IU/ml, 5.87±.174 mlU/L) respectively, while in subclinical was (75.52±14.98 U/ml, 139.17±22.97 IU/ml, 5.940± 0.52 mlU/L) respectively and in euthyroid was (40.46±4.29 U/ml, 0.169±0.0057 IU/ml, 1.39±0.050 mlU/L) respectively.

Table 4: Comparison of study parameters according to clinical status of Hashimoto's disease

Laboratory Estimates (Mean ±SE)	Study sample (RA) (N=140) (Mean. ± Standard error)			P value
	Subclinical HT, n=9	Overt HT; n=36	Euthyroid; n=95	
ESR mm/h	43.88±6.39	38.05±0.2.46	30.33±1.96	0.019
Anti-CCP U/ml	75.52±14.98	73.78±5.38	40.46±4.29	0.0001
TSH mlU/L	5.940±0.52	5.87±0.174	1.39±0.050	0.0001
T4 ng/dl	1.257± 0.08	0.51± 0.034	1.36± 0.023	0.0001
Anti-TPO IU/ml	139.17± 22.97	142.98±10.29	0.169 ±0.0057	0.0001
BMI kg/m2	35.24±1.86	35.68±0.82	31.63±0.65	0.002

That means there were a highly significant differences (P-value = 0.0001) among RA patients with HT and euthyroid RA regarding to the concentration of Anti-CCP, Anti-TPO, TSH. Besides, T4 shows a highly significant difference (P-value = 0.0001) among RA patients with HT and euthyroid RA patients, the mean concentration in overt HT was (0.51± .034 ng/dl) and subclinical HT was (1.257± .08 ng/dl) compared to the mean concentration of the euthyroid RA patients (1.36± .023 ng/dl). BMI has significant differences (P-value = 0.002) among RA patients with HT and euthyroid RA patients, the mean concentration in overt HT was (35.68± .82 kg/m2) and subclinical HT was (35.24±. 1.86 kg/m2) compared to the mean concentration of the Euthyroid patients (31.63±. .65 kg/m2).

DISCUSSION

The current study involved 140 adult RA patients, 16 males (11.4%) and 124 (88.6%) females. HT was present in 45 (32.14%) RA patients including subclinical HT 9(6.4) and overt HT 36(25.7) which agrees with (11) that show 36 (24%) RA patients had overt hypothyroidism, while 6 (4%) had subclinical hypothyroidism; And near similar to (12) who found that 20 (38.4 %) patients had hypothyroidism. The correlation in our study was a significant among RA patients with HT and ACCP (P= 0.0001), BMI (P=0.002), and ESR (P= 0.019). This indicates that hypothyroid present in patients with high ESR, obese, and positive ACCP. These results are similar to (11), (12), and (5) who found that patients with RA and hypothyroidism had a statistically significant correlation with BMI, and ESR, (P< 0.05). In addition, the present study has found no significant association among RA patients with HT in regards to age that have P value= 0.382 and gender (P=0.158). This is compatible with (12), (11), and (5), who find no significant association of age and gender P value >0.05. Besides, (13) finds that the P value of age =0.32**,** and Gender =0.18 and disagrees with (8) who documented a rise in the occurrence of hypothyroidism as individuals age, along with a greater prevalence among females compared to males. A recent study shows a significant difference (p<0.05) between RA patients with HT and treatment response (P=0.018). HT is higher in patients with poor response compared to good response; this disagrees with (8) who found that there is no association between medication for RA and an increased risk of hypothyroidism.

In the recent study, no significant difference between RA patients with HT and disease duration (P=0.44); this agrees with an Egyptian study by (3) who found that the disease duration has no significant differences (p=0.49) and disagree with (11), (12) and (5). They reported a statistically significant correlation (P<0.05) between RA patients with HT and disease duration. In a recent study that compared the sociodemographic characteristics of the RA patients with HT and euthyroid RA patients according to residency, it has been found that there was no significant difference of p > 0.05. Family history of RA was more in RA patients without HT, as there was a significant difference P-value <0.05 compared to RA patients with HT

CONCLUSIONS

HT is frequent among patients with RA. Therefore, there is a need of screening of thyroid hormone dysfunction as well as presence of Anti-TPO antibodies as markers of HT in RA patients particularly in young

patients, females, and those with high disease activity**.** The association was a significance among RA patients with HT and ACCP, BMI, and ESR.

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