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Impact of Primary Hypothyroidism on Rheumatoid Arthritis Patients

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Abstract

Background: Rheumatoid arthritis is a systemic inflammatory disease with unknown etiology. There has been considerable debate about the relation between thyroid gland and rheumatic diseases.

Objective: To assessed the prevalence of primary hypothyroidism in patients with rheumatoid arthritis, as well as the association between hypothyroidism and the severity of rheumatoid arthritis.

Patients and Methods: This study is a cross-sectional observational study involving 65 participants 18 years of age and older who were diagnosed with RA. Patients had thyroid function tests and patient disease activity was determined using the DAS28 Modified Disease Activity Score .the data were analyzed using the chi-square significance test with a P-value of ≤0.05. The data will be collected during the direct patient interview and the information from the questionnaire once verbal approval has been received from the study participant.

Results: Hypothyroidism (thyroid stimulating hormone) level >4.20 µIU/L) was observed in 26 (40%) parameters of disease activity such as DAS-28, counts tender joints significantly associated with hypothyroid patients RA.

Conclusion: Hypothyroidism was significantly associated with disease severity of RA, disease duration, BMI (Body Mass Index), and ACPA (Anti Citrullinated Protein Antibody). Identification of thyroid function tests in patients with RA is important.

Keywords: Rheumatoid arthritis, hypo-thyrodism, rheumatoid arthritis activity

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Introduction

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease without known etiology. It is characterized by symmetrical arthritis and progressive destruction of joint cartilage and bone, affecting primarily the peripheral joints symmetrically [1]. Thyroid dysfunction can be widely categorized as hypothyroidism and hyperthyroidism, the central characteristic of hypothyroidism is a reduction in thyroid hormone production, Permanent loss or destruction of the thyroid through processes such as autoimmune destruction, or radiation injury is described as primary hypothyroidism [2]. Central or secondary hypothyroidism resulting from inadequate stimulation of a normal gland is the result of hypothalamic or pituitary disease or defects in the TSH molecule [3]. approximately 99% of cases of hypothyroidism are due to

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Primary hypothyroidism, with less than 1% being due to TSH deficiency or other causes [4]. The relationship between thyroid dysfunction and RA has been the subject of discussion, with several studies suggesting a relationship between Hashimoto's thyroiditis and RA. Other studies have shown that abnormal or changing thyroid conditions can exacerbate or precipitate musculo-skeletal disease, especially when the common features and symptoms of hypothyroidism, such as discomfort, tiredness, weight gain and dyslipidemia, can be masked by the original symptoms of RA [5]. In addition, thyroid dysfunction was found at least three times more often in women with RA than in women with demographic characteristics similar to those of women with non-inflammatory rheumatic diseases such as fibromyalgia and osteoarthritis [6]. This study was designed to assess the prevalence of primary hypothyroidism in patients with rheumatoid arthritis, as well as the association between hypothyroidism and the severity of rheumatoid arthritis. There were some limitation in our study it was an observational cross-sectional study, the sample size was relatively small and the patients were not co-operative.

Patients and Methods

This study is a cross-sectional observational study; all parts of the study were performed at the outpatient clinic and inpatient of rheumatology department at Erbil teaching hospital and Rizgary teaching hospital of Erbil city. The period of the study was 6 months from October 2021 to March 2022. The study enrolled 65 participants aged >18 years. All adult rheumatoid arthritis patients who were previously and newly diagnosed were considered. The diagnosis of RA has been established according to the new 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) criteria for RA and ACR revised criteria of RA 1987. Were chosen by the convenience method of sampling. participants aged < 18 years, with Other rheumatological diseases like systemic lupus arthritis, psoriatic arthritis…, Pregnant women, Diabetic Mellitus, Patients on medication causing hypothyroidism(lithium),History of thyroidectomy, Evidence of malignancy, Infectious disease excluded from our study. The study's purpose was clearly explained to each patient who participated in it, to do this study need to get verbal acceptance from them, taking into account the privacy of each patient. The data were collected during the direct interview with patients and information from the questionnaire after taking verbal approval from the study participant. It wasincluded demographical and clinical data such as sex, age, disease duration, treatment method, and other variables, the medical and rheumatological history was evaluated by focusing on symptoms of thyroid problems (e.g., palpitations, duration of RA disease, cold intolerance, morning stiffness, weight gain, tender joints, swollen joints, etc.).

General and musculoskeletal examination and of BMI were performed. It was used DAS28 to assess the activity of disease. The scores of activity were graded as follows:

1. (Remission) ≤2.6
2. (Low activity). >2.6 and ≤3.2
3. (Moderate activity) >3.2 and ≤5.1
4. (High activity) >5.1

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C-reactive protein (CRP), ESR, rheumatoid factor (RF), ACPA, and other variables were collected.

For the Thyroid Function Test venous blood sample (3-5) ml was obtained from every participant and assessed by radioimmunoassay, the level of free thyroxine (FT4), free triiodothyronine (FT3) and (TSH), by combination of clinical symptoms and thyroid hormones. Thyroid dysfunction was assed, and classified into(subclinical or overt) hypothyroidism . subclinical hypothyroidism (SCH) mean those with increased TSH levels with normal FT4 levels Overt hypothyroidism mean an increased level of TSH and decreased FT4.

All patients were on regular treatment:

DMARDs (disease modifying anti rheumatic agent) like methotrexate, hydroxychloroquine, leflunomide…+folic acid +NSAID (nonsteroidal anti-inflammatory drugs)±steroid. Or biological DMARDs (etanarcept, adalimumab, infliximab and rituximab) +NSAID) ±steroid Or conventional +biological± NSAID or steroid.

Statistical Analysis

The data were entered by using SPSS program (version 25) and the results will be analyzed through frequency and percentage. To determine relation between the severity of disease and hypothyroidism, A Fisher exact test and chi-square were used. For statistical significant we considered a p-value ≤ 0.05.

Results

It involved 65 adult patients with RA 61 (93.8%) female and 4(6.2%) male, and their ages ranged from 19 to 70 years old (mean 51 ± 12.2 years). most of the patients (92%) were married, 85% of them were urban residents, and 80% of them were unemployed. It was observed most of the patients had BMI > 30 kg/m (obese 30(46 %).and they had disease duration from 5-10 years n=32(49%). Most RA patients had positive RF 41(63%) and ACPA 38 (58.5%),,and (50.8) % of them were ESR ranging from 18-39 mm/hour.

According to the activity of disease of rheumatoid arthritis patients (n=65):

(1) Patients with remission were7 (9.2%).

(2) Patients with low disease activity were 7 (9.2%).

(3) Patients with moderate disease activity were 21 (32.2%) 1.

(4) Patients with high disease activity were 30 (46.2%).

Table (1): Thyroid dysfunction definitions for free thyroxine (T4) and serum stimulating thyroid hormone (TSH)

Thyroid dysfunction	TSH (µIU/L)	Free T4 (pmol/L)
Euthyroidism	0.45–4.20 (normal)	(12.0–22.0) (normal)
Subclinical hypothyroidism	>4.20 (increased)	(12.0–22.0) (normal)
Overt hypothyroidism	>4.20 (increased)	<12(decreased)

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Table (2): Descriptive data of participants

Variables	category	No.	(%)
Age	18-39	12	18.5
	40-49	11	16.9
	50-59	23	35.4
	60-69	15	23
	≥70	4	6.2
Gender	Female	61	93.8
	Male	4	6.2
Marital status	Married	60	92.3
	Single	5	37.7
Residence	Rural	10	15
	Urban	55	85
Employment	Yes	13	20
	No	52	80
Disease duration	1-<5 years	15	23
	5-10 years	32	49
	>10 years	18	28
BMI	Normal	11	17
	Overweight	24	37
	obese	30	46
DAS 28	Remission	7	11
	Low	7	11
	Moderate	21	32
	High	30	46
RF	Positive	41	63
	Negative	24	36.5
ACPA	Positive	38	58.5
	Negative	27	41.5
CRP	Positive	31	47.7
	Negative	34	52.3
ESR	<18	8	12.3
	18-39	33	50.8
	40-59	14	21.5
	60-79	7	10.8
	≥80	3	4.6

A total of 26 (40%) patients had TSH levels >4.20µIU/mL and FT4<12pmol/L, therefore we classified them as having hypothyroidism, and 5 (19%) patients with TSH levels >4.20µIU/mL and normal FT4 as subclinical hypothyroidism.

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Table (3): Number and percent of thyroid dysfunction

Thyroid dysfunction	No.	(%).
Euthyroidism	34	52.3
Subclinical hypothyroidism	5	7.7
Overt hypothyroidism	26	40

It was Classified RA patients with hypothyroid (n = 26) according to the activity of disease, 1 (3.8% %) patient was in remission, 1 (3.8%) had low activity of disease, 10(38.4%) patients had moderate activity of disease and 14 (54%) patients had high activity of disease. The association was a significant between patients with hypothyroid and DAS28, disease duration, BMI, and ACPA were P-value < 0.05.

Table (4): Association between RA patients with Hypothyroidism and different measures

Measures	Category	RA with hypothyroidism		P value <0.05
		Yes	No	
DAS28	Remission Low Moderate High	0 (0%) 1(3.8%) 11(42.3%) 14(53.8%)	7(17.9%) 6(15.4%) 10(25.6%) 16(46.2%)	0.01
Disease duration	1-<5 5-10 >10	0(0%) 19(73%) 7(27%)	15(38.5%) 13(33.3%) 11(28.2%)	0.03
BMI	Normal Overweight Obese	4(15.4%) 5(19.2%) 17(65.4%)	7(17.9%) 19(48.7%) 13(33.3%)	0.04
ACPA	Positive Negative	20 (77 %) 6 (23 %)	18 (46.2%) 23 (53.8 %)	0.01
ESR	<18 18-39 40-59 60-79 ≥80	0(0%) 14(53.8%) 6(23.1%) 4(15.4%) 2(7.7%)	8(20.5%) 21(53.8%) 6(15.4%) 3(7.7%) 1(2.6%)	0.03

We observed no significant association of age, gender, RF, and CRP with the occurrence of hypothyroidism P-value >0.05.

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Table (5): Association between RA patients with hypothyroidism and diffrent variable

Measures	Category	RA patients with hypothyroidism		P value <0.05
		Yes	No	
Age	18-39 40-49 50-59 60-69 ≥70	4(15.4%) 5(19.2%) 12(42.2%) 4(15.4%) 1(3.8%)	8(20.5%) 6(15.4%) 11(28.2%) 11(28.2%) 3(7.7%)	**0.5**
Gender	Male female	0 26(42.6)	4(10.3 %) 35(57.4%)	**0.1**
RF	Positive Negative	18(69.2%) 8(30.8%)	23(59%) 16(41%)	**0.2**
Crp	Positive Negative	16(61.5%) 10(38.5%)	15(38.5%) 24(61.5%)	**0.06**

Discussion

Since the 1960s relation between RA patients and hypothyroidism has been demonstrated [7]. There has been considerable debate about the relation between thyroid and rheumatic diseases. Many researchers suggested that hypothyroidism could worsen rheumatoid disease with destructive arthropathy primarily affecting proximal interphalangial joints [8].

The study focused on studying the impact of primary hypothyroidism and RA and its association with the severity of the disease. It is involved 65 adult RA patients, 61 (93.8%) Female, and 4 (6.2%) Male.

Hypothyroidism was present in 26 (40%) RA patients which is disagree with Elattar *et. al* 36 (24%) RA patients had evidence of hypothyroidism [8]. And near similar to Joshi et. al. who found that 20 (38.4 %) patients had hypothyroidism [1], The association was a significant between RA hypothyroid patients and DAS28 (P=0.01), duration of disease (P=0.03), ACPA (P= 0.01) , BMI (P=0.04), and ESR in our study. This indicates that hypothyroid present in patients with high activity of disease, ESR, obese and positive ACPA, and these results similar to Elattar et al , Kumar DV *et al*. [] and Joshi *et al.* [1] they found association was a significant between RA patients with hypothyroid and DAS28 (P<0.05), disease duration(P<0.05),BMI(P<0.00))and ESR(p< 0.00).and DAS28 (P=0.001), disease duration(P=0.001),BMI(P=0.002))and ESR(p= 0.001) and DAS28 (P=0.007), disease duration(P=0.03),BMI(P=0.006))and ESR(p= 0.03), respectively.

In addition, It was found that there are no significant association between RA hypothyroid patients and Age(p=0.5,) Gender(p=0.1), RF(p=0.2) , and Crp (p=0.06) and This compatible with Joshi et al (1) Age(p=0.09) Gender(p=0.06), Elattar *et al* Age(p>0.05) Gender(p>0.05) (8), ,and kumar DV *et al*. Age(p=0.3) Gender(p=0.4) [9]. It was found that there are no significant association between RA hypothyroid patients and RF(p=0.2) , and CRP (p=0.06) This results compatible with Joshi *et al*. [1] RF(p=0.1) CRP(p=0.9), and with) Elattar et al. CRP (p>0.05) [8] ,and not compatible with kumar DV *et al.* RF(p=0.02)and

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CRP(p=0.009) [9] were significantly associated with RA hypothyroid patients.

Conclusions

Primary hypothyroidism has been significantly associated with the severity of RA, duration of illness, BMI and ACPA. The thyroid function of patients with RA should be determined. In this study.

Recommendations

It was recommended that all patients who received a diagnosis of RA should follow their thyroid function.

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Conflict of interest: Nil

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تأثير قصور الغدة الدرقية الأولي على مرضى التهاب المفاصل الروماتويدي

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الملخص

خلفية الدراسة: التهاب المفاصل الروماتويدي هو مرض التهابي جهازي (مزمن) مجهول السبب ، كانت العلاقة بين مرض الغدة الدرقية والاضطرابات الروماتيزمية موضوع نقاش كبير في دراستنا.

اهداف الدراسة: لتقييم انتشار قصور الغدة الدرقية الأولي بين مرضى التهاب المفاصل الروماتويدي وتقييمها العلاقة بين قصور الغدة الدرقية وشدة التهاب المفاصل الروماتويدي.

المرضى والطرائق: الدراسة عبارة عن دراسة رصدية مقطعية شملت ٦٥ مشاركًا تتراوح أعمارهم بين ١٨ عامًا وما فوق تم تشخيص إصابتهم بالتهاب المفاصل الروماتويدي. خضع المرضى لاختبار وظائف الغدة الدرقية وتم تحديد نشاط المرضى باستخدام مقياس نشاط المرض المعدل باستخدام DAS28 (تشير درجة نشاط مرض DAS والرقم ٢٨ إلى ٢٨ مفصل تم فحصها في هذا التقييم. تم تحليل البيانات باستخدام اختبار الأهمية كان Chi كانت قيمة الاختبار المربع والقيمة $P < 0.05$ ، وسيتم جمع البيانات أثناء المقابلة المباشرة مع المرضى والمعلومات من الاستبيان بعد أخذ الموافقة الشفوية من المشارك في الدراسة.

النتائج: لوحظ قصور الغدة الدرقية (يُعرَّف على أنه مستوى هرمون (TSH> 4.20 µIU / L) في ٢٦ (٤٠٪) من مؤشرات نشاط المرض مثل DAS-28-ESR ، وعدد المفاصل الرقيق المرتبط بشكل كبير بمرضى قصور الغدة الدرقية RA.

الاستنتاجات: ارتبط قصور الغدة الدرقية بشكل كبير مع شدة مرض التهاب المفاصل الروماتويدي ، ومدة المرض ، ومؤشر كتلة الجسم ، و ACPA. من المهم تحديد اختبار وظائف الغدة الدرقية في مرضى التهاب المفاصل الروماتويدي.

الكلمات المفتاحية: التهاب المفاصل الروماتويدي ، قصور الغدة الدرقية ، نشاط مرض التهاب المفاصل الروماتويدي

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