Section: General Medicine

Original Research Article

THYROID DYSFUNCTION AMONG PATIENTS NEWLY DIAGNOSED WITH RHEUMATOID ARTHRITIS IN A TERTIARY CARE CENTER IN SOUTH INDIA – A CROSS SECTIONAL STUDY

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Abstract

Background: Rheumatoid arthritis (RA) is a chronic and systemic autoimmune disease which can result in constant inflammatory polyarthritis and continuous joint destruction, leading to increased disability and damaged mobility. An association between thyroid autoimmunity and rheumatoid arthritis has been established but the causality is not yet established. The objective of this study is to estimate the frequency of thyroid dysfunction among patients newly diagnosed with rheumatoid arthritis. **Materials and Methods:** Patients newly diagnosed with rheumatoid arthritis as per ACR EULAR 2010 criteria is included in the study. Sample size was calculated to be 39 and a semi structured questionnaire on socio demographic factors was administered. Data regarding the lab investigation tests, routinely done on the patients was recorded in the proforma. Descriptive statistics like mean, SD, median and range was calculated for continuous data such as age, TSH values, antibody scores and frequency and percentages for categorical characteristics of the study sample. **Results:** Early morning stiffness of joint and relief of stiffness with exercise were symptoms presented by 100% of the study subjects while 23.1% showed weight loss and nearly 50% showed fatigue. Two (5.1%) study participants had pulmonary manifestations while just one participant had nodules. More than 61% of study subjects had moderate disease activity while over 38% had high disease activity. In this study, 28.21% of the study subjects has thyroid dysfunction and of the patients with thyroid dysfunction, 18% has subclinical thyroid dysfunction while nearly 10 % has overt hypothyroidism. **Conclusion:** The prevalence of thyroid dysfunction in patients newly diagnosed with rheumatoid arthritis was found to be 28.21%. There is a statistically significant association between thyroid dysfunction and severity of rheumatoid arthritis. Thyroid autoantibodies and thyroid dysfunction need to be screened as part of the care and follow-up of RA patients.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic and systemic autoimmune disease which can result in constant inflammatory polyarthritis and continuous joint destruction, leading to increased disability and damaged mobility.[1] Rheumatoid arthritis (RA) is a multisystem, chronic, inflammatory disease. It is characterised by destructive synovitis. Disease onset can occur at any age, however it tends to peak around the sixth decade of life. Rheumatoid arthritis carries a substantial burden for the individual as well as the society. The individual burden results from musculoskeletal deficits, with accompanying decline in physical function, quality of life, and cumulative comorbid risk. The socioeconomic burden, aside from major direct medical costs, is a consequence of functional disability, reduced work capacity, and decreased participation in societal activities. Hence it's paramount to commence efforts to establish the diagnosis early, initiate treatment promptly, and design novel treatment

strategies to control inflammation and reduce or prevent consequent damage.[2,3] Extra-articular signs include keratitis, pulmonary granulomas (rheumatoid nodules), pericarditis/pleuritis, small artery vasculitis, and other non-specific extra-articular symptoms are possible in patients with poorly managed or severe illness.[4]

Rheumatoid arthritis is considered to be a disease that is mediated by type 1 helper T cells but now attention is also given to the role of type 17 helper T cells (Th17), a subset that produces interleukin-17A, 17F, 21, and 22 and tumour necrosis factor α (TNF-α). Humoral adaptive immunity is important to rheumatoid arthritis. Plasmablasts and plasma cells are distributed in the synovium and also in juxta-articular bone marrow.[5] Macrophages are central effectors of synovitis and they act through the release of cytokines (e.g., TNF-α and interleukin-1, 6, 12, 15, 18, and 23), reactive oxygen intermediates, nitrogen intermediates, production of prostanoids and matrix degrading enzymes and phagocytosis. Neutrophils results in synovitis by synthesizing prostaglandins, proteases, and reactive oxygen species. Mast cells contributes to pathogenesis by producing high levels of vasoactive amines, cytokines, chemokines, and proteases.[5]

Multimorbidity is reported in 60% to 75% of those with RA.[6] Common comorbidities include cardiovascular conditions such as coronary artery disease and cardiac failure, as well as mental health conditions such as depression.[7,8] Majority of the excess mortality observed in RA is accounted by cardiovascular disease, with raised inflammatory markers and shared risk factors implicated.[9] One well-known cardiovascular risk factor for RA is hypertension. There is conflicting evidence that suggests that obesity contributes to the pathophysiology of RA. The risk of cardiometabolic comorbidities should be reduced by using effective anti-rheumatic medications, which is indicated by current guidelines.[9]

An increased prevalence of autoimmune thyroid disease is seen in patients with rheumatoid arthritis and also, an increased prevalence of rheumatoid arthritis is seen in patients with autoimmune thyroid disease.[10,11] An association between thyroid autoimmunity and rheumatoid arthritis has been established but the causality is not yet established.[12] .Thyroid dysfunction mainly includes hyperthyroidism and hypothyroidism. Hyperthyroidism is defined by excess of thyroid hormones, and Graves' disease (GD) is its main etiology. Hypothyroidism is defined by insufficiency of thyroid hormones, and its most common etiology is Hashimoto's thyroiditis (HT).[1]

There are very limited data available on the association between RA patients and thyroid function, particularly in the South Asian region. Therefore, this study aims to further investigate the prevalence of thyroid dysfunction in RA patients.

MATERIALS AND METHODS

The cross-sectional study was conducted between January to November 2022 in Rheumatology clinic of Department of General Medicine of Pushpagiri Institute of Medical Sciences and Research Centre. The study group of 39 newly diagnosed patients with RA as per ACR EULAR 2010 criteria was enrolled in the study and were recruited consecutively. Patients with symptomatic thyroid disease, TSH > 20 who require hormone replacement, on treatment for thyroid dysfunction and on medication known to cause thyroid dysfunction (e.g. lithium, interferon alpha, etc.) were excluded. Pregnant women, those with any evidence of malignancy and having any collagen disease other than RA were also excluded. A semi structured questionnaire on socio demographic factors was administered. Data regarding the lab investigation tests, routinely done on the patients was recorded in the proforma.

Operational Definitions

Subclinical hypothyroidism: it was indicated by increased serum TSH in the presence of a normal Free serum thyroxin level (FT4).

Overt hypothyroidism: it was indicated by increased serum TSH with decreased serum FT4 level, at which stage most patients have symptoms and benefit from treatment.

Subclinical hyperthyroidism: it was indicated by normal serum FT4 and FT3 levels, with TSH levels below the normal range, usually undetectable.

Overt hyperthyroidism: it was indicated by increased serum FT4 and FT3 levels, with TSH levels suppressed below the normal range, usually undetectable.

DAS 28 score is a validated numerical scale from 0 to 10 indicating current RA

The following DAS-28 values relate to clinical status:

Remission: DAS-28 ≤ 2.6

Low disease activity: DAS-28 2.6–3.1

Moderate disease activity: DAS-28 3.2–5.1

High disease activity: DAS28 >5.1.

Data analysis and ethical consideration

Data obtained was coded and entered into Microsoft Excel© and analysed using the Statistical Package for the Social Sciences (SPSS v. 21.0) (IBM Corp). Descriptive statistics like mean, SD, median and range was calculated for continuous data such as age, TSH values, antibody scores and frequency and percentages for categorical characteristics of the study sample. The association between thyroid dysfunction and severity of rheumatoid arthritis was done using Fischer's exact test.

Ethical review board approval was taken from Pushpagiri Institute of Medical Sciences and Research Centre (PIMSRC/E1/388A/46/2021). Informed consent was obtained from each patient before data collection.

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RESULTS

Over 70% (n=28) of the study participants were females, while nearly 30% (n=11) were males. Among clinical features early morning stiffness of joint and relief of stiffness with exercise were symptoms presented by all the study subjects while 23.1% showed weight loss and nearly 50% showed fatigue. Two (5.1%) study participants had pulmonary manifestations while just one participant had nodules. (Table 1) More than 61% of study subjects had moderate disease activity while over 38% had high disease activity. [Table 2]

On thyroid examination three study subjects had swelling and one had tenderness. Mean values of thyroid function tests across the study population were FT3 being 6.1 (± 0.88), FT4 being 14.1 (± 3.27), and TSH being 5.2 (± 1.54). Among the study population diagnosed with RA, 28.21% (n = 11) had Thyroid dysfunction. [Table 3]. More than 46% of study subjects with high disease activity had sub clinical thyroid dysfunction and 100% of study subjects with moderate activity had no Thyroid dysfunction. The difference between the groups were found to be statistically significant (p value = <0.05) [Table 4].

Table 1: Clinical features

	Symptom (N = 39)	Present n (%)	Absent n (%)
Symptom	Early morning stiffness of joint	39 (100)	0
	Relief of stiffness with exercise	39 (100)	0
	Fever	0	39 (100)
	Weight loss	9 (23.1)	30 (76.9)
	Fatigue	19 (48.7)	20 (51.3)
	Depression	0	39 (100)
Extra articular manifestation	Nodules	1 (2.6)	38 (97.4)
	Pulmonary manifestations	2 (5.1)	37 (94.9)
	Sjogrens syndrome	0	39 (100)
	Cardiac manifestations	0	39 (100)
	Vasculitis	0	39 (100)

Table 2: Distribution according to RA disease activity from DAS 28 Scores

RA Disease Activity	Frequency (N = 39)	Percent
Moderate	24	61.5
High	15	38.5

Table 3: Distribution according to prevalence of Thyroid dysfunction

Thyroid dysfunction	Frequency (N = 39)	Percent
Sub clinical	7	17.95%
Overt	4	10.26%
No Thyroid dysfunction	28	71.79%

Table 4: Association between Thyroid dysfunction and Rheumatoid Arthritis activity

RA Disease Activity	Thyroid dysfunction			Total n(%)	Fischer's Exact value	p value
	Sub Clinical n(%)	Overt n(%)	No dysfunction n(%)			
Moderate n(%)	0 0.0%	0 0.0%	24 100.0%	24 100.0%	24.247	0.000*
High n(%)	7 46.7%	4 26.7%	4 26.7%	15 100.0%		
Total n(%)	7 17.9%	4 10.3%	28 71.8%	39 100.0%		

DISCUSSION

In this study, 28.21% of the study subjects has thyroid dysfunction and 72% of the study subjects didn't have any thyroid dysfunction. Of the patients with thyroid dysfunction, 18% has subclinical thyroid dysfunction while nearly 10 % has overt hypothyroidism. Our result was comparable to the findings of other studies. In a study conducted by Anoop et al, 22 % of the patients with RA were detected to have thyroid dysfunction. Of these, 15 % had hypothyroidism.[13] According to Hussein et al , the proportion of hypothyroidism among RA patients was 16.0%.[14] Evidence for thyroid disease was obtained in 30% of patients with RA in a study conducted by Jeffrey et al.[15] A study conducted by Amir et al revealed that hypothyroidism was the most common thyroid disorder associated with rheumatoid arthritis with a prevalence of 30.4% and there was no significant difference of mean DAS28 score in subgroups of thyroid disorders.[16] The most common thyroid dysfunction observed in RA was subclinical hypothyroidism in a study by Przygodzka et al. Also no correlations were found between presence of anti TPO antibodies and thyroid dysfunction in patients with RA.[17]

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In this study, more than 46% of study subjects with high disease activity had sub clinical thyroid dysfunction and 100% of study subjects with moderate activity had no Thyroid dysfunction. A positive correlation was observed between DAS28 Score and TSH levels.

In a study conducted by Enas et al, hypothyroidism was the most common disorder found in 24% patients. On comparing between TSH levels and the RA disease activity parameters, there were significant positive correlation.[18] Study done by Prakash et al has showed significant correlation between TSH levels and DAS28 scores.[19] In this study, it is found that there is a significant change in levels of TSH in patients with subclinical hypothyroidism after being started on Disease Modifying Anti-rheumatic Drugs (DMARDs).

Since both thyroid disorder and RA are autoimmune in nature, their origin may be similar. However, the exact mechanism is not yet understood. It is believed that genetic and environmental factors are involved in the association between RA and thyroid dysfunction. This study has a few limitations. First, since the study was conducted in a single institute, the sample size was very limited. Secondly, thyroid hormones were only evaluated at the time of enrolment, and not during the course of the disease. Hence, we do not know the impact of rheumatoid arthritis on thyroid over the course of time.

CONCLUSION

According to our findings, thyroid dysfunction is quite prevalent in RA patients. Based on our findings, it is recommended that thyroid autoantibodies and thyroid dysfunction be screened as part of the care and follow-up of RA patients. It is necessary to undertake more research to comprehend the mechanism underlying the link between thyroid function and RA.

Conflicts of Interest

None.

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