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Original Research Article

SPECTRUM OF THYROID DISORDERS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A HOSPITAL-BASED ANALYTICAL CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease characterized predominantly by persistent inflammatory polyarthritis and associated extra-articular manifestations. Autoimmune diseases frequently coexist, and thyroid dysfunction has increasingly been recognized among patients with RA. The coexistence of RA and thyroid disorders may be related to shared genetic, immunological, and inflammatory mechanisms. Thyroid dysfunction may also influence systemic inflammation, disease activity, functional status, and quality of life in patients with RA. The objective is to determine the prevalence and pattern of thyroid dysfunction among patients with rheumatoid arthritis, to compare disease activity between RA patients with thyroid dysfunction and those with normal thyroid function, and to assess the possible association between severe RA and thyroid dysfunction. **Materials and Methods:** A hospital-based analytical cross-sectional study was conducted among 165 patients with rheumatoid arthritis attending the General Medicine and Rheumatology outpatient facilities of the Department of General Medicine, Government Medical College Hospital, Dindigul. Patients aged 40–75 years of either sex who had rheumatoid arthritis and were receiving treatment were included. Patients with thyroid disease in the absence of rheumatoid arthritis and those with thyroid dysfunction diagnosed before rheumatoid arthritis were excluded. The study was conducted over a period of six months. Thyroid function was assessed using thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4). Thyroid autoimmunity was evaluated using anti-thyroid peroxidase antibody (anti-TPO) and anti-thyroglobulin antibody (TgAb). General inflammatory and routine laboratory investigations were also performed. RA disease activity was assessed and compared according to thyroid status. **Result:** Among the 165 patients with rheumatoid arthritis evaluated, thyroid dysfunction was identified in 38.2% of patients. Subclinical hypothyroidism was reported as the most common thyroid abnormality. Hypothyroidism represented the predominant thyroid disorder, while hyperthyroidism was less frequently observed. Thyroid autoantibodies, including anti-TPO and TgAb, were assessed to identify associated autoimmune thyroid disease. Patients with thyroid dysfunction demonstrated higher rheumatoid arthritis disease activity compared with euthyroid patients. The findings suggest an association between thyroid dysfunction and increased RA disease activity. **Conclusion:** Thyroid dysfunction is common among patients with rheumatoid arthritis, with subclinical hypothyroidism being the predominant abnormality. RA patients with thyroid dysfunction showed greater disease activity than euthyroid patients. Routine assessment of thyroid function, particularly TSH with appropriate thyroid hormone and antibody testing, may therefore be considered as part of the clinical evaluation of patients with rheumatoid arthritis.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease characterized by persistent synovial inflammation, progressive joint destruction, functional disability, and a wide range of extra-articular manifestations. It affects approximately 0.5–1% of the global population and represents an important cause of morbidity and impaired quality of life.[1] The pathogenesis of RA is complex and involves interactions between genetic susceptibility, environmental factors, immune dysregulation, and chronic inflammatory responses.[2] Autoantibodies such as rheumatoid factor and anti-citrullinated protein antibodies are important immunological features of the disease. Persistent systemic inflammation may also contribute to manifestations involving organs outside the musculoskeletal system.[3] Autoimmune thyroid disease is another common autoimmune disorder.[4] Hashimoto thyroiditis and Graves disease represent the major autoimmune thyroid disorders and may occur together with other systemic autoimmune diseases. The coexistence of rheumatoid arthritis and thyroid dysfunction has increasingly attracted clinical attention because both conditions share several immunological and genetic mechanisms.[5] Thyroid dysfunction in patients with RA may present as overt hypothyroidism, subclinical hypothyroidism, hyperthyroidism, or autoimmune thyroid disease. Hypothyroidism is reported more frequently than hyperthyroidism among RA patients.[6] Thyroid autoantibodies, particularly thyroid peroxidase antibodies and thyroglobulin antibodies, may be detected in patients with RA even in the absence of overt thyroid dysfunction.[7] The relationship between thyroid dysfunction and RA may be bidirectional. Chronic inflammation and immune dysregulation associated with RA may predispose susceptible individuals to autoimmune thyroid disease.[8] Conversely, thyroid dysfunction may influence inflammatory pathways, metabolic activity, fatigue, musculoskeletal symptoms, and functional status.[9] Symptoms such as fatigue, weakness, myalgia, and reduced physical performance can overlap between thyroid dysfunction and active RA, potentially complicating clinical assessment.[10] However, the prevalence and pattern of thyroid dysfunction may vary between populations. Local hospital-based data are therefore useful for identifying the burden of thyroid abnormalities and determining whether thyroid dysfunction is associated with greater RA disease activity.[11] The present study was undertaken to evaluate the spectrum of thyroid disorders among patients with rheumatoid arthritis and to determine the relationship between thyroid dysfunction and RA disease activity.

MATERIALS AND METHODS

Study Design: A hospital-based analytical cross-sectional study was conducted to evaluate the prevalence and spectrum of thyroid dysfunction among patients with RA and to assess the association between thyroid dysfunction and rheumatoid arthritis disease activity. The study was designed to compare clinical and laboratory characteristics of RA patients with thyroid dysfunction with those of RA patients having normal thyroid function.

Study Setting: The study was carried out in the Department of General Medicine, Government Medical College Hospital, Dindigul. Patients attending the General Medicine and Rheumatology outpatient facilities were screened for eligibility and recruited into the study. Patients admitted to the medical wards who fulfilled the eligibility criteria were also considered for inclusion.

Study Population: The study population consisted of adult patients with an established diagnosis of rheumatoid arthritis who were attending the General Medicine and Rheumatology services during the study period. Both male and female patients between 40 and 75 years of age were included. A total of 165 patients with rheumatoid arthritis were enrolled in the study. The study presentation specifies that the participants comprised RA patients attending the General Medicine and Rheumatology outpatient facilities.

Study Duration: The study was conducted over a period of six months.

Inclusion Criteria

Patients were eligible for inclusion if they fulfilled the following criteria:

- Diagnosed cases of rheumatoid arthritis.
- Age between 40 and 75 years.
- Both male and female patients.
- Patients receiving treatment for rheumatoid arthritis.
- Patients attending the outpatient department or admitted to the hospital during the study period.
- RA patients in whom thyroid dysfunction was detected during the study evaluation.

The source presentation specifies inclusion of both genders, an age range of 40–75 years, patients receiving RA treatment, and RA patients with thyroid dysfunction.

Exclusion Criteria

Patients were excluded from the study if they fulfilled any of the following criteria:

1. Patients with thyroid disease in the absence of rheumatoid arthritis.
2. Patients with thyroid dysfunction diagnosed before the diagnosis of rheumatoid arthritis.

These exclusion criteria were applied to reduce the possibility of including patients whose thyroid disease preceded RA and to focus the analysis on thyroid dysfunction occurring in the context of established rheumatoid arthritis.

Clinical and Laboratory Assessment: Demographic and relevant clinical details were recorded, and rheumatoid arthritis disease activity was assessed. Thyroid function was evaluated by measuring thyroid-stimulating hormone (TSH), free

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T3, and free T4. Thyroid autoimmunity was assessed using anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (TgAb) antibodies. Routine laboratory and inflammatory markers were also evaluated.

Assessment of Thyroid Dysfunction: Participants were classified according to their thyroid-function profile as euthyroid or having thyroid dysfunction. Thyroid dysfunction was further categorized into hypothyroidism, subclinical hypothyroidism, and hyperthyroidism based on thyroid-function test results.

Statistical Analysis: The prevalence and pattern of thyroid dysfunction were determined. RA disease activity was compared between patients with thyroid dysfunction and euthyroid patients, and the association between severe RA and thyroid dysfunction was assessed. Categorical variables were expressed as frequencies and percentages, while continuous variables were summarized using appropriate descriptive statistics. A p-value <0.05 was considered statistically significant.

RESULTS

Demographic Characteristics of the Study Population: A total of 165 patients with rheumatoid arthritis were included in the study. The mean age of the study population was 57.8 ± 8.6 years. Among the participants, 31 (18.8%) were aged 40–49 years, 61 (37.0%) were aged 50–59 years, 52 (31.5%) were aged 60–69 years, and 21 (12.7%) were aged 70–75 years. There were 63 (38.2%) male and 102 (61.8%) female patients [Table 1].

Table 1: Demographic characteristics of the study participants

Variable	n	%
Age group (years)		
40–49	31	18.8
50–59	61	37
60–69	52	31.5
70–75	21	12.7
Sex		
Male	63	38.2
Female	102	61.8
Total	165	100

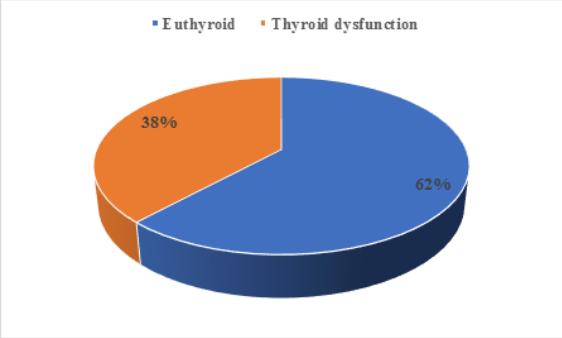

Figure1: Prevalence of thyroid dysfunction among RA patients

Prevalence of Thyroid Dysfunction: Among the 165 patients with rheumatoid arthritis, thyroid dysfunction was present in 63 (38%) patients, while 102 (62%) patients were euthyroid [Figure 1]

Spectrum of Thyroid Disorders: Among the 165 patients, subclinical hypothyroidism was identified in 36 (21.8%), overt hypothyroidism in 20 (12.1%), and hyperthyroidism in 7 (4.2%) patients. Among the 63 patients with thyroid dysfunction, subclinical hypothyroidism accounted for 36 (57.1%), overt hypothyroidism for 20 (31.7%), and hyperthyroidism for 7 (11.1%) patients [Table 2]

Table 2: Spectrum of thyroid disorders among RA patients

Thyroid disorder	n	% of total RA patients	% among thyroid dysfunction
Euthyroid	102	61.8	–
Subclinical hypothyroidism	36	21.8	57.1
Overt hypothyroidism	20	12.1	31.7
Hyperthyroidism	7	4.2	11.1
Total thyroid dysfunction	63	38.2	100

Thyroid Function Test Profile: The mean TSH level was 2.48 ± 0.91 mIU/L among euthyroid patients and 8.74 ± 6.18 mIU/L among patients with thyroid dysfunction. The mean free T3 level was 2.91 ± 0.43 pg/mL in the euthyroid group and 2.54 ± 0.51 pg/mL in the thyroid dysfunction group. The corresponding mean free T4 levels were 1.18 ± 0.21 ng/dL and 0.92 ± 0.27 ng/dL, respectively. The differences in TSH, free T3 and free T4 between the two groups were statistically significant (p<0.001) [Table 3]

Table 3: Comparison of thyroid function parameters

Parameter	Euthyroid RA (n=102)	Thyroid dysfunction RA (n=63)	p-value
TSH (mIU/L)	2.48 ± 0.91	8.74 ± 6.18	<0.001
Free T3 (pg/mL)	2.91 ± 0.43	2.54 ± 0.51	<0.001
Free T4 (ng/dL)	1.18 ± 0.21	0.92 ± 0.27	<0.001

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Thyroid Autoantibody Profile: Among the patients with thyroid dysfunction, anti-TPO antibodies were positive in 31 (49.2%) patients and negative in 32 (50.8%). TgAb positivity was observed in 22 (34.9%) patients, while 41 (65.1%) were negative. Positivity for either anti-TPO or TgAb was observed in 37 (58.7%) patients [Table 4]

Table 4: Thyroid autoantibody profile

Autoantibody	Positive n (%)	Negative n (%)
Anti-TPO	31 (49.2)	32 (50.8)
TgAb	22 (34.9)	41 (65.1)
Anti-TPO and/or TgAb	37 (58.7)	26 (41.3)

Comparison of Rheumatoid Arthritis Disease Activity: The mean disease activity score was 3.82 ± 0.74 among euthyroid patients and 4.61 ± 0.91 among patients with thyroid dysfunction. The mean ESR was 32.6 ± 13.8 mm/hour in the euthyroid group and 43.7 ± 17.2 mm/hour in the thyroid dysfunction group. Mean CRP levels were 8.9 ± 4.7 mg/L and 13.2 ± 6.1 mg/L, respectively. Severe RA was present in 21 (20.6%) euthyroid patients and 23 (36.5%) patients with thyroid dysfunction. The differences in disease activity score, ESR and CRP were statistically significant [Table 5]

Table 5: Comparison of RA disease activity according to thyroid status

Parameter	Euthyroid RA (n=102)	Thyroid dysfunction RA (n=63)	p-value
Disease activity score	3.82 ± 0.74	4.61 ± 0.91	<0.001
ESR (mm/hour)	32.6 ± 13.8	43.7 ± 17.2	<0.001
CRP (mg/L)	8.9 ± 4.7	13.2 ± 6.1	<0.001
Severe RA, n (%)	21 (20.6)	23 (36.5)	0.027

Association Between RA Severity and Thyroid Dysfunction: Among the 44 patients with severe RA, thyroid dysfunction was present in 23 (52.3%) patients and euthyroid status was observed in 21 (47.7%). Among the 121 patients with non-severe RA, 40 (33.1%) had thyroid dysfunction and 81 (66.9%) were euthyroid. The difference in the distribution of thyroid dysfunction according to RA severity was statistically significant (χ^2=5.06, p=0.024) [Table 6]

Table 6: Association between RA severity and thyroid dysfunction

RA severity	Thyroid dysfunction n (%)	Euthyroid n (%)	Total
Severe RA	23 (52.3)	21 (47.7)	44
Non-severe RA	40 (33.1)	81 (66.9)	121
Total	63 (38.2)	102 (61.8)	165

Disease Activity According to Anti-TPO Status: Among the patients with thyroid dysfunction, 31 were anti-TPO positive and 32 were anti-TPO negative. The mean disease activity score was 4.78 ± 0.82 in anti-TPO-positive patients and 4.45 ± 0.94 in anti-TPO-negative patients. The mean ESR values were 45.1 ± 16.4 mm/hour and 42.3 ± 18.1 mm/hour, respectively, while the corresponding CRP levels were 13.9 ± 6.4 mg/L and 12.5 ± 5.8 mg/L. The difference in disease activity score was statistically significant (p=0.041), whereas the differences in ESR and CRP were not statistically significant [Table 7]

Table 7: Disease activity according to anti-TPO antibody status

Parameter	Anti-TPO positive (n=31)	Anti-TPO negative (n=32)	p-value
Disease activity score	4.78 ± 0.82	4.45 ± 0.94	0.041
ESR (mm/hour)	45.1 ± 16.4	42.3 ± 18.1	0.508
CRP (mg/L)	13.9 ± 6.4	12.5 ± 5.8	0.358

DISCUSSION

Rheumatoid arthritis (RA) is a systemic autoimmune inflammatory disorder that may coexist with other autoimmune diseases, including autoimmune thyroid disease. In the present study, thyroid dysfunction was observed in 38.2% of patients with RA, with subclinical hypothyroidism being the most common thyroid abnormality. Patients with thyroid dysfunction also demonstrated higher RA disease activity compared with euthyroid patients. These findings support the clinical relevance of evaluating thyroid function in patients with RA. The prevalence of thyroid dysfunction observed in the present study is comparable with findings from previous studies. A study by Ramesh et al. involving 165 patients with RA reported a thyroid dysfunction prevalence of 38.2%, with subclinical hypothyroidism being the predominant abnormality.[12] Similarly, a study of 52 RA patients reported hypothyroidism in 38.4% of participants, and patients with hypothyroidism had significantly higher ESR and DAS28-ESR values.[13] In contrast, a recent study involving 58 female RA patients reported thyroid dysfunction in 19%, with hypothyroidism accounting for 17% and hyperthyroidism for 2%.[14] Differences between

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studies may be related to variation in patient characteristics, age, sex distribution, diagnostic criteria, duration of RA, treatment status, and the definitions used for thyroid dysfunction.

In the present study, subclinical hypothyroidism was the predominant thyroid abnormality. This finding is consistent with the study by Kumar et al., in which subclinical hypothyroidism was reported in 33.3% of RA patients and overt hypothyroidism in 3.6%.[12] Similarly, a study of newly diagnosed RA patients found that thyroid dysfunction was more frequent in RA than in controls and that subclinical hypothyroidism occurred in 13.0% of RA patients compared with 5.5% of controls.[15] A study of women with RA also reported subclinical hypothyroidism as the most common thyroid dysfunction.[16] These observations indicate that subclinical thyroid abnormalities may constitute an important component of thyroid dysfunction in RA and may remain clinically unrecognized because of overlapping symptoms such as fatigue, weakness and musculoskeletal complaints. The association between RA and thyroid dysfunction may be explained by common autoimmune mechanisms. Both diseases involve dysregulation of cellular and humoral immunity, genetic susceptibility and production of disease-associated autoantibodies. A systematic review and meta-analysis involving 29 studies and more than 35,000 RA patients demonstrated that RA was associated with an increased risk of thyroid dysfunction, particularly hypothyroidism, with a pooled odds ratio of 2.25.[4] Similarly, thyroid dysfunction and autoimmune thyroid disease have been reported to occur more frequently in patients with RA than in non-RA populations.[17] An important finding in the present study was the higher disease activity among RA patients with thyroid dysfunction. This observation is supported by a previous study in which hypothyroid RA patients had significantly higher ESR, tender joint counts, visual analogue scores and DAS28-ESR values than euthyroid patients.[2] A study involving 350 RA patients also demonstrated that thyroid dysfunction, anti-TPO positivity and autoimmune thyroid disease were significantly more common among patients with severe RA disease activity.[18] Furthermore, anti-TPO positivity was nearly three times more frequent among patients with severe disease compared with patients in remission.[18] However, the association between thyroid dysfunction and RA activity is not uniform across all studies. A large Swedish register-based cohort of 9,004 patients found that autoimmune thyroid disease was associated mainly with higher patient-reported measures at RA diagnosis, while objective disease activity measures showed only limited differences; the overall response to methotrexate was not substantially affected.[19] Similarly, a recent study of RA patients reported no significant association between thyroid dysfunction, thyroid hormone levels or thyroid autoantibodies and DAS28 or inflammatory markers.[14] These differences suggest that the relationship between thyroid dysfunction and RA activity may be influenced by disease duration, treatment, thyroid disease phenotype and the specific measures used to assess RA activity. Overall, the present findings demonstrate a substantial frequency of thyroid dysfunction among patients with RA, with subclinical hypothyroidism being the predominant abnormality and higher RA disease activity observed among patients with thyroid dysfunction. The findings support the consideration of routine thyroid function assessment in patients with RA, particularly in those with persistent or increased disease activity.

Limitations: The present study has several limitations. First, it was a hospital-based cross-sectional study conducted at a single tertiary-care centre, which may limit the generalizability of the findings to the wider rheumatoid arthritis population. Second, the study included a relatively small sample size of 165 patients, and a larger multicentre study would provide more robust estimates of the prevalence and pattern of thyroid dysfunction. Third, because of the cross-sectional design, a temporal or causal relationship between thyroid dysfunction and rheumatoid arthritis disease activity could not be established. Fourth, thyroid function was assessed at a single point in time, and longitudinal assessment would be useful to determine changes in thyroid status during RA treatment. Fifth, the influence of potential confounding factors such as duration of RA, individual antirheumatic medications, comorbidities, nutritional status and previous thyroid treatment was not comprehensively evaluated. Finally, although anti-TPO and TgAb were assessed, detailed evaluation of thyroid ultrasonography and other markers of autoimmune activity was not available. Therefore, larger prospective multicentre studies are required to further clarify the relationship between thyroid dysfunction and RA disease activity.

CONCLUSION

The present study demonstrated a considerable burden of thyroid dysfunction among patients with rheumatoid arthritis, with 38.2% of the study population showing thyroid abnormalities. Subclinical hypothyroidism was the most frequently observed thyroid disorder, followed by overt hypothyroidism, while hyperthyroidism was less common. Thyroid autoantibody positivity was also observed among patients with thyroid dysfunction. RA patients with thyroid dysfunction had higher disease activity compared with euthyroid patients, with increased inflammatory parameters observed in the thyroid dysfunction group. An increased frequency of thyroid dysfunction was also observed among patients with severe RA. These findings highlight the frequent coexistence of thyroid abnormalities in patients with rheumatoid arthritis. Routine assessment of thyroid function, particularly in patients with persistent or increased disease activity, may facilitate early identification and

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appropriate management of associated thyroid disorders. Further prospective, multicentre studies with larger sample sizes are required to establish the temporal relationship between thyroid dysfunction and RA disease activity.

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