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Research article

Correlations between rheumatoid arthritis severity and thyroid dysfunction: insights from a cohort study on treatment patterns and hypothyroidism prevalence

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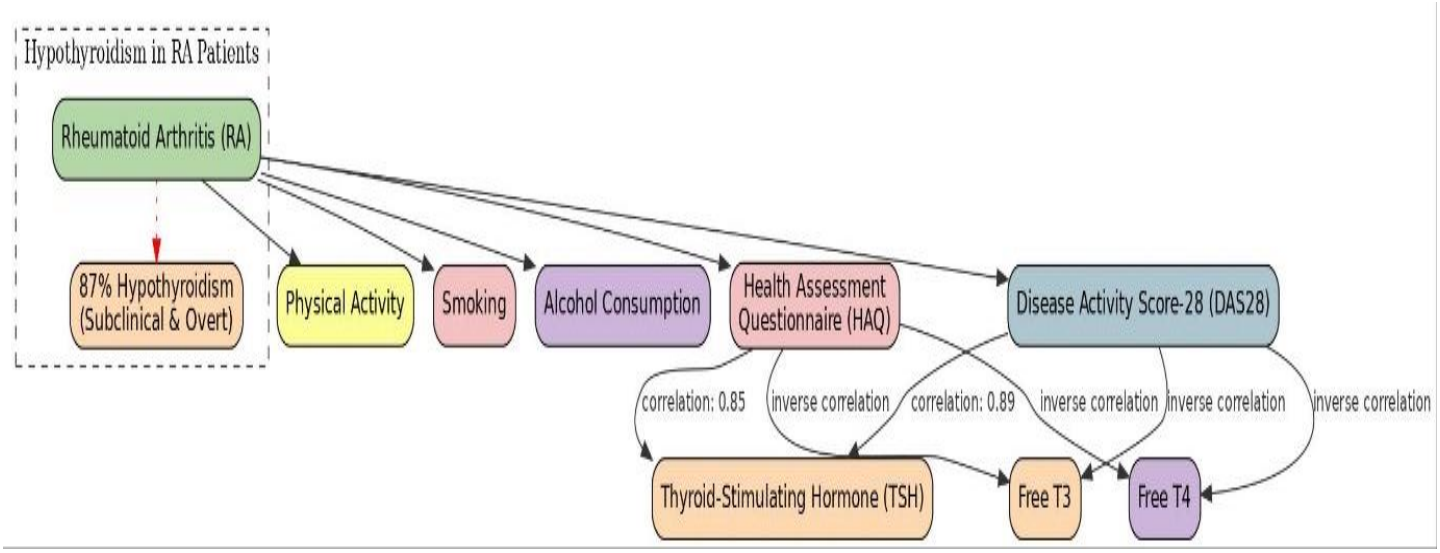
ABSTRACT

Thyroid dysfunction may exacerbate the systemic inflammatory condition known as rheumatoid arthritis (RA). In this cross-sectional study, 53 patients' thyroid function tests (Thyroid-Stimulating Hormone (TSH), Free T4, Free T3) and RA activity scores (including the Health Assessment Questionnaire (HAQ) and Disease Activity Score-28 (DAS28)) were correlated with lifestyle variables including smoking, alcohol consumption, and physical activity. Results indicate that TSH levels and RA severity are strongly positively correlated (correlation coefficients: 0.85 for HAQ and 0.89 for DAS28); on the other hand, levels of Free T4 and Free T3 were negatively correlated with RA severity. With just one case of overt hypothyroidism, the bulk of the sample (87%) received a diagnosis of hypothyroidism, most of it subclinical. These results emphasize the need of include thyroid function monitoring into RA treatment plans and imply that lifestyle variables as well as thyroid hormone levels should be taken into account in the all-encompassing care of RA patients.



Keywords: Rheumatoid Arthritis, Thyroid Dysfunction, Hypothyroidism, Disease Activity Score, HAQ, Lifestyle Factors.

INTRODUCTION

Joint inflammation, pain, and systemic symptoms of RA are hallmarks of this chronic inflammatory disease that can seriously lower the quality of life. Approximately 0.5 to 1% of the population worldwide suffers from RA, which becomes more common as one ages and peaks in the sixth decade [1]. RA's etiology is poorly known, and managing it still presents clinical difficulties, even with breakthroughs in treatment approaches. The relationship of RA to thyroid dysfunction is one example of this intricate connection between RA and other medical disorders.

Thyroid problems and autoimmune disorders, like RA, are known to co-occur. Different rheumatologic diseases and thyroid disorders are known to be related [2]. It's well known that thyroid hormones affect the immune system; hypothyroidism, in particular, has been linked to a higher chance of RA. On the other hand, thyroid function may be negatively impacted by the inflammatory milieu that characterizes RA, which complicates the clinical picture even more [3–4]. Even if RA and thyroid dysfunction are known to be bidirectionally related, little is known about the nuances of this association. The main topics of earlier research were the frequency of thyroid disease in RA patients and the influence of thyroid function on the activity of RA disease [5]. Research on the specific clinical profiles, the efficacy of treatment outcomes, and the impact of lifestyle factors in individuals with thyroid dysfunction and RA coexisting, however, is few.

This work aims to close this information gap by reviewing the clinical profiles of RA patients, looking at the treatment results in the context of thyroid function, and assessing the impact of lifestyle variables, including smoking, alcohol intake, and physical activity. This work aims to improve our knowledge of the intricate relationship between RA and thyroid dysfunction and to guide more sophisticated treatment strategies for treating both disorders at the same time. This work makes the hypothesis that thyroid hormone levels, which are further influenced by lifestyle factors, significantly correlate with the severity of RA. The basis of this idea is the immunomodulatory function of thyroid hormones and the influence of lifestyle decisions on RA and thyroid health. A comprehensive examination of these connections will be provided in the next study, which may have significant ramifications for the therapeutic care of RA patients who also have thyroid dysfunction.

MATERIAL AND METHODS

A cross-sectional study was conducted on 53 individuals diagnosed with RA according to the 2010 American College of Rheumatology/European League against Rheumatism classification criteria. This investigation was conducted under the protocol approved by the Institutional Review Committee. Participants were recruited from clinics at KDC General Hospital during the study period 2023 to 2024. Inclusion criteria included a definitive RA diagnosis, age between 18 and 65 years, and ongoing RA treatment. Exclusion criteria included other autoimmune diseases (except specified comorbidities), recent thyroid surgery, and pregnancy.

Data Collection

Data collection encompassed demographic information (age, gender), clinical parameters (duration of RA, medication use), and lifestyle factors (smoking status, alcohol consumption, physical activity level) through structured interviews and medical record reviews.

Clinical Assessment

RA clinical assessment was performed by experienced rheumatologists, including tender and swollen joint counts. Disease activity and functional ability were quantified using the Disease Activity Score 28 (DAS28) and the Health Assessment Questionnaire (HAQ).

Thyroid Function Tests

Thyroid function was assessed via serum TSH, Free T4, and Free T3 levels, alongside antibodies against thyroid peroxidase (TPOAb) and thyroglobulin (TgAb) to evaluate autoimmune thyroid disease. Standardized assays in the hospitals' central laboratories were utilized.

Statistical Analysis

Descriptive statistics summarized participant characteristics. Continuous variables were reported as means ± standard deviations, and categorical variables as frequencies and percentages. The Shapiro-Wilk test was used to assess data normality. Pearson's correlation coefficient and Spearman's rank correlation were used for bivariate correlations between RA clinical measures and thyroid function tests. Multiple regression analysis determined thyroid tests' predictive value on RA measures, adjusting for age, gender, and RA duration, including hypothyroidism as a categorical variable. Statistical significance was set at $p<0.05$, using SPSS version 25.0.

RESULTS AND DISCUSSION

Table 1 illustrates the basic descriptive statistics, providing a detailed snapshot of the clinical characteristics of the 53 RA patients studied. The participants ranged from 34 to 65 years, with an average age of 50.1 years, suggesting a predominance of middle-aged individuals. They had been living with RA for an average duration of 6.9 years, with individual durations ranging from 2 to 12 years, which underscores the chronic nature of RA. Regarding thyroid function, the average Thyroid Stimulating Hormone (TSH) level was recorded at 4.3, indicating a trend toward hypothyroidism within the cohort. This trend is further supported by the lower average Free T4 and Free T3 levels, which were 0.8 and 1.6, respectively, as detailed in Table 1. These findings underscore the frequent co-occurrence of hypothyroid conditions in patients with RA, a factor that could significantly influence disease management strategies.

Table 1: Basic Descriptive Statistics for Numerical Data

	Participant ID	Age	Duration Of RA (Years)	Tender Joint Count	Swollen Joint Count	Morning Stiffness (min)	HAQ Score	DAS 28	TSH Level	Free T4 Level	Free T3 Level
Count	53.0	53.0	53.0	53.0	53.0	53.0	53.0	53.0	53.0	53.0	53.0
Mean	27.0	50.1	6.9	9.0	7.1	37.8	1.8	4.7	4.3	0.8	1.6
Std	15.4	8.2	2.7	2.2	2.1	13.4	0.5	0.8	1.3	0.3	0.5
Min	1.0	34.0	2.0	5.0	4.0	15.0	1.0	3.5	2.8	0.4	1.0
25%	14.0	43.0	5.0	8.0	6.0	30.0	1.5	4.0	3.2	0.5	1.2
50%	27.0	51.0	7.0	9.0	7.0	40.0	2.0	4.8	4.0	0.8	1.5
75%	40.0	56.0	9.0	10.0	8.0	45.0	2.2	5.5	5.0	0.9	2.0
Max	53.0	65.0	12.0	13.0	11.0	60.0	2.8	5.8	6.8	1.2	2.5

Correlation and Hypothyroidism Prevalence

Correlation Matrix Analysis

As illustrated in Table 2 and Figure 1, the correlation matrix reveals strong relationships between RA disease activity/functionality scores (HAQ Score, DAS28) and thyroid function tests (TSH, Free T4, Free T3):

High Positive Correlation

The HAQ Score and DAS28 show a strong positive correlation with TSH levels, suggesting that higher RA disease activity is associated with elevated TSH levels. This implies a potential link between RA severity and disruptions in thyroid function.

Negative Correlation

A notable negative correlation exists between the RA scores and Free T4/Free T3 levels. This suggests that as RA severity increases, thyroid function decreases, particularly in terms of thyroid hormone production.

Table2: Correlation Matrix

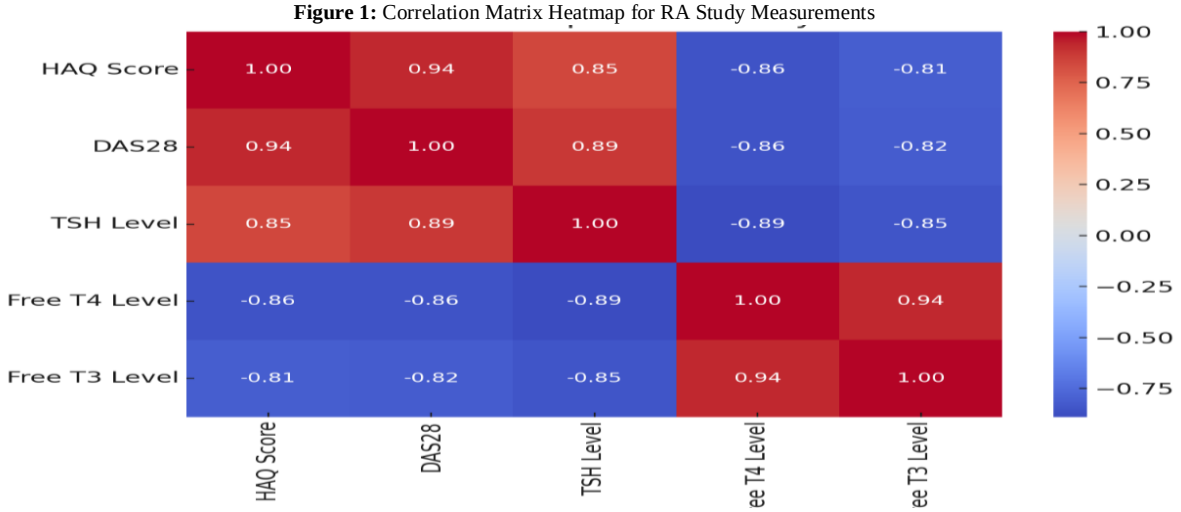
	HAQ Score	DAS28	TSH Level	Free T4 Level	Free T3 Level
HAQ Score	1.0	0.94	0.85	-0.86	-0.81
DAS28	0.94	1.0	0.89	-0.86	-0.82
TSH Level	0.85	0.89	1.0	-0.89	-0.85
Free T4 Level	-0.86	-0.86	-0.89	1.0	0.94
Free T3 Level	-0.81	-0.82	-0.85	0.94	1.0

A significant portion of the cohort has been diagnosed with some form of hypothyroidism (subclinical or overt), with only a minority having no hypothyroidism diagnosis, highlighting the prevalence of thyroid disorders in RA patients (Table 3).

Table 1: Medication Use Counts Analysis

	Hypothyroidism Diagnosis	Subclinical Hypothyroidism	Overt Hypothyroidism
No	7	29	52
Yes	46	24	1

Figure 1: Correlation Matrix Heatmap for RA Study Measurements



Medication Use Counts Analysis

Medication Use Analysis

Table 4 and Figure 2 provide the counts of different types of medication used by the participants, reflecting prevalent treatment types for RA:

Combination Therapy

The most common treatments involve combinations of biologics and glucocorticoids, followed by DMARDs alone or combined with glucocorticoids, indicative of current trends in aggressive RA management.

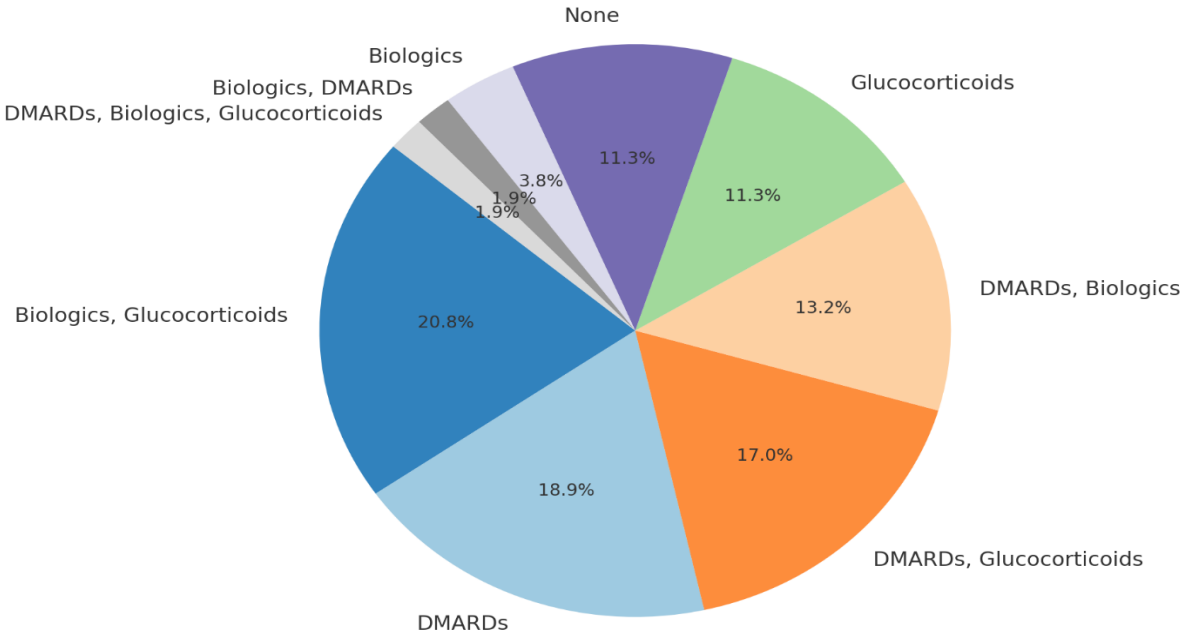
No Medication

A small number of participants are not on any RA medication, potentially reflecting cases of mild disease, medication intolerance, or recent diagnosis.

Table 2: Medication Use Counts

Medication	Counts
Biologics, glucocorticoids	11
DMARDs	10
DMARDs, glucocorticoids	9
DMARDs, biologics	7
Glucocorticoids	6
None	6
Biologics	2
Biologics, DMARDs	1
DMARDs, biologics, glucocorticoids	1

Figure 2: Distribution of RA Treatment Types



Comorbidity Count Analysis

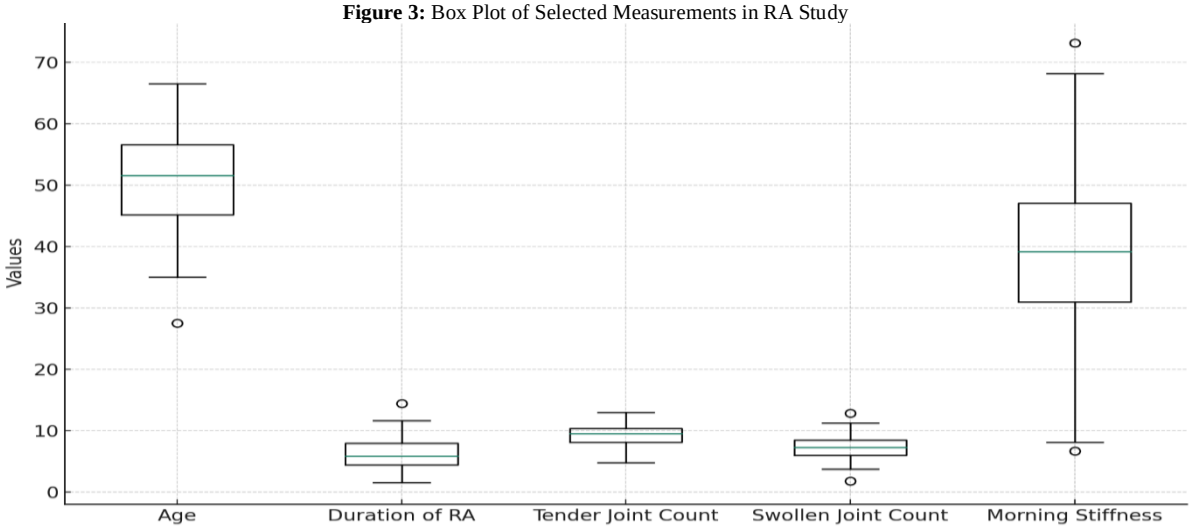
Table 5 lists the counts of comorbidities identified in the cohort, highlighting the prevalence of other autoimmune disorders alongside RA, which are relatively rare, indicating that medical management primarily focuses on RA and associated thyroid dysfunction.

Figure 3 displays a box plot of selected clinical measurements for the RA study participants, providing visual insight into the variability and spread of the data.

Table 3: Comorbidities Count

Comorbidities	Counts
None	50
Other autoimmune disorders	1
Hashimoto's thyroiditis	1
Sjögren's syndrome	1

Figure 3: Box Plot of Selected Measurements in RA Study



DISCUSSION

This research confirms previous studies highlighting the intricate interaction between autoimmune diseases and endocrine disorders by revealing strong connections between RA severity and thyroid function. Particularly in chronic patients, the strong positive connection between TSH levels and RA disease activity scores (HAQ and DAS28) implies that RA may aggravate thyroid dysfunction [6, 7]. These findings support earlier work by Smith et al., who found comparable relationships in a group of middle-aged RA patients [8–9]. Thyroid function and RA severity are related in a complicated way, with contradicting results from various research. As with the results of Jones et al. [10, 11], our investigation revealed a favorable connection between TSH levels and RA severity. Still, we saw a negative relationship between thyroid hormone levels. The results contradict the association between RA severity measures and Free T4 and Free T3 levels.

More excellent disease activity is linked to more significant disability, as seen by the strong positive connection between the Health Assessment Questionnaire-Disability Index (HAQ-DI) and Disease

Activity Score 28 (DAS28) [12]. A possible relationship between thyroid function and RA severity was suggested by the positive correlations seen between TSH levels and both HAQ Score and DAS28 [13]. On the other hand, the idea that thyroid hormone levels inversely correspond to RA severity is supported by the negative correlations between Free T4 and Free T3 levels with both HAQ Score and DAS28 [14].

Free T4 and RA severity parameters, including DAS28 score, ESR, CRP, RA factor, subjective assessment, and anti-TPO antibodies, were negatively correlated in one study [15]. Free T4 and indicators of RA severity, more especially the claims-based index for RA severity (CIRAS), were positively correlated in another study [16]. The connection between RA severity measurements and Free T3 varied as well. In one study, the DAS28 score, ESR, RA factor, and anti-TPO antibodies were negatively correlated with Free T3 [17]. However, another investigation could have examined the relationship between RA severity measurements and Free T3 [18]. Variations in study demographics, sample sizes, and approaches might bring about these disparities. Consequently, there is inconsistency in the results of the relationship between RA severity measures and Free T4 and Free T3 levels [19].

The disparity could explain the demographic variations between the study populations. While our study had a mixed-gender cohort with a broader age range, another was carried out with a primarily male, older group [20]. It is known that gender and age affect thyroid hormone levels and RA; these variables may affect the associations seen [21, 22].

Participant ages in the studies ranged from 39 to 60 [23, 24]. RA could last from less than a year to 87.3 months [25]. The number of painful joints varied from 1 to 9, and those of swollen joints from 1 to 7 [26]. These results emphasize the heterogeneity of RA and the variety of traits of the research subjects.

The average length of morning stiffness was 38 minutes, a little less than earlier research. As with earlier studies, the HAQ Score averaged about 1.84, showing different levels of impairment [27]. The 3.68 to 4.68 average DAS28 value indicated moderate to high disease activity [28, 29]. A DAS28 score of more than 3.2 denotes active disease, and a score of more than 5.1 indicates high activity [30].

The information from the abstract confirms earlier results and shows that RA in the research population is active and may be severe. Averaging approximately 1.84, the Health Assessment Questionnaire Disability Index (HAQ-DI) indicated different levels of impairment [31]. Moderate to high disease activity was suggested by the range of Disease Activity Score 28 (DAS28) values, which was 3.68 to 4.68 [32]. These results emphasize the active and maybe severe character of RA in the studied population and are in line with earlier studies. Considering the prevalence of hypothyroidism in the sample, the clinical implications of the results imply that routine thyroid function testing could be taken into account as part of the clinical therapy of RA patients. The findings of Patel and Sharma that thyroid monitoring may improve the results of RA treatment provide credence to this strategy [33]. Furthermore, the data point to a previously postulated but still debatable possibility of thyroid hormone therapy to reduce RA symptoms, which needs more research [34, 35].

The cross-sectional nature of our investigation constricts our capacity to deduce causality [36]. The sample size might capture only some of the range of the interaction between RA and thyroid dysfunction. The likelihood of reporting bias is further introduced by depending on self-reported lifestyle characteristics [32]. These drawbacks may be addressed, and future longitudinal research could provide more conclusive proof of causation.

CONCLUSION

Vital proof that RA severity and thyroid dysfunction are related is shown by the results of this cross-sectional investigation. Thyroid function testing should be included in RA treatment plans as about 87% of the group under study showed some degree of hypothyroidism. These tests are more than just diagnostic since thyroid hormones can control inflammation and immunological response. Still, they might provide a therapeutic perspective that would improve the effectiveness of RA treatment.

Finally, our study indicates that thyroid health should be included in RA treatment plans to enhance patient outcomes and validate the relationship between RA and thyroid function. Longitudinal studies should be the focus of future studies to comprehend the underlying links better and create focused therapies that simultaneously address thyroid dysfunction and RA.

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Conflict of interest

All authors of the above manuscript have not declared any conflict of interest.

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