folia medica

Folia Medica 67(6)
DOI: 10.3897/folmed.67.e165686

Research Article

Clinical and immunological assessment of thyroid pathology in rheumatoid arthritis

Elena Deseatnicova[1], Eugeniu Russu[1], Alexandru Corlateanu[1], Luana Andrea Macovei[2], Nistor Alesea[1], Lucia Andries[1], Elena Rezus[2], Liliana Groppa[1]

1 *State University of Medicine and Pharmacy Nicolae Testemitanu in Chisinau, Chisinau, Moldova*
2 *Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania*

Corresponding author: Elena Deseatnicova, State University of Medicine and Pharmacy Nicolae Testemitanu in Chisinau, Chisinau, Moldova; Email: edeseatnicova@yahoo.com

Received: 19 July 2025 ♦ **Accepted:** 5 September 2025 ♦ **Published:** 18 December 2025

Citation: Deseatnicova E, Russu E, Corlateanu A, Macovei LA, Alesea N, Andries L, Rezus E, Groppa L. Clinical and immunological assessment of thyroid pathology in rheumatoid arthritis. Folia Med (Plovdiv) 2025;67(6):e165686. doi: 10.3897/folmed.67.e165686.

Abstract

Introduction: Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease characterized by joint inflammation and significant extra-articular comorbidities. The autoimmune thyroid disease (AITD) is among the most frequent endocrine disorders associated with RA, reflecting potential shared immunopathogenic mechanisms.

Aim: To evaluate the prevalence and clinical characteristics of thyroid dysfunction and autoimmunity in female patients with RA in comparison with a matched cohort of healthy controls and assess their association with disease activity and anti-cyclic citrullinated peptide antibodies (ACPA) positivity.

Materials and methods: A cohort of 139 female RA patients was compared to 97 healthy controls. Thyroid function (TSH, fT4) and thyroid-specific antibodies (TPOAb, TgAb) were measured. RA disease activity was assessed using DAS28-ESR, with statistical analyses examining associations between thyroid pathology and RA features.

Results: The prevalence of thyroid dysfunction among RA patients was 40.2%, which was significantly higher than the 8.24% observed in controls (p<0.001). Clinical hypothyroidism occurred more frequently in the RA group (20.86%). RA patients also had higher rates of TPOAb and TgAb positivity (37.28% and 30.5%, respectively) compared to controls. ACPA and TPOAb levels demonstrated a strong positive correlation (r=0.6375). Moreover, higher RA disease activity correlated with an increased prevalence of thyroid pathology.

Conclusion: Thyroid dysfunction and autoantibody positivity are significantly more prevalent in RA patients, suggesting shared autoimmune mechanisms. Routine thyroid function and antibody screening in RA management may facilitate early detection and improve outcomes.

Keywords

autoimmune thyroid disease, hypothyroidism, systemic inflammation, thyroid dysfunction

Introduction

Rheumatoid arthritis (RA) is a persistent inflammatory condition marked by inflammation, pain, and degradation of synovial joints, resulting in significant disability and early death.[1] While synovitis is the defining pathological characteristic of RA, other extra-articular symptoms and comorbidities likely arise from the intricate, chronic, inflammatory, and autoimmune nature of RA.[2] RA affects approximately 0.5% to 1% of the population, with prevalence tending to decline from north to south and from urban to rural areas.[3] Women are at higher risk of devel-

Copyright by authors. This is an open access article distributed under the terms of the Creative Commons Attribution License (CC-BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

PENSOFT.

oping RA, which can manifest at any age but has a peak incidence around 50 years.[4]

The pathogenic processes that initiate and subsequently sustain the chronicity of the synovial lesion remain incompletely elucidated. Recent investigations in genetics, epidemiology, translational biology, and therapeutics have yielded significant insights.[3,5] Autoimmunity is widely recognized as an essential factor in the chronicity and progression of the illness. The identification of autoimmune reactions to citrullinated self-proteins signifies a notable advancement. ACPA identifies citrullinated residues on several self-proteins, such as vimentin, fibronectin, fibrinogen, and type II collagen. The tissue source of this reaction is unclear.[6]

The main characteristic of rheumatoid arthritis is a systemic autoimmune process characterized by persistent synovial inflammation driven by aberrant immune activation and proinflammatory cytokine release. Beyond joint destruction, its pathogenesis involves widespread immune dysregulation that contributes to extra-articular manifestations and multiple organ involvement, including the cardiovascular, pulmonary, and endocrine systems.[7,8] Understanding these systemic effects is essential for comprehensive disease management and reducing overall morbidity.

AITD comprises a spectrum of disorders characterized by an immune-mediated assault on the thyroid gland. Its prevalence is estimated to be around 5%, though antithyroid antibodies are more common. Women are disproportionately affected, and the prevalence of AITD is higher in iodine-sufficient regions than in iodine-deficient areas. Clinically, autoimmune thyroid disease is most commonly manifested as Hashimoto's thyroiditis, which causes hypothyroidism, or Graves' disease, which causes hyperthyroidism.[9,10] Nearly all forms of AITD are characterized by the presence of serum antibodies directed against thyroid peroxidase (TPOAb) and thyroglobulin (TgAb).[11] Although frequently described as a classic form of single-organ autoimmunity, the AITD burden in a subset of patients extends well beyond the thyroid gland.[12]

RA and AITD frequently co-occur, reflecting shared genetic and immunological mechanisms, as well as similar clinical and serologic features.[12] Both conditions involve dysregulated T-cell responses, autoantibody production, and increased levels of proinflammatory cytokines, such as tumor necrosis factor (TNF-α) and interleukin (IL-6), suggesting a shared autoimmune predisposition. Clinically, RA patients exhibit a higher prevalence of hypothyroidism and thyroid autoantibodies. Some authors suggest that hypothyroidism may exacerbate rheumatoid disease.[13] These considerations highlight the importance of systematic thyroid function screening in rheumatoid arthritis patients in order to detect and manage comorbid endocrine disorders early on. Therefore, we aimed to assess the presence of thyroid pathology, including its autoimmune component, in patients with RA and to determine its correlation with ACPA positivity and disease activity, as well as to analyze variability in its clinical presentation.

Aim

This study aims to assess the functional status of the thyroid gland, analyze the symptomatology of thyroid dysfunction, and evaluate the presence of thyroid-specific antibodies in patients diagnosed with rheumatoid arthritis in direct comparison with a matched cohort of healthy controls.

Materials and methods

The study group consisted of 139 female patients with RA, with a mean age of 59.1±11.7 years. The mean duration of rheumatoid articular syndrome was 9.9±3.7 years. Patients were recruited consecutively at the university clinic of the Department of Rheumatology starting from 2022. The control group (CG) consisted of 97 female patients without RA, recruited at the center of family medicine, homogeneous by physiological parameters, including a mean age of 58.1±11.3 years (p>0.05).

For the recruitment of patients into the study group, inclusion and exclusion criteria were used, which remained unchanged throughout the study. Thus, the inclusion criteria for the study group were a diagnosis of RA established according to the ACR/EULAR 2010 classification criteria[1], female sex, and treatment with methotrexate (MTX) as the sole disease modifying anti-rheumatic drug (DMARD). The exclusion criteria for the study group included other inflammatory rheumatic diseases besides RA, diabetes mellitus, malignancy, pregnancy at the time of inclusion, treatments affecting thyroid function, and decompensated somatic diseases. The control group was defined as people who did not have any evidence of inflammatory rheumatic or metabolic diseases, as well as being female. Exclusion criteria were the same as for the RA group. Clinical and demographic data of the study groups are presented in **Table 1**.

Laboratory investigations included the immuno-inflammatory syndrome [rheumatoid factor (RF), ACPA, C-reactive protein (CRP)] and erythrocyte sedimentation rate (ESR). Disease activity in RA was assessed using the DAS28-ESR score.[14] Assessment of thyroid status: thyroid-stimulating hormone (TSH), free thyroxine level (fT4), TgAb, and TPOAb. The reference range for TPOAb was 0–34 IU/mL and for TgAb 0–115 IU/mL. Reference values used to evaluate thyroid functional status are presented in **Table 2**.

Thyroid gland ultrasound was performed in all the patients to confirm the diagnosis of autoimmune thyroiditis and exclude nodular lesions or other structural abnormalities of the gland.

The study was approved by the Research Ethics Committee on April 18, 2022 (Approval No. 1). To achieve the research objective, a Type 1 cohort study (prospective study with retrospective components) was planned. Statistical analysis was performed using the StatSoft Statistica 9.0 software package. For quantitative variables with normal distribution, results are presented as mean values and standard deviations (M ± SD). For variables not following

Table 1. Clinical and demographic profile of the study group

Parameters	Study group (n=139) M±SD (%)	Me±ES [CI]
Mean age, y.o.	59.1±11.7	[48.2-71.4]
Age at RA onset, y.o.	48.7±9.4	[39.1-57.8]
Disease duration	9.9±3.7	[1.8-14.5]
Disease evolution		
Slow progressive	71 (51.1%)	
Fast progressive	68 (48.9%)	
Disease activity (DAS28) [14]		
<2.6 (remission)	17 (12.23%)	1.9±0.05 [1.3-2.59]
≥2.6-3.2 (low)	44 (31.65%)	2.81±0.07 [2.69-3.17]
>3.2 <5.1 (moderate)	62 (44.6%)	4.72±0.05 [3.26-5.05]
≥5.1 (high)	16 (11.51%)	6.2±0.03 [5.4-7.21]
X-ray stage [15]		
I	4 (2.88%)	
II	58 (41.72%)	
III	55 (39.57%)	
IV	22 (15.83%)	

Note: Baseline parameters of RA patients (n=139) and healthy controls (n=97), including age, disease duration, disease activity (DAS28-ESR), and radiographic stage. Data are presented as mean ± SD, median (ES, CI), or n (%).

Table 2. Classification of thyroid gland pathology

	TSH, μIU/mL	fT4, pmol/L
Clinical hypothyroidism	>4.20	<12
Subclinical hypothyroidism	>4.20	12-22 (normal)
Euthyreosis	0.27-4.20	12-22
Subclinical hyperthyroidism	<0.27	12-22 (normal)
Clinical hyperthyroidism	<0.27	>22

a normal distribution, the median (Me) and interquartile range (25th percentile; 75th percentile) were used. To assess the significance of differences between the mean values of numerical parameters, Student's t-test was applied. In cases of non-normal distribution and high data dispersion, the non-parametric Mann-Whitney test was used.

Results

We characterized the obtained data based on the clinical symptoms characteristic of thyroid gland pathology. The distribution of these symptoms, including dry skin, intolerance to low environmental temperatures, loss of appetite, and hair loss, showed a higher prevalence in patients with RA compared to the control group **(Table 3)**.

In patients with rheumatoid arthritis (RA), symptoms such as cold intolerance, hair loss, and fatigue were the most frequently reported, occurring in 97.84%, 80.58%, and 75.54% of cases, respectively. These findings demonstrated a statistically significant difference compared to the healthy control group ($p<0.001$). Other symptoms, including loss of appetite, constipation, and weight gain, were observed in a smaller proportion of cases but likewise showed statistically significant differences compared to controls

Table 3. Distribution of symptoms of thyroid pathology

Symptoms	Frequency of symptoms, n (%)		
	RA (n=139)	CG (n=97)	*p*
Fatigue	105 (75.54%)	36 (37.11%)	0.0067
Dry skin	98 (70.5%)	15 (15.46%)	0.0041
Cold intolerance	136 (97.84%)	5 (5.15%)	0.00034
Loss of appetite	38 (27.34%)	5 (5.15%)	0.012
Hair loss	112 (80.58%)	25 (25.77%)	0.0078
Constipation	58 (41.73%)	9 (9.28%)	0.036
Weight gain	23 (16.55%)	12 (12.37%)	0.089
Abnormal sensations (paresthesias)	12 (8.63%)	2 (2.06%)	0.041

Folia Medica

(p<0.005). Paresthesia was reported in 8.63% of RA patients versus 2.06% of controls (p<0.05).

The graphical analysis **(Fig. 1)** clearly illustrates the higher prevalence of symptoms indicative of thyroid dysfunction among patients with RA compared to the CG, emphasizing a comorbidity often neglected in clinical rheumatology. Classic hypothyroid symptoms, such as cold intolerance (97.84%), hair loss (80.58%), dry skin (70.5%), and fatigue (75.54%), are significantly more common in the RA cohort, where these values far exceed those in the CG (all below 37.11%). This distribution suggests that the association is not merely coincidental but may reflect a shared, immunologically mediated pathogenic mechanism linking RA with AITD.

Additionally, less specific symptoms such as constipation (41.73% vs. 9.28%), loss of appetite (27.34% vs. 5.15%), and paresthesia (8.63% vs. 2.06%) further illustrate the complexity of thyroid involvement that may remain unacknowledged in RA without a comprehensive evaluation of the hypothalamic–pituitary–thyroid axis. This clinical relationship raises critical questions about the interaction between chronic inflammatory processes and endocrine dysfunctions, underscoring the importance of regular thyroid function assessments in patients with RA. This study's results enhance our understanding of the systemic characteristics of RA and highlight the need for a multidisciplinary treatment approach that incorporates endocrinological assessment into conventional care regimens.

Among the patients with RA, 56 (40.2%) were diagnosed with thyroid dysfunction. Based on TSH and fT4 laboratory results, clinical hypothyroidism was identified in 29 RA patients (20.86%), while subclinical hyperthyroidism was observed in 17 (12.23%). Clinical hyperthyroidism and subclinical hypothyroidism were each diagnosed in 5 patients (3.59%) within the RA group. In contrast, clinical hypothyroidism was reported in only 2 control subjects (2.06%), with no cases of clinical hyperthyroidism observed. Subclinical hyperthyroidism was present in four control patients (4.12%), and subclinical hypothyroidism in two (2.06%). Overall, thyroid pathology was significantly less prevalent in the healthy control group, affecting only eight individuals (8.24%) **(Fig. 2)**.

Fig. 3 illustrates the marked differences in the prevalence of thyroid autoantibodies TgAb and TPOAb between patients with RA and healthy controls. TgAb were detected in 30.5% of RA patients compared to only 4.16% of controls, while TPOAb were present in 37.28% of RA patients versus 6.25% in the CG. The statistically significant differences highlight a complex immunological environment where the presence of both systemic and organ-specific autoantibodies indicates a common, systemic immune dysregulation.

The increased occurrence of thyroid autoantibodies in RA patients substantiates the theory of autoimmune "crosstalk" between the joints and endocrine systems, by sustained T-helper cell activation and common inflammatory pathways including IL-6, TNF-α, and type I interferons. This immunological comorbidity carries important clinical implications, as TPOAb and TgAb often precede overt thyroid dysfunction and predict the development of clinical hypothyroidism. Accordingly, systematic screening for thyroid antibodies in RA patients could facilitate early detection of autoimmune thyroiditis, help prevent progression to clinical endocrine dysfunction, and improve the overall management of autoimmune disease **(Fig. 3)**.

Inflammatory and autoimmune profiles were compared between the two groups. Patients with RA were positive for RF in 88.14% of cases and positive for ACPA in 71.19% of cases. The mean RF value was 226.75±57.9 IU/mL, while the mean ACPA level was 173.25±21.32 IU/mL. Inflammation markers such as ESR (35.5±24.2 vs. 18.4±5.0 mm/h) and CRP (62.1±8.3 vs. 4.2±1.05 mg/L) were significantly higher in RA patients, as expected given the presence of systemic inflammation **(Table 4)**.

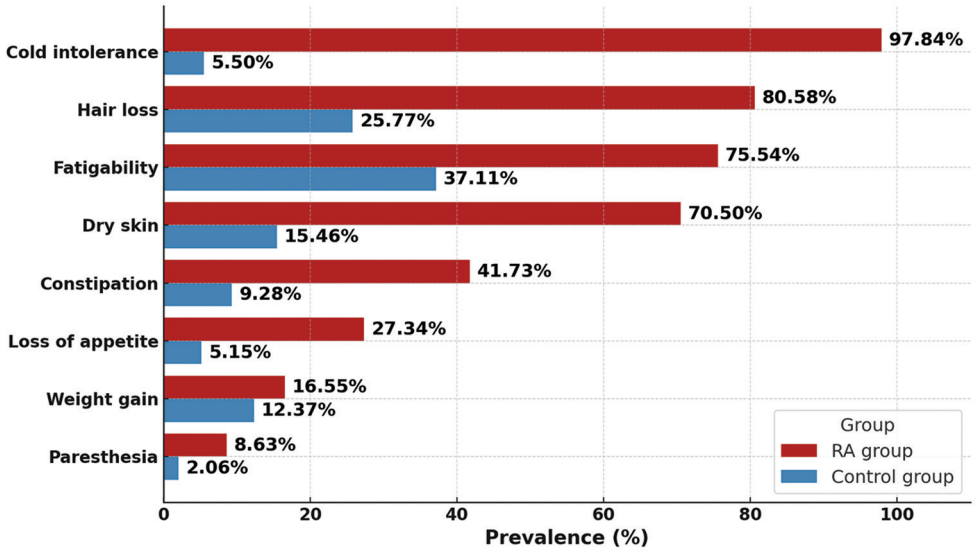

Figure 1. Comparative prevalence of thyroid dysfunction symptoms in rheumatoid arthritis and control groups.

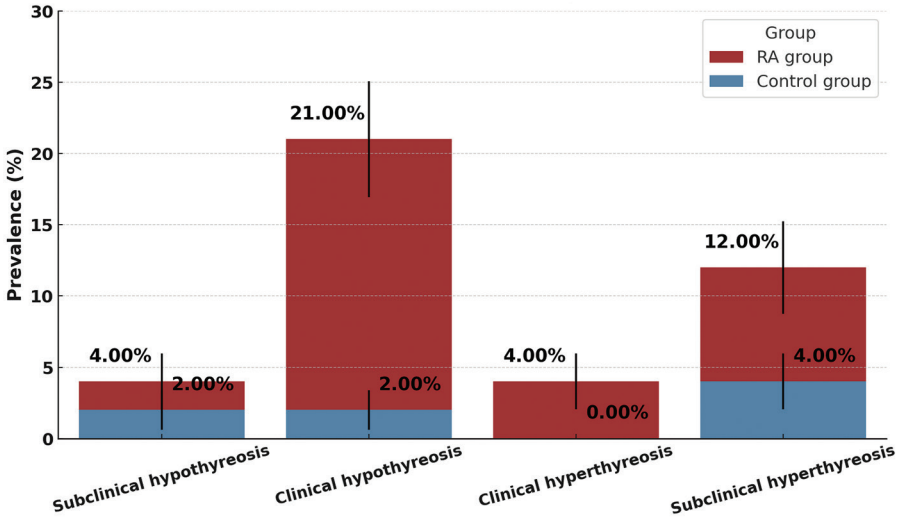

Figure 2. Prevalence of thyroid pathology in patients with RA (%).

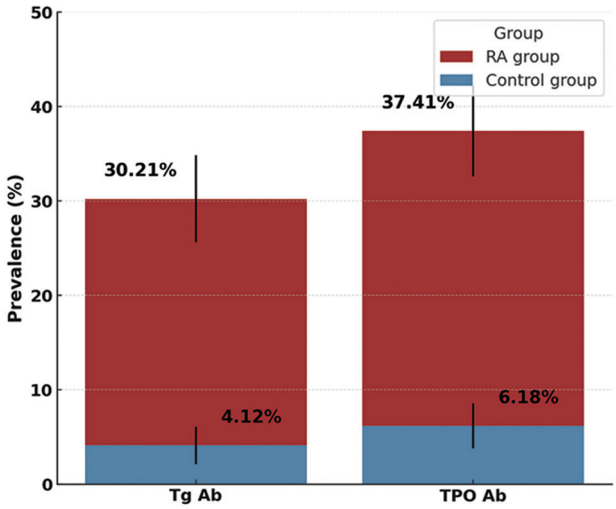

Figure 3. Frequency of thyroid gland antibodies presence in rheumatoid arthritis and control groups.

The scatterplot shows a significant positive connection between serum levels of anti-TPO and ACPA, suggesting a strong association between thyroidal immune activation and articular autoimmunity in RA **(Fig. 4)**. The linear regression line has a positive slope (coefficient β=0.8848), indicating that each unit increase in ACPA levels corresponds to a proportional rise in TPOAb titers. The Pearson correlation value (r=0.6375) reflects a reasonably strong relationship with potentially substantial therapeutic relevance.

This result highlights a potential immunological link between the etiopathogenic processes of RA and autoimmune thyroiditis, suggesting that individuals with elevated ACPA titers may be at a significantly increased risk of developing autoimmune thyroid dysfunction. Moreover, this pattern of association supports the hypothesis of a shared autoimmune basis, characterized by persistent T-helper cell activation and the stimulation of proinflammatory interleukins (IL-6, IL-17, IFN-γ), which may synergistically drive both citrullinated synovitis and autoantibody-mediated thyroid involvement. Clinically, these findings underscore the importance of comprehensive screening for thyroid dysfunction in seropositive RA patients, especially those with high ACPA titers, to enable early detection of subclinical endocrine involvement with systemic implications.

In the study group, 5 patients had low disease activity of RA (3.59%), 28 had moderate disease activity (20.14%), and 106 had high disease activity (76.25%). According to our findings, increased disease activity, as measured by DAS28-ESR, was associated with a higher proportion of patients exhibiting thyroid pathology. A positive correlation was observed between elevated disease activity and the presence of thyroid dysfunction (r=0.34) (**Fig. 5**).

Discussion

Our research reveals a significantly increased prevalence of thyroid dysfunction, including both clinical and subclinical variants, along with a higher occurrence of thyroid-specific autoantibodies in female patients with RA relative to a matched control cohort. Notably, RA disease activity, as assessed by DAS28-ESR, exhibited a positive correlation with the presence of thyroid pathology, indicating a relationship between the systemic inflammatory load of RA and the likelihood of thyroid dysfunction.

Our data show that 40.2% of patients with RA exhibited laboratory-confirmed thyroid dysfunction, compared to only 8.24% in the CG. Clinical hypothyroidism was particularly prevalent in the RA cohort (20.86% vs. 2.06%), with additional cases of subclinical hyperthyroidism and other thyroid abnormalities also identified. These findings align

Folia Medica

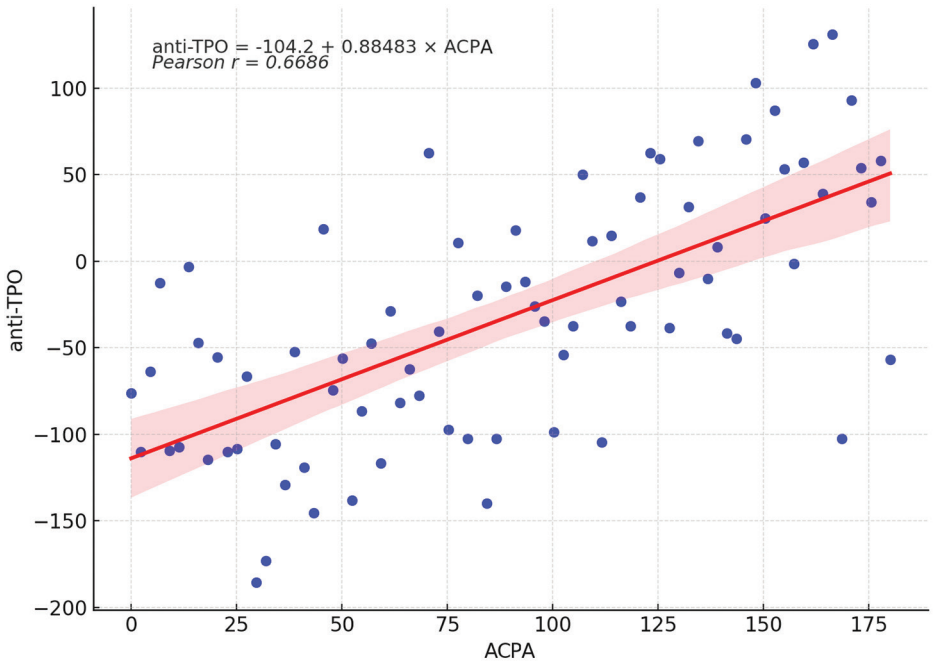

Figure 4. Relationship between serum levels of anti-thyroid peroxidase antibodies and anti-cyclic citrullinated peptide antibodies.

Table 4. Immune-inflammatory profile of the rheumatoid arthritis patients and control group

	RA group	CG
ESR, mm/h (M±SD [CI])	43.2±9.84 [5.0-52.0]	12.4±4.0 [8.0-17.0]
CRP, (N 0.5 mg/L) (M±SD [CI])	62.1±8.3 [4.0-96.0]	4.2±1.05 [0.6-3.9]
RF, n (%), (N<18 IU/ml) (M±SD [CI])	128 (92.1%), (226.75±57.9 [16.0-1020.0])	6 (6.18%), (48.0±12.0 [32-64])
ACPA, n (%), (N<17 U/ml)	71.19% (173.25±21.32)	0

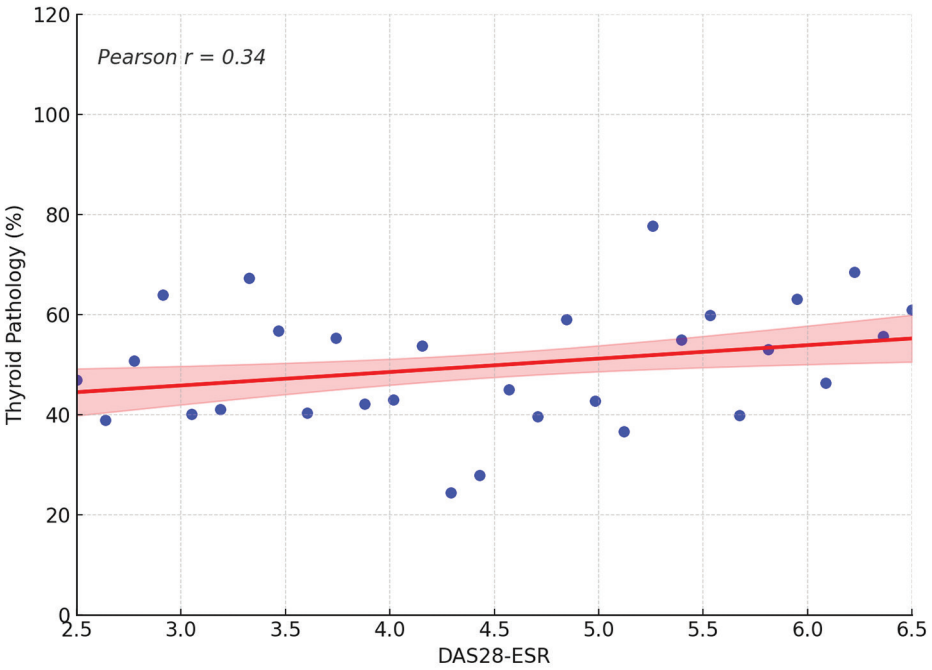

Figure 5. Correlation of DAS 28-ESR levels with the presence of thyroid gland pathology.

with previous studies reporting a higher prevalence of both clinical and subclinical hypothyroidism in individuals with RA compared to the general population.[16,17] The presence of TgAb and TPOAb in 30.5% and 37.28% of RA patients, respectively, compared to the markedly lower rates in controls (4.16% and 6.25%), further supports the autoimmune nature of this comorbidity.

These data support the hypothesis of a shared autoimmune mechanism between RA and AITD. Both conditions are characterized by dysregulated T-cell responses, sustained B-cell activation, and elevated pro-inflammatory cytokines such as IL-6 and TNF-α.[6,18-20] A significant positive correlation was observed between serum levels of ACPA and TPOAb (r=0.6375), strongly suggesting a link between articular and thyroidal autoimmunity. This association is clinically meaningful, as elevated ACPA titers are indicative of more severe joint involvement, and their correlation with thyroid autoimmunity may help identify a subset of patients at increased risk for systemic immune dysregulation.

Our findings align with the prevalence rates reported in international studies **(Table 5)**. The observed 40.2% prevalence of thyroid dysfunction in our cohort is at the upper end of reported values, which have ranged from approximately 20% to 38.5% in other populations.[19-28] Similarly, our TPOAb (37.28%) and TgAb (30.5%) positivity rates are among the highest documented, comparable only to select high-prevalence settings such as India and Turkey. Variations across studies likely reflect differences in genetic predisposition, iodine sufficiency, inclusion criteria, diagnostic methods, and our study's limitation of a female-only cohort. The consistently elevated rates of anti-thyroid antibodies across cohorts, including the studied cohort, reinforce the concept of shared autoimmune mechanisms linking RA and AITD. These findings support routine screening for thyroid dysfunction and antibodies in RA patients, particularly in high-risk populations, to facilitate early detection, integrated management, and prevention of endocrine complications that may exacerbate systemic inflammation and disease burden.

Clinically, the patients with RA in our study reported significantly more symptoms consistent with hypothyroidism, including cold intolerance (97.84%), hair loss (80.58%), dry skin (70.5%), and fatigue (75.54%) compared to controls, even after accounting for subjective reporting. Although these symptoms may overlap with constitutional features of RA, their significantly higher prevalence among RA patients (all p<0.001) suggests an under-recognized burden of thyroid dysfunction in this population. These findings emphasize the importance of routine screening for both thyroid hormone levels and thyroid-specific autoantibodies, as subclinical dysfunction and preclinical autoimmunity can progress to overt disease over time.

Our study revealed a moderate positive correlation (r=0.34) between RA disease activity, as measured by DAS28-ESR, and the presence of thyroid pathology. This finding suggests that systemic inflammation may exac-

Table 5. Comparison of prevalence of thyroid dysfunction and thyroid autoantibodies in rheumatoid arthritis patients across studies

Study	Country/Setting	Sample size (RA)	Thyroid dysfunction (%)	Clinical hypothyroidism (%)	TPOAb positivity (%)	TgAb Positivity (%)
Current study (2025)	M., University clinic	139 (female)	40.2%	20.86%	37.28%	30.5%
Atzeni et al. (2008)[21]	Italy, Outpatient clinic	186 (mixed)	25.3%	9.7%	37.1%	22.9%
Cárdenas Roldán et al. (2012)[22]	Colombia, Cross-sectional	800 (mixed)	35%	12.4%	34.3%	25.6%
Boelaert et al. (2010)[19]	UK, Population-based	N/A (AITD focus)	N/A	N/A	30–40% (AITD patients)	20–30% (AITD patients)
Li et al. (2024)[23]	China, Cross-sectional	402 (mixed)	29.8%	11.2%	36.4%	23.9%
Mahagna et al. (2018)[24]	Israel, Registry-based	3,686 (registry)	22.4%	~10–12%	~30–35% (review)	~20–25% (review)
Anoop et al. (2018)[25]	India, Tertiary care	122 (mixed)	38.5%	22.1%	41.8%	26.2%
Yavaşoğlu et al. (2009)[26]	Turkey, Outpatient	62 (mixed)	N/A	N/A	43.5%	32.2%
Shiroky et al. (1993)[27]	Canada, Prospective	106 (mixed)	19.8%	12.3%	~35% (literature)	~20–25% (literature)
Silman et al. (1989)[28]	UK, Family study	66 (mixed)	N/A	N/A	34.8%	27.3%

Folia Medica

erbate thyroid dysfunction, or, alternatively, that uncontrolled thyroid disease may contribute to sustained inflammatory activity in RA. The underlying mechanism may involve shared pro-inflammatory cytokine networks and prolonged activation of autoreactive Th cell subsets, such as Th1 and Th17, which are implicated in both synovial and thyroidal inflammation.[6,18,19]

These findings reinforce the systemic nature of RA as a multiorgan autoimmune disease with significant endocrine comorbidities. Recognition of this association has important clinical implications for rheumatologic care. Early detection and management of thyroid dysfunction in RA patients may improve overall disease control, reduce extra-articular morbidity, and enhance quality of life. Furthermore, our results underscore the need for a multidisciplinary approach, incorporating routine endocrinological evaluation into standard RA management protocols.

Conclusion

Our study demonstrates that thyroid dysfunction, particularly of autoimmune origin, is a frequent and clinically significant comorbidity in female patients with RA. We observed a markedly higher prevalence of both clinical and subclinical thyroid dysfunction, as well as significantly elevated rates of thyroid-specific autoantibodies in comparison to healthy controls. A strong positive correlation between ACPA and TPOAb further supports the hypothesis of shared autoimmune mechanisms linking articular and thyroidal autoimmunity in RA.

These findings underscore the systemic nature of RA as a multiorgan autoimmune disease and highlight the need for comprehensive management strategies that incorporate routine assessment of thyroid function and autoantibody screening, particularly in patients with high disease activity or ACPA seropositivity. Early identification and appropriate treatment of thyroid dysfunction may reduce endocrine-related morbidity, improve overall disease control, and enhance quality of life in this patient population.

Given the observed associations and high prevalence rates in our cohort, we recommend integrating systematic thyroid evaluation into standard rheumatological practice, supported by multidisciplinary collaboration between rheumatologists and endocrinologists. Further longitudinal research is warranted to elucidate causal relationships, evaluate the impact of thyroid disease management on RA outcomes, and establish evidence-based screening protocols.

Limitations of the study

Our study has several limitations that should be taken into account. First, although the sample was carefully selected and matched, it included only female patients, which limits the generalizability of the findings to male populations. Second, the cross-sectional design, while supplemented by prospective elements, does not allow for definitive conclusions regarding causality. Third, while we assessed thyroid function using TSH and free T4 (fT4) levels, additional diagnostic methods such as dynamic testing or thyroid imaging were not employed, limiting the characterization of thyroid pathology. Another limitation is that only patients on methotrexate monotherapy were included. This design improves cohort homogeneity but limits generalizability, as patients receiving biologics or combination DMARDs may exhibit different thyroid outcomes. Future studies including more heterogeneous treatment groups are warranted to better define these associations. Lastly, environmental influences, such as iodine intake, which may affect the prevalence of AITD, were not formally controlled in our cohort.

Despite these limitations, our findings contribute significantly to the growing body of evidence indicating that thyroid dysfunction, particularly of autoimmune origin, is a frequent and clinically significant comorbidity in patients with RA. Our data support the integration of systematic screening protocols for thyroid function and thyroid-specific autoantibodies into routine RA care, especially in patients with high disease activity or ACPA seropositivity. Such measures may facilitate earlier diagnosis, reduce endocrine-related morbidity, and enhance comprehensive disease management in RA.

Funding

The authors have no funding to report.

Competing interests

The authors have declared that no competing interests exist.

Acknowledgements

The authors have no support to report.

References

1. Aletaha D, Neogi T, Silman AJ, et al. 2010 Rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis and Rheumatism 2010; 62(9):2569–81.
2. Figus FA, Piga M, Azzolin I, et al. Rheumatoid arthritis: extra-articular manifestations and comorbidities. Autoimmun Rev 2021; 20(4):102776.
3. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. The Lancet 2016; 388(10055):2023–38.
4. Van Der Woude D, Van Der Helm-van Mil AHM. Update on the epidemiology, risk factors, and disease outcomes of rheumatoid arthritis.

Best Pract Res Clin Rheumatol 2018; 32(2):174–87.
5. Gulati M, Farah Z, Mouyis M. Clinical features of rheumatoid arthritis. Medicine 2018; 46(4):211–5.
6. McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. N Engl J Med 2011; 365(23):2205–19.
7. Prete M, Racanelli V, Digiglio L, et al. Extra-articular manifestations of rheumatoid arthritis: An update. Autoimmun Rev 2011; 11(2):123–31.
8. Cutolo M, Kitas GD, Van Riel PLCM. Burden of disease in treated rheumatoid arthritis patients: Going beyond the joint. Semin Arthritis Rheum 2014; 43(4):479–88.
9. Waldenlind K, Saevarsdottir S, Bengtsson C, et al. Risk of thyroxine-treated autoimmune thyroid disease associated with disease onset in patients with rheumatoid arthritis. JAMA Netw Open 2018; 1(6):e183567.
10. Ferrari SM, Fallahi P, Ruffilli I, et al. The association of other autoimmune diseases in patients with Graves' disease (with or without ophthalmopathy): Review of the literature and report of a large series. Autoimmun Rev 2019; 18(3):287–92.
11. McLeod DSA, Cooper DS. The incidence and prevalence of thyroid autoimmunity. Endocrine 2012; 42(2):252–65.
12. Lichtiger A, Fadaei G, Tagoe CE. Autoimmune thyroid disease and rheumatoid arthritis: where the twain meet. Clin Rheumatol 2024; 43(3):895–905.
13. Joshi P, Agarwal A, Vyas S, et al. Prevalence of hypothyroidism in rheumatoid arthritis and its correlation with disease activity. Trop Doct 2017; 47(1):6–10.
14. Prevoo MLL, Van't Hof MA, Kuper HH, et al. Modified disease activity scores that include twenty-eight-joint counts development and validation in a prospective longitudinal study of patients with rheumatoid arthritis: modified disease activity score. Arthritis Rheum 1995; 38(1):44–8.
15. Steinbrocker O. Therapeutic criteria in rheumatoid arthritis. JAMA 1949; 140(8):659.
16. Nazary K, Hussain N, Ojo RO, et al. Prevalence of thyroid dysfunction in newly diagnosed rheumatoid arthritis patients. Cureus [Internet] 2021 Sep 23 [cited 2025 Jul 12]; Available from: https://www.cureus.com/articles/71279-prevalence-of-thyroid-dysfunction-in-newly-diagnosed-rheumatoid-arthritis-patients
17. Liu YJ, Miao HB, Lin S, et al. Association between rheumatoid arthritis and thyroid dysfunction: A meta-analysis and systematic review. Front Endocrinol 2022; 13:1015516. Available from: https://www.frontiersin.org/articles/10.3389/fendo.2022.1015516/full
18. Choy EHS, Panayi GS. Cytokine Pathways and joint inflammation in rheumatoid arthritis. Epstein FH, editor. N Engl J Med 2001; 344(12):907–16.
19. Boelaert K, Newby PR, Simmonds MJ, et al. Prevalence and relative risk of other autoimmune diseases in subjects with autoimmune thyroid disease. Am J Med 2010; 123(2):183.e1–183.e9.
20. Frunze V, Deseatnicova E. [Thyroid gland pathology in rheumatoid arthritis]. Revista de Ştiinţe ale Sănătăţii din Moldova. 2021; 1(26):91–9. [Rumanian]
21. Atzeni F, Atzeni F, Doria A, et al. Anti-thyroid antibodies and thyroid dysfunction in rheumatoid arthritis: Prevalence and clinical value. Autoimmunity 2008; 41(1):111–5.
22. Cárdenas Roldán J, Amaya-Amaya J, Castellanos-de La Hoz J, et al. Autoimmune thyroid disease in rheumatoid arthritis: a global perspective. Arthritis 2012; 2012:1–15.
23. Li L, Jiao F, Zhao J, et al. Risk factors of thyroid dysfunction in patients with rheumatoid arthritis. Cent Eur J Immunol 2024;49(2):126–31.
24. Mahagna H, Caplan A, Watad A, et al. Rheumatoid arthritis and thyroid dysfunction: A cross-sectional study and a review of the literature. Best Pract Res Clin Rheumatol 2018; 32(5):683–91.
25. Anoop J, Geetha F, Jyothi I, et al. Unravelling thyroid dysfunction in rheumatoid arthritis: History matters. Int J Rheum Dis 2018; 21(3):688–92.
26. Yavasoglu I, Senturk T, Coskun A, et al. Rheumatoid arthritis and anti-thyroid antibodies. Autoimmunity 2009; 42(2):168–9.
27. Shiroky JB, Cohen M, Ballachey ML, et al. Thyroid dysfunction in rheumatoid arthritis: a controlled prospective survey. Ann Rheum Dis 1993; 52(6):454–6.
28. Silman AJ, Ollier WER, Bubel MA. Autoimmune thyroid disease and thyroid autoantibodies in rheumatoid arthritis patients and their families. Rheumatology 1989; 28(1):18–21.