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Original article

Hypothyroidism and rheumatoid arthritis: a cross-sectional study.

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Abstract

Background: Autoimmune diseases may cluster in a single patient. A higher prevalence of hypothyroidism in Rheumatoid arthritis (RA) patients has been noted. **Objective:** To study the

prevalence of hypothyroidism in a Brazilian cohort of RA patients and its possible association with disease activity indexes. **Methods:** Cross sectional study in 176 RA patients for the prevalence of hypothyroidism diagnosis, data on RA (epidemiological variables, comorbidities, disease activity indexes and treatment). RA patients with and without hypothyroidism were compared. **Results:** The prevalence of hypothyroidism in this cohort was 43.2%. Patients with thyroid dysfunction were older (63.5 vs. 58.4 years; p=0.001), had later RA diagnosis (49.4 vs. 43.8 years; p=0.003), and had higher type 2 diabetes prevalence (27.6% vs. 14%; p=0.02). No differences were observed in presence of rheumatoid factor and disease activity indexes (all with p>0.05). However, prednisone requirement was lower in the group with hypothyroidism (21% vs. 42%; p=0.003).

Conclusions: Hypothyroidism is prevalent in RA patients, and associated with advanced age and diabetes, without direct impact on RA inflammatory activity but with reduced corticosteroid requirement.

Keywords: Rheumatoid arthritis. Hypothyroidism. Prevalence.

Resumo

Justificativa: Doenças autoimunes podem se agrupar em um único paciente. Uma maior prevalência de hipotireoidismo em pacientes com artrite reumatoide (AR) foi observada. **Objetivo:** Estudar a prevalência de hipotireoidismo em uma coorte brasileira de pacientes com AR e sua possível associação com índices de atividade da doença. **Métodos**: Estudo transversal com 176 pacientes com AR para avaliar a prevalência de diagnóstico de hipotireoidismo, coletando dados sobre AR (variáveis epidemiológicas, comorbidades, índices de atividade da doença e tratamento). Pacientes com AR com e sem hipotireoidismo foram comparados. **Resultados**: A prevalência de hipotireoidismo nesta coorte foi de 43,2%. Pacientes com disfunção da tireoide eram mais velhos (63,5 vs. 58,4 anos; p=0,001), tinham diagnóstico de AR mais tardio (49,4 vs. 43,8 anos; p=0,003) e maior prevalência de diabetes tipo 2 (27,6% vs. 14%; p=0,02). Nenhuma diferença foi observada quanto à presença do fator reumatoide e índices de atividade da doença (todos com p>0,05). No entanto, o uso de prednisona foi menor neste grupo (21% vs. 42%; p= =0,003). **Conclusões:** O hipotireoidismo é bastante prevalente em pacientes com AR, e está associado à idade avançada e ao diabetes, sem impacto direto na atividade inflamatória da AR, mas com redução na necessidade de corticosteroides.

Palavras-chave: Artrite reuamtoide. Hipotireoidismo. Prevalência.

Introduction:

In recent years, there has been a notable rise in autoimmune diseases, conditions in which the immune system fails to distinguish between self and non-self, leading to immune-mediated attacks on the body's own cells [1]. This increase is attributed to multiple factors, including genetics, ambiental exposures and dietary quality. Among autoimmune diseases, rheumatoid arthritis (RA) stands out as a chronic, progressive, non-communicable inflammatory disorder that primarily affects the synovial membrane of peripheral joints, often resulting in cartilage and bone destruction and impaired mobility [2].

Autoimmune diseases frequently coexist, complicating diagnosis and management due to overlapping symptoms. In RA, there is a recognized association with autoimmune hypothyroidism, particularly Hashimoto's thyroiditis, characterized by anti-thyroid peroxidase (anti-TPO) antibodies [3,4]. Both conditions share symptoms such as fatigue and joint pain, which can obscure diagnostic interpretation.

Several studies have investigated this relationship. Mendelian randomization analyses and meta-analyses indicate a bidirectional genetic and causal link between RA and hypothyroidism: the presence of one increases the likelihood of developing the other [5]. Therefore, clinicians should perform screening tests for thyroid dysfunction in RA patients and vice versa. Early detection is crucial, as untreated hypothyroidism may mimic or exacerbate RA symptoms, influencing disease activity scores and management accuracy.

Herein, a study to assess the prevalence of hypothyroidism in patients with rheumatoid arthritis and evaluate its relationship with disease activity and seropositivity was done.

Methods:

The present study was approved by the Ethics Committee of the Mackenzie Evangelical Faculty of Paraná under protocol number 6.874.637, in accordance with national ethical guidelines. All participants provided written informed consent. This investigation was designed as a cross-sectional, analytical, and descriptive study, based on the systematic review of 176 medical

records and laboratory reports from patients followed at the Rheumatology Outpatient Clinic of the Mackenzie Evangelical University Hospital in Curitiba, Paraná.

Data Collection: Data collected from medical records included demographic variables (age, sex, race, and years of formal education), comorbidities, current medications, and clinical information related to RA —such as disease duration, presence of rheumatoid factor, radiographic erosions, age at diagnosis, and disease activity indices (DAS28-ESR, DAS28-CRP, SDAI, and CDAI). In addition, the presence of thyroid disorders and laboratory parameters (TSH and T4 levels) were recorded.

The Disease Activity Score 28 (DAS28) evaluates the number of tender and swollen joints (out of 28 predefined joints), the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and the patient's global health assessment using a visual analog scale (VAS). DAS28 values <2.6 indicate remission; <3.2, low disease activity; <5.1, moderate activity; and >5.1, high disease activity [6].

The Clinical Disease Activity Index (CDAI) is a fully clinical tool that does not require laboratory tests, facilitating its use in real-time evaluations. It is obtained by summing the tender and swollen joint counts and both patient and physician assessments (each on a 0–10 cm VAS). Scores ≤2.8 indicate remission, 2.9–10 low activity, 10.1–22 moderate activity, and >22 high disease activity [6].

Similarly, the Simplified Disease Activity Index (SDAI) incorporates the same parameters as the CDAI, with the addition of CRP (mg/dL) as an inflammatory marker. SDAI values ≤3.3 indicate remission, 3.4–11 low activity, 11.1–26 moderate activity, and >26 high disease activity [6].

After data collection, patients were stratified into two groups—those with and without hypothyroidism—for comparative analysis.

Inclusion criteria: Male and female patients aged over 18 years, regularly followed at the Rheumatology Outpatient Clinic of the Mackenzie Evangelical University Hospital, with a diagnosis of RA according to the 2010 ACR/EULAR classification criteria [7] and complete medical records for data extraction.

Exclusion criteria: Patients with other concomitant inflammatory diseases were excluded.

Data analysis: All data were entered into an Excel® spreadsheet. The prevalence of hypothyroidism was expressed as a percentage. Comparisons between groups (with and without hypothyroidism) were performed using Fisher's exact or chi-square tests for

categorical variables and unpaired t-test or Mann–Whitney test for continuous variables. A significance level of 5% was adopted for all analyses.

Results:

About 176 RA patients were studied. The description of studied sample is at **table 1** that shows that most of included individuals were Caucasian female with seropositive RA.

Table 1- Description of studied sample

Female sex (n)		159/176 (90.3%)
Ethnic background (n)	Euro descendente	145/176 (82.3%)
	Afro descendente	28/176 (15.9%)
	Others	3/176 (1.7%)
Years of formal study -median (IQR)		10.0 (4.0 - 10.0)
Age – Median (IQR) years		62.0 (54.0-68.0)
Age at diagnosis – Median (IQR) – years		46.0 (37.0-76.0)
Disease duration- Median (IQR) – years		13.0 (8.0-19.0)
Presence of rheumatoid fator (n)		125/175 (71.0%)
X Ray erosions – n		80/146 (54.7%)
DAS 28 ESR – Median (IQR)		2.74 (2.28 a 3.70)
DAS 28 CRP – Median (IQR)		1.99 (1.54 a 2.85)
SDAI – Median (IQR)		4.20 (0.80 a 9.30)
CDAI – Median (IQR)		3.0 (0-8.80)
Comorbidities (n)	Hypertension	103/176 (58.5%)
	Diabetes	35/176 (19.8%)
	Osteoporosis	42/176 (23.8%)
	Dyslipidemia	99/176 (56.2%)
Treatment	Methotrexate	74/176 (42.0%)
	Leflunomide	87/176 (49.4%)
	Prednisone	58 /176 (32.9%)
	Anti TNF alpha	35/176 (19.8%)
	Anti-IL6	15/176 (8.5%)
	Jak Inhibitors	32/176 (18.1%)

DAS= Disease activity score; ESR= erythrocyte sedimentation rate; CRP= C reactive protein, SDAI= simplified disease activity index; CDAI= clinical disease activity index; IL= interleukin; n= number; IQR= interquartile range.

In this sample 76/176 (43.1%) had hypothyroidism of whom 63 (35.7%) used hormonal reposition.

The comparison of RA patients with and without hypothyroidism showed the results on **Table 2.** Age and age at diagnosis as well as prevalence of type 2 DM were lower in those without

hypothyroidism. The treatment requirement was similar in both groups but for prednisone use more commonly seen in those without hypothyroidism.

Table 2. Comparison of RA characteristics in patients with and without hypothyroidism.

	With hypothyroidism	Without hypothyroidism	p
Number	76	100	
Female sex (n)	71/76 (93.4%)	88/100 (88%)	0.22
Eurodescendants (n)	66/75 (88%)	79/98 (80.6%)	0.19
Mean Age – years (SD)	63.5±8.48	58.4±11.03	**0.001**
Median disease duration – years (IQR)	12.0 (8.0-18.0)	13.0 (8.5 - 19.0)	0.62
Mean age at diagnosis (SD)	49.4±12.6	43.8±12.4 (49.4%)	**0.003**
Positive rheumatoid fator (n)	53/76 (69.7%)	72/99 (72.7%)	0.664
X Ray erosions (n)	37/69 (53.6%)	43/87 (49.4%)	0.602
Comorbidities (n)			
hypertension	42/76 (55.2%)	61/100 (61.0%)	0.44
diabetes	21/76 (27.6%)	14/100 (14.0%)	**0.02**
osteoporosis	19/76 (25%)	22/100 (22.0%)	0.64
dyslipidemia	47/76 (83.9%)	52/100 (52.0%)	0.19
Disease activity indexes			
DAS VHS	3.05±1.18	2.95±1.10	0.74
DAS PCR	2.33±1.26	2.39±1.04	0.28
CDAI	6.69±9.92	6.75±7.41	0.38
SDAI	5.71±8.73	6.23±7.34	0.17
Treatment			
Methotrexate	34/76 (44.7%)	40/100 (40.0%)	0.52
Leflunomide	38/76 (50.0%)	49/100 (49.0%)	0.89
Prednisone	16/76 (21.0%)	42/100 (42.0%)	**0.003**
Anti TNF alpha	16/76 (21.0%)	19/100 (19.0%)	0.70
Anti IL-6	3/76 (3.9%)	12/100 (12.0%)	0.09
Jak inhibitors.	13/76 (17.1%)	19/100 (19.0%)	0.74

DAS= Disease activity score; ESR= erythrocyte sedimentation rate; CRP= C reactive protein, SDAI= simplified disease activity index; CDAI= clinical disease activity index; IL= interleukin; n= number; IQR= interquartile range.

The comparison of disease activity indexes in patients with hypothyroidism using e not using hormonal replacement showed no statistical differences (all with p>0.05).

Discussion:

This cross-sectional study examined the prevalence of hypothyroidism among patients with RA and its association with inflammatory activity parameters, based on data from 176 individuals treated at a single rheumatology outpatient clinic. The findings align with trends reported in the literature. The prevalence of hypothyroidism in this cohort was 43.2% (76/176), markedly

higher than the average rates observed in the general population (0.3–5.3%)[7,8,9] . Liu et al.'s meta-analysis [3] had already indicated an increased incidence of hypothyroidism in RA patients (OR: 2.24), attributed to shared genetic mechanisms (e.g., HLA gene polymorphisms) and systemic immune dysregulation. The elevated prevalence observed in this study supports the recommendation for routine thyroid screening in RA patients.

Notably, individuals with hypothyroidism were older (63.5 vs. 58.4 years), reinforcing the influence of demographic factors on comorbidity. Interestingly, the age at RA diagnosis was also higher in the hypothyroid group (49.4 vs. 43.8 years), suggesting that thyroid dysfunction may emerge as a late comorbidity in the natural course of RA. No significant differences were found in disease activity indices (DAS-ESR, DAS-CRP, SDAI, CDAI) between patients with and without hypothyroidism. This finding contradicts the initial hypothesis that hypothyroid symptoms (e.g., arthralgia, fatigue) might lead to an overestimation of disease activity. However, it is interesting to note that most hypothyroid patients (63/76) were receiving hormone replacement therapy, thereby mitigating systemic effects. Nevertheless, despite the absence of marked changes in inflammatory markers, patients without hypothyroidism required higher doses of corticosteroids to manage underlying RA. This may suggest that disease activity indices were elevated on this group, but the result was masked by increased glucocorticoid use.

Additionally, the study revealed a higher prevalence of type 2 diabetes mellitus among hypothyroid patients (21/76 vs. 14/100), consistent with the role of insulin resistance in the pathophysiology of both conditions. A study by Baruah et al. showed that HbA1c in diabetic patients correlated negatively with total T3 and total T4.

Limitations of this study include selection bias due to its single-center design and the absence of anti-TPO testing, which precluded specific analysis of Hashimoto's thyroiditis. Nonetheless, the findings reinforce existing evidence of an increased risk of hypothyroidism in RA patients.

Conclusions:

This study confirms a significantly higher prevalence of hypothyroidism among patients with rheumatoid arthritis compared to the general population. It also highlights associations with older age, later onset of RA, and increased prevalence of type 2 diabetes mellitus. The presence of rheumatoid factor did not influence hypothyroidism prevalence.

Although hypothyroidism did not alter RA inflammatory indices, affected patients required greater corticosteroid use, suggesting a potential underlying impact on disease activity that warrants further investigation.

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