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Frequency of Thyroid Disorders in Rheumatoid Arthritis Patients and its Association with Disease Activity: A Hospital Based Study

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ABSTRACT

Objective: To establish the frequency of thyroid disorders among Rheumatoid Arthritis patients and its association with disease severity measured by DAS28-ESR.

Study Design: Prospective longitudinal study.

Place and Duration of Study: Department of Rheumatology, Federal Government Policlinic Hospital, Islamabad Pakistan, from Jan to Jun 2021.

Methodology: The study included 87 consecutive patients either gender with Rheumatoid Arthritis visiting Rheumatology OPD. Thyroid profile and DAS28-ESR were performed in all the patients.

Results: Out of 87 patients, 73(83.9%) were females, and 14(16.1%) were males. The mean age was 45.54±13.50 years. The mean DAS28-ESR was 4.45±0.68, with a minimum DAS28-ESR of 1.25 and a maximum of 8.40. The Disease severity calculated by DAS28-ESR was mild in 19(21.8%), moderate in 44(50.6%) and severe in 24(27.6 %) patients. The thyroid gland was abnormal in 23(26.1%) patients. 18(78.2%) of 23 patients with thyroid disorders belonged to the moderate to severe Rheumatoid arthritis disease activity group.

Conclusion: Thyroid disorders are very common in Rheumatoid Arthritis patients. Thyroid workup should be part of investigations of Rheumatoid Arthritis for early detection of thyroid disorder and better disease control.

Keywords: DAS28-ESR, Rheumatoid arthritis, Thyroid antibodies.

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INTRODUCTION

Rheumatoid arthritis is a chronic inflammatory disease of autoimmune origin. The reported prevalence of Rheumatoid arthritis varies from 0.5%-1% in the community.[1] The pathogenesis of Rheumatoid Arthritis is still not clearly understood.[2] The prevalence of thyroid disorder has been reported in 6%-34% of patients with Rheumatoid Arthritis.[3] The rise in thyroid antibodies is reported to be about 38% despite normal thyroid function.[4] This shows that subclinical thyroid abnormalities are higher in Rheumatoid arthritis patients. The thyroid disorder can be hypothyroid, hyperthyroid or simple goitre.[5]

There is evidence of an association between thyroid disorder and Rheumatoid Arthritis, but the study results are inconclusive.[6] This could be because these clinical trials stressed the clinical aspect of thyroid disorder, and they did not consider the disease severity of Rheumatoid Arthritis and its impact on thyroid disorder and the treatment response of Rheumatoid Arthritis on thyroid disorder.[7] A previous study concluded a relation between higher Rheumatoid Arthritis severity and hypothyroidism.[8] The frequency of thyroid disorders is increased in Rheumatoid Arthritis; as a result, thyroid disorder increases the co-morbidity in these patients. Therefore, this makes thyroid disorders the prevalent extra-articular disease in Rheumatoid Arthritis.[9] No such study was performed in our local set-up, so our study was designed to establish the frequency of thyroid disorders in Rheumatoid Arthritis patients in our local scenario and to establish the association of thyroid disorders with disease severity measured by DAS28-ESR. In addition, it will help us develop our local guidelines for performing thyroid investigations in our Rheumatoid arthritis patients and managing thyroid disorders in rheumatoid arthritis patients to decrease morbidity.

METHODOLOGY

The prospective longitudinal study was conducted at the Department of Rheumatology, Federal Government Polyclinic Hospital, Islamabad Pakistan, from January to June 2021. Prior Ethical

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Committee permission was taken (letter No: FGPC.1/12/2021-Ethical Committee). The WHO calculator was used for sample size estimation, taking the population proportion of Rheumatoid Arthritis patients at 6 %.[8]

Inclusion Criteria: Patients of either gender, aged 19 to 70 years, presenting in the Outpatient Department with Rheumatoid Arthritis, were included in the study. Rheumatoid Arthritis patients with Diabetic and Hypertensive patients were also included in the study.

Exclusion Criteria: Patients with Juvenile Rheumatoid Arthritis, Pregnant females, Rheumatoid Arthritis patients taking Amiodarone for cardiac issues and patients with known allergies to Disease-modifying agents were excluded from the study

All patients were informed about the purpose of the study, the procedure for gathering data and the possible advantages of this research work. The confidentially and anonymity of patients and their responses were maintained during the study. Baseline characteristics regarding gender, age, education, and disease duration were recorded. Patients with comorbid conditions or other chronic diseases were also included in the study as these conditions were unlikely to affect the outcome of the disease, so these were not mentioned in the study as separate variables.

DAS28-ESR measures disease activity using the number of tender joints out of 28, the number of swollen joints out of 28, global assessment of health and ESR.[9] These results were fed into a mathematical formula to produce the overall disease activity score. A DAS28-ESR of greater than 5.1 implies active disease with high severity, and between 5.1-3.2 implies moderate severity, less than 3.2 low disease activity, and less than 2.6 remissions.[10] DAS28-ESR was calculated at the time of inclusion in the study. To assess the frequency of thyroid disorders in Rheumatoid Arthritis patients, thyroid profile (T3, T4 & TSH) was advised to all Rheumatoid Arthritis patients and autoimmune thyroid antibodies, including TSHR antibodies and Anti-TPO antibodies, were performed in all patients. In addition, the patient's treatment with DMARD and steroids and the treatment duration were also recorded. A structured proforma was used to enter the collected data.

Data were analysed by using Statistical Package for Social Sciences (SPSS) version 21:00. Descriptive statistics were applied for categorical data. In addition, Mean±SD were measured from continuous numerical variables. The Chi-square test was used for inferential statistics. The *p*-value of ≤0.05 was set as the cut-off value for significance.

RESULT

The study included a total of 87 patients with Rheumatoid Arthritis. Of 87 patients, 73(83.9%) were females, and 14(16.1%) were males. The Mean age was 45.54±13.5 years (Table-I).

Table-I: Patients Demographic (n=87)

Characteristic	Frequency(%)
Gender	
Male	14(16.1%)
Females	73(83.9%)
Marital Status	
Married	84(96.6%)
Unmarried	3(3.4%)
Literacy	
Literate	68(78.2%)
Illiterate	19(21.8)
Duration of Disease	
Newly Diagnosed	
1 year	4(4.6%)
<1 Year	13(14.9%)
1-5 Years	36(41.4%)
6-10 Years	21(24.1%)
11-15 years	4(4.6%)
16-20 Years	5(5.7%)
>10 Years	4(4.6%)
Treatment	
Steroids	63(72.4%)
DMARDS	46(97.7%)

About 85(97.7%) patients were on DMARD. 44(50.6%) patients were on single DMARD, and 41(47.1%) were on multiple DMARD. 63(72.4%) were on steroids, while 24(27.6%) were not taking any steroids. 59(67.81%) patients were already on treatment. The Mean DAS28-ESR score was 4.45±0.68. The Disease severity calculated by the DAS28-ESR score was mild in 19(21.8%), moderate in 44(50.6%) and severe in 24(27.6 %) of the patients (Table-II).

Table-II: Disease Severity (n=87)

Severity	n(%)
Mild--DAS28-ESR score <3.2	19(21.8%)
Moderate--DAS28-ESR score 3.2-5-1	44(50.6%)
Severe--DAS28-ESR score >5.1	24(27.6%)
Total	87(100%)

Thyroid antibodies were positive in 29(33.3%), Thyroglobulin antibodies in 22(25.3%), Thyroid peroxidase antibodies in 16(18.4%) and thyrotropin receptor antibodies in 11(12.6%). Thyroid Disorders were present in 23 (26.1%) of the patients. Hyperthyroidism was in 6(6.8%) and, hypothyroidism was in

15(17%) patients, and simple goitre was present in 2(2.3%) patients. It was found that 18(78.2%) out of 23(26.5%) patients with thyroid disorders belonged to the moderate to severe Rheumatoid arthritis disease group (Table-III).

Table-III: Thyroid Disorder and association with Disease Severity (n=87)

Thyroid Disorder	Disease Severity		*p*-value
	Mild (n=87)	Moderate to Severe (n=87)	
Present	2(2.27%)	21(24.13%)	0.001
Not Present	17(19.54%)	47(54.02%)	0.68

DISCUSSION

Rheumatoid Arthritis is a disease of joints that gradually destroys the joint's articular surfaces.[11] It is a long-standing disease which causes pain, swelling, deformity and limitation of the movements of the joints.[12] Rheumatoid Arthritis is not limited to the joints, and it is known to involve the extra-articular tissues.[13] Disorder of the thyroid glands is very common with Rheumatoid Arthritis. The reported incidence is from 6-30% with Rheumatoid Arthritis.[14] The thyroid disorder may mimic autoimmune thyroiditis. Sometimes these patients may need replacement therapy for hypothyroidism or antithyroid drugs to control hyperthyroidism.[15]

A previous study conducted by Emamifar *et al.* showed that there is a correlation between Rheumatoid Arthritis severity which is measured by DAS 28 score, and thyroid disorders in Rheumatoid Arthritis.[3] It was further stated that an initial higher DAS 28 score at the time of diagnosis of Rheumatoid Arthritis is associated with a higher incidence of thyroid disorder. Pan *et al.* conducted a meta-analysis and showed that thyroid disorder in Rheumatoid Arthritis patients further influences the disease effect of Rheumatoid Arthritis.[6] The Disease-modifying drugs are the treatment of choice to control or slow the progression of disease in Rheumatoid Arthritis patients.[16] Disease-modifying agent decreases the production of the autoantibodies and immune complex. These agents slow the progression of the disease or control not only the articular cartilage but the extra-articular tissues as well.[17] As a result, good initial treatment and response to the treatment are associated with less thyroid involvement in Rheumatoid Arthritis. This may result in a decrease in the use of the medications for thyroid disorders, or this medicine may not be needed for thyroid disorders.[18]

Our result showed that there was thyroid disorder present in 26.1% of Rheumatoid Arthritis patients. Our results are in accordance with a previous study, which reported that 25.5% of the Rheumatoid Arthritis patients had thyroid abnormalities.[19]

In our study, 17% of Rheumatoid Arthritis patients had hypothyroidism, 6.8% had hyperthyroidism, and 2.3% had a simple goitre. Li *et al.* analysed subgroups and showed a positive correlation between Rheumatoid Arthritis with hypothyroidism (OR=2.28, p=0.006) and hyperthyroidism (OR=8.95, p<0.001). We found that 18(78.2%) out of 23 patients with thyroid disorder belonged to the moderate and severe Rheumatoid arthritis disease group.[5]

There we ascertain that thyroid abnormality is very common in patients with Rheumatoid arthritis, and its involvement increases with the severity of the disease. Therefore, the quality of life of Rheumatoid Arthritis patients with moderate to severe disease is already very disturbed, and thyroid problem further adds to the health problem of such patients. Being autoimmune, we recommend testing for thyroid abnormalities in all Rheumatoid Arthritis patients for early detection and appropriate treatment.[20] Similarly, thyroid antibodies should also be frequently checked and monitored, which may indicate underlying subclinical thyroid disorders. We suggest a multicentre randomised control trial on this topic so that our guidelines can be made.

CONCLUSION

Thyroid disorders are very common in Rheumatoid Arthritis patients and increase the co-morbidity in Rheumatoid Arthritis patients. Therefore, we suggest testing for thyroid disorders in all patients with Rheumatoid Arthritis for early detection and initiation of treatment for better disease control.

Conflict of Interest: None

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

SHQ & SFS: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

TK & SHQ: Data interpretation, critical review, approval of the final version to be published.

AHQ & SHS: Study design, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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