ORIGINAL ARTICLE

Tendency of Thyroid dysfunction in Rheumatoid Arthritis patients

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Abstract

Objective: To determine the prevalence of thyroid dysfunction among Rheumatoid Arthritis patients.

Background: Association of thyroid dysfunction among rheumatoid arthritis patient is found to be so common in various studies but it is still substantially debatable topic among researchers because of the risk of thyroid dysfunction in rheumatoid arthritis has not been well-defined. Many studies were conducted in the past to find out correlation among thyroid dysfunction and rheumatoid arthritis including the earliest study was conducted in 1963 but still there is lots of research work has to be done to find their exact correlation.

Material and Methods: Cross-sectional study conducted from January 2018 to December 2020. Total of 351 patients with diagnosis of Rheumatoid Arthritis were registered in our study as per inclusion criteria. Sample of all enrolled patients from venous blood collected for serum TSH, FT3 and FT4 levels. Quantitative data was presented as mean and standard deviation while frequencies and percentages were used for qualitative data presentation purpose. Moreover, for the purpose of observing the impact of the independent variable on the dependent variable, the effect of modifiers likes age, gender, smoking status, steroid use and disease duration were controlled through stratification. Data was analyzed by using SPSS version 16.

Results: Among 351 patients mean age was 40.80±7 years, while 197 (56.1%) were female and 154 (43.9%) were male. Duration of disease and treatment duration was 13.64±6.56 months and 18.45±5.55 months respectively. Thyroid dysfunction was noticed among 183 (52.1%) patients of Rheumatoid arthritis out of 351 which is statistically significant as p-vale is ≤ 0.05

Conclusion: In our study we observed high prevalence of Thyroid dysfunction among rheumatoid Arthritis patients, so we recommend thyroid dysfunction screening with FT3, FT4 and TSH before the commencement of their treatment and their re-evaluation at 3 and 6 months interval for proper and successful treatment.

Keywords: Rheumatoid arthritis and thyroid dysfunction, Thyroid stimulating hormone, triiodothyronine

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Introduction:

Approximately about 0.1% to 0.5% of the worldwide population of adult is affected by rheumatoid arthritis (RA). Rheumatoid arthritis predominantly affects peripheral joints with chronic symmetric and erosive synovitis, causing a range of physical disabilities.[1]

Prevalence of rheumatoid arthritis relatively high in North Pakistan than South Pakistan as it is estimated about 0.9 to 1.98/1000 in South while in North Pakistan it's about 148/1000. Rheumatoid arthritis (RA) patients have relatively reduced life expectancy because of increased incidence of cardiovascular events among rheumatoid arthritis patients.[2,3]

Thyroid disorders in rheumatoid arthritis pa-

tients are thought to be most often of autoimmune nature because they are accompanied by elevated thyroid auto-antibody titers. Many patients diagnosed initially to have rheumatoid arthritis develop thyroid disorders at a later point in time.[4] The converse is also frequently observed, i.e., musculo-skeletal disorders, including rheumatoid arthritis are known to develop in patients with various thyroid disorders.[5]

Prevalence of thyroid disorders among Pakistani population is estimated about 5.1% and 5.8% in hyperthyroidism and in sub-clinical hyperthyroidism respectively, while those with hypothyroidism and sub-clinical hypothyroidism are 4.1% and 5.4% respectively.[6-8]

Both hyperthyroidism and hypothyroidism are associated with considerable morbidity, are often mis-diagnosed, under appreciated, and neglected, and affect almost every aspect of health.

Hyperthyroidism and hypothyroidism together account for considerable morbidity and are often mis-diagnosed, mis-understood, and frequently overlooked affects almost every aspect of health. As the clinical assessment alone lacks both sensitivity and specificity, only 40% of thyroid disorders can be detected with clinical assessment alone and many of them remain undiagnosed.[9-11]

Symptoms of thyroid disease can be confused with those of rheumatoid arthritis. An abnormal thyroid function may be present in up to 34% of patients with rheumatoid arthritis.[12-13] Several international studies showed variable frequencies. Mosli et al, found the frequency of thyroid dysfunction in rheumatoid arthritis patients 26.3%.[14] Porkodi et al, confirmed that the prevalence of thyroid dysfunction is present in 5.1% in rheumatoid arthritis.[15] Chan et al. using the same criteria found prevalence to be 10.9%.[16] Another Canadian and Indian study found the prevalence to be 31% and 35.2%.[17-18] Accordingly, the purpose of the current study is to establish a local perspective since there are few local data. Investigations into the relationship between rheumatoid arthritis and the thyroid disorders have yielded conflicting results. As a result, screening of patients with Rheumatoid Arthritis for thyroid dysfunction should be recommended more often and more rigorously than in normal populations. Thyroid disorder management is emerging as a great challenge to deal with thereby effective management plan could be made on the basis of data from this study to prevent cardiovascular, neurological and other metabolic complications.

Material and Methods:

This study was conducted in the medicine department of tertiary care hospital. WHO calculator was used to estimate a population with specified absolute precision, a sample size of (n) 351 patients was determined with confidence interval of 95%. Enrollment of patients carried out by using non-probability, consecutive sampling technique. Patients with more than two years diagnosis of rheumatoid arthritis from 30 to 60 years of age without discrimination of gender were enrolled in the study. While non-consenting, critically ill, known cases of thyroid disease, known cases of IHD and pregnant patients were excluded from the study. Ethical committee approval was taken prior to begin study, all enrolled patients, written and informed consent was taken at the time of registering to study as per inclusion criteria. Sample of all enrolled patients from venous blood collected for serum TSH, FT3 and FT4 levels. Preformed proforma was used to enter demographic details, brief history of rheumatoid patients, and laboratory findings of thyroid dysfunction.

Quantitative data was presented as mean and standard deviation while frequencies and percentages were used for qualitative data presentation purpose. Calculation of qualitative variables were calculated in frequencies and percentages for gender, duration of disease, smoking status, steroid use, disease activity (CRP >5 mg/L) and thyroid dysfunction (yes/no). Moreover, for the purpose of observing the impact of the independent variable on the dependent variable, the effect of modifiers likes age, gender, smoking status; steroid use and disease duration were controlled through stratification.

Table 1: Descriptive statistics of age, duration of disease and treatment were analyzed

Variable	Mean	Standard Deviation	Min-max
Age (years)	40.80	±7.00	27-54
Duration of disease (months)	13.64	±6.56	04-21
Duration of treatment (months)	18.45	±5.55	13-24

Table 2: Distribution of Rheumatoid patients with respect to gender, thyroid dysfunction, use of steroid and smoker were analyzed

Total no of Patients	Gender		Thyroid Dysfunction		Disease Status		Steroid Use		Smoker	
	Male	Female	Yes	No	Active	Non Active	Yes	No	Yes	No
351	154	197	183	168	281	70	210	141	98	253
	43.9%	56.1%	52.1%	47.9%	80.1%	19.9%	59.85%	40.2%	27.9%	72.1%

Table 3: Thyroid dysfunction according to duration of disease

	Thyroid dysfunction		
Duration of disease (years)	Yes	No	Total
3-5	127 (69.4%)	56 (33.1%)	183(52.1%)
6-8	14 (7.7%)	84 (50%)	98(27.9%)
9-11	42 (23%)	29 (16.7%)	70(19.9%)
TOTAL	183 (100%)	168 (100%)	351(100%)
P-VALUE		0.00	

Table 4: Thyroid dysfunction according to steroid use

	Thyroid dysfunction		
Steroid use	Yes	No	Total
Yes	126 (68.9%)	84 (50%)	210(59.8%)
No	57 (31.1%)	84 (50%)	141(40.2%)
Total	183 (100%)	168 (100%)	351(100%)
P-value		0.00	

Data was analyzed by using SPSS version 16. Chi square test was applied post-stratification and p-value of ≤ 0.05 taken asstatistically significant.

Results:

The average age among 351 patients was 40.80±7, and the range between 27 and 54 years. Table 1 shows the mean duration of disease and treatment in our study as 13.64±6.56 months and 18.45±5.55 months respectively. Descriptive statistics like gender distribution, presence of thyroid dysfunction, disease status, use of steroids and smoking are shown in Table 2.

In terms of age distribution, 186 patients (53%) have 30-40 year olds; 85 patients (24.2%) have 41-50 year olds; and 80 patients (22.8%) have 51-60 year olds. On average, 183(52.1%), 98(27.9%) and 70(19.9%) patients had a disease duration of 3-5 years, 6-8 years, and 9-11 years, respectively.

In a stratified analysis based on age, 138 (75.4%), 8(4.4%), and 37(20.2%) patients in the 30-40, 41-50, and 51-60 year age groups had thyroid dysfunction. There were no thyroid dysfunction cases among the 48(28.5%), 77(45.6%), and 43(25.6%) patients who were in the 30-40 year, 41-50 year, and 51-60 year age groups respectively. Statistically significant as P-value was 0.00.

When stratified by gender, 84(45.9%) of the males and 99(54.1%) of the females had thyroid dysfunction. When stratifying by duration of disease, thyroid dysfunction was diagnosed in 127(69.4%) of patients with duration of 3-5 years' disease and in 56(33.3%) of patients did not have thyroid dysfunction. Whereas patients who had the disease for 6-8 years 14(7.7%) and 84(50%) had and did not have thyroid dysfunction. Furthermore, 42(23%) of these patients had thyroid dysfunction compared to 28(16.7%) of those who did not have thyroid dysfunction. A P-value 0.00 was obtained. Table 3 used to mention this stratification.

Stratification for smoking status with respect to thyroid dysfunction showed that patients who smoked, 42(23%) and 56(33.3%) had and did not have thyroid dysfunction. Whereas patients who did not smoke, 141(77%) and 112(66.7%) had and did not have thyroid dysfunction. P-value was 0.02.

With regards to thyroid dysfunction, steroid use was stratified according to whether patients had or did not have thyroid dysfunction. There were 126(68.9%) had the disease while 84(50%) did not have thyroid dysfunction. On the other hand, of those without steroid use, 57(31.1%) and 84(50%) had and did not have metabolic syndrome. Statistically a P-value 0.00 was ob-

tained. Table 4 used to mention this stratification.

With regard to disease activity status and thyroid dysfunction, 141(77%) of patients with active disease and 140(83.3%) of patients without active disease had thyroid dysfunction. Whereas patients who did not have active disease, 42(23%) and 28(16.7%) had and did not have thyroid dysfunction. P-value was 0.09.

Discussion:

Association of thyroid dysfunction among rheumatoid arthritis patient is found to be so common in various studies but it is still substantially debatable topic among researchers because of the risk of thyroid dysfunction in rheumatoid arthritis has not been well-defined.[19]

Many studies were conducted in the past to find out correlation among thyroid dysfunction and rheumatoid arthritis including the earliest study was conducted in 1963 but still there is lots of research work has to be done to find their exact correlation.[20] In a study thyroid related auto-antibodies were found to be significantly elevated among rheumatoid arthritis patients and it further signify the importance of evaluation of rheumatoid arthritis patients for thyroid dysfunction.[21]

In our study out of 351 patients mean and standard deviation of age, duration of disease and duration of treatment was 40.80±7 years, 13.64±6.56 months and 18.45±5.55 months respectively. 154(43.9%) were male and 197(56.1%) were female. Out of 351 rheumatoid arthritis patients, 183(52.1%) had thyroid dysfunction and 168(47.9%) did not have thyroid dysfunction.

In Mosli et al, study, 151 patients had their thyroid function evaluated. We found that the incidence of thyroid disorders 26.3% in rheumatoid arthritis patients was higher than that in non-rheumatoid arthritis patients which was 7%. These patients presented with varying degrees of thyroid dysfunction: sub-clinical hypothyroidism in 29(26.3%), hypothyroidism in 6(4%) and sub-clinical hyperthyroidism in 4(2.6%), and hyperthyroidism in 1(0.7%). None of patient evaluated as euthyroid sick syndrome. Positive significant correlation were found between C - reactive protein and serum thyroid stimulation hormone(r=0.22, P=0.029).[22]

Porkodi et al, evaluated 798 rheumatoid arthritis patients 41(5.1%) had thyroid dysfunction. There were 40 females and one male. Hyperthyroidism was seen in 7.3% (mean age was 30.7 years). Sub-clinical hypothyroid occurred in 17.1% (mean age was 35.7 years). Clinical hypothyroid was present in 73.2% (mean age of 48.3 years). 2.4% of patients, (mean age 30.7 years) had euthyroid state with raised antibodies alone.[23]

Shiorky et al,[32] documented 91 women with rheumatoid arthritis evaluated, 29(30%) had evidence of thyroid dysfunction compared with 10(11%) of 93 controls. The excess thyroid dysfunction is due to either hypothyroidism or Hashimoto's thyroiditis and was independent of age, increasing duration of disease, rheumatoid factor, and antinuclear antibodies.[24]

Despite a higher prevalence of thyroid disorders among patients with rheumatoid arthritis, Kumar et al, did not report this to be statistically significant. In his study 19/54 (35.2%) had thyroid dysfunction while 12/54 (22.2%) did not had thyroid dysfunction and P- value was 0.201.

Levothyroxine was being used to treat 9-patients with rheumatoid arthritis who had hypothyroidism. A significantly higher rate of autoimmune thyroid disease (AITD) was found among remaining rheumatoid arthritis patients (n=45), (10/45 versus 4/54; 2=4.437, p=0.045) and a positive anti-thyroid peroxidase antibody (4/45 versus 0/54; 2=5.002, p=0.040) was associated with sub-clinical hypothyroidism compared with healthy control subjects.[25]

Recently a study was conducted on association of thyroid dysfunction among rheumatoid arthritis patients by Nazary K et al, and showed comparable result with our study because they

also observed the high tendency of thyroid dysfunction among rheumatoid arthritis patients and signify the screening of thyroid dysfunction in these patients.[26]

It is concluded from this study that there is significant association between thyroid dysfunction and rheumatoid arthritis, and it highlights the importance of thyroid function tests in these patients.

Conclusion:
According to our results, rheumatoid arthritis patients had high prevalence of thyroid dysfunction. Females were found to be more affected than males. Screening for free T3, T4, and TSH is recommended before the treatment and their re-evaluation at 3 and 6 months intervals. Patients should be informed for the risk of thyroid dysfunction before the commencement of treatment. Patients suffering from thyroid dysfunction can suffer from longer disability periods, lower quality of life and more hospitalizations, which is why it is very important to detect and treat these conditions early. It could prove beneficial for these patients if rheumatologists and endocrinologists worked with close collaboration.

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Role and contribution of authors:
Izia Batool, collected the data, references and did the initial write up.

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Muhammad Fahad Waseem, collected the references and also helped in discussion and result writing.

Syed Kamran Ali Shah, critically went through the article and made useful changes.

Mehrunnisa Umar, collected the data, references and helped in discussion writing.

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