ORIGINAL RESEARCH PAPER

General Medicine

# PROPORTION OF ANTI TPO ANTIBODY POSITIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A TERTIARY CARE CENTRE IN NORTH INDIA

**KEY WORDS:** Anti TPO Antibody, Rheumatoid Arthritis, Thyroid dysfunction, Autoimmune thyroid disease

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## INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, progressive autoimmune systemic disease leading to joint destruction and organ impairment and subsequently leading to increased morbidity and mortality. RA is a systemic disease having many extraarticular manifestations including fatigue, subcutaneous nodule, lung involvement, pericarditis, peripheral neuropathy, vasculitis, endocrine and hematological abnormalities. Patients with RA commonly present a clinical picture of other autoimmune disorders, including AITD. Both disorders are associated because of similar pathogenic mechanisms and genetic susceptibility. Autoimmune thyroid disease (AITD) is a term used to bring together a group of pathologies that has thyroid dysfunction and an autoimmune response against this endocrine organ as its hallmark. Autoimmune thyroid disease (AITD) is the most prevalent organ-specific autoimmune disease characterised by the presence of antibodies against thyroid-specific components such as thyroglobulin (aTG), thyroid peroxidase (aTPO), thyrotropin receptor antigen (aTSHr) and sodium iodine symporter (NIS). AITDs, specifically Graves' disease (GD) and Hashimoto's thyroiditis (HT), are currently the most common causes of goitres in countries where iodine deficiency is not present, with a prevalence of up to 5% in the general population.

For several decades an increased occurrence of thyroid disorders in patients suffering from RA has been documented—both autoimmune and nonautoimmune in nature.(1-4) In addition, rheumatologic and non-rheumatologic manifestations of AITD have been described.(5) Within these manifestations, it is noteworthy that the most common symptoms are polyarthralgia and unclassified arthritis, which are the main features of RA.

The frequency of AITD in RA varies greatly over the world, ranging from 0.5 percent in Morocco(6) to 27 percent in Slovakia. Thyroid-specific antibody prevalence ranges from 6 to 31% for TgAb 5 to 37% for TPOAb and 10.4 to 32% for both. Certain reasons may account for the large prevalence variability. To begin with, identifying AITD is complicated because it is dependent on the presence of a past diagnosis of thyroid disease. However, there has been a lot of controversy about how to define hypothyroidism or hyperthyroidism; the normal reference range is not universally acknowledged, therefore writers and physicians all over the world use different normal ranges. Iodine ingestion is a third possibility. Iodine is well known for its ability to trigger an autoimmune reaction against the thyroid.(7)

When it comes to thyroid antibodies, there is also a wide range of prevalence. TPOAb, as opposed to TgAb, is largely considered as the most common of these thyroid antibodies.

### Aims and objectives

### PRIMARY OBJECTIVE

- To study the proportion of anti-TPO antibody in rheumatoid arthritis patients attending Medicine OPD of SRG Hospital, Jhalawar, Rajasthan.

### SECONDARY OBJECTIVE

- To study the association between anti TPO antibody and RA disease activity.
- To study the clinical profile of patients with Rheumatoid Arthritis.

### Materials and methods

### STUDY DESIGN

Hospital based cross sectional study

### STUDY POPULATION

All patients satisfying inclusion criteria.

### INCLUSION CRITERIA:

Patients diagnosed as rheumatoid arthritis according to the 2010 ACR/EULAR criteria presenting to Medicine OPD of SRG Hospital and Medical College, Jhalawar, Rajasthan.

### EXCLUSION CRITERIA:

1)Patients with congenital thyroid disorders
2)Patients who are not willing to give consent for the study

### PROCEDURE

165 patients were enrolled to my study – all those who satisfied the inclusion criteria and had given consent to take part in the study. All these patients were examined and evaluated. A detailed history and clinical examination were done. A semi structured questionnaire was used to collect data from patients. Blood sample was collected from patients for routine blood investigations like complete blood count, anti TPO antibody, thyroid function test, ESR, CRP and serology for RA.

### STATISTICAL ANALYSIS

Data was entered into excel sheet. Data analysis was done using SPSS SOFTWARE. Categorical variables were expressed as frequencies and proportions and quantitative variables as mean and standard deviation. Association between qualitative variable was tested using Chi Square test.

### OBSERVATIONS AND RESULTS

In our study more than half of the patients were in the age group 41-60 years. Only 3% of patients were below 30 years and 6.1% patients were above 70 years.

The mean age of the study population is 50.8(SD = 11.9) with maximum age of 78 years and minimum age of 24 years. The mean age of disease onset is 45.1 years (SD =10.2).

Out of the 165 patients with Rheumatoid arthritis,149 were females (90.3%) and only 16 were males (9.7%).

Of the studied population of 165 patients with RA, 66 patients (40%) were in the lower middle class background according to the Modified Kuppuswamy Scale.48 patients (29.1%) were from Upper lower class and 25 patients (15.2%) were from

Upper middle class background. Only 10 patients (6.1%) and 16 patients (9.7%) were from upper class and lower class respectively.

Most of the patients (about 70%) were from rural area and 30.3% were living in urban area in our study.

Only 22.4% patients had positive family history of RA. Rest 77.6% patients with the disease had no first degree relatives with RA.

**Table 1 : Distribution of the study sample based on Anti-TPO antibody**

| Anti-TPO | Frequency | Percent |
|---|---|---|
| Negative | 106 | 64.2 |
| Positive | 59 | 35.8 |
| Total | 165 | 100 |

Out of the 165 patients with RA,59 patients (35.8%) were positive for Anti-TPO antibody

**Figure 1 : Distribution of the study sample based on Anti-TPO antibody.**

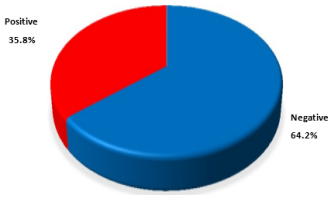



**Table 2 : Distribution of the study sample based on thyroid status**

| Thyroid Status | Frequency | Percent |
|---|---|---|
| Euthyroid | 124 | 75.2 |
| Hypothyroidism | 36 | 21.8 |
| Hyperthyroidism | 5 | 3 |
| Total | 165 | 100 |

About 25% of patients with RA had abnormality in their thyroid function of which 21.8% patients had hypothyroidism and 3% had hyperthyroidism.

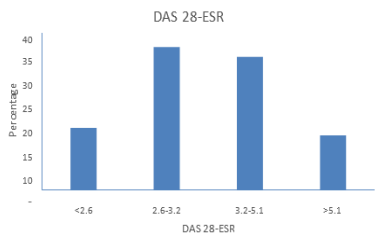
Out of the 36 patients with Hypothyroidism, 6 patients had only subclinical hypothyroidism.

**Table 3 : Distribution of the study sample based on RA factor.**

| RA FACTOR | Frequency | Percent |
|---|---|---|
| Negative | 35 | 21.2 |
| Positive | 130 | 78.8 |
| Total | 165 | 100 |

78.8% patients with RA in our study were RA factor positive. Only 35 patients out of 165 were RA factor negative. Anti CCP was positive in 73.3% of patients with RA in our study. Almost all patients in our study (97%) had elevated ESR. Only 3% had normal ESR.. CRP was elevated in 44.8% of patients in our study.

**Figure 2 : Distribution of the study sample based on disease activity.**

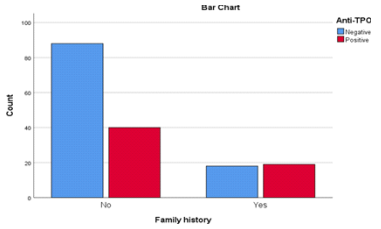



In our study, out of 165 patients, 26 patients (16%) were in remission. 36.4% of patients had low disease activity. About 34% had moderate disease activity and 23 patients( 14%) had high disease activity.

**Table 4 : Association between Anti-TPO and family history of RA.**

| Family history | Anti-TPO | | | | Total | | x2 | df | P |
|---|---|---|---|---|---|---|---|---|---|
| | Negative | | Positive | | | | | | |
| | N | % | N | % | N | % | | | |
| No | 88 | 83 | 40 | 67.8 | 128 | 77.6 | 5.049 | 1 | 0.025 |
| Yes | 18 | 17 | 19 | 32.2 | 37 | 22.4 | | | |
| Total | 106 | 100 | 59 | 100 | 165 | 100 | | | |

**Figure 3 : Association between Anti-TPO and family history of RA.**




There was significant association between Anti TPO and family history of RA.

**Table 5 : Association between Anti TPO and TSH.**

| TSH | Anti-TPO | | | | Total | | x2 | df | P |
|---|---|---|---|---|---|---|---|---|---|
| | Negative | | Positive | | | | | | |
| | N | % | N | % | N | % | | | |
| Normal | 91 | 85.8 | 33 | 55.9 | 124 | 75.2 | 18.195 | 2 | 0.000 |
| Increased | 13 | 12.3 | 23 | 39 | 36 | 21.8 | | | |
| Decreased | 2 | 1.9 | 3 | 5.1 | 5 | 3 | | | |
| Total | 106 | 100 | 59 | 100 | 165 | 100 | | | |

**Table 6 : Association between Anti TPO and Ft3.**

| FT3 | Anti-TPO | | | | Total | | x2 | df | P |
|---|---|---|---|---|---|---|---|---|---|
| | Negative | | Positive | | | | | | |
| | N | % | N | % | N | % | | | |
| Normal | 94 | 88.7 | 36 | 61 | 130 | 78.8 | 18.852 | 2 | 0.000 |
| Decrease | 10 | 9.4 | 22 | 37.3 | 32 | 19.4 | | | |
| Increased | 2 | 1.9 | 1 | 1.7 | 3 | 1.8 | | | |
| Total | 106 | 100 | 59 | 100 | 165 | 100 | | | |

**Table 7 : Association between Anti TPO and Ft4.**

| FT4 | Anti-TPO | | | | Total | | x2 | df | P |
|---|---|---|---|---|---|---|---|---|---|
| | Negative | | Positive | | | | | | |
| | N | % | N | % | N | % | | | |
| Normal | 94 | 88.7 | 36 | 61 | 130 | 78.8 | 18.852 | 2 | 0.000 |
| Decreased | 10 | 9.4 | 22 | 37.3 | 32 | 19.4 | | | |
| Increased | 2 | 1.9 | 1 | 1.7 | 3 | 1.8 | | | |
| Total | 106 | 100 | 59 | 100 | 165 | 100 | | | |

There was significant association between Anti TPO and TFT in patients with RA.

**Table 8 : Association between Anti TPO and Serology in RA.**

| Serology | P value |
|---|---|
| RA factor | 0.838 |
| Anti CCP | 0.642 |

There was no significant association between Anti TPO and RA factor or Anti CCP.

## DISCUSSION

Rheumatoid arthritis patients have a higher incidence of

thyroid disorders especially autoimmune thyroid disorders.[1-3]

This is a hospital based cross sectional study. 165 patients diagnosed as RA according to the 2010 ACR/EULAR Criteria[8] presenting to the Medicine OPD of SRG Hospital, Jhalawar were taken for the study.

The mean age of the study population is 50.8 years (SD =11.9) . Out of the 165 patients, 90.3% (149) were females and 9.7% (16) were males. Most of the studies show that females are more commonly affected by rheumatoid arthritis than males. Crowson et al showed that the lifetime risk for developing RA was 3.6% for females and 1.7% for males.

In our study, majority of patients with RA belonged to lower SES and live in rural areas. This result is comparable with many other studies conducted across the world. 22.4% (37 out of 165) patients had at least 1 first degree relative with RA.

In this study, 35.8% patients (59 out of 165) tested positive for anti TPO antibody. This is much higher compared to the general population with positive anti TPO antibody which is about 13%(128) . Studies conducted all over the world shows that the prevalence of anti TPO antibody in rheumatoid arthritis patients vary widely.

Coming to the thyroid status, about 75% patients with RA were euthyroid in our study. Only 24.8% patients had abnormal thyroid hormone levels of which the most common abnormality seen was hypothyroidism (21.8%). Hyperthyroidism was seen only in 3% cases. Out of the 36 patients with hypothyroidism, 6 patients had only subclinical hypothyroidism. This is in parallel with the study conducted in Slovakia where 24% patients with SLE and RA had thyroid disorder.

In the 59 patients with anti TPO antibody positive, 26 patients (44.1%) patients had thyroid dysfunction of which 23 patients (38.9%) had hypothyroidism and only 3 (5.08%) had hyperthyroidism. Where as in 106 patients with negative anti TPO antibody, only 15 (14.2%) patients had thyroid dysfunction. 91 out of 106 patients (85.8%) with negative anti TPO were euthyroid. This suggests that there is significant association between anti TPO and thyroid function in RA patients ($p<0.05$).

78.8% patients (130 out of 165) with RA in our study were RA factor positive. Only 35 patients out of 165 were RA factor negative. Akil et al have reported that 80% of patients with rheumatoid arthritis are seropositive for rheumatoid factor. Lindqvist et al reported that in their study on 168 cases of RA, 71% were positive for rheumatoid factor. Thus, the rheumatoid factor positivity in this study is comparable to that of other studies.

Anti CCP was positive in 73.3% of patients with RA in our study. Its diagnostic specificity approaches 95%, so a positive test for anti-CCP antibodies in the setting of an early inflammatory arthritis is useful for distinguishing RA from other forms of arthritis. The presence of RF or anti-CCP antibodies also has prognostic significance, with anti-CCP antibodies showing the most value for predicting worse outcomes. The detection of a disease-specific autoantibody like anti-CCP could be of great diagnostic and therapeutic importance in early cases of RA while symptoms are mild.

Coming to acute phase reactants, ESR was elevated in 97% of patients with RA in our study, where as CRP was elevated only in 44.8% of patients. Both ESR and CRP are important for assessing the disease activity of RA and modifying the treatment accordingly.

About 64.8% patients in our study had anemia as a complication. According to Wilson et al.[9], prevalence of mild anaemia ranged between 33% and 60% in various studies done across the world.

It was noted that there was significant association between anti TPO and family history of RA in our study ($p = 0.025$). This may be because of the common genetic factors involved in AITD and RA.

Association between anti TPO and RA disease activity (measured by DAS 28 ESR score) was evaluated in our study. It was noted that there was no significant association between anti TPO antibody and RA disease activity ($p=0.223$). But in a study by Koszarny et al.[10], there was significant association between antithyroid antibodies and RA disease activity.

It was also noted that there was no significant association between anti TPO antibody and RA factor ($p=0.838$) or anti CCP ($p=0.642$).

## CONCLUSION

1. The prevalence of anti TPO antibody in RA is high (35.8%) as compared to the general population.
2. Thyroid disorders are common in RA patients.
3. Most common thyroid disorder is hypothyroidism.
4. There was significant association between anti TPO antibody and thyroid function in RA patients.
5. There was significant association between anti TPO antibody and family history of RA.
6. No significant association was seen between anti TPO antibody and RA disease activity.
7. Patients with RA should be screened for thyroid disorders especially AITD by testing FT3, FT4, TSH and anti TPO antibody for early detection and management.

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