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Thyroid Profile in Rheumatoid Arthritis

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Abstract
Rheumatoid Arthritis (RA) and thyroid disorders have autoimmunity as one of the aetiological factors. This study aims to find the thyroid profile in RA patients. This is a descriptive cross-sectional study of 164 RA patients who attended Rheumatology OP department of Government Medical College Thiruvananthapuram over a period of one year in 2016, diagnosed according to ACR/EULAR 2010 criteria for RA. Activity index is calculated using DAS 28 scoring based on ESR. All the patients were tested for TSH, FT4, FT3, and Anti-TPO by chemiluminescent Immunoassay method. Thyroid status is defined based on the Dutch National Healthcare Consensus Committee. The mean age at diagnosis of RA was 43.3years ±11.7 years and mean duration of symptoms of RA were 4.7± 2.3 years. 90.2% were females and 9.8% were males. Thyroid abnormalities are found in 29.3% and relatively more among those between 41-50 years. 24.4% were hypothyroid, 3.7% had subclinical hypothyroidism, and 2% had subclinical hyperthyroidism. 14.6%) had Thyroid swelling, 6.1% had multi nodular goitre, and 8.5% had diffuse goitre. Among the patients with thyroid dysfunction, all had constitutional symptoms and 24.4% had morning stiffness for more than an hour. Mean duration of symptoms of thyroid dysfunction were5.1±3.0 years compared to 4.5±1.8 years in normal. There was significant correlation of patients with thyroid dysfunction to positive anti TPO antibodies. 27 patients with thyroid abnormalities were on treatment with NSAIDS or DMARDs. There was a significant correlation between RA and thyroid dysfunction and the commonest abnormality was hypothyroidism.
Keywords: *Rheumatoid arthritis, Thyroid dysfunction, Hypothyroidism, Anti-TPO antibody, DAS score.*

Introduction

Rheumatoid arthritis (RA) is the most common chronic inflammatory arthritis affecting 0.5 to 1% worldwide and in India, it is about 0.65 % to 0.75%[(1)]. Non organ specific antibodies and autoimmunity has been considered in the aetiopathogenesis of RA. In areas which are iodine sufficient autoimmunity has been projected as an aetiological factor for thyroid diseases. Because of these common aetiology and overlap of symptoms, various studies were conducted to find out the association between RA and thyroid dysfunction. Many studies have shown an increased incidence of thyroid dysfunction in RA[(2, 3)]. Studies have also found that there is clinical improvement of hypothyroidism with treatment of RA[(4)]. Increased incidence of coronary disease in patients with RA was reported[(5)] anti TPO antibodies were also implicated in the development of cardiovascular disease[(6)]. Hence this study was done to find out the

thyroid profile of patients with rheumatoid arthritis.

Materials and methods

This was a descriptive cross sectional study conducted among patients attending Rheumatology-Out patient clinic, under Department of Internal Medicine and patients admitted in The Medical wards of Internal Medicine Department, Government Medical College Hospital, Thiruvananthapuram Kerala over a period of one year from January 2015 to January 2016. Institutional Ethical clearance was obtained prior to starting the study. Patients aged more than 12 years, diagnosed based on the American College of Rheumatology (ACR)/EULAR 2010 classification criteria for rheumatoid arthritis were included in the study [(7)]. Patients on medication known to cause thyroid dysfunction, patients with evidence of malignancy, connective tissue disorder other than RA, chronic liver or renal diseases, Diabetic patients, Hypertension, patients who had undergone thyroidectomy and pregnant women were excluded.

Sample size was calculated based on the formula-sample size, n=164 ($n=4pq/l^2$ p-prevalence in previous study, q=100-p, l=20% of p) All patients were evaluated with detailed history age, sex, duration of RA, duration of morning stiffness, chest symptoms, list of painful joints, presence of other systemic disease, presence of extra-articular manifestations of RA and thyroid swelling were documented. A systematic examination of all joints for tenderness, swelling, deformity, and range of movements possible at the joint was done. System examination was conducted, neck examined for thyroid swelling which was confirmed by ultrasonogram of neck

Data Collection Tools

Structured data collection proforma DAS-28 scoring based on ESR[(8)]

The following investigations were done with special emphasis.

Erythrocyte sedimentation rate was measured using Westergrens method.

Rheumatoid factor (IgG): quantitative assay was performed using a latex fixation lab kit. A value of more than 12 IU/ml was taken as positive. C - reactive protein was done using a quantitative assay was performed using ELISA. Value >6mg/l was considered as positive. Thyroid Function test S.TSH,S.FT4,S. FT3 was performed by chemiluminescent Immunoassay assay .Thyroid stimulating hormone (TSH) normal range of TSH- 0.25-4.75 IU/ml [> 4.75 -hypothyroidism; <0.25 hyperthyroidism] Free serum thyroxine (FT4) normal range 0.9-1.71 ng/dl [<0.9 – hypothyroidism; >1.71 hyperthyroidism, Free serum triidothyronine (FT3) normal range 1.82-4.62 pg/ml ,anti-TPO was performed by chemiluminescent Immunoassay, value > 34 IU/ml was considered as positive.

Clinical hypothyroidism and hyperthyroidism were defined based on the criteria of thyroid abnormalities as defined by the Dutch National Healthcare Consensus Committee. Disease activity score (DAS28) was calculated for all of them using DAS28 calculator for ESR.

Chi square test/Fischer exact test has been used to find the significant association of clinical factors between patients with and without thyroid dysfunction. Student t test (two tailed, independent) has been used to find the significance of investigation parameter between two groups of patients.

The statistical software namely SPSS 23.0 was used for the analysis of the data and Microsoft word and excel have been used to generate graphs, tables etc.

Results

The study was conducted among 164 RA patients. 41-50 age group had the maximum representation. 148 females and 16 male patients were studied, ratio being 9:1. The mean duration of symptoms among RA patients was 4.7 years with a range of 2 to 14 years. 29.3% had thyroid dysfunction 24.4% had hypothyroidism (table 3) but only 15.9% had symptoms of hypothyroidism. Subclinical hypothyroidism formed 3.7%, subclinical hyperthyroid 1.2% .Overt hyperthyroidism was

not observed. multinodulargoiter (MNG) was found in 10 (6.1%) and diffuse enlargement was found in 14 (8.5%).Out of 48 patients who had thyroid function abnormality, 40 (83.3%) had morning stiffness, which found to be significant. All 48 patients had constitutional symptoms. Duration of symptoms is longer in patients with thyroid dysfunction groups in comparison to normal thyroid status groups but it was not found to be significant. There is no difference in the number of swollen joints. Mean value of Rheumatoid Factor was significantly higher in the thyroid dysfunction group. Mean ESR, Mean CRP and anti TPO values were significantly higher in patients with thyroid dysfunction .Mean DAS28 score for patients with thyroid dysfunction group was 6.1±1.07 as compared to 5.7±1.03 in normal thyroid status group with significant p value of 0.032. In this study group 26 patients (15.9%) were Anti-TPO positive, all patients are in the thyroid dysfunction group, which is statistically significant p<0.001

Table 1: Age in years of patient studied

Age in years	No of patients (%)
<30	25(15.2%)
31-40	40(24.4%)
41-50	58(35.45%)
51-60	29(17.7%)
>60	12(7.3%)
total	164(100%)

Table 2: Thyroid dysfunction in Rheumatoid Arthritis patient

Thyroid status	No of patients %
Normal	116(70.7%)
Thyroid dysfunction	48(29.3%)
total	164(100%)

Table 3: thyroid status in Rheumatoid arthritis patient

Thyroid status	No of patients (%)
Euthyroid	116(70.7%)
Hypothyroid	40(24.4%)
Subclinical hypothyroid	6(3.7%)
Subclinical hyperthyroid	2(1.2%)
total	164(100%)

Table 4: mean of the study parameters

Study parameters	Thyroid dysfunction		P*
	Absent (N=116)	Present (n=48)	
Age	43.1±11.7	43.8±11.8	0.723
Duration in years	4.5±1.8	5.1±3.0	0.116
Tender joints	11.0±6.8	12.2±5.6	0.276
Swollen joints	12.4±6.5	12.4±6.0	0.998
DAS 28	5.7±1.03	6.1±1.07	0.032
ESR	57.2±30.3	73.0±34.5	0.004
CRP	19.87±16.97	26.97±14.14	0.020
RA FACTOR	109.22±111.35	155.93±132.29	0.020
S.TSH	2.5±0.8	7.99±3.2	0.001
S.FT4	1.2±0.2	0.43±0.4	0.001
S.FT3	2.6±0.6	1.42±0.8	0.001
Anti TPO	7.1±7.5	290.6±284.8	0.001
Ht (cm)	162.4±5.0	157.9±5.6	0.001
Wt((kg)	67.1±10.9	65.4±11.6	0.348
BMI	25.4±3.5	26.1±3.9	0.236

Table 5: Study parameters between normal and thyroid dysfunction groups

Study parameters	Thyroid dysfunction		P*
	Absent (N=116)	Present (n=48)	
Female: male	105:11	43:5	0.854*
Joints involved QL:BUL:BLL	72:37:7	30: 18:0	0.200**
Morning stiffness	109(94%)	40(83.3%)	0.032**
Constitutional symptoms	106(91.5)	48(100%)	0.036**
Deformed joints		9(18.8%)	0.040**
Restriction joint movements	3(2.6%))	6(12.5%)	0.011**
Rheum nodules	13(11.2%)	7(14.6%)	0.458**
purpura	3(2.6%)	0	0.458**
Thyroid swelling absent	109(94%	31(64%)	
MNG	3(2.6%)	7(14.65)	0.001**
Diffuse swelling	4(4.3%)	10(20.8%)	
*independent sample t-test,**chi -square test			

Discussion

Rheumatoid arthritis is a chronic inflammatory arthritis-affecting woman of the 40-50 age group. The mean age of the study population was 43.3yrs Maximum number of patients were in the 41-50 age group (35.4%).) There was no significant difference in the mean age of patients with normal thyroid status and thyroid dysfunction. Similar observations made by Malaviya et al. and Chopra in their epidemiological studies[9,10]. Even though

rheumatoid arthritis is a disease affecting predominantly women in the ratio 3:1 this study showed a higher than normal ratio 9:1 higher ratio is also reported by F Mohammed (7:1) Kumar et al ; 8:1,studies.Sougandha concluded that in South India, RA affects females predominantly[11, 12, and 13]

Out of 48 patients with thyroid dysfunction, there were 43 females and 5 males. Females are more affected than males but, there is no statistically significant correlation with gender (p>0.05),

In this study48 patients (29.3%) showed thyroid dysfunction40 patients (24.4%) had hypothyroidism the finding was similar to other studies where prevalence of thyroid dysfunction in RA ranged from 29% to 37% (14).Li et al. in a case control study in China reported an incidence of thyroid dysfunction of 32.3% and hypothyroidism 26.2 % (15). Most common thyroid abnormality is hypothyroidism in all the studies and 3.7% had subclinical hypothyroidism, Elattar et al[16] reported similar incidence. A few studies have reported a higher incidence of subclinical hypothyroidism 7% to 19%. Przygodka et al and, Mosli et al had more number of subclinical hypothyroidism than overt hypothyroidism [17, 18]

In this study, two patients (1.2%) had subclinical hyperthyroidism; Elattar et al[16] showed prevalence of1.3% subclinical hyperthyroidism, which is similar to our results. Mosli et al in a retrospective study showed a higher prevalence of Subclinical hyperthyroidism in 2.6%, they also notedovert hyperthyroidism in one patient.[18] Lietal reported higher rate 6.2% patients[15]. Hyperthyroidism is a manifestation of early disease where there is inflammation of cells and release of hormones. This is followed by subclinical hypothyroidism and later stages overt hypothyroidism. Age in thyroid dysfunction patients were 43.8± 11.8years, mean duration of symptoms is 5.1±3.0 years, The mean duration of symptoms were longer in patients who had thyroid dysfunction (5.1±3.0 years) as compared to patients with normal thyroid status 4.5±1.8years but it is not statistically significant . 40 out of 48(83.3%) has morning stiffness more than 60 minutes (p0.045) which is statistically significant, this observation was also made by Singh et al[19]. In this study group 93.9%, patients had constitutional symptoms like anorexia, tiredness. In patients with thyroid dysfunction, all had constitutional symptoms, which is statistically significant between normal and thyroid dysfunction groups (p0.036). Out of the total 164, only 20 patients had rheumatoid nodules. In patients with thyroid, dysfunctions only 9 out of 48 had rheumatoid nodules. Duration of symptoms in our study was less and rheumatoid nodule is a manifestation of chronicity.

Cardenas etal observed that the incidence of AntiTPO varies with ethnicity and can range from 0.5 to 27%.Our incidence was 15.9%. Positive AntiTPO antibody is seen in all of the patients with thyroid dysfunction. Some authors have reported increased association of autoantibodies with risk for developing diabetes and cardiovascular disease. Hence, the high incidence in our study requires further studies.

Thyroid disorders are the result of the anti-thyroid activity of one of the antibodies produced in RA along with genetic and environmental factors contributing[18]. In RA, thyroid involvement may remain unnoticed for a long period in a reversible subclinical stage, which has to be identified and corrected. This study was conducted in a Tertiary care centre where advanced cases of RA was referred hence many early manifestations of thyroid dysfunction like hyperthyroidism, subclinical hypothyroidism were missed.

Conclusion

There is a strong association between RA and thyroid dysfunction. Commonest thyroid dysfunction noted was hypothyroidism.

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Conflicts of interest nil

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