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PATTERN OF THYROID DYSFUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ITS ASSOCIATION WITH DISEASE ACTIVITY AND DURATION

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ABSTRACT

BACKGROUND/PURPOSE: Cardiovascular complications are one of the most common comorbid conditions in rheumatoid arthritis (RA). Hypothyroidism and RA are both relatively common autoimmune diseases associated with increased Cardiovascular Disease (CVD) morbidity and mortality, further research into the interaction between these two diseases is worthwhile. Thus the study was done to determine the pattern of thyroid dysfunctions in Rheumatoid Arthritis patients.

Materials & Methods: A hospital based case-control study was done among patients who were admitted or attending various Out Patient Departments of Assam Medical College and Hospital, Dibrugarh, Rheumatology clinic in Assam Medical College & Hospital has been enrolled. 103 patients based on the Classification Criteria for Rheumatoid Arthritis (ACR/EULAR, 2010)were taken in the study and 103 healthy volunteers were taken in the control group.Patients age less than 13 and pregnant women were excluded.

Results: This study showed that thyroid dysfunction was present in 22(21.35%) patients, 12 patients had subclinical hypothyroidism and 6 had hypothyroidism, 4 patients had subclinical hyperthyroidism whereas in the control group 5 (4.85%) had thyroid dysfunction. Majority of the thyroid dysfunction patients (25%) were in the low disease activity group and amongst the Anti-CCP–/RF+ group thyroid dysfunction were observed to be the highest (33.33%)

Conclusion: The study shows that abnormal thyroid function tests, particularly subclinical hypothyroidism were seen more commonly in patients with Rheumatoid Arthritis compared to controls. The presence of non-specific suggestive symptoms in a RA patient inspite of a low disease activity may be a clinical pointer to the underlying thyroid disorder requiring laboratory evaluation. Thus Physicians should be aware of screening RA patients periodically for this comorbidity, especially those who are at high risk (female gender and positive thyroid autoantibody) and accordingly manage when patients become symptomatic or develops overt hypothyroidism.

KEYWORDS : *M. fortuitum*, Cutaneous ulcer, IndiaRheumatoid Arthritis(RA), Autoimmune disease, Thyroid Dysfunction, ACR-EULAR 2010

Introduction:

Rheumatoid arthritis (RA) is an autoimmune disease in whichchronic inflammation predominates. Inflammation is systemic,targeting articular tissues, and predisposing to cardiovascularcomorbidity and increased susceptibility to infectious pathogens,combining to reduce life expectancy by up to 10 years in severecases.1Rheumatoid Arthritis cases with high disease activity were having comparatively more cardiovascular involvement than the non-high disease activity group.One of the most common causes of death in patients with RA is cardiovascular disease. The incidence of coronary artery disease and carotid atherosclerosis is higher in RA patients than in the general population. The presence of elevated serum inflammatory markers appears to confer an increased risk of cardiovascular disease in this population.[2]

Hypothyroidism is one of the cause of cardiovascular morbidity and overt hypothyroidism is associated with increased systemic vascular resistance(SVR), decreased cardiac contractility, decreased cardiac output, and accelerated atherosclerosis and coronary artery disease.[3,4]Hypothyroid patients may have hypertension, particularly diastolic. Fazio S et al., (2004) showed that in patients with systemic hypertension, overt hypothyroidism is associated with higher blood pressure.[5]Hypothyroidism is consistently associated with elevations of total cholesterol and low-density lipoprotein (LDL) cholesterol, which improve with T4 replacement.[6]

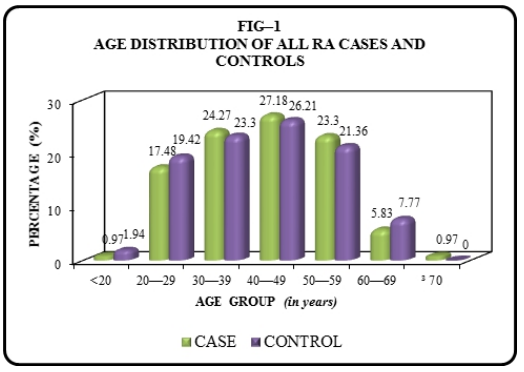
Materials & Methods:

Arthritis patients of 13 years or above diagnosed by the 2010 Rheumatoid Arthritis Classification Criteria an American College of Rheumatology (ACR) /European League Against Rheumatism (EULAR) Collaborative Initiative, who were admitted or attending various Out Patient Departments of Assam Medical College, Rheumatology clinic in Assam Medical College & Hospital, Dibrugarh has been enrolled. A hospital based case-control study was done among 103 patients and 103 healthy volunteers.Pregnant women and patientswith infections or sepsis and those known to have previous thyroid dysfunction or on antithyroid medication were excluded from the study.Statistical analysis was performed by using GraphPadInStat version 3.1, continuous data was expressed as mean ± standard deviation (SD) and categorical variables as counts and percentages. Tests employed were Student unpaired t-test for quantitative data and for qualitative data Chi square test. P value of <0.05 was considered statistically significant in this study.

Results & Observations:

The present study was conducted in the Department of Medicine, Assam Medical College and Hospital. Patients fulfilling the ACR/EULAR criteria (2010) were included in the study. A total of 103 patients with Rheumatoid arthritis and 103 controls were studied.

All the cases were subjected to a thorough history, clinical examination and laboratory investigations. The following tables and charts illustrate the results and important features of the study.



The study shows that maximum patients have presented in age group of age group of 40-49 years (27%). The mean age group in the study was 41.60 ± 11.36 years in cases and 41.17 ± 12.53 years in controls.

TABLE 1: SEX DISTRIBUTION OF ALL RA CASES AND CONTROLS

SEX	CASES		CONTROL	
	n	%	*n*	%
Male	24	23.30	23	22.33
Female	79	76.70	80	77.67
TOTAL	103	100.00	103	100.00
RATIO (M : F)	**1 : 3.29**		**1 : 3.48**	

TABLE 2: JOINT INVOLVEMENT OF ALL RA CASES

JOINT INVOLVEMENT	NUMBER *(n)*	PERCENTAGE *(%)*
1 Large Joint	0	0.00
2-10 Large Joint	2	1.94
1-3 Small Joint	26	25.24
4-10 Small Joint	47	45.63
> 10 Small Joints	26	25.24

From the above table it is observed that 45.63% patients had 4-10 small joints involvement followed by 25.24 % in two groups i.e. >10 small joints and 1-3 small joints. The least was 1.94% with 2-10 large joint involvement. 21.35% RA patients had thyroiddysfunction and 4.85% healthy volunteers had thyroid dysfunction in the control group. The study showed that of the 22 patients with thyroid dysfunction;90.9% were females and 9.1% males. Mean duration of RA disease was 5.9 ± 5.83 years in patients with thyroid dysfunction and 4.19 ± 3.55 years in patients with normal thyroid function. No significant difference was observed in between the mean duration of two groups.

TABLE 3 :PATTERNS OF THYROID DYSFUNCTION IN THE CASES AND CONTROLS

THYROID DYSFUNCTION	CASES	CONTROLS			*p value*
	n	%	*n*	%	
Normal	81	78.64	98	95.15	0.006543
Subclinical Hypothyroidism	12	11.65	4	3.88	
Hypothyroidism	6	5.83	1	0.97	
Subclinical Hyperthyroidism	4	3.88	0	0.00	
TOTAL	103	100.00	103	100.00	

TABLE 4: DISTRIBUTION OF THYROID DYSFUNCTION WITH DISEASE ACTIVITY

DAS28	PRESENT		ABSENT		TOTAL
	n	%	*n*	%	(n)
<2.6	0	0.00	1	100.00	1
2.6—<3.2	2	25.00	6	75.00	8
3.2—</=5.1	13	21.67	47	78.33	60
>5.1	7	20.59	27	79.41	34
TOTAL	22	21.36	81	78.64	103

**percentage were calculated row-wise*

The above table shows that 25% of patients in the low disease activity had thyroid dysfunction, followed by 21.67% in the moderate disease activity and 20.5% in the high disease activity group The above table shows that 5.82% RA patients with thyroid dysfunction was positive for Anti-TPO and 9.1% positive for anti-Tg and 9.1% for both Antibodies.

TABLE 5 : PATTERNS OF THYROID DYSFUNCTION AND ANTI THYROID ANTIBODIES

VARIABLES			THYROID DYSFUNCTION			
			Subclinical Hypothyroidism (n=12)	Subclinical Hyperthyroidism (n=4)	Subclinical Hyperthyroidism (n=4)	Total
Anti-Thyroid Antibody	Absent		7	2	3	12
	Present	Anti- TPO	4 (33.33%)	1 (16.6%)	1 (25%)	6
		Anti- Tg	0	2 (33.33%)	0	2
		Anti-TPO + Anti-Tg	1 (8.3%)	1 (16.6%)	0	2
	TOTAL		12	6	4	22

Percentage calculated column wise

From the above table it is observed that in the subclinical hypothyroidism group; 33.33% patients had Anti-TPO Antibody positive, and 8.3% had Anti-TPO + Anti-Tg Antibody. In the hypothyroisism group 33.33% patients had Anti- Tg Antibody followed by 16.6% patients in both the Anti- TPO and Anti-TPO + Anti-Tg. In the subclinical hyperthyroidism group only Anti-TPO was positive in 25% of patients.

TABLE 6: DISTRIBUTION OF ANTIBODY STATUS WITH THYROID DYSFUNCTION

ANTIBODY STATUS	PRESENT	ABSENT			TOTAL (n)	χ^2	*p value*
	n	%	n	%			
Anti-CCP+/ RF+	11	22.45	38	77.55	49	2.5482	0.4667
Anti-CCP+/RF–	7	18.92	30	81.08	37		
Anti-CCP–/RF+	4	33.33	8	66.67	12		
Anti-CCP–/RF–	0	0.00	5	100.00	5		
TOTAL	22	21.36	81	78.64	103		

It was observed that in the Anti-CCP–/RF+ group thyroid dysfunction was observed to be the highest (33.33%) followed by 22.45% in the Anti-CCP+/ RF+, 18.95 in the Anti-CCP+/RF– group. None of the patients with Anti-CCP–/RF– had thyroid dysfunction.

DISCUSSION

The present study was done to evaluate the spectrum of Thyroid Dysfunction in Rheumatoid Arthritis, and its relation to disease duration and disease activity.

In the present study, majority of the patients (27.18%) were in the age group of 40-49 years which is in accordance with the findings of Alamanos Y et al (2006)7; where disease incidence appeared to be greatest for women between 40 and 50 years of age.

In this study male to female ratio was 1: 3.29, it is comparable to the study by Fatima N et al (2013)8 in which the ratio was 1: 3.2 and the study by S. Chandrashekaraet al (2012)9with the ratio of 1: 3.96.

In the present study Thyroid dysfunction was 21.35% compared to 4.85% in controls. It is similar to the study byJeffrey et al (1993)10in which thyroid abnormalities was found in 24.26% compared to 11 % in the controls.In the study by Enas A et al (2013)11 thyroid abnormalities was seen in 29.3% compared to 8% in the control group. Kumar B et al (2014)12 study found thyroid disorders in

35.2% patients with RA and 22.2% in controls.

In our study it was observed that 25% of patients in the low disease activity had thyroid dysfunction, followed by 21.67% in the moderate disease activity and 20.5% in the high disease activity group. However, in the study by Enas a et al11in which hypothyroidism was the most common thyroid disorder, thyroid dysfuction was associated with high disease activity.

In the present study Subclinical hypothyroidism was seen in 12 (11.65%) , Hypothyroidism in 6 patients (5.83%), Subclinical hyperthyroidism in 4(3.88%) patients. It is comparable to HalaH et al13 in which Subclinical hypothyroidism was seen in 19%, Hypothyroidism in 4%, Subclinical hyperthyroidism in 2.6% and hyperthyroidism in 0.7% patients. In the study by El- Saadanyaet al14 Subclinical hypothyroidism was seen in 10.2% patients, hypothyroidism in 10.2%, and hyperthyroidism in 4.5%.

Mean duration of RA disease with thyroid dysfunction was 5.9 ± 5.83 years and 4.19 ± 3.55 years in patients with normal thyroid function. The difference was not statistically significant in between the two groups.

In the Anti-CCP–/RF+ group thyroid dysfunction was observed to be the highest (33.33%) followed by 22.45% in the Anti-CCP+/ RF+, 18.95% in the Anti-CCP+/RF– group. None of the patients with Anti-CCP–/RF– had thyroid dysfunction.In the study by Hala H et al(2014)13presence of RA markers and markers of inflammation revealed a statistically significant association between RF-positive RA and clinical hypothyroidism, and 4.9% of patients had both diseases with positive RF (P=0.027). Anti-CCP was not found to have a significant presence in co-existing RA and thyroid dysfunction.

In the present study anti-thyroid antibodies was seen in 10 RA patients (9.7%). anti-TPO Ab alone was found in 6 patients (5.8%) followed by anti –Tg in 2 patients (1.9%) and both in 2 patients (1.9%).In the study by Enas A et al11anti-TPO and anti-Tg antibodies in RA patients was present in 9.3 and 3.3%, respectively. In the study by Mousaet al(2012)15anti-TPO and anti-Tg antibodies was found in 10% and 6% of Egyptian RA patients.

CONCLUSION

Our study showed that abnormal thyroid function tests, particularly subclinical hypothyroidism was seen more commonly in patients with Rheumatoid arthritis compared to controls.Thyroid dysfunction was found more in the low disease activity group and is not associated with disease duration. Thus the presence of non-specific suggestive symptoms in a RA patient in spite of a low disease activity may be a clinical pointer to the underlying thyroid disorder requiring laboratory evaluation.Physicians should be aware of screening RA patients periodically for this comorbidity, especially when the specific symptoms may overlap between both diseases and accordingly manage on becomingovert hypothyroid orsymptomatic.

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