

CLINICO-BIOCHEMICAL PROFILE OF HYPOTHYROIDISM IN RHEUMATOID ARTHRITIS

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ABSTRACT

Objectives: The incidence of co-occurrence of multiple autoimmune diseases in a single patient is constantly increasing. Conditions with auto immune backgrounds such as rheumatoid arthritis and thyroid dysfunction have an immense relationship. This study was designed to evaluate the association biochemical parameters and disease progression in rheumatoid arthritis cases with hypothyroidism.

Methods: A total of 120 adult participants diagnosed with rheumatoid arthritis with suggestive hypothyroidism between 21 and 55 years of age were included in this study. All cases underwent complete laboratory investigations including thyroid profile. Depending on the diagnostic outcome of the thyroid profile, the participants were divided into two groups, that is, group 1 consists of rheumatoid arthritis with hypothyroidism and group 2 consists of rheumatoid arthritis without hypothyroidism.

Results: The higher mean values of FT3 and FT4 were observed in RA with hypothyroidism and mean levels of thyroid function test were statistically significant in between the study groups ($p < 0.05$). The hypertriglyceridemia in 43.3% cases, hypercholesterolemia in 58.3%, hyperuricemia in 26.6%, and diabetes mellitus in 35% cases were commonly observed metabolic complications.

Conclusion: The higher levels of metabolic complications, namely, hypercholesterolemia, hyperuricemia, hypertriglyceridemia, and diabetes mellitus were noticed in rheumatoid arthritis with hypothyroidism. Regular screening of patients is recommended to monitor the status of the condition and to maintain a healthy lifestyle.

Keywords: Rheumatoid arthritis, Thyroid function test, Hypothyroidism.

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory condition that affects around 0.5–1% of the general population and is 3 times more common in women [1]. This idiopathic disease affects multiple tissues and organs but mainly affects the synovial joints. Malaise, fatigue, and morning stiffness are the characteristic symptoms of RA [2]. RA is associated with several autoimmune diseases including autoimmune thyroiditis which leads to hypothyroidism [3]. Thyroid dysfunction has an inverse relationship with rheumatoid arthritis. Moreover, this relationship is still an ongoing debate. The thyroid dysfunction was 3 times more common in women with RA than women with rheumatic conditions such as osteoarthritis and fibromyalgia [4].

Several studies have reported that thyroid dysfunction and RA are strongly associated, probably due to autoimmunity but could not justify. Few other studies assessed clinical characteristics and the impact of thyroid dysfunction on diseases activity [5]. This study was designed to evaluate the association biochemical parameters and disease progression in rheumatoid arthritis cases with hypothyroidism.

METHODS

A total of 120 adult participants diagnosed with rheumatoid arthritis with suggestive hypothyroidism were recruited for this cross-sectional study carried out in the Department of General Medicine at East Point college of Medical Sciences and Research Centre, Bangalore from January 2021 to December 2021.

Inclusion criteria

The diagnosis was made according to the American College of Rheumatology (ACR) criteria for rheumatoid arthritis [6]. According to the Dutch National Health-care Consensus Committee, the elevated

level of TSH >4.2 μ IU/ml with lower than reference range of T3/T4 considered as hypothyroidism.

Exclusion criteria

Cases below 21 years and above 55 years of age, in pregnancy, history of thyroid surgery, and under medication for hypothyroidism were excluded from the study. After briefing the study procedure, written informed consent was obtained from all the study participants and Institutional Ethics Committee approval was obtained.

The patients attending the OPD of rheumatology with a history of thyroid complications and newly diagnosed with thyroid diseases were undergone thyroid function tests to evaluate TSH, FT3, and FT4 levels. Depending on the diagnostic outcome values, the participants were divided into two groups, that is, group 1 consists of rheumatoid arthritis with hypothyroidism and group 2 consists of rheumatoid arthritis without hypothyroidism. The parameters include serum lipid profile and LFT. RFT and their link to the disease progression and severity were assessed.

Statistical analysis

The recorded data were extracted into the Microsoft Excel sheet. The SPSS version 16.0 was used to carry out statistical analysis relevant to the study. The demographic and categorical variables were represented in the form of frequency and percentages. The continuous variables were represented in mean and standard deviation. The Student "t" test was used to test the significant difference of mean. $p < 0.05$ was considered statistically significant.

RESULTS

The mean age was 44.64 ± 6.25 in rheumatoid arthritis cases with hypothyroidism and 45.80 ± 6.92 in rheumatoid arthritis cases without

hypothyroidism. The mean difference of age was statistically significant ($p < 0.001$). Female participants were dominant in both the study groups. The mean difference in waist circumference was statistically not significant ($p = 0.256$) (Table 1).

The mean levels of thyroid function test were statistically significant in between both the study groups ($p < 0.05$) (Tables 2 and 3).

DISCUSSION

Rheumatoid arthritis is widely associated with various autoimmune diseases, autoimmune thyroiditis is important among, which resulting hypothyroidism [7]. The mean age was 44.64 ± 6.25 in group 1 and 45.80 ± 6.92 in group 2 and the difference was statistically significant ($p < 0.001$). Hypothyroidism was observed more common in females than males [8-10]. The above findings were similar with the present study where female dominance was observed in RA with hypothyroidism (female 36 and male 24). A study by Haitham *et al.* reported a higher prevalence of hypothyroidism in females (76.66%) [11].

The higher mean values of FT3 and FT4 were observed in RA with hypothyroidism. The mean levels of thyroid function test were statistically significant in both the study groups ($p < 0.05$). The FT3 ($p < 0.001$), FT4 ($p < 0.001$), and TSH ($p < 0.001$) levels showed a significant difference in the RA cases with hypothyroidism. The higher levels and positive correlation TSH are associated with the higher grades of RA disease activity [8]. A study by Haitham *et al.* reported a positive correlation between TSH and ESR, which indicate higher disease activity when TSH levels were high [11]. A study by Israa M. Saqre *et al.* noticed higher T3 and T4 levels in female cases with RA. However, TSH levels were higher in males than females [12].

The common metabolic complications associated are hypertriglyceridemia in 43.3% cases, hypercholesterolemia in 58.3%, hyperuricemia in 26.6%, and diabetes mellitus in 35% cases (Table 4). The elevated level of cholesterol was observed in cases with hypertriglyceridemia which may be responsible for the triggering of cardiovascular complications and diminishing the eGFR. The group 1 cases with hypertriglyceridemia and diabetes may be reasons for the escalation of serum bilirubin and serum AST levels.

Hypercholesterolemia was the common metabolic complication noticed in 58.3% of cases which were associated with reduced ejection fraction, eGFR, and lung disease in 40%, 22.85%, and 8.57% cases, respectively. Around 26.6% of cases reported hyperuricemia and associated with diminishing in eGFR in 43.75% of cases. Diabetes mellitus was noticed in 35% cases and associated with the lower levels of eGFR in 52.38%.

The ESR levels were higher in RA cases with autoimmune thyroid disorders (AITD) than without AITD. A significant elevation in ESR levels is associated with RA cases with hypothyroidism [12]. Similar findings were observed with elevated ESR levels were observed in RA with hypothyroidism (26.94 ± 10.26). A study by Joshi *et al.* found elevated levels of ESR in cases with RA with hypothyroidism (36.3 ± 24.2) than only RA (24.6 ± 9.0) [13]. The elevated ESR levels strengthen the role of hypothyroidism in the triggering of inflammatory mechanisms in rheumatoid arthritis. However, few studies reported no significant increase in the ESR with hypothyroidism in RA [11,14,15].

Anne *et al.* stated the prevalence of hypothyroidism more in cases with RA, especially among young women [2]. Enas *et al.* concluded that hypothyroidism was commonly associated with rheumatoid arthritis and has a significant association with the parameter triggering disease activity [8]. Haitham *et al.* and Nadeem *et al.* concluded that thyroid dysfunction commonly associated with RA and hypothyroidism is the most prevalent form among [11]. In the present study, the majority of cases in group 1 had vulnerable metabolic complications such as hypercholesterolemia, hyperuricemia, and diabetes mellitus. In addition, these metabolic complications are associated with renal

Table 1: Descriptive data of demographic variables in two study groups

Demographic variable	Group 1 (n=60)	Group 2 (n=60)	p-value
Age (In years)	44.64±6.25	45.80±6.92	0.001
Gender (M: F)	24:36	28:32	-
Waist circumference	78.63±6.55	76.78±6.84	0.256

Table 2: Comparison of thyroid function test between two study groups

Thyroid parameters	Group 1	Group 2	p-value
FT3	100.14±15.26	136.28±24.30	0.003
FT4	6.28±2.32	9.56±2.88	0.002
TSH	2.84±2.52	1.87±1.02	0.026

Table 3: Laboratory investigation profile between the two study groups

Parameters	Group 1	Group 2	F	p-value
	Mean±SD	Mean±SD		
FBS (mg/dl)	119.23±39.98	92.34±28.65	11.45	0.002
PBS (mg/dl)	168±26.24	140±20.18	19.64	0.002
HBA1C	5.89±0.84	5.69±0.64	1.78	0.314
TGL (mg/dl)	141.23±28.02	104.44±30.58	8.10	0.002
Serum cholesterol (mg/dl)	189.2±31.20	163.48±28.94	5.88	0.002
LDL (mg/dl)	114.06±37.64	96.22±35.45	5.62	0.028
HDL (mg/dl)	45.34±10.41	48.67±8.82	5.12	0.004
Serum creatinine (mg/dl)	1.02±0.24	0.28±0.56	1.48	0.075
Serum uric acid	8.98±4.57	6.32±2.35	12.684	0.001
Serum bilirubin	0.75±0.26	0.76±0.53	0.168	0.538
eGFR	84.35±28.51	92.38±30.18	1.91	0.003
Ejection fraction value	53.38±7.74	57.20±7.28	1.786	0.048
Hb levels	10.99±3.62	12.45±3.84	1.538	0.074
ALT levels	29.99±5.42	29.36±5.08	0.043	0.065
ESR	26.94±10.26	18.12±8.76	8.612	0.004

*FBS: Fasting blood sugar, PBS: Postprandial blood sugar, TGL: Triglycerides, LDL: Low density cholesterol, HDL: High density cholesterol, ESR: Erythrocyte sedimentation ratio. * $p < 0.05$ is statistically significant.

Table 4: Elevated levels of factors associated with development hypothyroidism (n=60)

Factors	Frequency	Percentage
Hypertriglyceridemia	26	43.3
Hypercholesterolemia	35	58.3
Hyperuricemia	16	26.6
Diabetes mellitus	21	35

and cardiovascular complications which strengthen the role of hypothyroidism in triggering rheumatoid arthritis. Further studies are needed to evaluate the natural history of thyroid dysfunction in RA cases to formulate standardized duration between assessments of thyroid function.

CONCLUSION

The higher levels of metabolic complications, namely, hypercholesterolemia, hyperuricemia, hypertriglyceridemia, and diabetes mellitus were reported in rheumatoid arthritis with hypothyroidism than without hypothyroidism. Regular screening of patients is recommended to monitor the status of the condition and to maintain a healthy lifestyle.

AUTHOR CONTRIBUTION

Conceptualization, data Acquisition, data analysis and interpretation, manuscript preparation, revision of manuscript, and approval of final version of manuscript: Dr. Preema Khan.

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CONFLICT OF INTEREST

Nil.

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