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RESEARCH ARTICLE

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## STUDY OF THE BIOCHEMICAL DETERMINATION, ANTICIPATION AND COMPLEXITIES INTERRELATED WITH THE SIMALTANEOUS OCCURANCE OF HYPOTHYROIDISM IN RHEUMATOID ARTHRITIS

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### ABSTRACT

**Introduction:** In rheumatoid arthritis, Chronic inflammation of rheumatoid arthritis can cause permanent joint destruction and deformity. **Objective:** To study the disruption of biochemical assessment, the prognosis and the development of complications associated with the occurrence of hypothyroidism and rheumatoid arthritis. **Method:** The patients included in our study 50 case study and 50 control were collected from all RA patients who attended rheumatology outpatient department or those who were admitted as inpatients in medical wards in Rajeev Gandhi College and General Hospital, Bhopal .MP. India. Determination of thyroid function TSH, T3, T4, lipid profile and hypertensive also in rheumatoid arthritis patients was performed. **Result:** This study shows that out of the 50 patients with RA and hypothyroidism, most of these patients, nearly 62% had dyslipidaemia. There was no significant difference noticed in Sr. Bilirubin, ALT and AST levels between the study and control groups There was a significant elevation in ESR levels among the RA patients with hypothyroidism when compared with the control group. **Conclusion:** The metabolic alterations reported in RA patients with hypothyroidism has been significantly higher than that of the control group. The role of screening and prompt initiation of treatment for hypothyroidism in all RA patients should be considered and implemented. The importance of thyroid screening in RA patients and its impact on better prognosis and prevention of complications has been well established.

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## INTRODUCTION

Rheumatoid arthritis is an autoimmune disease that causes chronic inflammation of the joints and other areas of the body, characterized by periods of disease flares and remissions. In rheumatoid arthritis, multiple joints are usually, but not always, affected in a symmetrical pattern. Chronic inflammation of rheumatoid arthritis can cause permanent joint destruction and deformity. Damage to joints can occur early and does not always correlate with the severity of the disease (Firestein, 2003). Among the RA patients who were screened for thyroid function abnormality, hypothyroidism accounted to a clearly large number present in nearly 27% patients. It has also been proved that Hypothyroidism is associated with an Increased Risk of Cardiovascular Events in Patients with Rheumatoid Arthritis (Delamere, 1982). Rheumatoid arthritis (RA) patients are at increased risk of cardiovascular disease (CVD), which is even more pronounced in hypothyroid RA patients. An unfavourable cardiovascular risk profile conferred by a higher prevalence of the metabolic syndrome

(MetS) and a higher Framingham risk score might explain this amplified cardiovascular morbidity. This study compared first, MetS (features) and second, the Framingham 10-year CVD risk in RA patients with hypothyroidism compared with euthyroid RA patients. (Joshi, 2011). In case of RA synovitis, there is massive effusion within the joint space. Thus, the flexion of the knee causes an increase in the intra- articular pressure which causes out pouching of the posterior components of the knee joint there by leading on to popliteal or Baker's cyst. This high pressure may even cause rupture down into the calf space or less often into the posterior aspect of the thigh. The rupture usually occurs between the medial head of the gastrocnemius and the tendinous insertion of the biceps. An intact popliteal cyst can cause the compression of the superficial venous flow to the thigh thereby leading on to dilatation of the veins, edema or both. Systemic symptoms like fever and leukocytosis may be seen when there is rupture of the cyst into the posterior aspect of the calf. The physical sign is manifested by the appearance of crescentic hematoma beneath one of the malleoli. Oxidative stress in rheumatoid

arthritis results due to increased pressure in synovial cavity, reduced capillary density, vascular changes, increased metabolic rate of synovial tissue and locally activated leukocytes. The repeated ischemic perfusion injury in the joint causes the production of reactive oxygen species. The free radical reactions are facilitated by the release of iron, heme and copper ions. Electron transport chain are affected in the mitochondria and this also contributes to the disease pathology. Around 8 to 15% of the patient have acute onset of the symptoms that peaks within few days. The patients with acute onset have less symmetrical pattern of joint involvement than those with the insidious onset, whereas those people with intermediate onset have more noticeable systemic symptoms.

### Aims & Objectives

**Aims:** To study the disruption of biochemical assessment, the prognosis and the development of complications associated with the occurrence of hypothyroidism and rheumatoid arthritis.

### Objectives

1. To diagnose the biochemical determination in rheumatoid arthritis patients with hypothyroidism.
2. To study the concatenation of disease activity of rheumatoid arthritis due to hypothyroidism.
3. To assess the issue associated with the concurrent incidence of hypothyroidism in rheumatoid arthritis.

## METHODOLOGY

**Study Design:** Case control study (comparative cross-sectional study).

**Source of Subjects:** The patients included in our study were collected from all RA patients who attended rheumatology outpatient department or those who were admitted as inpatients in medical wards in Rajeev Gandhi College and General Hospital, Bhopal .MP. India.

**Source of Data:** The source of the entire data was from the patients diagnosed to have RA and RA with hypothyroidism either in OPD or wards in Rajeev Gandhi College and General Hospital, Bhopal .MP. India.

**Duration of study:** January 2023-July 2023.

### Inclusion Criteria

1. Age group – 20 to 50 years
2. Newly or previously diagnosed rheumatoid arthritis patients with thyroid function test suggestive of hypothyroidism.

### Exclusion Criteria

1. Patients < 20 years and > 50 years of age
2. Patients with primary thyroid disease including neoplasm
3. History of intake of drugs known to cause hypothyroidism
4. Any collagen vascular disorder other than rheumatoid arthritis
5. Patients who have undergone thyroid surgery
6. Pregnant women

## MATERIALS AND METHOD

Assessment of thyroid function in rheumatoid arthritis patients was performed using the following:

1. Thyroid stimulating hormone (TSH)
2. Free serum tri-iodothyronine (FT3) level
3. Free serum thyroxin level (FT4)
4. Normal range for these parameters are as follows: TSH: 0.28-5.0 IU/ml, free T3: 2.37-4.58 pg/ml, and Free T4 : 0.89-1.81 ng/dl.

5. All these parameters were measured from serum sample of patients collected in the early morning using immunometric assays and quantitative values were obtained. Subclinical hypothyroidism: it is indicated by increased serum TSH in the presence of a normal serum FT4 level. Clinical hypothyroidism is diagnosed based on an increase in the serum TSH levels with low levels of serum FT4 level, along with the presence of clinical symptoms and signs of hypothyroidism.

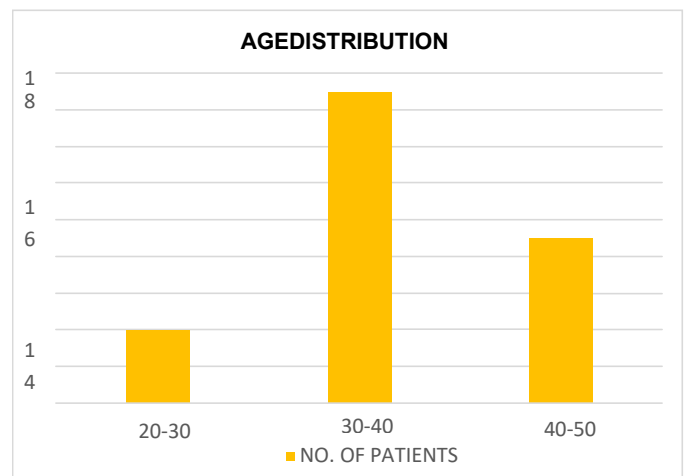
Based on the thyroid function tests, the rheumatoid arthritis patients were classified into two groups: rheumatoid arthritis with hypothyroidism and rheumatoid arthritis alone. The biochemical parameters such as liver function tests, serum lipid profile is compared in two subgroups: rheumatoid arthritis patients with coexisting hypothyroidism and patients with rheumatoid arthritis alone. The incidence of complications in the two-sub group of patients was analysed in the study. The prognosis and the severity of disease progression is analysed according to the derangement in biochemical parameters and with the development of complications. The results are tabulated and analysed for statistical significance using SPSS statistical tool version 17.0.

## RESULTS

### AGEDISTRIBUTION

**Table 1. According to distribution pf population**

AGEGROUP	CENSUS
20-30	2
30-40	33
40-50	15



**Chart 1. Showing age distribution of the study group**

According to the above results, a greater number of RA patients with hypothyroidism fall into the age group of 30-40 years. This is in accordance with the results of previous studies and is significant.

**Table 2. Illustrates the HBA1C levels among the RA Patients with and without hypothyroidism**

### Report

Normality	Mean	N	Std.Deviation
Control	5.764	50	0.5572
Study	5.938	50	0.8790
Total	5.851	100	0.7374

Hba1C values of the control and study group do not differ. From the above two variables namely FBS values and HbA1c values, the prevalence of Diabetes Mellitus among the control group and study group is estimated. This is done considering either one of the two being positive for the diagnosis of Diabetes Mellitus. In our study, we have analyzed the various metabolic parameters in patients with

Rheumatoid Arthritis. The patients were initially screened for presence of hypothyroidism using TSH levels, Free T3 and T4 levels and further divided into two groups- one group with hypothyroidism and those without hypothyroidism. There was a significant difference in the prevalence of metabolic abnormalities like elevated Sr. cholesterol, Sr. TGL, fasting blood sugars between the two groups studied.

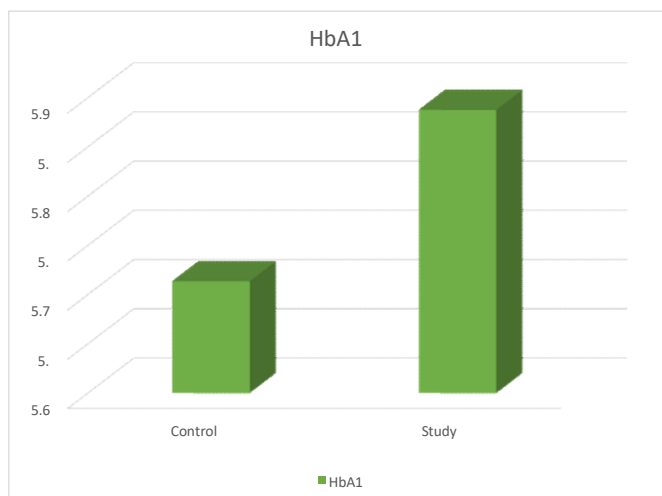


Chart 2. Showing distribution of HbA1c levels in control and studygroup

## DISCUSSION

The simultaneous occurrence of hypothyroidism in RA has been proved to have significant impact over the development of metabolic alterations in comparison with patients without hypothyroidism. This duration of this study was one year and it was conducted at Coimbatore Medical College Hospital. It was a comparative cross-sectional study. According to this study, a close association was established between the RA patients with hypothyroidism and the above-mentioned metabolic alterations. Hypercholesterolemia was found to be the most common metabolic abnormality among the RA patients with hypothyroidism. In this study of 50 patients of RA with hypothyroidism, the prevalence of hypercholesterolemia was noted in 31 patients accounting to about 62% of the study population. Among these patients with elevated sr. cholesterol (n=31), renal impairment in the form of reduced eGFR was noted in 6 patients (19.6%). In our study, out of these 31 patients with hypercholesterolemia, 11 patients had a significant reduction in the Ejection Fraction. Interstitial lung disease was found in only two patients among those with hypercholesterolemia. Hypertriglyceridemia stands to be the second commonly reported metabolic derangement. Nearly 12 patients with hypertriglyceridemia had significantly elevated total cholesterol levels and about 9 patients had borderline cholesterol levels. All these factors combined together had a significant impact over the development of complications like reduced eGFR and cardiovascular events in RA patients with hypothyroidism.

Hyperuricemia was noted in 15 RA patients with hypothyroidism (n=50) which accounts to about 30%. Among these 15 patients with hyperuricemia, reduction in eGFR was noted in about 12 patients (82%). Hence, a positive correlation was established between those with hyperuricemia and renal failure. The subgroup of RA patients with hypothyroidism had a fairly low serum HDL levels, which further contributed to the ill effects. All these metabolic derangements occurred at a much higher rate among RA patients with concomitant hypothyroidism. This proves that hypothyroidism is associated with an acceleration of ongoing inflammatory and pathological processes in RA. This also results in devastating cardiovascular, renal and CNS complications which are preventable to some extent with earlier identification and treatment of hypothyroidism. This study shows that out of the 50 patients with RA and hypothyroidism, nearly 22 patients had reduction in ejection fraction and 11 among them showed

echocardiographic evidence of regional wall motion abnormality. Most of these patients, nearly 62% had dyslipidemia. There was no significant difference noticed in Sr. Bilirubin, ALT and AST levels between the study and control groups. The standard distribution of the measurements of waist circumference were almost equal among both the groups. There was a significant elevation in ESR levels among the RA patients with hypothyroidism when compared with the control group. This strongly proves the role of hypothyroidism in the acceleration of the underlying inflammatory mechanisms in RA. Almost one third of the study group had all the three main metabolic abnormalities namely hypercholesterolemia, diabetes mellitus and hyperuricemia. The cardiovascular and renal manifestations were also found to be significant in this group, thereby proving the role of hypothyroidism in the acceleration of the disease process in RA. Also, hypothyroidism has been shown to increase the all-cause mortality and morbidity associated with RA.

## Summary

we conclude from our study that the existence of serum metabolic alterations correlated well with hypothyroidism in RA patients. Thus, there has been various postulates for classifying these patients and also in the determination of prognosis and complications of the disease. Thus, the occurrence of hypothyroidism in RA could be either an immune mediated phenomenon or any metabolic disease that might mimic hypothyroidism. Thus, to help us in the diagnosis of hypothyroidism in RA patients, an updated criteria should be postulated in order to facilitate earlier identification and initiation of thyroxine treatment.

## CONCLUSION

The biochemical parameters available at our hospital namely – sr. cholesterol, sr. triglycerides, sr. LDL, blood glucose levels and sr. uric acid levels were studied. Also, the presence of various complications of the disease process has been studied and shortlisted. The metabolic alterations reported in RA patients with hypothyroidism has been significantly higher than that of the control group. The role of screening and prompt initiation of treatment for hypothyroidism in all RA patients should be considered and implemented. The importance of thyroid screening in RA patients and its impact on better prognosis and prevention of complications has been well established.

**Limitations:** Limitation of this study is that the outcome of patients who received immune modulators and biological agents could not be studied. Moreover, the cause for the reduction in the glomerular filtration rate, whether it was an immune mediated process or a metabolic alteration leading on to a reduction in the eGFR couldn't be established properly. Being an invasive procedure renal biopsy was not attempted in these patients.

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