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Original Research Article

Evaluation of Thyroid Function in Autoimmune Connective Tissue Disorder

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Abstract

Introduction: Autoimmune connective tissue disorders (ACTDs) such as systemic lupus erythematosus, rheumatoid arthritis, and scleroderma often coexist with other autoimmune conditions, including autoimmune thyroid disease. Thyroid dysfunction can significantly influence disease activity and patient outcomes in ACTDs. Early identification of thyroid abnormalities is crucial for comprehensive management.

Aims: This study aims to evaluate the prevalence and pattern of thyroid function abnormalities in patients diagnosed with autoimmune connective tissue disorders and to analyze the correlation between thyroid dysfunction and clinical parameters of ACTDs.

Methods: The present study was a cross-sectional observational study conducted in the Department of General Medicine, Endocrinology Clinic at Calcutta National Medical College and Hospital. The study population comprised patients attending the outpatient department as well as those admitted to the general medicine ward. The study was carried out over a period of one year, from 2015 to 2016. A total of 110 patients diagnosed with Autoimmune Connective Tissue Disorders (ACTDs) were included in the study to evaluate thyroid function in this specific population.

Results: In this study of hypothyroid patients, a high prevalence of anemia was observed, with 84.04% having hemoglobin levels below 12 gm%. The most common anemia type was normocytic normochromic (61.05%), followed by microcytic hypochromic (35.78%) and macrocytic hyperchromic (3.15%). Hematological indices showed that 78.46% had low packed cell volume (<40), while most had normal mean corpuscular volume (75.38%) and normal mean corpuscular hemoglobin (63.84%). Elevated red cell distribution width was present in 67.69%, indicating anisocytosis. Total red blood cell counts mostly indicated mild to moderate reduction. Bleeding and clotting times were largely normal. Total leukocyte counts were normal in 88.46%, with some cases of leukopenia and leukocytosis. Platelet counts were generally normal, with mild thrombocytopenia in a small fraction and no severe thrombocytopenia detected, suggesting thrombocytopenia is uncommon in hypothyroidism.

Conclusion: Thyroid dysfunction, particularly hypothyroidism, is common in patients with autoimmune connective tissue disorders. Routine screening for thyroid abnormalities should be incorporated into the clinical evaluation of ACTD patients to enable timely intervention and potentially improve disease prognosis.

Keywords: Autoimmune Connective Tissue Disorder, Thyroid Function, Autoimmune Thyroid Disease, Rheumatoid Arthritis, Endocrine Dysfunction.

Introduction

Autoimmune connective tissue disorders (ACTDs) represent a heterogeneous group of systemic diseases characterized by immune-mediated inflammation primarily targeting connective tissues, resulting in multi-organ involvement and significant morbidity [1]. Common ACTDs include systemic lupus erythematosus (SLE), systemic sclerosis, rheumatoid arthritis (RA), polymyositis, dermatomyositis, and mixed connective tissue disease (MCTD) [2]. The pathogenesis of these disorders involves complex interactions between genetic susceptibility, environmental triggers, and dysregulation of immune tolerance, leading to production of autoantibodies and chronic

inflammation [3]. Thyroid dysfunction, particularly autoimmune thyroid disease (AITD), has been increasingly recognized as a frequent comorbidity in patients with ACTDs, reflecting shared immunogenetic pathways and overlapping autoimmunity [4].

The thyroid gland, an essential endocrine organ, regulates metabolism, growth, and development through secretion of thyroid hormones (thyroxine - T4 and triiodothyronine - T3) [5]. Autoimmune thyroid diseases, including Hashimoto's thyroiditis and Graves' disease, are characterized by lymphocytic infiltration of the thyroid gland and the presence of circulating autoantibodies such as anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-Tg) antibodies [6]. These autoimmune processes can result in hypothyroidism or hyperthyroidism, with systemic manifestations that can overlap or exacerbate symptoms of ACTDs, complicating clinical assessment and management [7].

Several studies have reported a higher prevalence of thyroid dysfunction among patients with various ACTDs compared to the general population [8]. For instance, hypothyroidism is commonly observed in SLE and RA patients, potentially due to the coexistence of autoimmune thyroiditis or as a consequence of chronic inflammation and immune dysregulation [9]. Moreover, subclinical thyroid dysfunction, often underdiagnosed, may contribute to fatigue, arthralgia, and mood disturbances, symptoms that overlap with those of ACTDs, thus necessitating routine thyroid function evaluation in these patients [10]. Early detection and treatment of thyroid abnormalities may improve overall disease outcomes and quality of life in ACTD patients.

The assessment of thyroid function in ACTD involves clinical evaluation along with biochemical tests measuring serum levels of thyroid-stimulating hormone (TSH), free T4, free T3, and thyroid autoantibodies [11]. Despite the recognized association, the exact mechanisms linking thyroid autoimmunity and ACTDs remain incompletely understood, and variability in thyroid dysfunction prevalence has been reported among different ACTD subtypes and ethnic populations [12]. Further research is warranted to elucidate the immunopathological links and to develop standardized screening protocols for thyroid function in ACTD patients. To assess the prevalence of left ventricular diastolic dysfunction associated with subclinical hypothyroidism and reducing frequency of these manifestation which can provide better understanding of epidemiology.

Materials and Methods

Sample design: Cross sectional observational study.

Study Area: Department of General Medicine**,** Endocrinology Clinic, Calcutta National Medical College and Hospital.

Study Population: Patient attending outpatient department and admitted in the general medicine ward.

Study Period: One year (2015 -2016).

Sample Size: 110 Autoimmune Connective Tissue Disorder Patients.

Inclusion Criteria

1. Patient age between 05- 70 year
2. Normal level of S.T3, S.T4
3. Elevated S.TSH value
4. Not taking any drug affecting t2dm HTN

Exclusion Criteria

1. Patients those unwilling to participate in the study.
2. Cigarette smoking or use of any drug.
3. Malignancy, surgery and major trauma in the last six months.

Study Tools

Lab Investigation

Essential investigation in all cases

- S.T3, S. T4, S.TSH
- TWBC
- TRBC
- HB
- MCHC
- MCH
- MCV
- RDW
- TPC
- Peripheral blood morphology

Special investigations

- ECG
- CXR PA view
- 2D colour Doppler

Statistical Analysis: For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5).

Numerical variables were summarized using means and standard deviations, while Data were entered into Excel and analyzed using SPSS and GraphPad Prism. Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Two-sample t-tests were used to compare independent groups, while paired t-tests accounted for correlations in paired data. Chi-square tests (including Fisher's exact test for small

sample sizes) were used for categorical data comparisons. P-values ≤ 0.05 were considered statistically significant.

Result

Table 1: Distribution of Hemoglobin Levels and Types of Anemia among Study Patients

Parameter		No. of patient	%
Hb %	>12 gm	15	15.96
	< 12 gm	79	84.04
	Total	94	100
Type of anaemia	Microcytic Hypochromic anaemia	34	35.78%
	Normocytic Normochromic anaemia	58	61.05%
	Macrocytic Hyperchromic anaemia	3	3.15%
	Total	95	100

Table 2: Distribution of Red Blood Cell Indices (PCV, MCV, MCH, MCHC) Among Study Patients

Parameter		Number of patients	%
PCV	< 40	102	78.46
	40–50	24	18.46
	>50	4	3.07
	Total	130	100
MCV	<80	29	22.3
	80-100	98	75.38
	>100	3	2.3
	Total	130	100
MCH	<27	37	28.46
	27-32	83	63.84
	>32	10	7.69
	Total	130	100
MCHC	<32	31	23.84
	32-35	94	72.3
	>35	5	3.84
	Total	130	100

Table 3: Distribution of Red Blood Cell Indices (PCV, MCV, MCH, MCHC) Among Study Patients

Parameter		Number of patients	%
Red Cell Distribution Width	<14	42	32.3
	>14	88	67.69
	Total	130	100
TRBC /cmm	<1.5	5	3.84
	2-4	118	90.7
	>4	7	5.38
	Total	130	100

Table 4: Distribution of Bleeding Time, Clotting Time, and Total Leukocyte Count among Study Patients

Parameter		Number of patients	%
Bleeding Time	<6 mins	124	95.39
	>6 mins	6	4.61
	Total	130	100
Clotting Time	<10 mins	130	100
	>10 mins	0	0
	Total	130	100
Total Leucocyte count/ cmm	>4000	11	8.46
	4000-11000	115	88.46
	>11000	4	3.07
	Total	130	100

Table 5: Distribution of Platelet Count among Study Patients

Parameter		No. of patient	%
Platelet count/cmm	<10000	0	0
	10000-20000	0	0
	21000-30000	0	0
	30000-40000	1	0.76
	40000-1 lakhs	10	7.69
	1-1.5 lakhs	14	10.76
	1.5-4 lakhs	100	76.92
	>4 lakhs	5	3.84

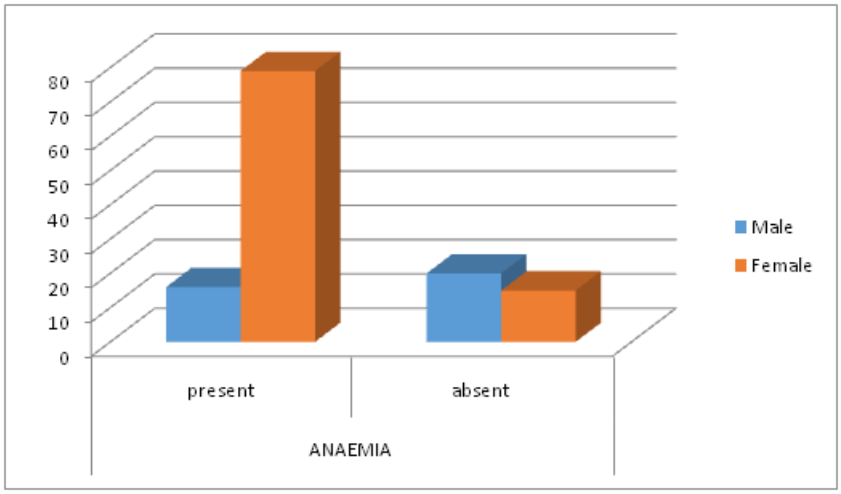

Figure 1: Distribution of Anemia among Hypothyroid Patients in Relation to Sex in the Study Population

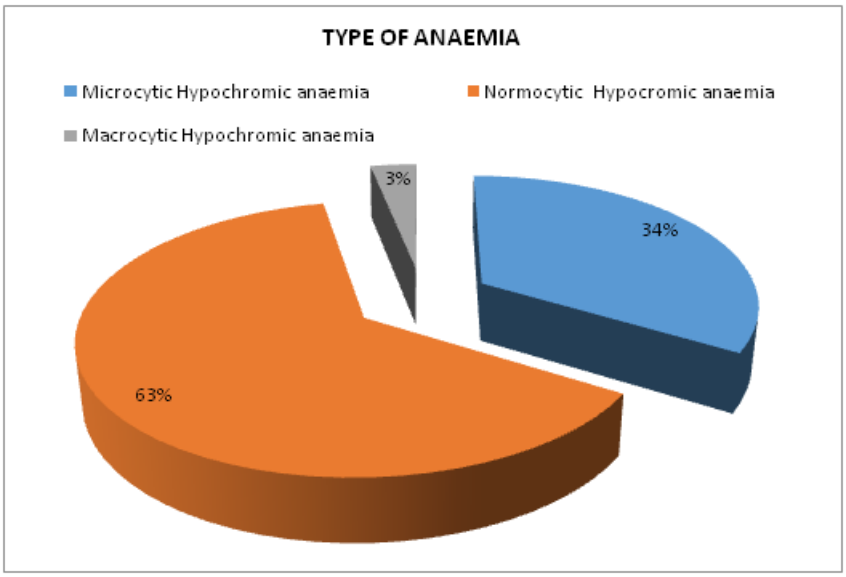

Figure: 2. Distribution of Types of Anemia in the Study Population

In the present study, out of 94 hypothyroid patients evaluated for hemoglobin levels, 84.04% (n=79) were found to have hemoglobin levels less than 12 gm%, indicating a high prevalence of anaemia in this population. Only 15.96% (n=15) had normal hemoglobin levels (>12 gm%). Regarding the type of anaemia, among 95 patients assessed, normocytic normochromic anaemia was the most common type, observed in 61.05% (n=58) of cases, followed by microcytic hypochromic anaemia in 35.78% (n=34), and macrocytic hyperchromic anaemia in 3.15% (n=3). In the present study involving 130 hypothyroid patients, hematological indices revealed significant variations. Packed Cell Volume (PCV) was found to be less than 40 in 102 patients (78.46%), indicating a high prevalence of anemia, while 24 patients (18.46%) had PCV between 40–50, and only 4 patients (3.07%) had values above 50. Mean Corpuscular Volume (MCV) was within the normal range (80–100 fL) in

98 patients (75.38%), while 29 patients (22.3%) had microcytosis (MCV <80 fL), and 3 patients (2.3%) had macrocytosis (MCV >100 fL). Mean Corpuscular Hemoglobin (MCH) was low (<27 pg) in 37 patients (28.46%), normal (27–32 pg) in 83 patients (63.84%), and elevated (>32 pg) in 10 patients (7.69%). Mean Corpuscular Hemoglobin Concentration (MCHC) was reduced (<32 g/dL) in 31 patients (23.84%), normal (32–35 g/dL) in 94 patients (72.3%), and increased (>35 g/dL) in 5 patients (3.84%).

Red Cell Distribution Width (RDW) was elevated (>14) in 88 patients (67.69%), indicating significant anisocytosis, while 42 patients (32.3%) had normal RDW values (<14). Total Red Blood Cell (TRBC) count showed that the majority of patients (118; 90.7%) had TRBC values between 2–4 million/cmm, suggesting a mild to moderate reduction in red cell mass. A small proportion had values <1.5 million/cmm (5 patients; 3.84%) or >4 million/cmm (7 patients; 5.38%).

In this study, bleeding time was found to be within normal limits (<6 minutes) in 124 patients (95.39%), while 6 patients (4.61%) had prolonged bleeding time (>6 minutes). Clotting time was normal (<10 minutes) in all 130 patients (100%), with no prolongation observed. Regarding total leukocyte count (TLC), 115 patients (88.46%) had counts within the normal reference range (4000–11000 cells/cmm), 11 patients (8.46%) had leukopenia (<4000 cells/cmm), and 4 patients (3.07%) showed leukocytosis (>11000 cells/cmm).

Platelet counts were within or close to the normal range for the majority of patients. Specifically, 100 patients (76.92%) had platelet counts between 1.5 to 4 lakh/cmm, which is considered normal. Counts between 1 to 1.5 lakh/cmm were observed in 14 patients (10.76%), and 10 patients (7.69%) had counts ranging from 40,000 to 100,000/cmm, indicating mild thrombocytopenia. Only 1 patient (0.76%) had a platelet count between 30,000 to 40,000andcmm. Elevated platelet counts (>4 lakh/cmm) were seen in 5 patients (3.84%). No cases of severe thrombocytopenia (<30,000/cmm) were observed. Overall, platelet profiles suggest that thrombocytopenia is uncommon in this hypothyroid cohort.

Discussion

The present study demonstrates a high prevalence of anemia among hypothyroid patients, with 84.04% (n=79/94) exhibiting hemoglobin levels below 12 gm%, consistent with previous literature that identifies anemia as a common hematological abnormality in hypothyroidism [13, 14]. The predominance of normocytic normochromic anemia (61.05%) aligns with findings reported by Das et al. [15] and Krishnan et al. [16], where normocytic normochromic anemia was the most frequently observed pattern, likely reflecting a chronic disease anemia component linked to thyroid hormone deficiency. The presence of microcytic hypochromic anemia in 35.78% of cases may indicate concomitant iron deficiency or impaired iron metabolism, as documented in studies by Dorgalaleh et al. [17] and Desai et al. [18]. Macrocytic anaemia, though less common (3.15%), could be attributed to associated vitamin B12 or folate deficiency, which has also been documented in hypothyroid patients [19].

Our hematological indices further corroborate the high anemia burden, with 78.46% of patients having a packed cell volume (PCV) below 40%, and 22.3% showing microcytosis on mean corpuscular volume (MCV) assessment. Elevated red cell distribution width (RDW) in 67.69% of patients signifies marked anisocytosis, consistent with previous observations by Sanyal et al. [20], suggesting a heterogeneous population of erythrocytes possibly due to nutritional deficiencies or ineffective erythropoiesis. The majority of patients exhibited normal or mildly reduced total red blood cell counts, reflecting a mild to moderate degree of anemia rather than severe bone marrow suppression.

Coagulation parameters in this cohort showed normal clotting times across all patients, while a small percentage (4.61%) had prolonged bleeding time. This finding aligns with the work of Kanwal et al. [21], who reported subtle platelet function abnormalities in hypothyroid patients despite normal platelet counts. Platelet counts in our study were predominantly within the normal range, with only a minority exhibiting mild thrombocytopenia and very few showing thrombocytosis, consistent with the observations by Chaudhary et al. [22]. This supports the concept that while hypothyroidism can impact platelet function, significant thrombocytopenia is uncommon.

Total leukocyte counts were largely within normal limits, though leukopenia was present in 8.46% of patients. This finding has been variably reported in hypothyroid populations, with some studies indicating mild leukopenia due to decreased bone marrow stimulation [23].

Conclusion

We conclude that, in this study of hypothyroid patients, anemia was highly prevalent, with 84% exhibiting hemoglobin levels below 12 gm%. Normocytic normochromic anemia was the predominant type, followed by microcytic hypochromic anemia. Most patients showed reduced packed cell volume (PCV <40%) and a majority had normal mean corpuscular volume (MCV), although microcytosis was also noted in about one-fifth. Mean corpuscular hemoglobin (MCH) and concentration (MCHC) were decreased

in a significant subset, while red cell distribution width (RDW) was elevated in over two-thirds, indicating anisocytosis. Total red blood cell counts were mildly to moderately reduced in most cases. Coagulation parameters were largely normal, with only a small fraction showing prolonged bleeding time and no clotting time abnormalities. Total leukocyte counts were normal in most patients, though leukopenia and leukocytosis were observed in a minority. Platelet counts predominantly fell within the normal range, with mild thrombocytopenia being uncommon. Overall, these findings indicate that anemia with varied red cell indices is a frequent hematological abnormality in hypothyroid patients, whereas coagulation and platelet profiles remain mostly unaffected.

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