(IJRST) 2023, Vol. No. 13, Issue No. 3, Jul-Sep **e-ISSN: 2249-0604, p-ISSN: 2454-180X**

# Study of Prevalence of Thyroid Dysfunctions in Connective Tissue Disorders[1]

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*DOI:10.37648/ijrst.v13i03.003*

*Received: 02 June 2023; Accepted: 08 July 2023; Published: 10 July 2023*

**ABSTRACT:**

Thyroid dysfunctions are detected in 41% of connective tissue disorders. Majority have autoimmune thyroid dysfunction; however Indian data is missing.

**Aims & Objectives:** To evaluate thyroid dysfunctios in connective tissue disorders. in This study was conducted of patients, having connective tissue disorders like Systemic Lupus Erythematosus, Rheumatoid Arthritis, Systemic Sclerosis, Sjogren's syndrome, Dermatomyositis, Sarcoidosis, vasculitis and Spondyloarthropathy were studied. Patients were evaluated for coexisting thyroid dysfunctions.

**Material & Methods:** All patients were tested for T3, T4, and TSH and anti thyroid antibodies having Connective tissue disorders.

**Result:** Our study demonstrates, autoimmune connective tissue diseases have high prevalence of thyroid dysfunctions. Hypothyroidism is the commonest thyroid dysfunction documented in our study. Therefore it is clinically important to screen patients early with systemic autoimmune diseases for the co-existence of thyroid disorders.

**Keywords**: *Connective tissue disorders (CTD); Thyroid Function Test (TFT); Rheumatoid Arthritis (RA); Systemic Lupus Erythematosus (SLE); Systemic Sclerosis (SS); Sjogren's syndrome; Syndrome (SjS); Spondyloarthropathy (SPA); Dermatomyositis (DM).*

## INTRODUCTION

Thyroid dysfunctions in connective tissue disorders (CTD) are common than in general population [1]. Aim of our study was to evaluate prevalence of thyroid dysfunctions in connective tissue disorders patients like Systemic Lupus Erythematosus, Rheumatoid Arthritis, Systemic Sclerosis, Sjogren's syndrome, Dermatomyositis, Sarcoidosis, and Spondyloarthropathy. Various patterns of thyroid dysfunctions like hypothyroidism, hyperthyroidism, and autoimmune thyroiditis were studied.

[1] How to cite the article: Kalekar L., Thakur L., Bhavsar P., Digole A., Bagul A. (July 2023); Study of Prevalence of Thyroid Dysfunctions in Connective Tissue Disorders; *International Journal of Research in Science and Technology*, Vol 13, Issue 3, 40-49, DOI: http://doi.org/10.37648/ijrst.v13i03.003

## MATERIALS AND METHODS

This is cross sectional; observational study was conducted during Jan 2018- June 2019 in Rheumatology services of a tertiary care centre in Western India. Study was approved by institutional ethics committee. 100 CTD patients fulfilling American College of Rheumatology Criteria for classification [2] were enrolled from IPD and OPD. All data was collected using a predefined protocol. Pregnant females and children were excluded. Patients diagnosed with Systemic Lupus Erythematosus, Rheumatoid Arthritis, Systemic Sclerosis, Sjogren's syndrome, Dermatomyositis, Sarcoidosis, and Spondyloarthropathy were included in the studies.

Complete history, physical examination and laboratory investigations were done. Presence of thyroid dysfunction was detected by T3, T4, TSH and thyroid antibodies tests.

**Statistical Analysis:** Statistical analysis was carried out for 100 patients with various connective tissue disorders. The data was analyzed by percentage analysis, Chi Square test and SPSS version 22.0.

## RESULTS

In our study out of 100 patients with CTD, which includes 30 SLE ,20 RA,10 Systemic sclerosis,5 each of Vasculitis, Sjogren's Syndrome, Dermatomyositis, Sarcoidosis, Seronegative RA and SPA, and 10 of Spondyloarthropathy respectively from age group 18-75 years.

Out of 100 CTD patients, 83 were female (45 females < 40 and 38 females > 40 years of age group) and 17 were males (13 males < 40 and 4 males > 40 years of age) Statistically significant correlation was found between thyroid dysfunction with age and sex in connective tissue disorders ($p<0.001$). (Table 1).

Out of 36 patients with thyroid dysfunction, 34(94.44%) were females (16 were <40 and 18 were > 40 years old and 2(5.55%) were males, 1 each from > 40 and < 40 age group. 64 patients were euthyroid ( 48 females and 16 males) with 41(64.06%) patients were < 40 and 23 ( 35.93%) patients were > 40 .Out of 48 (75%) females 29(60.41%) were < 40 and 19(39.58%) were > 40. Out of 17 males 13 were < 40 and 4 were > 40 years old. This suggests female preponderance with CTD and thyroid dysfunction (significant $p < 0.001$).

Out of 100 CTD patients, 64 were euthyroid and 36 had thyroid dysfunction. Out of 36 patients with thyroid dysfunction, 38.88% SLE(14/30), 11.11% Systemic sclerosis (4/10), 19.44% RA (7/20), 2.77% Vasculitis (1/5) and 5.55% each in Ankylosing Spondylitis (2/5) , Sjogren's syndrome (2/5), Dermatomyositis(2/5), Seronegative RA (2/5) respectively had thyroid dysfunction. (Table 2)

Out of 30 SLE, 14 patients had thyroid dysfunction (6 subclinical hypothyroid and 8 autoimmune $p <0.001$).Out of 20 RA patients 7 had thyroid dysfunction (4 overt hypothyroidism and 3 autoimmune =0.556).Out of 10 Systemic sclerosis 5 had thyroid dysfunction (2 hyperthyroidism, 1 subclinical hypothyroidism,1 subclinical hyperthyroidisms and 1 autoimmune thyroiditis, $p<0.015$).Out of 5 vasculitis patient,1 had hyperthyroidism<0.001,. Out of 2 dermatomyositis patients 2 had hypothyroidism $p=0.239$, out of 5 Sarcoidosis patients 2 had overt hypothyroidism=0.329. Out of 10 patients of Ankylosing Spondylitis 2 had hypothyroidism. Out of 5 Seronehative RA patients $p<0.019$. So significant p value <0.005) was seen in SLE, Sjogrens syndrome, Systemic Sclerosis, Vasculitis and Seronegative RA. (Table 3).

Out of 36 patients with thyroid dysfunction, 14(38.88%) had autoimmune thyroid dysfunction and 22(61.11%) had clinical thyroid dysfunction. Out of 14 autoimmune thyroid dysfunction, 8(66.66%) had autoimmune hypothyroidism, 2(16.66%) had autoimmune subclinical hypothyroidism, 1(8.33%) had autoimmune subclinical hyperthyroidism and 4 (28.57%) had autoimmune thyroiditis.

31(86.11%) patients had hypothyroidism. Out of 31 patients, 22 (70.96%) had clinical hypothyroidism and 9(29.03%) had autoimmune hypothyroidism. ( (Table 4 & Table 5)

**DISCUSSION:**

In our study, 100 patients of connective tissue disorders were enrolled. 36 patients had thyroid dysfunction. Out of 83 female patients of connective tissue disorders 34(94.44%) females had thyroid dysfunction and out of 17 males,2 (5.55 %) male patients had thyroid dysfunction. So thyroid dysfunction is more common in females than in male patients with connective tissue disorders patients.

Thyroid dysfunction is more common in < 40 years of age in connective tissue disorders patients. Mainly hypothyroidism was more common. Statistically significant correlation was found between thyroid dysfunction with age of connective tissue disorders patients in our study.
Out of 100 patients of connective tissue disorders, 36% had thyroid dysfunction out of that, 14(36.11%) had anti TPO positive test.

Out of 14 patients who had autoimmune thyroid dysfunction, 8 had autoimmune hypothyroidism,1(16.66%) had subclinical hypothyroidism, 1(8.33%) each had hyperthyroidism and subclinical hyperthyroidism respectively. So Statistically significant correlation was found between thyroid dysfunction and connective tissue disorders in our study.

In a study done by Arnaout MA [3,] et al.Scand J prevalence of thyroid dysfunction was 3.2 %, Prevalence of hypothyroidism was 3% and Prevalence of autoimmune thyroid pathology was 7 %. Our correlation is supported by Y Gokhale [4]. According to this study prevalence of thyroid dysfunction (30%) and in our study it was 40 % and autoimmune thyroid pathology was found in 14 % patients and .in our study it was 20%.

Out of 30 SLE patients, 14 (46.66%) had thyroid dysfunction. 7(50%) had autoimmune thyroid dysfunction (3 autoimmune hypothyroid, 2 autoimmune thyroiditis,1 autoimmune subclinical hypothyroid, and 1 autoimmune hyperthyroid) 5(35.51%) had subclinical hypothyroidism.So Statistically significant correlation was found between thyroid dysfunction and systemic lupus erythematous in our study. It correlates with study done by Miry Blich et al, [5],S.A Chambers et al [6], Hui Wu et al(7)and Namijou B et al [8].

Out of 20 patients of RA, 5(25%) had thyroid dysfunction, All had hypothyroidism 4(20%) had subclinical hypothyroidism, 1(5%) had autoimmune overt hypothyroidism) . So Statistically significant correlation was found between thyroid dysfunction and Rheumatoid arthritis in our study. Our correlation was supported by study done by Shiroky JB et al [9], Porkodi R et al [10].

Out of 10 patients of Systemic Sclerosis, 4(40%) had thyroid dysfunction, all had hypothyroidism (2(20 %) had subclinical hypothyroidism,(1(10% )had autoimmune overt hypothyroidism, 1 had autoimmune subclinical hypothyroidism) and 20 % had autoimmune thyroid pathology (10% had autoimmune overt hypothyroidism, 10 % had autoimmune subclinical hypothyroidism). So Statistically significant correlation was found between thyroid dysfunction and systemic Sclerosis in our study. Our correlation was supported by Gordon MB et al study [11].

Out of 5 patients of vasculitis, 20 % had thyroid dysfunction (20 % autoimmune overt hyperthyroidism) . Statistically significant correlation was found between thyroid dysfunction and vasculitis in our study.
In contrast to our study in YAVNE Y study [12] . Prevalence of hypothyroidism was 18.2 % and prevalence of hyperthyroidism was 2.56.

Out of 5 patients of Sarcoidosis 40% had thyroid dysfunction, all had hypothyroidism (20 % had subclinical hypothyroidism,20% had autoimmune overt hypothyroidism) and 20 % had autoimmune thyroid pathology (all had autoimmune overt hypothyroidism). So the prevalence of thyroid dysfunction in our study population was higher than control group (6% hypothyroidism and 1% autoimmune thyroid pathology). Statistically significant correlation was found between thyroid dysfunction and Sarcoidosis in our study. According to Atonally A et al [13].

Out of 10 patients of Ankylosing Spondylitis , 20% had thyroid dysfunction, all had hypothyroidism (20% had subclinical hypothyroidism, 20 % had overt hypothyroidism.

However no statistically significant correlation was found between thyroid dysfunction and AS in our study. According to Lange u study [14]. prevalence was lower than our study group (10%vs 20%) while prevalence of autoimmune thyroid pathology was found higher than our study ( 13% vs 0%) and Peluso R et al [15] .

Statistically significant correlation was found between thyroid dysfunction and Sjogren syndrome in our study and study done by Zeher M et al .[16]

Out of 5 patients of Dermatomyositis 40% had thyroid dysfunction all had hypothyroidis.Statistically significant correlation was found between thyroid dysfunction and Dermatomyositis in our study . and study by Newman et al.[17]

Out of 5 patients of Seronegative Spondyloarthropathy (SRA) patients, 40% had thyroid dysfunction and all had subclinical hypothyroidism. So the prevalence of thyroid dysfunction in our study population was higher than control group (6% hypothyroidism and 1% autoimmune thyroid pathology). Statistically significant correlation was found between thyroid dysfunction and SRA in our study.

## CONCLUSION

Prevalence of thyroid dysfunction is high with connective disorders as compared to in normal population. Autoimmune thyroid dysfunction is common in female less than 40 years of age. Prevalence of hypothyroidism (mostly subclinical) is common than hyperthyroidism in connective tissue disorders. Occurrence of autoimmune thyroid pathology is 16% in connective tissue disorders. Thyroid dysfunctions are more common in Systemic lupus erythematous, Rheumatoid arthritis, Sarcoidosis, Systemic sclerosis, Jorgen syndrome, Dermatomyositis, Seronegative Rheumatoid arthritis than vacuities' and spondyloarthropathies.

In summary, polyautoimmunity is frequent in connective tissue disorders, and is influenced by clinical and immunological features. Systemic and thyroid autoimmune diseases often overlap with each other. Therefore it is clinically important to screen patients with systemic autoimmune diseases for the co-existence of thyroid disorders. Patients with co-existing thyroid disease and connective tissue disorders may escape clinical detection because of overlapping clinical features. Hence serological testing for autoimmune thyroid disease and appropriate treatment is warranted in this subset of patients for better quality of life.

## LIMITATIONS

Sample size: Only 100 patients were enrolled in the study. Study could have been more effective with larger sample size.

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**TABLE 1: Correlation between thyroid dysfunction, AGE and**

**And Sex in CTD (p<0.001 Significant).**

| **CTD STATUS** | **N=100** | **AGE <40** | **AGE >40** |
|---|---|---|---|
| FEMALES | 83 | 45(54.21%) | 38(45.78%) |
| MALES | 17 | 13(76.47%) | 4(23.52%) |
| **THYROID STATUS** | **36** | **17(47.22%)** | **19(52.77%)** |
| FEMALES | 34(94.44%) | 16(47.05%) | 18(52.95%) |
| MALES | 2(5.55%) | 1(5.55%) | 1(50%) |
| **EUTHYROID STATUS** | **64** | **41(64.06%)** | **23 (35.93%)** |
| FEMALES | 48(75%) | 29(60.41%) | 19(39.58%) |
| MALES | 16(25%) | 12(75%) | 4 (25%) |

**TABLE 2: CORRELATION BETWEEN DEMOGRAPHIC DATA WITH CTD.**

| SR NO | CTD(N= 100) | CTD N=100 | FEMALE (82 ) | MALE ( 18 ) | THYROID DYSFN | EU THYROID |
|---|---|---|---|---|---|---|
| | | | <40 >40 | <40 >40 | | |
| 1 | SLE | 30 | 16 12 | 2 0 | 14 (38.88%) | 16((25%) |
| 2 | RA | 20 | 7 11 | 0 2 | 7(19.44%) | 13(20.31%) |
| 3 | SYSTEMIC SCLEROSIS | 10 | 8 2 | 0 0 | 4(11.11%) | 6(9.37%) |
| 4 | VASCULITIS | 5 | 3 2 | 0 0 | 1(2.77%) | 4(6.25%) |
| 5 | SJOGREN'S SYNDROME | 5 | 4 1 | 0 0 | 2(5.55%) | 3(4.68%) |
| 6 | DERMATOMYOSITIS | 5 | 2 3 | 0 0 | 2(5.55%) | 3(4.68%) |
| 7 | SARCOIDOSIS | 5 | 3 1 | 1 0 | 2(5.55%) | 3(4.68%) |
| 8 | SPONDYLOARHROPATHY | 10 | 0 1 | 8 1 | 2(5.55%) | 8(12.5%) |
| 9 | SERO-NEG RA | 5 | 1 4 | 0 0 | 2(5.55%) | 3(4.68%) |
| 10 | SERO-NEG SPA | 5 | 1 1 | 2 1 | 0 | 5(7.81%) |
| | TOTAL | 100 | 45 38 | 13 4 | 36 | 64 |
| | | | 83 | 17 | | |

**TABLE 3: Thyroid Dysfunction in CTD with demographic features**

| **SR. NO** | **TYPE OF THYROID DYSFUNCTION(32)** | **FEMALE (30)** | **MALE (2)** | **TOTAL (32 )** | **%** |
|---|---|---|---|---|---|
| | Age | <40 > 40 | <40 >40 | | |
| 1 | Autoimmune Thyroiditis | 2 2 | 0 0 | 4 | 12.5% |
| 2 | Autoimmune Hypothyroidism | 8 0 | 0 0 | 8 | 25% |
| 3 | Autoimmune Hyperthyroidism | 0 1 | 0 0 | 1 | 3.12% |
| 4 | Autoimmune Subclinical Hypothyroidism | 1 0 | 0 0 | 1 | 3.12% |
| | **TOTAL AUTOIMMUNE THYROID DISEASE (A)** | **11 3** | **0 0** | **14** | **43.75%** |
| 5 | Subclinical Hypothyroidism | 5 15 | 1 0 | 21 | 65.6% |
| 6 | Hypothyroidism | 0 0 | 1 0 | 1 | 3.12% |
| 7 | Subclinical Hyperthyroidism | 0 0 | 0 0 | 0 | 0% |
| 8 | Hyperthyroidism | 0 0 | 0 0 | 0 | 0% |
| | **OTHER THYROID DYSFN (B)** | **5 15** | **2 0** | **22** | **68.75%** |
| | **A+B** | **16 18** | **2 0** | **36** | **36%** |
| | | **34** | **2** | **36** | |
| | **Euthyroid** | **29 19** | **12 4** | **68** | **68%** |
| | **TOTAL** | **48** | **16** | **64** | |

**Table 4: TABLE OF CORRELATION BETWEEN CTD AND THYROID DYSFUNCTION WITH P VALUE**

| | CTD (N=100) | NO. OF PATIENTS | THYROID DYSFUN | EU | HYPO | HYPER | SUBCL HYPO | SUBCL HYPER | AUTO HYPO | AUTO HYPER | AUTO EU | AUTO SUBCL HYPO | AUTO SUBCL HYPER | P Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 100 | 36 | 64 | 15 | 2 | 6 | 0 | 4 | 1 | 6 | 1 | 1 | 36 |
| 1 | SLE | 30 | 14 (46.6%) | 16 | 0 | 0 | 7 | 0 | 3 | 1 | 2 | 1 | 1 | <0.001 Significant |
| 2 | RA | 20 | 7 (32.5%) | 15 | 4 | 0 | 0 | 0 | 1 | 0 | 2 | 0 | 0 | 0.556 |
| 3 | Sjogren's Syndrome | 5 | 2 (40%) | 3 | 1 | 1 | O | 0 | 0 | 0 | 0 | 0 | 0 | 0.015 Significant |
| 4 | Systemic Sclerosis | 10 | 4 (40)%) | 6 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0.002 Significant |
| 5 | Vasculitis | 5 | 1 (20%) | 4 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.001 Significant |
| 6 | Dermatomyositis | 5 | 2 (40%) | 3 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.329 |
| 7 | Sarcoidosis | 5 | 2 (40%) | 3 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.329 |
| 8 | Ankylosing Spondylitis | 10 | 2 (20%) | 8 | 2 | 0 | 0 | | 0 | 0 | 0 | 0 | 0 | 0.257 |
| 9 | Seronegative RA | 5 | 2 (40%) | | 0 | 0 | 0 | | 0 | 0 | 3 | | 0 | 0.019 Significant |

**TABLE 5: Prevalence of Thyroid dysfunction and Autoimmunity in CTD patients.**

| SR N O | THYROID DYSFUNCTN | FREQUENCY | ANTI TPO POSITIVE | TOTAL |
|---|---|---|---|---|
| | **TOTAL** | 83 | 17 | 100 |
| 1. | **EUTHYROID** | 60(93.75%) | 4(6.25%) | 64 |
| 2. | **THYROID DYSFUNCTION** | 22(61.11%) | 14(38.88%) | 36 |
| A | SUBCLINICAL HYPOTHYROIDISM | 21(58.33%) | 1(4.54%) | 22 |
| B | SUBCLINICAL HYPERTHYROIDISM | 0 | 1(8.33%) | 1 |
| C | Overt HYPOTHYROIDISM | 1(2.77%) | 8(22.22%) | 9 |
| D | Overt HYPERTHYROIDISM | 0 | 0 | 0 |
| E | THYROIDITIS | 0 | 4 (11.11%) | 4 |