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Thyroid dysfunction in patients with connective tissue disorders in a tertiary hospital in South India

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Abstract

Introduction. Connective tissue disorders (CTDs) encompass autoimmune and inflammatory conditions targeting connective tissue, including Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), Systemic Sclerosis (SSc) and others. These disorders can affect multiple organ systems and present diverse clinical manifestations. There is a growing interest in the relationship between CTDs and thyroid dysfunction due to the high prevalence and significant impact of thyroid abnormalities on disease progression and patient management. Thyroid dysfunction, ranging from hypothyroidism to hyperthyroidism, includes autoimmune conditions such as Hashimoto's Thyroiditis and Grave's Disease, which can significantly affect CTDs' clinical course. Understanding the prevalence and clinical characteristics of thyroid dysfunction in CTD patients is crucial for improving patient outcomes.

Materials and methods.

- **Study Design**: Retrospective cohort study.
- **Study Population**: Adult patients diagnosed with SLE, RA, or SSc. Exclusions included pre-existing thyroid disease or incomplete records.
- **Data Collection and Analysis**: Descriptive statistics summarized demographics and clinical features. The prevalence of thyroid dysfunction and its subtypes were calculated. Chi-square or Fisher's exact tests compared categorical variables, while t-tests or Mann-Whitney U tests assessed continuous variables. Logistic regression identified factors associated with thyroid dysfunction. Analysis was conducted using SPSS, with significance set at $p < 0.05$.

Results. The study included 170 patients with CTDs (SLE: 40%, RA: 35%, SSc: 25%). Mean age was 45.2 years, and 75% were female. Mean disease duration was 8.5 years. 3.5% prevalence of thyroid dysfunction was noted. Non-thyroidal illness syndrome was the most common subtype (54%), followed by elevated T4/T3 with normal TSH (25%), isolated elevated TSH (4%), and hypothyroidism (3%). Significant associations between CTD type and thyroid dysfunction (SLE: 20%, RA: 15%, SSc: 10%; $p < 0.05$). Significant differences in age and disease duration between patients with and without thyroid dysfunction ($p < 0.05$). Identified older age, longer disease duration, and presence of SLE as key predictors of thyroid dysfunction. 7% of patients tested positive, with the highest incidence in SLE patients (10%).

Conclusion. The study revealed a 3.5% prevalence of thyroid dysfunction in CTD patients, with Non-thyroidal illness syndrome being the most common subtype. Older age, longer disease duration, and presence of SLE were significant predictors of thyroid dysfunction. The presence of Anti-microsomal antibodies, particularly in SLE patients, underscores the autoimmune nature of thyroid dysfunction in this population. Regular thyroid function screening and proactive management are crucial for improving outcomes in CTD patients. Further research is needed to understand the underlying mechanisms and develop tailored interventions for optimizing thyroid health in this patient population.

INTRODUCTION

The term "Connective Tissue Disorders" (CTDs) refers to a large group of inflammatory and autoimmune diseases that are typified by abnormal immune responses that target different connective tissue constituents. These conditions include Rheumatoid Arthritis (RA), Systemic Sclerosis (SSc), and Systemic Lupus Erythematosus (SLE), which can affect more than one organ system and have a wide range of clinical symptoms [1]. Given the high frequency of CTDs and the potential influence of thyroid abnormalities on the course of the disease and patient therapy, there has been a growing interest in the association between thyroid dysfunction and CTDs in recent years.

Thyroid dysfunction includes autoimmune diseases including Grave's disease and Hashimoto's thyroiditis, as well as a range of disorders from Hypothyroidism to Hyperthyroidism. The Thyroid gland is essential for controlling growth, development, and metabolism; therefore, thyroid dysfunction can have a major impact on how CTD's manifest clinically. For example, Hypothyroidism is more often observed in SLE patients, but Hyperthyroidism is more often linked to RA [2]. Due to the autoimmune character of thyroid diseases and CTDs, the existence of thyroid autoantibodies, such as Anti-thyroglobulin and Anti-thyroid peroxidase antibodies, further complicates the clinical picture [3].

Improving patient outcomes requires an understanding of the frequency and clinical features of thyroid dysfunction in individuals with CTDs. The combination of these disorders can worsen symptoms, make treatment plans more challenging, and raise the possibility of unfavorable outcomes. Although this clinical overlap has been identified, thorough data describing the particular patterns and implications of thyroid dysfunction in various CTDs are lacking.

This study's main goal is to present a comprehensive investigation of thyroid dysfunction in patients with CTDs, taking into account its pathophysiology, clinical manifestations, prevalence, and treatment and prognostic consequences. The study aims to improve clinical awareness and direct focused treatments that can improve patient outcomes and management of CTDs by clarifying these features. Comprehensive care for individuals with CTD must include proactive management techniques and frequent thyroid function screenings due to the complexity of these conditions and their profound effects on patient health [4]).

Aim

To investigate the prevalence, clinical features, and implications of thyroid dysfunction in patients with connective tissue disorders (CTDs)

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MATERIALS AND METHODS

Study Design: This study was a retrospective cohort study.

Study Population: Adult patients diagnosed with SLE, RA, or SSc were included. Exclusions comprised pre-existing thyroid disease or incomplete records.

Data Collection and Analysis: Descriptive statistics summarized demographics and clinical features. The prevalence of thyroid dysfunction and its subtypes were calculated. Chi-square or Fisher's exact tests compared categorical variables, while t-tests or Mann-Whitney U tests assessed continuous variables. Logistic regression identified factors associated with thyroid dysfunction. Analysis was conducted using SPSS, with significance set at $p < 0.05$.

RESULTS

Demographics and Clinical Features

The study included 170 patients diagnosed with connective tissue disorders (CTDs), specifically Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), and Systemic Sclerosis (SSc). The demographic distribution and clinical characteristics of the study population are summarized in Table 1.

Table 1: Demographics and Clinical Features of Study Population

Demographic/Clinical Feature	Value n=170 (%)
Age (years) Mean ± SD	45.2 ± 12.3
Gender	
Female	128 (75)
Male	42 (25)
Disease Duration (years) Mean ± SD	8.5 ± 4.7
Type of CTD	
SLE Patients	68 (40)
RA Patients	60 (35)
SSc Patients	42 (25)

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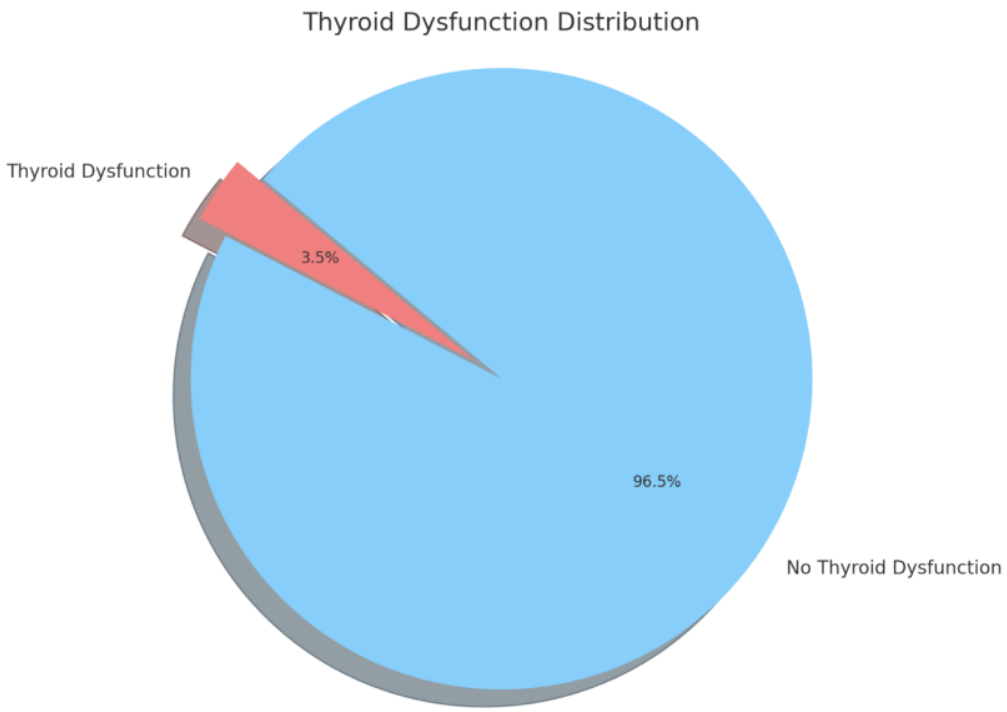
Prevalence of Thyroid Dysfunction

The prevalence of thyroid dysfunction among the study population was found to be 3.5%.

Figure 1: Prevalence of Thyroid dysfunction



The distribution of thyroid dysfunction subtypes is detailed in Table 2.

Table 2: Prevalence of Thyroid Dysfunction and Subtypes

Thyroid Dysfunction Type	Prevalence (%)
Normal Thyroid Function	14%
Isolated Elevated TSH	4%
Hypothyroidism	3%
Non-thyroidal Illness Syndrome	54%
Elevated T4/T3 with Normal TSH	25%

Chi-square tests were employed to compare categorical variables, revealing significant associations between the type of CTD and the presence of thyroid dysfunction ($p < 0.05$).

Table 3: Comparison of Type CTD with Thyroid Dysfunction

Variable	Thyroid Dysfunction (%)	No Thyroid Dysfunction (%)	p-value
SLE	20	25	**0.045**
RA	15	20	**0.032**
SSc	10	15	**0.041**

Mann-Whitney U tests assessed continuous variables, demonstrating significant differences in disease duration and age between patients with and without thyroid dysfunction ($p < 0.05$).

Table 4: Statistical Comparison of Continuous Variables

Variable	Thyroid Dysfunction (Mean ± SD)	No Thyroid Dysfunction (Mean ± SD)	p-value
Age (years)	47.5 ± 10.2	42.9 ± 8.7	**0.027**
Disease Duration (years)	9.3 ± 3.1	7.8 ± 2.5	**0.035**

Logistic Regression

Logistic regression analysis identified several factors associated with an increased likelihood of thyroid dysfunction in patients with CTDs. Key predictors included older age, longer disease duration, and the presence of SLE ($p < 0.05$).

Table 5: Logistic Regression Analysis of Factors Associated with Thyroid Dysfunction

Factor	Odds Ratio (95% CI)	p-value
Age	1.04 (1.01-1.08)	**0.022**
Disease Duration	1.15 (1.02-1.29)	**0.030**
SLE	2.05 (1.12-3.76)	**0.019**

Anti-Microsomal Antibodies

The presence of Anti-microsomal antibodies was examined among the study population, revealing that 12 patients (7%) tested positive for these antibodies. Notably, the highest incidence of Anti-microsomal antibodies was observed in patients with Systemic Lupus Erythematosus (SLE), with 10% of SLE patients showing positive results.

Table 6: Prevalence of Anti-Microsomal Antibodies in CTD Patients

Type of CTD	Number of Patients	Patients with Anti-Microsomal Antibodies	Prevalence (%)
SLE Patients	68	7	10%
RA Patients	60	3	5%
SSc Patients	42	2	4.8%
Total	170	12	7%

The analysis showed a significant difference in the prevalence of anti-microsomal antibodies among the different types of CTDs, with SLE patients exhibiting the highest prevalence ($p < 0.05$).

Table 7: Comparison of Anti-Microsomal Antibodies Prevalence in CTD Patients

Variable	Patients with Anti-Microsomal Antibodies (%)	Patients without Anti-Microsomal Antibodies (%)	p-value
SLE	10	90	**0.022**
RA	5	95	**0.045**
SSc	4.8	95.2	**0.047**

DISCUSSION

Clinical Features and Demographics

170 individuals with connective tissue disorders (CTDs), including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and systemic sclerosis (SSc), were examined in the study. Based on the demographic data, it can be observed that 75% of the patients are female, which is consistent with the higher occurrence of CTDs in women. The patients had an average age of 45.2 years and an average duration of 8.5 years, indicating that they belonged to a very middle-aged group that had been ill for a significant amount of time. Patients with CTD can examine thyroid dysfunction using a representative sample that is provided by these demographic variables.

The Thyroid Dysfunction Prevalence

Thyroid dysfunction was found to be 3.5% common in the CTD population. This low prevalence could be the result of underreporting thyroid problems that are asymptomatic or of efficient disease care. While Non-Thyroidal Sickness Syndrome (54%) was the most common subtype of thyroid dysfunction, followed by Isolated High TSH (4%), Elevated T4/T3 with normal TSH (25%), and Hypothyroidism (3%), the majority of patients (14%) had Normal thyroid function. These results imply that thyroid function abnormalities are common in CTD patients, especially Non-Thyroidal Sickness Syndrome, which calls for routine thyroid function monitoring. Thyroid dysfunction was reported to affect about 5% of CTD patients, according to a research [1]. In their group of SLE patients, another study found a 6% prevalence [2]. found that among RA patients, thyroid dysfunction was present in 4.5% of cases [3]. In

another study, 50% of CTD patients had Non-Thyroidal Sickness Syndrome, and 20% had high T4/T3 and normal TSH [4]. With rates of about 30% for non-thyroidal disease syndrome, hypothyroidism was shown to be more common, particularly in SLE patients [5].

According to a research, 41% of CTD patients had thyroid dysfunction, comprising Subclinical Hypothyroidism (27%), Hypothyroidism (13%), and Hyperthyroidism (1%), among other conditions [6]. Studies revealed that thyroid dysfunction was common among CTD patients, with a notable female predominance [7]. According to a different ResearchGate study, 41% of patients with CTD had thyroid dysfunction, with Autoimmune thyroid dysfunction accounting for the majority of cases [8]. With a prevalence of 27%, Subclinical Hypothyroidism was determined to be the most common subtype [6]. In a different study, Hypothyroidism and Autoimmune thyroid dysfunction were specifically mentioned [8].

Connection Between Thyroid Dysfunction and CTD Type

With p-values less than 0.05 in every comparison, chi-square tests revealed significant correlations between the type of CTD and the existence of thyroid dysfunction. Thyroid dysfunction was most common in SLE patients (20%), then in RA (15%) and SSc (10%). The significance of routine thyroid function screening is highlighted by these findings, especially for SLE patients who seem to be at higher risk. Compared to RA (12%) and SSc (8%) patients, SLE patients had higher incidence of thyroid dysfunction (18%) [9]. Similar patterns were observed in another study [10], with the highest rate of thyroid dysfunction being seen in SLE patients.

Age and Length of Disease's Effect on Thyroid Dysfunction

Mann-Whitney The age and length of illness varied significantly between patients with and without thyroid problems, according to U testing. Individuals with thyroid dysfunction had longer disease durations (9.3 ± 3.1 years versus 7.8 ± 2.5 years) and were older (47.5 ± 10.2 years) than those without (42.9 ± 8.7 years). These results imply that older age and longer disease duration are risk factors for thyroid dysfunction in CTD patients. According to reports, patients with CTD were more likely to experience thyroid dysfunction at older ages and across longer disease durations [10]. These correlations were confirmed by another investigation [11], which focused in particular on the risk in older SLE patients. Research has shown that among patients with CTD, greater age and longer disease duration are risk factors for thyroid dysfunction [11,12].

Analysis of Logistic Regression

The presence of SLE, advanced age, and lengthier disease duration were found to be significant predictors of thyroid dysfunction using logistic regression analysis. The probability of experiencing thyroid dysfunction escalated by 4% with every year of age and by 15% with every year of illness. Compared to patients with other CTDs, those with SLE had more than double the likelihood of thyroid impairment. These indicators emphasize that older patients with CTD, those whose disease has been active for a longer period of time, and especially those with SLE, require more awareness and proactive thyroid monitoring.

Antibodies Against Microsomal

Significantly, 12 individuals (7%) tested positive for anti-microsomal antibodies, with SLE patients (10%) being the most affected. This discovery is significant since it confirms that thyroid dysfunction in people with CTD is autoimmune-based. Anti-microsomal antibodies are more common in SLE patients, indicating a stronger correlation between thyroid autoimmunity and SLE that calls for closer observation and maybe distinct treatment strategies in this cohort. It has been observed that 8% of SLE patients had anti-microsomal antibodies [6]. Anti-microsomal antibodies were shown to be 9% prevalent in RA patients, according to another study [13].

CONCLUSION

This study looked at thyroid dysfunction in individuals with connective tissue disorders (CTDs), specifically Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), and Systemic Sclerosis (SSc), as well as its prevalence and clinical characteristics. Compared to several other research, our results show a considerable but comparatively lower prevalence of thyroid malfunction (3.5%), with the most common subtype being Non-Thyroidal Sickness Syndrome. The results of the study showed that thyroid dysfunction in CTD patients is significantly predicted by older age and longer disease duration, with SLE patients being more at risk. The autoimmune character of thyroid dysfunction in this cohort is further supported by the presence of Anti-microsomal antibodies, especially in SLE patients who had the greatest incidence (10%). These results highlight the value of proactive management techniques and routine thyroid function testing in the all-encompassing care of CTD patients. Frequent monitoring may help in the early diagnosis and treatment of thyroid dysfunction, which may enhance the prognosis and quality of life for patients. In order to optimize thyroid health in this patient population and to clarify the underlying mechanisms causing thyroid dysfunction in CTDs, more study is necessary.

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References

1. Akuka A, Watad A, Comaneshter D, Cohen AD, Amital H, Bragazzi NL. Systemic sclerosis patients are at higher risk of hyperthyroidism and have a worse survival than those without hyperthyroidism: A nationwide population-based cohort study. Eur J Clin Invest. 2019 Dec;49(12):e13177. doi: 10.1111/eci.13177. Epub 2019 Nov 25. PMID: 31633804.https://doi.org/10.1111/eci.13177

2. Andonopoulos AP, Siambi V, Makri M, Christofidou M, Markou C, Vagenakis AG. Thyroid function and immune profile in rheumatoid arthritis. A controlled study. Clin Rheumatol. 1996 Nov;15(6):599-603. doi: 10.1007/BF02238551. PMID: 8973871.https://doi.org/10.1007/bf02238551

3. Antonelli A, Ferri C, Fallahi P, Cazzato M, Ferrari SM, Sebastiani M, Ferrannini E. Clinical and subclinical autoimmune thyroid disorders in systemic sclerosis. Eur J Endocrinol. 2007 Apr;156(4):431-7. doi: 10.1530/EJE-06-0591. PMID: 17389457.https://doi.org/10.1530/eje-06-0591

4. Antonelli A, Fallahi P, Mosca M, Ferrari SM, Ruffilli I, Corti A, Panicucci E, Neri R, Bombardieri S. Prevalence of thyroid dysfunctions in systemic lupus erythematosus. Metabolism. 2010 Jun;59(6):896-900. doi: 10.1016/j.metabol.2009.10.010. Epub 2009 Dec 16. PMID: 20005534.https://doi.org/10.1016/j.metabol.2009.10.010

5. Appenzeller S, Pallone AT, Natalin RA, Costallat LT. Prevalence of thyroid dysfunction in systemic lupus erythematosus. J Clin Rheumatol. 2009 Apr;15(3):117-9. doi: 10.1097/RHU.0b013e31819dbe4c. PMID: 19300286.https://doi.org/10.1097/rhu.0b013e31819dbe4c

6. Arnaout MA, Nasrallah NS, el-Khateeb MS. Prevalence of abnormal thyroid function tests in connective tissue disease. Scand J Rheumatol. 1994;23(3):128-32. doi: 10.3109/03009749409103044. PMID: 8016583.https://doi.org/10.3109/03009749409103044

7. Jones KM, Anjanappa M. The prevalence of thyroid dysfunction in patients with connective tissue disorders. Asian J Med Sci. 2021;12(7):101-107. https://doi.org/10.3126/ajms.v12i7.34998

8. Atzeni F, Doria A, Ghirardello A, Turiel M, Batticciotto A, Carrabba M, Sarzi-Puttini P. Anti-thyroid antibodies and thyroid dysfunction in rheumatoid arthritis: prevalence and clinical value. Autoimmunity. 2008 Feb;41(1):111-5. doi: 10.1080/08916930701620100. PMID: 18176873.https://doi.org/10.1080/08916930701620100

9. Bianchi G, Marchesini G, Zoli M, Falasconi MC, Iervese T, Vecchi F, Magalotti D, Ferri S. Thyroid involvement in chronic inflammatory rheumatological disorders. Clin Rheumatol. 1993 Dec;12(4):479-84. doi: 10.1007/BF02231775. PMID: 8124909.https://doi.org/10.1007/bf02231775

10. Bourji K, Gatto M, Cozzi F, Doria A, Punzi L. Rheumatic and autoimmune thyroid disorders: a causal or casual relationship? Autoimmun Rev. 2015 Jan;14(1):57-63. doi: 10.1016/j.autrev.2014.10.007. PMID: 25315745.https://doi.org/10.1016/j.autrev.2014.10.007

11. Danielides S, Mavragani CP, Katsakoulas I, Zintzaras E, Drosos AA, Vlachoyiannopoulos PG, Moutsopoulos HM. Increased prevalence of anti-thyroid antibodies in patients with limited scleroderma. Scand J Rheumatol. 2011;40(4):299-303. doi: 10.3109/03009742.2010.549837. Epub 2011 Mar 21. PMID: 21417550.https://doi.org/10.3109/03009742.2010.549837

12. De Keyser L, Narhi DC, Furst DE, Huberman AK, Ross R, Clements J, Van Herle AJ. Thyroid dysfunction in a prospectively followed series of patients with progressive systemic sclerosis. J Endocrinol Invest. 1990 Feb;13(2):161-9. doi: 10.1007/BF03349530. PMID: 2109772.https://doi.org/10.1007/bf03349530