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# A CROSS-SECTIONAL STUDY ON PATTERN OF THYROIDITIS IN MULTIPLE SCLEROSIS

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## ABSTRACT

**Background and Aim:** Multiple sclerosis (MS) is a neurodegenerative disease characterized by an autoimmune response to the central nervous system (CNS), resulting in inflammation, demyelination and axonal detachment. The present study aimed to assess the thyroiditis pattern in multiple sclerosis.

**Patients and Methods:** This was a cross-sectional study conducted on 142 multi-sclerosis patients in the department of medicine, Ayub Teaching Hospital, Abbottabad from March 2022 to March 2023. Patients who met the criteria for infectious thyroiditis, and exhibited symptoms such as painful thyroid palpation, neck pain, and fever in addition to the laboratory investigation. Clinical examination and positive antibodies presence was the baseline criteria for the diagnosis of autoimmune thyroiditis.

**Results:** The overall mean age of MS with thyroiditis (Group-I) (n=62) and MS without thyroiditis (Group-II) (n=84) was 28.7 ± 5.86 and 29.92 ± 6.78 years respectively. The mean duration of disease in Group-I and Group-II was 6.78 ± 0.89 and 5.84 ± 0.85 years respectively. The incidence of autoimmune thyroiditis and infectious thyroiditis was 37% (n=54) and 5.5% (n=8) respectively. For disease-modifying drugs (DMD), the prevalence of thyroiditis was higher in MS, patients treated with interferon-beta-1b. Among Group-I patients, the clinical presentation of MS in autoimmune thyroiditis vs. infectious thyroiditis were as follows: Sensory (32 (59.3%) vs. 4 (50%)), Motor (39 (72.2%) vs. 5 (62.5%)), Speech (8 (14.5%) vs. 3 (37.5%)), and visual (42 (77.8%) vs. 6 (75%)).

**Conclusion:** The present study found that the prevalence of thyroiditis was 42.5%. Thyroiditis is significantly related to relapsing-remitting multiple sclerosis (RRMS) and interferon beta-1B as a treatment option for MS. Autoimmune thyroiditis is frequently related to interferon beta-1B which causes Cytomegalovirus (CMV) infection.

**Keywords:** Multiple Sclerosis, Thyroiditis, relapsing-remitting multiple sclerosis, Pattern

## INTRODUCTION

Multiple sclerosis (MS) is a disease characterized by inflammatory neuropathy, autoimmune metastasis to the central nervous system (CNS), and manifestations such as demyelination, axonal degeneration [1]. Various disease-modifying treatment have been advised for multiple sclerosis and Interferon beta (IFN-β) is recognized as an important disease-modifying agent for relapsing MS [2, 3]. This interacts with cell surface receptors for IFN α/β to help maintain an anti-inflammatory state in the immune system. IFN-β has been extensively studied due to its strong association with several autoimmune pathologies reported in MS patients [4]. Studies in the region have reported varying MS prevalence rates, ranging from 5.3 to 74.28 per 100,000 individuals [5, 6].

Increasing evidence suggests that multiple sclerosis (MS) is associated with other autoimmune diseases, and has common genetic or environmental factors [7]. In addition, newer treatments, which can increase the autoimmune-related risk conditions, show an association with most immunosuppressants treat MS and various immunosuppressive diseases in this short-term or intermittent approach (such as pulsed therapy or induction therapy) between treatments. Immunomodulatory drugs are associated with an increased risk of opportunistic infections or more susceptible infections [8]. Disease-modifying drugs (DMDs) play an important role in improving the status of patients with multiple sclerosis (MS), and these include intravenous interferon beta-1a, and fingolimod [9]. This drug's primary mechanism of action balance the immune system and inhibit antibodies against infection, preventing autoimmune cells from attacking the myelin sheath of nerves [10, 11]. Thyroid dysfunction (TD) is a common autoimmune disorder that is frequently seen in in individuals treated for DMDs autoimmune disease. In addition, autoimmune DMD is associated with an increased risk of opportunistic infections [12].

## METHODOLOGY

This was a cross-sectional study conducted on 142 multi-sclerosis patients in the department of medicine, Ayub Teaching Hospital, Abbottabad from March 2022 to March 2023. Patients who met the criteria for infectious thyroiditis, and exhibited symptoms such as painful thyroid palpation, neck pain, and fever in addition to the laboratory investigation. Clinical examination and positive antibodies presence was the baseline criteria for the diagnosis of autoimmune thyroiditis. Patients with prior history of neurological, cardiovascular, and liver disease and pregnant women were excluded. After an overnight fast, blood specimen were collected. In addition, TSH, FT3, FT4, anti-TG, and anti-TPO were measured by enzyme-linked immunosorbent assay (ELISA). Anti-cytomegalovirus (CMV) IgM and IgG were detected in serological blood samples by electrochemiluminescence immunoassay (ECLIA) method.

Descriptive statistics was done using SPSS version 27. Data were presented and analyzed using descriptive statistics (mean ± standard deviation). Independent sample t-test (t) was used to compare two groups and parametric variables; while non-parametric variables were analyzed using Mann–Whitney test (z). Significance was determined as $P < 0.05$, with 95% confidence interval (CI).

## RESULTS

The overall mean age of MS with thyroiditis (Group-I) (n=62) and MS without thyroiditis (Group-II) (n=84) was 28.7 ± 5.86 and 29.92 ± 6.78 years respectively. The mean duration of disease in Group-I and Group-II was 6.78 ± 0.89 and 5.84 ± 0.85 years respectively. The incidence of autoimmune thyroiditis and infectious thyroiditis was 37% (n=54) and 5.5% (n=8) respectively. For disease-modifying drugs (DMD), the prevalence of thyroiditis was higher in MS, patients treated with interferon-beta-1b. Among Group-I patients, the clinical presentation of MS in autoimmune thyroiditis vs. infectious thyroiditis were as follows: Sensory (32 (59.3%) vs. 4 (50%)), Motor (39 (72.2%) vs. 5 (62.5%)), Speech (8 (14.5%) vs. 3 (37.5%)), and visual (42 (77.8%) vs. 6 (75%)). Table-I represents the incidence of thyroiditis. Demographic, clinical, and laboratory parameters compared between group-I and group-II are shown in Table-II. Clinical presentation of MS compared in autoimmune thyroiditis vs. infectious thyroiditis are depicted in Figure-1. Comparison

of demographic, clinical, and laboratory parameters in autoimmune thyroiditis vs. infectious thyroiditis are shown in Table-III.

Table-I incidence of thyroiditis (N=62)

| **Thyroiditis** | **N (%)** |
|---|---|
| Autoimmune thyroiditis | 54 (37%) |
| Infection thyroiditis | 8 (5.5%) |
| **Total N (%)** | 62 (42.5%) |

Table-II comparison of demographic, clinical, and laboratory parameters

| **Parameters** | **Group-I (N=62)** | **Group-II (N=84)** |
|---|---|---|
| Age (years) | 28.7 ± 5.86 | 29.92 ± 6.78 |
| Duration of disease (yrs) | 6.78 ± 0.89 | 5.84 ± 0.85 |
| Frequency of relapse | 3.58 ± 0.89 | 2.98 ± 0.94 |
| **Laboratory Investigations** | | |
| FT3 (pg/ml) | 1.02 ± 0.78 | 2.61 ± 0.29 |
| FT4 (ng/ml) | 1.09 ± 0.75 | 1.27± 0.32 |
| anti-TG (IU/ml) | 1.7 ± 1.49 | 1.09 ± 0.3 |
| anti-TPO (IU/ml) | 139.76 ± 54.2 | 33.78 ± 7.9 |
| TSH (µIU/ml) | 4.32 ± 3.39 | 3.59 ± 1.82 |
| Hemoglobin (Cell/ $10^3$/µl) | 8.49 ± 1.57 | 9.7 ± 2.68 |
| Platelet (Cell/ $10^3$/µl) | 78.2 ± 44.9 | 112.7 ± 28.09 |
| Fasting plasma glucose (mg/dl) | 89.3 ± 3.8 | 88.1 ± 4.6 |

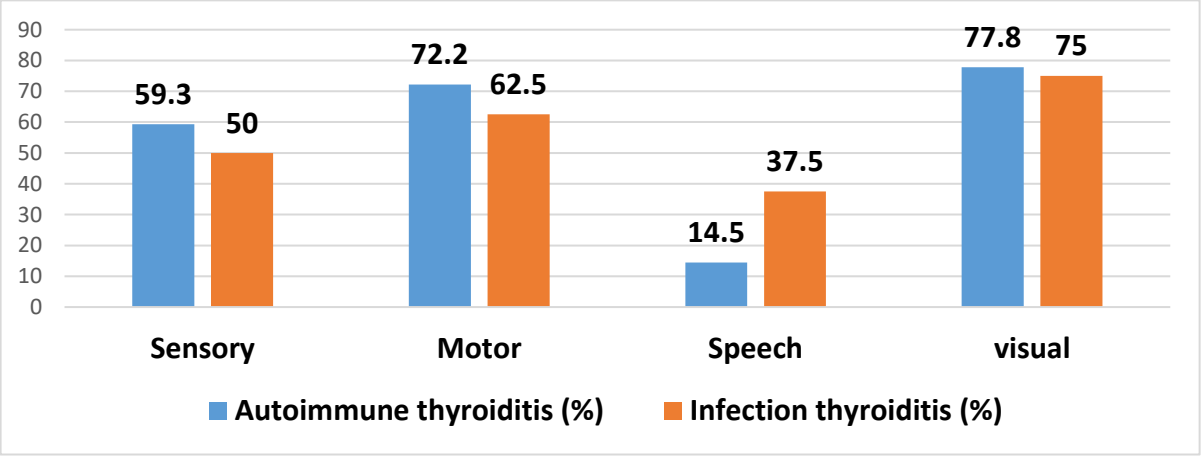


**Figure-1** Comparison of clinical presentation MS in autoimmune and infectious thyroiditis (N=62)

Table-III Comparison of demographic, clinical, and laboratory parameters in autoimmune thyroiditis vs. infectious thyroiditis (N=62)

| **Parameters** | **Autoimmune Thyroiditis (N=54)** | **Infection thyroiditis (N=8)** |
|---|---|---|
| Age (years) | 28.9 ± 4.45 | 28.5±7.27 |
| Duration of disease (yrs) | 6.4 ± 0.95 | 7.2±0.83 |
| Frequency of relapse | 3.2± 0.97 | 3.96± 0.79 |
| **Laboratory Investigations** | | |
| FT3 (pg/ml) | 1.59±0.647 | 0.54±0.91 |
| FT4 (ng/ml) | 1.2±0.61 | 0.98±0.89 |
| anti-TG (IU/ml) | 1.8±1.51 | 1.6±1.47 |
| anti-TPO (IU/ml) | 191.2±70.82 | 88.32±37.58 |
| TSH (µIU/ml) | 5.98±1.4 | 2.66±1.2 |
| Hemoglobin (Cell/ $10^3$/µl) | 8.4±2.69 | 8.58±0.45 |
| Platelet (Cell/ $10^3$/µl) | 113.6±27.6 | 42.4±62.2 |

## DISCUSSION

The present study mainly focused on the thyroiditis pattern in multiple sclerosis patients and observed that thyroiditis is frequently seen in individuals who relapse with RRMS, and increased with interferon beta-1B as a treatment. Multiple sclerosis (MS) stands out as the most common chronic neurological disorder affecting young adults, likelihood for enduring impairment or lasting disability [13]. Numerous investigations have shown that diseases where the body is resistant to diseases such as thyroiditis and MS coexist [14-16]. A notable finding in our study was that 42.5% of patients who had relapsing MS (RRMS) at relapse had thyroiditis, 37% had autoimmune involvement, and 5.5% had symptoms of infected Indicates that there may be a clinical relationship. For inflammatory markers, the thyroiditis group showed a significant increase in white blood cell (WBC) count, neutrophil count, and high-sensitivity C-reactive protein (hs-CRP) compared with those without thyroiditis. Manso et al. [17] reported similar results with thyroiditis found in 12.3% patients.

A recent study examined thyroid profiles including TSH, FT3 and FT4 in 100 drug-naïve multiple sclerosis (MS) patients compared to age-matched healthy volunteers. The results showed normal thyroid profiles in both groups [18]. Baghizadeh et al. [19] conducted another study that examined the relationship between thyroid and autoimmunity in drug-naïve MS patients. This study involved 106 MS patients and healthy volunteers, found significant differences between the two groups in terms of thyroid antibodies. Interestingly, there was no significant difference in thyroid issues between the two groups, which is in line with research findings in the earlier investigations [20].

Previous studies have suggested that older age at disease onset is associated with less distress, which may enhance central nervous system (CNS) repair and improve recovery in younger patients improved [21]. The relationship between sex, age at onset, and disease severity remains under investigation. Horkova et al. [22] Age at disease onset and female sex have been reported to be associated with higher rates of relapse within two years. In addition, several studies have identified female gender as a potential risk factor for multiple sclerosis (MS) but multivariable analysis showed that gender did not have a significant impact on long-term prognosis [23].

Various immunosuppressants are used to treat multiple sclerosis (MS) improving quality of life and considered as protective and have promising profile in risk-benefit by avoiding potentially disabling neurological conditions [24]. The present study observed the high prevalence of multiple sclerosis (MS) patients with thyroiditis treated with interferon beta-1b. In contrast, MS patients without thyroiditis treated with interferon beta -1a treated their disease had significantly higher rates. These findings highlight a possible association between specific types of interferon therapies and thyroiditis in patients with MS.

Guzel et al. [25] reported the IFN-β the importance of interferon-beta (IFN-β) in chronic inflammation, emphasizing its role in the anti-inflammatory state of the immune system emphasizes; it stands out as one of the most widely used drugs for the treatment of multiple sclerosis (MS). However, due to its immunomodulatory effects, IFN-β therapy may improve immune function [26].

## CONCLUSION

The prevalence of thyroiditis was 42.5%. Thyroiditis is significantly related to relapsing-remitting multiple sclerosis (RRMS) and interferon beta-1B as a treatment option for MS. Autoimmune thyroiditis is frequently related to interferon beta-1B which causes Cytomegalovirus (CMV) infection.

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