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# ASSOCIATION OF ALLERGIC RHINITIS AND THYROID DYSFUNCTION: A CROSS-SECTIONAL OBSERVATIONAL STUDY IN A TERTIARY CARE CENTER

## ABSTRACT

**Aims and Objectives:** Allergic rhinitis can be a presenting symptom of underlying thyroid dysfunction. This study aims to assess thyroid function status and to explore prevalence of underlying thyroid dysfunction in allergic rhinitis patients.

**Methods:** This was a cross-sectional observational study carried out from July 2021 to June 2022 at Department of Otorhinolaryngology, Bir Hospital, Kathmandu, Nepal. A total of 91 allergic rhinitis patients without known thyroid disorders were included in this study. Severity and type of allergic rhinitis was categorized according to ARIA classification and their thyroid function status was assessed.

**Results:** Out of 91 total cases, there were 47 (51.6%) males and 44 (48.4%) females. Most patients (39.56%) were in the age group 21-30 years with mean age of 30.55 years. By ARIA classification, 30.76% had mild intermittent, 19.78% had mild persistent, 30.76% had moderate-severe intermittent type and 18.68% had moderate-severe persistent type of allergic rhinitis. Thyroid function assessment revealed mean TSH value 3.57mIU/L and median TSH 2.50 mIU/L. Out of total 91 cases, 82.4% (n=75) had normal TSH, 13.2% (n=12) had high TSH, 4.4% (n=4) had low TSH. Total 16 (17.58%) patients had undiagnosed underlying thyroid dysfunction. Out of 16 cases with thyroid dysfunction, 81.25% (n=13) had moderate to severe type of allergic rhinitis. The prevalence of underlying thyroid dysfunction in allergic rhinitis patients was statistically significant ( $p < 0.05$ ).

**Conclusion:** There is some association between allergic rhinitis and underlying thyroid dysfunction. Thyroid dysfunction is more common in moderate/severe type of allergic rhinitis. Serum TSH could be a screening tool to identify underlying thyroid dysfunction in allergic rhinitis patients.

**Keywords:** allergic rhinitis, thyroid disease, thyroid function test

## INTRODUCTION

Allergic rhinitis (AR) is a clinical hypersensitivity of nasal mucosa to foreign substances mediated through Immunoglobulin E (IgE) antibodies.<sup>1</sup> Four hundred million people in the world suffer from allergic rhinitis.<sup>2</sup> It is the most common form of non-infectious rhinitis, contributing to missed or unproductive time at work and school, sleep problems, and decreased outdoor activities in affected children.<sup>3</sup>

Allergic Rhinitis and its Impact on Asthma (ARIA) classifies allergic rhinitis into intermittent (IAR) or persistent (PER) disease and severity is classified into mild or moderate to severe. Intermittent AR refers to symptoms present for less than four days a week or for less than four consecutive weeks, and persistent AR refers to symptoms present for more

than four days a week and for more than four consecutive weeks. Mild AR implies that symptoms are present but not troublesome; especially not disturbing sleep and daily activities. Moderate to severe AR implies presence of one or more of the followings: sleep disturbance, impairment of daily activities and troublesome symptoms.<sup>4</sup>

Thyroid dysfunction can be classified as overt hyperthyroidism (TSH < 0.1 mIU/L or undetectable) with elevated T4 or T3, overt hypothyroidism (TSH > 4.5 mIU/L) with low T4, subclinical hyperthyroidism (Low TSH with normal T4 and T3), and subclinical hypothyroidism (High TSH with normal T3, T4).<sup>5</sup> In the western region of Nepal, prevalence of thyroid dysfunction was 17.42% with higher prevalences of hypothyroidism (2.26%) and subclinical hypothyroidism (10.50%) as compared to hyperthyroidism (1.59%) and subclinical hyperthyroidism (3.05%).<sup>6</sup> Subclinical

hypothyroidism and hyperthyroidism are associated with increased cardiac problems.<sup>7</sup> Maternal hypothyroidism may adversely affect fetal neural development.<sup>8</sup>

Thyroid Stimulating Hormone (TSH) serves as the most useful physiologic marker of thyroid function, the change in its level preceding FT3 and FT4 level in blood.<sup>8</sup> A normal TSH measurement is a good indicator of normal thyroid function except in rare situation of pituitary dysfunction.

Hypertrophy of mucous glands and markedly increased connective tissue in sub mucosa of septum and turbinates in hypothyroid patients lead to nasal obstruction and nasal discharge.<sup>9,10</sup> Helper T cells (Th2) up-regulation is found in Graves' disease. Similarly, over activation of the Th2 cytokine pattern is also a dominant feature of AR.<sup>11</sup>but it is not clear whether Graves' disease is T-helper cell type 2 (TH2A suppressor T-cell defect is responsible for both atopic disease and thyroid autoimmunity.<sup>12</sup>

In light of this situation, this study aims to assess thyroid function status and to explore prevalence of underlying thyroid dysfunction in patients with AR. Any linkage between them, if present would prompt for early testing for thyroid dysfunction leading to better management of AR.

**METHODS**

This was a cross sectional observational study conducted in Otorhinolaryngology Head and Neck Surgery (ORL HNS) Department, Bir Hospital, National Academy of Medical Sciences (NAMS), Kathmandu, from July 2021 to June 2022. Ethical approval was obtained from Institutional Review Board of NAMS and written informed consent was taken. The inclusion criteria included patients not more than 50 years with clinical features that included combination of two or more nasal symptoms; rhinorrhea, nasal obstruction, nasal itching, and sneezing and newly diagnosed as Allergic rhinitis by serum Ig E level (>300IU/ml)<sup>13</sup> and absolute eosinophil count (>450 eosinophils/uL).<sup>14</sup> The exclusion criteria included patients with sino-nasal mass, occupation associated with compost and chemical exposure, pregnant and post-partum (till 6 weeks) women, patients on hormonal contraceptives, patients with pituitary/hypothalamic disease , patients on angiotensin-converting enzyme (ACE) inhibitors, phosphodiesterase-5-selective inhibitors, phentolamine, alpha-receptor antagonists, aspirin, immunomodulators, steroids dopamine agonists or somatostatin analogues and other non steroidal anti-inflammatory drugs (NSAIDs), diagnosed case of thyroid function disorder or thyroid mass, history of any thyroid surgery in the past. A total of 91 cases fulfilled the criteria and were enrolled in the study.

A history taking and examination of all study participants were carried out in OPD and particulars were recorded.

Allergic Rhinitis was diagnosed on basis of clinical features, serum IgE level and absolute eosinophil count. Allergic rhinitis was classified according to Allergic Rhinitis and its Impact on Asthma (ARIA) classification and recorded. Thyroid function test of each patient was done in Bir Hospital Laboratory. Thyroid Function test was done by Chemiluminescence Immunoassay (CLIA) method using Vitros ECi Immunodiagnosics Machine. Test results were recorded and thyroid function status of patients was classified according to Serum TSH level. TSH level was considered within normal range if it was 0.46 to 4.68 mIU/L, low if below 0.46 mIU/L and high if above 4.68 mIU/L.

The collected data were stored in an electronic database (MS-Excel Sheet). Statistical analyses was performed with statistical software (SPSS 21.0 for Windows). Mean, standard deviation, median, frequency values were used for descriptive data analysis. Chi Square Test was used for quantitative data analysis. All analyses were done with statistical significant level set at p<0.05.

**RESULTS**

The mean age was found to be 30.55 ± 9.58 years (Range 13-50 years, Median 30 years). 47 patients (51.6%) were males while 44 patients (48.4%) were females. Out of 91 allergic rhinitis patients in the study, most of them had mild intermittent (30.76%) and moderate severe intermittent (30.76%) type of allergic rhinitis (Table 1). Least number of patients had moderate/severe persistent (18.68%) type of allergic rhinitis.

**Table 1: Frequency Distribution of Allergic Rhinitis Severity and Type.**

Allergic Rhinitis Severity and Type	Number	Percentage
Mild Intermittent	28	30.76
Mild Persistent	18	19.78
Moderate/Severe Intermittent	28	30.76
Moderate/Severe Persistent	17	18.68
Total	91	100

The mean serum TSH was 3.57mIU/L (median 2.50 mIU/L and S.D. 8.23 mIU/L). The distribution of TSH values was positively skewed with high standard deviation because of a single value of TSH 79.14mIU/L in one of the patient. The frequency distribution of TSH value in allergic rhinitis patients (Table 2) showed that 82.4% had normal TSH, 4.4% had low TSH and 13.2% had high TSH. Hence, 17.6% of allergic rhinitis patients had underlying covert thyroid dysfunction. Among patients with thyroid dysfunction, most of the patients with high TSH were in age group 31 to 40 years and most of the patients with low TSH were in age group 21 to 30 years.

**Table 2: Table showing frequency distribution of patients according to serum TSH value.**

Thyroid function status (by TSH value)	Number	Percentage
Low TSH	4	4.4
Normal TSH	75	82.4
High TSH	12	13.2

Comparing distribution of serum TSH value with severity and type of allergic rhinitis (Table 3), patients with moderate/severe persistent type of allergic rhinitis were more likely to have thyroid dysfunction. Pearson correlation analysis revealed that the relationship between severity and type of Allergic Rhinitis and thyroid function status was significant.

**Table 3: Thyroid status according to serum TSH value and severity of Allergic Rhinitis.**

	Mild Intermittent n	Mild Persistent n	Moderate/ Severe Intermittent n	Moderate/ Severe Persistent n
Low TSH	0	2	1	1
Normal TSH	27	16	24	8
High TSH	1	0	3	8
Total	28	18	28	17

Pearson Chi-Square value = 25.838; p value=0.0004

## DISCUSSION

Thyroid hormones are directly or indirectly associated with all biological phenomena in the body. Thyroid dysfunction causes a number of clinically identifiable changes in the ear, nose and throat region as well. There are few studies in the literature that indicate thyroid dysfunction can lead to nasal symptoms. There have been various studies in literature on relationship between allergic disorders like allergic rhinitis, allergic dermatitis, urticaria, asthma and thyroid disorders like hypothyroidism, hyperthyroidism, Graves' disease, Hashimoto's thyroiditis, autoimmune thyroiditis. Up-regulation of Th1-inducing cytokines has been found in association with Hashimoto thyroiditis and Th2 up-regulation in Graves' disease. Overactivation of the Th2 cytokine pattern is a dominant feature of allergic rhinitis.<sup>15</sup> Moens et al. suggested that a suppressor T-cell defect is responsible for both atopic disease and thyroid autoimmunity.<sup>12</sup> A total of 91 allergic rhinitis patients who fulfilled the inclusion criteria were included in the study. All the patients in the study were tested for their serum TSH level. The objective of this study was to find out the prevalence of thyroid dysfunction in allergic rhinitis patients using serum TSH as a screening tool.

In this study, patients with age ranging from 13 years to 50 years were present. Mean age of allergic rhinitis patients was 30.55 years and the median age was 30 years. Male to

Female ratio was 1.06:1. Degirmenci et al. carried out a study enrolling 1239 patients with allergic rhinitis and 700 healthy subjects. Of these 1239 patients, 631 were female (51%), and 607 were male (49%) with male to female ratio being 0.96. The mean age of the patients was 35.71 ±11.14 (standard deviation [SD]) years (range; 17-63 years).<sup>16</sup> Akkoca et al. conducted a study which included 62 adult allergic rhinitis patients. The mean age was 41.6±18.14 years while gender distribution was 54.8% female, 45.2% male with male to female ratio of 0.82.<sup>17</sup>

Analyzing the thyroid function status in our study, the mean TSH was 3.57 mIU/L and median TSH was 2.50 mIU/L. Out of 91 patients, there were 75 (82.4%) patients with normal TSH, 4 (4.4%) low TSH and 12 (13.2%) with high TSH. By gender distribution, in male population low TSH was present in 4.25% and high TSH in 8.5%. However, in female population, low TSH was present in 4.5% and high TSH in 18.18%. Analyzing the age wise distribution of thyroid function status in present study, low TSH was found more in age group 21-30 years and high TSH in 31-40 years. In a study by Amino et al., the mean age of Graves' disease was 36.5±13.7 years, painless thyroiditis was 37±14 years, Hashimoto's thyroiditis was 45.5±14.3 years. Graves' disease, painless thyroiditis, Hashimoto's thyroiditis were common in female.<sup>11</sup> The age group with higher prevalence of thyroid dysfunction in our study did match with mean age in this study as well and thyroid dysfunction was found to be common in females than males like in this study. In a Turkish study by Demir et al. in 2008 to 2011 skin prick tests were evaluated in 83 hypothyroid patients with symptoms of allergic rhinitis which had 75 patients (90.3%) female and 8 (9.7%) male and the mean age was 39±11.6 years<sup>18</sup> which supported the present study that thyroid dysfunction is common in female and common age group affected is 21-40 years.<sup>18</sup>

Out of 91 allergic rhinitis patients of present study, 16 (17.58%) patients had undiagnosed underlying thyroid dysfunction. In a study done by Reisacher et al., among all 212 patients, 23 (10.8%) had autoimmune thyroid disease. Of these 23 patients, 14 (60.9%) had hypothyroidism, 4 (17.4%) had hyperthyroidism, and 5 (21.7%) had euthyroid thyroiditis. AITD was found in 8 (10.4%) of the AR group.<sup>15</sup> Degirmenci et al carried out a study to analyze the incidence of autoimmune thyroid disease in patients with allergic rhinitis enrolling 1239 patients with allergic rhinitis and 700 healthy subjects. Their thyroid hormone levels were measured. Results showed that 171(13.8%) participants with allergic rhinitis had euthyroid Hashimoto's thyroiditis and 31 (2.5%) had hypothyroid Hashimoto's thyroiditis. On the other hand, 688 (98.2%) healthy participants had normal thyroid function, 10 (1.4%) had euthyroid Hashimoto's thyroiditis, and two (0.4%) had hypothyroid Hashimoto's thyroiditis.<sup>16</sup> Lindberg et al. investigated the coexistence of thyroid

autoimmunity in 140 children and adolescents with various allergic diseases and 370 control children with no allergic diseases in Malmo University Hospital, University of Lund, Sweden and found that thyroid peroxidase autoantibodies was found to be higher among the patients than in the control group (11.4% vs 5.4%).<sup>19</sup> In a study by Akkoca et al., subclinical hyperthyroidism was found in 4.8%, euthyroid status in 61.3%, subclinical hypothyroidism in 29% and clinical hypothyroidism in 4.8% in allergic rhinitis patients group. In control group, subclinical hyperthyroidism was found in 9.5% patients, euthyroid status in 68.3%, subclinical hypothyroidism in 12.7% patients and clinical hypothyroidism in 9.5% patients.<sup>17</sup> A study was conducted by Gurlek et al. in 2016 in Turkey with 319 patients in which no significant difference was found between the allergic rhinitis patient and control groups in terms of anti-Tg and anti-TPO values. There was no significant difference between patient and control groups in terms of TSH, FT3, and FT4 values.<sup>20</sup> Analyzing these literatures, the prevalence of thyroid dysfunction in allergic rhinitis patients ranges from 10 to 30% which did not match with our study's prevalence of 17.58%.

Conversely, various studies suggest that allergic conditions co-exist in patients with thyroid disorders. Amino et al. examined the prevalence of seasonal allergic rhinitis in patients with Graves' disease, painless thyroiditis and Hashimoto's thyroiditis, and compared them to healthy controls in Osaka, Japan in 2003. The prevalence of seasonal allergic rhinitis was significantly high in patients with Graves' disease (42.9%) and low in patients with painless thyroiditis (13.0%) but was not different in patients with Hashimoto's thyroiditis (26.1%) compared to that of healthy controls (32.6%).<sup>11</sup> Yamada et al. conducted a study on 193 patients with hyperthyroid Graves' disease, which showed elevation of serum Ig E was found in 35.5% of patients with hyperthyroid Graves' disease and serum levels of T4, T3, anti-microsomal antibody and TSH Binding Immunoglobulins were significantly greater in patients with Ig E elevation than in those with normal serum IgE.<sup>21</sup> According to Sato A et al. study in 1998 in Japan on possible role of immunoglobulin E in patients with hyperthyroid Graves disease, elevation of serum Ig E levels (>170 U/mL) was found in 19 of 66 patients (29%), 11 of whom had hereditary and/or allergic conditions.<sup>22</sup> In a study by Lindberg et al. in 1998 in 140 children and adolescents with various allergic diseases and 370 control children with no allergic diseases, thyroid peroxidase autoantibodies were found to be higher among the patients than in the control group (11.4% vs 5.4%).<sup>19</sup> Various study throughout the world has established some association between allergic rhinitis and thyroid disorders but still more study is needed to be conducted in our part of the world to understand the association and underlying pathophysiology.

Thyroid disorders have a wide range of presenting clinical

manifestations of which allergic rhinitis could be one. If all the allergic rhinitis patients could be screened for thyroid function status with at least serum TSH estimation, the underlying covert thyroid dysfunction could be diagnosed and managed much earlier than usual. The early detection and treatment of thyroid dysfunction will lead to optimal management of allergic rhinitis along with the prevention of complications associated with thyroid disorders.

A small sample size is the main limitation of the present study. Future prospective studies in larger population with appropriate control is needed to establish an association of allergic rhinitis and thyroid disorders. Serum TSH value does not encompass all the thyroid disorders including autoimmune thyroid diseases. It would be better if results could be analyzed with serum FT3, FT4 and anti-thyroid antibodies as well. Confounding factors may affect the thyroid function status as for example; patients with allergic rhinitis may have other form of rhinitis or non-allergic rhinitis, or may have elevated serum Ig E because of any other causes like worm infestation. Population of Nepal belong to different geographical regions like mountains, hills and terai, which have diverse climate zones and ethnicity that may have played role in diverse thyroid physiology and hence thyroid function status.

## CONCLUSION

There is some association between allergic rhinitis and underlying thyroid dysfunction. Patients with thyroid dysfunction may present with manifestations of allergic rhinitis. Patients with underlying thyroid dysfunction may present with moderate to severe type of allergic rhinitis affecting their daily activities, work or sleep. Serum TSH can be used as a screening tool to identify underlying undiagnosed thyroid dysfunction in allergic rhinitis patients.

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**CONFLICT OF INTEREST:** None

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