

## Clinical Association of Anti-TPO in Patients with Chronic Urticaria

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### Abstract

#### Background:

Chronic urticaria may occur when the body's immune system attacks its self-tissues. It is a skin condition marked by brief purpuric wheals that last longer than six weeks. Uncertainty surrounds the disease's etiopathogenesis. Autoimmunity and endocrine dysfunction may both be at play, according to the available research.

#### Objective:

This study aimed to evaluate if thyroid immunity is statistically linked with chronic urticaria.

#### Methods:

This case-control study was held from June 2022 to March 2023 at Department of Dermatology & Venereology in IMCH, Popular diagnostic center and Digital Hospital in Gazipur. We examined the prevalence of autoantibodies (Anti-TPO) in 50 chronic urticaria patients and 50 healthy volunteers. In all participants, thyroid hormone and thyroid auto-antibodies were assessed.

#### Results:

Thyroid function abnormalities were found 7 (13.42%) patients and Anti-TPO is positive in 38(76%) patients respectively. Only 2 (4%) of the individuals in the control group had positive anti-TPO tests. With chronic urticaria, anti-TPO levels were considerably greater (P 0.05) than in the control group.

#### Conclusions:

This study shows a significant association between chronic urticaria and thyroid auto-immunity. The test is conducted to detect thyroid auto-antibodies is relevant in patients with chronic urticaria.

**Keywords:** Chronic urticaria, Autoantibodies

### Introduction:

Chronic urticaria (CU) is an autoimmune skin disease defined as wheals, flares, and itching that occur virtually every day for at least six weeks.<sup>1</sup> Chronic urticaria is a common cutaneous disorder with an estimated prevalence of 8-10% of the general population.<sup>2</sup> The pathophysiology of chronic urticaria is not well understood, however, most scientists concur that the activation of cutaneous mast cells is the main event. The pathophysiological events are most prominent during the initial stage of inflammation, which develops into a complex interplay of various pro-inflammatory mediators, cytokines, chemokines, and adhesive molecules that regulate vasoactivity and specific kinetics of cellular infiltration before

evolving into lymphocytes and granulocytes mediated hypersensitivity type-I reaction and producing inflammatory urticaria wheals.<sup>3,4</sup> A perivascular non-necrotizing cellular infiltration around tiny skin venules is the defining feature of chronic urticaria. It largely comprises CD4(+) lymphocytes, with a predominance of the T helper (Th)2 subtype but including Th1 cells and high plasma levels of cytokines produced by Th17 cells.<sup>5</sup> The majority of cases with chronic urticaria have an unknown etiology and, appropriately, 30-40% have autoimmune pathogenesis.<sup>6</sup> The most widely recognized theory that accounts for the improper activation and degranulation of mast cells in urticaria is one with an autoimmune etiology.<sup>7</sup> This theory is supported by the clinical association

of chronic urticaria with various autoimmune disorders.<sup>8</sup> The frequent detection of circulating autoantibodies, positive association with HLA subtypes DRB-04 and DQB1-0302, and response to plasmapheresis and intravenous immunoglobulin.<sup>9</sup> The association of chronic urticaria with thyroid autoimmunity has been known since 1983.<sup>10</sup> The frequency seems to vary in different reports, and among them, the prevalence of thyroid autoantibody or autoimmunity in patients with chronic urticaria varies from 4.3% to 57%, and 5–10% have clinically apparent thyroid disease.<sup>11</sup> The aim of this study is to determine whether chronic urticaria is statistically associated with thyroid autoimmunity.

#### Material & Methods:

This case - control study was held from June 2022 to March 2023 at Department of Dermatology & Venerology in IMCH, Popular diagnostic center and Digital Hospital in Gazipur. A total of 50 chronic urticaria patients (30 female and 20 male) were included in this case-control research. All study subjects were taken with a detailed history and examination, including patients' age of onset, criteria, and duration of disease, other associated diseases, and the history of thyroid disorders and the extent and severity of the disease. Chronic urticaria was identified on the basis of clinical evidence. The control group in this study comprised of 50 people (30 female and 20 male), all of whom had skin conditions other than chronic urticaria. There were no patients who had thyroid dysfunction identified before the investigation. Blood samples were taken and a physical examination with ultrasonography of the thyroid gland was performed. Thyroid autoantibodies (Anti-TPO) and Thyroid Stimulating Hormone (TSH), Tri-iodothyronine (T3), and Thyroxine (T4) were measured in all subjects. TSH (Normal range 0.30-4.20 mIU/l) was measured by use of immunoradiometric assay (IRMA) (BRAHMS AKtiengesellschaft Hennigsdorf, Germany), Total T3 (Normal range 1.3 – 3.3 nmol/l) and Total T4 (normal range 70-180 nmol/l) were measured by radio-immunoassay (RIA). Serum level of Anti\_TPO (borderline value 35 IU/ml) was measured by Beckmen Coulter-Access – 2 Germany, Electrochemiluminescence immunoassay (ECLIA). The clinical Characteristics for these two groups were compared with the use of the student's t-test for continuous variables, and the chi-square test for

categorical variables as appropriate. Data were entered into a computer with the help of software SPSS for Windows programmed version 17.

#### Results:

The study focused on the anti-TPO in chronic urticaria patients encountered in the Department of Dermatology & Venerology in IMCH, Popular Diagnostic Center, and Digital Hospital in Gazipur. In this study, a total of 100 persons were included. Of them, 50 (fifty) persons were in the case group and 50 were in the healthy control group. Age and sex matched with the case group and in the case of the control group chronic urticaria or any major illness were excluded. The mean age of the case group is approximately 41.27 years, with a standard deviation of 14.10 years. The control group was 40.71 years old with a standard deviation of 14.50, respectively of p-value was 0.796. The youngest and the oldest people were 16 and 65 years (Table-I). The duration of chronic urticaria ranged from 3 to 60 months. A family history of the same disease was present in 3(6.10%) patients. Thyroid function abnormalities were found in 7(13.42%) patients. In the control group, only one person 1(1.72%) had abnormalities in hormonal status. In this study, regarding sex distribution, female patients predominate in both groups with 60% persons female while 40% persons were male (Table-I). The female: male ratio was roughly 1.7:1. All chronic urticaria patients of the study had hypo-echogenic thyroid tissue, which was seen in 7(14%) who all had elevated levels of thyroid autoantibodies. The Thyroid gland was enlarged in 5 (8.14%) patients. The goiter was diagnosed in 4(6.12%) cases. The ultrasound examination of the thyroid gland in the control group was interpreted as normal in 44(92.14%) and 6 (7.8%) persons who had simple goiter. The thyroid volume did not differ significantly between the case and control group ( $p > 0.05$ ). In Patients with chronic urticaria, estimated anti-TPO antibody titers from 15.10 to 705.40 IU/ml. In the control group, anti-TPO antibody titers were from 4.30 to 100.00 IU/ml. Here anti-TPO antibody of 38 (76%) cases were positive and 12(24%) cases were negative of titer. In the control group, anti-TPO antibodies of 2(4%) and 48(96%) were respectively positive and negative in antibody titer. The frequency of thyroid autoantibodies was significantly higher in the chronic urticaria case group than in the control

group (Table-II). A chi-square test for independence indicated a significant association between higher values of anti-TPO (values more than 38 IU/ml) and chronic urticaria,  $X^2 (1, n = 100) = 19.458$ ,  $p$ -value  $< 0.001$

**Table-I: The Demographic data of Patients of Chronic urticaria case group and control group**

	Chronic urticaria Group (Case group), n(%)	Control group, n(%)
Man	20(40)	20(40)
Women	30(60)	30(60)
Age range (years)	16-65	16-65
Age, mean years (SD)	41.27(14.10)	40.70(14.50)
$p$ -Value = 0.796		

SD = Standard Deviation,  $p$ -Value = 0.796

**Table-II: The frequencies of detectable thyroid auto-antibody Anti-TPO of Chronic urticaria case group and control group**

Group	Anti-TPO (threshold value 38 IU/ml) case group	Anti-TPO (threshold value 38 IU/ml) control group
	Positive n(%) Negative n(%)	Positive n(%) Negative n(%)
ChronicUrticaria (case group), n = 50	38(76) 12(24)	-
Control group n = 50	-	2(4) 48(96)
Total (case+ control)	Positive 40(40) Negative 60(60)	
Difference n(%)	20(28%)	

$X^2 (1, n = 100) = 19.458$ ,  $p$ -Value  $< 0.001$ .

### Discussion:

Chronic urticaria has been linked to numerous endocrine problems in studies. Patients with chronic urticaria had a wide range of thyroid auto-immunity prevalence rates, ranging from 4.3% (7) to 57.4% (8).<sup>12</sup> According to previous

studies, we also found that anti-thyroid autoantibodies were significantly increased in patients with chronic urticaria in comparison to healthy persons.<sup>13</sup> We detected the Anti-TPO level elevated in 38(76%) of patients with chronic urticaria. Usually, 5-10% of the general population has positive anti-thyroid antibodies.<sup>14</sup> In this study, autoantibodies are substantially less common in the control group than was predicted. In this study, those with chronic urticaria had considerably more anti-TPO antibodies than those in the control group. This study's findings are comparable to those of a clinical trial carried out by Palma-Carlos et al.<sup>15</sup> They conducted a case-control study to evaluate thyroid antibodies in chronic urticaria patients, and detected anti-TPO positively in 26.8%. However, 93% of chronic urticaria patients showed normal thyroid function test. In contrast, feibelman et. al found that thyroid auto-antibody prevalence in chronic urticaria patients was greater than Control group.<sup>16</sup> As regards the type of thyroid antibody our study showed a higher prevalence of anti-TPO. This is consistent, and similar to the result of Amir et al.<sup>17</sup> In this study demonstrated that anti-TPO had a higher prevalence in the case group. Anti-TPO antibody, historically referred to as the anti-chromosomal antibody, is established as a sensitive tool for the detection of early subclinical autoimmune thyroid diseases and the identification of risk cases for autoimmune thyroid diseases.<sup>18</sup> According to a study by Gilbert et al, anti-TPO antibodies are more frequently associated with thyroid dysfunction. It has not yet been conclusively shown how thyroid disease development and chronic urticaria are related. It is often believed that disease develops because a patient is prone to developing reactions to themselves. According to a theory, thyroid dysfunction might make urticaria worse by triggering the complement system.<sup>19</sup> Kirpasic noted that C4 levels decrease when thyroid disease is treated, resulting in remission of chronic urticaria.<sup>20</sup> As a result, although it is assumed that thyroid illness and chronic urticaria may coexist because of a patient's propensity for autoimmunity, thyroid disease may also make the condition worse through direct processes that activate the complement system.<sup>21</sup> O'Donnell et al. observed that patients with positive anti-TPO antibodies were more likely to demonstrate histamine-releasing autoantibodies as predicted by positive autologous intradermal skin testing and positive release in

vitro of histamine from donor basophil leukocytes.<sup>22</sup> The patient's T cells exhibited greater levels of CD-401 expression and bcl-2 expression in activated T and B lymphocytes. Though not proven, it is conceivable that cellular immunity that began in the thyroid gland may be the origin of the skin problem. According to Unnikrishnan et al., anti-TPO antibodies are more prevalent in females than men (P 0.05) in eight Indian cities, which is consistent to our findings that is displayed in Table-I.<sup>23</sup> Anti-thyroid autoantibodies largely cause pathology through complement-dependent cytotoxicity, and there is a complicated link between the existence of these antibodies and the eventual onset of thyroid disease.

### Conclusion:

Our study demonstrated a substantial correlation between thyroid autoimmunity and chronic urticaria, as well as the relevance of the thyroid autoantibody test in patients with chronic urticaria. Although cutaneous evident autoimmune thyroid illnesses are extensively documented and it is known that thyroid hormone controls how the skin develops and functions, further research is necessary to fully comprehend these processes. The fact that a considerable portion of older adults may have anti-thyroid antibody positivity adds to the need for screening.

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