Association of Pro-Inflammatory Cytokines and Rubella Virus in Patients with Hashimoto's Thyroiditis

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Abstract

Background: Hashimoto's thyroiditis is an autoimmune disorder characterized by chronic lymphocytic infiltration of the thyroid and elevated proinflammatory cytokines. Environmental triggers, including viral infections, may contribute to disease pathogenesis. **Objectives:** This study evaluated the association of Rubella virus seropositivity, TNF-α levels, and body mass index with Hashimoto's thyroiditis in an Iraqi population. **Materials and Methods:** A case-control study was conducted on 40 patients with Hashimoto's thyroiditis and 40 healthy controls. Serum Rubella virus IgM was assessed using rapid test, TNF-α level was measured via enzyme linked immune sorbent assay and body mass index was calculated. Statistical comparisons were performed using Fisher's exact and Welch's t-test. **Results:** Females predominated in the Hashimoto's thyroiditis group (92.5%) compared to controls (72.5%), though statistically significant (P = 0.037). Rubella IgM positivity was detected in 10% of Hashimoto's thyroiditis patients and none of the controls (P = 0.116). Mean age (53.34 ± 11.39 vs. 42.95 ± 11.41 years), BMI (29.9 ± 3.27 vs. 21.5 ± 1.4 kg/m²), and TNF-α levels (60.42 ± 41.08 vs. 22.07 ± 7.32 pg/ml) were significantly higher in Hashimoto's thyroiditis patients compared to controls (P ≤ 0.001). **Conclusion:** Hashimoto's thyroiditis patient's exhibit significantly higher BMI and TNF-α level compared to healthy controls, suggesting a pro-inflammatory and metabolic component in disease pathogenesis. Although Rubella IgM positivity was more frequent in patients, the difference was not statistically significant. Larger studies are needed to confirm viral contributions to Hashimoto's thyroiditis.

Keyword: Hashimoto's thyroiditis, Rubella virus, TNF-α, Body Mass Index, Autoimmunity

Introduction

Hashimoto's thyroiditis (HT) is the most common autoimmune thyroid disorder, characterized by lymphocytic infiltration of the thyroid gland, progressive destruction of thyroid tissue, and fluctuating thyroid hormone levels [1]. The etiology of HT involves a complex interaction between genetic predisposition, environmental triggers, and immune dysfunction, leading to immune system attack on thyroid cells and the subsequent development of autoimmune thyroid disease (AITD) [2]. Thyroid disorders are highly prevalent in the general population, and in areas with low iodine levels, HT is the leading cause of hypothyroidism. The main features of Hashimoto's disease include lympho-

cytic invasion of thyroid tissue, the presence of anti-thyroid autoantibodies, and thyroid cell death, which ultimately leads to the destruction of thyroid follicles [2,3]. Pro-inflammatory cytokines, particularly tumor necrosis factor-alpha (TNF-α), play a pivotal role in thyroid tissue inflammation and autoantibody production in HT [4]. Elevated TNF-α level have been reported to correlate with disease activity and severity [5]. Viral infections have been suggested as environmental triggers for autoimmune thyroid disease. Rubella virus infection, in particular, has been implicated in immune dysregulation leading to autoimmunity [6]. Additionally, body mass index (BMI) has been associated with autoimmune thyroid disorders, potentially reflecting metabolic and inflamma-tory contributions [7]. This study aimed to investigate the association of Rubella virus IgM, TNF-α levels, and BMI with HT in an Iraqi patient population.

Materials and Methods

Study of design and participants

In this case-control study, 80 serum samples were obtained, divided into 40 patients with clinically and serologically confirmed HT and 40 control groups, from Al-Imam Al-Sadiq Teaching Hospital /Babylon from March 2024 to December 2024. In addition, Demographic data, including age and sex, were recorded. Height and weight were measured to calculate BMI (kg/m²). Exclusion criteria included pregnancy, other autoimmune diseases, or recent infection.

Measurement of a serological assay

A quantitative Sandwich ELISA kit was used to measure TNF-α level (Elabscience Biotechnology Co., Ltd, Wuhan, P.R.C.) in all samples. Rubella virus was detected by Rubella IgM rapid test cassette (CTK biotech, Inc. USA). The parameter was measured according to the instructions of the manufacturing company.

Statistical analysis

For the statistical study, IBM Co., Chicago, IL's SPSS software, version 25.0, was utilized. The data were displayed as number (n), percentage, mean, and standard deviation, and the means of the various groups were compared using Fisher's exact and Welch's t-test. A P value of 0.05 indicated that the difference was statistically significant.

Ethical approval

The study was carried out in compliance with the moral guidelines found in the Helsinki Declaration. Before taking a sample, the patient's verbal and analytical consent was obtained. An ethical committee at the University of Babylon, Hammurabi College of Medicine, Babylon, Iraq, evaluated and approved the study protocol as well as the subject information and permission form.

Results

The results in Table (1) shows that HT group included 37 females (92.5%) and 3 males (7.5%), while the control group had 29 females (72.5%) and 11 males (27.5%) (P = 0.037). Mean age was significantly higher in HT patients (53.34 ± 11.39 years) compared to controls (42.95 ± 11.41 years, P = 0.001). Rubella IgM was positive in 4 HT patients (10%) and negative in all controls (0%), though this difference was not statistically significant (P = 0.116). BMI was significantly higher in HT patients (29.9 ± 3.27 kg/m²) than controls (21.5 ± 1.4 kg/m², P < 0.001). TNF-α levels were also elevated in HT patients (60.42 ± 41.08 pg/ml) compared to controls (22.07 ± 7.32 pg/ml, P < 0.001).

Table 1: Demographic and Laboratory Characteristics of Study Participants

Parameters		Hashimoto's Thyroiditis (n=40)	Controls (n=40)	P value
Sex	Male	3 (7.5%)	11 (27.5%)	0.037*
	Female	37 (92.5%)	29 (72.5%)	
Age (years)		53.34 ± 11.39	42.95 ± 11.41	0.001**
BMI (kg/m²)		29.9 ± 3.27	21.5 ± 1.4	<0.001**
TNF-α (pg/ml)		60.42 ± 41.08	22.07 ± 7.32	<0.001**
Rubella IgM positivity		4 (10%)	0 (0%)	0.116*

*Fisher's exact, **Welch's t-test for categorical variables.

Discussion

This study demonstrates that HT patient's exhibit elevated TNF-α levels and BMI compared to healthy controls, supporting the role of inflammation and metabolic factors in disease pathogenesis. TNF-α is a key mediator of thyroidal inflammation, promoting lymphocyte infiltration and thyroid cell apoptosis [4, 5]. Hashimoto's disease is characterized by the loss of thyroid epithelial cells, which are gradually replaced by mononuclear cells, without any involvement of cytotoxic T cells in the thyrocyte destruction [8, 9]. Tumor necrosis factor-alpha (TNFα) plays a pivotal role in initiating and amplifying inflammatory responses. Its levels are elevated in various autoimmune diseases, cancers, and viral infections, making it a central target of immunological research [10, 11]. Functionally, TNFα enhances inflammatory pathways and interacts with pattern recognition receptors (PRRs) to promote the production of interleukin-1β (IL-1β), leading to activation and recruitment of immune cells [12]. These activated immune cells further stimulate Th1 and Th17 cell-mediated immune responses, both of which are crucial in the development of autoimmune and infectious immune reactions through the secretion of pro-inflammatory cytokines [3, 13]. Based on these findings, the present study suggests that the immune response against thyroid self-antigens may be intensified due to TNFα's role in driving Th1 and Th17 activation and promoting immune cell infiltration and accumulation within thyroid tissue [13]. Although Rubella IgM positivity was observed in 10% of HT patients, the difference from controls was not statistically significant. This finding may indicate a limited role of recent Rubella infection in triggering HT or may reflect the small sample size. Previous studies have suggested a potential link between viral infections and autoimmune thyroid disease [6]. Higher BMI in HT patients aligns with evidence that obesity-related inflammation can exacerbate autoimmune processes [7]. These results highlight the interplay between metabolic and immune factors in HT.

Conclusion

HT patients have significantly elevated TNF-α levels and BMI, suggesting an inflammatory and metabolic contribution to disease pathogenesis. Rubella virus IgM positivity was observed but not statistically significant, indicating a limited or indirect role in HT development. Further studies are warranted to explore viral triggers and their immunological impact.

Limitations of study

The study is limited by a relatively small sample size and cross-sectional design. Future longitudinal studies with larger cohorts are needed to clarify causal relationships.

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