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Research Article

### A CORRELATION BETWEEN INFERTILITY AND THYROID AUTO-ANTIBODIES IN WOMEN OF REPRODUCTIVE AGE GROUP: A RETROSPECTIVE CROSS-SECTIONAL STUDY

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**Abstract:**

*Objective:* This study intends to ascertain the prevalence of thyroid auto-antibodies in reproductive age group female patients with infertility referred to our centre in Bengaluru.

*Materials and Methods:* Our retrospective cross-sectional study was carried out at MVJ Medical College and Research Hospital, Bengaluru, India from June 2015 to May 2019. A total of 1392 female infertile women was included in the study population and were assessed for the presence of thyroid auto-antibodies (anti-TPO and anti-TG).

*Results:* We detected the presence of either anti-TPO or anti-TG antibodies in 287 patients (20.7%). The mean age of patients with positive thyroid auto-antibodies is  $28.4 \pm 0.84$  years, while it is noted to be slightly higher among those with negative lab results with  $29.7 \pm 0.44$  ( $p$ -value= 0.72). It has been found that, 192 (66.8%) patients tested positive for Anti-TPO antibodies and 95 (33.2%) of them for Anti-TG antibodies.

*Conclusion:* As the prevalence of thyroid auto-antibodies are found to be high among infertile and sub-fertile women, It is therefore suggested to screen for the elevated titres of thyroid auto-antibodies to minimize the adverse pregnancy outcomes.

**Keywords:** Infertility, Autoimmune thyroid disease (AITD), thyroid auto-antibodies, Hypothyroidism, Hyperthyroidism, Subfertility.

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**INTRODUCTION:**

Auto-Immune Thyroid disorders (AITD) are estimated to be one the commonest causes of morbidity worldwide and more so in infertile women of reproductive age group [1]. Its prevalence is predicted to be about 2-4% among women with infertility [2]. AITD commonly include Graves' disease and Hashimoto's thyroiditis among other entities under AITD, and their incidence is reported to be higher in female [3]. The mechanism of pathogenesis in AITD is complex and involves Immune intolerance of self-antigens in genetically susceptible individuals which can be triggered by infections, medication, Iodine intake, smoking and stress [4]. The diagnosis of Graves' disease and Hashimoto's thyroiditis involves demonstrating circulating autoantibodies to Anti-thyroid peroxidase antibodies (anti-TPO) and Anti-thyroglobulin antibodies (anti-TG) even without the overt clinical manifestations [5]. Anti-thyroid peroxidase antibodies (anti-TPO) are directed against the glycoprotein which catalyse the oxidation of Iodine and thyroglobulin reactions in the thyroid gland [6]. Anti-TPO antibodies are highly specific and are found in 90% of patients with Hashimoto's thyroiditis, also, they are detected among 75% of the Graves' disease individuals. An estimated 10-20% of nodular goitre and thyroid cancer patients were found to be positive for anti-TPO antibodies, with 10-15% of healthy individuals having above normal serum levels of anti-TPO titres [7]. AITD has been implicated in recurrent abortions, placental abruption, preterm delivery and overall increased perinatal mortality [8]. With increasing evidences and advancements, it has been a common clinical practice to assess the thyroid functions in women with reproductive age to prevent the unfavourable pregnancy outcomes [9]. In this article, we intend to offer an insight on the prevalence of Thyroid autoantibodies i.e; Anti-thyroid peroxidase antibodies (anti-TPO) and Anti-thyroglobulin antibodies (anti-TG).

**DISCUSSION:**

In our investigative study, it was observed that a large proportion of infertility issues were attributed to the causes related to AITD, 20.7% of overall infertility etiological causes. The AACE guidelines recommends that anti-thyroid antibodies be measured in women with Infertility or Subfertility and in patients with history of miscarriages and Subclinical Hypothyroidism [10]. Thyroid hormones have a critical role in the various aspects of reproductive health, therefore, thyroid hormone imbalance (hypothyroidism and hyperthyroidism) impair normal ovarian function and have deteriorating pregnancy outcomes [11]. In a study conducted by McGrogan et

al. it was inferred that the prevalence of AITD in general population was 8-14%, which is lower than the percentage of individuals with infertility reported in our study [12]. In addition, a study undertaken by Korevaar et al. concluded that women with AITD are associated with lower ovarian reserve [13]. A meta-analysis study by Prummel MF et. al found that serum TSH titres in thyroid auto-antibody positive but euthyroid women were higher than in antibody negative women, with a difference of  $0.81 \pm 0.58$  mU/L ( $p$ -value=0.005), which further reinforce the association between AITD and miscarriages [14]. Treatment modalities have reflected the underlying pathophysiological mechanism in AITD. Regulating the Immune process in patients with the use of Intravenous Immunoglobulin (IVIG) has proven to be beneficial in the previous studies [15]. Furthermore, a prospective study by Negro et al. suggested that substitutive treatment with Levothyroxine (T4) have shown to lower the risk of miscarriage and premature delivery. This study should be further confirmed by double-blinded placebo controlled Randomized clinical trials (RCT) with adequate sample size [16].

**MATERIALS AND METHODS:**

This is a retrospective cross-sectional study employed at MVJ Medical College and Research Hospital, Bengaluru, India from June 2015 to May 2019. The study subjects who were unable to conceive with thyroid or gynaecological issues were primarily referred by general practitioner to our centre. Overall, a total of 1382 patients with laboratory serum titres of anti-thyroid antibodies (anti-TPO) as well as anti-thyroglobulin antibodies (anti-TG) were included in this study. We included patients with anti-TPO antibodies  $\geq 40$  IU/mL and anti-TG antibodies  $\geq 45$  IU/ml, and excluded patients above 40 years and below 18 years. The immunoassay tests were performed using Cobas c 111 analyzer (Roche Diagnostics). This instrument is a random-access auto-analyzer with closed system. Statistical analysis was done using the Statistical program for Social Sciences (Version 25; IBM Corporation, Armonk, NY, USA). A  $p$ -value  $\leq 0.05$  was considered statistically significant with an alpha-criterion set at 5%.

**RESULTS:**

Of the total 1392 study subjects included in the study with provisional diagnosis of infertility, we detected the presence of either anti-TPO or anti-TG antibodies in 287 patients (20.7%). The mean age of patients with positive thyroid auto-antibodies is  $28.4 \pm 0.84$  years, while it is noted to be slightly higher among those with negative lab results with  $29.7 \pm 0.44$  ( $p$ -value= 0.72). (Table-I)

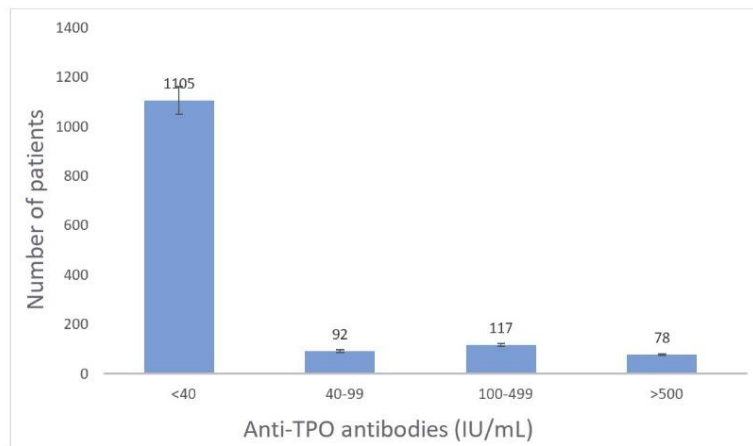
Patient characteristics	Auto-antibody status		Total (N=1392)	p-value
	Positive n (%)	Negative n (%)		
Number of patients (n)	287	1105	1392	
Age (in years)	28.4 ± 0.84	29.7 ± 0.44	29.05 ± 0.64	0.72

It has been found that, 192 (66.8%) patients tested positive for Anti-TPO antibodies and 95 (33.2%) of them for Anti-TG antibodies. Our results emphasize

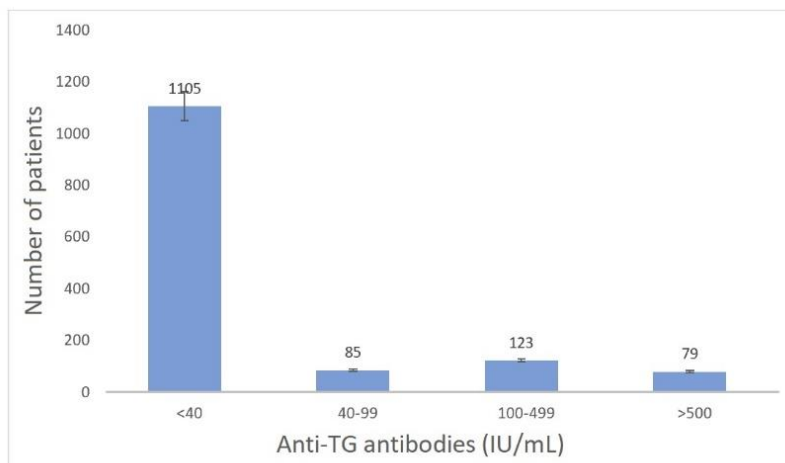
the fact that Anti-TPO antibodies are the most common thyroid auto-antibodies among patients with AITD. (Table-2)

Year of the study	Auto-antibody status		Total (N=287)	p-value
	Anti-TPO n (%)	Anti-TG n (%)		
2015	38 (67.8)	18 (32.2)	56 (19.5%)	0.372
2016	42 (68.8)	19 (31.2)	61 (21.2%)	0.182
2017	35 (60.3)	23 (39.7)	58 (20.2%)	0.144
2018	48 (68.5)	22 (31.5)	70 (24.3%)	0.791
2019	29 (69.0)	13 (31.0)	42 (14.6%)	0.211

Majority of the study population, 117 (40.7%) and 123 (42.8%) of the patients have the Anti-TPO and Anti-TG antibodies respectively between 100-499 (IU/mL).



**Figure 1: Serum anti-TPO antibodies titres (Anti-TPO: Anti-thyroid peroxidase)**



**Figure 2: Serum Anti-TG antibodies  
(Anti-TG: Anti-thyroglobulin)**

**CONCLUSION:** Owing to the fact that thyroid hormones play a critical role in the reproductive health and pregnancy, an imbalance could have catastrophic pregnancy outcomes. Therefore, screening for thyroid auto-antibodies are recommended in cases with infertility. In this study, it was found that 20.7% of the patients with failure to conceive have elevated thyroid auto-antibodies titres. Further studies are required to establish the causality between AITD and infertility so that the adverse pregnancy outcomes can be minimised.

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