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Original Research Article

Association of Anti-Thyroid Stimulating Hormone Receptor Antibodies with Female Infertility: A Comprehensive Analysis

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Abstract: ***Background*:** Infertility affects 10-15% of couples globally with female factors contributing to nearly half of cases. Thyroid dysfunction, particularly involving thyroid-stimulating hormone (TSH) and anti-TSH receptor antibodies (TRAbs), plays a crucial role in reproductive health. Autoimmune thyroid diseases like Hashimoto's thyroiditis and Graves' disease are linked to infertility, miscarriage, and pregnancy complications. This study investigates the association between anti-TSH receptor antibodies and female infertility, aiming to clarify their impact on reproductive outcomes. ***Objectives:*** To investigate the relationship between anti-TSH receptor antibodies and Female infertility. ***Methods and Materials:*** This cross-sectional study was conducted from July to December 2023 at Dhaka Medical College in collaboration with the National Institute of ENT. Ninety infertile women aged 18–40 years were recruited using purposive sampling. Blood samples were collected and analyzed for anti-TSH receptor antibodies and serum TSH levels. Data were processed using SPSS version 25 with ethical approval obtained. ***Result:*** Among 90 infertile women, 68.9% were aged 21-30 years (mean: 26.82 ± 5.37) and 74.4% had a normal BMI (23.47 ± 2.54 kg/m²). The IQR for marital age (4.25) was higher than for infertility duration (2.62). Median Anti-TSH receptor antibody was 0.82 IU/L (IQR: 0.56–1.14), and serum TSH was 2.65 μIU/mL (IQR: 1.30–5.35). Elevated Anti-TSH receptor antibody is strongly correlated with high TSH ($p < 0.001$). ***Conclusion:*** Thyroid autoimmunity, marked by elevated Anti-TSH receptor antibodies, significantly impacts female infertility, highlighting thyroid dysfunction's role in reproduction.

Keywords: Infertility, Thyroid autoimmunity, Anti-TSH receptor antibodies, Thyroid dysfunction.

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Introduction

Infertility is a significant global health concern, affecting approximately 10-15% of couples worldwide, with female factors contributing to nearly 50% of cases.[1] Among the myriad causes of female infertility, endocrine disorders, particularly thyroid dysfunction, have garnered increasing attention due to their profound impact on reproductive health.[2] The thyroid gland plays a pivotal role in regulating metabolism, growth, and development, and its dysfunction can disrupt the

delicate hormonal balance required for successful conception and pregnancy.[3] Thyroid-stimulating hormone (TSH) is a key regulator of thyroid function, and its dysregulation has been implicated in various reproductive disorders, including infertility.[4] Recent studies have highlighted the potential role of anti-thyroid antibodies, particularly anti-TSH receptor antibodies (TRAbs), in the pathogenesis of thyroid-related infertility.[5] These antibodies can interfere with the normal function of TSH, leading to either hyperthyroidism or hypothyroidism, both of which are associated with adverse reproductive outcomes.[6] Autoimmune thyroid diseases (AITDs), such as Hashimoto's thyroiditis and Graves' disease, are characterized by the presence of these antibodies and have been linked to an increased risk of infertility, miscarriage, and other pregnancy complications.[7]

Despite the growing body of evidence suggesting a connection between anti-TSH receptor (anti-TSHR) antibodies and female infertility, the exact mechanisms underlying this association remain poorly understood.[8] The prevalence of anti-TSH antibodies in women with infertility is significantly higher than in the general population, suggesting a potential role in the etiology of reproductive dysfunction.[9] Some studies have proposed that these antibodies may directly affect ovarian function, impairing folliculogenesis and oocyte quality.[10] Others have suggested that the inflammatory milieu associated with AITDs may disrupt endometrial receptivity, thereby hindering embryo implantation.[11] Additionally, the presence of anti-TSH receptor antibodies has been correlated with elevated levels of thyroid peroxidase (TPO) antibodies, further complicating the endocrine landscape and exacerbating reproductive challenges.[12] Given the potential implications of anti-TSH receptor antibodies on female fertility, there is a pressing need for further research to elucidate their role and explore potential therapeutic interventions.[13] This cross-sectional descriptive study aims to investigate the association between anti-TSH receptor antibodies and female infertility, with the goal of providing valuable insights into the pathophysiology of thyroid-related reproductive disorders.[14]

Objectives

General Objective

To assess the link between anti-thyroid stimulating hormone receptor antibodies and infertility in women.

Specific Objectives

To measure anti-TSH receptor antibody levels in infertile women

To measure TSH levels in infertile women

To evaluate the relationship between serum TSH levels

Methods And Materials

Study design: This cross-sectional descriptive study was conducted to investigate the association between anti-thyroid stimulating hormone antibodies and female infertility. The research took place in the Department of Biochemistry, Dhaka Medical College, Dhaka, in collaboration with the National Institute of ENT, Tejgaon, Dhaka, over a period from July 2023 to December 2023. The study population consisted of women aged 18 to 40 years, diagnosed with infertility, who were attending the Reproductive Endocrinology and Infertility Unit at Dhaka Medical College Hospital (DMCH

Inclusion Criteria

Women aged 18–40 years, diagnosed cases of infertility based on history and clinical examination by an infertility specialist.

Exclusion Criteria

Infertility due to male factors, Women unwilling to provide consent.

Study Procedure

Participants were selected from the Reproductive Endocrinology and Infertility Unit at DMCH. The study's objectives were explained to the participants, and written informed consent was obtained. A structured data collection sheet was used to record demographic and clinical information.

Blood Sample Collection

5 ml of venous blood were collected under aseptic conditions. Blood was clotted and centrifuged at 3000 rpm to separate serum, which was stored at -20°C for further analysis.

Statistical Analysis: Data were processed and analyzed using SPSS (version 25). Quantitative data were expressed as mean ± standard deviation, and qualitative data as frequency and percentage. Statistical significance was assessed using a p-value < 0.05.

Ethical Considerations

The study protocol received approval from the Department of Biochemistry and the Ethical Review Committee (ERC) of Dhaka Medical College. Written informed consent was obtained from all participants, ensuring confidentiality and voluntary participation.

Operational definitions

It included normal TSH levels (0.4–5.5 μIU/mL), normal anti-TSH receptor antibody levels (<1.5 IU/L). Infertility was defined as the inability to conceive after one year of unprotected intercourse.

Results

Table 1: Age and BMI Distribution among Infertile Women (n=90)

Variable	Frequency (n)	Percentage (%)
Age (years)		
≤ 20	7	7.8
21–30	62	68.9
≥ 31	21	23.3
Total	90	100
Mean ± SD	26.82 ± 5.37	
Range	18–40	
BMI (kg/m²)		
<18.5 (Underweight)	2	2.2
18.5–24.9 (Healthy)	67	74.4
25.0–29.9 (Overweight)	20	22.2
≥30.0 (Obese)	1	1.1
Total	90	100
Mean ± SD	23.47 ± 2.54	
Range	18.0–31.0	

Table 1 highlights the demographic and clinical characteristics of 90 infertile women. Most participants (68.9%) were aged 21-30 years, with a mean age of 26.82 ± 5.37 years, ranging from 18 to 40 years. Regarding BMI, 74.4% had a healthy BMI (18.5-24.9 kg/m²), 22.2% were overweight (25.0-29.9 kg/m²), 2.2% were underweight (<18.5 kg/m²), and 1.1% were obese (≥30 kg/m²). The average BMI was 23.47 ± 2.54 kg/m², indicating a predominantly normal weight population. These findings suggest that most women in the study were of reproductive age with a healthy weight, factors that may influence fertility outcomes.

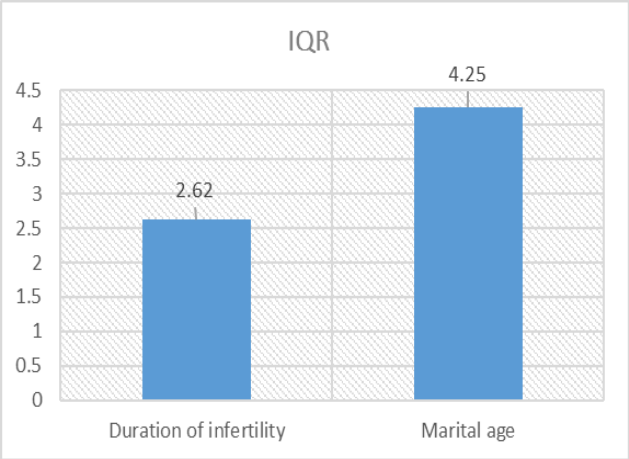

Figure 1: Distribution of Duration of Infertility, and marital status of the study participants (n=90)

Figure 1 illustrates the interquartile range (IQR) for two variables: the duration of infertility and marital age among the study participants. The IQR for marital age is notably higher at 4.25 compared to the duration of infertility, which has an IQR of 2.62.

Table 2: Thyroid Autoantibody Status of Infertile Women (n=90)

Thyroid Hormone Status	Median	IQR (Q1–Q3)
Anti-TSH receptor antibody (IU/L)	0.82	0.58 (0.56–1.14)
TSH (μIU/ml)	2.65	4.05 (1.30–5.35)

Table 2 presents the thyroid autoantibody status among 90 infertile women, showing the median values and interquartile ranges (IQR) for Anti-TSH receptor antibody and TSH levels. The median Anti-TSH receptor antibody level was 0.82 IU/L, with an IQR of 0.56–1.14, indicating a relatively narrow distribution. The median TSH level was 2.65 μIU/mL, with a wider IQR range of 1.30–5.35, suggesting greater variability in thyroid-stimulating hormone levels among the participants.

Table-3: Distribution of thyroid autoantibodies among the study subjects according to serum TSH level (n=90)

Thyroid Autoantibodies	Serum TSH (μIU/mL)		p-value
	High (>5.5) n (%)	Normal (0.4 to 5.5) n (%)	
Anti TSH receptor antibody			
Normal (<1.5)	22 (95.7)	55 (96.5)	<0.001[s]
High (>1.5)	1 (4.3)	2 (3.5)	

Table 3 presents the distribution of thyroid autoantibodies among study participants based on serum TSH levels. Among participants with high TSH levels (>5.5 μIU/mL), 95.7% had normal Anti-TSH receptor antibody levels (<1.5), while 4.3% had elevated levels (>1.5). Similarly, in participants with normal TSH levels (0.4–5.5 μIU/mL), 96.5% had normal Anti-TSH receptor antibody levels, whereas 3.5% exhibited elevated levels. A statistically significant association was found between Anti-TSH receptor antibody levels and serum TSH levels (**p < 0.001**), suggesting that the majority of participants in both groups had normal antibody levels, with only a small proportion presenting elevated values.

Discussion

The demographic profile of the study cohort revealed that the majority of infertile women were aged 21–30 years (68.9%), with a mean age of 26.82 ± 5.37 years. This aligns with global trends where infertility evaluations peak among women in their third decade, reflecting heightened awareness and early intervention in reproductive health.[15] The predominance of healthy BMI (74.4%) and low obesity rates (1.1%) contrasts with studies linking obesity to ovulatory dysfunction, suggesting that weight-related factors may not be the primary driver of infertility in this population.[16] However, the observed variability in marital age (IQR: 4.25) compared to the duration of infertility (IQR: 2.62) underscores the multifactorial nature of infertility, where delayed marriage or delayed childbearing intentions may contribute to prolonged infertility despite optimal physiological conditions.[17] The median Anti-TSHR antibody level of 0.82 IU/L (IQR: 0.56–1.14) falls within the reference range for thyroid autoimmunity, yet the significant association between elevated Anti-Receptor antibodies and high TSH levels (>5.5 μIU/mL) highlights a potential thyroid-fertility axis. These findings mirror studies demonstrating that thyroid autoimmunity, even in euthyroid women, may impair ovarian reserve and endometrial receptivity.[18] This suggests that thyroid dysfunction, particularly when autoimmune in origin, may exacerbate infertility risks, necessitating routine screening of thyroid antibodies in fertility assessments.[19]

The strong statistical association ($p < 0.001$) between elevated TSH and Anti-TSH receptor antibodies supports the hypothesis that thyroid autoimmunity disrupts hypothalamic-pituitary-thyroid feedback, leading to subclinical or overt hypothyroidism.[20] Such dysregulation is linked to menstrual irregularities, anovulation, and recurrent pregnancy loss, even in the absence of overt thyroid disease.[21] However, the absence of elevated Anti-receptor antibodies in women with normal or low TSH levels implies that thyroid autoimmunity alone may not always drive thyroid dysfunction, necessitating individualized diagnostic approaches.[22] These results align with recent guidelines advocating for integrated thyroid and reproductive hormone profiling in infertility workups.[23-30] The study has several limitations that should be considered when interpreting the findings. The relatively small sample size of 90 participants, due to time constraints, limits the generalizability of the results. Being a single-center study, the findings may not fully represent the broader population of infertile women in Bangladesh.

Conclusion

This study highlights the significant association between anti-TSH receptor antibodies and infertility in women, emphasizing the impact of thyroid autoimmunity on reproductive health. Elevated levels of anti-TSH receptor antibodies were observed among the study participants, underscoring the role of thyroid dysfunction in impairing fertility.

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