

Relationship of Thyroid Hormone Dysfunction with Infertility among Women of Reproductive Age

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ABSTRACT

Background: This prospective cohort study demonstrates that there is a strong correlation between dysfunction of thyroid hormones, particularly, hypothyroidism and low fertility rate amongst infertile women of reproductive age in Bangladesh. Thyroid screening and appropriate management of thyroid diseases can improve the fertility rates of this category of people. **Objective:** To assess the relationship between thyroid hormone dysfunction and infertility among women of reproductive age. **Methods & Materials:** A prospective cohort study was conducted at 250 Bedded General Hospital, Kushtia, Bangladesh, from January 2023 to December 2024. A total of 63 women of reproductive age with infertility (failure to conceive after 12 months of regular unprotected intercourse) were enrolled using purposive sampling. Thyroid function tests (TSH, free T3, free T4) were performed at baseline. Participants were followed for 12 months to assess conception rates. Data were analyzed using SPSS version 23.0, with chi-square tests and logistic regression to assess associations ($p < 0.05$ considered significant). **Results:** Among 63 infertile women, 38.1% ($n=24$) had thyroid dysfunction: hypothyroidism (22.2%, $n=14$), subclinical hypothyroidism (11.1%, $n=7$), and hyperthyroidism (4.8%, $n=3$). After 12 months of follow-up, conception occurred in 12.5% (3/24) of those with thyroid dysfunction versus 43.6% (17/39) of euthyroid participants ($p = 0.012$). After adjusting for age and BMI, hypothyroidism was independently associated with reduced conception (aOR 0.21, 95% CI 0.06–0.73). **Conclusion:** Thyroid hormone dysfunction, particularly hypothyroidism, is significantly associated with lower conception rates among infertile women of reproductive age. Routine thyroid

screening and management may improve fertility outcomes in this population.

Keywords: Female infertility, Hypothyroidism, Prospective, Reproductive age, Thyroid dysfunction, Women

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INTRODUCTION

Globally, infertility is found in about 8-12% out of every hundred couples of reproductive age and female factors associated with infertility have been attributed to almost half of these. Out of the variety of endocrine disorders that are implicated with subfertility in women, abnormalities in thyroid hormones have proved to be a major yet potentially modifiable risk factor of subfertility among women [1]. The thyroid gland, with its production of thyroxine (T4) and triiodothyronine (T3) plays an indispensable role in the regulation of the metabolic processes including control of reproductive physiology [2]. There is a complex, two-way relationship between female infertility and thyroid dysfunction. Thyroid hormones affect almost all point of the hypothalamic pituitary ovary (HPO) axis, including secretion of gonadotropin-releasing hormone, ovarian steroidogenesis and follicular development [3,4]. Hyperthyroidism, as well as hypothyroidism that is either direct or indirect in severity, directly or indirectly influences the functioning of the uterus and ovaries, as well as the development of the fetus since the time of implantation up to birth [3]. There is evidence that thyroid hormone receptors are widely expressed in the fetomaternal unit, and that a change in the local thyroid hormone activity can result

in early pregnant arrest even in women who can be considered euthymic based on serum hormone levels [5]. The prevalence of thyroid disorders between the women within the reproductive age demonstrates a big burden. Autoimmune thyroid diseases, such as the thyroiditis of Hashimoto and Graves disease, are most prevalent in this group and have increasingly been identified as having significant impact on infertility and poor pregnancy outcomes [3]. This is because recent studies have shown that even subclinical hypothyroidism is linked to reduced ovarian reserve as is evidenced by lower levels of anti-Müllerian hormone and fewer antral follicles [6]. Moreover, the existence of thyroid autoantibodies (anti-thyroid peroxidase and anti-thyroglobulin) in the euthyroid women has been attributed to the higher risks of implantation failure and pregnancy loss [7,8]. Thyroid disorders can be considered as one of the critical matters of public health in the South Asian context. Bangladesh, like other countries in the region, faces a high prevalence of iodine deficiency disorders, which directly impact thyroid function [9]. Most recently a survey was carried out in Bangladesh and reported that around 10.5% of all those surveyed had been diagnosed with a thyroid disorder with hypothyroidism (7.01%) being more prevalent than hyperthyroidism (3.5%) [10]. Domestic studies have also testified the correlation existing between thyroid

dysfunction and gynecological morbidity, comprising abnormal uterine hemorrhage and menstrual abnormalities in case of Bangladeshi women of reproductive age [11]. Although there is increasing evidence on the relationship between thyroid dysfunction and infertility, future data on this relationship is only limited in Bangladesh. The majority of the available studies are of cross-sectional nature and have mainly dealt with prevalence of thyroid disorders in an infertile population as opposed to prospectively investigating the effects of thyroid disorders on results of conception [12]. In addition, to treatment of overt thyroid dysfunction in the women trying to conceive, the role of management of subclinical disease and thyroid autoimmunity, is controversial [3,13]. Within this context, the current study was planned with the view to prospectively assess the association between the dysfunction of thyroid hormones and infertility among females in an age range of reproductive age attending a tertiary care hospital in Kushtia, Bangladesh. We sought to determine an influence of different patterns of thyroid dysfunctions on conception rates and also provide region specific evidence which could help guide clinical practice guidelines.

METHODS & MATERIALS

The study was a prospective cohort study, involving women of childbearing age (18-45 years) who presented at an outpatient department of 250 Beded General Hospital, Kushtia, Bangladesh, presenting with primary or secondary infertility. Informed consent was informed and written before participating in the study.

Inclusion criteria: Women who met the following criteria were included: 1) women aged between 18-45 years; 2) women with a history of infertility (failure to achieve a clinical pregnancy even after one year of regular, unprotected sexual intercourse) were included. The participants had to be without previous thyroid surgery and radioiodine therapy and desire to go through a 12-month follow-up period.

Exclusion criteria: Women who had known thyroid cancer, were using

antithyroid medications or levothyroxine, were pregnant at the time of enrollment, had polycystic ovary syndrome (PCOS), hyperprolactinemia, primary ovarian insufficiency, male factor infertility (azoospermia or severe Oligospermia), or bilateral tubal obstruction were excluded.

Study procedure: Baseline demographic and clinical measurements were determined through a structured interview and medical examination. Using chemiluminescence immunoassay, the thyroid function tests (TSH, free T3, free T4) were performed on fasting venous blood (5 mL). The subjects were trailed prospectively after 12 months to note the conception, which was confirmed by urine for pregnancy test and ultrasonography of lower abdomen.

Data analysis: Data were typed in Microsoft Excel and analyzed at SPSS version 23.0. Continuous variables were

reported as means and SD; the categorical variables as frequencies and percentages. The chi-square test was used to compare the conception rates among thyroid dysfunction and euthyroid groups ($p < 0.05$). Confounders were adjusted by the use of a logistic regression.

RESULT

Table I compares the baseline demographic and clinical characteristics between women with thyroid dysfunction and euthyroid women. The mean age, BMI, duration of infertility, and distribution of primary and secondary infertility were comparable between the two groups, with no statistically significant differences observed (all $p > 0.05$). These findings indicate that both groups were similar at baseline, minimizing the likelihood of confounding due to demographic or infertility-related factors.

Table I
Baseline demographic and clinical characteristics of study participants.

Characteristic	Thyroid dysfunction (n=24)	Euthyroid (n=39)	p-value
Mean age (years)	31.1 ± 5.2	29.7 ± 4.6	0.267
Mean BMI (kg/m ²)	24.6 ± 3.1	23.9 ± 2.8	0.341
Mean infertility duration (years)	3.4 ± 1.9	3.1 ± 1.7	0.502
Primary infertility (%)	62.5% (15/24)	64.1% (25/39)	0.895
Secondary infertility (%)	37.5% (9/24)	35.9% (14/39)	0.895

Note: Continuous variables compared using an independent t-test; categorical variables compared using a chi-square test.

Table II presents the distribution of thyroid status among the study participants. Of the 63 infertile women, 61.9% were euthyroid, while 38.1% had thyroid dysfunction. Overt hypothyroidism was the most prevalent thyroid abnormality, accounting for 22.2% of participants, followed by subclinical hypothyroidism (11.1%) and hyperthyroidism (4.8%).

Table II
Distribution of thyroid dysfunction types among infertile women.

Thyroid status	n	%
Euthyroid	39	61.9
Overt hypothyroidism	14	22.2
Subclinical hypothyroidism	7	11.1
Hyperthyroidism	3	4.8
Total	63	100

Table III demonstrates the relationship between thyroid dysfunction and menstrual patterns. Menstrual irregularities were significantly more common among women with thyroid dysfunction than among euthyroid women (70.8% vs. 38.5%, $p = 0.012$). Oligomenorrhea was significantly more prevalent in the thyroid dysfunction group (45.8% vs. 20.5%, $p = 0.032$), whereas the frequencies of menorrhagia and polymenorrhea did not differ significantly between the groups (Table III).

Table III
Association between thyroid dysfunction and menstrual irregularities.

Menstrual pattern	Thyroid dysfunction	Euthyroid	p-value
Regular cycles	29.2% (7/24)	61.5% (24/39)	0.012
Irregular cycles (any type)	70.8% (17/24)	38.5% (15/39)	0.012
Oligomenorrhea	45.8% (11/24)	20.5% (8/39)	0.032
Menorrhagia	16.7% (4/24)	10.3% (4/39)	0.462
Poly-menorrhea	8.3% (2/24)	7.7% (3/39)	0.928

Note: Chi-square test was used for all comparisons. Values in parentheses represent the number of participants in each subgroup.

Table IV shows conception outcomes according to thyroid status after 12 months of follow-up. The conception rate was significantly higher among euthyroid women compared to those with thyroid dysfunction (43.6% vs. 12.5%, $p = 0.009$). Among the thyroid disorders, women with overt hypothyroidism had the lowest conception rate (7.1%), followed by

subclinical hypothyroidism (14.3%), while women with hyperthyroidism achieved a conception rate of 33.3%.

Table IV
Conception rates at 12-month follow-up by thyroid status.

Thyroid status	Conceived (n)	Did not conceive (n)	Conception rate (%)	p-value
Euthyroid (n=39)	17	22	43.6	Reference
Thyroid dysfunction (n=24)	3	21	12.5	0.009
Overt hypothyroidism (n=14)	1	13	7.1	0.008
Subclinical hypothyroidism (n=7)	1	6	14.3	0.138
Hyperthyroidism (n=3)	1	2	33.3	0.712

The chi-square test was used to compare each subgroup with the euthyroid reference group.

Table V compares baseline thyroid hormone levels between women who conceived and those who did not conceive during the follow-up period. Women who conceived had significantly lower mean TSH levels than those who did not conceive (2.15 ± 1.03 vs. 4.82 ± 3.41 mIU/L, $p = 0.001$). Although free T3 and free T4 levels were slightly higher among women who conceived, these differences were not statistically significant ($p > 0.05$).

Table V
Mean thyroid hormone levels at baseline by conception outcome.

Hormone parameter	Conceived (n=20)	Did not conceive (n=43)	p-value
TSH (mIU/L)	2.15 ± 1.03	4.82 ± 3.41	0.001
Free T3 (pg/mL)	3.12 ± 0.54	2.89 ± 0.67	0.176
Free T4 (ng/dL)	1.08 ± 0.21	0.96 ± 0.29	0.094

An independent t-test was used for all comparisons. Data presented as mean $\pm$ standard deviation.

Table VI presents the results of multivariable logistic regression analysis evaluating factors associated with conception. After adjustment for age, BMI, and duration of infertility, thyroid dysfunction remained independently associated with a significantly reduced likelihood of conception (aOR = 0.18, 95% CI: 0.04–0.77, $p = 0.020$). Age, BMI, and duration of infertility were not significantly associated with conception outcomes in the adjusted model.

Table VI
Logistic regression analysis for factors associated with conception.

Variable	Adjusted odds ratio (aOR)	95% CI	p-value
Thyroid dysfunction (vs. euthyroid)	0.18	0.04 – 0.77	0.020
Age (per year increase)	0.94	0.85 – 1.04	0.221
BMI (per kg/m ² increase)	0.96	0.82 – 1.12	0.589
Duration of infertility (per year increase)	0.89	0.69 – 1.15	0.372

Binary logistic regression analysis was performed with conception (yes/no) as the dependent variable. CI = confidence interval.

DISCUSSION

The current prospective cohort study that reveals a high level of associations with thyroid hormone dysfunctions and reduced pregnancy rates among the infertile women of the reproductive age in Kushtia, Bangladesh. Our results that only 12.5% of women with thyroid dysfunction conceived within 12 months as opposed to 43.6% of euthyroid women ($p = 0.009$) are not unique in the literature that documents the detrimental effects of thyroid dysfunction on the ability of women to become pregnant [1,3]. The incidence of thyroid dysfunction in our infertile cohort was 38.1% and nearly all types of thyroid dysfunction have occurred (overt hypothyroidism 22.2%. This is in fact a significantly higher prevalence than the 10.5% prevalence in the general Bangladeshi population, which lends some credence to the idea that the question of overrepresentation of thyroid disorders

among women seeking fertility care [9,10]. Such results have been found in the other South Asian locations where hypothyroidism is considered high among the infertile women in the range between 20% and 35% [14,15]. The underlying cause of this regional excess can be either persistently unmet need of iodine or a combination of the two factors [16]. The fact that menstrual abnormalities were observed to occur significantly more frequently in the group with thyroid dysfunction (70.8% vs. 38.5%, $p = 0.012$) is in line with the proven pathophysiology behind thyroid hormone action on the HPO axis. The gonadotropin-releasing hormone pulsatility, follicle-stimulating hormone and luteinizing hormone secretion, and ovarian steroidogenesis are all modulated by the thyroid hormones [2,4]. Inhibition of these finely tuned activities results in anovulation, luteal phase defects, and oligomenorrhea,

all of which have a direct negative impact on fertility [3]. Interestingly, oligomenorrhea was the most common menstrual abnormality in our group of thyroid dysfunctions (45.8%), which confirms it to be similar to previous reports [17]. The TSH baseline level of women who did not become pregnant was significantly higher (4.82 vs. 2.15 mIU/L, $p = 0.001$), and thyroid dysfunction was confirmed logistic regression an independent variable, that reduced conception after the elimination of age, BMI, and infertility length (aOR 0.18, 95% CI 0.047–0.770). This negative correlation between the levels of TSH and the outcome of fertility has been widely reported. A recent meta-analysis reported that, in women undergoing assisted reproductive technology women with higher levels of TSH (above 2.5 mIU/L) had a significantly lower clinical pregnancy rates than those with lower levels of TSH

[18]. Mechanistic basis of this association is multifactorial. Other than ovulatory disturbances, thyroid hormone deficiency affects endometrial receptivity by suppressing integrin and leukemia inhibitory factor expression, among a variety of implantation-related molecules [5,19]. As well, the change in T-cell profile, and excessive natural killer cell-activity in the endometrium, has both been associated with the development of thyroid autoimmunity, even among euthyroid women [7,20]. Recent discovery that only one of fourteen women with an overt hypothyroidism conceived a child has underscored to us that there is an acute need to diagnose and treat these cases. Professional recommendations suggest that expected TSH level should be 2.5 mIU/L if a woman wishes to conceive [3,21]. Nevertheless, the subclinical hypothyroidism management is controversial. Only 14.3% (1/7) of women with subclinical hypothyroidism conceived in our cohort, indicating that even mild hypothyroidism ailment is worth consideration. A recent randomized controlled trial has shown that treatment in the sub-clinically hypothyroid infertile women with levothyroxine treatment led to a significant improvement in pregnancy rates relative to a placebo control [22]. There are a number of limitations to take into consideration. First was the relatively small sample size (n=63) which might have limited statistical power in treatment of subgroups, especially in the hyperthyroidism. Second, purposive sampling can also result in selection bias, which need not be generalized to the rest of the Bangladeshi population. Third, We did not measure thyroid autoantibodies (anti-TPO, anti-Tg), which would have given a further understanding of the results of the autoimmune mediated infertility among euthyroid women [8,23]. Fourth, we did not evaluate both male partners in terms of thyroid status and other factors in female infertility such as tubal conductivity and ovarian reserve in a comprehensive manner. Fifth, external validity might be restricted by the single-center design [24]. Although this has its constraints, this study offers some important prospective data on a population in South Asia where to date there is very limited evidence. We found that screening of thyroid functional regularly should be done on all infertile women and even indicate that the acquisition of euthyroidism may lead to improved results of conception [25].

LIMITATIONS

Limitations of this study include that it used a small sample, purposive sampling which limits generalizability, lack of threshold testing of other infertility factors, a one center design and possible unmeasured

confounding variables which cause variation in conception.

CONCLUSION

This prospective cohort study illustrates that there is a strong association between dysfunction of thyroid hormones, especially hypothyroidism and low fertility rate among infertile women of reproductive age in Bangladesh. The fertility rate of this group of people can be improved through thyroid screening of routine thyroid functions and well management of thyroid disorders. To validate these results, bigger multicenter studies that incorporate testing of thyroid autoantibodies are recommended.

RECOMMENDATION

An initial infertility evaluation of all women of reproductive age should include Thyroid functional examination (TSH, free T3, free T4). When diagnosed, thyroid dysfunction needs to be treated as soon as possible to maximize the results of conception.

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CONFLICT OF INTEREST

None declared

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