

## Original Research Article

# Thyroid status and treatment responses of hypothyroid infertile women: a study in a tertiary care hospital of Bangladesh

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### ABSTRACT

**Background:** Recently, the prevalence of hypothyroidism in the reproductive age group is found up to 4%. In many studies it had been claimed that, thyroid status is directly involved in women reproductive system. Hypothyroidism can be easily detected by assessing serum thyroid stimulating hormone (TSH) levels. The aim of this study was to dig out the prevalence of hypothyroidism in infertile women and to assess their responses in treatment procedures.

**Methods:** This observational study was conducted National Institute of Traumatology and Orthopedic Rehabilitation (NITOR), Dhaka, Bangladesh during the period from January 2019 to December 2019 in total 236 women of Endocrinology Department treatment. Patients were followed up for six months even if pregnancy was attained.

**Results:** In total 22% (n=52) patients were hypothyroid. Among them 35 (15%) were subclinical hypothyroid and 17 (7%) were frank hypothyroid. Besides these, 73% (n=172) were euthyroid and the rest 5% (n=12) were hyperthyroid. On the other hand, in analysing the outcome (treatment responses) among the hypothyroid subjects we observed regular menstruation, normal ovulation, clinical pregnancy and chemical pregnancy were achieved by 92.31% (n=48), 88.46% (n=46), 50% (n=26) and 69.23% (n=36) subjects respectively.

**Conclusions:** According to the study, the careful diagnosis and treatment of hypothyroidism can ensure benefit a lot rather than going for unnecessary hormone assays and costly invasive procedures in for women of infertility.

**Keywords:** Hypothyroidism, Infertility, PRL level, Thyroid disorder, TSH

### INTRODUCTION

Now a day, the prevalence of hypothyroidism in the reproductive age group is found up to 4%. In many studies it had been claimed that, thyroid status is directly involved in women reproductive system. Although it differs in several places, communities, geographic areas and age-groups but it deserves more attention from the reproductive health physicians and even from world communities. Hypothyroidism can be easily detected by assessing serum thyroid stimulating hormone (TSH) levels. We need a clear concept on this issue. Infertility is a world health issue affecting approximately 8-10% of couple's worldwide.<sup>1</sup> WHO estimates the overall prevalence of primary infertility in India to be 3.5-

16.8%.<sup>2</sup> Both hyperthyroidism and hypothyroidism have profound effects on estrogen and androgen metabolism, menstrual function and fertility.<sup>3</sup> They may cause delayed onset of puberty, menstrual abnormalities, anovulatory cycles, miscarriages and infertility.<sup>4</sup> Hypothyroidism can be easily detected by assessing serum thyroid stimulating hormone (TSH) levels. A slight increase in TSH levels with normal T3 and T4 indicates subclinical hypothyroidism whereas high TSH levels accompanied by low T3 and T4 levels indicate clinical hypothyroidism. Elevated thyrotropin-releasing hormone levels due to hypothyroidism are often associated with increased prolactin (PRL) levels and a delayed LH response to GnRH.<sup>5</sup> Thyroid dysfunction is implicated in a broad spectrum of reproductive disorders, ranging from

abnormal sexual development to menstrual irregularities and infertility.<sup>6</sup> It has been proved that for normal sexual function, thyroid secretion of T3, T4 need to be approximately normal. We had conducted this study to collect some specific information regarding hypothyroidism in infertile women and to assess their responses in treatment procedures.

### Objectives

#### General objective

To dig out the prevalence of hypothyroidism in infertile women and to assess their responses in treatment procedures.

#### Specific objective

To collect information regarding the thyroid status of participants and to collect information regarding hormone level in hypothyroid participants.

### METHODS

This was a descriptive observational study and it was conducted in National Institute of Traumatology and Orthopedic Rehabilitation (NITOR), Dhaka, Bangladesh, during the period from January 2019 to December 2019. In total 236 women attended Endocrinology Department treatments were finalized as the study population of this study. The study was approved by the ethical committee of the mentioned hospital. Proper written consents were taken from all the participants before starting data collection. The routine investigations such as CBC, blood sugar of 2 hours post prandial or GTT, TSH and prolactin was done. Subclinical hypothyroidism was diagnosed when there was increased TSH and normal FT4. Hypothyroid patients were given levothyroxin depending upon TSH levels and continued until end of the study. Patients were followed up for six months even if pregnancy was attained. TSH and PRL were measured by the electro-chemiluminescence method as per the instruction manual for Elecsys, 2010 (Roche, USA). Normal TSH and PRL levels were 0.27-5.0 U/ml and 1.9-25 ng/ml, respectively, as per kit supplier's instruction. Therefore, hypothyroidism was considered at TSH levels of >5.0  $\mu$ IU/ml and hyperprolactinemia at PRL levels of >25 ng/ml and subclinical hypothyroidism when increased TSH and normal FT4. Hypothyroid patients were given levothyroxin depending upon TSH levels and continued until end of the study. Patients were followed up for six months even if pregnancy was attained. The primary endpoint was pregnancy and secondary endpoint were serum TSH, FT4, regular menstruation and ovulation. Sign of ovulation was assessed by TVS, day 21 serum progesterone. Chemical pregnancy when serum  $\beta$ -HCG was >15 mIU/ml and clinical pregnancy was confirmed by observing gestational sac with or without embryo with or without visible cardiac activity on USG. Statistical analysis was done by SPSS version 23.

### Inclusion criteria

This study was simple random sample, every member of the population has an equal chance of being selected. Inclusion criteria were patients of infertile women, patients with hypothyroid patients were given levothyroxin depending upon TSH levels.

### Exclusion criteria

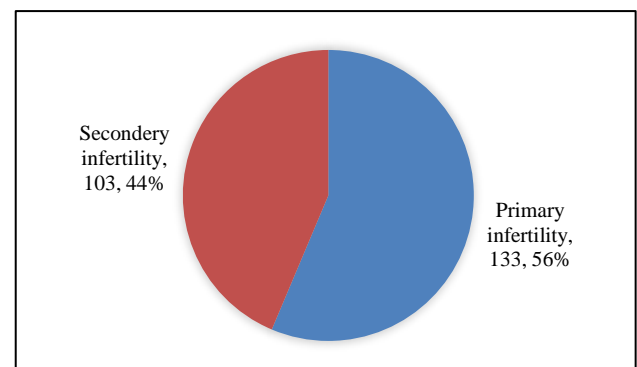
Exclusion criteria were patients who would not give consent, unstable patients with hypothyroid patients were given levothyroxin depending upon TSH levels.

### RESULTS

The total study people were 236 in number. In this study we found the mean $\pm$ SD age of the participants was 24.75 $\pm$ 4.50 years. Besides this, the mean $\pm$ SD BMI was 25.18 $\pm$ 3.16 and the mean $\pm$ SD duration of suffering from infertility was 4.3 $\pm$ 1.25 years (Table 1). Out of total 236 participants 56% (n=133) were with primary infertility and the rest 44% (n=103) were with secondary infertility (Figure 1).

**Table 1: General characteristics of participants (n=236).**

Variables	Mean $\pm$ SD
Age (years)	24.75 $\pm$ 4.50
BMI	25.18 $\pm$ 3.16
Mean duration of infertility (years)	4.3 $\pm$ 1.25



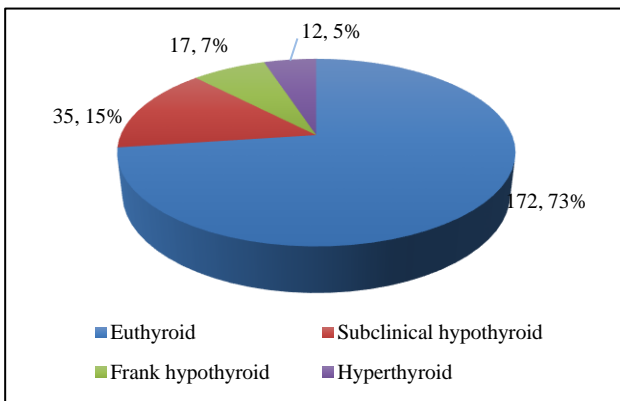
**Figure 1: Types of infertility among participants (n=236).**

In analyzing the thyroid status of the participants we found that, in total 22% (n=52) patients were hypothyroid. Among them 35 (15%) were subclinical hypothyroid and 17 (7%) were frank hypothyroid. Besides these, 73% (n=172) were euthyroid and the rest 5% (n=12) were hyperthyroid (Figure 2). In analyzing the hormone levels of the hypothyroid subjects we found, the mean $\pm$ SD serum TSH, serum FT4 and serum prolactin were 7.22 $\pm$ 2.44 mIU/l, 16.94 $\pm$ 3.31 pmol/l and 51.82 $\pm$ 10.69 ng/ml respectively (Table 2). On the other hand, in analyzing the treatment responses among the

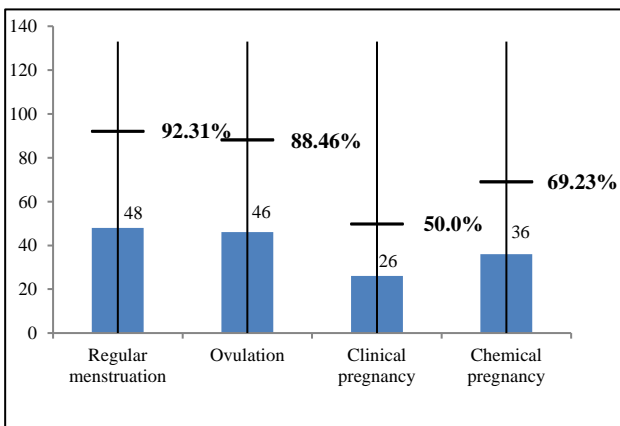
hypothyroid subjects we observed regular menstruation, normal ovulation, clinical pregnancy and chemical pregnancy were achieved by 92.31% (n=48), 88.46% (n=46), 50% (n=26) and 69.23% (n=36) subjects respectively (Figure 3).

**Table 2: Mean hormone level in hypothyroid subjects (n=52).**

Variables	Mean±SD
Serum TSH (mIU/L)	7.22±2.44
Serum FT4 (pmol/l)	16.94±3.31
Serum prolactin (ng/ml)	51.82±10.69



**Figure 2: Thyroid status of participants (n=236).**



**Figure 3: Outcome of hypothyroid subjects (n=52).**

**DISCUSSION**

The aim of this study was to dig out the prevalence of hypothyroidism in infertile women and to assess their responses in treatment procedures. In our study, out of total 236 participants 56% (n=133) were with primary infertility and the rest 44% (n=103) were with secondary infertility. In many previous studies it has been claimed that, hypothyroidism is an important cause of both primary and secondary infertility. Therefore, it is important to predict hypothyroidism during infertility to prevent its occurrence. Many reports have described the use of serum thyroid hormones biochemical parameter to

predict the development of infertility, but with controversial results.<sup>7</sup> TSH and PRL levels are usually checked at the time of the couple’s initial consultation for infertility. In our study, the prevalence of hypothyroidism was 22% and hyperthyroidism was 5%, which is higher than in USA.<sup>8</sup> Thyroid hormones have profound effects on reproduction and pregnancy. Thyroid dysfunction is implicated in a broad spectrum of reproductive disorders, ranging from abnormal sexual development to menstrual irregularities and infertility.<sup>6</sup> The percentage of conception in euthyroid women who were positive for antithyroid antibodies was near about half of the patients after levothyroxine treatment. The result of the present study was not consistent with Negro et al who reported that the pregnancy rate was not affected either by the presence of antithyroid antibodies or treatment with levothyroxine.<sup>9</sup> It has been proved that for normal sexual function, thyroid secretion of T3, T4 need to be normal. Undiagnosed and untreated thyroid disease can be a cause for infertility and sub-fertility. Problems in fertility can occur at any point in the process of conception that is in the development and release of egg, in fertilization or transportation of the fertilized egg from the fallopian tube to the uterus and in implantation of the embryo in endometrium. Hormone therapy with thyroxine is the choice of treatment in established hypothyroidism. It normalizes the menstrual cycle, PRL levels and improves the fertility rate. Therefore, with simple oral treatment for hypothyroidism, about 50% infertile women conceived after 6 weeks to 6 months of therapy. We tried to maintain normal TSH levels. Compliance and adequacy of hypothyroid drug dose were checked by TSH measurement at 6 to 8 weeks interval.

There are some limitations of the study. Our study wasn’t a blinded study so patient bias was present along with observer bias in subjective recording and the small sample size, single center study, blinding was not done, short follow up period.

**CONCLUSION**

According to the findings of this study we can conclude that, careful diagnosis and treatment of hypothyroidism can ensure benefit a lot rather than going for unnecessary hormone assays and costly invasive procedures. The normal TSH levels are the pre-requisite for fertilization. The decision to initiate thyroid replacement therapy in subclinical hypothyroidism at early stage is justified in infertile women. This was a single centered study with a small sized sample. So the findings of this study may not reflect the exact scenario of the whole country. For better management of infertility cause and for getting more specific findings we would like to recommend for conducting more studies regarding the same issue with larger sized sample.

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*Conflict of interest: None declared*

*Ethical approval: Not required*

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