

# Hypothyroidism and hyperprolactinemia in infertility: Bangladesh perspective

Gopa Sarker<sup>a</sup>, Hasina Akhter<sup>a</sup>, Nahid Yusuf<sup>b</sup>, Nasrin Rahman<sup>a</sup>, Md. Kabiruzzaman<sup>c</sup>

## Abstract

**Background:** Infertility is the highest in Bangladesh among all South Asian countries. Hypothyroidism specially subclinical hypothyroidism is a prevailing cause of infertility and habitual abortion. **Objective:** To find out the prevalence of hypothyroidism specially subclinical hypothyroidism as well as hyperprolactinemia in infertility. **Methods:** This was a cross-sectional comparative type of study conducted at Obstetrics & Gynaecology Out Patient Department (OPD) of Rajshahi Medical College Hospital (RMCH), Bangladesh. The sample size was 94. Data on nature of infertility, clinical presentations and biochemical findings were collected by a preformed Data Collection Sheet. Serum hormone assay TSH, T3, T4, and prolactin (PRL) were done in Institute of Nuclear Medicine and Allied Sciences (INMAS), Rajshahi, Bangladesh. Pearson's chi-square and student's 't' test were applied to determine differences in proportions and means respectively. **Results:** Prevalence of clinical hypothyroidism, subclinical hypothyroidism and hyperprolactinemia were 10.6%, 29.8% and 22.3% respectively in study subjects. Prevalence of hypothyroidism and hyperprolactinemia were significantly higher in primary than in secondary infertility. Prevalence of subclinical hypothyroidism was 37.7% in primary and 15.2% in secondary infertility. Prevalence of hyperprolactinemia was 27.9% in primary and 12.1% in secondary infertility. The mean TSH and Prolactin values in primary infertile women ( $3.14 \pm 2.21$  mIU/L and  $507 \pm 206$  mIU/L) were significantly higher than those of secondary infertile women ( $1.35 \pm 1.87$  mIU/L and  $422 \pm 136$  mIU/L). There was no correlation between TSH and prolactin levels in both primary and secondary infertility. **Conclusion:** Hypothyroidism specially subclinical hypothyroidism and hyperprolactinemia are important health disorders in Bangladeshi infertile women. Further studies are needed to clarify the etiology of the hypothyroidism and hyperprolactinemia for better management of infertility cases.

**Key words:** infertility, hypothyroidism, hyperprolactinemia, Bangladesh.

## Introduction

Infertility is not a physically debilitating disease. However, the desire to have a child is the strongest that people experience, and no wonder that infertility is ranked among life's greatest stresses, similar in intensity of having a life threatening illness.<sup>1</sup> Infertility affects at least 12% of couples worldwide.<sup>2</sup> It is 10 – 15% in Western countries.<sup>3</sup> Infertility rate is approximately 15% in Bangladesh, which is the highest among all South Asian countries.<sup>4,5</sup>

Prevalence of hypothyroidism in the reproductive age group is 2-4% and has been shown to be the cause of infertility and habitual abortion.<sup>6,7</sup> Hypothyroidism can be easily detected by assessing thyroid stimulating hormone (TSH) levels in the blood. A slight increase in TSH levels with normal triiodothyroxine (T3) and thyroxine (T4), indicates subclinical hypothyroidism whereas high TSH level accompanied by low T<sub>3</sub> and T<sub>4</sub> levels indicate clinical hypothyroidism.<sup>8</sup> Subclinical hypothyroidism is more common. It can cause anovulation directly or by causing elevation in PRL. It is extremely important to diagnose and treat the subclinical hypothyroidism for pregnancy and to maintain it unless there are other independent risk

factors. Many infertile women with hypothyroidism had associated hyperprolactinemia due to increased production of thyrotropin releasing hormone (TRH) in ovulatory dysfunction.<sup>9,10</sup> Traditionally, measurements of prolactin and thyroid stimulating hormone have been considered important components of the evaluation of women presenting with infertility.<sup>11</sup> Hypothyroidism in females, maternal hypothyroidism and sub-clinical hypothyroidism, have all come under a lot of discussion recently.<sup>12</sup>

Due to the lack of infertility data of women with hypothyroidism in Bangladesh, it is intended to find out the prevalence of hypothyroidism specially subclinical hypothyroidism as well as hyperprolactinemia and correlation between TSH and prolactin levels both in primary and secondary infertility.

## Methods

This was a cross-sectional descriptive type of study conducted at Obstetrics & Gynaecology Out Patient Department (OPD) of Rajshahi Medical College Hospital (RMCH), Bangladesh. All the infertile women attending at the OPD of RMCH for seeking fertility treatment constitute the study population. A

<sup>a</sup>Department of Gynaecology and Obstetrics, Barind Medical College, Rajshahi, Bangladesh.

<sup>b</sup>Department of Gynaecology and Obstetrics, Rajshahi Medical College, Rajshahi, Bangladesh.

<sup>c</sup>Institute of Nuclear Medicine and Allied Sciences (INMAS), Rajshahi, Bangladesh.

Correspondence to :  
G Sarker  
gopasarkerme@yahoo.com

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total of 94 infertile women attended at the OPD were included in this study. The women who were with liver, renal or cardiac diseases; those already on treatment for thyroid disorders or hyperprolactinemia; or whose male partner identified as infertile were excluded from the study. Before selecting the women, informed written consent was taken from each of them.

Data were collected by a preformed Data Collection Sheet (DCS). The DCS was designed to record the nature of infertility, clinical presentations and biochemical findings. The information were recorded from the patients' treatment slips, investigation reports, interview with the patients and consultation with the concerned doctors when necessities. Serum hormone assay TSH, T3, T4, and prolactin (PRL) were done in Institute of Nuclear Medicine and Allied Sciences (INMAS), Rajshahi, Bangladesh. Normal TSH and PRL levels were 0.3-3.0 mIU/L (as per American Association of Clinical Endocrinologists)<sup>13</sup> and < 460 mIU/L<sup>12</sup> respectively. Therefore, hypothyroidism was considered at TSH levels of > 3 mIU/L and hyperprolactinemia at PRL levels of >460 mIU/L. Depending upon the T3 & T4 levels, hypothyroid infertile women were further subdivided into clinical and subclinical hypothyroidism. Clinical hypothyroidism was considered at TSH levels of > 3 mIU/L with decreased serum T3 (<1.1 nmol/L) and T4 (<54.0 nmol/L) levels than normal. Subclinical hypothyroidism was considered at TSH levels of >3mIU/L with normal serum T3 (1.1-2.7 nmol/L) and T4 (54.0-173.0 nmol/L) levels.

Chi-square test was applied to find out the association between nature of infertility and patients' clinical presentation, hypothyroidism and hyperprolactinemia. Student's t test was applied to observe any significant difference of mean TSH and Prolactin values between primary and secondary infertile women. Correlation between serum TSH and Prolactin level in both primary and secondary infertility was calculated.

### Results

A total of 94 women with primary (n=61) and secondary (n=33) infertility were included in this study. Out of 61 primary infertile women, 29(47.5%), 31(50.8%), 32 (52.5%) and 45 (73.8%) women had irregular menstrual cycle, hirsutism, polycystic ovary and body mass index 25 or more. Among the secondary infertile women these clinical

findings except body mass index 25 or more were significantly lower than those of primary infertile women (Table 1).

Table 1. Clinical findings of women with primary and secondary infertility.

Clinical findings	Infertility		P-value
	Primary N= 61	Secondary N = 33	
Irregular menstruation	47.5% (29)	21.2% (7)	0.015
Hirsutism	50.8% (31)	12.1% (4)	0.000
Polycystic Ovary (PCO)	52.5% (32)	12.1% (4)	0.000
Body Mass Index 25 or above	73.8% (45)	63.6% (21)	0.214

A total of 94 infertile women, 10(10.6%) were clinical hypothyroid, 28 (29.8%) were subclinical hypothyroid and the rest 56 (59.6%) were euthyroid women. None of the infertile women was hyperthyroid. Prevalence of clinical hypothyroidism was 14.8% in primary infertile and it was only 3.0% in secondary infertility. Prevalence of subclinical hypothyroidism was 37.7% in primary infertile women. It was 15.2% in secondary infertile women. Prevalence of hyperprolactinemia was 27.9% in primary and 12.1% in secondary infertile, and over all prevalence was 22.3% (Table 2).

Table 2. Serum thyroid stimulating hormone and Prolactin levels in primary and secondary infertility.

Hormones	Status	Type of fertility		Total N(%)	P Value
		Primary N(%)	Secondary N(%)		
TSH (mIU/L)	Clinical hypothyroidism	9 (14.8)	1 (3.0)	10 (10.6)	10.64, p=.005
	Subclinical hypothyroidism	23 (37.7)	5(15.2)	28 (29.8)	
	Euthyroidism	29(47.5)	27 (81.8)	56 (59.6)	
	Total	61(64.9)	33 (35.1)	94(100.0)	
Prolactin (mIU/L)	Hyperprolactinemia	17 (27.9)	4 (12.1)	21 (22.3)	3.06, p= 0.065
	Normal	44 (72.1)	29 (87.9)	73 (77.7)	
	Total N(%)	61 (64.9)	33 (35.1)	94 (100.0)	

The mean TSH value in primary infertile women (3.14±2.21 mIU/L) was significantly higher than that of secondary infertile women (1.35±1.87 mIU/L). The mean Prolactin value in primary infertile women (507±206 mIU/L) was too significantly higher than that of secondary infertile women (422±136 mIU/L) (Table 3). There was no



correlation between TSH and prolactin levels in both primary and secondary infertility.

Table 3. Serum TSH and prolactin level in primary and secondary infertile women.

Type of infertility	TSH level mean $\pm$ SD mIU/L	Prolactin level mean $\pm$ SD mIU/L
Primary	3.14 $\pm$ 2.21	507 $\pm$ 206
secondary	1.35 $\pm$ 1.87	422 $\pm$ 136
P-value	0.000	0.019

## Discussion

The prevalence of hypothyroidism, specially subclinical hypothyroidism among the present study population was much higher than (those previously reported in Bangladesh) that reported by Akter et al.<sup>12</sup> in Mymensingh, Bangladesh. They were reported that prevalence of sub-clinical hypothyroidism was 6.5% in primary and 15% in secondary infertility. The higher prevalence of hypothyroidism reported in this present study may be due to use of narrow reference range of TSH which is recently recommended by American Association of Clinical Endocrinologists.<sup>13</sup> But the present study findings and the previous report of Akter et al.<sup>12</sup> suggested that hypothyroidism, specially subclinical hypothyroidism in infertility is a major health problem in Bangladesh like other countries of the world.<sup>14-17</sup> In the present study, the prevalence of hyperprolactinemia was 22.3%, which is much lower (37.5%) than in Mymensingh, Bangladesh<sup>12</sup>, but similar with the findings in North India (18.3%).<sup>15</sup> The prevalence of hyperprolactinemia was higher in Iraq (60%)<sup>18</sup> and in Hyderabad, India (41%)<sup>19</sup> as compared to the present study in Northern part of Bangladesh. Hyperprolactinemia may result from stress, and the variable prevalence may be due to the different stress levels in different areas.

In this study, prevalence of hypothyroidism both clinical and subclinical was significantly higher ( $P=0.005$ ) in primary infertility than in secondary infertility and mean serum TSH in primary infertility (3.14 $\pm$ 2.21 mIU/L) was also comparatively higher than in secondary infertility group (1.35 $\pm$ 1.87 mIU/L). As Northern part of Bangladesh is an iodine-deficient zone, this may be one of the reasons for the higher prevalence of hypothyroidism in primary infertility. But it is not consistent with a previous study by Akter et al.<sup>12</sup> Akter et al.<sup>12</sup> reported higher prevalence of hypothyroidism in secondary than primary infertility. They suggested that the higher prevalence of hypothyroidism in secondary infertility due to antibody reaction. They

considered the sequel of previous autoimmune thyroid diseases (AITD) which caused the thyroid function to worsen after the first conception leading secondary infertility. Although they did not evaluate thyroid antibodies in their study.

Hypothyroidism is associated with increased production of thyrotropin-releasing hormone (TRH), which stimulates pituitary to secrete TSH and PRL release.<sup>20,21</sup> So the higher prevalence of hyperprolactinemia and higher mean serum prolactin in primary than secondary infertility found in this present study may be explained by this phenomenon. A significantly higher prevalence of oligomenorrhea, hirsutism, polycystic ovaries and body Mass Index 25 or above reflected the higher prevalence of hypothyroidism / high TSH level and hyperprolactinemia / high PRL level in primary than secondary infertility also consistent with this phenomenon. In a study by Cramer et al.<sup>11</sup>, TSH and prolactin were positively correlated in women undergoing In Vitro Fertilization (IVF). In this study, no correlation was observed between TSH and PRL levels in primary or secondary infertility.

This study has some limitations. The sample size was small. Identification of clinical and subclinical hypothyroidism was done on the basis of biochemical (TSH, T3 and T4) analysis, clinical findings of hypothyroidism were not considered.

The findings of this study have some implications for further research on hypothyroidism and hyperprolactinemia in infertility in Bangladesh. Further studies are recommended with a large sample size and long follow-up to validate the variation in TSH and prolactin levels in primary and secondary infertility and to clarify the etiology of the hypothyroidism and hyperprolactinemia for better management of infertility cases.

## Conclusion

Hypothyroidism specially subclinical hypothyroidism and hyperprolactinemia are important health disorders in Bangladeshi infertile women. Further studies are needed to clarify the etiology of the hypothyroidism and hyperprolactinemia for better management of infertility cases.

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