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Original Research Article

Study of serum insulin and thyroid hormones levels among infertile females in Bangladesh

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ABSTRACT

Background: Infertility affects 8-10% of couples worldwide, with altered insulin and thyroid levels as potential factors. This study examines fasting serum insulin and thyroid hormones in women with primary and secondary infertility.
Methods: The study included 100 women, with 50 experiencing primary infertility (Group A) and 50 with secondary infertility (Group B). Age-matched fertile women served as the control group. Data were recorded on a standardized data sheet following written consent. Statistical analysis was performed using unpaired Student's t-tests with SPSS software, version 12.
Results: In this study, the mean fasting serum insulin and TSH levels were significantly higher in infertile women compared to fertile women ($p<0.001$). Within the infertility group, serum fasting insulin was higher in women with primary infertility than in those with secondary infertility, although this difference was not statistically significant. The mean TSH levels in both infertility groups were significantly elevated compared to the fertile group. Among those with infertility, 28% of women with primary infertility and 24% with secondary infertility had hypothyroidism, while elevated serum insulin levels were observed in 22% and 20% of these groups, respectively. Among the hypothyroid infertile women, 64.2% (9 of 14) with primary infertility and 58.3% (7 of 12) with secondary infertility also had hyperinsulinemia.
Conclusions: The study found higher fasting serum insulin and TSH levels in infertile women, often linked to hypothyroidism, menstrual irregularities, and ovulatory dysfunction. It emphasizes the need to assess TSH and insulin levels in infertility evaluations.

Keywords: FT3, FT4, Hyperinsulinemia, Hypothyroidism, Infertility, TSH

INTRODUCTION

Infertility is an important health problem in Bangladesh. In Bangladesh, the rate of infertility has been reported as 4% to 15%. [1-3] The alteration of thyroid and insulin hormone is associated with infertility.[4-7] Thyroid hormones, particularly thyroid-stimulating hormone (TSH), are recognized as key factors in infertility. Thyroid dysfunctions can disrupt various aspects of reproductive health and pregnancy. Numerous studies have linked hypothyroidism and hyperthyroidism with menstrual disturbances, anovulatory cycles, reduced fertility, and increased pregnancy complications.[8,9] Hypothyroidism, in particular, may directly contribute to infertility, as thyroid hormones play a crucial role in the optimal production of both estradiol and progesterone. High level of insulin can be as a metabolic state where normal glucose homeostasis mechanisms fail to operate properly. The American Diabetes Association has characterized hyperinsulinemia or insulin resistance is a state of impaired metabolic response to insulin, to achieve euglycemia, the pancreas over secretes insulin.[10,11] High level of insulin may be due to reduced number of insulin receptors, insulin resistance, and altered the insulin to receptor interaction or postreceptor failure. In infertile women, post receptor defect is the main cause of hyperinsulinemia. High level of insulin in infertile women is the risk for metabolic syndrome and coronary artery disease and also leads to an increase risk of miscarriage, pre- mature birth and birth defects.[12] Again, increase level of insulin may cause hormonal imbalance in the pituitary gland and ovary. This leads to an increased secretion of lutenizing hormone (LH). Increased LH secretion then causes ovulation disorders, menstrual irregularities and infertility.[13,14] Thyroid disorder and high level of insulin alters the hypothalamopituitary ovarian axis and causes reproductive dysfunction.[11-19] Women with hyperinsulinemia have been found to have primary hypothyroidism. Hence, it is necessary to screen serum thyroid hormones along with insulin in women with infertility problems.

Therefore, this study aimed to determine the status of thyroid function and fasting serum insulin in women with infertility.

METHODS

This cross-sectional study was carried out in the Department of Physiology at Dhaka Medical College, Dhaka, from July 2010 to June 2011, following approval from the Ethical Review Committee of Dhaka Medical College. The study included a total of 150 women, with 50 women experiencing primary infertility (Group A), 50 with secondary infertility (Group B), and 50 age-matched, apparently healthy fertile women as controls (Group C). Participants ranged in age from 23 to 34 years, and the mean age across the groups was similar, showing no statistically significant difference. Additionally, there was no significant difference in the mean body mass index (BMI) between Groups A and B. Women with primary and secondary infertility were included, with an equal number of age-matched healthy fertile women serving as the control group. Primary infertility referred to women who had never conceived, while secondary infertility was defined as the inability to conceive after a previous pregnancy. [12] Fertility was defined as the capacity to conceive. The study included infertile women whose husbands had normal semen analyses and those with normal genitalia, uterus, and adnexa. Women with tubal factors, congenital anomalies of the urogenital tract, organic lesions, pelvic inflammatory diseases, or those who were lactating were excluded, as were infertile women with subclinical or secondary thyroid conditions. Only cases of primary hypothyroidism and primary hyperthyroidism were considered. The study's purpose and benefits were explained to each participant, and written informed consent was obtained. Comprehensive medical, personal, family, and socioeconomic histories were recorded using a structured questionnaire. Data were analyzed using SPSS version 12, with statistical methods including one-way ANOVA, Tukey's HSD post-hoc test, unpaired Student's t-test, and Z-test. The Institutional Ethical Review Committee provided ethical clearance for the study.

RESULTS

The mean serum levels of TSH, FT4, FT3 and serum fasting insulin (SFI) of Group A, B and C are shown in Table 2. The mean serum TSH levels of women with primary (4.83±0.54 mIU/l) and secondary (6.40±0.59 mIU/l) infertility were significantly ($p<0.001$) higher than that of women with normal fertility (1.98±0.18 mIU/). The mean serum FT4 levels of women with primary (10.54±0.66 pmol/l) and secondary (7.64±0.44 pmol/l) infertility were significantly ($p<0.005$) lower than that of women with normal.

Table 1: Age and body Mass index (BMI) of study population.

Study population	Number	Age (years), Mean±SD	BMI (kg/m^2), Mean±SD
Groups A (Primary infertility)	50	27.08±4.15	28.05±4.08
Groups B (secondary Infertile)	50	28.98±4.81	27.62±3.68
Groups C (Control)	50	27.82±4.65	25.35±3.48

Note: Gr A= Primary sterility, Gr B= Secondary sterility, Gr C= women with normal fertility (Control); One-way ANOVA and Tukey's post-hoc tests were performed to compare among the groups. Age -Gr A vs Gr C: p=0.7918, Gr B vs Gr C: p=0.4372, Gr A vs Gr B: p=0.2375. BMI- Gr A vs Gr C: p=0.0118, Gr B vs Gr C:p=0.0071, Gr A vs Gr B: p=0.8882

Table 2: Serum TSH, FT4, FT3 and fasting insulin levels of study population.

Study population	No	Mean±SD serum level			
		TSH (mIU/l)	FT4 (pmol/l)	FT3 (pmol/l)	Serum fasting insulin (mIU/l)
Group A	50	4.83±0.54	10.54±0.66	4.12±0.32	20.04±3.46
Group B	50	6.40 ±0.59	7.64±0.44	3.9±0.23	19.13±2.62
Group C	50	1.98±0.18	14.48±0.64	4.93±0.20	17.37±3.05

Table 3: Statistical analysis.

Group	Serum TSH (P value)	Serum FT4 (P value)	Serum FT3 (P value)	Serum insulin (P value)
A vs C	0.000***	0.000**	0.035*	0.0001***
B vs C	0.000***	0.000***	0.001**	0.003**
A vs B	0.05*	0.003	0.584	0.140^{ns}

Note: Gr A = Primary infertility, Gr B = Secondary infertility, Gr C = Control; One-way ANOVA and Tukey's post-hoc tests were performed to compare among the groups fertility.
*For TSH-Gr A vs Gr C: p<0.001, Gr B vs Gr C: p<0.001, Gr A vs Gr B: p = 0.05; **For FT4-Gr A, Gr B and Gr C were significantly different from each other: p<0.005; ***For FT3-Gr A vs Gr C: p = 0.03, Gr B vs Gr C: p = 0.001, Gr A vs Gr B: p = 0.58; For prolactin – Gr A vs Gr C: p = 0.017, Gr B vs]Gr C: p = 0.003, Gr A vs Gr B: p = 0.834

The mean serum FT3 levels were significantly lower in women with primary infertility (4.12±0.32 pmol/l) and secondary infertility (3.9±0.23 pmol/l) compared to women with normal fertility (4.93±0.20 pmol/l), with p-values of 0.03 and 0.001, respectively. However, there was no significant difference in serum FT3 levels between Group A (primary infertility) and Group B (secondary infertility).

The mean serum fasting insulin levels of women with primary (20.04±3.46 mIU/l) and secondary (19.13±2.62 mIU/l) infertility were significantly (p<0.000) higher than that of women with normal fertility (17.37±3.05 mIU/l). However, no statistical significance difference was observed between primary and secondary infertility women.

Table 4: Compare thyroid function status with serum fasting insulin levels in women with primary and secondary infertility.

Study population	Serum TSH level		Serum fasting insulin level			
	Number (%)	Mean±SE (mIU/l)	High		Normal	
Group A (n=50)			N (%)	Mean±SE (mIU/l)	N (%)	Mean±SE (mIU/l)
Euthyroid	35 (70)	3.12±0.21	02 (5.7)	25.73±2.7	33 (94.2)	15.12±1.4
Hypothyroid	14 (28)	5.14±0.85	09 (64.3)	27.63±3.6*	05 (35.7)	18.23±0.2
Hyperthyroid	1 (2)	1.14±0.27	0	0	01 (100)	16.73±1.3
Group B (n=50)						
Euthyroid	36 (72)	4.12±0.16	01 (2.7)	25.12±3.4	33 (91.6)	14.42±2.7
Hypothyroid	12 (24)	7.97±0.72*	08 (66.7)	26.83±3.2	05 (41.6)	17.23±1.6
Hyperthyroid	2 (4)	1.07±1.04	0 (0)	-	02 (100)	15.86±0.4
Group C (n=50)						
Euthyroid	50 (100)	1.98±0.18	-	-	50 (100)	17.37±3.05

Note: Normal range of fasting serum insulin (SFI) = 5-15 or 5-12 mIU/l. High serum insulin = >25; Z test was performed; Gr A vs Gr B with euthyroid: Z = 0.82, p = 0.22; Gr A vs Gr B with hypothyroid: Z = 0.45, p = 0.54; Gr A vs Gr B with hyperthyroid: Z = 0.580, p = 0.55. Z proportionat test was performed. Gr A vs Gr B with euthyroid and high SFI;- Z= 0.53, p=0.61 ;Gr A vs Gr B with hypothyroid and high SFI ; Z= 0.31, p= 0.74and Gr A vs Gr B with euthyroid and normal SFI: - Z=0.61, p=0.54 ; Gr A vs Gr B hypothyroid and normal SFI: - Z=0.61, p=0.54
Unpaired student t test were performed to compare among the groups. To the respective group of Gr A vs Gr B with euththyroid and normal SFI: - p=0.42 Gr A vs Gr C p=0.17; Gr B vs C; p=0.003*; Gr A vs Gr B with Euthyroid with high SFI: p=0.86; Gr A vs Gr B with hypothyroid and normal SFI, p= 0.63; hypothyroid with high SFI P= 0.35; Gr A vs Gr B with hyperthyroid and normal PRL P = 0.74.

According to the thyroid function status, 70% and 72% of the women having primary and secondary infertility were euthyroid respectively while 28% and 24% were suffering from hypothyroidism (Table 4). The mean serum TSH level in hypothyroid cases of the secondary infertility group (7.97±0.72 mIU/l) was significantly higher than in the primary infertility group (5.14±0.85 mIU/l), with a p-value of 0.02. Elevated serum insulin levels were noted in 64.3% of hypothyroid women with primary infertility and 66.7% with secondary infertility.

The Pearson's correlation coefficient was calculated for serum TSH and insulin in primary and secondary infertile women. In primary infertile women serum insulin levels were significantly positively correlated with corresponding TSH levels (r=0.536, p<0.001; Figure 1). In women with secondary infertility, serum prolactin levels showed a significantly positive correlation with serum TSH levels (r=0.561, p<0.001, Figure 2). This finding indicates a strong association between hypinsulinemia and hypothyroidism in both primary and secondary infertile women.

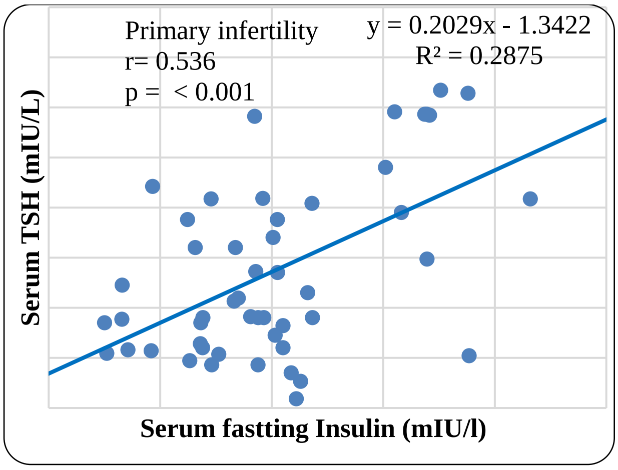

Figure 1: Correlation of serum fasting insulin SFI with TSH in primary infertile women.

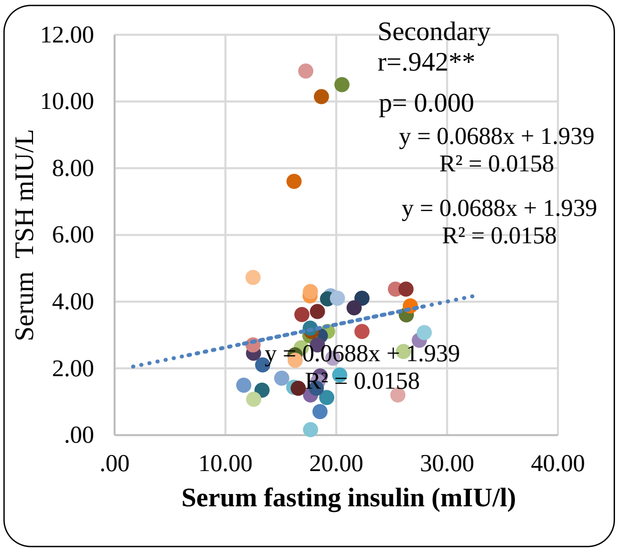

Figure 2: Correlation of serum SFI with TSH in secondary infertile women.

DISCUSSION

In the present study, thyroid dysfunction and altered insulin levels have been identified as contributing factors to female infertility.[8-10,15] We explored the possible correlation between serum TSH and insulin levels in infertile women attending a tertiary care hospital in Dhaka, finding that hypothyroidism was present in 24%-28% of women with primary and secondary infertility, mirroring other studies.[8-15,18,20] With researchers from various countries observing a positive correlation between serum TSH, fasting serum insulin, and infertility.[12-20] Thyroid hormones, T3 and T4, help maintain glucose homeostasis by acting as insulin agonists and antagonists. Hypothyroidism can disrupt this balance, leading to altered glucose metabolism and insulin resistance. Insulin resistance is a key pathophysiological factor underlying metabolic syndrome, and previous studies have established overt hypothyroidism as a risk factor for insulin resistance.[19,20] Many investigators of different countries reported that high level of insulin may cause increase secretion of androgens (male hormones) in the female which worsen the symptom of infertility. In addition, hyperinsulinemia produces the hyperandrogenism by increasing ovarian androgen production, particularly testosterone. The high levels of androgenic hormones interfere with the pituitary ovarian axis, leading to increased LH levels, anovulation, amenorrhea, recurrent pregnancy loss and infertility. [9-18] Some investigators suggested that hyperinsulinemia inhibits hepatic synthesis of SHBG which may causes infertility. Decrease level of SHBG may causes increase testosterone and estrogen level. Increased estrogen section causes increased LH and decreased FSH level. Suboptimal FSH action leads to follicular stimulation but no maturation or ovulation. As a result numerous small and immature follicles undergo atresia and also prevent normal follicular growth and causes premature follicular atresia which leads to anovulatory cycle and infertility. [9-18] In infertile females, if hypothyroidism is associated with hyperinsulinemia, it is important to treat the hypothyroidism first and maintain TSH levels at the lower limit. Evidence from both experimental and clinical studies has highlighted a close relationship between the hypothalamic-pituitary-ovarian (HPO) axis and the hypothalamic-pituitary-thyroid (HPT) axis.[13] In our study, about 50% of hypothyroid cases exhibited hyperinsulinemia, which aligns with similar findings reported by other researchers.[7,8,15,20] Therefore, this study demonstrates that a significant proportion of women with primary and secondary infertility have altered thyroid function and elevated serum fasting insulin levels compared to fertile women.

CONCLUSION

This study concludes that fasting serum insulin and TSH levels were higher in infertile women compared to healthy fertile women. These alterations may contribute to menstrual irregularities, ovulatory dysfunction, and infertility. The study also highlights a high prevalence of hypothyroidism with elevated fasting serum insulin levels in infertile women.

Recommendations

It is recommended that clinicians include both serum TSH and fasting insulin level assessments as part of the routine evaluation for women presenting with infertility. Identifying and managing elevated insulin and TSH levels may help address underlying hormonal imbalances that contribute to menstrual irregularities, ovulatory dysfunction, and infertility.

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