Original Article

Frequency and pattern of thyroid dysfunction in diabetic and non-diabetic women with primary infertility: experience in a tertiary care hospital in Dhaka, Bangladesh

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Abstract

Background*: Thyroid hormones have profound effects on reproduction and pregnancy. A relationship between the thyroid gland and the gonads is suggested by the far more frequent occurrence of thyroid disorders in women. Hormonal disorders of female reproductive system are comprised of a number of problems resulting from dysfunction of hypo-thalamic-pituitary ovarian axis. These relatively common disorders often lead to infertility. Concomitant Diabetes and other metabolic abnormalities or endocrinopathy flare up the condition. This study was conducted to find out any difference in thyroid function among diabetic and non-diabetic patient presenting with primary infertility.*

Methods*: In this study total 174 patients were included and allocated into two groups, 87 in each group. Group I were diabetic infertile women and group II were non diabetic infertile women. Thyroid hormone profile were done and compared between groups. The data were based on the answers came from interviews and medical records registered in the OPD follow up, investigation report, treatment paper and notes in hospital file sheet. Data processing work was consisted of registration schedules, editing computerization, preparation of dummy table, analyzing and matching of data.*

Results*: No difference was observed in respect of demographic profile. It was observed that, majority of patients 73(41.9%) belonged to age 26-33 years, mean age was found 26.3±10.9 years in Group-I and 26.7±11.6 years in Group-II. Low T_3 was found in 15(17.2%) patients and in 9(10.3%) patients group I and group II respectively. Mean FT4 was found 8.25±1.5 pmol/L in group I and 10.57±1.82 pmol/L in group II. Raised TSH was found in 23(26.4%) patients and 13(14.9%) patients in group I and group II respectively. On interpretation of thyroid function test, 71.8% (125/174) patients had normal finding or in euthyroid status (64.3% in group I and 79.3% in group II). Present study shows that, frequency of thyroid dysfunction was common in group-I patients than group-II (35.6% vs. 20.6%). primary hypothyroidism was predominant abnormality, noted 15(17.2%) patients in group I and 9(10.3%) patients in group II patients.*

Conclusion: *Hypothyroidism is the most common thyroid dysfunction found in infertile females and it is predominant in diabetic infertile group. Hence assessment of thyroid function should be considered as an important component in infertility work up of women.*

Key-words: *Hypothyroidism, hyperthyroidism, diabetes mellitus, fertility, infertility.*

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Introduction

The thyroid gland plays a major role in the metabolism, growth and development of the human body. It helps to regulate many body functions. It has long been recognized that thyroid dysfunction may have profound effects on the female reproductive system. Thyroid disorders are more common in women with menstrual irregularities as compared to general population. Endocrine as well as immune system abnormalities can impair fertility[1] and thyroid abnormality considered as important cause of infertility. Infertility is defined as

the failure to conceive, with no contraception, after one year of regular intercourse in women < 35 years and after 6 months in women > 35 years. Epidemiological data suggest that around 10% to 15% of couples are infertile. Anovulatory problems are responsible from 25% to 50% of causes of female infertility.[2]

In female, thyroid dysfunction is a condition known to reduce the likelihood of pregnancy and to adversely affect pregnancy outcome.[3] Increasing evidence derived from experimental and clinical studies suggests that the hypothalamic-pituitary-thyroid axis and hypothalamic-pituitary-ovarian axis are physiologically related.[4] Thyroid hormones receptors have direct effects of iodine and thyroid hormone on ovarian function are proposed recently.[5] There is a known association of hyperthyroidism and hypothyroidism with menstrual disturbance, anovulatory cycles and decreased fecundity.[4]

The infertility problem is more common phenomenon among the women now days. There was a higher prevalence of hypothyroidism in the infertile women as compared to the fertile ones.[6] In a case-control study demonstrated that, 33.3% women had been suffering from thyroid disease.[7] A close interconnection is present between hypothyroidism and hyperprolactinemia. Failure to ovulate regularly in women of the reproductive age group may occur owing to hypothyroidism.[8] Hyperprolactinemia badly affects the fertility possibility by ruining the pulsatile secretion of gonadotropin releasing hor-mone (GnRH), thereby interfering with ovulation. This is implicated in menstrual and ovulatory dysfunctions such as amenorrhea, oligomenorrhea, anovulation, inadequate corpus luteal phase, and galactorrhea.

Autoimmune thyroid disease is present in 5–20% of unselected pregnant women. Isolated hypothyroxinemia has been described in approximately 2% of pregnancies, without serum TSH elevation and in the absence of thyroid autoantibodies. Overt hypothyroidism has been associated with increased rates of spontaneous abortion, premature delivery and/or low birth weight, fetal distress in labor, and perhaps gestation-induced hypertension and placental abruption. The links between such obstetrical complications and subclinical hypothyroidism are less evident. Thyrotoxicosis during pregnancy is due to Graves' disease and gestational transient thyrotoxicosis.[9] Hypothalamic amenorrhea results from a change in the normal pattern of episodic secretion of the GnRH pulse generator, with ovulation failure and amenorrhea. It can be due to congenital GnRH deficiency, hypothalamic lesions, or it may be functional.[10] The prevalence of primary or secondary infertility is also common in hyperthyroidim.

Diabetes mellitus added the burden of this condition. Diabetic patients have higher prevalence of thyroid disorder and hypothyroidism is more common than thyrotoxicosis.[11] The actual mechanism is unknown. But several studies showed that, in diabetic patients the nocturnal TSH peak is blunted or abolished, and the TSH response to TRH is impaired. Reduced T_3 level have been observed in uncontrolled diabetic patients. This "low T_3 state" could be explained by impairment in peripheral conversion of T_4 to T_3.[12]

According to the Endocrine Society[13], studies are now focusing on the potential impact of subclinical hypothyroidism and subclinical hyperthyroidism on maternal and fetal health, the association between miscarriage and preterm delivery. Thyroid hormones and reproduc-tive functions interact with each other although their precise mechanism is poorly understood.[12] The present study was carried out to correlate thyroid hormones with infertility in the reproductive age group of women.

Methods

This was a observational, cross sectional study. A total of 174 women with primary infertility, aged 18 to 40 years attended in BIRDEM General Hospital were included after fulfillment of selection criteria. Approval of the study was obtained by the local Ethical Committee. All subjects who were included in the study signed on informed consent after careful explanation of the study procedures. Diagnosis was made on the basis of patient's statement, characteristic features of illness, clinical examination and available records. Patients were allocated into two groups, of which 87 was as diabetic and 87 patients as non-diabetic. Method of sampling was purposive according to the availability of the patients. A thorough clinical examination including general physical examination, neck examination, systemic and gynecologic examinations was conducted meticulously. Under full aseptic precaution 5 ml of venous blood was drawn by disposable syringe and transferred to a clean dry test tube and taken to the laboratory. The sample was sent instantly for testing as fresh sample in hospital lab. Then all patients subjected to FT_3, FT_4, TSH and blood

glucose. The parameters were observed & recorded in pre-structured Case Record Form (CRF). The case definitions of operational variable were described. Patient data such as age, sex, clinical presentation, etc were noted. This questionnaire was used for collection of information by interviewing patients. All the collected data were checked very carefully to identify errors in collecting data. Data processing work consisted of registration of schedules, editing, coding and computerization, preparation of dummy tables, analysis and matching data. The technical matters of editing, encoding and computerization looked by researcher.

Results

In this series, majority of patients 73(41.9%) belonged to age 26-33 years, followed by 65 patients (37.3%) belonged to age 18-25 years. The mean age was found 26.3±10.9 years in Group-I and 26.7±11.6 years in Group-II. There was no significant difference between two groups. In this study almost two third (60.3%) patients hailing from urban area, 39.7% from rural site. It was observed that, 47(54.0%) of patients were housewives in group I and 45(51.7%) in group II. The difference was not statistically significant (p>0.05) between two groups. (Table I)

Table I Demographic characteristics of the study patients (n=174)

Variables		Group-I(n=87)		Group-II(n=87)	
		No.	(%)	No.	%
Age (yr.)	18-25	31	(35.6)	34	(39.0)
	26-33	37	(42.5)	36	(41.3)
	34-40	19	(21.8)	17	(19.5)
	Mean±SD	26.3±10.9	26.7±11.6		
Occupational status	Service	18	(20.6)	21	(24.1)
	House wife	47	(54.0)	45	(51.7)
	Teachers	12	(13.7)	7	(8.0)
	Others	10	(11.4)	14	(16.0)
Residence	Urban	48	(55.1)	56	(64.3)
	Rural	39	(44.8)	31	(35.6)

Table II Evaluation of thyroid hormone status (THS) among study subject (n=174)

	Group-I(n=87)		Group-II(n=87)		P value
	No.	(%)	No.	(%)	
Serum FT_3 (pmol/L)					
<1.86	15	(17.2)	9	(10.3)	
1.86–6.43	63	(72.4)	72	(82.7)	
>6.43	9	(10.3)	6	(6.8)	0.046[s]
Mean±SD	2.86	±1.3	3.62	±1.8	
Serum FT_4 (pmol/L)					
<9.14	15	(17.2)	9	(10.3)	
9.14–23.18	64	(73.5)	73	(83.9)	
>23.18	8	(9.1)	5	(5.7)	0.044[s]
Mean±SD	8.25	±1.5	10.57	±1.82	
Serum TSH (uIU/ml)					
<0.47	8	(9.1)	5	(5.7)	
0.47–5.01	56	(64.3)	69	(79.3)	
>5.01	23	(26.4)	13	(14.9)	0.026[s]
Mean±SD	7.38	±3.17	4.56	±0.86	

On evaluation of thyroid function test, it was observed that normal FT_3 was found in 63(72.4%) patients of group I and in 72(82.7%) patients of group II. Low FT_3 was found in 15(17.2%) and 9(10.3%) patients in group I and group II respectively. Mean FT_3 was found 2.86±1.3 pmol/L in group I and 3.62±1.8 pmol/L in group II patients. The difference was not statistically significant ($p>0.05$) between two groups. We found that serum thyroxine (FT_4) level was decreased in 15(17.2%) patients of group I and in 9(10.3%) patients of group II. The mean FT_4 was found 8.25±1.5 pmol/L in group I patients and 10.57±1.82 pmol/L in group II patients. It was observed that raised TSH was found in 23(26.4%) and 13(14.9%) patients in group I and group II respectively. Mean TSH was found 7.38±3.17 uIU/ml in group I and 4.56±0.86 uIU/ml in group II patients. The mean TSH level was significantly ($p<0.05$) higher in group I. (Table II).

Table III Frequency and pattern of thyroid abnormality in the study population (n=49)

Thyroid status	Group-I (n=31)		Group-II (n=18)	
	No.	(%)	No.	(%)
Primary hypothyroidism	15	(48.3)	9	(50.0)
Subclinical hypothyroidism	8	(25.8)	4	(22.2)
Primary hyperthyroidism	8	(25.8)	5	(27.7)
Subclinical hyperthyroidism	0	0	0	0

Present study demonstrated that, thyroid disorders were prevalent in 35.6% patients in group I and 20.6% in group II patients. Among thyroid dysfunction, 15(17.2%) in group I and 9(10.3%) in group II patients was detected as primary hypothyroidisms and it was the predominant type of thyroid abnormality among infertility women. The prevalence of subclinical hypothyroidism was detected in 8(9.1%) patients and 4(4.5%) patients in group I and II respectively. The prevalence of hyperthyroidism was detected in 8(9.1%) and 5(5.7%) patients in group I and II respectively. None of the case was as subclinical hyperthyroidism (Table III).

Discussion

In this study, mean age was 26.3±10.9 years in patients of Group-I and 26.7±11.6 years in patients of Group II. The difference was not statistically significant ($p>0.05$) between groups. Findings are consistent with result of other study. In a case-control study most of the patients were in the age group of 25-30 years.[14] Elahi S, et al reported that mean (± SD) age of the infertile and control women was 26.9 ± 5.0 years and 28.3 ± 6.1 years respectively in their study.[1] Nasir S, et al demonstrated that mean age of primary infer-tile women was 26.74±4.82 years and secondary infertile women 30.52±4.74 years in their study.[15]

In this study, mean FT_3 was found 2.86±1.3 pmol/L in group I and 3.62±1.8 pmol/L in group II patients. Serum thyroxine (FT_4) level had decreased in 15(17.2%) patients of group I and 9(10.3%) patients of group II. Mean FT4 was detected 8.25±1.5 pmol/L in group I patients and 10.57±1.82 pmol/L in group II patients. On evaluation of TSH, raised level of TSH was in 23(26.4%) patients of group I and in 13(14.9%) patients of group II.

Result consistent with other study. In a study postulated that, serum T_3 and T_4 levels had found to be significantly decreased in infertile females as compared to controls ($p<0.05$). Serum TSH levels were found to be significantly increased in infertile females as compared to controls.[14] Fupare S et al[16], reported that, prevalence of hyperthyroidism in the cases and the controls were 4% and 7.5%, respectively. Goswami Binita et al (2009)[17], in their study reported prevalence of hypothyroidism was seen in 8% of the infertile subjects.

In this study on evaluation of thyroid function test, hypothyroidism was detected as predominant thyroid disorder, overall frequency of thyroid dysfunction was higher in group-I patients than group-II. Findings are consistent with result of other study. In a case-control study[16] showed that mean value of FT_4 is slightly lower in infertile group than control. Mean value of TSH is increased in infertile women as compared to control. The prevalence of hyperthyroidism in the cases was 5/120 (4%) and hypothyroidism was seen in 22/120 (18%) of the infertile women. The crude prevalence of hypothyroidism was higher when compared to hyperthyroidism in the infertile group. The rise in serum FT_4 and FT_3 in the infertile group with hyperthyroidism was found to be non significant as compared to the control group with hyperthyroidism[16]. In another study found that higher prevalence of hypothyroidism in the infertile women. Hypothyroidism is commonly associated with ovulatory failure.[16]

Present study demonstrated that, among thyroid dysfunction, 15(17.2%) in group I patients and 9(10.3%) in group II patients detected as primary hypothyroidisms and it was the major thyroid abnormality among infertility women patients. On comparison between groups, study shows that thyroid disorder was predominant in Group I subject or patients having history of diabetes mellitus.

Elahi et al[1], demonstrated that incidence of hypothyroidism (6.4%) was slightly higher as compared to hyperthyroidism (4.3%) in their study. Where as in other study found 16.2 & 22.5% hypothyroid women in primary and secondary infertility respectively.[16] These findings of above studies correlate with findings of our study in which we get high prevalence of hypothyroidism in infertile. The prevalence of hypothyroidism in women of reproductive age (20-40 years) varies between 2% to 4%.[17]

Possible explanation is infertility in hypothyroidism due to altered peripheral estrogen metabolism, hyperprolactinemia, defects in homeostasis, and disturbances in GnRH secretion that result in an abnormal pulsatile release of LH are some of the main causes to explain the high frequency of infertility in hypothyroid women.[18] Our study concludes that thyroid dysfunction plays a significant role in female infertility. Thyroid profile can help us in prompt diagnosis and timely initiation of therapy. Therefore thyroid hormone profile must be included in the routine workup of infertile women in our setup.[15]

Conclusion

Present study shows higher prevalence of hypothyroidism in the infertile women and predominant in diabetic individual. In this study hypothyroidism is commonly associated with diabetic infertile women. Hence, assessment of thyroid function test is mandatory in the work up of all infertile women, especially those presenting with H/O diabetes.

Conflict of interest: Nothing to declare.

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