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THYROID DISORDERS IN FEMALE SUBFERTILITY

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Abstract

The study was done to find out the prevalence, the different type of thyroid disorder and the clinical presentation of thyroid dysfunction in our subfertile women. The study was carried out in the infertility outdoor of infertility unit, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka and a private tertiary infertility centre in Dhaka during the period of 16th March 2007 to 15th September 2007. Sixty women of child bearing age were recruited for the study out of which 30 subfertile women of reproductive age was taken as case and 30 non pregnant, reproductive aged, parous women without a history of reproductive problem as control.

In both control and case groups, most of the subjects were belonged to age group 26-35 years.

33.3% of the women had been suffering from thyroid disease in the case group. In the study group 26.7%, had been suffering from subclinical hypothyroidism, 6.7% from hypothyroidism, where as in control group, 3.3%, had been suffering from hypothyroidism and 3.3% from hyperthyroidism. Menstrual cycle was regular in 6.7% of women with hypothyroidism, 3.3% in subclinical hypothyroidism and 36.7% who had no thyroid disease in study group, where as in control group menstrual cycle was regular in 3.3% in hypothyroidism, 3.3% in hyperthyroidism and 83.4% who had no thyroid disease.

10% women had history of abortion those who had been suffering from subclinical hypothyroidism. Prevalence of thyroid disorder seems to be higher in female subfertile patient than the general population.

Key words : thyroid dysfunction; female subfertility

Introduction

Globally around 10% of the population in the reproductive age is facing problem to conceive with a rough estimate of 80 million couples worldwide suffering from the problem. 26 - 44 % of the female infertility is due to anovulation. Thyroid dysfunction is four to five times more common in females than in males. Both hyperthyroidism and hypothyroidism has significant effects on estrogen and androgen metabolism, menstrual function and fertility [1].

The prevalence of abnormal TSH level in infertile women was reported as 6.3% , 4.8% , 2.6% , and 1.5% for women in couples diagnosed with anovulatory infertility, unexplained infertility, tubal infertility, and male infertility respectively [2]. Thyroid disease interferes with the physiology of reproduction. Women are at a higher risk of most types of thyroid disorders early in life and about 10% of women will have thyroid dysfunction following pregnancy. After puberty, hyperthyroidism may cause infrequent and scanty period, or may lead to amenorrhoea. In hypothyroidism the periods often become too frequent and heavy, sometimes with prolonged bleeding that may even result in anaemia. Both hyperthyroidism and hypothyroidism have significant effects on estrogen and androgen metabolism, menstrual function and fertility. In women of fertile age, hypothyroidism can lead to oligomenorrhoea and amenorrhoea, polymenorrhoea and menorrhagia. The later is probably due to estrogen break-through bleeding secondary to anovulation[3]. Defect in hemostasis such as the decreased level of factors VII, VIII, IX and XI that have been demonstrated in hypothyroidism, may also contribute to polymenorrhoea and menorrhagia[4]. In women severe hypothyroidism is commonly associated with diminished libido and failure to ovulation [5].

Thyroid dysfunction can halt ovulation by upsetting the balance of the body's natural reproductive hormones and in some women can cause short lutcal phase. A shortened luteal phase can cause what appears to be infertility but in fact failure to sustain a fertilized egg, with loss of the very early pregnancy at around the same time menstruation would typically begin. Hypothyroidism can cause an increase in prolactin, prolactin level which has negative impact on ovulation. Hypothyroidism can

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also be associated with an increased risk of cysts formation in the ovaries, or polycystic ovaries, which is also associated with decreased fertility [6].

Subclinical hypothyroidism is associated with ovulatory dysfunction and infertility[7]. The worldwide prevalence of subclinical hypothyroidism ranges from 1 to 10 percent. Subclinical hypothyroidism may be of greater clinical importance in subfertile women with menstrual disorders-especially when the luteal phase is inadequate[8]. Undetected subclinical hypothyroidism during pregnancy may adversely affect the neuropsychological development[9] and survival of the fetus [10] and can be associated with hypertension and toxemia [11].

An increased risk of spontaneous abortion is noted in women with thyrotoxicosis. An increased incidence of congenital anomalies, particularly aplasia cutis occurs in the offspring of women with Methimazole[12]. Women who have antithyroid antibodies before and after conception appears to be at an increased risk for spontaneous abortion. It has been suggested that immunological factors may play important role in the reproductive process of fertilization, implantation and placental development.

Autoimmunity can result in unexplained infertility, and recurrent pregnancy loss. Autoimmune thyroid disorders are characterized by the presence of antithyroid antibodies, specifically antithyroglobulin and antithyroid peroxidase (microsomal antibodies). Women who have antithyroid antibodies miscarry at approximately twice the rate of women who have no antithyroid antibodies. Approximately 30% of women experiencing recurrent pregnancy loss have one or both antithyroid antibodies. Antithyroid antibodies have also been associated with implantation failure after in vitro fertilization (IVF) and embryo transfer (ET)[13]. The study was done to find out the prevalence, the different type of thyroid disorder and the clinical presentation in our subfertile women.

Materials and methods

The study was carried out in the Infertility outdoor of infertility unit of BSMMU in Dhaka and a tertiary infertility centre in Dhaka during the period of 16th March 2007 to 15th September 2007. Blood tests were carried out in a private diagnostic laboratory in Dhaka. Sixty women of child bearing age were recruited for the study out of which 30 subfertile women of reproductive age was taken as case and 30 non pregnant, reproductive aged, parous women without a history of reproductive problem as control.

Women with both primary and secondary subfertility within 18 to 45 years of age was taken into the study. Women with organic lesion in uterus or ovary or with history of abdominal surgery was excluded from the study. Required permissions was taken from the authorities of BSMMU and tertiary infertility centre. Informed verbal and written consents were taken from the study patients.

10 ml of venous blood from the antecubital vein was collected from each women and TSH , T3 and T4 , anti TG ab and TPO ab were measured using a third generation chemiluminescent immunoassay system (DPC - Diagnostic Products Corporation, Los Angeles, USA). The reference values were 0.4 - <4.5 _ IU / ml for TSH , 1.2 - 2.7 n mol / L for T3 , 60 - 160 n mol / L for T4 , upto 40 IU / ml for anti TG ab and < 35 IU / ml for TPO ab. Anti TG ab and TPO ab considered positive when they were exceeding the reference range.Lipid profile includes serum Cholesterol, HDL, LDL and Triglycerides were measured using a semi automated flow cell chemistry analyzer

(1021 Mertech , Italy). The reference values were 220 mg / dl for serum cholesterol , >55 mg / dl for HDL , < 150 mg / dl for LDL , 10-190 mg / dl for serum triglycerides.

Results

In both control and case groups, most of the subjects belonged to age group 26-35 years (50% and 60%), followed by 25 years (30%) and >35 years (20%) in control group, and >35 years (23.3%) and 25 years (16.7%). Occupation was almost similar in both the groups. 13.3% of the cases was from high socioeconomic group and the rest of the women belonged middle socioeconomic group.

Table-I shows that in control group, proportion of women suffering from thyroid disease was significantly low (6.7%), but in case group 33.3% of the women had been suffering from thyroid disease. Comparison mean (±SD) of BMI between control and case groups showed significance difference (Table II). Table- III Shows in case group women were suffering from subclinical hypothyroidism about 26.7%, hypothyroidism about 6.7% where as in control group, women were

suffering from hypothyroidism in about 3.3%, hyperthyroidism about 3.3%.

In the case group menstrual cycle was irregular in 23.3% women with subclinical hypothyroidism and in 30% of women who had no thyroid disease. In the control group irregular menstrual cycle was in 10% of women without any thyroid disease.

Menstrual cycle was regular in 6.7% women in hypothyroidism, 3.3% in subclinical hypothyroidism and 36.7% who had no thyroid disease in case group, where as in control group menstrual cycle was regular in 3.3% in hypothyroidism, 3.3% in hyperthyroidism and in 83.4% who had no thyroid disease. 10% women had history of abortion in women suffering from subclinical hypothyroidism, 3.3% in hypothyroidism, and 6.7% who had no thyroid disease in case group. In the control group 3.3% had history of abortion in hyperthyroidism and in 6.7% in women where thyroid disease was absent. Diabetes was present in 10% of subclinical hypothyroidism and 6.7% who had no thyroid disease in case group. 6.7% women had hypertension in subclinical hypothyroidism 3.3% in hypothyroidism, and 20% who had no thyroid disease in case group, where as in the control group no women had any other medical problem. Hypercholesterolaemia was present in one (5%) woman of case group without thyroid disease.

Table I : Prevalence of thyroid disease

Study group	Thyroid disease absent		Thyroid disease present		P value
	No.	(%)	No.	(%)	
Control (n=30)	28	(93.3)	2	(6.7)	<0.001s
Case (n=30)	20	(66.7)	10	(33.3)	>0.10ns

Z-test
s = Significant
ns = Not significant

Table II : Comparison of BMI between control and case

Parameters	Control (n=30)	Case (n=30)	P value
	Mean±SD	Mean±SD	
BMI (kg/m2)	24.16±3.77	27.98±5.42	<0.01s

s = Significant

Table III : Type of Thyroid Disorder In Case & Control Groups.

Thyroid Disorder	Case (30)		Control (30)	
	No.	(%)	No.	(%)
Subclinical Hypothyroidism	8	(26.7)	0	
Hypothyroidism	2	(6.7)	1	(3.3)
Hyperthyroidism	0		1	(3.3)
No Thyroid disease	20	(66.6)	28	(93.4)

Discussion

The study was done to find out the prevalence of thyroid disorder and the different type of thyroid disorder in subfertile women. Most of the patient in the control and case groups was in the age range of 26-35 years. In a study done by Petta A in 2007 the prevalence of thyroid dysfunction was 12.2% in women with surgically and histopathologically confirmed endometriosis and 10.8% in the control group [14]. In this study out of 30 subfertile women screened for thyroid disorder, thyroid disease was present in 33.3% of the patients where as in the control group only 6.7% suffered from thyroid disease which was statistically highly significant.

In a study done by Achita Sadera incidence of hypothyroidism was in 4% of the general population where both male and female were included [15] where as in this study prevalence of hypothyroidism was in 6.7% of the infertile women. Subclinical hypothyroidism can be an early stage of hypothyroidism and is characterized by an exaggerated TSH response to thyrotrophin releasing hormone. Bals- Pratsch M showed in his study the incidence of subclinical hypothyroidism to be 25% in infertile women[16]. In Raber's W study, subclinical hypothyroidism was in 34% of infertile women[17] where as in this study 26.7% subfertile women were suffering from subclinical hypothyroidism.

Petta A showed prevalence of hyperthyroidism to be 3.2% in female population of reproductive age where as in this study, prevalence of hyperthyroidism in female population of reproductive age was 3.3%. Scott and Mussey found that 56% of hypothyroid patient had menstrual irregularities [18]. Joshi et al found that 68.2% hypothyroid patients had menstrual irregularities [19]. In this study 53.3% subfertile women had menstrual irregularities. BMI is significantly higher in case group than in control group and this may be due to possible low metabolism rate due to hypothyroidism.

In a study done in 2003 abortion rate was 13% in infertile women with thyroid disorder which was not associated with the presence of autoimmune thyroiditis [17]. In this study abortion was 13.3 % in infertile women with thyroid disorder and not associated with thyroid antibodies. Stagnaro-green showed there was strong association between abortion and the presence of elevated thyroid antibodies [20] which was in contrast with this study.

Diabetes and hypertension were in 10% of the subfertile women with thyroid disease where as in the control group no woman had any medical disorders.

Poppe K, in his study showed serum TSH levels in patients with infertility was significantly higher compared with control patients i,e, mean serum TSH level was 1.6±2.6 mIU/L and 1.2±0.7mIU/L in infertile patient and control group respectively[36]. In this study mean serum TSH level in case group was 3.38±2.86 mIU/ml and in control group was 2.46±1.87mIU/ml which was higher in patients with subfertility compared with control patients.

Only one patient was suffering from hyperthyroidism in control group where as no hyperthyroidism patient was seen in case group in this study. As the sample size was small comment on hyperthyroidism in subfertile women will required large population study. There was no difference in the lipid profile of the control and case group.

Conclusion

Prevalence of thyroid disorder seems to be higher in female subfertile patient than the general population. BMI in the infertile group was significantly higher. Subfertile women who had been suffering from thyroid disorder had menstrual irregularities. Subclinical hypothyroidism was significantly higher in subfertile women. History of abortion is higher in subclinical hypothyroidism than control group. Hypothyroidism seems to be the dominant thyroid disorder in female subfertility.

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