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Thyroid Status of Infertile Women Attending at Infertility Outdoor in BSMMU

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Summary:

Aim: To evaluate the thyroid status in infertile women.

Materials and methods: A cross sectional study was conducted in the department of Infertility of Bangabandhu Shaekh Mujib Medical University from January 2012 to December 2012. A total 400 patients of infertility were studied. The thyroid function status of the subjects were assessed and analyzed.

Results: Of the 400 women enrolled for the study, 221(55%) patients with primary infertility and 179 (45%) patients were with secondary subfertility. The mean age of the responders were 22.3±4.6 years, the mean duration of marriage were 4.5±1.2 years and mean BMI were 23.2±3.1 kg/m^2.Among the 400 patients 70.50% that is 293 patients were euthyroid, TSH level was increased in 23% or in 92 subjects. Depending upon the TSH levels, hypothyroid infertile women were further subdivided into subclinical hypothyroidism where TSH 4–6 mIU/L with normal FT4 (9-24 pmol/L) and clinical hypothyroidism where TSH > 6 mIU/L with raised FT4 level. It was found that 66 (71.74%) of hypothyroid infertile women were with subclinical and remaining 26 (28.26%) were with clinical hypothyroidism.Hyperthyroidism that is low TSH level (<.5 mIU/L) found in 15(3.75%) subjects and visible goiter was present in only 2 patients. In 96 hypothyroid infertile females, the mean TSH levels were 7.34 ± 2.13 mIU/L, and mean FT4 level was 17.34±3.23pmol/L. The mean PRL levels were 52.46 ±11.17 ng/ml.

Conclusion: Thyroid dysfunction is an important factors for infertility. Early diagnosis and timely intervention can reduce the burden of infertility due to thyroid dysfunction.

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Introduction:

Infertility is defined as a failure to achieve pregnancy during 1 year of frequent, unprotected intercourse[1]. In the general population, it is estimated that 84% of females would conceive within 1 year of regular unprotected sexual intercourse. This rises cumulatively to 93% after 3 years [2-3.]

The relation of infertility and thyroid disorder is not yet clear. Undiagnosed and untreated thyroid disease can be a cause for infertility as well as sub-fertility. Thyroid hormones are essential for normal growth, sexual development and reproductive function. Thyroid dysfunction can affect fertility in various ways resulting in anovulatory cycles, luteal phase defect, high prolactin (PRL) levels, and sex hormone imbalances. Therefore, normal thyroid function is necessary for fertility, pregnancy, and to sustain a healthy pregnancy, even in the earliest days after conception.[4-5]

Thyroid glands produce hormones that regulate metabolism and important organ functions like reproduction and mental health[4]. However, it is true that thyroid problem can sometimes be an impediment to getting pregnant for anovulation and menstrual irregularities with no eggs to fertilize, conception becomes impossible[6]. In addition, some women experience a short luteal phase- The luteal phase is the time frame between ovulation and onset of menstruation. Luteal phase needs to be of sufficient duration (13-15 days) to nurture fertilized egg.[7] Luteal phase defect has been diagnosed in 3-20% who in infertile patients.[8]

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Hypothyroidism may also increase circulating active estrogen and interfere with ovulation. This increased bioactive estrogen may be due to decreased metabolism of estrogen in the liver or decrease level of protein that binds it in the circulation, like sex hormone binding globulin (SHBG) in adequate amount binds to hormone and reduces free fraction of estrogen. This persistent elevation of bioactive estrogen disrupts the midcycle preovulatory LH and FSH surges as required for ovulation[9]. Since thyroid hormones are involved in the gonadotropin induced estradiol and progesterone secretion by human granulosa cells, hypothyroidism would interfere with ovarian function and fertility.[10] Hyperprolactinemia resulting from longstanding primary hypothyroidism has been implicated in ovulatory dysfunctions ranging from inadequate corpus luteal progesterone secretion when mildly elevated to oligomenorrhea or amenorrhea when circulating prolactin levels are high.[11]

Thyroid evaluation should be done in any woman who wants to get pregnant with family history of thyroid problem or irregular menstrual cycle or had more than two miscarriages or is unable to conceive after 1 year of unprotected intercourse. The comprehensive thyroid evaluation should include T_3, T_4, thyroid stimulating hormone (TSH), and thyroid autoimmune testing such as thyroid peroxidase (TPO) antibodies, thyroglobin/ antithyroglobin antibodies, and thyroid stimulating immunoglobulin (TSI). Thyroid autoimmune testing may be included in the basic fertility workup because the presence of thyroid antibodies doubles the risk of recurrent miscarriages in women with otherwise normal thyroid function.[12–14]

Thyroid dysfunction can be easily detected by assessing TSH levels in the blood. A slight increase in TSH levels with normal T_3 and T_4 indicates subclinical hypothyroidism whereas high TSH levels accompanied by low T_3 and T_4 levels indicate clinical hypothyroidism.[15] Subclinical hypothyroidism is more common. It can cause anovulation directly or by causing elevation in PRL. Many infertile women with hypothyroidism had associated hyperprolactinemia due to increased production of thyrotropin releasing hormone (TRH) in ovulatory dysfunction.[16,17]

So, awareness of the thyroid status in the infertile couple is crucial, because of its significant, frequent and often reversible or preventable effect on infertility. Many aspects of the role of thyroid disorders in infertility need further research.With this background, the present study has been contemplated to investigate the prevalence and etiology of different thyroid disorders in infertile patients attending at infertility outdoor BSMMU.

AIM

To evaluate the thyroid status in infertile women.

Materials and Methods:

The cross sectional study was conducted on 400 women (age group 20–40 years) on their first visit to Infertility outdoor of Gynecology and Obstetrics Department of BSMMU from January 2012 to December 2012. The study was approved by the Institutional Ethical Committee and was conducted after taking informed, written consent of the participants. Subjects were selected purposively according to the availability of the patients. Sample size was determined from "Tables of minimum sample size"

Inclusion criteria:

- Age 20-40 years
- Duration of marriage >1 year

Exclusion criteria:

- Infertile women having pelvic pathology, like- Fibroid Uterus, tubular blockage, pelvic inflammatory disease, endometriosis on diagnostic laparoscopy or hysteroscopy and with genital TB (PCR-positive); with liver, renal or cardiac diseases
- Patients having systemic diseases, (Diabetes Mellitus, Hypertension, Renal disease, Liver disease, Cardiac disease) those already on treatment for thyroid disorders or hyperprolactinemia
- Male factor abnormalities also were excluded from the study.

Routine investigations such as random blood sugar (RBS), hemogram, urine routine examination, and ultrasound were done. TSH and PRL were measured by the electrochemiluminesence method as per the instruction manual for Elecsys, 2010 (Roche, USA). Normal TSH and PRL levels were 0.27–4.5 ìIU/ml and 1.9–25 ng/ml, respectively and FT4 (9-24 pmol/L), as per kit supplier's instruction. Therefore, hypothyroidism was considered at TSH levels of > 4.5 ìIU/ml and hyperprolactinemia at PRL levels of >25 ng/ml.

Statistical analysis of results was carried out using percentages.

Results:

Of the 400 women enrolled for the study, 221(55%) patients with primary infertility and 179(45%) patients were with secondary subfertility.76[19.29] The mean age of the responders were 22.3±4.6 years, the mean duration of marriage were 4.5±1.2 years and mean BMI were 23.2±3.1 kg/m^2

Among the 400 patients 70.50% that is 293 patients were Euthyroid, TSH level was increased in 23% or in 92 subjects. Depending upon the TSH levels, hypothyroid infertile women were further subdivided into subclinical hypothyroidism where TSH 4–6 mIU/L with normal FT4 (9-24 pmol/L) and clinical hypothyroidism where TSH > 6 mIU/L with raised FT4 level. It was found that 66 (71.74%) of hypothyroid infertile women were with subclinical and remaining 26 (28.26%) were with clinical hypothyroidism. Hyperthyroidism that is low TSH level (<.5 mIU/L) found in 15(3.75%) subjects and visible goiter was present in only 2 patients.

In 96 hypothyroid infertile females, the mean TSH levels were 7.34 ± 2.13 mIU/L, and mean FT4 level was 17.34±3.23pmol/L. The mean PRL levels were 52.46 ±11.17 ng/ml.

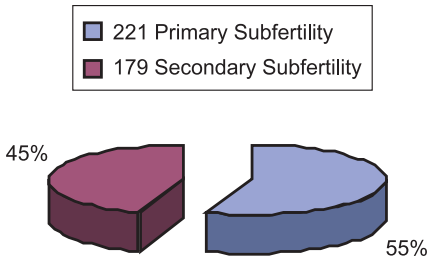

Fig.-1: *Distribution of the subjects according to the type of infertility (n=400)*

Table-I

Socio-demographic variables in study subjects (n=400)

Variables	Study subjects (n = 400)	Range
Age (Years)	22.3±4.6	18.6-28.6
BMI (kg/m^2)	23.2±3.1	20.2-30.1
Mean duration of infertility (years)	4.5±1.2	3.1-5.8

Table-II

Distributions of study subjects according to thyroid function (n=400)

Types of thyroid status	Number	Percentage (%)
Euthyroid	293	73.25
Hyperthyroid	15	3.75
Subclinical hypothyroid	66	16.50
Clinical hypothyroid	26	6.50

Table-III

Comparison of Biochemical examination between groups (n=400)

Hormons	Mean level	Range
Serum FT_4 (micromole/L)	17.34±3.23	13.69-22.44
Serum TSH (mIU/L)	7.34 ± 2.13	2.73-9.54
Serum PRL(ng/ml)	52.46±31.17	20.11-70.60

Discussion:

Prevalence of hypothyroidism in the reproductive age group is 2–4% and has been shown to be the cause of infertility and habitual abortion.[18] Thyroid dysfunction is a common cause of infertility which can be easily managed by correcting the appropriate levels of thyroid hormones.[19,20] 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.[21] Hypothyroidism is associated with increased production of TRH, which stimulates pituitary to secrete TSH and PRL. Hyperprolactinemia adversely affects fertility potential by impairing GnRH pulsatility and thereby ovarian function.[20]

The current cross sectional study of 400 infertile women showed 221(55%) patients with primary infertility and 179(45%) patients were with secondary subfertility. The mean age of the responders were 22.3±4.6 years, the mean duration of marriage were 4.5±1.2 years. Nambiar et al. and Mbah et al. found the mean age of the subjects were 25.19 (±4.17) years which are higher than the current study[22-23]. In this study, data reflecting early marriage prevalent in Bangladesh. The higher age of the above mentioned authors may be due to increased

life expectancy, geographical and racial influences may have significant impacts.

In the present study the mean BMI were 23.2±3.1 kg/m^2.Mbah et al.[23] found the statistically significant differences in body weight as found between the hypothyroid and non-hypothyroid pregnant women[15]. The relationship of thyroid function with BMI also described by Glinoer et al. and Vermiglio, Presti and Argentina[24-25].

An elevated TSH indicates primary hypothyroidism, and serum-free T4 levels will help to categorize this as either overt or subclinical hypothyroidism. Among the 400 patients 73.25% that is 282 patients were Euthyroid, TSH level was increased in 23% or in 92 subjects. Depending upon the TSH levels, hypothyroid infertile women were further subdivided into subclinical hypothyroidism where TSH 4–6 mIU/L with normal FT4 (9-24 pmol/L) and clinical hypothyroidism where TSH > 6 mIU/L with raised FT4 level. It was found that 66 (16.50%) of hypothyroid infertile women were with subclinical and remaining 26 (6.50%) were with clinical hypothyroidism. These findings are very close to the study done by Janssen *et al* .[26]

The prevalence of hypothyroidism in women of reproductive age (20-40 years) varies between 2% to 4%.[18] Relatively higher crude prevalence rate of hypothyroidism (8%) in the infertile women found in our study could be due to special referral pattern of the patients who were referred to the hospital based on suspicion of thyroid abnormalities.

Hyperprolactinemia was found in 20.75% cases, which is higher than in USA. The prevalence of hyperprolactinemia was higher in Iraq (60%) and even in Hyderabad, India, it is higher (41%) as compared to the present study. Hyperprolactinemia may result from stress, and the variable prevalence may be due to the different stress levels in different areas.[13,17]

Hyperthyroidism was found in 3.75% of the infertile patients in the present study. Joshi *et al* [27] evaluated 53 hyperthyroid patients and found 5.8% of them to be infertile. In this study goiter was present in only two patients.

Therefore, the normal TSH levels are the pre-requisite requirements for fertilization. For these reasons, TSH and prolactin are commonly-ordered clinical tests in evaluating infertile women. The decision to initiate thyroid replacement therapy in subclinical hypothyroidism at early stage may be justified in infertile women. Our data also indicate that variations in TSH levels in the narrower range or borderline cases, i.e. 4–5, 5–6, and >6.0 ìIU/ml, should not be ignored in infertile women which are otherwise asymptomatic for clinical hypothyroidism. This group of infertile women, if only carefully diagnosed and treated for hypothyroidism, can benefit a lot rather than going for unnecessary battery of hormone assays and costly invasive procedures. For better management of infertility cause, we should plan further studies with the large sample size and long-term follow-up which are necessary to validate the variation in TSH and PRL levels.

It may be concluded that thyroid dysfunction could initiate, maintain or worsen the infertility status and thereby correcting thyroid state, infertility could be managed in a better way. This hypothesis seems to hold true even now but it lacks appropriate evidence based systematic analysis to establish the necessity of routine screening of all the infertility patients for thyroid function and thyroid-specific autoantibodies even without clinical evidence of overt thyroid disorders because patients with anti-TPO and anti Tg autoantibodies are much likely to develop thyroid dysfunction later in the later life.

Conclusion:

The present study was done to see the thyroid status of infertility women. In the light of the findings of the present study and discussion thereof, it is found that thyroid disorder are very commonly found in women who are suffering from infertility, and the most common thyroid disorder is sub clinical hypothyroidism. So, it is recommended to undertake further study with larger sample size to find whether Thyroxin therapy in sub clinical hypothyroid improves fertility status. It is also recommended to see whether those having sub clinical hypothyroidism associated with thyroid peroxidase antibody are more prone to become infertile and overt hypothyroidism.

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