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PREVALENCE OF THYROID DYSFUNCTION IN WOMEN WITH INFERTILITY

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ABSTRACT Human conception and pregnancy is both a vulnerable and a robust process. Thyroid hormones have profound effects on reproduction and pregnancy. There is a known association of hyper- and hypothyroidism with menstrual disturbances and decreased fecundity. Women with reproductive failure also have an increased prevalence of organ specific autoimmunity compared to fertile women. The present study was undertaken in 186 women (ages, 28 ± 5 years) with various causes of infertility, and in 100 age-matched (29 ± 5 years) healthy controls with the aim of assessing the prevalence of undisclosed alterations of thyroid function in women with infertility. Female origin of the infertility was diagnosed in 52% of the couples, with specific causes including endometriosis (11%), tubal disease (30%), and ovarian dysfunction (59%). Male infertility represented 38% and idiopathic infertility 17% of the couples. Overall, median thyrotropin (TSH) was significantly higher in patients with infertility compared to controls: 2.0 (0.9) versus 1.4 (0.8) mIU/L. Serum TSH above normal (>4.2 mIU/L) or suppressed TSH (<0.27 mIU/L) levels were not more prevalent in the infertile women than in controls. When thyroid antibodies were positive, both hypothyroidism and hyperthyroidism were more frequent in all women of infertile couples and in the women with a female infertility cause, compared to women in the same groups but without positive TPO-Ab. The present study shows that in infertile women, thyroid dysfunction features are significantly more frequent than in healthy fertile controls.

KEYWORDS : TSH, Thyroid, infertility, controls

I. Introduction

Human conception and pregnancy is both a vulnerable and a robust process. Thyroid hormones have profound effects on reproduction and pregnancy. There is a known association of hyper- and hypothyroidism with menstrual disturbances and decreased fecundity (1). Infertility is defined as the inability to conceive after one year of regular intercourse without contraception. The prevalence of infertility is estimated between 12 and 14% and remains stable in recent years [1], [2]. It thus represents a common condition, with important medical, economic and psychological implications (2). According to a standard protocol infertility evaluation usually identifies different causes, including, male infertility (30%), female infertility (35%), the combination of both (20%), and finally unexplained or "idiopathic" infertility (15%). Female causes of infertility comprise endometriosis, tubal damage and ovulatory dysfunction (OD) (3).In 52% of the infertile couples a female cause of infertility was identified: endometriosis (11%), tubal disease (30%) and ovarian dysfunction (59%). Male infertility was diagnosed in 38% and idiopathic infertility in 17% of the couples (4).

Thyroid dysfunction is a condition known to reduce the likelihood of pregnancy and to adversely affect pregnancy outcome (4) .Data on the relationship between thyroid disorders and infertility remain scarce and the association with a particular cause of infertility has not thoroughly been analyzed (5, 6) . We therefore performed this case-control study to determine the relative frequency of thyroid dysfunction and -autoimmunity in women of a large group of infertile couples, according to the underlying cause of infertility and in comparison to age matched control women (7).

This cohort will be monitored in time; in order to identify the impact of thyroid autoimmunity on the outcome of the IVF procedure, in terms of pregnancy rate and life-birth.

Recently, it has been suggested that infertility may be caused by the presence of auto antibodies, among them thyroid immunity has been incriminated (8).

II. Methodology

186 consecutive women, aged 18-50 years (mean 28 ± 5 years) consulted at the King George Hospital and Padmasri Clinic Visakhapatnam between June 2017 and November 2017. All women were systematically screened on the third day of their menstrual cycle (when present) for the presence of serum thyrotropin (TSH) and thyroxine (T4). The standard infertility workup included medical history, gynaecological examination, transvaginal ultrasonography, hormonal profile, screening for infectious disease and whenever indicated hystero-salpingography and/or laparoscopy. Female causes of infertility were defined, according to WHO criteria: endometriosis (except stage I) (8), tubal damage or OD. Male infertility was identified when the semen was abnormal and no female cause was present. In the case of a normal sperm analysis and the absence of a female cause of infertility, the couple was considered to have idiopathic infertility. One hundred randomly selected, age-matched parous women with a mean age of 29 ± 4 years, and no history of reproductive problems, were screened for the same thyroid parameters and served as controls. Serum TSH and T4 were measured using a third generation electro-chemiluminescence immunoassay (Roche; Mannheim; Germany). Normal TSH and PRL levels were 0.27–4.2 μIU/ml and 1.9–25 ng/ml, respectively, as per kit supplier's instruction.

III. Results

Female origin of the infertility was diagnosed in 52% of the couples, with specific causes including endometriosis (11%), tubal disease (30%), and ovarian dysfunction (59%). Male infertility represented 38% and idiopathic infertility 17% of the couples. Overall, median thyrotropin (TSH) was significantly higher in patients with infertility compared to controls: 2.0 (0.9) versus 1.2 (0.8) mIU/L. Serum TSH above normal (>4.2 mIU/L) or suppressed TSH (<0.27 mIU/L) levels were not more prevalent in the infertile women than in controls. When thyroid antibodies were positive, both hypothyroidism and hyperthyroidism were more frequent in all women of infertile couples and in the women with a female infertility cause, compared to women in the same groups but without positive TPO-Ab. The present study shows that in infertile women, thyroid dysfunction features are significantly more frequent than in healthy fertile controls. Therefore, hypothyroidism was considered at TSH levels of > 4.2 μIU/ml and hyperprolactinemia at PRL levels of >25 ng/ml. Correlations between variables were assessed using Spearman's test, and differences between mean values by the Mann-Whitney-U test. All statistical tests were considered statistically significant whenever P <0.05.

IV. Discussion

Normal thyroid function is necessary for fertility, pregnancy, and to sustain a healthy pregnancy, even in the earliest days after conception (9). Undiagnosed and untreated thyroid disease can be a cause for infertility as well as sub-fertility. Both these conditions have important medical, economical, and psychology implications in our society. Thyroid dysfunction can affect fertility in various ways resulting in anovulatory cycles, luteal phase defect, high prolactin (PRL) levels, and sex hormone imbalances. 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 (3). 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) (9). Thyroid autoimmune testing may or may not 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 (8, 9).

The relationship of infertility with thyroid dysfunction was overlooked in a retrospective study in 186 infertile women showing an overall prevalence of hypothyroidism (both subclinical and overt) of 4% . In this study, subgroup analysis identified 6% of hypothyroid women among those with OD, 2.6% among those with tubal infertility, 0% among those with endometriosis, 1.5% in male infertility and 5% among women with idiopathic infertility. In two other prospective studies, increased serum TSH was identified in 0.7% and 2.3% respectively of women with infertility, the majority of them presenting infertility due to OD (10).The clinical implication of overt thyroid dysfunction in infertile women is explained by the direct effects of thyroid hormones on granulosa and luteal cells, and on oocytes; hence suggesting an interference with normal ovarian function. In case of overt thyroid dysfunction, treatment should be instituted as a primary therapeutically act (11).

In the present work, the overall mean serum TSH was significantly higher in the women of infertile couples than in the controls and in particular in women of the OD subgroup (9-11). In spite of the overall mean higher TSH, only 1% of these women actually presented supranormal TSH values, except for women with tubal infertility with a prevalence of 3% of increased TSH (ns) (12). The low prevalence of overt thyroid dysfunction does not allow speculations on thyroid dysfunction and associated infertility in the tubal and OD subgroup (13). In conclusion, the present study showed that the relative risk to have positive TPO-Abs in infertility due to a female cause and in particular related to endometriosis was significantly increased. Thyroid dysfunction itself is a condition interfering with normal ovarian function and was more frequent in women with positive TPO-Abs (10).

We therefore propose that a systematic screening of TSH, free T4 and TPO-Abs could be considered in all women with a female cause of infertility Stress management is imperative. Stress results in elevated levels of cortisol, the main hormone released by the adrenal glands. Increased cortisol will inhibit the conversion of T4 to the active T3 hormone and will stop the active T3 entering cells sufficiently. Exercise is beneficial as it will stimulate thyroid hormone secretion and increases tissue sensitivity to thyroid hormones (13).

V. Conclusion

Undiagnosed and untreated thyroid disease can be a cause for infertility as well as sub-fertility. Both these conditions have important medical, economical, and psychology implications in our society. Treating thyroid function is not a magic cure for all fertility issues but we found that for many women, once thyroid health has been improved, their fertility issues were resolved and they have gone on to have a healthy pregnancy and enjoyed the treasures of parenthood.

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