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Study of Thyroid and Reproductive hormones levels in fertile and infertile women

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Abstract :

Hormones are actual messengers in endocrine signaling. Thyroid gland as endocrine glands holds a critical place in controlling brain and somatic development in embryos and metabolic activities in adults . There is an Coordination between hypothalamus-pituitary-thyroid and hypothalamus-pituitary- gonadal axes, Therefore hypo- and hyper-thyroidism affect women fertility and prolonged exposure to altered thyroid physiology could lead to women infertility . This study was done to illustrate some hormones(sex and thyroid) changes , the study included 73 infertile women and 23 fertile women24-35years old between March 2013 and June 2013, in Endocrines and diabetes medical center in Nassirhyia city . The results of the study were revealed the significantly increase in the level of LH , FSH , and prolactin and T4 in infertile womens compared with fertile womens(control) while no significant differences was observed in T3 level between two groups .

Keywords: Thyroid hormone and sex hormone , female Reproduction , female infertility.

الخلاصة :

تعتبر الهرمونات الوسائط نقل الاشاره الكميائيه بين الغدد الصم ، وهرمونات الغدة الدرقية تسيطر على عمل الدماغ ونمو الخلايا الجسمية في الاجنة والفعالية الايضيه للخلايا عند الكبار , وهناك تناسق بين هرمونات الغدة الدرقية وهرمونات الغدد التناسلية التي تفرز بايعاز من الغدة النخامية . فالزيادة والنقصان في هرمونات الغدة الدرقية يؤثر في هرمونات الغدد التناسلية . جاءت هذه الدراسة لتحديد التغير الذي يحصل بين هذه الهرمونات ومعرفة هل هناك تاثير لهذا التغير على خصوبة النساء .حيث اجريت الدراسة في المركز الطبي لامراض الغدد الصم والسكري على 73 امراءة تعاني من مشاكل الخصوبه ولعمر من 24–35 ومجموعة سيطرة 23 للفترة مابين اذار 2013 الى حزيران 2013 في مدينة الناصريه واظهرت النتائج ان هناك زيادة في الهرمونات الجنسية .Pro, LH,FSH والدرقية T_4, TSH.

مفتاح الكلمات: هرمونات الغدة الدرقية ، هرمونات الجنس ،تكاثر المرأة ، خصوبة المرأة

Introdution :

Endocrine system is the controller of organ functions in human body where Hormones are messengers in endocrine system . The main function of thyroid gland controlling for nervous system ,somatic development in embryos and have a main role in controlling basal metabolic rate, growth, as well as the development and differentiation of many cells in the body. There are two major types of thyroid hormones, the biologically of thyroid hormones form thyroxine (T4) secretion it comprises ~80% of the thyroid hormones secreted, the main secretory product and pro-hormone triiodothyronine (T3) ~20% , T4 is transformed to T3 by (DOI), containing proteins which founds in three isoforms. DOI1 and DOI2 are involved in the alteration from T4 to T3 while DOI3 catalyzes the alteration of T4 to an revesible T3 form of T3, (Song et al., 2011). Thyroid peroxidase or thyroperoxidase (TPO) enzymatic protein that plays an critical role in thyroid Hormones synthesis . Infertility and reproductive related to abnormalities in the endocrine or immune system, or both. These systems are also directly linked to the thyroid gland since the most thyroid autoimmunity frequent causes is hypothyroidism in women of reproductive age the most women with thyroid dysfunction occurrence menstrual irregularities, infertility and increased pregnancy miscarriage .(Harbeck B. and Brabant G. 2012). The thyroid gland and gonadal axes interact continuously before and during pregnancy (Poppe K.et al., 2008).In

Hypothyroidism influences ovarian function by decreasing levels of sex-hormone-binding globulin and increasing the secretion of prolactin , In women without thyroid autoimmunity these changes are transient, hypothyroidism and hyperthyroid in women suffer mainly from menstrual disturbances and men from erectile abnormalities and defects in sperm motility.(Rajender,2011)Pathophysiologically, hypothyroidism and thyrotoxicosis may impair the course of pregnancy and may negatively affect the fetus therefore, thyroid function should be tested in patients with infertility,clinically hypothyroidism in men is associated with adverse effects on spermatogenesis whereas in women of fertile age hypothyroidism results in menstrual disturbances. In this study, therefore the study aimed to study the interaction between thyroid disorders and infertility

Material and Method:

The study consisted of 73 infertile women and 23 fertile women with age 24-35 between March 2013 and June 2013. In Endocrines and diabetes center in Nasirhyia city , 5 ml of blood collected from each women and left to clot for 1-2 hour at room temperature and then centrifuged at 3000 rpm for 10 minutes, ,serum was stored at – 20Cº until was used . tested for the determination of prolactin, thyroid and sex hormone levels: (TSH, T3, T4, FSH, LH and Prolactin) using a miniVidas system. Is an automated quantative test for use on the VIDS family instrument ,for the enzyme immunoassay determination of human hormones in human serum or plasma (lithium heparin) using the ELFA technique ((Enzyme Linked Fluorescent Assay). (Biomerieux ,France).

Statistical analysis:

Values were expressed as mean ± SD, differences between the mean values were analyzed by chi-square test.while correlation between the data obtainedwere analyzed by using analysis of variance (A Y VOVA)to determine the level of significance by using minitab under windows The criterion for significance was ($p < 0.05$) .

Results:

A total of 73 subjects infertile women and 23 fertile women covered in this study.

Table:1 The level of TSH ,T4 ,T3 ,LH ,FSH and Pro.hormones in fertile and infertile women

Hormone test	Fertile women Mean ± SD	Infertile women Mean ± SD	P value
TSH mIu/l	2.33 ± 0.32	17 ± 14	0.310
T_4 nmol/l	82 ± 3.8	289 ± 205	0.314
T_3 nmol/l	1.754± 0.08	1.831 ± 0.06	0.473
LH mIu/l	2.80 ± 0.25	6.73 ± 0.94	0.000 *
FSH mIu/l	1.319 ± 0.076	8.49 ± 1.2	0.000 *
Prol. pg/l	3.96 ± 1	19.5 ± 2	0.000 *

*P value ≤ 0.005

The present study showed asignificantly increase(p=000)hormone level of LH,FSH , Prol. While the mean thyroid hormone level of level of T_4 and TSH increase but not significant ,T_3 remain the same level and not reach asignificant when compared with fertile women Table (1).

Table (2): Correlations: TSH,T_4, T_3, FSH, LH and Prol. In infertile women

hormone	TSH mIu/l	T_4 nmol/l	T_3 nmol/l	LH mIu/l	FSH mIu/l
T_4	-0.017 0.889				
T_3	-0.039 0.743	-0.037 0.758			
LH	-0.042 0.722	0.050 0.673	0.070 0.557		
FSH	-0.007 0.950	-0.045 0.703	-0.060 0.615	-0.001 0.992	
Pro. pg/l	-0.003 0.979	0.003 0.980	-0.186 0.115	-0.013 0.916	-0.101 0.396

Cell Contents: Pearson correlation, P-Value

All parameters in table (2) no significant correlation .

Table (3): Correlations: TSH,T4, T3, FSH, LH and Prol. In fertile women

Hormone test	TSH mIu/l	T_4 nmol/l	T_3 nmol/l	FSH mIu/l	LH mIu/l
T_4	0.042 0.848				
T_3	-0.094 0.668	0.688 0.000			
FSH	0.472 0.023	0.282 0.192	0.270 0.212		
LH	0.085 0.701	-0.376 0.077	-0.300 0.164	-0.004 0.987	
Pro .pg/l	-0.211 0.333	0.708 0.000	0.590 0.003	-0.077 0.728	-0.784 0.000

Cell Contents: Pearson correlation P-Value

There were a positive Significant correlation between T4 and T3 , Pro. and positive Significant correlation between T3 and Pro. ,while Significant negative correlation between LH and Pro. ,and there were no Significant correlation between other parameters

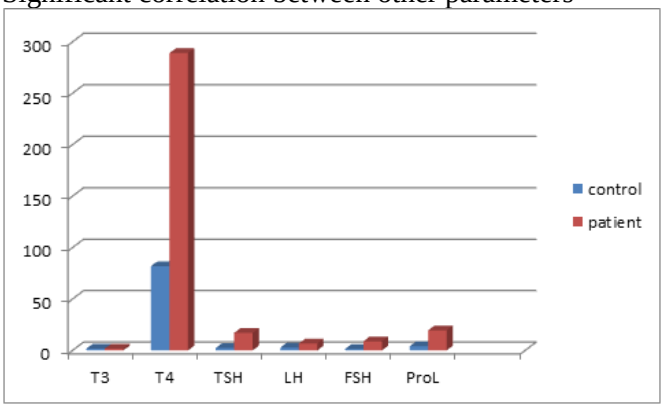

Figure (1): Thyroid hormone and serum sex hormone level in fertile and infertile women

The figure explain high level of T4 in infertile women and elevated TSH, LH, FSH, Pro. , compared with fertile women.

Discussion:

many studies have observed the incidence of thyroid autoimmune disease in women with infertility.(Poppe K *et al*., 2002; Abalovich M. *et al*., 2007; Petta C. *et al*,. 2007; Krassas *et al*., 2010.) The present study showed increase significantly in the level serum LH, FSH and Prol. Hormone associated with increase secretion of T4,TSH. Thyroid hormone effected to modulate the level of sex hormone-binding globulin (SHBG) in serum.(Krassas E.*et al.*, 1999).Also the levels are higher in hyperthyroidism (Stephen R. 2013; Vierhapper H.et al.,1998) The Leydig and Sertoli cells, respectively are less stimulated to differentiate into mature cells In cases of delayed hypothyroidism due to drop in LH and FSH level (Mandel, 2004).Thyroid gland is important for both follicular and embryo development that indicate the thyroid hormones and TSH affect in endometrium and ovary on the paracrine level (Evers , 2012),Therefore thyroid autoimmunity has been associated with an increased rate of miscarriage mainly in the first trimester (Poppe, et al., 2008).There are several paracrine factors are of importance for successful embryo implantation, leukemia inhibitory factor (LIF), and Leptin being among the most studied (Cioffi et al., 1997 ; Gonzalez et al., 2004., Aghajanova, 2004). TSH increase LIF and LIF receptor expression in endometrial epithelial cells and in thyroid cells. (Aghajanova et al., 2011). TSH release leptin in human adipose tissue culture (Evers ,2012), and it is possible that this effect is present also in the human endometrium, thereby playing a role for successful implantation . (Zelenko et al., 2012) refer to effect directly TRH in endometrium from women with endometriosis compared to health controls Thyroxine-binding globulin binds concentrations elevated with the greatest elevation found in patients with the highest serum T4 concentrations (Vierhapper H, et al., 1998) . The majority of circulating endogenous T4 and T3 is transported in serum bound to thyroxine-binding globulin, transthyretin and albumin. Thyroxine-binding globulin has the highest affinity constant for T4 Thyroxine-binding globulin binds about 75% of circulating T4, During pregnancy, levels of thyroxine-binding globulin double, which obviously increases the number of T4 binding sites.(Glinoer , 1997) .Thyroid hormone receptors have been described in human oocytes, where they synergize with the luteinizing hormone and human-chorionic- gonadotropin receptor, mediated by follicle-stimulating hormone(FSH) to exert direct stimulatory effects on granulosa cell function and on trophoblastic differentiation (Aghajanova , et al,. 2009) Pregnancy causes a number of physiological alterations in thyroid hormones metabolism (Verthelyi, 2001) may be due to pathophysiological states of thyroid dysfunction.We are found the thyroid hormones is significantly higher in infertile women than fertile women, the risk of miscarriage may be higher if anti-TPO are present. (Harbeck,et al., 2009) and the risk of early miscarriage is substantially raised mainly in the first trimester (Krassas , 2010) Considering that significantly higher serum TSH and the incidence of TPO antibodies is higher in infertile women compared to fertile controls (Poppe and Glinoer, 2003). Inconsistent results prolactin levels were seen in thyrotoxic patients from different studies some of found normal prolactine (Hudson, and Edwards 1992) (Abalovich M .et al ., 1999) . while others found elevated serum prolactine (Cooper, 1979 ; Onishi et al., 1975) .In another hand (Reh et al., 2010) showed no differences in the rates of clinical pregnancy ,delivery or miscarriage were experiential.

Conclusion :

Thyroid hormones play an important part in normal reproductive function, by direct effects on the ovaries and also indirectly by multiple interactions with other sex hormones. Thyroid dysfunction can lead to menstrual irregularities and infertility. The physiology

of the interaction between sex hormones and immune function and its potential pathological consequences may provide insight into the autoimmune disease.

Refrence :

Abalovich M., Levalle O., Hermes R., Scaglia H., Aranda C., (2007) Subclinical hypothyroidism and thyroid autoimmunity in women with infertility. *Gynecol Endocrinol* 23: 279–283

Aghajanova L. (2004). Leukemia inhibitory factor and human embryo implantation. Ann. N. Y. Acad. Sci. 1034, 176–183

Aghajanova L., Giudice L. C. (2011). Molecular evidence for differences in endometrium in severe versus mild endometriosis. Reprod. Sci. 18, 229–251

Aghajanova L., Stavreus-Evers A., Lindeberg M., Landgren B. M., Sparre L. S., Hovatta O. (2011). Thyroid-stimulating hormone receptor and thyroid hormone receptors are involved in human endometrial physiology. Fertil. Steril. 95, 230–237

Aghajanova L, Lindeberg M, Carlsson IB, Stavreus-Evers A, Zhang P, Scott JE, Hovatta O, Skjöldebrand-Sparre L (2009) Receptors for thyroid-stimulating hormone and thyroid hormones in human ovarian tissue , (Sweden)Reprod Biomed Online.;18(3):337-47.(Abstract)

Cioffi J. A., Van Blerkom J., Antczak M., Shafer A., Wittmer S., Snodgrass H. R. (1997). The expression of leptin and its receptors in pre-ovulatory human follicles. Mol. Hum. Reprod. 3, 467–472.

Cooper D., Ridgway E., Kliman B., Kjellberg N., Maloof F.(1979) Metabolic clearance and production rates of prolactin in man. J Clin Invest 64: 1669-80.

Donnelly P, White C.(2000) .Testicular dysfunction in men with primaryhypothyroidism; eversal of hypogonadotropic hypogonadism with replacement thyroxine. Clin Endocrinol; 52: 197-201.

Evers A.S. (2012) Paracrine Interactions of Thyroid Hormones and thyroid Stimulation Hormone in the Female Reproductive Tract have an impact on Female Fertility Endocrinol. 3: 50.

Glinoer ,D. (1997) The regulation of thyroid function in pregnancy: pathways of endocrine adaptation from physiology to pathology. Endocr Rev 18: 404–433

Gonzalez R., Rueda B. R., Ramos M. P., Littell R. D., Glasser S., Leavis P. C. (2004). Leptin-induced increase in leukemia inhibitory factor and its receptor by human endometrium is partially mediated by interleukin 1 receptor signaling. Endocrinology 145, 3850–3857

Harbeck·H., Lehnert H., Mönig (2009) GynäkologischeEndokrinologieSchilddrüsenentzündungen in Schwangerschaft und Stillzei ,Medizin Verlag 7:224–230(Abstract)

Harbeck and Brabant (2012) Experimentelle und klinischeMedizinischeKlinikI,Universitätsklinikum Medizini sche Klinik I, Universitätsklinikum Schleswig-Holstein, Campus Lübeck, Lübeck . Gynäkologische Endokrinologie 10:26–30 . (Abstract)

Hudson R., Edwards A. (1992) Testicular function in hyperthyroidism. J. Androl 13: 117-24.

Krassas G. E., Pontikides N., Kaltsas T., Papadopoulou P., Paunkovic J., Paunkovic N., Duntas L. H. (1999). Disturbances of menstruation in hypothyroidism. Clin. Endocrinol. (Oxf.) 50, 655–659.

Krassas G. E., Poppe K., Glinoer D. (2010). Thyroid function and human reproductive health. Endocr. Rev. 31, 702–755.

Mandel S .J. (2004) Hypothyroidism and chronic autoimmune thyroiditis in the pregnant state: maternal aspects. Best Pract Res Clin Endocrinol metab 18: 213–15

Onishi T., Kiyai K., Izumi K., Nakanishi H., Kumahara Y. (1975) Prolactin response to chlorpromazine and thyrotropin releasing hormone in

hyperthyroidism. J Clin Endocrinol Metab 40: 30-2.

Petta C. A., Arruda M. S., Zantut-Wittmann D. E., Benetti-Pinto C. L. (2007). Thyroid autoimmunity and thyroid dysfunction in women with endometriosis. Hum. Reprod. 22, 2693–269710.1093 (Abstract)

Poppe K. and Glinoer D. (2003) Thyroid autoimmunity and hypothyroidism before and during pregnancy Hum Reprod Update 9: 149–161.

Poppe K., Glinoer D., Van Steirteghem A., Tournaye H., Devroey P., Schiettecatte J., Velkeniers B. (2002). Thyroid dysfunction and autoimmunity in infertile women. Thyroid 12, 997–1001

Poppe K., Velkeniers B., Glinoer D. (2007). Thyroid disease and female reproduction. Clin. Endocrinol. (Oxf.) 66, 309–321.

Poppe,K. Velkeniers B. and Glinoer D .(2008) The role of thyroid autoimmunity in fertility and pregnancy .Nature Clinical Practice endocrinology & Metabolism vol 4, 394-405.

Rajender.S. , Alaa. J. H. and Ashok. A. ,(2011) Thyroid Hormones in Male Reproduction and Fertility The Open Reproductive Science Journal, , 3, 98-104.

Reh A., Grifo J., Danoff A. (2010). What is a normal thyroid-stimulating hormone (TSH) level? Effects of stricter TSH thresholds on pregnancy outcomes after in vitro fertilization. Fertil. Steril. 94, 2920–2922.

Ris-Stalpers C., Bikker H. (2010). Genetics and phenomics of hypothyroidism and goiter due to TPO mutations. Mol. Cell. Endocrinol. 322, 38–43.

Song Y., Yao X., Ying H. (2011). Thyroid hormone action in metabolic regulation. Protein Cell 2, 358–368.

Stephen r. plymate , louis a. matej, robert e. jones, and karl e. friedl. 2013. Inhibition of Sex Hormone-Binding Globulin Production in the Human Hepatoma (Hep G2) Cell Line by Insulin and Prolactin. Published Online: July 01,

VerthelyiD. (2001). Sex hormones as immunomodulators in health and disease. Int Immunopharmacol. Jun;1(6):983-93.

Vierhapper H, Bieglmayer C, Nowotny P, Waldhäusl W(1998) with hyperthyroidism due to subacute thyroiditis. Thyroid. dec;8(12):1107-11.

Zelenko Z., Aghajanova L., Irwin J. C., Giudice L. C. (2012). Nuclear receptor, coregulator signaling, and chromatin remodeling pathways suggest involvement of the epigenome in the steroid hormone response of endometrium and abnormalities in endometriosis. Reprod. Sci. 19, 152–16210.