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Effect of Anti Mullerian Hormone (AMH) on Hyperthyroidism with and without polycystic ovarian syndrome (PCOS) in female patients

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Abstracts

Effect Anti-Mullerian Hormone (AMH) on thyroid levels in patients with and without polycystic ovarian syndrome PCOS was studied, The results showed an increase in AMH, T3, T4 with increase of age while TSH, BMI decreased with increase of age comparing to control in hyperthyroidism with PCOS patients. Otherwise an increase in AMH, TSH, BMI, T3 and T4 with increase of Age compared to healthy group in hyperthyroidism without PCOS. Effect of ovarian hormones (AMH) on inventory levels of thyroid and perturbations in terms of increases and its impact obesity as well as fertility in women was declared in this research. Serum Anti-Müllerian Hormone (AMH) was assessed using enzyme linked immunosorbent kit [Elisa] while Thyroid stimulating hormone (TSH), Triiodothyronine (T3), Thyroxin (T4) were determined by VIDAS kit method (enzyme linked fluorescent assay).

Keywords: Anti- Mullerian hormone, Hyperthyroidism and PCOS

تأثير هرمون مخزون المبيض (AMH) على فرط نشاط الغدة الدرقية مع وبدون متلازمة المبيض المتعدد الكيسات (PCOS) في المرضى الإناث

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الخلاصة

دراسة تأثير هرمون مخزون المبيض على مستويات الغدة الدرقية في المرضى الذين يعانون من وبدون متلازمة تكيس المبايض المتعدد الكيسات، وأظهرت النتائج زيادة في T3، T4، AMH مع زيادة في العمر بينما انخفاض في BMI، TSH مع زيادة في العمر مقارنة مع مجموعة صحية في فرط نشاط الغدة الدرقية مع مرضى متلازمة تكيس المبايض. خلاف ذلك زيادة في BMI، TSH، T3، T4 وAMH مع زيادة العمر مقارنة مع مجموعة صحية في فرط نشاط الغدة الدرقية دون متلازمة تكيس المبايض، وتأثير هرمونات المبيض (AMH) على مستويات الغدة الدرقية والاضطرابات من حيث الزيادة في الوزن (السمنة) وكذلك الخصوبة لدى النساء. في هذا البحث تم تقييم مصل هرمون مخزون المبيض (AMH) باستخدام مجموعة مناعية مرتبطة بالإنزيم [Elisa] في حين تم تحديد هرمونات الغدة الدرقية ثلاثي يودوثيرونين (T3)، ثيروكسين (T4) والهرمون المحفز للغدة (TSH) بواسطة طريقة VIDAS.

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Introduction

Anti-Mullerian hormone (AMH) is a dimeric glycoprotein belonging to the transforming growth factor-beta (TGF- β) super family, which acts on tissue growth and differentiation. It is composed of two 55KDa N-terminal and two 12.5KDa C-terminal homodimers, non-covalently linked by disulfide bridges [1]. Recent study have shown that the AMH C-terminal homodimer is much less active than the noncovalent complex, but almost all activity can be restored by associating with the N-terminal pro-region, which reforms a complex with the mature C-terminal homodimer. This finding raises the possibility that the AMH noncovalent complex is the active form of protein. It was reported that the cleaved AMH noncovalent complex binds to AMHRII and stimulates intracellular signaling, whereas full-length AMH shows only minimal activity [2]. In females, AMH is produced by the granulosa cells of small growing follicles from the 36 th week of gestation onwards until menopause when levels become undetectable. Potential clinical applications of low end anti-mullerian hormone (AMH) have been published in premature ovarian insufficiency, ovarian tumors, menopause and many more. AMH serum concentrations in females are thought to reflect the size of the ovarian follicle pool [3]. In general AMH production rate is considered to reflect the amount of growing follicles in ovaries and the reservoir of ovarian function in females [4]. Circulating AMH concentration predicts responsiveness to in vitro fertilization [5] decreases with aging [6]. AMH levels appear to remain constant throughout the menstrual cycle and thus can be reliably measured at any time unlike FSH, LH, estradiol and other hormone markers that must be measured in the early follicular phase. The VIDAS T4 assay aids in assessing thyroid function, which is characterized by increase in patients with hyperthyroidism [7]. Hyperthyroidism is a condition caused by unregulated production of thyroid hormones. Thyrotoxicosis is a serious sequela of hyperthyroidism that corresponds to an overt tissue exposure to excess circulating thyroid hormones [8], It is characterized by tremor, emotional instability, intolerance to heat, sinus tachycardia, marked chronotropic and ionotropic effects, increased cardiac output (increased susceptibility to congestive heart failure), hypertension, increased appetite and weight loss. It can be caused by thyroid hyperfunction, metabolic imbalance or extraglandular hormone production [9-11] .Since AMH levels reflect the number of developing follicles, their measurement may be used as a marker of ovarian follicle impairment in Polycystic ovary syndrome. PCOS is clinically diagnosed when at least two of the following three features are present : chronic oligo- or anovulation, biochemical hyperandrogenemia or hyperandrogenism and polycystic ovarian morphology in ultrasound examination (PCO) [12]. Polycystic ovary syndrome is also associated with metabolic aberrations. The incidence of metabolic syndrome is two to three – fold higher among women with PCOS compared to healthy women of similar age and body mass index (BMI), while 20% of women with PCOS, aged less than 20 years have already manifested the metabolic syndrome [13]. It is known that AMH levels decrease with age women with normal ovulatory cycles. A similar decline is observed in women with PCOS, but at a slower reduction rate [14]. Women with PCOS have an increased number of small follicles in the pre-antral and antral stage, and therefore it is observed that their AMH serum concentrations are higher than their counter part [15]. Not only is AMH elevated in women with PCOS but it also correlates with the severity of PCOS. It is not just the mere increase in the number of these follicles that produce raised AMH levels but it is also the individual's follicles from polycystic ovary that produces more AMH than their size – matched counterparts from a normal ovary [16].The study aimed to investigate the effect of Anti-Mullerian Hormone (AMH) on thyroid disorders in terms of increases and decreases and its impact on obesity, as well as fertility in women.

Material & methods

Patients:

The current study was applied on 150 female, the age range within 15-55 years ,selected sample of patients who attend the Endocrinology and Diabetes center Canadian hospital and AL-Yarmouk teaching hospital during the period from November -2016 till March -2017.All the patient's body max index [BMI] were measured. Serum Anti-Müllerian Hormone (AMH) was assessed using enzyme linked immunosorbent kit [Elisa] while Thyroid stimulating hormone (TSH), Triiodothyronine (T3), Thyroxin (T4) were determined by VIDAS kit method (enzyme linked fluorescent assay) .These patients were divided into three groups according to their hyperthyroidism with PCOS and without

PCOS group B and C respectively , each group contain 50 sample. In addition to fifty (50) apparently healthy matching the person were selected as a control group (group A).

Collection of blood specimens

Ten ml of venous blood sample was obtained from each female. The blood samples which were collected from all subjects were transferred into plain tube ,allowed to stand for 15 minutes at room temperature then centrifuged at 3000rpm for 5 minutes .The resulting serum was separated and frozen at -20 C till used for estimation of levels TSH ,T3 ,T4 and AMH.

Statistical analysis

The statistical analysis system SPSS version 20 (2012). T-test Chi- Square program used was to effect of difference factors in study parameters. In this study, correlation coefficient estimated between difference parameter[17].

Results & Discussion

.Results showed a non-significant increase was found in GC when comparing with group A in Age and BMI, while non-significant increase seen between GB in Age, non-significant decrease in BMI comparing with group A as shown in Tables- (1 and 2) and Figures- (1 and 2). Results revealed a significant $p \leq 0.05$ increase in T3 and T4 in GB and GC comparing to GA, but there are non-significant increase in GC, decrease in GB comparing to GA in TSH levels.. Results in Tables- (1 and 2) illustrated non-significant increase in AMH levels in GB and GC comparing to GA . Earlier data showed that in women with PCOS, serum and follicular AMH levels are higher than in healthy controls [18, 19]. Subsequent data confirmed this finding and indicated that the elevated levels of AMH were related to increased number of follicles with a diameter of 2-5mm in women with PCOS [20]. The main tool for detection of hyperthyroidism is measurement of the blood TSH level which is secreted by the pituitary gland. The measurement of TSH should result in low or undetectable levels in cases of hyperthyroidism. If the excessive amount of thyroid hormone is due to a TSH – secreting pituitary tumor, then the levels of TSH will be abnormally high. This uncommon disease is known as "secondary hyperthyroidism"[21]. In anovulatory women with PCOS, the follicular development is halted when follicular diameter is 6-9 mm, that is just before the selection of the dominant follicle [22]. In a large prospective study of adolescent population, although AMH serum levels were higher in adolescents with PCOS, the hormone was not proven to be a reliable predictor of PCOS [23]. In recent study it was found that AMH production per granulosa cell was increased by up to 75% in women with PCOS compared to controls [24] High AMH levels were observed in adolescent girls, aged 12-18 years, with polycystic ovary syndrome compared to controls [25]. In the study of Mehri et al AMH levels were evaluated in obese women of variable age before and after the performance of bariatric surgery [26]. Despite the small size of the sample, significant AMH reduction was found after the decrease of BMI in the group of young women but not in older age groups. AMH is produced by small growing follicles, from primary up to small antral follicles and, therefore, reflects what is called functional ovarian reserve (FOR) [27]. If thyroid function affects follicular growth and development, higher AMH concentrations should be observed in women with lower TSH levels independent of thyroid autoimmunity and female age. Furthermore, AMH levels are positively correlated with individual features of PCOS, mean ovarian volume and the number of ovarian follicles [28]. AMH could be used as a marker of ovarian aging given that the reduction in hormone levels reflects the age dependent fall in the follicular potential of the ovary. AMH concentration remains stable throughout the menstrual cycle and AMH levels decrease with age in women with normal ovulatory cycles. A higher AMH levels seen in normal-weight women with PCOS compared to obese women. AMH levels were lower in overweight and obese women with PCOS than in normal-weight women with the syndrome and healthy controls [29]. Female sufferings with PCOS have higher levels of AMH whether obese or lean as compared to a female with no PCOS [30].

Table 1- Levels of Age, BMI, TSH , T3, T4 and AMH hyperthyroidism with PCOS patients and control group.

Parameters	Group A (G _A)	Group B(G _B)	P-value
Age 15-55year	25.9±7.81	37.08±12.655	0.51
BMI Kg/m ²	28.29±6.18	27.39±5.71	0.72
TSH μIU/L	1.89±0.89	0.34±0.67	0.15
T3 nmol/L	2.09±0.304	4.95±1.905	0.005
T4 nmol/L	114.4±4.004	154.24±48.78	0.01
AMH ng/ml	7.422±2.508	12.85±2.264	0.84

Significant ($p \leq 0.05$), highly significant ($p \leq 0.01$), non-significant ($p \geq 0.05$).

Table 2- Levels of Age, BMI, TSH, T3, T4 and AMH hyperthyroidism without PCOS patients and control group.

Parameters	Group A (G _A)	Group C (G _C)	P-value
Age 15-55year	25.9±7.81	27±8.485	0.75
BMI Kg/m ²	28.29±6.18	30.09±6.88	0.621
TSH μIU/L	1.89±0.89	4.3±14.34	0.11
T3 nmol/L	2.09±0.304	3.717±1.84	0.001
T4 nmol/L	114.4±4.004	138±55.1	0.028
AMH ng/ml	7.422±2.508	7.85±1.74	0.39

Significant ($p \leq 0.05$), highly significant ($p \leq 0.01$), non-significant ($p \geq 0.05$).

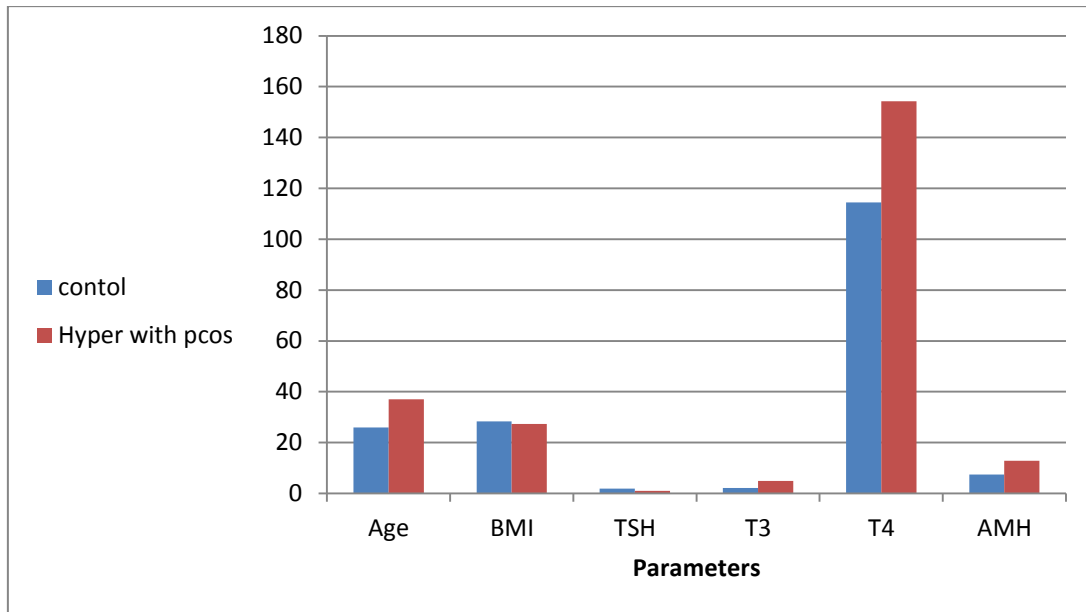


Figure 1- comparison between patient hyperthyroidism with PCOS and control group for Age, BMI,TSH,T3,T4 and AMH.

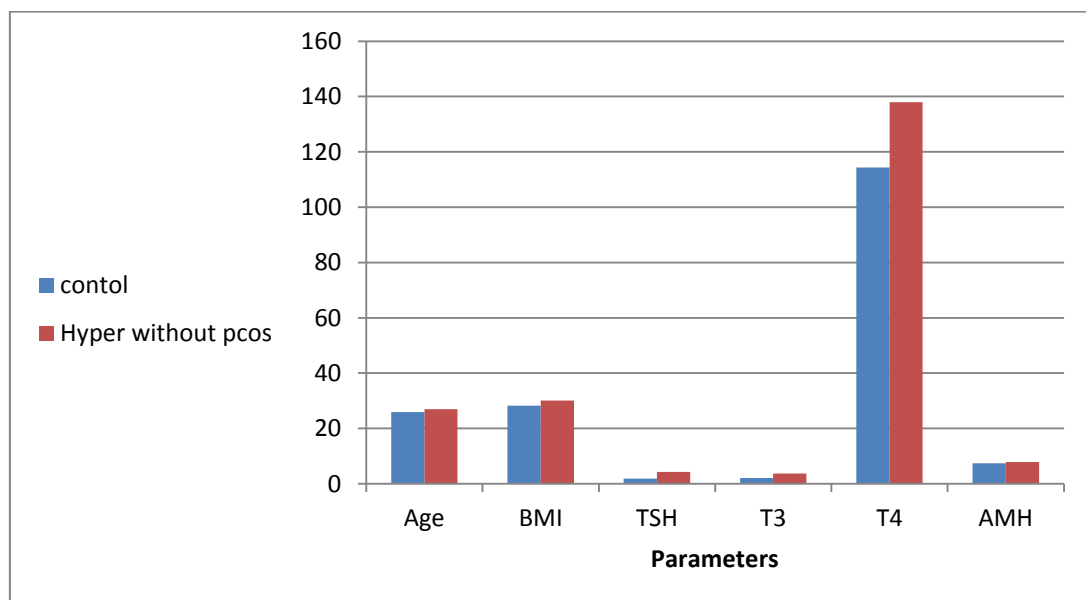


Figure 2- Comparison between hyperthyroidism without PCOS and control group for Age, BMI,TSH,T3,T4 and AMH.

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