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Thyroid Stimulating Hormone among Sudanese Women with Polycystic Ovary Syndrome, A pilot Study in Khartoum.

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Abstract
Infertility frequently present in both women with polycystic ovary syndrome (PCOS) and subjects with thyroid dysfunction. This study aimed to determine the variation of thyroid-stimulating hormone (TSH) level among PCOS patients. One hundred participants; fifty women were diagnosed as PCOS and 50 without P COS were enrolled in this cross-sectional comparative study, during the period from June to November 2019. Serum TSH, total triiodothyronine hormone (TT3) and total thyroxin hormone (TT4) levels were measured using enzyme-linked immunosorbent assay (Cobas-e-411), while anti mullerian hormone (AMH) was determined using ultrasensitive method by Electrochemiluminesent (ECL) immunoassay (Roche's e411), and results statistics were computed using SPSS 20. The mean age of PCOS group was (26.08 ±3.92) and non-PCOS group (25.8 ± 3.91) years. Bilateral cyst in the ovary and irregular menstrual cycle were predominant among PCOS women. A significant increased mean of TSH among PCOS women occur when compared to non-PCOS P.value <0.05. A significant positive correlation between TSH and body mass index (BMI) in PCOS women P. value <0.05, r= 0.3. In conclusion study results revealed that PCOS status was associated with increased TSH level that considered an indicator to subclinical hypothyroidism among Sudanese women with PCOS.

Keywords: PCOS, TSH, BMI, TT3, TT4, AMH.

المستخلص

العقم موجود بشكل متكرر في كل من النساء المصابات بمتلازمة تكيس المبايض والأشخاص الذين يعانون من أختلال نشاط الغدة الدرقية. هدفت هذه الدراسة إلى تحديد تباين مستوى الهرمون المنشط للغدة الدرقية (TSH) بين مرضى متلازمة تكيس المبايض. تم تسجيل 100 مشارك ؛ خمسون امراءه تم تشخيصهم بالاصابه بمتلازمه التكيس وخمسون ليس لديهم المتلازمه لهذه الدراسه المقارنة المقطعية. تم قياس مستويات TSH وهرمون ثلاثي يودوثيرونين الكلي (TT3) ومستويات هرمون التيروكسين الكلي (TT4) في مصل الدم باستخدام مقايسة الممتز المناعي المرتبط بالإنزيم (Cobas−e−411) ،

بينما تم قياس هرمون مولر المضاد (AMH) باستخدام طريقة فائقة الحساسية بواسطة (ECL) Electrochemiluminesent

تم حساب المقايسة المناعية (Roche's e411) وإحصاءات النتائج باستخدام برنامج SPSS . كان متوسط عمر المشاركين

(26.08 ± 3.92) سنة لمجموعة متلازمة تكيس المبايض والمجموعة غير المصابة بمتلازمة تكيس المبايض (25.8 ±

3.91) سنة. ان الكيسات الثنائية في المبيض والدورة الشهرية غير المنتظمة سائدة بين النساء المصابات بالمتلازمة. ان

هنالك زيادة ذات دلاله احصائيه في متوسط هرمون TSH بين النساء المصابات بمتلازمة تكيس المبايض عند مقارنتها بغير

المصابات بالمتلازمة تكيس المبايض P <0.05 . ان هنالك علاقة ارتباط موجبة معنوية بين TSH ومؤشر كتلة الجسم

(BMI)عند النساء المصابات بالمتلازمة.

الخاتمة: ان مرض متلازمة تكيس المبايض مرتبطة بزيادة مستوى الهرمون المحفز للدرقية الذي يعتبر مؤشراً على قصور

الغدة الدرقية تحت الإكلينيكي بين النساء السودانيات المصابات بالمتلازمة.

Introduction

Polycystic ovary syndrome (PCOS) is the most common female endocrinopathy. The global prevalence of PCOS among women is 25% (Helen., 2017). It is characterized by hyperandrogenism /hirsutism, oligo or amenorrhea, and polycystic ovaries (PCO). PCOS is also a heterogeneous disorder that affects many body functions, resulting in several health complications, including infertility and menstrual dysfunction (Cai et al., 2019).

Thyroid hormone disorders or thyroid autoimmunity is associated with increased risk of infertile, spontaneous miscarriage, preterm delivery, and metabolic dysfunctions, which is also commonly observed in PCOS (Thangaratinam et al.2011,Vissenberg et al., 2015). In PCOS population, the prevalence of subclinical hypothyroidism (SCH) and thyroid autoimmunity are reported higher than that for women in general (Cooper and Biondi 2012).

Sub-clinical hypothyroidism (SCH) is observed in PCOS women and has been found to be associated with hyperlipidemia and affect pregnancy rate in both PCOS and general population (Benetti-Pinto et al.,2013.

Huang et al., 2014). Bakker et al. reported serum thyroid stimulating hormone (TSH) value is associated with a higher risk for dyslipidemia and severe cardiovascular risk factors (Bakker et al., 2001).

Thyroid hormones not only plays an important role in regulating metabolism but also in reproductive health (Cai et al., 2019). Both thyroid receptor and TSH receptor are expressed in ovary, uterus and widely expressed in the feto-maternal unit during implantation (Escobar-Morreale., 2018). Deficiency of thyroid hormones may affect gonadal function and fertility, leading to delayed puberty onset and an-ovulatory cycles (Colicchia et al., 2014). TSH has been described as the most sensitive parameters for detecting minor degrees of primary thyroid hormone deficiency (Alexander et al., 2017).

Serum anti- mullerian hormone (AMH) concentration is higher in women with PCOS and correlates with the number of 2–6 mm antral follicles observed by trans-vaginal ultrasound of the ovaries (Pigny et al., 2003. Dewailly et al 2011). It has been proposed as a more sensitive and specific marker of antral follicle count (AFC) than ultrasound (Dewailly et al., 2011). Additionally, serum

AMH concentration is related to the severity of hyperandrogenism and oligoan-ovulation in PCOS (Piouka., 2009). The study aimed to investigate the differences in serum TSH and thyroid hormones among newly diagnosed females with PCOS which can be used with AMH as a biochemical profile in the diagnosis of infertility among females in reproductive age.

Materials and Methods

This a cross-sectional comparative hospital-based study approved by the clinical chemistry department scientific committee in Sudan University of Science and Technology. After obtaining informed consent, a total of 100 females were randomly selected from Dr. Alsir Abu-alhassan Fertility Center. Clinical diagnosis of PCOS based on fertility hormonal profile and ultrasound and confirmed by Anti-mullrien hormone above 4ng/ml. Blood samples were collected from 50 women with PCOS, and 50 age and sex –matched non PCOS women. Women who used steroids drug, contraceptive pills, pregnancy, hyperthyroidism, or had hypothyroidism, neoplasia of thyroid or adrenal gland were excluded from this study.

Anthropometric measurements, including height and weight, were taken using standard protocols. BMI was calculated as weight (in kilograms) divided by height (in meters squared). Waist circumference was taken as the minimum circumference at the umbilicus level, and hip circumference as the maximum circumference around the buttocks. Waist to hip ratio (WHR) was calculated as waist circumference divided by hip circumference.

Serum TSH (Wu., 2006), TT3 and TT4 (Kronenberg *et al.,* 2011) levels were measured using enzyme-linked immunosorbent assay (Cobas-e-411), while the anti mullerian hormone was determined using ultrasensitive method (Burtis et al., 2008) by Electrochemiluminesent (ECL) immunoassay (Roche's e411).

Statistical analysis of the data was performed using the SPSS version 20 program to the arithmetic mean, standard deviation, *t*-test, and Pearson's test of correlation. The level of confidence (P<0.05) was considered as a cutoff value for significance.

Results

The mean age of participants was 26.08 ±3.92 years for PCOS group and 25.8 ± 3.91 years non-PCOS group.

Table1: In PCOS group 42 (84%) out of 50 women had a bilateral cyst, 36% had an irregular menstrual cycle, and 17% were overweight and 21% obese.

Table 2: shows the statistics of measured TSH,TT3,TT4 and AMH parameters computed for PCO and non-PCO women, which indicate that results were found to be significantly increased for TSH, AMH respectively P<0.05, while insignificant change in means of TT3, and TT4 P >0.05.

Table 3: shows that among PCOS women there was 9% (9/50) had elevate in serum TSH level (upper the reference value (normal (0.4 to 4 mU/L), 13% decreased in TT3level, and 19% decreased in TT4level,while in non-PCOS group all the participant had normal TSH level.

Figure1: shows Pearson's correlation results, which reflect statistically significant, positive correlation between the TSH and BMI.

Table 1: shows the frequency of cyst site in the ovary, regulation of menstrual cycle and BMI in the study group.

Variables& parameters	Frequency (Percentage)	
	non-PCOS women n= 50	PCOS women n= 50
Site of cyst:		
bilateral	00 (0%)	42 (84%)
unilateral	00 (0%)	08 (16%)
Menstrual cycle:		
regular	44 (44%)	14 (14%)
irregular	06 (6%)	36 (36 %)
Family history of PCOS		
Yes	18 (18%)	45 (45%)
No	38 (38%)	05 (05%)
BMI (Kg/m^2):		
Normal weight (18.5 – 25)	40 (40%)	12 (12%)
Overweight (25.1 – 29.9)	10 (10%)	17 (17%)
Obese (≥ 30)	00 (0%)	21 (21%)

Table 2: Comparison between age, BMI, TSH,TT3,TT4 and AMH levels in PCOS and non-PCOS women.

Variables& parameters	mean± SD		P value
	Non-PCOS women	PCOS women	
Age/ year	25.8 ± 3.91	26.08 ±3.92	0.700
BMI kg/m^2	23.8 ± 2.34	29.26 ± 7.30	0.000
TSH mIU/L	2.09 ± 0.8	2.80 ±2.10	0.030*
TT3 ng/dL	95.94±22.07	95.34 ± 22.07	0.917
TT4µg/dL	1.57 ± 0.743	1.69 ±0.70	0.377
AMH (ng/ml)	2.40 ± 1.0	14.11 ± 9.2	0.000*

PCOS, polycystic ovarian syndrome; BMI, body mass index; TSH, thyroid-stimulating   hormone; TT3, total triiodothyronine hormone; TT4, total thyroxin hormone; AMH, Anti-Mullerian hormone.

Table 3: Distribution of TSH, TT3 and TT4 hormones level among the study group according to the reference range

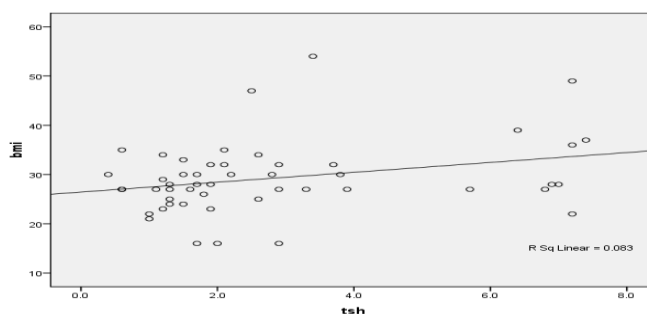| Variable	Frequency (%)	
	PCOS group	Non-PCOS group
TSH level (0.4-4mIU/L)		
Normal	41 (41%)	50 (50%)
Decreased	00 (0%)	00 (0%)
Elevated	09 (9%)	00 (0%)
TT3 level (6-12 µg/dL)		
Normal	37 (37%)	43 (43%)
Decreased	13 (13%)	07 (7%)
Elevated	00 (0%)	00 (0%)
TT4 (70–204 ng/dL)		
Normal	31 (31%)	50 (50%)
Decreased	19 (19%)	00 (0%)
Elevated	00 (0%)	00 (0%)

Figure 1: positive significant correlation between TSH (**U/L**) level and BMI (kg/m^2) r= 0.289, P=0.042.

Discussion

PCOS and thyroid disorders are two of the most common endocrine disorders in women, they cause infertility in females amid the reproductive age. Thyroid disease and PCOS are interconnected by both genetic and environmental factors which are believed to be contributing to thyroid disorders in PCOS and known to cause PCOS-like ovaries and overall worsening of PCOS and insulin resistance.

This study revealed that there was a significant increase in BMI among PCOS women, 21 out of 50 were obese, this agrees with a previous study (Kumar et al.,2016. Bjorntorp.,1992). Obesity, mainly central obesity, is present in varying degrees 30-70% in women with PCOS (Bjorntorp.,1992. Azziz *et al.,*2001). Central obesity, being a prominent feature of the so-called metabolic syndrome, is directly linked to increased peripheral insulin resistance (Azziz et al.,2001) . It has been shown that insulin resistance is responsible for the development of polycystic ovaries in PCOS women although obesity seems to be the major cause (Azziz *et al.*,2001) .

In this study, there were 9 out of 50 PCOS patients with elevated TSH levels, 41 patients reported TSH levels in the normal range, this agreed with previous studies by previous study (Eldar-Geva et al., 2007. Yasmin et al.,2008. Anwary *et al.,* 2013). Hypothyroidism is the disease state caused by insufficient production of thyroid hormone by the thyroid gland. Some authors have declared that insulin resistance and increased androgen production can cause hypothyroidism. Insulin resistance has also been considered to be the principal factor in the genesis of PCOS (Eldar-Geva et al., 2007).

Conclusion

The study conclude that most women with PCOS had some degree of thyroid dysfunction, especially subclinical hypothyroidism. Hence we recommend screening of PCOS for TSH and thyroid hormones which will help in the management and treatment of PCOS for a better outcome.

Limitation

A small sample size is an evident limitation of this study which is due to the limited availability of data within the short duration of the study.

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Conflicts of Interest: The authors declare no conflicts of interest regarding the publication of this paper.

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