# Effect of Thyroid Disorder in Polycystic Ovarian Syndrome in the Women of Diyala Province

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## Abstract

Polycystic ovarian syndrome (PCOS) is the most endocrine disorder common effect (5-10) % in women at reproductive age. Thyroid dysfunction with PCOS is both representing parts of the endocrine system; this link leads to problems of ovulation and pregnancy. **Aims**: to investigate the prevalence of thyroid disorder in PCOS woman, and associate the outcome with obesity. This study was conducted in Al-batol Teaching Hospital in Baquba City /Iraq. The results reviewed included 63 women: 45 PCOS were diagnosed on the basis of Rotterdam criteria, 18 as control, aged 17- 44 year. The samples have been collected at second day of menstrual cycle, to test fT3, fT4, fTSH in serum. Information was collected for (Age, BMI, LH, and FSH) to be part of this study. A significant increasing in fT3 was found in PCOS women comparison with control pvalue<0.05. T3 showed in significant differences between lean PCOS matched against control Pvalue > 0.05, along with statistically increasing of TSH level in (lean, overweight) PCOS comparison with control pvalue<0.05. **Conclusion**: PCOS is associated with hypothyroidism. Obesity or overweight is a key factor leads to increased risk of thyroid disorder.

**Keywords:** Polycystic ovary syndrome**,** BMI, Thyroid function, hypothyroidism.

# Introduction

Polycystic ovary syndrome (PCOS), is one of the most common endocrine disorders which female suffers from, many researches have shown that the proportion of women with PCOS, ranging from 5% to 10% of reproductive age [1]. PCOS can be diagnosed through Rotterdam criteria 2004: chronic oligo and / or anovulation, biochemistry test, including increased secretion of androgens and/ or detected by ultrasound waves [2]. On the other hand Diagnosis is made too by the external appearance through the emergence of gain weight, patches darker skin, facial hair, acne and difficulty getting pregnant [3]. There is a special relationship between PCOS and auto-immune thyroiditis (AIT) in many findings [4]. The thyroid gland is a butterfly-shaped organ located in the base of the neck. It releases hormones that control metabolism and evolution [5]. Chronic autoimmune thyroiditis (AIT) or know Hashimotos thyroiditis: Is a more popular disease because of hypothyroidism in parts that do not suffer from iodine deficiency, it is identified by apoptosis of thyroid, produced from the failure in the synthesis of hormones, which regulate vital body functions [6]. Disorder system of the thyroid gland is more common in women more than men; there is a special relationship between hypothyroidism and PCOS [7]. A rise of ovarian size and appearance of cyst on the ovary are initial signs of hypothyroidism [8]. Initially Hypothyroidism is a deficiency in the secretion of thyroid hormone, associated with elevation of Thyrotrophic- releasing hormone (TRH) that will increase the concentration of TSH [9]. All of that produce disorder in Gynecological Profile. Furthermore, increasing level of prolactin participate in forming of polycystic ovaries, has a specific role in preventing ovulation resulting from the change in the proportion of Follicle stimulating hormone (FSH) and luteinizing hormone (LH) [10].

# Materials and methods

This study was carried out in Al-Batol Teaching Hospital in Baquba City /Iraq. The duration of this study was from September 2016 to April 2017, including 63 women divided into two groups: 18 female without PCOS as control were matched to another 45 women selected with PCOS, the diagnosis was based on at least 2 of 3 Rotterdam criteria 2004 [11] at reproductive age, which are:

1- Oligo and /or anovulation

As known as presence of menstrual dysfunction meaning:

a) They had not any menstrual bleeding for last 3 months

b) And /or had six cycles over more than 35 days [12].

2- Hyperandrogenism by clinical and /or biochemistry.

3- Polycystic ovaries on ultrasound

All subjects were within (17- 44) year age. Approximately (5) ml of blood was collected from Venipuncture by disposable syringe, after overnight fasting at second day in period (Follicular phase), then dispensed into plane tube and left for one hour to separate the serum by 300 rpm centrifuge for 10 minutes then was left for freezing (-20 $C^0$) for 30 day to estimate Thyroid profile: Thyroid stimulation hormone (TSH), Triiodothyronine (fT3), Thyroxine (fT4) by ELIZA method, using commercially available Kit from D-65205 Wiesbaden – Germany.

Body Mass index was calculated for each woman by an equation which divided body weight (Kg unit) by the square of the height ($m^2$ unit) according to the European Society of Human Reproduction and Embryology, 2009, BMI divided into three groups: normal weight (18.5- 24.9) $Kg/m^2$, overweight (25- 29.9) $Kg/m^2$, obesity (≤30) $Kg/m^2$. In this study PCOS were divided as normal (<25 $Kg/m^2$), and obese (≤25 $Kg/m^2$) [13]. Excluded from this study woman whom: (1) younger than 17 years (2) elder than 45 year (3) lactating or pregnant

woman (4) taking contraceptive pills (5) suffering Thyroid disorder and problems with blood pressure.

### Statistical analysis

The Statistical Package for Social Sciences (SPSS) software, version 20 was applied to analyze all our data. Expression of data was by (mean $\pm$ standard error). For comparison of Thyroid functions and finds the statistical differences between two groups using Student's t-test. While one-way analysis of variance (ANOVA) was performed to test the differences among three groups. Considered P value < 0.05 was a standard of significant.

## Result and discussion

As shown in table (1) this study was based on many variables, such as (Age, BMI, LH/FSH, LH, and FSH). The samples, 63 donor women, were divided based on the number and proportion. The donor women included (45 PCOS woman, 18 as a control), their ages were ranging from (17- 44) years old. The results indicated that 48.5% of women with PCOS was in the age group under 25 year, 26.7% in group 25-32 year, and only 24.8% in aged 32-44 year.

This work showed that more than two thirds of women, who are suffering from PCOS were less than 32 year, as shown table (1), the majority of PCOS reports referred to prevalence of this phenomenon in young women with ages less than 35 year, these results agree with Rita K (2001) who emphasized that decreasing physiological efficacy of the ovarian follicles leading to tendency of ovary to return to its normality with age. Where, low secretion LH associated with declining number of ovarian follicles at progression age of the normogonadotropic in anovulation infertile women [14]. In addition Hyperandrogenism is a pre-eminent factor in women who are suffering from disorder of the menstrual cycle. Many research pointed to declining of level testosterone in middle age (more than 25 year) in PCOS woman and this declining of androgen level is one of the reasons that regulate the menstrual cycle in PCOS woman when become growing old [15].

The results showed that 20% of women with PCOS have a fatty body, their BMI were ($\geq$30) Kg/M$^2$, (WHO Expert Consultation, 2004) this observation agrees with [16]. The greatest proportion of PCOS women (more than half (55.5%), 25 out of 45 were suffering from overweight (>25<30) (conventional criteria for overweight). Whereas, only 11 out of 45 PCOS woman (24.5%) have less than (25 Kg/M$^2$), the high of BMI value affect metabolism and become more disorder than in those who have normal weight which in turn increase the insulin resistance, consequently, lead to hyperandrogenism. However, the BMI varies according to the ethnic as pointed by several researches [17] who are originally from Shanghai but live currently in New York have low BMI, these individuals seem to have increasing level of body fat more than white population who have same sex and age. On the other hand, the results showed that most of woman in the control group (66.6%) were within healthy scale (18-24.9) Kg/M$^2$, while the remaining percentage revealed a rise in BMI due to lack in exercise and/or as wrong lifestyle.

Also table (1) showed that women with PCOS have a raised ratio of LH/FSH. The raising of ratio may be a result of disorder in the secretion for both (LH, FSH) in PCOS which is a heterogeneous turbulence in gonadotropin profile at reproductive age [18].

The present study showed that 23 out of 45 PCOS (51.2%) suffering from hyper production of LH (> 10 mlU/ml) while the most of healthy women (17 from 18, 94.5%) have normal secretion of LH (<10 mlU/ml). This agreed with (19) who indicates the formation of ovary poly bag related to raise secretion of (LH), this deals with the current result. Furthermore, decreasing level of FSH will lead to high ratio of LH/ FSH among 75.5 PCOS woman

(Basically this ratio is considered an essentially standard for diagnosis PCOS). The FSH level was normal in 61.2 % of control; Secretion of progesterone by corpus luteum can help to regulate the concentration of LH versus elevation level of FSH which has an important role to mature of follicles for next bleeding [20]. In contrast PCOS woman, abnormality of LH associated with less response for progesterone and defect in the frequency of FSH, this leads to a high ratio of LH/FSH. Consequently, ratio LH/FSH increases in women with PCOS 0%, 55.5%, 44.5%, respectively which approach with [21], compared with a women in control group as the ratio of LH/FSH was (<1) in all individuals of control , as shown in table (1).

**Table (1): Distribution of study group by (number, proportion)**

| Variable | Patient | | Control | |
|---|---|---|---|---|
| **Total 63** | **Total 45** | **Percentage %** | **Total 18** | **Percentage %** |
| **Age** | | | | |
| (17- 25) year | 22 | 48.5% | 7 | 38.8% |
| (25-32) year | 12 | 26.7% | 4 | 22.3% |
| (32-44) year | 11 | 24.8% | 7 | 38,9% |
| **BMI** | | | | |
| Normal (18- 24.9)Kg/$M^2$ | 11 | 24.5% | 12 | 66.6% |
| Overweight(25-29.9) Kg/$M^2$ | 25 | 55.5% | 6 | 33.4% |
| Obese(<30)Kg/$M^2$ | 9 | 20% | - | - |
| **LH/FSH** | | | | |
| Control <1 | - | - | 18 | 100% |
| Normal >1 | 25 | 55.5% | - | - |
| Abnormal >2 | 20 | 44.5% | - | - |
| **LH** | | | | |
| Normal> 10 mlU/ml | 22 | 48.8% | 17 | 94.5% |
| Hyper <10 mlU/ml | 23 | 51.2% | 1 | 5.5% |
| **FSH** | | | | |
| Normal > 7 mlU/ml | 34 | 75.5% | 11 | 61.2% |
| Hyper <7 mlU/ml | 11 | 24.5% | 7 | 38.8% |

During follow-up for all subjects, several differences were found in Thyroid gland function between PCOS and control women. Table (2) recorded a statistically significant increase (P value < 0.05) in $T_3$ concentration (2.422 $\pm$ 0.104) in PCOS woman when compared with control (2.005 $\pm$ 0.064). The results also showed non-significant differences (P value > 0.05) in $T_4$ concentration between PCOS and control women (112.236 $\pm$ 2.448, 105.938+_3.578) respectively. Table (2) showed a rising in TSH concentration in PCOS woman (2.826 $\pm$0.340) when compared with control (1.7817 $\pm$ 0.129) but, this increasing wasn't within the limit of significance, (P value = 0.61).

Both of the thyroid gland and the ovary are part of the endocrine system, most of the cases that suffering from thyroid disorder (hypothyroidism). Mostly of women with PCOS are to get hypothyroidism [22] this may be due to insufficient secretion of thyroid hormone resulting from dysfunction of hypothalamic-pituitary ovarian axis [23] which agrees with present work. A disorder of the thyroid gland system leads to decrease in sex binding globulin hormone (SBGH) which in turn increases the testosterone also, non-regularity of menstrual cycle helps to impair ovulation and increase the chance of abortions [24].

Free tri iodothyronine (fT3) exist in follicular fluid [25] in addition to TSH has an important role with its receptor (TRα1, TRα2, TRβ1, and TRβ2 mRNA) to change of ovarian shape,

such as oocytes, cumulus. Furthermore the placenta has transporter membrane for thyroxin (T4) and triiodothyronine (T3) which arrange the performance of thyroid hormone in placenta. There are other processes participated in releasing of thyroid hormone like evolution, growth, metabolism of the body and menstrual irregularities [26] TSH is divided into two types: thyroxin (T4) and the main portion is triiodothyronine (T3) which has more influence. This fact enhances the absence of statistically differences of (fT4), where T4 suffering to change to T3 by thyroglobulin (TG) remove one iodine atom from T4, this catalyze is done by deiodenase I, II in body [27].

**Table (2): The level of thyroid hormone and TSH in patients and healthy controls**

| Groups | T3( Mean ± SE) nmol/L | T4( Mean ± SE) nmol/L | TSH ( Mean ± SE) µU/ml | LH/FSH( Mean ± SE) |
|---|---|---|---|---|
| Patient | 2.422 ±0.104 | 112.236 ± 2.448 | 2.826 ±0.340 | 2.288 ± 0.194 |
| Control | 2.005 ± 0.064 | 105.938 ± 3.578 | 1.7817 ±0.129 | 0.649 ± 0.364 |
| P value | P value< 0.05 | P value > 0.05 | P value > 0.05 | P value<0,001 |

**P value < 0.05 considering statistically significant

In table (3), the women with PCOS were further classified depending on BMI into two groups (A): Normal weight PCOS (18 -24.9) Kg/m$^2$ and (B): overweight PCOS (≥25) Kg/m$^2$. The purpose of this classification is to find the differences of thyroid function between (normal, overweight) PCOS women and the control (C). This result showed slight increase of T3 value (P value > 0.05) between (A), (B) (2.356+_0.220) (2.444_+0.120) respectively, which tends to increase statistically significant when comparing group (B) with (C) (2.005+_0.064, P value < 0.05). Increase significantly TSH for both (A), (B) (2.697 +_0.402) (2.868 +_0.433) respectively when compared with (C) (1.7817+-0.129) P value < 0.05. From these results, it was concluded that no statistical differences in T4 among groups: (A) (114.029_+5.822), (B) (111.657 +_2.685) and (C) (105.938 +_3.578). These results deal with (Wunder et al 2008). In this study, it was shown increasing of TSH concentration in PCOS women compared with control refers to diagnosis of hypothyroidism. The serious hypothyroidism in turn leads to increase ovary size and/or generation of cysts. The thyroid hormones take part in regulating the metabolic system, thermogenesis and lipid metabolism [28]. BMI and PCOS have a specific role in ovarian activity. Overactive ovaries leads to the accumulation of oocytes, which indicate increase probability of PCOS with overweight woman, this obesity and excess weight, occur as a result of change of metabolism which can lead to involution [29]. Obesity linked to insulin resistance (IR) [30] and estradiol (E2) in fatty tissue inhibits the secretion of FSH making obesity pathological factor [31].

**Table (3): Mean distribution of thyroid hormone and TSH concentration in the studied groups (dividing them according to BMI)**

| Cases | T3 | T4 | TSH |
|---|---|---|---|
| PCOS Normal BMI **(A)** | 2.356 ±0.220 | 114.029 ±5.822 | 2.697 ±0.402 |
| PCOS Overweight **(B)** | 2.444 ±0.120 | 111.657 ±2.685 | 2.868 ±0.433 |
| Control **(C)** | 2.005 ± 0.064 | 105.938 ±3.578 | 1.7817 ±0.129 |
| P value( Significant) | B,C | N.S | A,C and B,C |

**P value < 0.05 considering statistically significant, (B, C) = Significant differences Pvalue <0.05 between overweight PCOS and control, (A, C) = Significant differences Pvalue <0.05 between lean PCOS and control, (B, C)= Significant differences Pvalue <0.05 between overweight PCOS and control. N.S= there are no significant differences

## Conclusion

Most cases of polycystic ovaries are accompanied by disorder in the functions of thyroid gland, spatially hypothyroidism which is associated with increase the size of the ovary or formation of oocytes, PCOS be more influential in younger in women less than 25 year. Moreover continually monitoring for all thyroid profile even TSH within normal range. Weight gain causes disorders in hormonal distribution correctly; obesity may be key factor for disturbance thyroid function. We need more investigation to get results about causes of PCOS.

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