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Original Research Article

Impact of Metformin on Blood Levels of Thyroid Function Tests, and Some Biochemical Parameters Levels in Polycystic Ovarian Women

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Abstract: Polycystic ovary syndrome (PCOS) is the most common form of chronic female disease associated with androgen excess; perhaps occurring in 5-10% of the reproductive age group in women. PCOS is viewed as a heterogeneous disorder of multifactorial etiology. It is also associated with increased metabolic and cardiovascular risk factors. ***Objectives:*** The purpose of this study is to evaluate the serum level of hormones TSH, T3 and T4 in women with PCOS and to investigate the effect of metformin on hormones TSH, T3, and T4 levels in subjects with PCOS. ***Patients and methods:*** The present study was conducted at Kirkuk General Hospital and Azadi General Hospital from March 2023 to January 2024.One hundred forty-one women with PCOS were selected as the PCOS group, while 120 healthy women matched for age with the PCOS patients were selected as the control group. The body mass index is determined before and after therapy. They take metformin 850 mg twice daily for three months and provide fasting blood samples on the second day of menstruation before and after treatment. The data collection done through a designed closed and open-ended questionnaire, by using direct interviewing, and Ultrasound examination, Data were analyzed using SPSS for Windows 7. ***Results:*** Treatment resulted in a significant decrease in in body mass index at p-values 0.05. This study reveals that the thyroid hormones TSH, T3 and T4 were highly significantly increased ($P < 0.001$) in the serum of PCOS patients compared to the control group. Serum levels of TSH in women with PCOS were high significantly elevated compared to healthy control group. However, the study found no significant difference ($p > 0.05$) in TSH level in treated group with metformin compared with pre-treatment. ***Conclusion:*** Metformin can induce changes of TSH levels in patients with polycystic ovary syndrome.

Keywords: Metformin; PCOS; TSH; T3 and T4.

INTRODUCTION

Thyroid disorder is a common endocrine disorder in women of reproductive age, the most prevalent cause of thyroid dysfunction is thyroid autoimmunity. the regulation of thyroid hormone synthesis and thyroid hormone release to the circulation are driven by the pituitary-gland-derived TSH in a classical negative feedback loop. This explains why hypothyroidism in the presence of a functional hypothalamic–pituitary axis results in increased TSH levels while the reverse occurs in hyperthyroidism [1]. The human thyroid predominantly produces the biologically inactive prohormone thyroxine (tetraiodotyrosine, T4) and only a small amount of the bioactive hormone triiodothyronine (T3). Less than 0.1% of the total amount of circulating thyroid hormone (T4 and T3) is in the free or unbound form that can be transferred across the plasma membrane into a target cell. It was long thought that thyroid hormones diffuse passively across plasma membranes [2]. The intracellular availability of the biologically active thyroid hormone T3 is the net result of a finely tuned system of three distinct iodothyronine deiodinases with tissue-specific expression that are responsible for thyroid hormone outer ring (type I and II) and inner ring (type I and III) deiodination [3]. DIO1 and DIO2 can convert inactive T4 to biologically active T3, whereas both DIO1 and DIO3 are able to inactivate T3. Biologically active T3 finally enters the nucleus and exerts its function through the nuclear thyroid hormone receptors (THR), thyroid hormone receptor alpha (THRA) and beta (THRB) that are expressed in a tissue-specific manner. Since their initial identification, (THRs) have

evolved into central players in a complex system of co-activators and co-repressors [4]. Both hypothyroidism and hyperthyroidism have been associated with altered ovarian function, menstrual irregularities, subfertility and higher (recurrent) miscarriage rates, and thyroid hormone affects female reproductive organs. Thyroid disorders and polycystic ovary syndrome (PCOS) are two of the most common endocrine disorders in. Although the etiopathogenesis of hypothyroidism and PCOS is completely different, these two entities have many features in common. An increase in ovarian volume and cystic changes in ovaries have been reported in primary hypothyroidism. In the other direction, it is increasingly realized that thyroid disorders are more common in women with PCOS as compared to the normal population whether this is due to some common factors predisposing an individual to both disorders, or due to polycystic ovary syndrome (PCOS) and thyroid disorders and are two of the most common endocrine disorders in the women. Although the etiopathogenesis of PCOS and hypothyroidism is completely different, these two entities have many features in common [5,6]. An increase in ovarian volume and cystic changes in ovaries have been reported in primary hypothyroidism. In the other direction, it is increasingly realized that thyroid disorders are more common in women with PCOS as compared to the normal population. Whether this is due to some common factors due to a pathophysiological connection between the two disorders has not been established until now. The purpose of descriptive and exploratory review is to explore the relationship between these two disorders. To generate a hypothesis linking these disorders, terms "PCOS," "autoimmunity," "subclinical hypothyroidism," "thyroid autoimmunity," thyroid autoantibodies, obesity and thyroiditis, [7]. In hypothyroidism the presence of hypothyroidism, ovarian morphology becomes poly-cystic. Hence, thyroid disorders are one of the exclusion criteria before making a diagnosis of PCOS in any women. Rise in thyrotropin-releasing hormone (TRH) in primary hypothyroidism leads to increased prolactin and thyroid stimulating hormone (TSH). Prolactin contributes toward polycystic ovarian morphology by inhibiting ovulation as a result of the change in the ratio of follicle stimulating hormone (FSH) and luteinizing hormone and increased dehydroepiandrosterone from the adrenal gland. Increased TSH also contributes due to its spill-over effect on FSH receptors. Increased collagen deposition in ovaries as a result of hypothyroidism has also been suggested [7-8].

MATERIALS AND METHODS

Study Design

This cross-sectional study, used for investigation of some biochemical marker in patients with PCOS before and after metformin treatment.

Study Population

The present study was conducted at Kirkuk General Hospital and Azadi General Hospital from March 2023 to January 2024, with One hundred forty-one patients newly diagnosed PCOS women, complete the follow-up study and agreed to continue on metformin treatment during three months, the duration of the follow-up.

In addition, a group of One hundred twenty healthy women without PCOS matching in the mean age and BMI to the PCOS women were also recruited in the study as a control group, and their ages between 16-40 years old.

The diagnosis of PCOS was made according to the Rotterdam criteria. Specifically, patients with anovulation and clinical and/or biochemical hyperandrogenism were enrolled.

After their visit to the gynecologist physicians and diagnosed according to their symptoms and signs and to the picture of ovarian ultrasound, their weight and height are measured, and other related information such as age, duration of infertility, number of children.

Treatment

All patients received metformin (Glucophage) at a dosage of 850 mg daily for 3 months. In addition, standard clinical evaluations and laboratory analyses were performed at baseline and after 3 months of treatment as safety measures. After the treatment period, in each patient, all of the above parameters were reevaluated as at baseline.

Inclusion Criteria

1. Women newly Diagnosed with PCOS according to modified Rotterdam criteria which include:
   a. The presence of clinical and/or biochemical signs of hyperandrogenism; and
   b. At least one of the following: oligo- or anovulation and/or polycystic ovaries, depending on ultrasound examination, clinical features and laboratory hormonal tests by specialist gynecologist.
2. The women with PCOS were given metformin drug 850 mg daily during the meal for three months. The changes in clinical and biochemical parameters were measured (before treatment) and then after three months of treatment with above mention drugs.

Exclusion Criteria of Women with PCOS

1. Women who had diabetes mellitus, hyperprolactinemia, congenital adrenal hyperplasia, thyroid disorders, Cushing syndrome, androgen-secreting tumors, hypertension, and smoking.
2. Women had been treated with any hormone and confounding medications, including oral contraceptive agents, antilipidemic drugs, and insulin-sensitizing drugs that might affect the ovarian function and /or metabolic criteria; within 3 months before enrollment.

Statistical Analysis

Data are expressed as the means ± SD. Statistical analyses were performed using Student's t-test or one-way analysis of the variance (ANOVA). All the data were analyzed by T-test, data were considered to be statistically significant at P value < 0.01 and < 0.05. All data were analyzed using SPSS (version 20).

RESULTS & DISCUSSION

Demographic characteristics of the two groups are given in Table 1.

Table 1: Demographic characteristics of the studied population

Variables	PCOs	Control	P. Value
Mean of age	31.43±6.42	29.45±10.05	0.264
Diabetic/Non Diabetic	66(46.8)/75(53.2)	33(27.5)/87(72.5)	0.001**
Hypertensive/Non-Hypertensive	30(21.3)/111(78.7)	30(25)/90(75)	0.004
Smoker/Non-Smoker	21(14.9)/120(85.1)	6(5)/114(95)	0.009**
BMI	72(51.1)/69(48.9)	91(75.8)/29(24.2)	0.004**
Occupation -House wife -Employee	 -69(48.9) -72(51.1)	 -33(27.5) -87(72.5)	0.000**
-Hirsutism	31.49±2.80	30.50±1.95	0.467
Menstruation: -Regular -Irregular	 -27(19.1) -114(80.9)	 -93 (77.5) -27(22.5)	0.0001**
Chi-square test used for analyzing categorical variables, while unpaired t-test used for numerical variables. Probability (P) value >0.05 considered as non-significant, *P-value <0.05 means significant differences, while **P. value<0.01 highly significant differences. Mean± Standard deviation (SD) used for numerical variables.			

In regard to the sociodemographic features of the PCOS and the control group, the current study showed non-significant differences (P=0.264) between the mean age of the PCOs and control group as revealed in Table 1. The current study reveals that the majority of women with PCOS were from the age 20 to 30 years, this finding initiated the idea that younger age groups are more prone to PCOS, this finding may be related to that the ovaries are more physiologically active in women at the childbearing age, therefor the ovaries are more liable to undergo cystic changes. This finding was in agreement with the finding of Jamal AF *et al.*, 2019 in Iraq [9] who found that the highest prevalence (32.7% and 43%) was among the age group 18-27 years. Alhindawi Zena [10]. Found that the highest prevalence of PCO among the mean age of women (25.8 ± 5.9 SD (ranging between 18-47 years old).

Concerning the diabetes mellitus status, the present study showed highly significant differences (P=0.001) between the diabetic and non-diabetic individuals of both PCOs and control groups This finding was in agreement with the finding OF *Mana st, et al.*, [11] 2022 in Iraq women with a history of PCOS considered an important risk factor for the development T2DM and we found 7.6% of T2DM individuals were diagnosed as PCOS earlier, which was supported by a previous local study [12]. PCOS is considered a hallmark trigger for the development of dysglycemia due to an insulin secretory defect, and the high risk for glucose intolerance.

It is evident from Table 1 that there were significant variances (P<0.05) between the proportion of the hypertensive and non-hypertensive individuals among the PCOs and control groups, the relationship between PCOS and hypertension remains controversial [13-15]. The World Health Organization (WHO) defines arterial hypertension as a permanent increase of systolic blood pressure over 140 mmHg and an increase of diastolic blood pressure over 90 mmHg [14]. Among the general population, hypertension is considered a significant risk factor for cardiovascular disease. Despite increasing studies demonstrating a higher prevalence of hypertension among women with PCOS, the evidence so far has been inconsistent. Several studies suggest an increased prevalence of hypertension among women with PCOS. This finding was in agreement with the finding of Anju E Joham *et al.*, [16].

Highly significant differences (P<**0.001**) were noticed between the PCOs and control groups in regards to smokers and non-smokers percentages. This study agrees with Reem Alariqi *et al.*, [17].

Regarding the BMI mean levels, the present study demonstrated highly -significant results (P<**0.001**) between the PCOs and the control group. This study goes with Jamal AF *et al.*, 2019 in Iraq [9] who found that the highest prevalence (43%) of PCO which was also found among participants of high BMI (≥ 30) and 22.5% among overweight women.

Patients with PCOS, especially those of high BMI, require specific therapy to decrease their weight; usually, those patients could not achieve weight loss easily, because of different frustration such as their bad mood, depression, feeling of distress and bad quality of life. Therefore, resolving of emotional problem is very important to encourage those patients to change their lifestyle and hence decrease their weight. It is well known that most common symptoms of PCOS are daily fatigue, sleep disturbances and changes of appetite, which highlight an importance of changing lifestyle by decreasing high fat diet and high carbohydrate diet with increasing physical activity as well as resolving mental and emotional status by incorporation and encouragement [18, 19].

In the current study, the women with PCOS were found to be significant reductions in BMI after three months of treatment. Our study are also consistent with those of Fattah *et al.*, revealed that patients who were on Metformin had a mean decrease in BMI of 6.7 ± 3.01 kg/m2 [20]. Metformin reduces appetite and caloric intake in the gastrointestinal tract. It also alters the adenosine monophosphate-activated kinase in the hypothalamus and mediates anorectic effects, in this way metformin reduces body weight resulting in a reduction of body mass [8]. In regards to the comparing to house wives, this was true for both the PCOs and control group, the results were highly significant (P. value =0.000) World Health Organization study on health behaviors of 35 countries showed that 60% of people's quality of life and health depends on their lifestyle and personal behaviors. One of the objectives of WHO for 2020 is to promote healthy lifestyle, reduce health risk factors including inappropriate physical activity, bad diet, defective interpersonal relationships, alcohol use, and substance use correcting lifestyle, first introduced by the Austrian psychoanalyst Alfred Adler, is an important concept that is mostly used to express people's lifestyle and covers different dimensions including nutrition, exercise, self-care, cigarette smoking, alcohol and substance use, social support, and stress control [21].

Regarding the Hirsutism, the present study demonstrated not significant results (P. value =0.467). The presence of hirsutism in 88.33% of the patients in the given PCOS group, this finding agreed with several studies, they reported that hirsutism rates was around 80% among women with PCOS [17,20,21]. The underlying cause of hirsutism is commonly attributed to increased androgen production from either the ovaries or adrenal glands. Androgens are male sex hormones, but both men and women produce them, although in different amounts. In PCOS, there can be an excess production of androgens, leading to hirsutism among other symptoms [22]. Elevated serum levels of androgens, including testosterone, androstenedione, and dehydroepiandrosterone sulfate (DHEAS), are commonly observed in women with PCOS. These elevated androgen levels contribute to the development of various symptoms associated with PCOS [22].

The results of this study observed that were a highly significant differences in the mean levels of Menstruation regularity and irregularity (P. value =0.000) between cases (PCOS) and control menstrual cycle irregularity is indeed a useful clinical marker in assessing ovulation and reproductive health. It can provide valuable information about hormonal balance and potential underlying conditions such as PCOS or other menstrual disorders [23]. The menstrual cycle is regulated by a complex interplay of hormones, including estrogen, progesterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH). Ovulation, the release of an egg from the ovary, is a key event in the menstrual cycle. Regular menstrual cycles typically indicate the occurrence of ovulation, as they reflect the coordinated hormonal changes necessary for successful ovulation [32, 33]. Therefore, menstrual cycle pattern might serve as a marker of IR in patients with PCOS, as IR can induce oligo- or anovulation and thus menstrual cycle irregularity by exacerbating hyperandrogenemia and by disrupting follicular growth [24, 25]. Some studies have explored the potential associations between menstrual irregularities and endocrine or metabolic parameters in PCOS. For example, elevated levels of androgens, such as testosterone, have been found to correlate with menstrual irregularities in some studies. Additionally, insulin resistance, which is common in PCOS, has been implicated in menstrual disturbances and may contribute to the metabolic features of the condition [26, 27]. Ovulatory dysfunction, defined as oligomenorrhea and amenorrhea, is a common complaint in women of reproductive age. Hyperandrogenemia is thought to increase cardiovascular and metabolic risks in women with PCOS [28, 29]. Indeed, according to the ESHRE and the ASRM definition of PCOS, at least two of the following three features should be present to establish the diagnosis of PCOS: a) oligoor anovulation, b) biochemical hyperandrogenemia or clinical manifestations of hyperandrogenemia and c) polycystic ovaries on ultrasound, resulting in four different PCOS phenotypes. Therefore, ovulatory women with hyperandrogenemia and polycystic ovaries (phenotype 3) are considered to suffer from PCOS. However, it is unclear whether the severity of menstrual cycle irregularity, a surrogate marker of anovulation, differs between the three different anovulatory PCOS phenotypes [30, 31]. In addition, women with PCOS are frequently obese and obesity is associated with menstrual cycle abnormalities in the general population.

Table 2: Comparison of thyroid hormone levels between PCOs and control groups

Thyroid hormones	PCOs	Control	P. Value
T3	1.62±0.82	1.34±0.29	0.392
T4	3.25±0.31	2.49±0.12	0.146
TSH(µIU/ml)	93.32±15.37	85.67±12.11	0.029

The study was performed on 141 infertile women and 120 age-matched healthy fertile control age (31 ± 6 yea rs). Overall, serum (TSH) assay is for the diagnosis and management of hypo and hyperthyroidism. The present study, the aim was made to identify the Impact of metformin on blood levels of anti-mullerian hormone, Evaluation of, 17-hydroxyprogesterone; dehydroepiandrosterone sulfate, and some biochemical parameters level in polycystic ovarian women and the relationship between thyroid autoimmunity and female infertility. The study was performed on 141 infertile women and 120 age-matched healthy fertile control age (31 ± 6 years). Overall, serum thyroid stimulating hormone (TSH) assay is the key test for the diagnosis and management of hypo and hyperthyroidism. The mean ± SD of serum (TSH) (**93.32±15.37**) µIU/ml was significantly (**0.01**) in infertile group compared with control (**85.67±12.11**) µIU/ml.

According to recent study, many evidences showed that women who suffered from PCOS present in most cases thyroid disorders which is often associated with hypothyroidism or at risk of future hypothyroidism could be explained by the presence of thyroid hormone receptors in human oocytes and effects on differentiation of the trophoblast. Another pathway through which hypothyroidism may impact on fertility is by altering the peripheral metabolism of oestrogen and by decreasing sex hormone binding globulin SHBG production; both pathways may result in an abnormal feedback at the pituitary [32].

The present study agree with Zahiri Z [33], who found that PCOS patients were found to have higher mean TSH level than that of the control group. Duran [1], found that increased thyroid disorders in females with PCOS compared with controls and found significant higher prevalence of goiter (27.5% *vs.* 7.5%). The effect size revealed that the TSH level was higher in PCOS patients than in non-PCOS patients. Our study showed in PCOS patients there is raised levels of TSH as compared to healthy females.

Hypothyroidism itself can aggravate PCOS symptoms. Hypothyroidism can lead to low levels of (SHBG) which in turn can lead to higher concentrations of free testosterone and increased testosterone throughout the body and aromatization to estradiol and reducing the metabolic clearance rates of androstenedione and estrone. Since thyroidhormones are involved in the gonadotropin induced estradiol and progesterone secretion by human granulosa cells, hypothyroidism will interfere with ovarian function and fertility [34].

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Table 3: Serum Level of thyroid tests in Women with PCOs before and after treatment

Thyroid hormones	Before metformin	After metformin	P. Value
T3(µIU/ml)	1.62±0.82	1.37±0.61	0.423
T4(µIU/ml)	93.32±19.37	95.05±18.84	0.642
TSH (µIU/ml)	3.25±0.31	2.66±0.25	0.159

In the present study, we found a non-significant difference (**0.159**) in **TSH** levels in PCOS patients before and after taking metformin compared with healthy subjects (85.67±12.11 vs 93.32±15.37).

Contrary to our results, Sinha U [33], who found that PCOS patients were found to have higher mean TSH level than that of the control group (4.547 ± 2.66 and 2.67 ± 3.11 respectively; P value = 0.00001). Duran [1], found that increased thyroid disorders in females with PCOS compared with controls and found significant higher prevalence of goiter (27.5% *vs.* 7.5%). The effect size revealed that the TSH level was higher in PCOS patients than in non-PCOS patients. Our study showed in PCOS patients there is raised levels of TSH as compared to healthy females ($p<0.0001$).

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hypothyroidism will interfere with ovarian function and fertility [33].

Metformin is the first-line recommended and commonly used drug for T2DM. The Endocrine Society recommends metformin in women with PCOS who have T2DM or impaired glucose tolerance (IGT) who fail lifestyle modification and also as a second-line therapy in women with menstrual irregularities who cannot take or tolerate hormonal contraceptives. Metformin may directly decrease ovarian androgen production. Metformin has been shown to improve ovulation rates when combined with clomiphene citrate in women resistant to it South Asians are more insulin resistant and have significantly lower insulin sensitivity compared to Caucasians and Europeans. with the same BMI. Metformin monotherapy for 6 months resulted in regular menses within 4 months of treatment, but a consistent reversal toward pretreatment conditions was observed within 3 months of metformin withdrawal Recently, there have been some reports that metformin can influence thyroid function tests, mainly by a decrease in serum levels of thyrotropin (thyroid-stimulating hormone [TSH]). In contrast, in other study, metformin was not associated with changes in TSH levels in euthyroid patients without underlying thyroid dysfunction Dhanpal *et al.,* [35].

The data suggest that in PCOS women who have thyroid dysfunction, i.e., either overt or subclinical, metformin use was associated with a non significant change in TSH levels. The dose of metformin used in the current study was 1000 mg OD, and this is similar to the study conducted by Ibraheem *et a*., [17].

Patients were followed up for 3 months in our study; this is similar to the study conducted by Ibraheem *et al.,* where they had followed the patients for three monthsbut in contrast to other studies where follow-up was 6 months] and 4 months, respectively [36].

The significant effect of metformin on TSH in patients with thyroid dysfunction was in concurrence with other studies conducted by Rotondi *et al.,* [37] in which they observed no significant change in the euthyroid group and that agree with the recent study.

In a study done by Dunaif, Andrea, *et al.,* [38], it was shown that metformin not only has TSH-lowering effect in patients with type 2 DM and hypothyroidism but also in euthyroid TPOab-positive and There was no significant change in total T4 and total T3 levels in either group, and these results were similar to the studies conducted by Morteza Taghavi *et al.,* for free T4 and free T3 Ibraheem *et al.,* [36] for total T4 and total T3, and for free T4. Rotondi *et al.,*[39].

The mechanism of metformin action on the thyroid axis is complex and multifactorial. The affinity or the number of thyroid hormone receptors may be changed by metformin. It may increase the central dopaminergic tone or may directly act on TSH regulation Rotondi *et al.,* [39].

Polycystic ovary syndrome is the most common endocrine and metabolic disease in women of childbearing age and can cause metabolic disorder, infertility, and increased anxiety and depression; as a result, it can seriously affect the physical and mental health of fertile women. PCOS is a highly clinically heterogeneous disease with unclear etiology and pathogenesis, which increases the difficulty of treatment. The thyroid gland has complex regulatory effects on metabolism, reproduction, and emotion, and produces hormones that act on almost all cells of the human body. The clinical manifestations of PCOS are similar to some thyroid diseases. Furthermore, some thyroid diseases, such as subclinical hypothyroidism (SCH), not only increase the incidence rate of PCOS, but also exacerbate its associated metabolic abnormalities and reproductive disorders. Interestingly, PCOS also increases the incidence of some thyroid diseases. However, the role of the thyroid in PCOS remains unclear [40].

Table 4: Study of thyroid hormones mean levels within diabetic and non-diabetic patients of PCOs

Thyroid hormones	Diabetic	Non-Diabetic	P. Value
T3	1.99±0.72	1.31±0.65	0.211
T4	91.01±22.36	95.26±16.69	0.465
TSH (µIU/ml)	2.89±0.87	3.55±0.44	0.503

The current study showed the mean levels (2.89±0.87µIU/ml) of TSH found among diabetic patients with PCOs in comparing to (3.55±4.44 µIU/ml) which was detected among non-dabetic group, but the results were not statistically significant were the P>0.05. This was also applicable for TSH, while T4 and T3 mean levels showed non significant variances (P>0.05) as shown in Table 4.

This study disagree with Fan, Huanhuan, *et al.,* [40] who reported that the incidence of hypothyroidism is higher in patients diagnosed with PCOS (11–14%) compared with control subjects (1–2%) [41] Metabolic changes observed in both hypothyroidism and PCOS include insulin resistance, dyslipidemia, increased weight, and obesity. Compared with

PCOS patients with normal thyroid function, women with PCOS and SCH combined have higher triglyceride levels, fasting insulin levels [42].

PCOS women were predicted to have a high risk for dyslipidemia because they are frequently obese and have elevated androgen levels. Furthermore, PCOS women frequently have hyperinsulinemia and IR, they would be suffered from an increased risk for dyslipidemia associated with IR, which was considered as the risk for CVD [30]. Currently, the dyslipidemia pattern in PCOS women is being investigated. IR, elevated androgen levels, estrogen, genetics, ethnicity, aging, obesity, lifestyle, and medication are putative factors. Altered glucose–insulin homeostasis is a stronger contributor to dyslipidemia in PCOS than either hyperandrogenism or chronic estrogen exposure. On the other hand, PCOS women frequently have higher TG, lower HDL- cholesterol, and higher LDL-cholesterol levels [34].

Table 5: Study of thyroid hormones mean levels within hypertensive and non-hypertensive patients of PCOS

Thyroid hormones	Hypertensive	Non-hypertensive	P. Value
T3	1.70±2.04	1.33±0.46	0.576
T4	93.77±19.46	91.70±19.99	0.768
TSH	3.44±0.70	2.56±0.8	0.466

This study reveals that serum level of **TSH** was non-significantly difference in hypertensive patients was (3.44±0.70µIU/ml), as compared with non-hypertensive patients (2.56±0.8 µIU/ml) and it is disagree with Trummer Christian *et al.,* (41). his study was to analyse the impact of elevated TSH levels on the metabolic and endocrine phenotype in 583 women with PCOS. Endocrine and metabolic parameters were measured in all patients and compared between women with and without elevated TSH levels. Of the 583 women with PCOS, 125 women (21.4%) had thyroid disturbances (thyroid replacement therapy: 109 women, subclinical hypothyroidism: 16 women). Patients with elevated TSH levels had significantly increased fasting insulin, area under the curve–insulin, homeostatic model assessment–insulin resistance, and TC/ HDL ratio and lower free thyroxin, insulin sensitivity and HDL ($p < 0.05$ for all). Euthyroid PCOS women with thyroid hormone substitution showed significant differences in TSH, age, body mass index, HDL and systolic blood pressure compared to those without hormone replacement therapy ($p < 0.05$ for all). We conclude that hypothyroid disturbances and elevated TSH levels are common findings in PCOS, which are associated with an adverse metabolic profile. Therefore, women with diagnosed PCOS should be screened for thyroid dysfunction.

Table 6: Distribution of PCOS women and control group mean according to systematic disorder

Condition	NO.	With condition%	NO.	Without condition%
Hirsutism	39	37.14	66	62.85
Hypertensive	45	42.85	60	57.15
Regular MS	15	14.28	90	85.72
BMI	50	47.61	55	52.38
$X^2 = 51.3024$ p= 0.0001 P ≤ 0.01 Highly Significant(HS)				

The results showed that an increased incidence of hypothyroidism in women of reproductive age is affecting the normal women's cycle, the regular MC were (85.72%) compared to the patient's women group were regular MC (14.28%) which means that alteration of thyroid hormones leads to change the normal cyclic patient's women. According to recent studies, much evidence showed that women who suffer from PCOS present, in most cases, thyroid disorders which is often associated with carbohydrate metabolism disorder or at risk of future diabetes. The results of this study shown in Table 6 indicate that there has been an elevation in blood pressure in obese PCOS women at reproductive age (31.72±0.91years) with (42.85%) compared with (57.15%) in healthy normal women.

Furthermore, the relation of body mass index with PCOS women as presented in Table 6 reveals that the patients with PCOS have high BMI (47.61%) compared to control group.

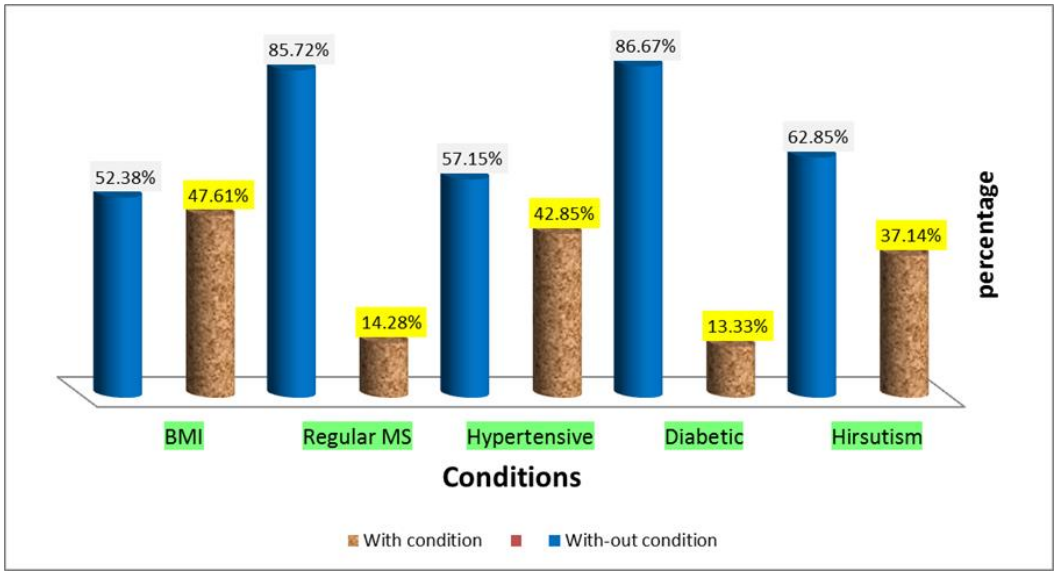

Figure 1: Distribution of PCOS women and control group mean according to systematic disorder

The diagnostic evaluation of the potentially systematic disorder irregular MC, hypertensive and hirsute patient first involves confirming the presence of irregular MC, hirsutism due to ovulatory dysfunctional and then hypertension patient's women excluding associated or etiological abnormalities and disorders (eg, diabetes, obesity) [42].

Moreover, PCOS is associated with hypertension in pregnancy a significantly increased risk of adverse pregnancy, fetal, and neonatal outcomes. Increased cancellation rate and lower fertilization rate. Some researchers observed a link between low thyroid hormones and decreased levels of hemostatic factors which may lead to changes in the menstrual cycle and increased bleeding [43].

Nandi *et al.*, [45] reported that both Gonadotropin hormone Gn and T_4 are important in achieving maximum level of success of fertilization and blastocyst development. Vaiarell *et al.*, [46] referred to the presence of thyroid hormone receptors in human oocytes, where they act together with the LH and human-chorionic- -gonadotropin HCG receptor, to enhance a stimulatory action that directly affects the function of granulosa cells and differentiation trophoblastic cells.

The present study was conducted on the factors that contribute to the onset of some symptoms of PCOS such as hirsutism, diabetes, hypertension, and high BMI. Data listed in Table 6 shows that hirsutism in the present study effects (37.14%) compared to healthy normal women (62.85%), primarily because the underlying endocrine disorders (eg, PCOS) and the factors regulating the development of hair growth (eg, androgen receptor activity) have a strong genetic component.

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