

Evaluation the Serum Level of Melatonin in Iraqi Patients with Polycystic Ovarian Syndrome

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Abstract

Background: Polycystic Ovarian Syndrome(PCOS) is one of the most frequent gynecological endocrinopathy that occur in premenopausal females, with a predominance range from 6%to10% among women of reproductive age.Melatonin (N-acetyl-5-methoxytryptamine), an neurohormone synthesized from the aromatic amino acid tryptophan mainly by the pineal gland of humans.The important of melatonin in human reproduction is still unidentified. A numerous study suggests that melatonin and reproductive hormones are closely related. This concept is based on observation of influence melatonin on sex steroid production at different stages of ovarian follicular maturation as melatonin receptors have been demonstrated at multiple sites in ovary and in intrafollicular fluid. **Aim :**The study aim to evaluate the role of melatonin in women with polycystic ovarian syndrome. **Materials and Methods:**A prospective cross-sectional study was designed taking 60 PCOS patients and 30 controls women whose ages were between 15-35 years old, from beginning of January 2019 to ending of April 2019. These patients admitted to obstetrics and gynecology unit at Babylon teaching hospital. And Five ml of blood sample was taken on day 2 of menstrual cycle by vein puncture from each subject enrolled in this study .Blood samples were collected between 07:00am – 08:00 am, and placed into sterile test tubes to serum melatonin estimation.**Result:** The study showed that there is the significant difference betweenPCOS women and the control group concerning melatonin level,and the highest mean of melatonin was occurred in PCOS women (61.21 ± 13.78 vs. 28.61 ± 6.73). And also This study showed that there were the higher means of melatonin in PCOS women with positive family history than PCOS women with negative family history (66.56 ± 11.25 vs. 59.26 ± 14.21) with significant relation. **Conclusions:** Women with PCOS have significant increase of serum melatonin in PCOS women. And also thisstudy could open the way for therapeutic role of melatonin in treatment of PCOS women.

Keyword : Melatonin ; Iraqi patients ;Polycystic Ovarian Syndrome

Introduction

Polycystic Ovarian Syndrome(PCOS) is one of the most frequent gynecological endocrinopathy that occur in premenopausal females⁽¹⁾, with a predominance range from 6%to10% among women of reproductive age⁽²⁾. It is characterized by hyperandrogenism (male hormone in female), menstrual disturbance, excess body and facial hair (hirsutism), acne, temperament disorder, endometrial cancer in addition, severe physiological disturbance are commonly detected among women with PCOS; for example, abdominal adiposity, inflammation, and infertility^(3,4,5). Polycystic ovarian syndrome diagnosis is based on two of the following three findings: Oligo- or anovulation, polycystic ovaries under ultrasonography,

and clinical or biochemical signs of hyperandrogenism⁽⁶⁾. Polycystic ovarian syndrome etiology and pathogenesis is still unknown, but some causative factors play important role in this syndrome such as hormonal disorders, adipose tissue dysfunction, oxidative stress have been blamed, but definitive consensus has not been reached⁽⁷⁾. However, in recent years, insulin resistance (IR) has been reported to play an important role in the progression of PCOS^(8,9,10). PCOS may present with metabolic abnormalities such as insulin resistance (IR) and visceral obesity at a young age. Long-term exposure to these abnormalities during fertile life may increase the reverse impacts and expose these women to higher risks of metabolic syndrome (MetS), cardiovascular diseases (CVDs) and type II diabetes mellitus (T2DM)

⁽¹¹⁾. While, melatonin (N-acetyl-5-methoxytryptamine), an neurohormone synthesized from the aromatic amino acid tryptophan mainly by the pineal gland of humans⁽¹²⁾. As a neurohormone, melatonin has numerous important physiological function and regulates varieties of central and peripheral actions related to circadian rhythms and reproduction. It act as a broad-spectrum antioxidant, powerful free radical scavenger, anti-inflammatory agent, potential immunoregulator, anticarcinogenic effector, sleep inducer, and regulator of the circadian rhythm in the body⁽¹³⁾. The important of melatonin in human reproduction is still unidentified. A numerous study suggests that melatonin and reproductive hormones are closely related⁽¹⁴⁾. This concept is based on observation of influence melatonin on sex steroid production at different stages of ovarian follicular maturation as melatonin receptors have been demonstrated at multiple sites in ovary and in intrafollicular fluid. Also several studies found that increased of melatonin concentration in serum of women with PCOS, and also indicating a feedback mechanism due to reduced melatonin concentration at the level of ovarian follicles. This could interpretation role of melatonin in the pathogenesis of PCOS⁽¹⁵⁾. The study aim to assess the role of melatonin in women with polycystic ovarian syndrome. Objectives: Clarify the relation of serum melatonin in PCOS women and the control group and Evaluate the association some clinical symptoms in PCOS women.

Materials and Method

Study design: A prospective cross-sectional study was designed taking 60 PCOS patients and 30 controls women whose ages were between 15-35 years old, from beginning of January 2019 to ending of April 2019. These patients admitted to obstetrics and gynecology unit at Babylon teaching hospital. An interview was carried out with these patients using questionnaire form designed by the investigator including their demographic characteristics, age, weight, length, BMI... etc.

Study population:

Inclusion criteria for selection of cases women:

The Rotterdam European Society for Human Reproduction and Embryology/American Society for Reproductive Medicine (ESHRE/ASRM) this criteria was used to diagnose PCOS and women with presence of any two of the following three features were included in the study:

- Menstrual disturbance or irregular.
- Clinical and/ or biochemical hyperandrogenism (hirsutism, acne, and alopecia)
- Polycystic ovaries morphology under ultrasound (more than 12 follicles in one or both ovaries, 2-9mm in diameter and/ or increased ovarian volume more than 10 ml).

Inclusion criteria for selection of controls women:

- Regular menstrual cycle
- Normal androgen, without (hirsutism, alopecia, and acne)
- Absence of polycystic ovary morphology under ultrasound
- Normal biochemical parameters including (S.Melatonin).

Exclusion criteria: All patients with metabolic or endocrinology disorders including thyroid disorder, diabetes mellitus, hypertension, Cushing's syndrome, acromegaly, premature ovarian failure, virilising adrenal or ovarian tumors, and history of using contraceptive through last of sex months were excluded from this study.

Sampling: Five ml of blood sample was taken on day 2 of menstrual cycle by vein puncture from each subject enrolled in this study .Blood samples were collected between 07:00am – 08:00 am, and placed into sterile test tubes, after blood clotting, centrifuged at 2500 RPM for 15 minute then clot removed and remain re-centrifuged at 2500 RPM for 10 minute and the obtained serum were aspirated using mechanical micropipette and transferred into clean test tubes which labeled and stored in deep freeze at -20 c for serum melatonin measurement.

Statistical Analysis

Computerized statistically analysis was performed using SPSS statistic program version 16.1. Comparison was carried out using; Chi-square(X^2) and T-Test probability (P value).

Finding

Comparison of age in PCOS and Control women.

A total of 60 PCOS women and 30 non PCOS women (control group) were examined for (melatonin).

Their age range group were between (15-35) years, showed in Table 1.

Table 1: Comparison of age in PCOS and Control women.

Age	PCOS group	Control group
No.	60	30
Mean	24.25	23.63
SD	5.12	4.06
P- Value	NS	

Comparison of melatonin level with PCOS women.

The study showed that there is the significant difference between PCOS women and the control group concerning melatonin level, and the highest mean of melatonin was occurred in PCOS women (61.21 ± 13.78 vs. 28.61 ± 6.73), showed in Table 2.

Table 2: Comparison of melatonin and PCOS.

Serum Melatonin (ng/ml)	PCOS group	Control group
No.	60	30
Mean	61.21	28.61
SD	13.78	6.73
P- Value	< 0.05	

Comparison of Melatonin with Family History in PCOS women.

This study showed that there were the higher means of melatonin in PCOS women with positive family history than PCOS women with negative family history (66.56 ± 11.25 vs. 59.26 ± 14.21) with significant relation, showed in Table 3.

Table 3: Comparison of melatonin and family history in PCOS.

Melatonin	Negative family history	Positive family History
No.	44	16
Mean	59.26	66.56
SD	14.21	11.25
P- Value	< 0.05	

Discussion

PCOS with Age :

Our study it was found that there was no significant difference between PCOS women and control group concerning age (24.25 ± 5.12 vs. 23.63 ± 4.06), Table 3.1, and Figure 3.1. This agreement with (Guilherme

Barbosa, *et al.*)⁽¹⁶⁾ study, that found PCOS affects women of childbearing age without higher prevalence by ethnic groups, but the signs and symptoms may differ by ethnicity. And disagreement with (Chhabra,*et al.*)⁽¹⁷⁾ who reported that PCOS varies with age but continues to be more common among women aged less than 35 years than in those above 35 years, this finding could be

attributed to that the women in that age are physiological active concerning the fertility and ovulation.

Melatonin level with PCOS.

The study showed that there is the significant difference between PCOS women and the control group concerning melatonin level and the highest mean of melatonin was occurred in PCOS women compared with control group (61.21 ± 13.78 vs. 28.61 ± 6.73), Table 3.2, and Figure 3.2.

Melatonin is normally synthesized in the ovary, as both melatonin synthesizing enzymes AANAT (arylalkylamine N-acetyltransferase) and HIOMT (hydroxyindole-O-methyl transferase) are present in ovarian tissue⁽¹⁸⁾. The study by (Tenorio, *et al.*)⁽¹⁹⁾ found that, the presence of melatonin receptors in the follicular cells of rats and mice, suggests possible melatonin production in the ovary. Its well-documented role as an antioxidant may be associated with follicular development and oocyte quality, interfering in processes such as oocyte maturation and ovulation⁽²⁰⁾. Melatonin, synthesized by the ovary, may be released into the follicular fluid. However, the capacity of melatonin detected in the ovary and preovulatory follicular fluid is derived from the circulation. There may be a reduction in the uptake of melatonin from circulation into the ovarian follicles of PCOS cases due to anovulation and increased number of atretic follicles and consequently serum melatonin concentration may increase in PCOS as a feedback response to decreased follicular concentration⁽¹⁵⁾. This study agreement with (Murcia-García, *et al.*)⁽²¹⁾, Experimental studies with female rats and hamsters reported that removal of the pineal gland leads to a decrease in melatonin levels with consequent premature vaginal opening, ovarian hypertrophy, increased cornification of vaginal cells and chronic anovulation, effect that can be reversed after administration of melatonin⁽²²⁾. The reduction of melatonin ovary can decrease embryo implantation, as well as interfere with pregnancy when rats are subjected to short photoperiods, showing an increase in melatonin levels accompanied by depressions in follicle stimulating hormone (FSH) and reduction in follicle development, becoming anestrous⁽¹⁹⁾. And also with (Woo, *et al.*)⁽²³⁾ study, found the expression of receptors for melatonin MT1 and MT2 has been identified in human reproductive tissues, including the mammary epithelium, myometrium, ovary and granulosa-luteal cells. In females, the influence of melatonin on the reproductive

function can be inferred from studies that indicate that high levels of melatonin cause amenorrhea⁽²⁴⁾, disturbance in gonadotropin secretion and the secretion of prolactin in response to the photoperiod⁽²⁵⁾. Studies have suggested that melatonin has a role in ovarian physiology, given that high concentrations of melatonin have been detected in follicular fluid⁽¹⁹⁾.

Melatonin and Family History in PCOS women.

The study showed that there is the significant difference between positive family history and negative family history concerning melatonin level and the highest mean of melatonin was occurred in positive family history compared with negative family history in PCOS women (66.56 ± 11.25 vs. 59.26 ± 14.21), Table 3.3 and Figure 3.3.

Our result agreement with (Sirmans, *et al.*)⁽²⁶⁾ study, that found family history of PCOS is a risk factor for PCO. Based on the clustering of cases in families, PCOS is considered to be a heritable disorder. A high prevalence of PCOS or its feature among first-degree relatives is suggestive of genetic influences. A increased prevalence of PCOS is associated with a number of condition. A history of weight gain often precedes the development of the clinical features of PCOS, and following healthy lifestyle has been shown to reduce body weight, abdominal fat, reduce testosterone, improve insulin resistance, and decrease hirsutism in women with PCOS. And also with (Begum, *et al.*)⁽²⁷⁾ study, that found The presence of a genetic component to PCOS and familial clustering of reproductive and metabolic abnormalities results in increased risk of PCOS among first-degree relatives of PCOS patients. This is evident agree with our study results where participants with a positive family history of PCOS carried little higher risk of development of PCOS.

Conclusions

- 1- There was significant increase of melatonin in PCOS women.
- 2- There was significant increase of melatonin with positive family history in PCOS women.

Conflict of Interest: Non

Source of Findings: Non

Ethical Clearance: Non

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