Study of a Hormonal Assay in PCOS Patients with Type 2 DM and their Correlation with Inhibin B

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Abstract

Background: inhibin B considered a sensitive marker for follicles numbers of the ovary. Inhibin B levels increased with overnighted, lipedema and PCOS women. PCOS affects women in menstrual age. Obesity and insulin resistance have an association with PCOS. This syndrome increases LH, FSH, Prolactin. and testosterone hormonal levels.

Aim: examine the role of inhibin B in polycystic ovary syndrome (PCOS) with type 2DM patients, and to investigate the correlation between these quantities with serum inhibin B for women on the 12th day of their ovulation developments and correlation of inhibin with other biochemical parameters in those patients.

Patient and Method: sixty women included in this study divided into two groups of 30 subjects. The first group is for women who had PCOS with type 2DM, and the second for control subjects. PCOS with type 2DM patients diagnosed according to Rotterdam ESHRE/ASRAM. The biomedical test is done for FBS, Cholesterol, TG, LDL, HDL, HbA1c for all subjects included in this study.

Results: BMI, weight, prolactin and testosterone, FBS, cholesterol, TG, LDL, HDL, HbA1c had significantly higher levels in PCOS women with type 2DM. while inhibin B level showed to be significantly lower in PCOS with type 2DM. when this study attempted to find the correlation between the inhibin B with the biochemical tests, only the TG and HbA1c show a significant correlation in PCOS with type 2DM women.

Discussion: The high levels of biochemical parameters for diabetic female patients' groups with PCOS are due to the association of PCOS with insulin resistance and obesity. So, the low inhibin B levels in PCOS with type 2DM and its correlation with HbA1c and TG in the PCOS group could be an indication for using inhibin B as a type 2 DM marker. This study supported by Katrine et al 2017 when found out that when they diagnosed type 2DM at a younger age the levels of event rate (HbA1c and FBS) was higher in PCOS compared with controls

Conclusion: There is a significant correlation in inhibin-B levels with HbA1c and TG levels in PCOS women with type 2 DM.

Keyword: *polycystic ovary syndrome (PCOS), Inhibin B, Triglycerides, LH, BMI, FSH*

Introduction

Some women in reproductive age had one of the common endocrinal disorders characterized by the state of anovulation called polycystic ovarian syndrome (PCOS) which may persist for any length of time. androgen excess, infertility, menstrual irregularity, and insulin resistance may appear as an endocrinological feature for PCOS patients. PCOS is associated with insulin resistance and obesity [(1)]. It was found that ovarian inhibin exerts negative feedback on pituitary

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gonadotrophin production, preferentially affecting follicle-stimulating hormone (FSH) secretion, inhibin has been shown to impact basal secretion of both FSH and LH, as well as gonadotrophin-releasing hormone (GnRH)-stimulated FSH with the isolation of inhibin.

PCOS found to be related to lipid abnormalities, dyslipidemia, cholesterol, low density of lipoprotein and triglycerides. All these increases the risk of type 2 diabetes in PCOS women [(2)].

Inhibin's are disulfide-linked heterodimers composed of an α-subunit and either a β_A-subunit (inhibin A) or a β_B-subunit (inhibin B) which belong to the transforming growth factor β (TGF-β) super family [(3, 4)]. Inhibin negatively regulates the secretion of FSH (follicle-stimulating hormone), even if there is no direct evidence of this phenomenon as well as locally enhancing the follicle development leading to reverse the growth of small antral follicle [(5)].

The investigations over decades show that in both male and female, inhibin B plays a physiological role in reproductive endocrinology applications. In a female, inhibin B considered as an earlier marker and more sensitive for ovarian follicle number as it is directly secreted by the granulosa cells of the small, developing follicles of the ovary when a low level clinically suggests a premature ovarian failure [(6)]. The inhibin B levels increase when women affected with weight gain, anorexia nervosa and with an increase in adipose tissue and leptin levels [(7)].

Throughout the menstrual cycle different secretory patterns displayed in Inhibin A and B. Levels of inhibin B serum and follicular fluid reach to maximum in the early to mid follicular phases, most likely under the stimulation of FSH. The information about factors regulating the shift production of inhibin in when the follicle becomes dominant [(8)]. Inhibin B levels are found to be inversely correlated with Body Mass Index (BMI) in PCOS [(9,10)].

In this case-control study, we aimed to examine the role of inhibin B in polycystic ovary syndrome (PCOS) with type 2DM patients and to investigate the correlation between these quantities with serum inhibin B for women in 12th day of their ovulation developments and correlation of inhibin with other biochemical parameters in those patients.

Patient and Method

This study approved by the scientific committee of the physiology department for al-Mustansiriyah college of medicine. The data of patients collected from Al-Yarmouk Teaching Hospital. Sixty females included in this study: 30 females are diagnosed as normal or control and 30 females with PCOS and with type 2DM. All patients examined with Ultrasonography on the 12th day of the menstrual cycle and diagnosed by a gynecologist according to Rotterdam ESHRE/ASRAM. To determine if female have PCOS, the doctor checked that whether they have at least 2 of these 3 symptoms:

1. Irregular periods or no periods, caused from lack of ovulation (amenorrhea or oligomenorrhea

2. Clinical Hyperandrogenism (acne, hirsutism)

3. Multiple small cysts on the ovaries found in ultrasound diagnosis.

The weight, height and Body Mass Index measured by electronic height and balance apparatus. The Biochemical tests include serum for Hormones of LH, FSH, Prolactin, and Testosterone. Biochemical tests for type 2DM are done which is: Fast Blood Sugar (FBS) , Cholesterol, Triglyceride (TG), HDL, LDL, HbA1c were measured by using KENZA 240 TX system (Bio IABO Diagnostics 2016) which is random access analyzers with microprocessor or control for measurement of lipid profile, HbA1c & glucose level. We use minividus for hormonal assay. All mentioned test is done for both control and diabetic PCOS groups.

Statistical Analysis

Analysis of data was carried out using the available statistical package of SPSS-25 (Statistical Packages for Social Sciences- version 25). Data were presented in simple measures of mean, standard deviation and range (minimum-maximum values). The significance of the difference of means (quantitative data) was tested using Students-test for the difference between two independent means. The significance of correlations was tested using the Pearson correlation test. Statistical significance was considered whenever the P-value was equal to or less than 0.05 [(12-14)].

Results

A. Comparison between control & PCOS with type 2DM groups:

Table (1) shows no significant difference between the two groups in age and height, while there is a significant difference between these two groups in weight, BMI and *p*-value (0.0001) for both of them. where the PCOS women with type 2DM tend to be obese more than the control group.

Table (1) characteristic of control and PCOS with type 2DM groups

	PCOS	**Controls**	**P value**
Age (years)	28.9±5.6 (20-40)	29.1±6.4 (20-41)	0.822
Weight (kg)	74.16 ± 10.29	59.66±70.01	0.0001*
Height (cm)	160.26 ± 7.99	159.1±5.32	0.5155
BMI (Kg/m²)	28.9±3.5 (22.46-35.96)	23.5±2.1 (19.72-28.84)	0.0001*
*Significant difference between proportions using Pearson Chi-square test at 0.05 level			

Table (2): shows that inhibin B levels had a significant difference in control (102.7±83.7) and PCOS group (58.6.6±356.4) with p-value 0.001. It appears that levels of inhibin B in PCOS women is less than control. While the level prolactin and testosterone are higher in PCOS women with PCOS with type 2 DM rather than control.

Table (2): hormonal assay for control and PCOS with type 2DM.

	PCOS	Controls	P value
Inhibin B	⁅58.6 ±35.6 (4 -100)⁆	⁅102.7±83.7 (15-400)⁆	⁅0.0001*⁆
LH (µIU/ml)	5.6±2.6 (1.2-10.1)	5.0±1.3 (3.0-7.1)	0.212
FSH (µIU/ml)	3.1±2.9 (0.1-12)	3.7±0.9 (2.1-5.6)	0.284
Prolactin (ng/ml)	31.3±14.6 (10-74)	18.6±6.0 (8-31)	0.0001*
Testosterone (ng/ml)	0.7±0.3 (0.2-1.1)	0.4±0.3 (0.05-0.9)	0.0001*

*Significant difference between two independent means using Students-test at 0.05 level

The tests of biochemical parameters for type 2 diabetes are listed in the table (3) it appears that all parameters are had a higher significant level in PCOS groups with significant value (p-value 0.0001).

Table (3): biochemical test for control and PCOS with type 2DM

	PCOS	**Controls**	**P value**
FBS (mg/dL)	128.4±35.1 (75-201)	85.2±7.1 (72-100)	0.0001*
HbA1c (mg/dl)	7.97±1.29 (5.2-10.6)	4.24±0.31 (3.7-5.0)	0.0001*
Cholesterol (mg/dl)	230.57±51.10 (170-344)	155.37±19.72 (105-190)	0.0001*
Triglycerides (mg/dl)	226.57±58.05 (165-368)	129.70±16.95 (100-155)	0.0001*
HDL (mg/dl)	55.87±7.85 (34-69)	41.53±3.78 (32-50)	0.0001*
LDL (mg/dl)	170.03±35.77 (107-235)	86.30±10.28 (65-101)	0.0001*
-Data were presented as Mean±SD (Range)			
*Significant difference between two independent means using Students-test at 0.05 level			

B. Correlation between inhibin B with parameters in PCOS type 2DM

The results of the correlation of hormone parameters with inhibin B for PCOS and Control groups listed in table 4. It appears that there is no correlation of mentioned hormones with inhibin B for both control and PCOS groups.

Table (4): correlation between hormones parameters with inhibin-B for PCOS and Control groups.

	PCOS		Control	
Parameters	**Correlation Coefficient**	**P-value**	**Correlation Coefficient**	**P-value**
LH	-0.0206	0 .9164	0.1877	0.3205
FSH	0.1031	0 .5877	0.0714	0.7077
Prolactin	0.1210	0.5241	-0.1949	0.3043
Testosterone	-0.0746	0.6975	0.0254	0.8940

* Pearson Correlation Coefficient Calculator at 0.05 level.

Discussion

Researches proved that one of the most common endocrinal metabolic disorder is PCOS which affect female fertility [15,16]. Being overweight is associated with PCOS and appear also in diabetic patients [17, 18]. Patient with high weight and PCOS is correlated with type 2DM [19].

Weight, BMI, Prolactin, testosterone, FBS, HbA1c, Cholesterol, Triglycerides, HDL, LDL significantly higher level in PCOS women considered as predictors for PCOS T2DM development. These results supported with Bhanu Kalra et al 2010 [5] when they found that in PCOS HbA1c, fasting plasma glucose, 2-hour plasma glucose, triglycerides, age, and BMI upon baseline were predictors of development of T2D. When models were corrected for age and BMI, fasting plasma glucose, 2-hour plasma glucose, and triglycerides were the best predictors of development of T2D. Hussain et al 2013 [20] compared hormonal levels in PCOS with control for cortisol, and testosterone is significantly high in the PCOS group.

The PCOS women with type 2DM with included in this study have higher BMI, prolactin, and lipids upon PCOS diagnosis. The significant of biochemical tests of type 2DM is agreed with Abbasi A et al 2012 [21] and Selvin E et al 2010 [22] where FBS is applied in many prediction models for risk of Type 2 DM developing in non-PCOS populations as control with PCOS patients HbA1c is a measure of average glucose levels and an indicator for increased risk of T2D in PCOS. It considered a better predictor of cardiovascular disease and overall mortality than fasting or 2-hour glucose.

The FSH levels result show no correlation with inhibin B in PCOS. The negative correlation of FSH with inhibin B for PCOS group of patients gives an indication that this hormone cannot be used to diagnose PCOS with type 2DM. These results are in agreement with Torgac et al [23] when they found out that the basal inhibin A or B levels give a significant positive correlation with the PCOS group and a negative correlation with FSH levels. As the previous studies showed that during the follicular phase, inhibin B is more important than inhibin A [24].

Prolactin and testosterone levels are higher in PCOS patients with type 2DM which demonstrated as a frequent condition in most PCOS patients increase of basal Prolactin levels or of an increased reserve of Prolactin in the pituitary gland. Prolactin heterogeneity behavior in secretion is a characteristic of PCOS [24]. The result agreed with Richard et al 2013 who showed that PCOS patients had hyperprolactinemia other than control [25]. The results of negative correlation for Testosterone and Prolactin with inhibin B agreed with Corrine K. et al. 2002 which reveals the fact that they had no direct effect on inhibin B levels but suggesting a stimulatory effect of insulin on Prolactin and testosterone [26].

We find in this study a significant correlation between inhibin B with HbA1c and TG lipids in PCOS women with type 2DM. There was no similar study (as we know) support this finding, but Corrine k. 2002 found that there are significant relationships between inhibin B and BMI including LH, insulin & SHBG. Katrine et al 2017 found out that when they diagnosed type 2DM at a younger age the levels of event rate (HbA1c and triglyceride) were higher in PCOS compared with controls [27].

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both MOH and MOHSER in Iraq

Conflict of Interest: Non

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