Correlation between Hormonal and Biochemical Changes with Kidney Function in Newly and Previously Diagnosed Women Diseased with Polycystic Ovary Syndrome

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Abstract

The objectives of our work was to identify the effects of insulin resistance and other hormonal changes on kidney function in newly and previously diagnosed women diseased with PCOS.

Method: This prospective study was done by collect serum samples and urine from three group (Control 60), (previously 50), (newly 50) patients. The withdrawal led samples were subsequently assay for hormonal and biochemical changes.

Results: The data of tests were available for both groups. We found significant differences in level of insulin, Homeostatic model assessment Insulin resistance (HOMA-IR), Homeostatic model assessment Beta function (HOMA-B), Progesterone among newly and previous women, also the data indicated a significant correlation between urea and testosterone in newly while direct significant correlation between urea and progesterone. There was significant correlation between Thyroid stimulating hormone (TSH) and creatinine in previously diagnosed PCOS, also direct correlation between uric acid and Body mass index (BMI), Fasting blood glucose (FBS), HOMA IR and inverse correlation with Triiodothyronine (T3) in new PCOS while in previously diagnosed PCOS there is inverse correlation between uric acid and T3. Finally, significant correlation between FBS, insulin, HOMA B and HOMA IR in previously diagnosed patients while correlation is seen between FBS, insulin and HOMA IR in newly patients.

Keywords: *Biochemical changes, kidney, women, polycystic ovary syndrome.*

Introduction

Polycystic Ovarian Syndrome: Polycystic ovarian syndrome (PCOS) is metabolic, endocrine and genetic disorders, chronic absence of ovulation of, with clinical and biochemical changes and presentation of hyperandrogenism [(1)]

PCOS affects as many as 10% of reproductive-age women when using the National institutes of health (NIH) standards in diagnosis. It is convenient that menstrual disturbances, insulin resistance and hyperandrogenism are currently existent, that includes anovulation, hirsutism, irregular and painful menstrual cycles, amenorrhea oligomenorrhea with small cysts in the ovaries, central obesity, and one more presentations related to the insulin resistance [(2,3,4)].

Epidemiology: The predisposing factors for PCOS include the following:

High maternal androgen: Prenatal exposure and Onset of type 1 diabetes mellitus before menarche, insulin resistance and obesity. Drugs: such as anti-epileptic drugs (e.g., Valproate) [(5)].Polycystic ovaries develop when the ovaries are stimulated to produce excessive amounts of (androgens), particularly testosterone, by either the release of excessive luteinizing hormone and

high levels of insulin in the blood or change due to levels of sex-hormone binding globulin (SHBG) resulting in increased free androgens [6] .

Women affect with PCOS reign elevated level of gonadotropin releasing hormone (GnRH), hence gives rise to a rise in ratio of Luteinizing hormone (LH)/ Follicle stimulating hormone (FSH) .The preponderance of women affected with PCOS have obesity and /or insulin resistance. The hypothalamic, pituitary and ovarian axis changes in PCOS are caused by insulin levels rises [7].

The state of hyperinsulinemia augments GnRH shoots frequency, LH upon FSH predominance, ovarian androgen output excess, follicles' maturation reduction and lowering binding of SHBG.[8] .

Autosomal dominant method sounds to be the genetic part of PCOS inheritance [9, 10]

Diagnosis of PCOS: NIH works proposed that diagnosis of PCOS is performed when patient has pictures of androgen rise in vivo and in vitro, whether patent endures oligoovulation, and when other conditions causing PCOS are excluded [11].

Standard Diagnostic Assessment: The diagnosis assessment includes the followings:

A-History-taking: women are inquired for menstrual manner, fatness, lack of breast evolution , acne and / or hirsutism, Lifestyle modality such as exercise , diet, and smoking require estimation and whether to consume any drugs and their influence should be scrutinized . Gynecological enquiry has to recognize age of menarche, menstrual disturbance , infertility and presence of relatives' hirsutism. [12]

Patients and Methods

Selection of patients:

This work was performed at the Obstetric and Gynecological Teaching Hospital in Karbala. It was carried out from July to November 2018. The age of patients and controls groups was (18-38) years. This study was carried on 100 patients with PCOS and 60 healthy individuals as controls, the patients were allocated into (2) groups:

Groups (A): include 50 patients with PCOS since above 1 year (as previously patients group).

Group (B): include 50 patients recently diagnosed with PCOS (as newly diagnosed group).

All patients were tested for fasting serum glucose and fasting insulin level , FSH, LH, progesterone , estradiol (E2), prolactin , testosterone, thyroid stimulating hormone (TSH), free T3, free T4,urea ,creatinine and uric acid were measured by using a ready-made kits and Microalbuminuria was measured by urinalysis reagent strips .

Statistical Analysis

Modeling and featuring of data was accomplished by using SPSS 22.0.0 (Chicago, IL), GraphPad Prism version 8.0.0 for Windows, GraphPad Software, San Diego, California USA, software package applied to predict analytic techniques, p value is counted significant if lower than 0.05.

Results

Hormonal and biochemical change in PCOS groups and control

The data presented in the table (3.1) and in the figures (3.1) indicated serum insulin was significantly elevated in previous PCOS compared to control. The data presented in the figure (3.2), (3.3), indicated a significant different in the HOMA-IR, HOMA-B, among the previous and new PCOS to control patients and in the figure (3.4) the data indicated a significant different in the progesterone among the previous and new PCOS compared to control.

Table 1: Hormonal and biochemical changes

	Control	Old PCOS	New PCOS	p-value
Number	60	50	50	-
Age (years)	28.4 ± 7.5	27.7 ± 5.2	26.9 ± 7.3	0.797
BMI (kg/m2)	29.8 ± 5.4	32.6 ± 4.4	33.6 ± 5.3	0.087
FBS (mg/dl)	119.9 ± 12.6	127.5 ± 17.8	125.7 ± 35.0	0.626
Insulin	11.0 ± 5.2	32.3 ± 38.5	21.1 ± 15.8	0.008 [S]
HOMA-IR	3.3 ± 1.6	11.1 ± 14.5	7.3 ± 8.6	0.014 [S]
HOMA-B	72.1 ± 37.7	161.7 ± 150.2	142.3 ± 126.9	0.006 [S]
Prolactin (ng/ml)	17.1 ± 8.0	17.8 ± 10.3	17.6 ± 8.1	0.971
Progesterone*(ng/ml)	0.7 ± 1.6	4.0 ± 8.4	0.2 ± 0.2	<0.001 [S]
Estrogen*(pg/ml)	37.8 ± 23.7	48.2 ± 44.2	38.6 ± 16.7	0.660
FSH (m.Iu/ml)	6.5 ± 2.0	5.9 ± 2.0	6.2 ± 2.2	0.685
LH* (m.Iu/ml)	5.5 ± 1.8	7.5 ± 5.4	7.7 ± 5.1	0.570
TSH* (uIU/ml)	2.4 ± 1.9	4.5 ± 8.9	2.9 ± 1.8	0.320
T3 (pmol/L)	5.0 ± 0.6	5.1 ± 0.6	5.1 ± 0.5	0.862
T4 (pmol/l)	16.2 ± 2.3	15.5 ± 3.2	16.3 ± 1.9	0.595
Urea (mg/dl)	24.0 ± 7.0	21.2 ± 6.2	22.8 ± 4.5	0.334
Creatinine* (mg/dl)	4.5 ± 13.6	0.6 ± 0.1	0.7 ± 0.5	0.954
Uric acid (mg/dl)	4.3 ± 0.7	4.4 ± 1.2	4.8 ± 1.3	0.409

Results were presented as mean ± SD

Relationship between urea and various variables

The data presented in the table (2) are indicated in the newly diagnosed PCOS; urea is negatively and significnatly coorelated with testesterone. While in previous PCOS urea is directly and signifincatly correlated with progesterone.

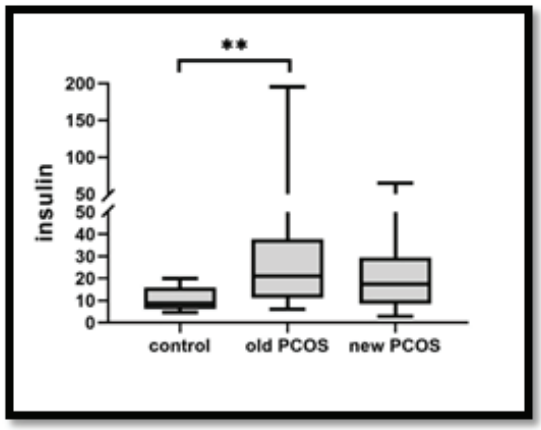

Figure 3.1 Insulin level in control, previously and newly diagnosed PCOSIs considered significantly different (P>0.05)

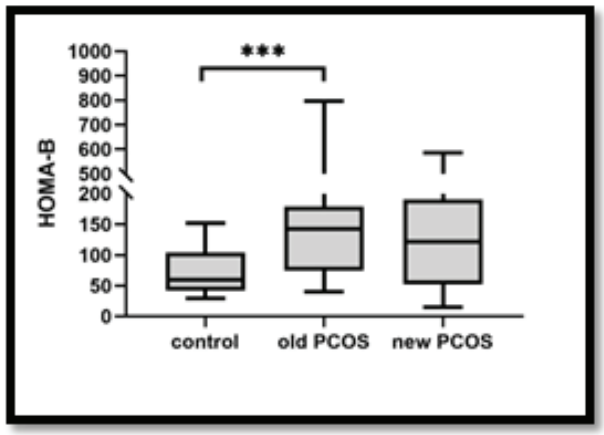

Figure3.3: HOMA-B level in control, previously and newly diagnosed PCOSIs considered significantly different (P>0.05)

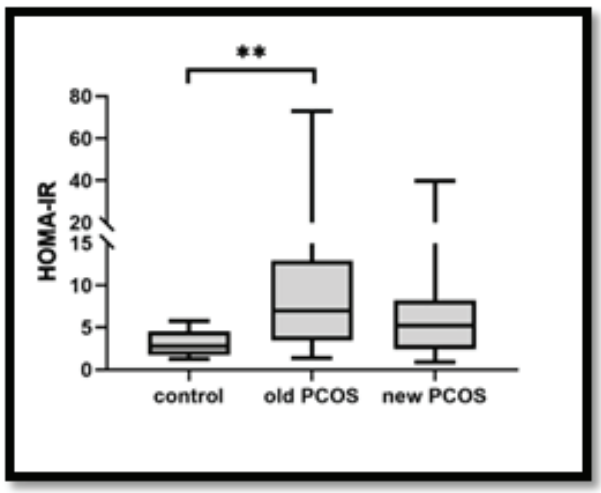

Figure 3.2: HOMA-IR level in control, previously and newly diagnosed PCOs Is considered significantly different (P>0.05)

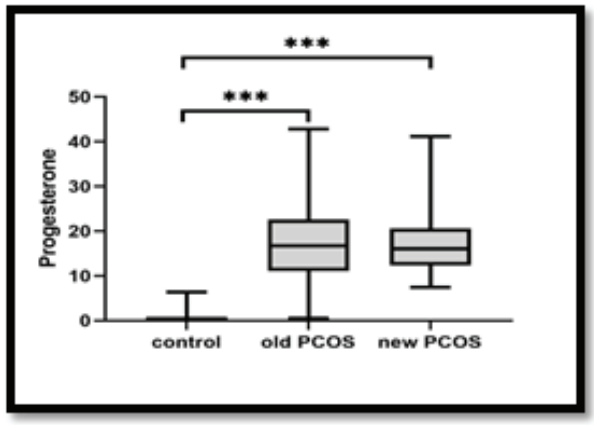

Figure 3.4 progesterone level in control, previous and newly diagnosed in PCOSIs considered significantly different (P>0.05)

Table 2: Relationship between urea and various variables

	Urea			
	Newly diagnosed PCOS		**Old PCOS**	
	Regression coefficient	**p-value**	**Regression coefficient**	**p-value**
Age	0.090	0.706	0.056	0.790
BMI	-0.023	0.923	-0.200	0.339
FBS	0.011	0.962	-0.135	0.519
Insulin	0.173	0.467	-0.170	0.417
HOMA-IR	0.138	0.562	-0.164	0.434
HOMA-B	0.095	0.690	-0.190	0.362

Cont.... **Table 2: Relationship between urea and various variables**

Prolactin	-0.205	0.387	0.150	0.473
Progesterone	-0.030	0.901	0.414	0.040 [S]
Estrogen	-0.146	0.539	-0.179	0.393
Testosterone	-0.552	0.012 [S]	0.254	0.221
FSH	-0.084	0.726	0.141	0.502
LH	0.001	0.995	-0.387	0.056
TSH	-0.312	0.181	0.146	0.487
T3	-0.334	0.150	-0.285	0.167
T4	-0.197	0.405	-0.165	0.430
Microalbuminuria	0.040	0.867	-0.257	0.215

Relationships between creatinine and various variables

The data presented in the table (3.3) indicated direct and significant correlation between creatinine and TSH In previous PCOS.

Table 3. relationship between creatinine and various variables

	Creatinine			
	Newly diagnosed PCOS		**Old PCOS**	
	Regression coefficient	**p-value**	**Regression coefficient**	**p-value**
Age	-0.156	0.511	0.174	0.406
BMI	0.218	0.357	-0.170	0.418
FBS	0.061	0.798	0.065	0.758
Insulin	0.090	0.707	-0.068	0.747
HOMA-IR	0.068	0.777	-0.061	0.771
HOMA-B	-0.012	0.961	-0.108	0.607
Prolactin	-0.315	0.176	-0.019	0.928
Progesterone	-0.328	0.158	0.303	0.141
Estrogen	-0.001	0.998	0.058	0.784
Testosterone	0.175	0.461	-0.043	0.838
FSH	-0.027	0.911	0.093	0.657
LH	0.227	0.336	0.007	0.972
TSH	0.068	0.776	0.537	0.006 [S]
T3	-0.187	0.430	-0.386	0.057
T4	0.188	0.427	-0.328	0.109
Microalbuminuria	-0.307	0.187	0.032	0.878

Relationship between uric acid and various variables

The data presented in the table (3.4) indicated direct correlation between uric acid and BMI, FBS, HOMA-IR and inverse correlation with T3 In newly diagnosed PCOS, while in previous PCOS there was inverse correlation between uric acid and T3.

Table 4: Relationship between uric acid and various variables

	Uric acid			
	Newly diagnosed PCOS		**Previous PCOS**	
	Regression coefficient	**p-value**	**Regression coefficient**	**p-value**
Age	0.068	0.776	0.338	0.099
BMI	0.535	0.015 [S]	0.072	0.731
FBS	0.508	0.022 [S]	-0.209	0.317
Insulin	0.389	0.090	0.156	0.457
HOMA-IR	0.512	0.021 [S]	0.145	0.488
HOMA-B	-0.063	0.793	0.203	0.329
Prolactin	0.116	0.625	-0.013	0.952
Progesterone	-0.441	0.051	-0.016	0.939
Estrogen	-0.149	0.530	-0.081	0.702
Testosterone	-0.443	0.051	-0.073	0.728
FSH	0.183	0.439	0.031	0.884
LH	-0.151	0.525	0.215	0.303
TSH	-0.043	0.857	-0.008	0.970
T3	-0.652	0.002 [S]	-0.452	0.023 [S]
T4	-0.211	0.372	0.197	0.345
Microalbuminuria	-0.010	0.968	0.258	0.213

Relationship between HOMA-IR and various variables

The data presented in the table (3.5) indicated significant correlation between FBS, insulin, HOMA-B and HOMA-IR in previous PCOS while there is correlation between FBS, insulin and HOMA-IR in newly PCOS patients.

Table 5: Relationship between HOMA-IR and various variables

	HOMA-IR			
	Newly diagnosed PCOS		**Previously diagnosed PCOS**	
	Regression coefficient	**p-value**	**Regression coefficient**	**p-value**
Age	0.401	0.080	0.278	0.179
BMI	0.357	0.123	0.085	0.686
FBS	0.804	<0.001 [S]	0.583	0.002 [S]
Insulin	0.911	<0.001 [S]	0.999	<0.001 [S]

Cont ... **Table 5: Relationship between HOMA-IR and various variables**

HOMA-B	0.170	0.472	0.981	<0.001 [S]
Prolactin	-0.142	0.551	0.017	0.936
Progesterone	-0.201	0.396	-0.206	0.323
Estrogen	-0.267	0.255	0.049	0.816
Testosterone	-0.203	0.391	-0.137	0.514
FSH	-0.002	0.995	-0.178	0.395
LH	-0.118	0.621	-0.048	0.819
TSH	-0.221	0.348	-0.170	0.418
T3	-0.383	0.096	0.014	0.946
T4	-0.016	0.945	0.135	0.519
Microalbuminuria	0.178	0.454	0.090	0.669

Discussion

The elevated insulin level in the PCOS women regarding to the table (1) figure (1), (2) indicate that insulin level in the two groups of PCOS women are higher matched to controls. The present study revealed that serum insulin levels in both new and old PCOS were higher than that reported in controls; this attributed to the presence of insulin secretion impairment besides state of insulin resistance. An agent outer to receptor of insulin, supposedly a serine/threonine kinase, impetuses mentioned aberrations and it is a model of paramount neoteric mechanism of resistance of insulin correlated to agents dominating insulin receptor coding. PCOS patients were noted to be insulin resistant, and had beta-cell dysfunction. The data presented in the table (1) figure (3) indicate a significant different in HOMA B function ,HOMA B was significantly higher in old PCOS compared to control.

The homeostasis model assessment (HOMA) is a technique applied to endue an evaluation of beta cell assignment and sensitivity of insulin from glucose levels and serum fasting insulin. In this study also, there is relationship between HOMA-IR with various variables as presented in the table (5):

The results in previously PCOS women showed a significant correlation between HOMA-IR and FBS, insulin and HOMA-B While in newly PCOS women illustrate a significant correlation between HOMA-IR and FBS and insulin. There is a strong association of PCOS with insulin resistance. This can be due to increase process of phosphorylation in insulin receptor proteins, which reduces its protein tyrosine kinase performance leading to abnormal insulin secretion. PCOS patients had significantly higher values of fasting glucose, fasting insulin and HOMA-IR compared with controls. This study clarify a significant elevation in insulin resistance (HOMA -IR) in both newly and previously diabetic patients compared to control and a significant elevation in beta cell assignment (HOMA-B) in previously patients group compared to newly patients group and control group, this increase develops initially to compensate for Hyperinsulinemia, as glucose level increase, beta cell function decreases further but insulin hypersecretion within time lead to beta cell exhaustion.

Conclusion

In newly diagnosed PCOS women the hormones (testosterone, progesterone) may have an effect on the kidney function, while in previous diagnosed PCOS women the hormones (progesterone, TSH) effect on the kidney function.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols

were approved under the Department of Pharmacology and Toxicology and all experiments were carried out in accordance with approved guidelines.

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