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Original Research Article

Evaluation of Insulin, Insulin Resistance LH, and FSHin Women with Polycystic Ovary Syndrome and Diabetic Mellitus Type 2

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Abstract

The polycystic ovary syndrome is one of the most common causes of infertility duo to anovulation in women.In this study there was 105 women, 75 patients of them divided in to three groups, (A) 30 women with diabetic mellitus type 2, (B) 30 women with polycystic ovary syndrome, (C) 15 women with diabetic mellitus type 2 and poly cystic ovary syndrome and 30 women asa control group.In this entire group were analyzed serum fasting glucose, HbA_{1c}, fastinginsulin,IR,LH, FSH, lipid profile, and total anti-oxidant. The result show significant increase in fasting insulin level, and insulin resistance in type 2 diabetic patient group and DMT2+PCOS group compared to those of control also there was a significant increase in level of LH compared to those of control($p<0.05$). Woman with diabetic mellitus type2 and polycystic ovary syndrome have high serum insulin levels and Luteinizing hormone Insulin resistance and compensatoryhyperinsulinemia can inhibit follicular development and ovulation.

Key words: IR,LH, Polycystic ovary syndrome (PCOS).

الخلاصة

متلازمة تكيس المبايض هو واحد من الامراض الشائعة التي تسبب العقم بسبب عدم التبويض. في هذه الدراسة ١٠٥ امراة, ٧٥ من المرضى قسمت الى ثلاثة اقسام (أ) ٣٠ امراة مصابة بمرض السكري النوع الثاني, (ب) ٣٠ امراة مصابة بمرض تكيس المبايض, (ت)١٥ امراة مصابة بكلا المرضين وايضا ٣٠ امراة اصحاء. في هذه المجاميع تم فحص سكر الصيام, السكر التراكمي, الانسولين, LH, FSH, الدهون , ومضاد الاكسدة الكلي. النتائج اظهرت زيادة في مستوى الانسولين ومقاومة الانسولين في المجموعة (ا) والمجموعة (ت) مقارنة مع الكونترول وكذلك هناك زيادة في مستوى هرمون LH مقارنة مع الكونترول($p<0.05$). النساء بمرض السكري النوع الثاني ومرض تكيس المبايض لديهن مستويات عالية من الانسولين ومقاومة الانسولين وهرمون LHوهذا يسبب تثبيط تطور البويضة وعدم التبويض.

الكلمات المفتاحية: متلازمة تكيس المبايض, مقاومة الانسولين, LH

Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrinedisorder affecting 6–21% of reproductive aged women,depending on population studied and diagnostic criteriaapplied is characterized by menstrual irregularity, insulin resistance, [1-4]chronic anovulation and hyperandrogenism, androgen excess, hirsutism, acne. PCOS has beenlinked to obesity,type 2 diabetes mellitus (T2DM), dyslipidemia,hypertension, and heart disease [5-7]. Endocrine abnormalitiesmay include in this syndrome increased free testosterone levels, low sexhormone binding globulin, and high luteinizing hormone/follicle-stimulating hormone ratio [8, 9]Some investigators consider insulin resistance (IR) to be an important risk factor for the development of the metabolic syndrome in women with PCOS [10].

(IR) is now known to be intrinsic to this disorder, present in approximately 50-70 % perphosphorylationcent of these women independent of obesity, and contributing in a major way to its pathogenesis [11]. Women with PCOS are frequently obese which contributes an extrinsic component of IR. It is known that IR progresses towards the development of compensatory hyperinsulinemia, which drives hyperandrogenemia in these women[4]. Excess androgen levels lead to menstrual disturbances, development of ovarian cysts, hirsutism and other related disorders. IR also increases the risk for development of glucose intolerance. T2DM, hypertension, dyslipidemia and cardiovascular abnormalities in these women [12].Hyperinsulinemia and hyperandrogenemia are thus two principal features of PCOS and their cause and effect relationship is still DMT2, however, several evidences suggest hyperinsulin-emia to be the primary factor contributing to the ovarian hyperandrogenemia. Pharmacological reduction of insulin levels has been found to improve hyperinsulinemia as well as hyperandro-genemia and restore ovulation in the women with PCOS. Pathways linking hyperinsulinemia and hyperandrogenemia and related disorders in addition of that, Insulin directly acting on ovary alone or/and along with LH can enhance ovarian androgen production. It indirectly also can increase androgen levels by reducing hepatic production of SHBG (sex hormone binding globulin) and IGFBP-1 (insulin like growth factor binding protein -1) and thus elevates free testosterone and free IGF-I, IGF-II (insulin like growth factor) levels[13].

In this study were analyzed serum fasting glucose, HbA1c, fasting insulin, IR,LH, FSH, lipid profile, and total anti-oxidant.

Materials and Methods

A total of 105 women were studied, 75 patients of themdivided in to three groups, (A) 30women with diabetic mellitus type 2 (15 normal weight and 15 over weight), (B) 30 women with polycystic ovary syndrome (15 normal weight and 15 over weight), (C) 15 women with diabetic mellitus type 2 and poly cystic ovary syndrome.The body max index was increase in this group.These entire group compared with healthy women as apparently control group (n=30).

The diagnosis of PCOS was based on the Rotterdam ESHRE/ASRM criteria from 2003.These criteria include two of the following**:**(Clinical and/or biochemical hyperindrogensim, Oligo-ovulation or anovulation, and polycystic ovaries) [14].

About five milliliters of venous blood was aspirated at day two of the menstrual cycle for all group of patients using disposable syringes. The blood is left for 10 – 15 minutes in room temperature for clotting and then centrifuged at 2000 ×g for 15 minutes and serum were separated and divided into 6 parts in labeled Eppendorf tubes and given a serial number together with the patients names then frozen at -20 C0 until time of use.

In this studyfasting glucose, HbA_{1c}, total cholesterol, TG, HDL, LH, FSH, insulin, and leptin were analyzed. Serum insulin levels was measured by enzyme linked immunosorbent assay kit (ELISA kit).

The homeostasis model assessment for insulin resistance (HOMA-IR) was calculated as fasting Insulin (mg/dl) x Fasting glucose (mg/dl) divided by405.Serum LH, FSH by mini VIDAS, and glucose, HbA1c, lipid profile by spectrophotometer.

Results

By using the *t-test*, there was a significant difference in mean of BMI in C group compared to the control group.There was asignificant increase in mean of fasting glucose, HbA1c, fasting insulin level, and insulin resistance in A and C groups compared to those of control, also there wassignificant ($p<0.05$) increasein mean of LH and total anti-oxidantin all patients groupscompared to those of control. ($p<0.05$), as shown in table(1).

Table 1 : Mean ± SD values of a Demographic and bio chemical characteristics of women with DMT2, PCOS, and DMT2+ PCOS groups comparison with control group.

parameters	Control Mean ± SD	Group A Mean ± SD	Group B Mean ± SD	Group C Mean ± SD
Number	30	30	30	15
Age (years)	34.57 ± 3.74	37.00 ± 3.00	32.67 ± 3.44	34.33 ± 3.35
BMI kg/m^2	24.51 ± 3.11	25.68 ± 2.44	24.42 ± 3.65	28.04 ± 1.06*
Glucose (mg/dl)	90.29±12.15	244.70±71.56*	86.29±10.16	197.07±44.78*
HbA_{1c}%	4.69 ±0.567	8.37 ±1.78*	4.68±0.877	9.09 ±0.936*
Insulin µIU/ml	6.63 ±2.28	9.54 ±3.63*	6.29 ±2.32	12.44 ±5.28*
HOMA-IR	1.45 ±0.45	5.37 ±1.39*	1.31 ±0.43	6.08 ±1.22*
LH mlU/ml	3.59± 1.51	7.02± 6.06*	10.61±4.08*	9.93± 4.43*
FSH mlU/ml	5.71± 2.18	6.11± 2.61	5.57± 3.28	6.98± 3.71
T-AOC (unit/ml)	6.97± 1.99	1.88± 0.88*	3.50± 3.81*	1.15± 0.42*

*significant $p<0.05$

Discussion

The association between IR and hyperindrogensim was described by Poretsky and Kahin [١٥] suggested that insulin acts in concert with several paracrine growth factor as a no pituitarygonadotrophin to modulate several parts of reproductive endocrine system not just ovarian stroma and under normal physiological situation not just pathologies like PCOS [١٦]. Hyperinsulinemia is often associated with increased BMI and insulin stimulates cholesterol transport into arteriolar smooth muscle cells and enhances the cholesterol synthesis and proliferation of these cells [١٧, ١٨]Woman with hyperindrogensim exhibit the worst metabolic features would be the most common clinical syndromes associated with insulin resistance [١٩, 20]. Elevated level of Blood glucose concentration in patients with DMT2 type 2(group A) and patients with diabetic DMT2 and PCOS (group C) may be duo to that blood glucose is not utilizing by all tissue leading to hyperglycemia which agree with (Suilbert R., 2014) [٢١]. Type 2 diabetes is usually preceded a long period of asymptomatic hyperglycemia that may last for years. The elevation of fasting glucose is used for the definition of impaired fasting glucose (IFG) [22].

High level of Luteinizing hormone in patients group compared to control group may association with increase insulin level this agree with study (Barbieri RL., 1988) [٢٣].Insulin resistance and compensatory hyperinsulinemia can inhibit follicular development and ovulation as a result of hyper androgenic intraovarian microenvironment and by altering gonadotropin [24].

In 1975, Berger was the first to emphasize that one can differentiate a separate type of PCOS with normal gonadotropin level. At that time it was not associated with insulin

resistance. Nowadays it is believed that elevated LH level occurs more rarely in a group of patients with insulin resistance and hyperinsulinemia, than in group without hyperinsulinemia [25]. The decrease in TAOC level in group A, B, and C may contributed to the resultant oxidative stress (OS) causes increased tissue/cellular damage manifested by lipid peroxidation and protein oxidation the generation of reactive oxygen species (ROS) is increase in diabetic that is closely associated with oxidative stress that agreement with (Reddy *et al*., 2011; Johanson*et al*., 2005) [26,27], formation of ROS is direct consequence of hyperglycemia, ROS and subsequent OS are believed to play a key role in the pathogenesis of late diabetic complication and causing insulin resistance [28, 29]. The inherent genetic susceptibility may include oxidative stress related candidate genes which may contribute to increased tissue/ cellular damage [30, 31]. Reduce level of total anti-oxidant duo to hyperglycemia, hyperinsulinemia in diabetic increase activity of the enzyme fatty acyl coenzyme A oxidase, which initiates B-oxidation of fatty acids, resulting in lipid peroxidation [32].

Conclusion

Woman with diabetes mellitus type2 and polycystic ovary syndrome have high serum insulin levels and Luteinizing hormone.Insulin resistance and compensatory hyperinsulinemia can inhibit follicular development and ovulation.

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