ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Association among liver enzymes and insulin resistance in Iraqi women with polycystic ovary.

Bushra F Hasan[1], Noor Alhuda Kh Ibrahim[2]*, Dhifaf A Abdulabass[3], ans Shahad F Obeid[1].

[1]Dept of biochemistry, College of Science for Women, University of Baghdad, Iraq
[2]Dept of biochemistry, College of Nursing, University of Baghdad, Iraq
[3]Department of Chemistry, College of Science / University of Al- Mustansiriyah.Baghdad / Iraq

ABSTRACT

This study was conducted to evaluate the liver enzymes as surrogate markers in Iraqi women with polycystic ovary syndrome (PCOS) according to body mass index (BMI) and their association with features of the syndrome**. T**hirty women with PCOS and 30 healthy women as control were studied. Clinical history, height and weight were obtained and metabolic and hormonal parameters were determined. The results revealed that there is a significant difference in serum liver enzymes levels between PCOS women and controls. The prevalence of elevated ALT and AST levels was significantly higher in women with PCOS than healthy control, subjects serum fasting insulin, HOMA – IR, triglyceride and total cholesterol were higher in women with PCOS compared to controls**.** The obesity, androgen excess dyslipidemia and insulin resistance are the main factors related to NAFLD in PCOS.

Keywords: Insulin resistance, liver enzymes, obesity, poly cystic ovary.

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most a common chronic endocrine disorder affecting women of reproductive age. Depending on the definition used for diagnosis the prevalence of the condition is estimated to be between 4% and 25% (1). The two main sets of symptoms typically associated with PCOS are disruption to fertility resulting from irregular menses (oligo menorrhea) or absence of menstruation (anovulation) and clinical signs of hyperandrogenism (including Hirsutism, acne and alopecia) (2). There may be secondary metabolic problems related to obesity and insulin resistance. This combination of outwardly visible and reproduction-inhibiting symptoms makes PCOS a particular distressing disorder suffered by a large number of women (3). For example acne and hirsutism have been identified as major causes of social and emotional stress and psychological morbidity. Irregular menses and infertility issues have been suggested to cause tensions within the family, altered self-perception, impaired sexual functioning and problems in the work place (4). Poly cystic ovary syndrome (PCOS) is the commonest cause of anovulation remains uncertain. The typical gross morphology of an ovulatory polycystic ovaries is the presence of multiple antral follicles 2-8 mm in diameter which signifies arrest of follicle elopement prior to the pre ovulatory phase. Ovulation can be including in most cases by treatment which increases serum concentration of follicle –stimulating hormone (FSH). But while serum levels of FSH are slightly lower than in the early follicular phase of the normal cycle, FSH deficiency is unlikely to be the primary abnormality in PCOS (5, 6).

PCOS is characterized by hyper secretion of LH, and it is possible that this alone may promote premature arrest follicular growth. However, many patients have normal serum concentration of LH. In cells derived form an ovulatory woman with polycystic ovaries, LH stimulated secretion of estradiol and progesterone in Granulosa cells from follicles small as 4 mm. Furthermore, antral follicles around 6-8 mm in diameter produced levels of estradiol and progesterone that were similar of those found in the normal preovulatory follicle (7).

Nonalcoholic fatty liver disease (NAFLD) is one of the most important hepatic manifestations of metabolic disturbances with a spectrum from hepatic steatosis, inflammation, fibrosis to hepatocellular carcinoma. Alanine aminotransferase (ALT), a sensitive indicator of liver cell injury, is a cytosolic enzyme and is thought to be a more specific indicator of liver damage also with aspartate aminotransferase (AST). ALT levels are sensitive in the detection of NAFLD in both obese and non-obese patients with PCOS (8, 9).

Subjects and methods

Thirty women were consecutive patients with PCOS attending PCOS – endocrine unit in medical city of Baghdad hospital, were studied. PCOS was defined according to the Rotterdam criteria (2). participants were diagnosed with PCOS if they had oligo/amenorrhea (menstrual intervals ≥35 days) combined with clinical sings of androgen excess (hirsutism, Ferriman – Gallwey score ≥ 8) and or elevated serum levels of total testosterone. This study excluded of other causes of irregular menstrual cycles, uncontrolled thyroid disease, congenital adrenal hyperplasia, tumor or pregnancy.

A group of 30 normal androgenic and regularly ovulating women, confirmed by progesterone levels on three consecutive cycles, served as the control group. Venous blood was sampled from each patient after a 12 – h overnight fast in the follicular phase of a spontaneous or progesterone induced menstrual cycle for the determination of hormone, liver enzyme, lipid profile, and insulin and glucose levels. This done after a complete history, all women underwent clinical assessment and anthropometric measurements (weight, height). The concentration of serum glucose, serum levels of total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides, AST and ALT were measured with biochemical auto analyzer (COBAS C11).

Serum insulin levels were determined by a micro particle enzyme immunoassay.

Homeostasis model assessment (HOMA) method for insulin resistance was calculated by the formula:-

Fasting serum insulin (micro units/ml) **x** fasting serum glucose (ml mole per liter)/22.5.

Hormones levels were assayed by protocols of kits and reading by TOSO.

ISSN: 0975-8585

RESULTS

Thirty patients with PCO met our biochemical characteristics of the PCO patient are shown in table (1).the clinical ,anthropometric ,and biochemical features of these patients were compared with a group of (30) healthy women of similar age and BMI.

The result of present study show that the mean age of PCO patients (27 ± 5) years, BMI (35± 6) Kg/m^2 range age between (18-35) years, while the mean age of control subjects (27± 4.5) , BMI (26± 3) Kg/m^2 range age between (16-38) years.

Mean of BMI was significantly higher in patients compared to control.

The mean of liver enzymes levels ALT, AST, and ALP were significantly higher in patients (21 ± 7),(6 21±), (106±17)U/L comparing with control (6± 2),(6 ± 2) and (87± 23) U/L respectively p=(0.00001),(0.0008)

The mean of lipid profile levels in PCO patient show non-significant increase comparing to control.

The mean of fasting insulin and HOMA-IR in PCO patient was significantly higher (11±36) UI/L,(2.4±6.7),comparing to control (6±14) UI/L,(1.2±2.7) respectively p=(0.00001).while there non-significant in F.B.G.

The mean of hormones levels FSH, LH, prolactin, and testosterone were significantly higher in patients (19±3.7) (51±),(11± 2.4), (0.7±.0.4) mlU/L comparing with control(14 ± 1) ,(42±),(9± 3) and (0.3±0.1)ml U/L respectively p=(0.00001).

Table (2) show a positive correlation in ALP level with HDL, and, FSH (0.29), (0.34) respectively, whereas they were negatively correlated with Cholesterol and LDL (-0.21),(-0.25) respectively.

ALT level found to be weakly correlated with BMI and LDL (0.22),(0.31) respectively, and negatively correlated with age ,TG. F.B.G and HOMA-IR (-0.30),(-0.52) (-0.20),(-0.20)respectively. Also AST level found to be weakly correlated with HDL (0.27), (0.31) and negatively correlated with TG. and F.B.G (-0.44),(-0.24)respectively

Table 1: Comparison of characteristics study participants and biochemical parameters between patients PCO and control

Parameters	Mean ± SD patient	Mean ± SD control	P value
Age	27 ± 5	27±4.5	0.8
BMI Kg/m^2	35± 6	26± 3	0.00001*
ALP U/L	106±17	87± 23	0.0008*
AST U/L	21± 6	6 ± 2	0.00001*
ALT U/L	21 ± 7	6 ± 2	0.00001*
CHO. mg/dl	195±27	178 ± 27	0.02*
TG. mg/dl	124± 34	118±35	0.4
HDL mg/dl	36 ± 3.5	40±41	0.1
LDL mg/dl	112± 26	107±29	0.3
F.B.G mmol/l	0.7±4.3	0.6±4.2	0.6

ISSN: 0975-8585

Insulin UI/L	11±36	6±14	0.00001*
HOMA IR	2.4±6.7	1.2±2.7	0.00001*
FSH mlU/ml	19±3.7	4 ± 1	0.00001*
LH ml U/ml	5±1	4 ± 2	0.00001*
Pro .mlU/ml	11±2.4	9 ± 3	0.00001*
Testo. mlU/ml	0.7±.0.4	0.3±0.1	0.00001*
* (P<0.01)			

Table 2: Correlation coefficient and p-value between liver enzymes and with other parameters in PCO patients

Parameters	ALP		ALT		AST	
	r	P	r	p	r	p
Age	0.18	0.34	-0.30	0.1	-0.16	0.39
BMI	0.16	0.39	0.22	0.24	0.13	0.49
CHO.	-0.21	0.26	0.01	0.95	0.09	0.63
TG.	0.10	0.59	-0.52	0.003	-0.44	0.01
HDL	0.29	0.12	0.17	0.36	0.27	0.14
LDL	-0.25	0.18	0.31	0.09	0.19	0.31
F.B.G	-0.15	0.42	-0.20	0.28	-0.24	0.2
Insulin	-0.04	0.98	-0.19	0.31	-0.12	0.52
HOMA IR	0.06	0.97	-0.20	0.28	0.18	0.34
FSH	0.34	0.06	0.02	0.91	-0.0006	0.99
LH	0.07	0.97	0.15	0.42	0.06	0.97
Pro.	-0.19	0.31	-0.03	0.87	0.03	0.87
Testo.	-0.009	0.96	0.09	0.63	0.05	0.97

DISCUSSION

POCS is the most common endocrinopathy affecting women of reproductive age. The consequences of the PCOS extend beyond the reproductive axis; perpetual sequence of hormonal and metabolic aberrations in PCOS patients may commence early and extend throughout life. women with this disorder are at substantial risk for developing metabolic abnormalities .in this study, we demonstrated that ALT level was significantly higher in women with PCOS than control subjects as shown in previous studies .we also found the higher levels of AST among women with PCOS .this might be give possible explanation that hyperandrogenemia of POCS is one of the most important determining factors accounting for the elevation of liver enzymes level (10, 11).

Elevated aminotransferase activity as ALT and AST levels might represent the potential degree of chronic liver disease, especially nonalcoholic fatty liver disease (NAFLD) (12).

Hyperandrogenism has not only been reported to be associated with the polycystic ovary morphology in women with PCOS ,but has also been reported to have a strong association with the presence of metabolic syndrome , dyslipidemia , and insulin resistance , independent of obesity, in women with PCOS . The excessive body fat, especially visceral fat contributes to the development of a complex network of potentially serious clinical condition such as insulin resistance, glucose intolerance, dyslipidemia, elevated blood pressure impaired fibrinolysis and endothelial dysfunction. Insulin resistance (IR), a hallmark of metabolic syndrome, is observed in about 50% to 80% of women with PCOS. Insulin resistance assessed using the hemostasis model assessment (HOMA-IR) was inpatients with NAFLD independently of obesity and diabetes (13).

The presence of hyperandrogenism in women with syndromes of extreme insulin resistance was the initiation for the investigation of the possible role of insulin resistance and compensatory hyperinsulinemia in the pathophysiology of PCOS. Metabolic dysfunction in PCOS patient leads to increased risk for cardio vascular disease with aging, particularly after menopause Classic components of an adverse cardiovascular risk profile (cemtrat adiposity, impaired glucose tolerance and diabetes mellitus, dyslipidemia and hypertension) are frequently present in PCOS patients of all ages, occurring in dependently of obesity (14,15). In addition increased levels of several biochemical inflammatory and thrombotic markers of cardiovascular risk are more prevalent in PCOS patients (16).

In conclusion, the findings of our study are consistent with hypothesis that women with PCOS have higher risk of elevated ALT and AST level independent of the confounding effects of obesity and dyslipidemia .Such high prevalence of elevated ALT level in women with PCOS was correlated with androgen level independent of age, insulin resistance, obesity and dyslipidemia.

CONCLUSION

Obesity, androgen excess dyslipidemia and insulin resistance are the main factors related to NAFLD in PCOS.

ACKNOWLEDGMENT

We would like to thank all the patients for their cooperation in completing this study

REFERENCES

[1] March WA, Moore VM, Willson KJ, Phillips DI, Norman RJ, Davies MJ. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. Hum Reprod.2010; 25:544–551.

[2] Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group, 2004 Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod 19: 41-47.

[3] Baranova A, Tran TP, Birerdinc A, Younossi ZM. Systematic review: association of polycystic ovary syndrome with metabolic syndrome and non-alcoholic fatty liver disease. Aliment Pharmacol Ther.2011; 33:801–814.

[4] Panidis D, Tziomalos K, Papadakis E, Vosnakis C, Chatzis P, Katsikis I, 2013 Lifestyle intervention and anti-obesity therapies in the polycystic ovary syndrome: impact on metabolism and fertility. Endocrine 44: 583-590.

[5] Panidis D, Tziomalos K, Misichronis G, et al, 2012 Insulin resistance and endocrine characteristics of the different phenotypes of polycystic ovary syndrome: a prospective study. Hum Reprod 27: 541-549.

[6] Naderi T, Akbarzadeh M, DabaghManesh M, Tabatabaei H, Zareh Z. Frequency of facial and body acne in 14- to 18- year-old female high school students and its relationship to polycystic ovary syndrome. JDC.2011; 2:124–131.

[7] Polycystic ovary syndrome with hyperandrogenism is characterized by an increased risk of hepatic steatosis compared to nonhyperandrogenic PCOS phenotypes and healthy controls, independent of obesity and insulin resistance. J ClinEndocrinol Metab.1997: 3709-3716.

[8] Vassilatou E, Lafoyianni S, Vryonidou A, et al, Increased androgen bioavailability is associated with non-alcoholic fatty liver disease in women with polycystic ovary syndrome. Hum Reprod. 2010; 25: 212-220.

[9] Baranova A, Tran TP, Birerdinc A, Younossi ZM, Systematic review: association of polycystic ovary syndrome with metabolic syndrome and non-alcoholic fatty liver disease. Aliment PharmacolTher. 2011; 33: 801-814.

[10] Vassilatou E, Lafoyianni S, Vryonidou A, et al, Increased androgen bioavailability is associated with non-alcoholic fatty liver disease in women with polycystic ovary syndrome. Hum Reprod. 2010;.25: 212-220.

[11] Sookoian S, Pirola CJ. Alanine and aspartate aminotransferase and glutamine-cycling pathway: their roles in pathogenesis of metabolic syndrome. World J Gastroenterol.2012 ;18:3775–3781.

[12] Gambarin-Gelwan M, Kinkhabwala SV, Schiano TD, Bodian C, Yeh HC, Futterweit W, Prevalence of nonalcoholic fatty liver disease in women with polycystic ovary syndrome. ClinGastroenterolHepatol. 2007;5: 496-501.

[13] Carmina E, PCOS: metabolic impact and long-term management. Minerva Ginecol .2012;64: 501-505.
[14] Panidis D, Macut D, Tziomalos K, et al, Prevalence of metabolic syndrome in women with polycystic ovary syndrome. ClinEndocrinol (Oxf). 2013;78: 586-592.
[15] Marino L, Jornayvaz FR. Endocrine causes of non-alcoholic fatty liver disease. World J Gastroenterol.2015; 21(39):11053 – 76.
[16] Velez LM, Motta AB.,Association between polycystic ovary syndrome and metabolic syndrome.2014;21(35):3999 – 4012.