

Is lipid profile in women with polycystic ovary syndrome related to calcium or magnesium in serum?

هل توجد علاقة بين تراكيز مختلف انماط الدهون وتراكيز الكالسيوم والمغنسيوم في مصول مريضات متلازمة تكيس المبيض؟

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Abstract

Polycystic ovary syndrome (PCOS) is a gynaecological disease that has multiple connections with many diseases. It has been estimated that myocardial infarction is more likely in patients with PCOS. The effect of serum calcium and magnesium on the risk of heart diseases is not yet established. In this work, the lipid profile (total cholesterol TC, triglycerides TG, and very low-density lipoprotein VLDL, and high density lipoprotein HDL-C), serum magnesium, and calcium have been estimated in PCOS patients in comparing with control group. Different atherogenic ratios ((TC/HDL-C, LDL-C/HDL-C, TG/HDL-C, and Log (TG/HDL-C)) were calculated to obtain the best indicative ratios for the risk of cardiovascular diseases. The results showed that there is a significant increase ($p < 0.05$) in TC, TG, and VLDL in PCOS patients as compared with control group. While HDL and serum calcium is decreased significantly ($p < 0.05$) in patients group in comparing with control group. No significant change in serum magnesium and Ca/Mg ratio between both groups. There is no correlation ($-0.50 < \text{Correlation Coefficient } (r) < 0.50$) between different forms of serum calcium and magnesium with each parameter of lipid profile of both groups. The tested atherogenic ratios are significantly increased in PCOS patients in comparing with healthy control. The ratios TC/HDL-C and LDL-C/HDL-C have the lowest p-values indicating the best change predictor between groups. It is concluded that PCOS patients are at higher risk of cardiovascular diseases than control group and the ratios TC/HDL-C ratio and LDL-C/HDL-C are the best atherogenic indices of these diseases. Serum calcium and magnesium are not correlated with lipid profile components even serum calcium is decreased in PCOS patients group.

Key words: Polycystic ovary syndrome, lipid profile, calcium, magnesium, cardiovascular diseases.

الخلاصة

تعتبر متلازمة تكيس المبيض (PCOS) من الامراض النسائية التي لها ارتباط وعلاقة مع انواع اخرى من الامراض. فنسبة الاصابة باحتشاء عضلة القلب يكون اكبر عند مرضى (PCOS) مقارنة بغير المصابات بهذه المتلازمة. ان تاثير التغير في تراكيز الكالسيوم والمغنسيوم في المصل على الاصابة بامراض القلب والشرايين لم يصل الى مرحلة البت النهائي لحد الان. في هذا العمل تم قياس انماط الدهون (الكوليستيرول الكلي TC و الدهون الثلاثية TG والدهون واطئة الكثافة جدا VLDL-C والدهون عالية الكثافة HDL-C). كما اختبرت مختلف نسب الاصابة بتصلب الشرايين (TC/HDL-C و LDL-C/HDL-C و Log (TG/HDL-C) و TG/HDL-C) لمعرفة افضل نسبة معبرة عن احتمالية الاصابة بتصلب الشرايين عند مرضى (PCOS). اظهرت النتائج ارتفاعا معنويا ($p < 0.05$) في تراكيز TC و TG و VLDL-C عند المرضى مقارنة بمجموعة السيطرة. بينما يوجد انخفاض معنوي في تراكيز HDL-C والكالسيوم الكلي في مرضى (PCOS) مقارنة بمجموعة السيطرة. لم يلاحظ وجود تغير معنوي في مستويات المغنسيوم ونسب الكالسيوم الى المغنسيوم في المصل بين المجموعتين. لا توجد علاقة ارتباط ($0.05 < \text{معامل الارتباط } (r) < -0.50$) بين تراكيز الاشكال المختلفة من الكالسيوم والمغنسيوم ومكونات انماط الدهون في مصول مجموعتي المرضى والاصحاء. اظهرت مختلف نسب الاصابة بتصلب الشرايين ارتفاعا معنويا عند مجموعة المرضى مقارنة بمجموعة السيطرة وافضل نسب تشير الى احتمالية التعرض للاصابة كانت النسب التي لها قيم احتمالية (p) اقل في اختبار الطالب (Student t-test) وهما النسبتان (TC/HDL-C and LDL-C/HDL-C). يستنتج من هذه الدراسة ان

مرضى (PCOS) لديهم احتمالية عالية للإصابة بأمراض القلب والشرابيين مقارنة بمجموعة السيطرة وان النسبتين (C)- (TC/HDL-C and LDL-C/HDL) هما افضل مؤشر يمكن حسابه لاحتمالية الاصابة بهذه الامراض. لا توجد علاقة ارتباط محسوبة من قيم معامل الارتباط بين تراكيز الاشكال المختلفة من الكالسيوم والمغنسيوم ومكونات انماط الدهون في مصول مجموعتي المرضى والاصحاء.
مفاتيح الكلمات: متلازمة تكيس المبيض، انماط الدهون، الكالسيوم، المغنسيوم، امراض القلب والشرابيين.

Introduction:

Polycystic ovary syndrome (PCOS) is a very important and common syndrome in women of reproductive age. Several studies have suggested a prevalence of PCOS of 5%–10% in women^(1, 2). PCOS is not only a gynaecological condition affecting women but, also, a comprehensive syndrome with a variety of associated endocrine^(3, 4) and metabolic disorders (insulin resistance, hyperinsulinaemia and dyslipidaemia)^(5, 6).

There is increasing evidence that patients with polycystic ovary syndrome (PCOS) have increased cardiovascular risk compared with age matched controls^(7, 8). It has been estimated that myocardial infarction is seven times more likely in patients with PCOS^(9, 10).

Dyslipidemia is found more frequently in women with PCOS, independently of the excess weight that is often found in PCOS patients⁽¹¹⁾. PCOS women had a high blood pressure and low density lipoprotein cholesterol (LDL-C), and a low high density lipoprotein cholesterol (HDL-C) and HDL-C/total Cholesterol (TC) ratio⁽¹²⁾. Different lipid ratios were used to estimate the risk of cardiovascular diseases. Some studies demonstrated that the TC/HDL-C and the LDL-C/HDL-C ratios are better predictors of Atherosclerosis and cardiovascular disease than any other single lipid marker^(13, 14). Likewise, the TG/HDL-C ratio was demonstrated to be as significant a predictor of cardiovascular disease as the two other lipid ratios⁽¹⁵⁾. Hence, the study of lipid profile in PCOS women is of importance matter to determine the risk of metabolic syndrome and the cardiovascular diseases in those patients.

The minerals are powerful modulators of several physiological functions that can be considerably perturbed in deficiency states⁽¹⁶⁾. The role of magnesium in metabolic and cardiovascular disorders is reviewed by Bo and Pisu (2008)⁽¹⁷⁾. Magnesium plays an important role in the functioning of the cardiovascular system. Magnesium is known to be a cardioprotective agent^(17, 18) despite of the fact that its beneficial effects on acute cardiac dysfunction remain to be elucidated. Magnesium deficiency is one of the most frequent electrolyte abnormalities in clinical practice⁽¹⁹⁾ that linked with hypertension⁽²⁰⁾, coronary artery diseases⁽²¹⁾, tachydysrhythmias, and increased mortality in patients with congestive heart failure and after an acute myocardial infarction⁽²²⁾.

The proper amount of elements including calcium and magnesium is helpful in preventing cardiovascular perturbations⁽²³⁾, reduce blood pressure, and coronary heart disease^(24, 25). Serum levels of calcium, total cholesterol, low-density lipoprotein and triglycerides were elevated in a higher proportion of ischemic heart disease patients, compared to controls.⁽²⁶⁾

Different clinical studies showed a beneficial modification of lipid profiles, especially decrease serum cholesterol, was observed after long-term supplementation with calcium preparations^(27, 28, 29).

The objective of the present work is to identify the possible risk of cardiovascular diseases using different lipid ratios (TC/HDL-C, LDL-C/HDL-C, TG/HDL-C, and Log (TG/HDL-C)⁽³⁰⁾, in women with PCOS. Additionally, to study the correlation between lipid profile and the level of each serum calcium and magnesium in PCOS patients.

Materials and Methods:

Sixty-five women with PCOS (mean age=23.3± 6.9 years). Patients with PCOS were recruited from the gynecological clinics in Najaf, Iraq. PCOS was diagnosed according to the criteria of Rotterdam

revised consensus meeting in 2003 ⁽³¹⁾. It was proposed that oligomenorrhoea, clinical or biochemical hyperandrogenaemia and the presence of polycystic ovaries should serve as the diagnostic criteria for PCOS ⁽³¹⁾. Control subjects were 33 healthy control women with a normal menstrual cycle and with no clinical features of hyperandrogenism. Serum lipid profile (total cholesterol, triglyceride, high density lipoprotein (HDL) cholesterol were measured by spectrophotometry; LDL-cholesterol was calculated using Friedewald's formula (LDL-cholesterol= total cholesterol minus HDL-cholesterol minus triglycerides/2.19). Serum calcium and magnesium were measured spectrophotometrically using Spinreact[®]-Spain and Human[®]-Germany kits, respectively.

Serum ionized calcium levels were estimated using the following equation ^(32, 33):

$$\text{Ionized calcium} = \frac{((6.25 * (\text{total calcium}) - ((\text{total protein}) * 3/8)) / ((\text{total protein}) + 6.5))}{1}$$

While serum magnesium levels were calculated according to the following formula ⁽³⁴⁾:

$$\text{Ionized magnesium in mmol/L} = (0.66 * (\text{total magnesium in mmol/L})) + 0.039$$

Statistical analysis used in this work involve pooled student-t-test for the comparison between the data of patients and control groups. The difference is significant if probability value (p) is less than 0.05. The correlation coefficient (r) values were calculated for the parameters of each group to estimate the correlation between them.

Results:

The biochemical results of PCOS patients and control group are shown in Table (1).

Table (1): Biochemical results of PCOS patients and control group expressed as (mean±standard deviation). The change is significant when (p<0.05).

Parameters	PCOS	Control	p-value
TC (mmol/L)	5.76±0.95	4.9±0.71	1.21E-05
TG (mmol/L)	2.65±0.81	2.11±0.59	0.0009
VLDL (mmol/L)	1.21±0.37	0.96±0.27	0.0009
HDL-C (mmol/L)	1.09±0.25	1.25±0.31	0.012
LDL-C v (mmol/L)	3.46±0.93	2.69±0.77	7.73E-05
TC/HDL-C	5.4±0.9	4.2±1.1	3.12E-07
TG/HDL-C	2.56±0.98	1.85±0.85	0.0006
log(TG/HDL-C	0.37±0.18	0.23±0.19	0.0004
LDL-C/HDL-C	3.24±0.82	2.31±0.91	4.99E-06

It is noticed that there is a significant increase (p<0.05) in total cholesterol, TG, VLDL, and LDL-C in PCOS patients as compared with control group. While HDL-C and serum calcium is decreased significantly in patients group in comparing with control group. There is a significant increase (p<0.05) in total and ionized calcium in PCOS patients in comparing with healthy control group.

From Table (2), there is no significant change in serum total and ionized magnesium between both groups. Total and ionized Ca/Mg ratios showed a significant increase (p<0.05) in PCOS group as compared with healthy control group.

Table (2): The results of different forms of Ca and Mg PCOS patients and control group expressed as (mean±standard deviation). The change is significant when (p<0.05).

Parameters	PCOS	Control	p-value
Ca (mmol/L)	2.45±0.14	2.33±0.15	0.0064
Ionized Ca (mmol/L)	1.02± 0.08	0.96±0.09	0.0011
Mg (mmol/L)	0.97±0.27	1.03±0.23	0.1573
Ionized Mg (mmol/L)	0.61± 0.16	0.65±0.13	0.2134
Ca / Mg	2.64±0.68	2.29±0.85	0.084
Ionized Ca / Ionized Mg	1.79±0.43	1.63±0.32	0.063

The tested atherogenic ratios (TC/HDL-C, TG/HDL-C, and LDL-C/HDL-C and log(TG/HDL-C)) are significantly increased in PCOS patients in comparing with healthy control. From the p-values listed in Table (1), it is noticed that the comparisons between groups of TC/HDL-C ratio and LDL-C/HDL-C have the lowest p-values (3.10863E-07 and 4.99093E-06 respectively) indicating the best change predictor between groups. There is no correlation between each elements (total and ionized forms), Ca and Mg, with all the measured lipid parameters (depending on correlation coefficient values).

Discussion:

The result of the present work (Table 1) showed severe dyslipidemia in PCOS patients in comparing with healthy control group. The level of HDL-C decreases significantly while TC, TG, and LDL-C increase significantly. These results are in agreement with many previous studies^(11, 12, 35, 36, 37). However, some other studies showed different profiles. Bickerton et al (2005)⁽³⁸⁾ found that there were no significant differences in Lipid or lipoprotein concentrations between the women with PCOS group and controls. Yilmaz et al (2005)⁽³⁹⁾ found no difference in serum TC, LDL-C, TG, levels between PCOS and control groups, whereas HDL-C was lower. Vrbíková (2003)⁽⁴⁰⁾ showed serum TC and TG did not differ significantly between PCOS and healthy women groups while HDL-C was lower and LDL-C was higher in PCOS than in controls

PCOS is associated with a more pronounced atherogenic Lipid profile and it seems to constitute an additional risk factor for an atherogenic Lipid profile⁽³⁷⁾. Changes in serum Lipid profile, which are possible risk factors for cardiovascular disorders, play important roles in the development of cardiovascular disease in both obese and non-obese patients with PCOS⁽³⁹⁾. Increased serum concentration of LDL-C is atherogenic, whereas increased HDL-cholesterol (HDL-C) is considered cardioprotective⁽⁴¹⁾. Hence, the present of high LDL-C and low HDL-C in PCOS patients made them at high risk of cardiovascular diseases. Many explanations have been postulated for the increased cardiovascular risk in PCOS including endothelial dysfunction⁽⁴²⁾, hyperandrogenism⁽⁴³⁾, increased oxidative stress and decreased antioxidant capacity⁽⁴⁴⁾ and abnormal Lipid metabolism⁽⁴⁵⁾. Increased serum concentrations of triglycerides (TGs) have also been recognized as a risk factor for cardiovascular disease⁽⁴⁶⁾. Serum triglyceride level is well known to be increased in obese individuals. Obesity might thus be considered the most important factor aggravating cardiovascular risks in PCOS women, just as it is in the general population⁽⁴⁷⁾.

Low HDL-C has been reported to be the most important lipoprotein profile predictor for the occurrence and mortality of cardiovascular disease especially in PCOS women^(48, 49). Some studies showed that more than half of PCOS women had a decrease in high-density lipoprotein (HDL) cholesterol⁽⁵⁰⁾. In the present work, 43.2% of PCOS patients have increase HDL-C.

The increase in (TC/HDL-C, TG/HDL-C, and LDL-C/HDL-C) ratios and decrease in log(TG/HDL-C) indicates an increase in the atherogenic risk in PCOS patients as compared with healthy control group. PCOS women are at high risk to cardiovascular disorders and the frequent monitoring is required to early diagnosis of these disorders. From the Table (1), depending on the p-values, TC/HDL-C ratio and LDL-C/HDL-C are the most important ratios for the prediction of the risk of cardiovascular disorders. Orio et al (2004)⁽⁵¹⁾ showed that, PCOS women had higher TC and LDL-C, and TC/HDL-C and lower HDL-C levels than controls which are in accordance with the results of the present work.

It is hypothesized that it is the ratio of TG/HDL-C in the plasma that determines the esterification rate of cholesterol⁽⁵²⁾. Furthermore, increased TG/HDL-C ratios also indicate the presence of atherogenic small, dense LDL particles^(52, 53), could serve as a good predictor of myocardial infarction⁽¹⁵⁾, and the presence of coronary atherosclerotic lesions⁽⁵⁴⁾. The increase in the Log (TG/HDL-C) in patients suggesting a more frequent occurrence of the atherogenic phenotype in these individuals. This parameter indicates the individuals' atherogenic risk, particularly when plasma Lipids are within the normal range⁽³⁰⁾.

The changes in serum Ca and Mg concentrations can affect such entities as the vasculature, synaptic transmission, and excitation-secretion coupling⁽⁵⁵⁾. Muneyvirici-Delale et al⁽⁵⁵⁾ found a change in the serum ionized Mg, Ca, and Ca/Mg ratio with the changes of the menstruation phases. A decrease in ionized Mg was found with increased testosterone levels. Serum calcium showed an increase in PCOS patients as compared with healthy control women. Some studies focused on the role of calcium intake on heart diseases and found various correlations. A positive effect of calcium supplementation on the treatment of patients with hypercholesterolaemia was found in one study⁽⁵⁶⁾. Furthermore, a high calcium intake is associated with a plasma lipoprotein-lipid profile predictive of a lower risk of coronary heart disease risk compared with a low calcium intake. The daily calcium intake was negatively correlated with plasma LDL cholesterol, total cholesterol, and HDL cholesterol⁽⁵⁷⁾. However, in the present work revealed and research by, the level of serum Lipids is not correlated with the serum calcium.

Table (2) showed no significant change in serum magnesium in PCOS patients as compared with control group. Although Mg does not seem to increase lipoprotein synthesis; it may be involved in the regulation of some enzymes responsible for lipoprotein synthesis⁽⁵⁸⁾, while there was a trend toward an increase of triglyceride levels with increasing magnesium levels. This could be due to changes in hepatic triglyceride metabolism induced by magnesium⁽⁵⁸⁾. This is not the same case in our research. Experimentally induced low plasma levels of magnesium accelerate atherogenesis by increasing LDL concentrations and their oxidative modifications, and by promoting inflammation⁽⁵⁹⁾.

There are some evidences about the correlation between sex hormones and ionized magnesium and calcium in the blood, serum estrogen and progesterone levels in women modulate the blood levels of circulating ionized Mg and the serum ionized Ca/Mg ratio⁽⁶⁰⁾. However, the correlation between testosterone, which increased in PCOS patients, to serum magnesium is not established yet.

There is no correlation between serum Ca and Mg with lipid profile parameters in the present work according to the correlation coefficient (r) values which is less than 0.50 for all correlations (data not included). Few studies showed a possible such correlation i.e., increased dietary magnesium intake ameliorates insulin resistance and serum lipid profiles⁽¹⁷⁾. Muneyvirici-Delale et al (2001)⁽⁶¹⁾ found significantly lower serum ionized and total magnesium and a significantly higher serum Ca^{+2}/Mg^{+2} ratio, a measure of cardiovascular problems, in the PCOS patients compared with the controls⁽⁶¹⁾.

Conclusions: It is concluded that PCOS patients are at higher risk of cardiovascular diseases than control group and the ratios TC/HDL-C ratio and LDL-C/HDL-C are the best atherogenic indices of these diseases. Serum calcium and magnesium are not correlated with lipid profile components even serum calcium is decreased in PCOS patients group.

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