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Serum Liver enzymes activity and some minerals level in the polycystic ovary patients in Salah Al-Deen governorate

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ABSTRACT

Polycystic ovary syndrome (PCOS) represents a commonly encountered metabolic- endocrinopathy that affects young women all over the world. It is characterized by hyperandrogenism, infertility and menstrual irregularity; as well as by being heterogeneous. PCOS was found to be associated with diabetes, insulin resistance, obesity and metabolic syndrome in large number of patients.

The aim of this study is to investigate the effect of this syndrome and its treatment on several parameters. To do so, 77 blood samples (from women in the reproductive age group) were collected in the private outpatients' clinics of Salah Al-Din governorate. The samples were divided into three groups (control, untreated PCOS and treated PCOS).

Their age, weight, length, medication history data were collected and biochemical tests were carried out to investigate the levels of liver enzymes (Serum glutamic oxaloacetic transaminase (SGOT), Serum glutamic pyruvic transaminase (SGPT), alkaline phosphatase (ALP) and serum phosphorus and iron. The average age was (26.23 ± 0.73 years) and the average body mass index (BMI) was in the overweight zone (26.57 ± 0.78).

We concluded that liver enzymes showed a trend of decreased levels of ALP and SGPT in the treated PCOS group compared to the control; and the decrease in the level was statistically significant in the ALP but was not significant in the SGPT. There was no significant difference in the SGOT levels.

Serum minerals assessment did not show any difference in the phosphorus level, while iron was lower in the treated group but it wasn't statistically significant.

Introduction

Leventhal and Stein were the first to report and link a group of conditions in female patients, these conditions are a triad: (polycystic ovary, hirsuitism and oligo-menorrhoea), and they reported them as PCOS in 1935.[1] Despite the advancement over the last two decades in the diagnosis of this syndrome and in the understanding of its pathophysiology, this syndrome is still underdiagnosed[2] In the reproductive age group women, PCOS represents the most common endocrine-metabolic disorder [2].

Polycystic ovary syndrome (PCOS) is one of the most commonly encountered conditions in the pre-menopausal women in the obstetrics and gynecology clinics. The affected women are usually in the reproductive age group and they usually present with a constellation of symptoms of endocrinological disturbances of which irregular menstrual cycle is a common presentation; side by side with features of hyperandrogenism and a polycystic ovary. This syndrome encompasses endocrine and metabolic pathologies in the affected women[3,4].

This syndrome is characterized by its complexity and having multiple factors playing a role in its pathogenesis. These factors could be environmental factors, genetic predisposition and epigenetic changes. The main driver of PCOS is having

excessive amount of androgen hormone. This increase in the amount of the hormone leads to several presentations including excessive hair growth, disturbance of the metabolism as well as it might affect the fertility. These signs and symptoms might lead to negative effects on the affected patients' life[3].

One of the most common presentations are irregularities in the menstrual cycle reflected in infrequent or light menstrual periods called (oligomenorrhoea) or absence of the menstrual period or (amenorrhoea). These are frequently associated with decreased fertility or even the patient will be infertile. The other very frequent presentation is excessive growth of abnormal hair on areas of the body that is called (hirsuitism), in addition to acne[4,5].

PCOS prevalence varies considerably and it was reported to affect between four to eight percent of women in the reproductive age group although other studies have reported variable incidence rates[3,4].

This syndrome was found to be predisposed by and associated with several metabolic diseases. Diabetes is the most commonly encountered metabolic disease associated with PCOS. Other metabolic diseases include obesity, insulin resistance, metabolic syndrome, hypertension, and dyslipidemia [3].

It performs a process called gluconeogenesis in which two of the involved enzymes are used as markers of liver injury. Those enzymes are aminotransferases, the first is aspartate aminotransferase (AST) or SGOT which transfers amino group from aspartic acid to ketoglutaric acid to produce oxaloacetic acid, and the other one is alanine aminotransferase (ALT) or SGPT which transfers alanine to ketoglutric acid to produce pyruvic acid. AST is present in the liver and many other organs, like the heart, myocytes, pneumocytes, neurons and pancreatic cells. This enzyme present in the cytoplasm and in the mitochondria. ALT on the other hand is specific to the hepatocyte cytoplasm and the increase in both enzymes denotes hepatocellular injury. They also increase in obese people and in those with a high body-mass index. [6].

Alkaline phosphatase (ALP) is another enzyme that is found in the canaliculi of the biliary channels in the liver. This enzyme is present in other tissues like the bone, placenta and the intestine. When there is obstruction to the biliary tree, the enzyme level increases, e.g. bile duct obstruction due to stones and cancer of the head of the pancreas, cirrhosis and in cholestasis. It also increases in cases of bone disease and in pregnant women and in chronic disease of the kidney and during growth of children[7].

In addition to its role in the musculoskeletal system, phosphorus is a key element that enters in a large number of metabolic processes the most important of which is the regulation and production of energy through its role in the adenosine triphosphate (ATP) formation that is the unit of energy for intracellular processes as we'll as its role in the genetic material maintenance in RNA & DNA[8]. Disturbances in phosphorus metabolism lead to abnormalities in the bone, renal problems (stones), myopathies and abnormal depositions in the soft tissues[8] .

Iron in the body is mainly bound and free iron is minimal due to its toxic effect on the cells through induction of radical injury to the cell. Therefore excess iron (whether due to increased intake or hereditary disorders) will lead to toxic damage of the body tissues and mainly the liver is affected. On the other hand, reduced intake and deficiency will manifest as iron deficiency anaemia.[9, 10].

Material and methods

Study Design

A total of 77 blood samples were collected in the private outpatients clinics of Salah Al-Din governorate for the period extending between the 28th of August 2020 till the 15th of January 2021. The age range was between 18-45 years old. An interview was carried out with these patients using questionnaire form designed by the investigator and was filled with data about their age, weight, length, and medication history. Out of the seventy seven samples, 57 patients had polycystic ovary syndrome, and those were further divided into two groups. Untreated PCOS included thirty patients who did not receive any treatment and the second group was Treated PCOS group and included twenty-seven patients who had taken the treatment for this disease. The remaining twenty samples were of healthy women and were the control group.

Sampling and preparation

Five milliliters of venous blood were collected from all the aforementioned women. Blood samples were centrifuged at 3000 rotation per minute (rpm) for 15 minutes, if a clot was formed then it had to be removed and the sample was re-centrifuged at 3000 rpm for 15 minutes and the obtained serum was aspirated using mechanical micropipette and transferred into clean test tubes. Then each sample was labelled and stored in the deep freezer at -20°C for biochemical measurement. The level of AST, ALT, ALP, phosphorus, iron, were assessed in each sample.

Estimating the level of biochemical variables:

The level of AST, ALT, ALP, phosphorus, and iron, were estimated according to the instructions of the kit's leaflet. The principle is via colormetric method by using the spectrophotometer and measuring a absorbance at a specified wavelength.

No.	Chemicals	Source	Kit number
1	Iron kit	Barcelona(Spain)	Biosystems 11509
2	Phosphorus kit	Barcelona(Spain)	Biosystems 11508
3	ALP KIT	Northen Ireland	Liquicolor no.FT677
4	AST KIT	Northen Ireland	Randox AL 147
5	ATP KIT	Northen Ireland	Randox AL 146

Statistical Analysis

All data were presented as the Mean ± standard error of the mean (SEM) unless otherwise specified. The p-

value was calculated using Microsoft Office, and GraphPad Prism 6 software with a p-value of < 0.05 considered statistically significant at the 95% confidence level. Paired and unpaired t-tests and one way ANOVA were used as appropriate for the comparison data type unless otherwise specified.

Results discussion

Liver function

Assessment of liver function test was included in the current study, and it involved three enzymes' levels, ALP, SGOT and SGPT.

Serum Alkaline phosphatase (ALP)

The overall serum ALP level (7.11 ± 0.26 IU/L) was within the normal range of (3-13 IU/L). The average ALP levels showed a decrease in those women with PCOS with and without treatment compared to the control. There was no significant difference across the three groups (p=0.083) (see table 1), that was probably due to the small sample size. A further detailed statistical analysis was carried out comparing the individual groups to the control showed a significant difference (p=0.012) between the control and the treatment groups (see figure 1). There was no significant difference between the treated and the untreated groups (p=0.18) nor between the untreated and the control groups (p=0.35) (see figure 1).

Table 1: Serum ALP levels in all of the study groups.

Groups	Serum ALP (IU/L) Mean ± SEM	p value One-way ANOVA
Control n=20	7.9 ± 0.50	0.083
Untreated (PCOD) n=30	7.21 ± 0.48	
Treated (PCOD) n=27	6.41 ± 0.32	

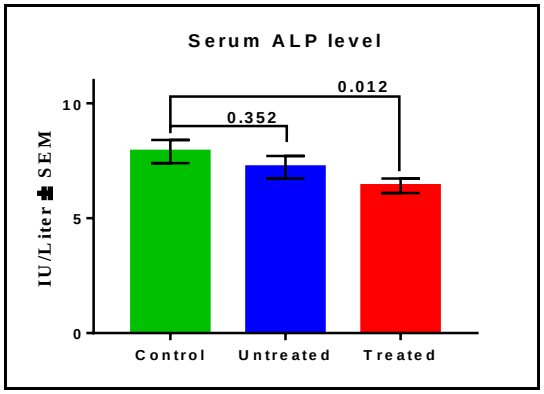

Figure 1: Serum ALP levels of the study groups. Data represents the mean ± standard error of the mean (SEM).

Serum Alanine transaminase

Assessment of serum SGPT enzyme levels average ((5.36 ± 0.30) has shown it to fall within normal range of up to 12 U/L. The average level of SGPT was (5.9 ± 0.47, n=20) in the control group, (5.6 ± 0.56, n=30) in the untreated group and (4.7 ± 0.47, n=27) in the treated group. Graphical presentation has shown a trend of decrease in the SGPT levels in the PCOS and treatment groups respectively compared to the control group, but this decrease was not significant statistically when the data were analysed across the three groups (p=0.263) (table 2); nor even when comparing individual groups (p= 0.71, 0.089, 0.23) for the control vs the untreated, control vs treated and treated vs untreated respectively (see figure 2).

Table 2: Serum ALT levels in all of the study groups.

Groups	Serum SGPT (U/L) Mean ± SEM	p value One-way ANOVA
Control n=20	5.9 ± 0.47	0.263
Untreated (PCOD) n=30	5.6 ± 0.56	
Treated (PCOD) n=27	4.7 ± 0.47	

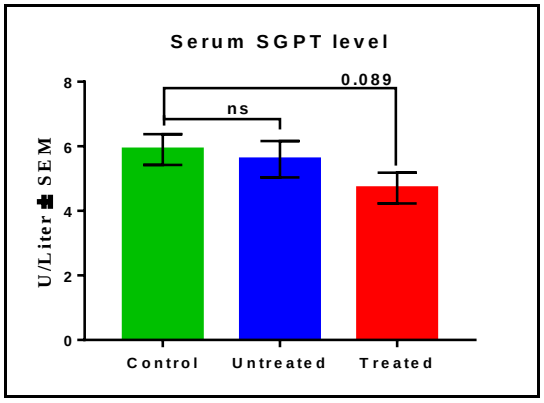

Fig. 2: Serum ALT levels of the study groups. Data represents the mean ± standard error of the mean (SEM). ns means non-significant.

Serum Aspartate transaminase

Serum SGOT analysis showed that the overall average level of this enzyme was within the normal range of up to 12 U/L. It was (6.1 ± 0.51, n=20) in the control group, and (6.03 ± 0.41, n=30) in the untreated group and (5.88 ± 0.46, n=27). Statistical analysis showed no significant difference neither between the individual groups (control vs untreated p=0.91, control vs treated p=0.76, treated vs untreated p=0.81) nor between the three groups (p=0.949). (See Table , Figure 3).

Table 3: Serum SGOT levels in all of the study groups.

Groups	Serum SGOT (U/L) Mean ± SEM	p value One-way ANOVA
Control n=20	6.1 ± 0.51	0.949
Untreated (PCOD) n=30	6.03 ± 0.41	
Treated (PCOD) n=27	5.88 ± 0.46	

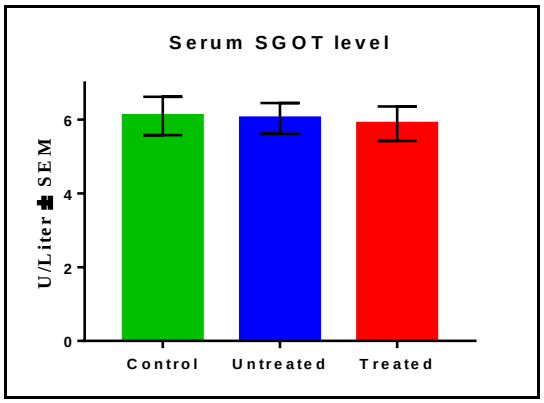

Figure 3: Serum SGOT levels of the study groups. Data represents the mean ± standard error of the mean (SEM).

Serum Phosphorus

The overall average of serum phosphorus was (3.51 ± 0.04 mg/dL) and it is within the normal range of (2.5-4.5 mg/dL). In the control group the average level was (3.61 ± 1.01, n=20), and (3.48 ± 0.07, n=30) in the untreated group, and (3.46 ± 0.07, n=27). Statistical analysis showed no significant difference neither between the individual groups (control vs untreated p=0.23, control vs treated p=0.26, treated vs untreated p=0.84) nor between the three groups (p=0.467) (See Table 4).

Table 4: Serum phosphorus levels in all of the study groups

Groups	Serum phosphorus (mg/dL) Mean ± SEM	p value One-way ANOVA
Control n=20	3.61 ± 1.01	0.467
Untreated (PCOD) n=30	3.48 ± 0.07	
Treated (PCOD) n=27	3.46 ± 0.07	

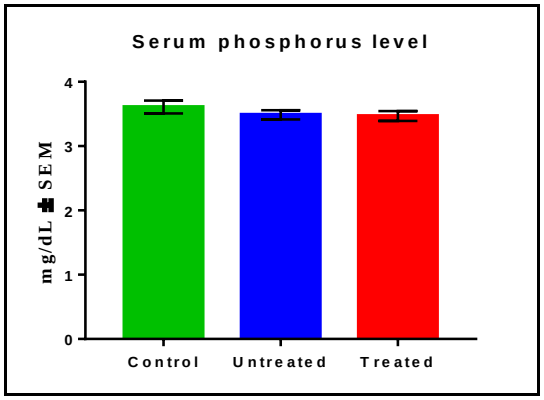

Fig. 4: Serum phosphorus levels of the study groups. Data represents the mean ± standard error of the mean (SEM).

Serum Iron

Serum iron was another essential mineral to be analysed in this study. The overall average of serum iron level was (144.40 ± 7.73 µg/dL), and it was within the normal range for women (50-170 µg/dL). It was (159.8 ± 18.63, n=20) in the control group, and (148.7 ± 11.06, n=30) in the untreated group and (128.2 ± 21.14, n=27). Although the plotted figure showed a trend of a negative effect of both the PCOS and treatment on the serum iron level, statistical analysis showed no significant difference neither between the individual groups (control vs untreated p=0.58, control vs treated p=0.14, treated vs untreated p=0.21); nor among the three groups (p=0.264) (See Table 5, Figure 5).

Table 5: Serum iron levels in all of the study groups.

Groups	Serum iron (µg/dL) Mean ± SEM	p value One-way ANOVA
Control n=20	159.8 ± 18.63	0.264
Untreated (PCOD) n=30	148.7 ± 11.06	
Treated (PCOD) n=27	128.2 ± 21.14	

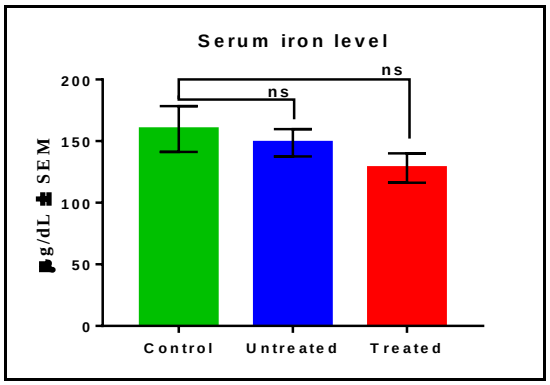

Fig. 5: Serum iron levels of the study groups. Data represents the mean ± standard error of the mean (SEM)

Discussion

Liver function is one of the variables that can be affected in patients with obesity and metabolic syndrome. Since it is well known that a large percentage of PCOS patients might have metabolic syndrome or obesity with or without insulin resistance; therefore; assessment of liver enzymes levels was included in the current study to have a better understanding of the relationship between liver function and the PCOS status. Despite the fact that the majority of our patients and control were overweight (reflected by their high BMI as mentioned before), the liver enzymes were within the normal range. Unexpectedly the liver enzymes level in the PCOS groups were lower than that of the control group and this was true in all of the assessed enzymes (SGOT, SGPT & ALP). ALP was significantly lower in the treated group than the control group.

[11] showed that the liver enzymes (SGOT & SGPT) were within normal range in PCOS patients in their study, and this comes in agreement with our results, but the enzymes levels were significantly higher in PCOS patients with high BMI compared to those with normal BMI. [12] assessed liver function in parallel to the BMI in PCOS patients. They classified their groups into PCOS with metabolic syndrome and PCOS without metabolic syndrome. Liver enzymes (SGOT & SGPT) were significantly higher in those with metabolic syndrome compared to those without it although the levels of the enzymes were within normal range in both groups. The above findings are rational as the higher the BMI might means higher fat content of the liver and therefore higher enzyme levels reflecting liver injury due to obesity. One caveat that needs to be kept in mind is that both papers (Won *et al* & Cai *et al*) did not have a control group to compare their findings with, but only disease groups with or without other conditions. One explanation for the difference between our results (lower levels of liver enzymes in PCOS) and the above two papers' results (high liver enzymes in disease groups) might be the role of the level of Sex hormone-binding globulin (SHBG). It is a glycoprotein synthesized by the liver and plays a role in regulating the hormones levels. It was found to be

inversely related to the severity of metabolic syndrome and liver enzymes elevation[13]; so low levels of SHBG were associated with high liver enzymes. Therefore the PCOS patients in our study might have had high levels of this glycoprotein and therefore had in turn low levels of the liver enzymes.

[14] found that PCOS patients had considerably higher levels of serum phosphorus than the control group. Furthermore, this high level was associated with insulin resistance in PCOS patients; however, phosphorus measurements in the current investigation revealed no significant differences between the study groups.

[14] also showed that there is no difference between PCOS group and the control group in regard to serum iron level. Although in that study there was lower level of serum iron in the PCOS group, but this low level in comparison with the control group was not statistically significant (p=0.72). This is in concordance with the current study results that showed similar findings. In the current study the serum iron level in the PCOS groups was lower than the control group but it wasn't statistically significant (p=0.264).

Conclusions

PCOS is a condition that affects women in their reproductive age in Salah-al Deen governorate, and it has an impact on their blood levels of several parameters. Despite the fact that all of the analyzed parameters were within normal limits, PCOS had a substantial impact on serum calcium (higher levels) and iron levels (lower levels) in the current investigation.

PCOS had a lowering effect on liver function reflected by the reduction of liver enzymes in PCOS patient, although the only statistically significant of them was alkaline phosphatase.

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فعالية إنزيمات الكبد وبعض المعادن في المريضات المصابات بتكيس المبايض في محافظة صلاح الدين

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الملخص

يمثل مرض تكيس المبايض اعتلالًا شائعًا في التمثيل الغذائي للغدد الصماء يصيب النساء في جميع أنحاء العالم. يتميز هذا المرض بفرط الأندروجينات والعقم وعدم انتظام الدورة الشهريةويرتبط مرض تكيس المبايض بمرض السكري ومقاومة الأنسولين والسمنة ومتلازمة التمثيل الغذائي.

صمم البحث الحالي لدراسة تأثير هذه المتلازمة على عدة عوامل وعلاجها. للقيام بذلك ، تم جمع 77 عينة دم (من النساء في سن الإنجاب) في العيادات الخارجية الخاصة بمحافظة صلاح الدين. تم تقسيم العينات إلى ثلاث مجموعات (مجموعة السيطرة ، مجموعة المابات بمتلازمة تكيس المبايض بدون علاج, و مجموعة المصابات بتكيس المبايض مع العلاج).

تم جمع بيانات العمر والوزن والطول والتاريخ الدوائي وأجريت اختبارات الكيمياء الحيوية للتحقق من مستويات إنزيمات الكبد (SGOT، SGPT، ALP) و كل من المعادن في المصل وهي (الفوسفور والحديد). كان متوسط العمر (26.23 ± 0.73 سنة) ومتوسط مؤشر كتلة الجسم (BMI) في منطقة الوزن الزائد (26.57 ± 0.78).

أظهرت إنزيمات الكبد اتجاهًا لانخفاض مستويات ALP و SGPT في مجموعة متلازمة تكيس المبايض PCOS المعالجة مقارنةً بالمجموعة الضابطة وكان الانخفاض في المستوى ذا دلالة إحصائية في ALP ولكنه لم يكن مهمًا في SGPT. لم يكن هناك اختلاف في مستويات SGOT. لم يظهر تقييم معادن المصل أي اختلاف في مستوى الفوسفور ، بينما كان الحديد أقل في المجموعة المعالجة ولكنه لم يكن ذا دلالة إحصائية.