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TESTOSTERONE TO ESTRADIOL (T/E2) RATIO, AS A LABORATORY PREDICTOR IN INFERTILE WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

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Abstract: : Polycystic ovary syndrome is a common endocrine disease in women, characterized by heterogeneous presentation of hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology. This study was carried out to assess plasma levels of testosterone, estradiol calcium and cholesterol levels among females with polycystic ovarian syndrome (PCOs).

Forty females aged 18-35 years diagnosed by ultrasonography and Anti-Müllerian hormone (AMH) test in Alsir Abu-Hassan center for fertility in Khartoum State, and forty apparently healthy individuals as control group participated in this study.

Plasma testosterone and estradiol measured by using ELISA, cholesterol measured by BS-380 chemistry analyzer, and calcium by colorimetric method. Results were analyzed using statistical package for social science (SPSS), computer programmed version 21. The study showed that, the mean plasma levels of testosterone and T/E2 ratio were significantly increased in PCOs female patients. For testosterone (1.4±1.1 versus 0.87±0.65ng/ml, p-Value =0.011). For T/E2 ratio (0.019±0.015 versus 0.01±0.008 ng/pg,p-Value =0.022). Also the finding of this study showed insignificant difference in estradiol levels between PCOs compared with control group. (Mean±SD: 86±39versus 101±38.6 pg/ml) respectively with P. Value 0.086. The mean plasma levels of cholesterol was significantly increased in PCOs female patients. (Mean±SD: 207.6±33.4 versus112±33.4 mmoL /L) respectively with P.vale 0.000. The mean level of plasma calcium was significantly decreased (p.value 0.000). It is concluded that: the plasma levels of testosterone, T/E2 ratio and cholesterol are higher in PCOs female patients, while calcium level decreased.

Keywords: PCOS, testosterone, estradiol, ratio, cholesterol, calcium.

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СООТНОШЕНИЕ ТЕСТОСТЕРОНА И ЭСТРАДИОЛА (T/E2) КАК ЛАБОРАТОРНЫЙ ПРОГНОЗ У БЕСПЛОДНЫХ ЖЕНЩИН С СИНДРОМОМ ПОЛИКИСТОЗНЫХ ЯИЧНИКОВ

Резюме: : Синдром поликистозных яичников — распространенное эндокринное заболевание у женщин, характеризующееся гетерогенной выраженностью гиперандрогении, овуляторной дисфункции и поликистозной морфологии яичников. Это исследование было проведено для оценки уровней тестостерона, эстрадиола кальция и холестерина в плазме среди женщин с синдромом поликистозных яичников (СПКЯ).

Сорок женщин в возрасте 18-35 лет, диагноз которых был поставлен с помощью УЗИ и теста на антимюллеров гормон (АМГ) в Алсире Абу-Хасане.

Центр рождаемости в штате Хартум, и в этом исследовании приняли участие сорок практически здоровых людей в качестве контрольной группы.

Тестостерон и эстрадиол в плазме измеряются с помощью ELISA, холестерин измеряется химическим анализатором BS-380, а кальций - колориметрическим методом. Результаты были проанализированы с использованием статистического пакета для социальных наук (SPSS), компьютерной версии 21. Исследование показало, что средние уровни тестостерона в плазме и соотношение T/E2 были значительно увеличены у женщин с поликистозными коклюшками. Для тестостерона (1,4±1,1 против 0,87±0,65 нг/мл, значение p=0,011). Для соотношения T/E2 (0,019±0,015 против 0,01±0,008 нг/пг, значение p = 0,022). Также результаты этого исследования показали незначительную разницу в уровнях эстрадиола между СПКЯ по сравнению с контрольной группой. (Среднее ±SD: 86±39 против 101±38,6 пг/мл) соответственно со значением P 0,086. Средний уровень холестерина в плазме был значительно повышен у женщин с поликистозными коклюшками. (Среднее ± стандартное отклонение: 207,6 ± 33,4 против 112 ± 33,4 ммоль/л) соответственно с P.vale 0,000. Средний уровень кальция в плазме был значительно снижен (значение p 0,000). Сделан вывод: у женщин с поликистозными коклюшками выше уровень тестостерона в плазме, соотношение T/E2 и холестерина, а уровень кальция снижается.

Ключевые слова: СПКЯ, тестостерон, эстрадиол, соотношение, холестерин, кальций.

1. INTRODUCTION PCOS, defined as oligomenorrhea (history of no more thanPolycystic ovary syndrome (PCOS) is characterized by eight spontaneous menses per year) and hyperandrogenemia chronic anovulation and

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hyperandrogenism which can be (elevated testosterone level documented within the previous present in a different degree of severity. The main year in an outpatient setting on the basis of local laboratory physiopathological basis of this syndrome includes Insulin- results. Any menopausal and women receiving resistance and hyperinsulinemia(1) . Many females with contraceptives were excluded. Consent was taken regarding PCOS have an increased risk of insulin resistance which, acceptance to participate in the study and re-assurance of with the prevalence of obesity, is a powerful risk factor for confidentiality. Before the specimen was collected, the progression to type 2 diabetes .They also have an increased donors knew that this specimen was collected for research long-term risk of endometrial hyperplasia /cancer (2) . PCOS purpose. About 2.5 ml of venous blood were collected from is a heterogeneous disorder (that is, capable of having each participant (both case and control). The samples were somewhat different manifestations in different people) and collected under aseptic conditions and placed in sterile the exact cause not known until now, and it is a very lithium heparin containers and centrifuged for 5 minutes at common problem among patients attending infertility clinics. 3000 RPM to obtain plasma then they obtained sample were The diagnosis depend on above criteria and rule out other kept in plain containers at 2-8˚C until the time of analysis. causes of hyperandrogenism. study conducted to assess Data was analyzed to obtain means standard deviation and serum Anti-Müllerian hormone as laboratory predictor in correlation of the sampling using statistical package for infertile women with PCOS (3).17B-oestradiol is the social science (SPSS) computer Programmed version 21, t principle hormone produce by the ovaries also synthesized in test and person correlation were used for comparison and the placenta from androgens secreted by the fetal adrenal correlation glands (4) Dyslipidemia is the most common abnormality in **Results:** PCOS (5) . Table (1): Illustrate the mean concentration of testosterone and estradiol and ratio between them serum calcium,

Materials and Methods: This cross sectional study was albumin in polycystic ovarian syndrome patients and control conducted in Khartoum state, the capital of Sudan, eighty group. volunteer included to participate in this study, 40 with polycystic ovarian syndrome, 40 healthy subjects without any diseases control group. All subjects were diagnosed with

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Variable	PCOS N=40 Mean±SD	Control N=40 Mean±SD	*P. Value*
Estradiol pg/mL	86.0±39.0	101±38.6	0.086
Testosterone ng/ml	1.40±1.10	0.87±0.65	0.011*
T/E2 ratio	0.019±0.015	0.01±0.008	0.022*
AMH	10.6±5.92	1.40±0.22	0.000*
Cholesterol mmol/L	207.6±33.4	112±33.4	0.000*
Calcium mg/dL	7.0±0.69	9.2±0.55	0.000*
Albumin g/dL	4.1±0.56	4.5±0.46	0.124

*Result given in mean ± SD, *P-Value* ≤ 0.05 Consider significant.

* Independent sample T test was used for comparison

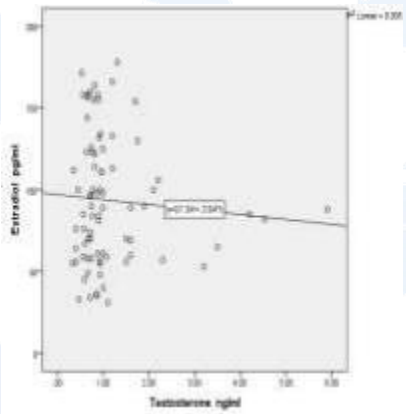

Figure (A)

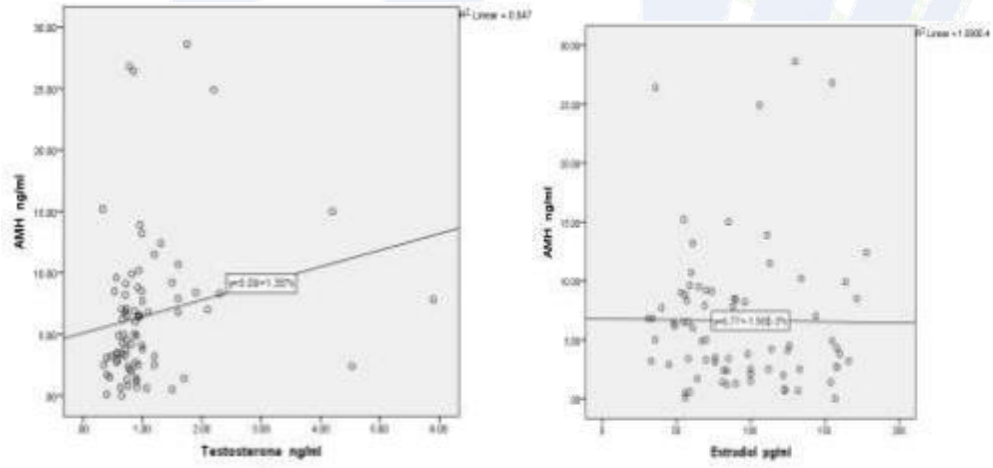

Figure: (1): (A) Show correlation between testosterone concentration and estradiol(r= -.073, P.Value = 0.522). (B) Show correlation between AMH and Testosterone (r= 0.216, P.Value = 0.055). (C) Show correlation between AMH and estradiol (r= -0.010- , P.Value = 0.927)

DISCUSSION:

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Polycystic ovary syndrome (PCOS) disrupt the fertility hormones in females by increasing or decreasing them, this study conducted to get the disrupt of testosterone / estradiol ratio among PCOS female patients. In research, the ages ranged from 17 to 29 years. In the past they thought PCOs presents during the reproductive years only, but now can be diagnosed from fetal life. In this study, the average age of woman was from (17 to 30 years).This finding is consistent with study by (6), who had reported that the proportion of women with PCO decreased with age . this can be caused by a decrease in the number of antral follicles throughout the reproductive years that occurs in normal women, a phenomenon that also applies to patients with PCOS (7).

Although PCOS classically presents during the reproductive years with menstrual irregularities, hyperandrogenism and metabolic complications, the origin of the disorder probably occurs very early starting from fetal life. In utero exposure to elevated testosterone levels coupled with gestational hyperglycemia may contribute to early differentiation of PCOS or may lead to amplification of the phenotype in genetically predisposed individuals. The spectrum of presentation of PCOS phenotype changes across the life span of a given individual. Improved understanding of the disease spectrum has allowed us to identify endocrine and metabolic changes in the very young subject with high risk of developing PCOS (8)

The present study revealed significant increase in mean testosterone and T/E2 ratio levels among case when compared to control group with p-value 0.011 and 0.022 respectively, while estradiol showed insignificant difference with p-value 0.086. This finding agreed with study done by (9) (Shang-Gwo et al., 2008), who reported that polycystic ovary syndrome (PCOS) had higher levels of T/E2 ratio as compared to control group. Also similar to study done on by (10) ,who approved that (PCOS) had higher levels of testosterone as compared to control and estradiol not significant difference in PCOs compared to control. Because the PCOs female produce excess LH and AMH hormone which can inhibit the ovarian production of estradiol, also inhibit the aromatase enzyme that can lead to prevent conversion of testosterone to estradiol in peripheral tissues.

In the present study of PCOs, there are no correlations were found between plasma levels of testosterone and estradiol. This finding was agreed with studies done by (10).

The result showed that, there was no correlations were found between AMH and plasma levels of testosterone and estradiol.This finding was agreed

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with estradiol and disagreement with testosterone in studies done by (11) . Also the result showed that, there was no correlations were found between age and plasma levels of testosterone and estradiol and T/E2 ratio. in our study, we found that there was highly elevation in the concentration of AMH in patients samples when compared with control group and the difference was significant (P. value 0.000), also the highly reduction in concentration of serum calcium was found and the difference was significant also (P.value 0.000), Several studies showed that the level of AMH in plasma was significantly increased in patients with polycystic ovarian syndrome but there was significant decrease level of calcium among them. These findings were similar with that obtained by (12) . The increased level of AMH was explained by the fact that AMH concentrations directly reflecting the increased number of early antral follicles. Moreover, the magnitude of AMH elevations in PCOS is associated with the extent of disease (13) .

Dyslipidemia is one of the important risk factor associated with PCOS. Abnormal lipid metabolism is one of the main metabolic characteristics of PCOS patients. The result of this study show that PCOS patients had higher total cholesterol concentration when compared with control group which are similer to the results observed in PCOS patients in another study (14) also in agreement with some studies suggested that PCOS patients are hyperlipidemic with higher total cholesterol compare to control group (7,15).

The reduced level of calcium was explained by the fact that Females with polycystic ovarian syndrome have vitamin D deficiency, 83% of all PCOS patients showed vitamin D deficiency while 35% were severely deficient (16) .Another study showed the opposite observations in which they suggest that abnormalities in calcium homeostasis may be responsible, in part, for the arrested follicular development in women with PCOS and may contribute to the pathogenesis of PCOS (17).

Also it showed that there were no significantly difference between serum albumin and estradiol levels among female patients with polycystic ovarian syndrome compared to healthy individuals (P.value0.283) and (P.value0.086) respectively. The possible explanation of the decreased level of estradiol is the evidence that decreased aromatase activity may be a possible mechanism underlying the arrested follicular growth in PCOS. This was suggested by the study which showed that follicles in women with PCOS contain low levels of estradiol, aromatase mRNA and aromatase activity. PCOS follicular fluid contains one or more endogenous inhibitors of aromatase activity. 5α -

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androstane- 3, 17-dione, a 5α- reduced androgen, is a competitive inhibitor of aromatase activity; it is markedly elevated in PCOS follicular fluid (18). In addition, 5α-reductase activity is substantially higher in PCOS follicles than in control follicles, leading to increased production of 5α- androstane- 3, 17-dione in women with PCOS. Collectively, the decreased estradiol production and increased androgen production in PCOS maybe a result of elevated 5α- reductase activity and decreased aromatase activity (18).

CONCLUSION

from the results and finding of this study, it is concluded that the plasma levels of testosterone and T/E2 ratio are higher in PCOs female patients. Decreased level of calcium and estradiol as well as albumin also decreased which may increase the risk of cardiovascular disease, osteoporosis and delay the course of treatment and recover of ovulatory problems. The plasma levels of total cholesterol is increase in PCOs female patient

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Conflicts of Interest:

The authors declare no conflicts of interest regarding the publication of this paper.

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