Study of some biochemical parameters in patients With polycystic ovarian syndrome In Al-Najaf Al-Ashraf province

Abbas .Sahib.Al-Naffakh *, Ali .M.AL-Gharawi ** and Sanad .B.Al-A'araji **.
*** M.Sc. , Al-Najaf Health Directorate. Technical Affairs Dep. Lab office.**
****Ph. D. ,College of Health and Medical Technology , Baghdad .**

الخلاصة

الموضوع:

متلازمة ألمبيض متعدد الكيسات (PCOS) هي من الأمراض الشائعة الانتشار بين الإناث خلال سن الإنجاب (12-45) سنه حيث تشكل نسبة الإصابة بهذا المرض من(5 - 10%) ومع ذلك فان تكون المرض غير واضح وقد يعزى نشوؤه الى بعض الاضطرابات الهرمونية في المبايض أو الغدة النخامية، مقاومة الأنسولين وأخيرا فان وجود الالتهابات المزمنة(chronic inflammation) قد تكون مرتبطة بحصول المرض.

الهدف من الدراسة:

تسليط الضوء على بعض التغييرات الكيموحيويه للمصابات بمتلازمة المبيض متعدد الكيسات للوصول إلى النتائج المتعلقة باليـة تكـوين المـرض مـن خـلال مقارنتهـا مـع مجموعـه مـن النسـاء غيـر المصـابات كمجموعـة ضـبط (Control).

المرضى وطرق العمل:

شملت الدراسة جمع مائة وست عينات من المصابات بمتلازمة المبيض متعدد الكيسات والتي تراوحت أعمارهن بين (15-45 سنه) إضافة الى (35) امرأة من غير المصابات انضموا للدراسة كمجموعة ضبط .تم أخذ التأريخ الطبي للمريضات والسليمات، وزن الجسم والطول و تم جمع عينات الدم منهن خلال الأيام من (2-6) من الدورة الشهرية في حالة الصيام.

تم قياس مستوى السكر ونسبة الدهون بجهاز المطياف الضوئي في حين تم قياس الهرمونات بجهاز الأيلايزا.

قسمت النساء المصابات إلى ثلاث مجموعاتٍ أعتماداً على العمر:

(ن1) 51 مريضه بعُمرَ(15-25 سنه)، (ن2) 41 مريضه بعُمرَ (26-35 سنه) و (ن3) 14 مريضه بعُمرَ (36-45سنه). تم أجراء الفحوصات المختبريه و مقَارنتُها بمجموعة السيطرةِ (35) من النساء الأصحاء بنفس المدى من العمر.

تم تشخيص المصابات (بمتلازمة المبيض متعدد الكيسات) طبقاً للجمعية الأوربية للتكاثر البشري وعلم الأجنَّةِ European society of human reproduction and embryology (ESHRE) والجمعية الأمريكية لمعايير الطبِّ والتكاثر American society for reproductive medicine Criteria (ASRM)

إن وجدت هناك أيّ اثنين مِنْ المعايير الآتية :

١. وجود أكياس في المبيض في فحص الأمواج فوق ألصوتيه PCOS in Ultra Sound(U/S).

٢. اضطرابات الدورة الشهرية.

٣. فرط هرمون الاندروجين (Hyperandrogenism).

أجريت الدراسة في مستشفى الحكيم العام ومستشفى الفرات الأوسط في محافظة النجف الاشرف للفترة بين تشرين الأول/ 2009 وآذار/ 2010 .

Abstract

Background: Polycystic ovarian syndrome(PCOS) is a common syndrome affecting 5-10% of women in reproductive age (12-45 years), though its pathogenesis is still unclear, but the probability of pathogenesis might be due to the hormonal disorders in the ovarian and pituitary gland, insulin resistance, and recently chronic inflammation may be associated .

The objective: To shed light on some biochemical parameters in patients with PCOS to reach some aspects of its pathogenesis through a comparison with normal women as control.

Patients and methods: One hundred and six infertile Iraqi women; aged (15-45) years in addition to 35 normal women as a control group were included in this study.
The medical history was taken and body mass index (BMI) was calculated. Blood samples were aspirated from all subjects from day(2 – 6) of menstrual cycle in fasting state.
The levels of fasting plasma glucose (FPG) and lipid profile were measured by spectrophotometer while hormones were measured by ELISA.
Patients were divided into three groups according to age , 51 (No.1) aged (15-25), 41(No.2) aged (26-35) and 14(No.3) aged (36-45)years .The control group were divided in to similar categories.
The study was conducted at Al-Hakeem and Al-Furat Hospitals in Al- Najaf Al-Ashraf province between October /2009 and March /2010.

Introduction

Polycystic ovary syndrome (PCOS)

Polycystic ovary syndrome is the most common female endocrine disorder affecting 5 - 10% of women of reproductive age (12 - 45years) and is thought to be one of the leading causes of female infertility.[1]

The disorder causes multiple abnormal cysts in enlarged ovaries, so they would not produce the normal number of eggs and do not ovulate normally .The disease is present at birth but does not cause symptoms until puberty.[2]

The principal features are obesity, anovulation (resulting in irregular menstruation), acne and excessive amount or effect of androgenic (masculinizing) hormones [3].While the causes are unknown, insulin resistance, diabetes, and obesity are all strongly correlated with PCOS.[4] PCOS patients had been already diagnosed according to European Society of Human Reproduction and Embryology(ESHRE) and American Society for Reproductive Medicine(ASRM): Rotterdam consensus workshop indicated PCOS is diagnosed for presence any of two of the following criteria:[5]

1. Polycystic ovaries are presented by the ultrasound.
2. High levels of male hormones(Androgen).
3. Menstrual dysfunction.

Their LH level is often two or three times that of the FSH level .This situation is called an elevated LH to FSH ratio. [6]

When women having PCOS means that their ovaries are not getting the right hormonal signals from their pituitary gland. Without these signals there will be no ovulation .The period ,therefore, may be irregular or absent. [7]

Most often, women with high testosterone levels develop male pattern hair growth (hirsutism) especially on their faces and chests.[8]

There is a significant increase in the incidence of impaired glucose tolerance (IGT) and Type 2 Diabetes Mellitus (T2DM) in women with PCOS. Studies indicated that on the initial evaluation with a 2-hour Glucose Tolerance Test (GTT) 30-40% of PCOS already have IGT or T2DM. [9]

Patients of PCOS are at increased risk of high levels of LDL , which if neglected, can lead to a heart attack or stroke. Conversely, women with PCOS have lower levels of HDL , which is another risk factor for cardiovascular disease(CVD) .[10]

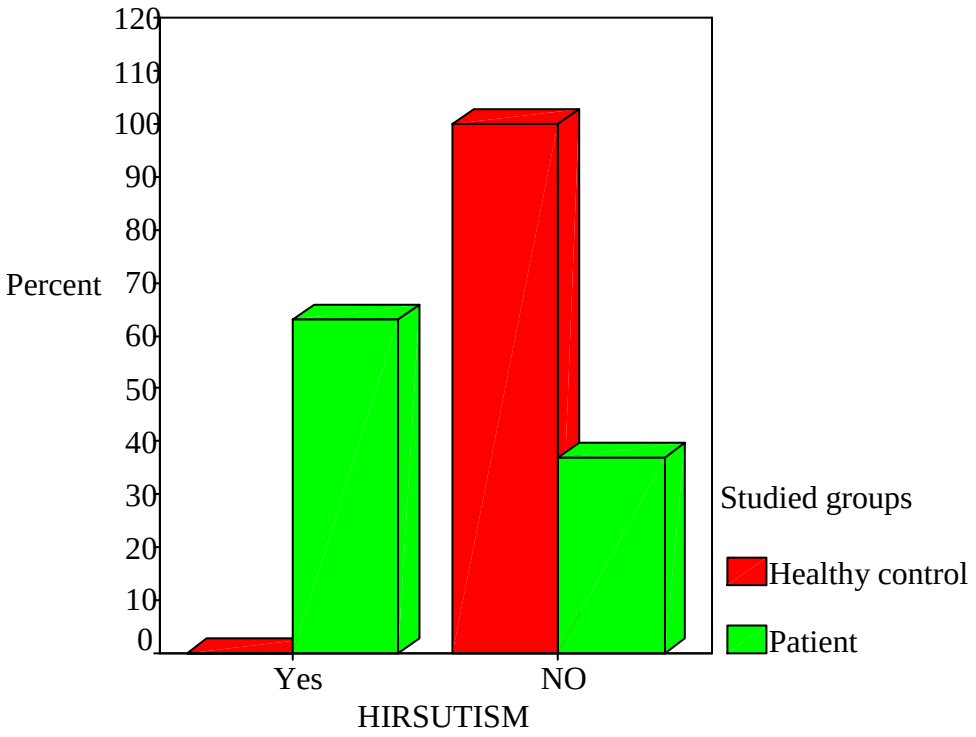
Results: It is exhibited that there is:
1.A highly significant positive correlation (P<0.01) between PCOS and marital status where PCOS is more prevalent in married women (78.3%) , than in unmarried (21.7%).
2.A highly positive correlation (P<0.01) between PCOS patients and hirsutism where 64.2% out of PCOS patients suffered from hirsutism.
3.A positive correlation between PCOS patients and disturbance of menstrual cycle where 78.3% had irregular menses while 21.7% had regular. This study also found that a high percentage of PCOS patients were with oligomenorrhea (66%) and 12.3% were with amenorrhoea in comparison with other groups in random sample population .
4.A positive correlation between BMI and(plasma sugar , cholesterol, triglyceride ,HDL, LDL and LH) while non significancy relationship observed between BMI and FSH ,testosterone ,and VLDL-cholesterol in PCOS patients .
5.A significant difference (P<0.05) in the mean of BMI (Kg/m^2) and menstrual regulation in PCOS patients was observed .
6.A significant correlation between miscarriage and PCOS patients were comprised 17.9 % from all patients , this state is associated with hormonal abnormalities.
7.The levels of LH and testosterone hormones were significantly higher(P<0.01) in the PCOS patients when compared with control group, while the FSH hormone had a significant decrease
(P<0.05) .
8.The levels of LH:FSH ratio were higher significantly(P<0.01) in the PCOS group when compared with the control group.
9.A highly significant increase(P<0.01) in glucose and triglyceride in PCOS patients when compared with control group, these positive correlation might be a good indication to diagnose PCOS.

Results:-
The following tables and figures show the results of some biochemical parameters investigated to evaluate 106 patients in addition to 35 control subjects .
Table 1 : Distribution of studied groups according to hirsutism.

			Studied groups		
			Healthy control	Patient	Total
HIRSUTISM	Yes	No.		68	68
		%		64.2%	48.2%
	NO	No.	35	38	73
		%	100.0%	35.8%	51.8%
Total		No.	35	106	141
		%	100.0%	100.0%	100.0%

P-value =0.00 HS

The data demonstrated in table and figure(1) showed that there is a highly significant positive correlation (P<0.01) in the prevalence of PCOS patients who showed the presence of hirsutism [68 (64.2%) for yes and 38 (35.8%) for no.



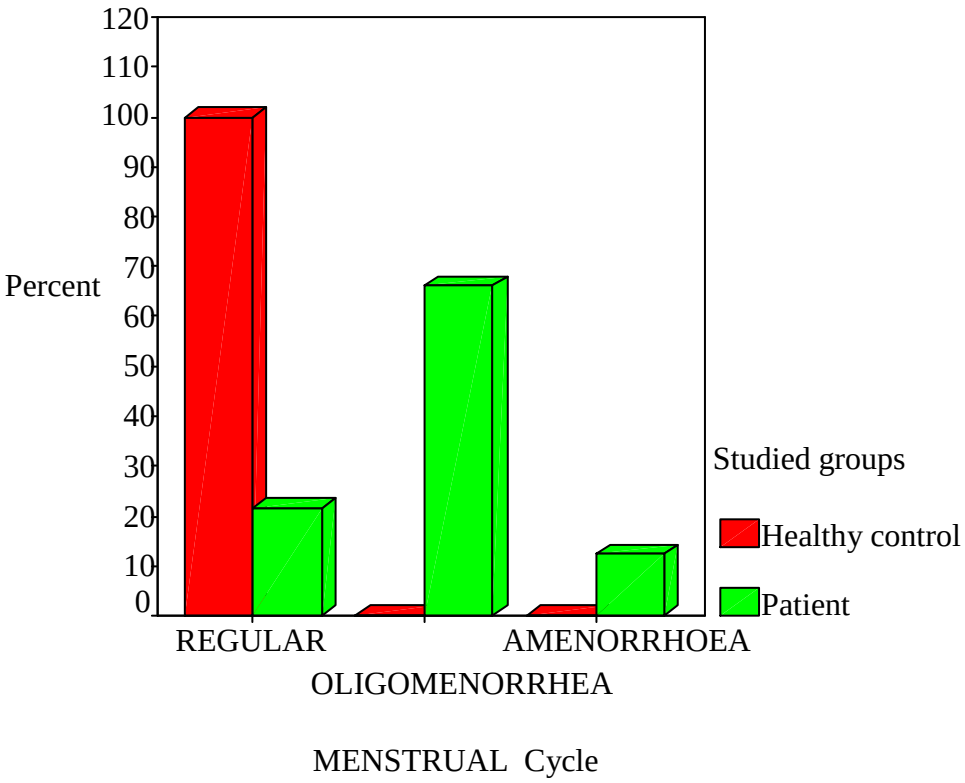
Figure(1) : Distribution of studied groups according to hirsutism.

Table(2) : Distribution of studied groups according to menstrual cycle.

			Studied groups		
			Healthy contro	Patient	Total
MENSTRUAL Cycle	REGULAR	N	35	23	58
		%	100.0%	21.7%	41.1%
	OLIGOMENORRHEA	N		70	70
		%		66.0%	49.6%
	AMENORRHOEA	N		13	13
		%		12.3%	9.2%
Total		N	35	106	141
		%	100.0%	100.0%	100.0%

P-value =0.00 HS

The results exhibited in table & figure (2) proclaim the effect of PCOS on menstrual cycle status which show a high frequency of oligomenorrhea patients [70 (66%)] while the regular are [23 (21.7%)] & amenorrhoea [13 (12.3%)], on the other hand all control groups were only regular [35 (100%], ($p<0.01$).



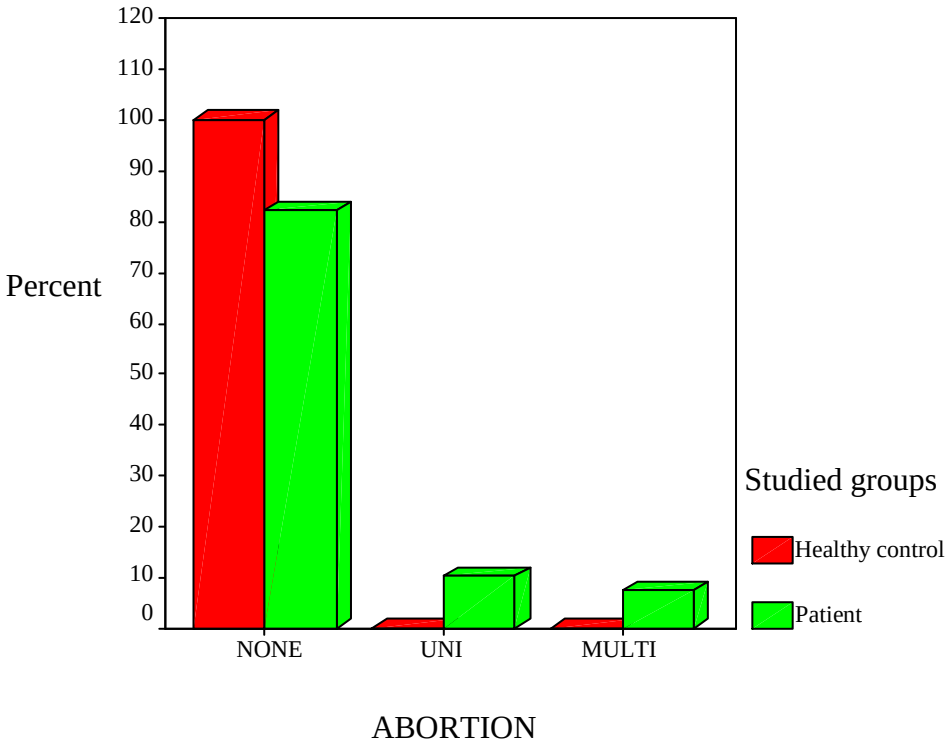
Figure(2) : Distribution of studied groups according to menstrual cycle.

Table(3) : Distribution of studied groups according to abortion.

			Studied groups		Total
			Healthy control	Patient	
ABORTION	NONE	N	35	87	122
		%	100.0%	82.1%	86.5%
	UNI	N		11	11
		%		10.4%	7.8%
	MULTI	N		8	8
		%		7.5%	5.7%
Total		N	35	106	141
		%	100.0%	100.0%	100.0%

P-value =0.027 S

The results in the table and figure (3) showed that all controls [35 (100%)] and most of patients [87 (82.1%)] were non aborted, uni abortion patients [11 (10.4%)] and multi abortion patients [8 (7.5%)], with a significant difference ($p<0.05$).



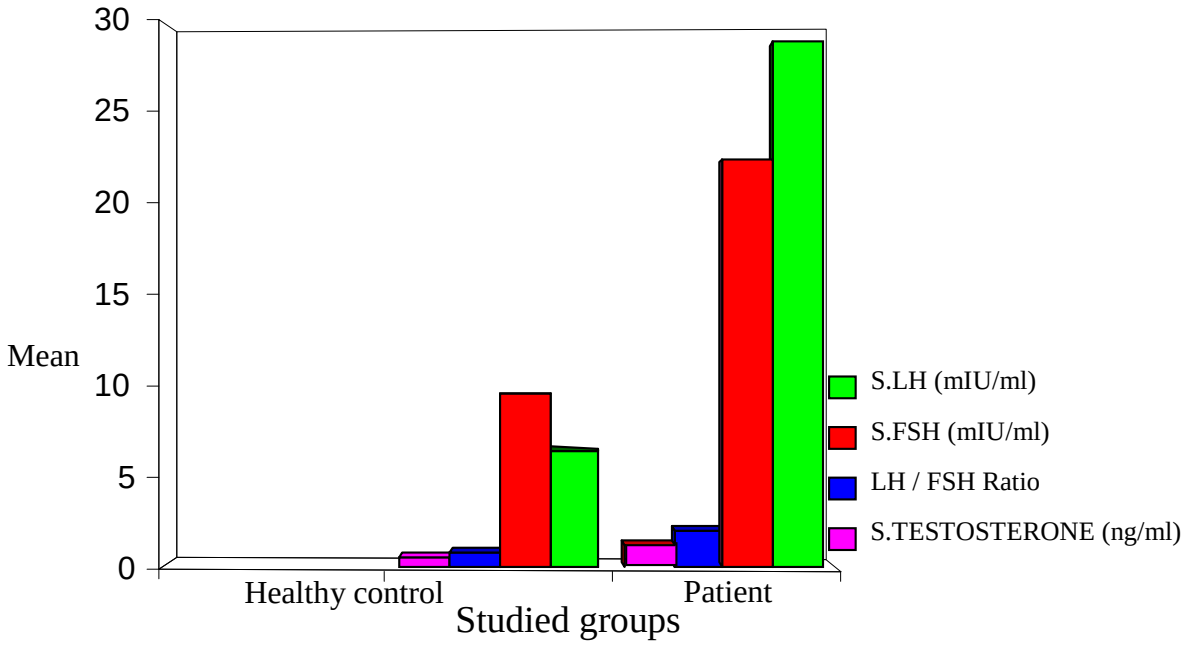
Figure(3) : Distribution of studied groups according to abortion.

Table(4): Mean distribution of hormone assay in sera among studied groups.

		N	Mean	Std Deviation	Std Error	Range		t-test (P-value)	Sig
						Min	Max		
S.LH (mIU/ml)	Healthy control	35	6.43	3.10	1.96	0.83	12.71		
	Patient	106	28.89	26.75	2.58	0.93	97.92	.000	HS
	Total	141							
S.FSH (mIU/ml)	Healthy control	35	9.52	4.09	1.21	2.98	19.14		
	Patient	106	22.46	20.22	1.99	1.04	140.00	.030	S
	Total	141							
LH / FSH Ratio	Healthy control	35	0.81	0.54	9.24	0.28	2.22		
	Patient	106	2.01	1.10	0.19	0.06	14.77	.001	HS
	Total	141							
S.Testosterone (ng/ml)	Healthy control	35	0.52	0.35	6.79	0.08	2.25		
	Patient	106	1.24	0.84	8. 17	0.08	3.89	.000	HS
	Total	141							

Table and figure(4) showed a highly significant elevation($P<0.01$) in the mean concentration of (LH, LH/FSH ratio and testosterone) hormones in sera of PCOS patients in comparison with the mean serum concentration of control [LH (28.89 ± 26.75

mIU/ml) and (6.43 ± 3.10 mIU/ml),respectively];[FSH (22.46 ± 20.22 mIU/ml) and (9.52 ±4.09 mIU/ml),respectively], with a significant difference (P<0.05)and [LH / FSH ratio (2.01 ± 1.10 mIU/ml) and (0.81 ± 0.54 mIU/ml),respectively], with a highly significant difference (P<0.01).Finally [testosterone (1.24 ±0.84 ng/ml) and (0.52 ±0.35 ng/ml),respectively], with a highly significant difference (P<0.01).



Figure(4): Mean distribution of hormone assay in sera among studied groups.

Discussion:-

The study in the table and figure(1)is in agreement with Knobil.E, [11] and Kalro.B,[12] who reported that out of PCOS patients 69% had hirsutism .Similarly Fossati P, [13] illustrated the presence of 70% out of PCOS in the United States complain from these hair problems(hair growth on face, chest, back, abdomen, thumbs and toes). This is explained by the increased level of androgen which lead to increased secretion of testosterone , the causative agent of the appearance of male pattern (hirsutism).

on the other hand 10-20% out of the Japanese PCOS women suffer from hirsutism when compared with united states or Iraq (this study). The difference might be associated with genetic factors ,life style and differences between the patients in response to androgen production. [14]

Effect of disease on menstrual cycle prevalence showed the result in table and figure (2) agreed with recent studies [15,16] which observed that the overall prevalence are 59.75% out of PCOS patients with oligomenorrhea , 25 % with regular cycle and 15.25% with amenorrhoea. PCOS- associated menstrual dysfunction usually extends beyond the typical irregularity association with the 1-2 years following menarche, and varies from subtle irregularity to amenorrhoea. The endometrium is in an unopposed estrogen state caused by antral follicle atresia and the resulting anovulation, leading to endometrium proliferation. Bleeding, often unpredictable and heavy, represents the sloughing of only

the top layer of the endometrium that can no longer be sustained by estrogen production. [17,18]

Effect of PCOS disease on abortion in the table and figure (3) agreed with recent study [19] which proved that miscarriages in PCOS patients are common, approximately 20% of pregnancies (one in five) end in miscarriage .

Miscarriage (or spontaneous abortion)[20] in PCOS patients associated with hormonal abnormalities.

Women with raised LH have a higher miscarriage rate (60% of pregnancies end in miscarriage) compared with those who have normal LH values (around 12 percent miscarriage rate) [21,22] . Most clinically apparent miscarriages (two thirds to three-quarters in various studies) occur during the first trimester.[23]Another study showed that 30-50% of pregnant women with PCOS being miscarried in the first trimester , and shown that the treatment with metformin lowers the rate of miscarriage to half .[24]

Another study [25]indicated that the miscarriage rate in women with PCOS is 20-40% , higher than the baseline rate in the general obstetric population. Miscarriages occurred in 62-73% of pregnancies without metformin and 9-36% of pregnancies when metformin has been taken[26].The cause of miscarriage is not known but there are other causes which may be linked to high insulin levels, low level of progesterone hormone ,delayed ovulation ,or other problems such as the quality of the egg or how the egg attaches to the uterus.[27]

Estimation of hormone levels in sera of studied groups in table and figure (4) appeared that these current study agreed with previous study [28] which proved that 60% and 70% of patients with PCOS had an increasing in their LH level than normal subjects. This elevation may give an explanation about increased male hormones production in ovary, or due to increased pulse frequency or episodic secretion of LH as reported previously. [29] Elevated LH has been described in women with hyperandrogenism of other causes ,such as androgen-secreting ovarian neoplasm.[30] Androgens are able to distort gonadotropin released by their aromatization to estrogens.[31] Although androgen levels of the normal male range suppress gonadotropin release in normal women [32], androgen levels do not directly alter gonadotropin release in women with PCOS or in normal women.[33]

While FSH level showed a significant difference ($P<0.05$) between PCOS patients and control, the result is in agreement with previous studies[34],and it fits with the criteria for the diagnosis of PCOS , where the levels of FSH hormone in PCOS patients and control group are within normal range.

The table & figure (4) also explain that the level of LH is more than two times of FSH level . These results agreed with previous studies[35],and with the criteria for diagnosis of PCOS .This change in the LH to FSH ratio is enough to disrupt ovulation. Although the effect of the increase in the ratio of LH to FSH is unclear but might be due to either primary central disorder involving GnRH secretion or secondary by pituitary sensitization to GnRH by abnormal feedback signals from ovaries.[36]Another cause suggested that the ability of Estrogen to increase LH response to GnRH compared with FSH [37], mainly if unopposed by progesterone which might lead to absence of negative feedback mechanism on LH secretion and might cause an increase of LH frequency in response to GnRH pulse pattern.[38]

Finally serum testosterone showed highly significant difference between PCOS patients and the control group, this study agreed with other studies[39,33] that proved 55-65% of patients with PCOS had abnormal testosterone values, one of these studies mentioned

above[33] has found that PCOS patients had markedly elevated LH level with a total serum testosterone level. So , the conclusion that in PCOS there is a probably increment in the amount of testosterone which acts to synergies the action of LH on theca cells which became reasonable, and this is possibly associated with the effect of increased level in hyperandrogenism. [40] The adrenal cortex glands always make a small amount of male hormone testosterone as a by-product of cortisone, the main hormone produced by the adrenal glands .[41] Other causes of increased testosterone include the follicles themselves, which are lined by two types of cells, theca and granulosa, when ovulation does not occur these cells should self-destructed.[42]

In PCOS ,the theca cells do not die and prevent the follicle from collapsing and this is how the cyst formed the theca cells take cholesterol from the blood stream and turn it into androstenedione, this is taken up by the chick granulosa cells to make estrone a weak female hormone after a failure of ovulation in PCOS and granulosa cells death; the theca cells are left to turn all the cholesterol into androstenedione and then into testosterone. [43]

Conclusions :

Polycystic Ovarian Syndrome (PCOS) is related to:

1.High elevation of the serum levels of testosterone , LH and LH : FSH ratio .

2.Hirsutism appeared at high percentage of PCOS patients .

3.Abnormal menstrual cycle high occurance .

4.Miscarriage comprised about 1/5th, out of PCOS patients. This state is associated with hormonal

abnormalities.

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