Association Between Lipid Profile ,BMI , and Some Pituitary Hormones Abnormalities In Sera of Iraqi Infertile Females

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Abstract

In this study , the clinical impact of interaction between gonadotrophin hormones (luteinzing hormone, LH, and follicle stimulating hormone ,FSH) and prolactin PRL in serum of seventeen Iraqi infertile female with the lipid profile . In addition to control group involving age matched fertile females .

Immunoradiometric assay (IRMA) technique for the determination of (LH , FSH and PRL) was utilized. The lipid profile { i.e. total cholesterol (Tc) , triglycerides (TG) , and high density lipoprotein – Cholestrol (HDLc)} ,were evaluated by using colorimetric method , while{ low density lipoprotein cholesterol (LDLc) and very low density lipoprotein – cholesterol (VLDLc)} , were evaluated by using a mathematical formulas. The body mass index (BMI) was calculated as weight (Kg) / height (m^2).

The results revealed that only(20%) of infertile female with abnormal hormonal levels are obese , while (40%)of them were overweight . Only (TG) in sera of infertile female showed a significant increase than that of control group. On the other hand no significant differences in (Tc) , (HDLc) were noticed in sera of groups under consideration .

A conclusion could be obtained from the above data , that (BMI)or obesity is not associated with infertility always.

Introduction

The reproductive system of women shows regular cyclic changes that may be regarded as periodic preparations for fertilization and pregnancy . This cycle is the menstrual cycle [1] .

Menstruation is dependent on the proper functioning of a chain made up of ; hypothalamus → pituitary →ovary(HPO) ; amenorrhea presupposes awakening or break in one or more of these links [2] .

Interaction (HPO) to produce cyclic expression of the appropriate hormones at the expected time or chronology age at which sexual maturation should normally occur [3]

The growth and the reproductive activities of the gonadal tissue are controlled by the gonadotrophins hormone LH and FSH from the interior pituitary gland . LH and FSH are called gonadotrophins because they regulate the function of the gonads (ovaries and testes) , in both sexes , FSH stimulates gamete (sperm or egg) production, while LH promotes production of gonadal hormones [4] .The secretion of both LH and FSH is stimulated by gonadotrophin releasing hormone from the hypothalamus , LH and FSH both are subjected to feed back loops regulation by the ovarian hormones [5].

In women , LH along with FSH are ordered as part of the workup of infertility and also useful in the investigation of menstrual irregularities , and to aid in the diagnosis delayed and precocious puberty [6].

Prolactin PRL stimulates mammary development and subsequent lactation , it is an episodic secretion that it produced by the lactotrophs of interior pituitary[7] .

High level of PRL is a biochemical finding and does not necessarily indicate the presence of a disease , this would increase in PRL level in the blood above the physiological concentration, it is now well documented to interfere with the female reproductive function [8] .

It was reported that obesity was a common finding in woman with ovarian hyperandrogenism , although the mechanisms underlying this relationship remain largely undetermined [9].

The aim of the present study is to evaluate the lipid profile of infertile woman with pituitary hormones dysfunction and compared with that for healthy fertile woman matched in age and body mass index BMI.

Experimental Part

Seventeen infertile female were selected from Elwyia Maternity Teaching Hospital during 2008, a careful history was obtained from the patients including menstrual disturbance , if any , associated with the symptom of infertility , weight and height and all patients, were free from medication affecting hormone level .

Evaluation of each patient is done by detecting body mass index, serum gonadotrophens hormones level LH , FSH and serum PRL. Excluding the test during the days (12 – 16)from the cycle period .

As control (17) normal female with normal regular menstrual cycles with body mass index within normal range ,patients and control aged (20 – 39) years were included in this study .

Blood samples (5ml) were collected in plain tubes , centrifuged at 3000 rpm for 10 min, after allowing the blood to clot at room temperature . The sera were a liquated and frozen until assay performed .

Body mass index uses a mathematical formula based on person's height and weight , BMI equals weight in kilograms divided by height in square meters (BMI = kg / m^2) [10].

Fost et al suggested that a BMI of (18.5 – 24.9) indicates a person of normal weight . A person with a BMI of (25 – 29.9) is overweight , while a person with a(BMI of $\geq$ 30) is obese [11] .

Immunoradiometric assay IRMA for the in vitro determination of FSH , LH , and PRL in human serum was utilized by kits from immunotech abeckman coulter company . The Immunoradiometric assay of luteinizing hormone FSH , LH , and PRL is a sandwich type assay the kit utilizes mouse monoclonal antibodies directed against two different epitopes of FSH , LH and PRL hence not competing . Samples or calibrators are incubated in tubes , coated with the first monoclonal antibody in the presence of the second monoclonal antibody labeled with iodine 125. The content of tubes is aspirated and rinsed after incubation and bound radioactivity measured values are calculated by interpolation from the standard curve . The radioactivity bound is directly proportional to the concentration of FSH , LH , and PRL in the samples.

The results are obtained from the standard curve by interpolation. The standard curve serves for the determination of FSH , LH and PRL concentration in samples measured at the same time as the calibrator .

Determination of total serum cholesterol [12] involves the use of three enzymes , cholesterol esterase , cholesterol oxidase and peroxidase . In the presence of the former mixture, (N- ethyl propyl – m – anisidine) and 4 – amino – antipyrine are condensed by hydrogen peroxide to form quinoneimine dye proportional to the concentration of cholesterol , when the absorbance of the samples measured against the reagent blank within 60 minutes at 500 nm.

The Triglycerides were determined after enzymatic hydrolysis with lipases . The indicator is aquinoneimine formed from hydrogen peroxide , 4-aminophenazone , and 4 – chlorophenol under the catalytic influence of perioxidase .

The absorbance was measured for test and standard against the reagent blank within 60 minutes at 500 nm [13].

In determination of high density lipoprotein – cholesterol HDLc [14], the method uses a selective precipitations of chylomicrones and the apolipoprotein containing lipoprotein VLDLc and LDLc by addition of 4% phosphotungstic acid solution , which contain 10 % magnesium chloride PH 6.2 . Sedimentation of the precipitant by centrifugation , and subsequent enzymatic analysis of HDLc as residual cholesterol remaining in the clear supernatant , from which the cholesterol can be determined as described as above according to [12].

Low density lipoprotein cholesterol LDLc was determined by using empirical Friedwald formula which was based on the assumption that VLDLc is present in serum at concentration equal to one fifth of the TG concentration .

This formula is as follow [15] :when all concentration are given in milligrams per deciliter :-

$$LDLc(mg / dl) = Total\ cholesterol - (HDLc + VLDLc)$$

Statistical Analysis of Data

To compare the significance of the differences in the mean values of any two groups student's t-test was applied and P value less than 0.05($p<0.05$) was considered statistically significant .

Results and Discussions

Table (1)and fig(1) showed the mean distribution of serum hormones concentration LH , FSH , and PRL of the infertile female patients with the minimum and maximum values to each hormonal level when compared with the mean concentration of the normal control . A significant difference was observed between normal and high hormonal levels of infertile female compared to the majority of infertile have hormonal levels higher than that of control with a percentage of 74.4%, on the other hand there was no significant differences in the level of FSH in 28% of infertile female compared with healthy control . The significant difference was found in the higher levels of FSH in 72% of infertile female compared with normal hormonal level of healthy control . The results agreed partly with other studies who concluded that different results could reflect variation in the selection of patients and / or the different lifestyle factors [16].

The mean serum level of LH / FSH ratio for patients was(0.8)and for control group was(0.8). The difference is not significant yet others studies reported higher or lower ratio and they stated that this variation might be due either to primary central disorders involving (GnRH) secretion or secondary pituitary sensitization to (GnRH) by an abnormal feed back signals from ovaries [17] .

The PRL level in (60%) of infertile female showed a significant increase compared to that of healthy control while lower significant values than control was depicted in the rest of the patient .High prolactin level are found in(30%)of women with different kind of amenorrhea leading to infertility [18] . About(60%)of patients

of high level of prolactin showed lower levels of FSH and LH than healthy control. These results are in agreement with other studies who suggested that a decline in gonadotrophine in hyperproctanemic patient showed the association between gonadatrophine deficiency and hyperprolactinemia which might be an indirect sign of functional hypothalamic pituitary interruption due to the inhibitory effect of PRL [19] .

Body mass index is a measurement that is associated with body fat and it is widely used by health care provider.

Table (2)represent mean±SD of BMI for both groups .Fig (2) showed the distribution of infertile female according to BMI.There was a significant difference between patients, patients were overweight (40 %), and(33.3 %) of patients were in a healthy weight range ,while the percentage of obese patient was(20%). The present results disagree with some reports of infertility association with obesity [20] .

Table (3) and fig (3) showed the lipid profile in serum of the infertile female and the healthy control. The mean serum level of total cholesterol Tc for the infertile group was (172.125± 35.58 mg /dl) and for the control group was (171± 14.83mg / dl). The values for triglycerides TG were (108.68 ±31.63 mg /dl) and (80 ±7.19mg /dl)for the infertile females and control respectively . The HDLc and LDLc were (57.75 ±7.56 mg / dl) and (97.68 ±27.14 mg / dl) in serum of the infertile female respectively , and were (54.7± 7.39mg/dl) and (100.1 ±10.38mg /dl)for the control group respectively .

The values for VLDLc were (21.68±6.33mg/dl)and(16±1.438mg/dl) for the infertile females and control respectively .A non significant elevation in total cholesterol as compared with control group was found .The result does not agree with other studies which found that women with different causes of infertility had increase Tc levels[21]. A significant elevation in TG in serum of infertility female patient compared to control was obvious as shown in table(3).

The pattern of dyslipidemia is mostly found in a wide range of causes of infertility , even studies reported that high TG levels are found in both obese and non obese women suffering from infertility [22&23] .

Abnormalities of LDLc had not been found consistently in some cases of infertility , even in those with a normal LDLc level had shown increase VLDLc and small dense LDLc relative to control subject [24] .

High TG and low HDLc in patients with hyperprolactinemia were reported due to acceleration of hepatic and adipose tissue biosynthesis of triglyceride and certain phospholipids factors [25].

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Table (1) Mean± S.D, range and distribution of(LH , FSH and PRL) levels in serum of infertile female and healthy control

Hormone	Levels	Number of subjects	(%) of subject	Mean ± S.D.	Min. value	Max value	P- value
LH (IU/L)							
Healthy Control		17	100	5.7± 1.76	0.7	7.8	
Patients	Normal	5	25.6	6.7± 1.4	4.2	7.7	
	High	12	74.4	11.3± 2.6	8.4	17.5	
	Low	Nil	Nil	Nil	Nil	Nil	
	Total	17	100	9.71±3.34	4.2	17.5	P<0.05
FSH (IU/L)							
Healthy Control		17	100	7.1±2.13	1.3	10	
Patients	Normal	4	28	7.7 ±2.03	5.5	10	
	High	13	72	14.1± 3.1	10.2	21	
	Low	Nil	Nil	Nil	Nil	Nil	
	Total	17	100	12.48±3.91	5.5	17.7	P<0.05
PRL (ngm/ml)							
Healthy Control		17	100	14.1± 3.05	7.03	18.2	
Patients	Normal	5	33.4	12.6 ± 1	11	14	
	High	11	60	21.2± 3.8	15	29	
	Low	1	6.6	7± 0.00	7	7	
	Total	17	100	17.56± 5.58	7	29	P<0.05

Table (2) BMI for infertile female and control group

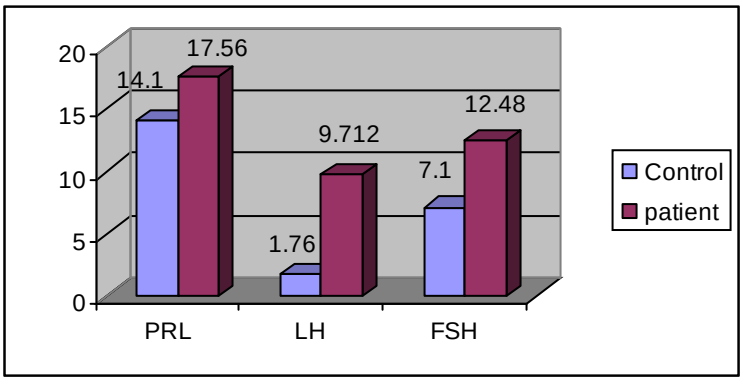
Groups	No. Of subjects	BMI (Kg/m^2) ±S.D
Patients	17	27.00 ±4.72
Control	17	25.8± 2.68
P-Value	--------	P>0.05

- **Each value represents mean ± standard deviation(S.D)**

Table (3) Serum level of lipid profile of infertile females and control subjects

Groups	No. Of subjects	Tc (mg/dl) ± S.D	TG (mg/dl) ± S.D	HDLc (mg/dl)± S.D	LDLc (mg/dl) ± S.D	VLDLc (mg/dl) ± S.D
Patients	17	172.125± 35.58	108.68 ±31.63	57.75 ±7.56	97.68 ±27.14	21.68± 6.33
Control	17	171± 14.83	80 ±7.19	54.7± 7.39	100.1 ±10.38	16± 1.438
P-Value	--------	P>0.05	P<0.05	P>0.05	P>0.05	P<0.05

Each value represents mean ± standard deviation(S.D)



Fig(1):Distributions of (PRL, LH, &FSH)levels in serum of infertile female and healthy control

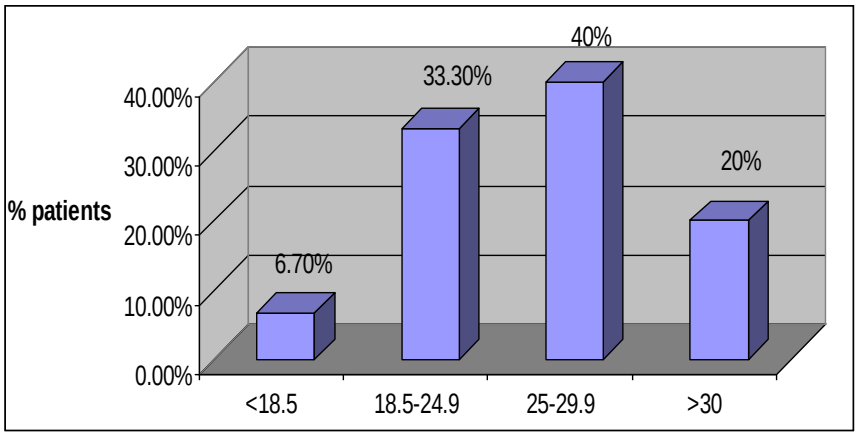


Fig.(2):Distributions of infertile females according to (BMI)

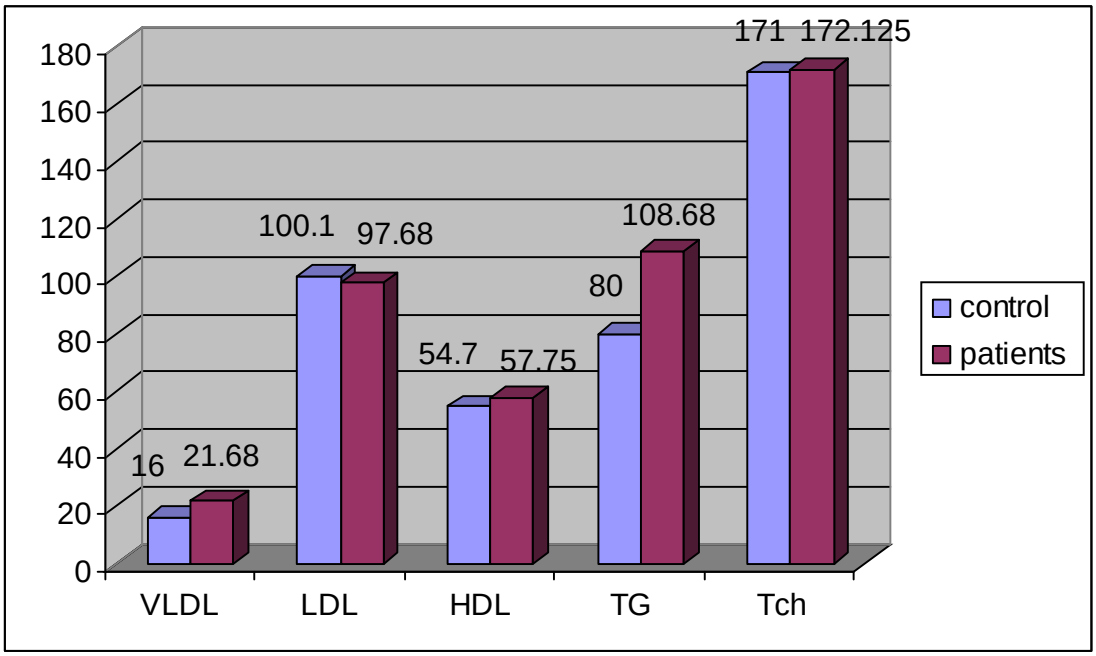


Fig.(3): Serum level of lipid profile of infertile females and control subjects

العلاقة بين صورة الدهون ومؤشر كتلة ا لجسم مع ا لخلل في بعض هرمونات الغدة النخامية في أمصال نساء عراقيات عقيمات

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الخلاصة

في هذه الدراسة تم تأكيد التداخلات بين هرمونات الجريبات {هرمونات الجسم الاصفر(LH) ، الهرمون المحفز للجريبة (FSH) والهرمون المحفز للحليب (PRL)} في أمصال (17) أمرأة عراقية عقيم مع صورة الدهون ، فضلا عن مجموعة سيطرة تشمل (17) أمرأة بحالة صحية جيدة وغير عقيمات ، وأعمارهن مقاربة لعمر النساء العقيمات.

أستعملت تقنية التحليل الاشعاعي المناعي (IRMA) لقياس الهرمونات المذكورة في أعلاه،أما صورة الدهون فتشمل مستوى مصل الدم من الكوليستيرول الكلي (Tc)، الكليسريدات الثلاثية (TG)، البروتينات الشحمية العالية الكثافة (HDLc) ، فقد قدرت باستعمال الطرائق اللونية ، واستخدمت المعادلات الرياضية في تقدير البروتينات الشحمية واطئة الكثافة (LDLc) والواطئة الكثافة جدا (VLDLc). أن مؤشر كتلة الجسم (BMI قدر بطريقة حسابية).

اظهرت النتائج ان (20%) فقط من النساء العقيمات نتيجة لخلل هرموني يعانين السمنة ,في حين أن(40%) منهن ذوات أوزان أعلى من الطبيعي .

أظهرت لنا الدراسة ارتفاعامعنويا في مستوى الكليسريدات الثلاثية (TG)عند النساء العقيمات بالمقارنة مع اقرانهن من النساء اللاتي بحالة صحية جيدة .

من ناحية أخرى لم تظهر أي فروق معنوية في مستويات الكوليستيرول الكلي (Tc)، البروتينات الشحمية العالية الكثافة (HDLc) والبروتينات الشحمية واطئة الكثافة (LDLc) بين المجاميع قيد الدراسة .

يمكن ان نستنتج من النتائج اعلاه بأن مؤشر كتلة الجسم (BMI) أو السمنة لاتقترن مع العقم دائما.