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Estimation of Leptin and Estrogen Hormones in Obese Women with Arthritis

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ABSTRACT

Background: Obesity is abnormal accumulation of fat in the body, which led to many health problems that will reduce the life expectancy. Arthritis is joints inflammation that cause many of symptoms such as swelling, tenderness, pain and stiffness of most joints. The arthritis is divided into many types, but the most common types are osteoarthritis and rheumatoid arthritis the last type is the focus of our topic. Rheumatoid arthritis (RA) is an auto-immune, chronic inflammation that can cause damage for joints and other body organs like skin, eyes, lungs, heart and blood vessels.

Objective: The study aimed to investigate the levels of leptin and estrogen hormones in obese women with arthritis. We focused on rheumatoid arthritis especially.

Patients and Methods: The research included ninety women They were distributed into three groups, 30 obese women with body mass index (BMI) more than 25 Kg/m^2 for overweight and more than 30 Kg/m^2 for obese, 30 obese women with rheumatoid arthritis which have positive rheumatoid factor (RF) and 30 control women with normal weight and BMI < 25Kg/m^2 and healthy from RA. BMI, WHR was calculated for all participants.

Result: The result of estrogen hormone showed highly significant difference (P≤0.01) in G1 (55.74 ± 9.23), G2 (55.35 ± 11.77) compared to G3 (129.85 ±16.69). While leptin hormone revealed no significant difference among G1 (2102.13 ±78.03), G2 (2005.80 ±23.81) and G3 (1931.27 ±22.91).

Conclusion: We concluded that leptin levels did not differ among the three groups. Conversely estrogen levels showed highly difference between the three groups.

Keywords: Obesity, Body mass index, Waist-hips ratio, Rheumatoid arthritis, Leptin, Estrogen hormones.

INTRODUCTION

Obesity is increase in body weight and amount of fat body because of increasing in food and calories intake with corresponding decrease in expenditure. This accumulates calorie that lead to build up more adipose tissue. In addition, less movement also increases body weight [(1)].

Obesity is associated with many diseases including cardiovascular disease (CVD), insulin resistance, type 2 diabetes mellitus (DM), hypertension, dyslipidemia, coronary heart disease (CHD), gallbladder disease, obstructive sleep apnea, nonalcoholic fatty liver disease and some malignancies including endometrial, breast, and colon cancer according to guidelines of The American Heart Association and the American College of Cardiology [(2)].

Obesity also have influence on fertility and It interferes with the pregnancy process in women by affecting spontaneous ovulation, interfering with the efficiency and outcomes of assisted reproductive technology (ART), and by worsening the physiological process and delivery in pregnancy [(3)]. Obesity is one of the causes that lead to polycystic ovary syndrome (PCOS) [(4)].

Obesity is a worldwide epidemic. In 2016, obesity rates increased 4 times what they were since 1975. In 2016, obesity rates reached about 1.9 billion in adults over the age of 18, who were overweight, while the number of people suffering from obesity is among these 650, and in general, the obesity rate in 2016 was only 13% (distributed between women and men by 15% and 11%, respectively) [(5)].

There are many measurements used to identify and classify obesity of these measurement is BMI, which are called previously Quetelet index [(6)]. The BMI equation used to calculate the value of BMI, which is dividing the weight in kilogram (Kg) on square of high in meter (m) [(7)]. Based on BMI values, obesity was classified to BMI<20 Kg/m^2underweight, BMI 20-24.9 Kg/m^2 normal weight, BMI (25-29.9) Kg/m^2 overweight, BMI (30-39.9 Kg/m^2) obese and BMI≥40 severely obese [(8)]. The other indicator or measurement of obesity is waist-hip ratio (WHR), which is calculated by dividing the narrowest point of waist on widest points around hips [(9)]. WHR can predict the central obesity in adult and adolescent, which are related to metabolic disorders (insulin resistance and dyslipidemia) and increase the risk of cardiovascular disease. The values of WHR differ among gender, WHR > 0.90 in men and > 0.85 in women [(10)].

Leptin is one of hormones that regulate the body weight and control of appetite and energy homeostasis so it has a significant role in obesity, it is secreted from adipose tissue [(11)]. The adipose tissue is considered as endocrine organ and not fat storage only as was thought previously [(12)].

Leptin sends the signal that is related to size and energy store in organism to brain [(13)], so it works on "brain gut axis" and thus it is transmitting the satiety signal to the

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leptin receptor within hypothalamus in CNS and thus suppress eat food and promote energy expenditure [14]. Leptin functions are metabolic control, insulin sensitivity regulation, growth control, immune regulation and reproduction but most important role is body weight regulation [15].

Estrogen thought is the first hormone determined, this hormone have essential role in reproduction processes in both genders especially in the women, also in other organs system like neuroendocrine, vascular, skeletal, and immune systems. Estrogen plays important role in many illnesses including obesity, metabolic disorder, a variety of cancers, osteoporosis, lupus, endometriosis, and uterine fibroids [16].

Rheumatoid arthritis is autoimmune inflammatory disorder, infected female more than males especially through 30 to 50 years of age. The most important symptoms are pain, swelling, and stiffness of multiple joints. In case long-term inflammation or chronic inflammation it is leading to Joint deformity and loss of function [17]. Obesity in rheumatoid arthritis patients' may increase the activity of disease. Obesity in many studies identified as inflammatory state characterized by increase of the levels of c-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and cytokines, which are called adipokines such as leptin, resistin, visfatin and low levels of adiponectin, which is an anti-inflammatory adipokine. All these pro inflammatory factors increase activity of RA disease [18]. Estrogen has pro-inflammatory effect and also has stimulatory and inhibitory effect on immune system some studies indicate that high or low exposure to estrogen hormone increase the risk of RA and proposed that decline of estrogen increases the dangerous effects of RA more than increase of estrogen levels, which is considered protective agent. One of the factors that cause decline estrogen level is post-menopause in women, which leads to increase incidence of risk in females more than males [19].

MATERIALS AND METHODS

This research was carried out at Baghdad Medical City Teaching Hospital in the period from January 2022 to November 2022. The study included 90 women (30 obese women, 30 obese with RA and 30 control), their ages ranged from 18 to 68 years old. All the women participating in the study were subjected to measurement of waist circumference (WC), hip circumference, waist-hip ratio (WHR) and height using tape. Weight was measured using a digital scale in order to obtain BMI. Venous blood was collected using 5 ml syringe (Cellotron, Malaysia), then was put in gel tube (SSGT, China) and left for 10 min then centrifugation at 3000 rpm for 10 min. The separated serum was used for measurement of leptin by ELISA kit (Mybiosource, U.S.A) and also estrogen according the instruction of kit (Roche, Germany) in the patients and healthy women.

Ethical consent:

The study was approved by The Ethics Board of the University of Baghdad, College of Science, and the participants were informed about the research, and a written consent was obtained from each participant in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

To identify the impact of various factors on research parameters, the Statistical Analysis System- SAS (2018) program was utilized. To statistically compare between means, the Least Significant Difference (LSD) test and analysis of variation (ANOVA) test were employed. In this study, a meaningful comparison between percentage (0.05 and 0.01 likelihood) was made using the Chi-square test.

RESULT

The age in the study revealed highly significant difference ($P \leq 0.01$) in G1 (44.67 ± 2.09) and G2 (44.73 ± 2.46) as compared to G3 (29.60 ± 1.61). The BMI (kg/m^2) showed highly significant difference ($P \leq 0.01$) in G1 (39.33 ± 1.12) and G2 (35.76 ± 1.27) as compared to G3 (28.70 ±1.46). The WHR (cm) revealed highly significant difference ($P \leq 0.01$) in G1 (0.869 ± 0.01) and G2 (0.873 ± 0.02) as compared to G3 (0.776 ±0.02) as shown in table (1) and figures (1), (2), and (3).

Table (1): Comparison between different groups regarding age, BMI and WHR

Group	Mean ± SE		
	Age (year)	BMI (kg/m2)	WHR (cm)
G1	44.67 ±2.09	39.33 ±1.12	0.869 ±0.01
G2	44.73 ±2.46	35.76 ±1.27	0.873 ±0.02
G3	29.60 ±1.61	28.70 ±1.46	0.776 ±0.02
LSD value	5.864 **	3.340 **	0.0338 **
P-value	0.0001	0.0001	0.0001

G1(Obese groups), G2 (obese with RA group), G3 (control group)
**** (P≤0.01).**

Leptin hormone:

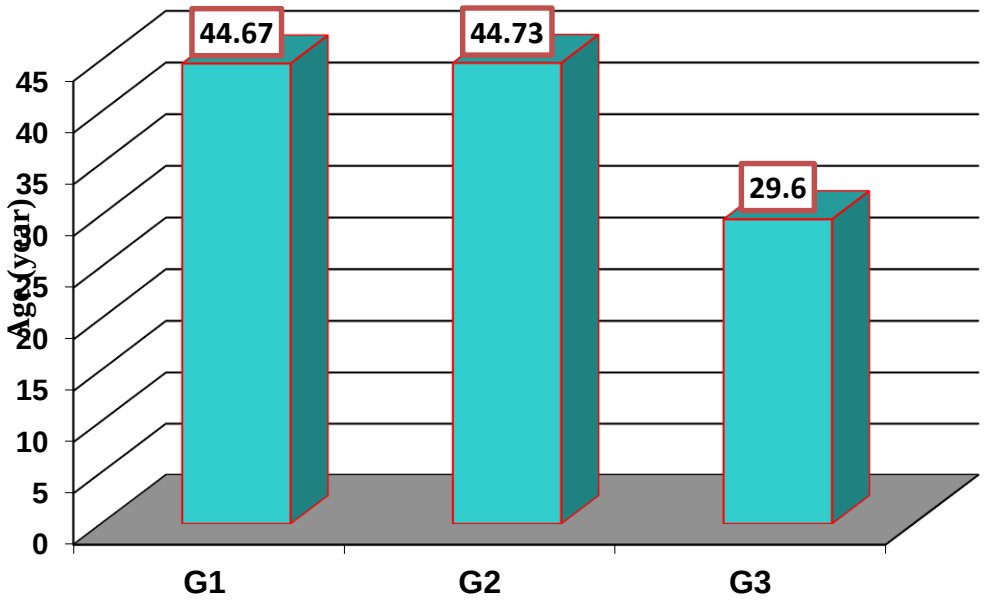

Figure (1): Comparison between different groups regarding age

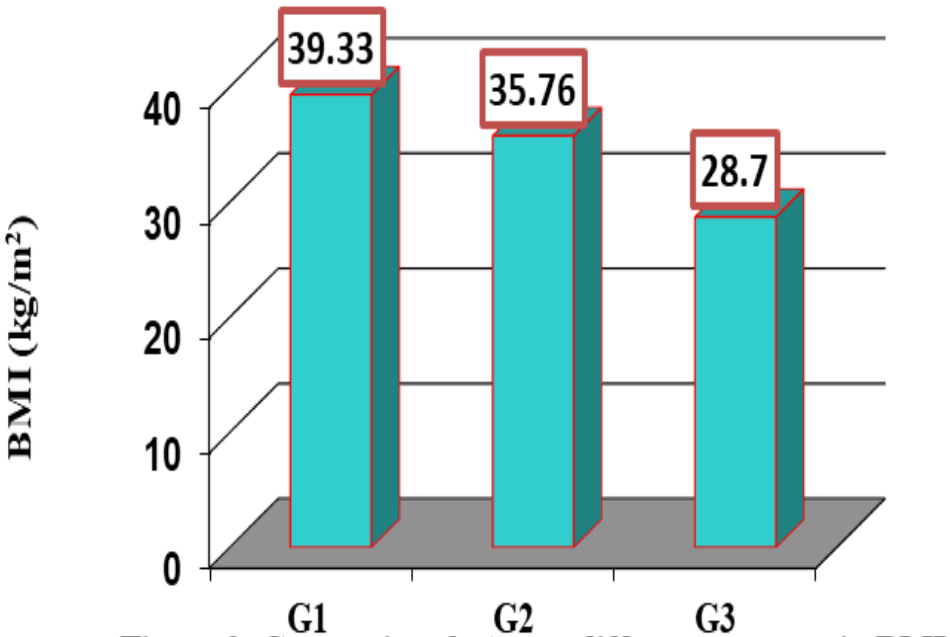

Figure 2: Comparison between difference groups in BMI

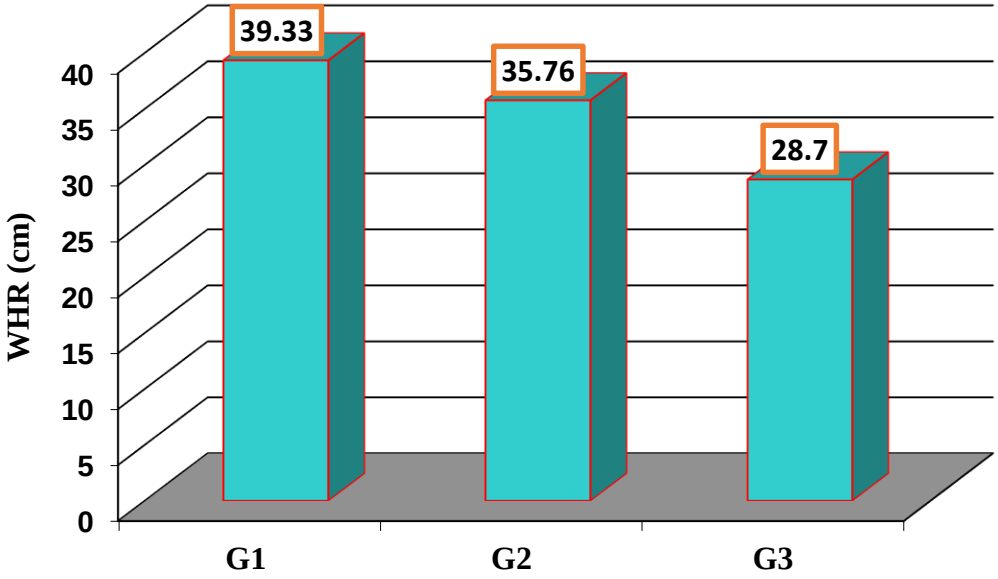

Figure (3): Comparison between different groups concerning WHR

Leptin hormone exhibited no significant difference (P>0.01) between G1 (2102.13 ± 78.03), G2 (2005.80 ± 23.81) compared to G3 (1931.27 ±22.91) as shown in the table (2) and figure (4).

Estrogen hormone:

The estrogen hormone showed highly significant difference (P≤0.01) among G1 (55.74 ± 9.23) and G2 (55.35 ± 11.77) as compared to G3 (129.85 ± 16.69) as shown in the table (2) and figure (5).

Table 2: Comparison between difference groups in Leptin and E2 hormones level

Group	Mean ± SE	
	Leptin (pg/ml)	Estrogen (pmol/L)
G1	2102.13 ±78.03	55.74 ±9.23
G2	2005.80 ±23.81	55.35 ±11.77
G3	1931.27 ±22.91	129.85 ±16.69
LSD value	137.53 NS	36.39 **
P-value	0.433	0.0001
G1(Obese groups), G2 (obese with RA group), G3 (control group) ** (P≤0.01).		

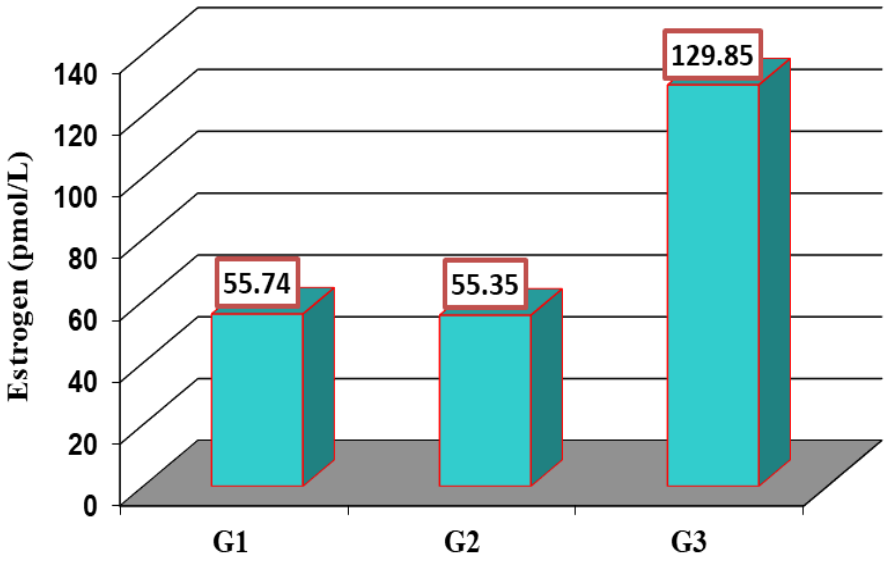

Figure 5. Comparison between difference groups in E2

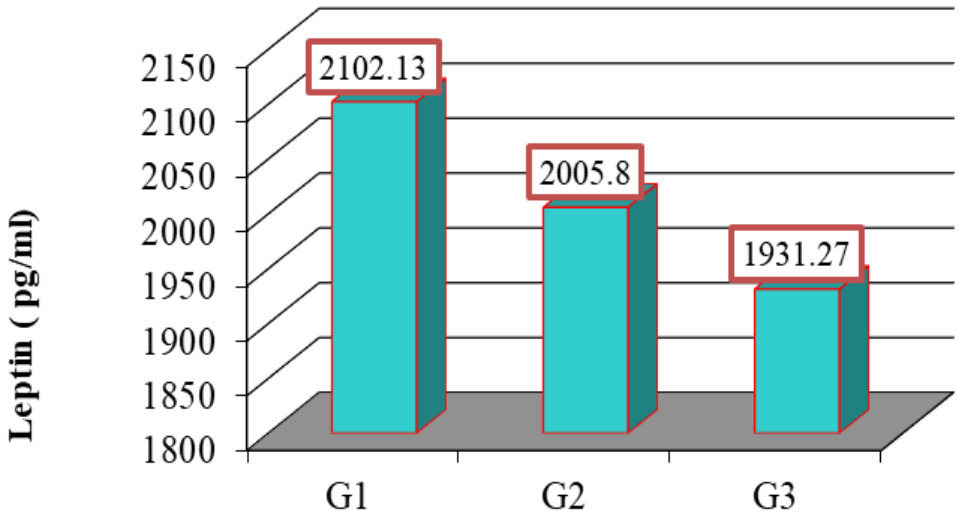

Figure 4: Comparison between difference groups in Leptin

In this study the age, BMI and WHR in obese and obese RA women showed highly significant difference compared to control and this finding agrees with another study [20].

There are many methods for measurement of obesity and overweight, BMI is considered the cheapest and most easily way to predict obesity but it has its disadvantages that it can't distinguish between lean and fat mass hence it is used to determined excess weight not excess fat, which made it less accurate [21 22]. There is a study examined the relationship between BMI and body fat percentage that was in an Urban African Setting and proved the strength relationships between body fat and BMI as get aging and this can be interpreted by many reasons including with age, the fat body increases, protein-energy malnutrition and muscle atrophy because of less activity and movement [23].

The WHR recorded highly significant difference among obese women compared to control women and this matches with another study [24]. WHR is considered from the point of view of WHO important indicator for obesity and it is correlated with obesity in the abdominal area hence it is considered high risk factor for occurrence of type 2 diabetes mellitus and cardiovascular risk conditions, such as coronary artery disease (CAD), stroke, and hypertension. The increase in visceral fat accumulation is associated with increased secretion of free fatty acids, hyperinsulinemia, insulin resistance,

hypertension, and dyslipidemia. WHR related to abdominal fat and it is the beast predicator for cardiovascular risk [25].

The results of leptin hormone in this study showed agreement with previous study which reported no significant difference among obese women and men in leptin hormone [26]. Leptin hormone produced by Lep gene control, is a 16-kDa non glycosylated peptide hormone. Its concentration is related to the amount of fatty tissues and BMI indicator. Leptin level is high in females than in males because its production is suppressed by testosterone and its production is stimulated by ovarian sex steroids. It is known that leptin controls weight and appetite by its effect on hypothalamus and hence limiting the size of adipose tissue stores [27]. Our study revealed that there was no difference in concentration of leptin between obese, obese RA and non-obese women. This result disagrees with previous study concluded that leptin hormone showed highly significant differences among obese and non-obese women [28].

One of explanation for this result is that the level of leptin in blood may be effected by the time of day (Morning, noon and evening). This is the conclusion of **Radić and others** where they measured the level of leptin in three different times (Morning, noon and evening) in obese and lean. Their results showed that leptin concentration in the noon was very low and in the evening was very high in general. In non-obese peoples the level of leptin in the morning was higher than in the evening. Conversely, in obese people the level of leptin in the noon was higher than in the morning period. Hence, because of night fasting the morning levels of leptin was high but decrease after eating and reach lowest value at noon and get rise at evening [29].

Most blood samples of obese women and obese with RA in this study were taken in the morning. Conversely, samples of control non obese women were taken at noon. It is possible that those periods of time had an effect on the level of leptin in the blood. The result of obese women with RA compared to control women disagrees with previous study revealed significant difference in median level of leptin between obese and non-obese patients [30].

Also, **Nishiya *et al.*** [31] and **Anders *et al.*** [32] revealed that there is no difference in leptin level among patients with RA and healthy peoples and there is no correlation between leptin and any indicators of disease activity but it is correlated with BMI or percentage of body fat (%BF).

Our study finding of estrogen hormone disagrees with **Zumoff** [33] result, which showed that estrogen level was high in obese than in non-obese. We noticed throughout the result that the mean levels of estrogen were decreased in obese women and obese women with RA compared to control women. One of the causes to explain this finding are that most obese women and obese women with RA that participated in study were in the postmenopausal period, which lead to low levels of estrogen. Conversely the control women were in premenopausal and this caused high levels of estrogen and this result agrees with previous study showed significant difference in E2 especially in patients with RA [34]. Estrogen produced principally from ovaries but also is produced from adipose tissues, which have roles in distribution of adipose tissues in the body. In pre-menopause females, estrogen stores fat tissue in subcutaneous and gluteo-femoral regions, whereas in the post-menopause stage the adipose tissue is stored at visceral compartment [35].

CONCLUSION

In our study on the evaluation of leptin and estrogen levels, the study found that there were high significant differences in estrogen levels between the two groups of obese women and obese women with RA compared to healthy women. On the contrary, leptin showed no significant differences between the three groups (obese women, obese women with RA and the control women).

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