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Relationship of Obesity to Serum Ferritin, Lipid Profile, uric acid and urea at Obesity Medical Center in Iraq

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Abstract

Obesity is a hyper assembly of energy in the form of adipose tissues which has worse effects on health. The major factors of obesity epidemic are : heavy mails which are rich in lipids, carbohydrates resulting in over weight and eventually obesity, decrease in physical activity that lead to defect in calories conception. In health care facilities ferritin assay is used as a screening test to detect iron deficiency; however, its reliability in obesity has been questioned. The aim of present study was to assess and compare the incidence of obesity, hyperferritinemia, hyperlipidemia and hypouricemia among middle aged hypertensive patients in the local setting as well as, examined ferritin concentrations and other classical indices in obese males and females .This limited population study was conducted at Obesity Medical Center at Al-Kindy Teaching Hospital, Baghdad, Iraq from January to march 2016. One hindered and eight patients were enrolled in this study plus to participate of 61 subjects as healthy control. On the basis of body mass index (BMI), 169 participants were divided into two groups: BMI ≥ 18.5–25 kg/m2 non obese (control), BMI ≥ 30 kg/m2 obese subjects. The main demographic features data of the study population appears that, systolic blood pressure and diastolic blood pressure were raised significantly in obese patients ($P<0.05$) compared with control. Serum hemoglobin level was decreased significantly in obese male when compared with the non-obese group and no difference in female group was observed. In addition, the levels of lipid profile and other studied parameters according to gender showed the following results: A significant elevation in TG, LDL, VLDL, glucose, ferritin in obese (for both genders) compared with the non-obese group. While a significant decrease was noticed in HDL-c, uric acid and urea level in obsess group compared with the non-obese group in both genders. The comparison results between obese males and females concluded that a significant elevation in BMI with a significant decrease in VLDL and ferritin levels in obese females compared with obese males. Present study includes examined all types of correlation between parameters .In obese patients (n=108), stepwise linear regression analysis showed that, serum ferritin levels were independently correlated with LDL, VLDL levels and age, ($P< 0.001$).

Keywords: Obesity, ferritin, lipid profile, Body Mass index, Obesity complications.

الخلاصة

تعرف السمنة بانها تجمعً عالي مِنْ الطاقةِ على شكل أنسجة دهنية والتي لَها تأثيراتُ سيئة على الصحة العامة. . إنّ العوامل الرئيسية للسمنةِ تتمثل ب: الوجبات الثقيلة الغنية بالدهون, تناول الكثير من السكريات, نقصان في النشاطِ الطبيعي والذي يؤدي لخزن المزيد من السعرات الحرارية .عادة يعتبر اختبار الفرتيين تحليل معتمد للكشف عن نقص الحديد في الجسم ولكن علاقة الفرتيين بالسمنة هي مصدر مثير للتساؤلات لدى الباحثيين . الهدف من الدراسة الحالية تقدير ومقارنة الاصابة بالسمنة, ارتفاع مستوى الفرتيين,ارتفاع مستوى الدهون وانخفاض مستوى اليوريا بين مرضى ارتفاع ضغط الدم بمنتصف الاعمارو كذلك قياس تركيز الفرتيين ومتغيرات كلاسيكية اخرى بين الذكور والاناث البدناء .اجريت الدراسة في مركز السمنة الطبي في مستشفى الكندي التعليمي في بغداد للفترة مِنْ يناير/كانون الثّاني إلى مارس/آذارِ 2016وذلك باخذ عينات من 109 مريض بالسمنة و61 كمجموعة سيطرة (اناس اصحاء).وتم اعتماد مقياس التصنيف العالمي BMI لتقسيم العينات حيث صنف الذين يمتلكو $BMI \geq 30\ kg/m^2$ مجموعة السمنة وممن يمتلكون $BMI \geq 18.5–25\ kg/m^2$ مجموعة االسيطرة. اما البيانات السكّانيةِ الرئيسيةِ لمجموعة الدراسةَ تَظْهرُ بأنّ، ضغط الدمّ الإنقباضي وضغط الدمّ

الانبساطي يرتفعان بشكل ملحوظ في مجاميع البدناءعن مجموعة السيطرة (بي <0.05)وملاحظة الانخفاض في مستوى الهيمكلوبين لدى الذكور البدناء مقارنة مع السيطرة وعدم التغير في مستواه لدى الاناث .اما مستوى الدهون والمتغيرات المقاسة الاخرى فقد اعطت النتائج التالية: ارتفاع معنوي في مستويات الفرتين, السكر,VLDL, LDL, Tg في البدناء من كلا الجنسيين مقارنة مع السيطرة .في حين ان هناك انخفاض ملحوظ في مستويات اليوريا, اليورك اسيد, HDL-c في مجموعة البدناء مقارنة بغير البدناء ولكلا الجنسيين .اما الدراسة المقارنة بين الذكور والاناث البدناء فقد اظهرت زيادة معنوية فيBMI ونقصان معنوي في مستوى الفرتيين وVLDL لدى الاناث البدينات مقارنة بالذكورالبدناء .وتضمنت الدراسة فحص معامل الارتباط بين جميع المتغيرات وفحص معامل الانحدار المعياري والذي اظهر الارتباط المعنوي بين الفرتين وكل من العمر ومستوى LDL,VLDL.

Introduction

Obesity is a wide world health complication. In 2014, 600 million adults and 42 million kids, less than five years of age, were obese [1] . This consider the main serious threat to human life by different studies and very common in women [2] . The normal body mass index (BMI) is 18–25 kg/m2. Anyone with a BMI of 25–30 kg/m2 is be overweight, at same time the term "obesity" is used, when BMI exceeds 30 kg/m^2[3] .Overweight and obese individuals have probability of developing health threat like diabetes, obstructive sleep apnea, corpulmonale, ischemic cardiac disease, and others [4] . While it raises the possibility of low Iron levels, leading to an anemia and other disease complecation [5-9]. Medically Obesity is defined as: Is a disorder of body weight regulatory systems characterized by an accumulation of excess body fat. Many metabolic pathways are included in the uptake, transport and storage of fats [10] . The high incidence of obesity results from the reaction of environmental, habitual, and genetic factors. In spite of, genetic factors are necessary for evaluate person ability to becoming overweight, widely defined environmental factors such as changes in food cooking, agriculture, physical activity, and marketing, transportation . These life style steps affect obesity through their effects on diet and physical activity [11, 12]. Obesity began to affect persons to ongoing sub inflammation. Many authors have reported that overweight and obese individuals are ready to sub inflammation which cause many disease like iron deficiency, tumors [13] .Ferritin is submitted as an indicator of low iron levels in wide clinical practice [14] . Ferritin concentration is be increases in overweight and obese individuals, because of generalized inflammation in them [15-17] . For these reason, Ferritin is a Marker of inflammation rather than Iron Deficiency in overweight and obese people [16-17]. Many authors have noticed a relation between ferritin levels and abdominal obesity. Oshang *et al.* [18] found that body mass index (BMI) were the greatest predictors of ferritin level. As well as, the Third National Health and Nutrition Examination Survey reported that ferritin level had a relation with obesity and other factors of fat distribution in body [19-20] Furthermore, Illouz *et al.* [21] Showed that the waist-to-hip circumference ratio was associated to ferritin concentrations in obese type 2 diabetic patients with metabolic syndrome .It must be cleared that ferritin level is an acute phase reactant [22] and, for these reason, every inflammatory events can raise ferritin concentrations. Put in consider that type 2 diabetic mellitus patients have a low inflammatory status [23-24]. This state has been observed in the diabetic persons with increases ferritin level [25].Additionally, not only type 2 diabetes but also insulin resistance and METs have been related with raise in ferritin concentration [19-21] . As raise incidence of METs and/or diabetes have been noted in obese persons, it could be provided that the increased ferritin concentrations tested in obese persons is due to these reasons rather than obesity itself .Therefore, present work will focus on correlating serum ferritin with lipid profile, hypertension and BMI to find out whether, it is right to consider ferritin as a true test of inflammatory in overweight and obese individuals or not.

Materials and Methods

This limited population study was conducted at Obesity Medical Center at Al-Kindy Teaching Hospital, Baghdad, from January to march 2016. One hindered and nine patients seen in the medical outpatient center were enrolled in the study plus to participate of 61 subjects as control. On the basis of body mass index

(BMI), 169 participants were divided into two groups: BMI ≥18.5–25 kg/m^2 non obese (control), BMI ≥ 30 kg/m2 obese subjects. Patients with endocrine disease, pregnancy, and renal disease leading to hypertension were excluded from the study. BMI was calculated using the formula:

$$\boldsymbol{BMI = \frac{Weight\ (kg)}{(Height\ (m))^2}}\ [4]$$

Laboratory analysis

The laboratory parameters were assessed on blood samples. The analyzed biochemical indices involved evaluated of serum glucose, uric acid, urea, total cholesterol, HDL cholesterol, low-density lipoprotein cholesterol, triglycerides and VLDL. These indices were assayed in clinical chemistry laboratories by using laboratory kits (Bio Systems, Spain).

Ferritin was carried out using the Cobas e 411 Analyzer. Two monoclonal mouse antibodies - M-4.184 and M-3.170- are used to form the sandwich complex in the assay. The analyzer automatically calculates the analytic concentration of each sample (ether in µg/L or ng/ml).

Statistical analysis

Statistical analyses were finished depending on the Statistical Package for the Social Sciences (version 20) . Parameters were presented and analyzed using descriptive statistic (mean ± standard deviation). The relation between all indices in obese patients with each other's was assessed using pearson correlation coefficient. The main predictors of ferritin levels in obese patients were detected using the linear regression analysis. The p-value ($p>0.05$), ($p<0.05$) and ($p<0.001$) were considered statistically non-significant, significant .and highly significant.

Results and Discussion

One hundred and sixty nine voluntaries (83 males; 86females) aged between 34-52 years participated in present study. The general demographic characteristics of these subjects are summarized in Table 1.

Table 1: Demographic characteristics of male and female participants.

Gender	Males			Females		
Parameter	Non obes. N=31 Mean ±SD	Obes. N=52 Mean±SD	P value ≤0.05	Non obes. N=30 Mean ±SD	Obes. N=56 Mean±SD	P value ≤0.05
Age (years)	34.02 ±4.425	43.85±4.370	0.0001*	38.31 ±6.858	52.05 ±8.060	0.001*
BMI (Kg/m^2)	26.340± 2.99	34.250± 3.915	0.0001*	24.34 ±2.179	37.48± 2.415	0.0001*
Systolic blood pressure (mmHg)	12.20 ±1.135	15.40 ±1.646	0.001*	11.9 ±1.197	16.20 ±1.619	0.0001*
Diastolic blood pressure (mmHg)	7.80± 1.032	9.90 ±1.197	0.001*	8.40± 0.966	9.70± 0.948	0.007*
Hb(g/dl)	15.36± 1.8422	12.73± 2.493	0.015*	11.53± 1.53	12.58± 2.10	0.218

The main demographic features data of the study population appeared the following results: Systolic and Diastolic blood pressures were significantly raised in obese patients ($P<0.001$) compared with control. Serum Hb was decreased significantly in obese male when compared with the non-obese group and no differences in female group were observed.

In addition, the levels of serum lipid profile and other parameters among groups according to gender are presented in Table 2. The mean levels of cholesterol, Tg, LDL, HDL, VLDL, glucose, ferritin in obese for both gender had

significantly higher when compared with the non-obese group. Dissimilarly, the mean concentration of HDL, uric acid, urea value in obese had significantly lower when compared with the control in both genders.

Table (3) shows a comparison between two obese genders, female subjects had significant increase in BMI compared to male subjects, and decreased in VLDL and ferritin levels compared to male subjects.

Table 2: parameters studied in Iraqi obese patients and control according to gender.

Gender	Males			Females		
Parameter	Nonobes N=31 Mean ± SD	Obes N=51 Mean±SD	P value ≤0.05	Nonobes N=30 Mean ± SD	Obes N=56 Mean±SD	P value ≤0.05
Cholesterol (mg/dl)	188.9± 15.05	253.00 ±44.8	0.001*	181.30 ±18.269	279.50 ±19.415	0.001*
Tg(mg/dl)	111.860 ±32.484	139.351± 26.139	0.05	114.30 ±32.57	143.85 ±18.064	0.022*
HDL-c(mg/dl)	56.13± 8.01	39.18 ±5.811	0.001*	54.20 ±8.641	42.35± 4.585	0.001*
LDL-c(mg/dl)	68.660 ±11.31	112.22 ± 14.056	0.001*	58.541± 9.977	108.23 ±32.210	0.001*
VLDL-c(mg/dl)	23.59± 5.300	36.72± 4.836	0.001*	18.780± 2.853	28.230± 5.374	0.0001*
Uric acid(mg/dl)	5.37± 1.391	2.290± 0.576	0.001*	4.80 1.251	2.240± 0.427	0.0001*
Urea(mg/dl)	34.50 ±4.453	24.900± 4.458	0.001*	35.100 5.216	24.78± 5.403	0.0001*
Glucose(mg/dl)	81.34 ±7.094	109.77± 17.599	0.001*	86.11 ±11.434	108.050± 12.956	0.0001*
Ferritin(ng/ml)	34.08± 4.216	45.410± 5.201	0.001*	20.88 ±6.023	27.81± 6.59	0.025*

Table 3: Comparison of studied parameters between obese males and females.

groups .

Gender	Males	Femals	P value ≤0.05
Parameter	Obes N=51 Mean±SD	Obes N=56 Mean±SD	
Age (years)	43.85±4.370	52.05 ±8.060	0.011*
BMI (Kg/m2)	34.250 ±3.915	37.48 ±2.415	0.039
Systolic blood pressure (mmHg)	15.40 ±1.646	16.20 ±1.619	0.288
Diastolic blood pressure (mmHg)	9.90 ±1.197	9.70 ±0.948	0.684
Hb(mg/dl)	12.73 ±2.493	12.58± 2.10	0.886
Cholesterol (mg/dl)	253.00± 44.8	279.50 ±19.415	0.104
Tg(mg/dl)	139.351± 26.139	143.85 ±18.064	0.660
HDL(mg/dl)	39.18 ±5.811	42.35 ±4.585	0.129
LDL(mg/dl)	112.22 ±14.056		0.724
VLDL(mg/dl)	36.72 ±4.836	28.230± 5.374	0.002*
Uric acid(mg/dl)	2.290 ±0.576	2.240 ±0.427	0.828
Urea(mg/dl)	24.900 ±4.458	24.78 ±5.403	0.957
Glucose(mg/dl)	109.77± 17.599	108.050 ±12.956	0.806
Serum ferritin (ng/ml)	45.410± 5.201	27.81± 6.59	0.001*

Correlation Study

The correlation coefficient (r) test was used for describing the association between the different studied parameters which appeared the following results:

It was noticed a significant correlation between serum cholesterol levels and BMI (-0.637, p=0.048), VLDL and age (0.876, p=0.001), uric acid and glucose (-0.686, p=0.028), urea and SP (0.778, P=0.008) ferritin and SP (0.709, P=0.022) in males group. As well as, a significant correlation in females group was found between cholesterol and HDL (-0.0665,P=0.036), cholesterol and BMI (0.724, P=0.018), urea and BMI (-0.633, p=0.050). Stepwise linear regression analyses in obese patients were performed to examine the influence of the main independent indices against ferritin levels (dependent variable revealed statistically that in

obese patients, ferritin level was independently correlated with LDL, VLDL levels and age, (P< 0.05; Table 6).

Table 6:-Linear regression analyses in obese patients to examine the influences of the main independent indices against ferritin levels (dependent variable).

Coefficients[a]						
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
	(Constant)	-15.013-	40.600		-.370-	.715
	Cholesterol (mg/dl)	-.003-	.046	-.014-	-.066-	.948
	Tg(mg/dl)	.053	.060	.153	.878	.388
	HDL(mg/dl)	.177	.213	.167	.833	.413
	LDL(mg/dl)	.169	.078	.483	2.161	.040
	VLDL(mg/dl)	.963	.234	.735	4.111	.000
	Uric acid(mg/dl)	-.247-	1.617	-.040-	-.153-	.880
	Urea(mg/dl)	.335	.358	.219	.937	.358
	Glucose(mg/dl)	.045	.113	.076	.398	.694
	Hb(mg/dl)	.450	.607	.103	.742	.465
	Systolic blood pressure (mmHg)	-.702-	1.106	-.156-	-.635-	.531
	Diastolic blood pressure (mmHg)	.295	1.550	.037	.191	.850
	Age (years)	-.495-	.200	-.421-	-2.469-	.020
	BMI (Kg/m2)	.018	.488	.011	.037	.971
a. Dependent Variable: ferritin						

Discussion

Obesity has become globally a main health risk in wide world, which lead to many medical and public health complications [25]. On the basis of body mass index (BMI), the World Health Organization (WHO) reported that billion persons at least in world are overweight, of whom three hundred million are obese [26].

Upper results has been appeared clearly increased in ferritin level, glucose, lipid profile and blood pressure in other hand, there was a decreases in Hb, urea, uric acid concentrations in obese patients compared with control, evidence suggests that the rate of synthesis of urea from precursors in obese was lower than in controls which may attribute to the activities of all the enzymes of the urea cycle are decreased in obese subjects [27]. Moreover, uric acid could originate from fructose metabolism, which is well known for inducing hepatic steatosis being directly metabolized to triglycerides in the liver, and be responsible for mitochon-

drial oxidative stress Despite these data, acute decreases seem to provide antioxidant protection, and uric acid contributes >50% of the antioxidant capacity of our organism[28]. Results reviled that obesity may cause inflammation according to ferritin levels which may lead in future at risks factors to have diabetic mellitus, hypertension, heart attacks, kidney dysfunction incidence. The major effect of obesity events are related to complications that include dyslipidemia, type 2 diabetes mellitus, cardic disease, hypertension and respiratory disorders.

Obesity raises cardiac disease risk through risk factors such as raised serum triglycerides, hypertension, high LDL-c cholesterol, low HDL-c cholesterol, and raised serum glucose and insulin levels [29]. Small dense LDL-c is dependent as metabolic risk factors related to obesity, hepatic overproduction of a prob containing lipoproteins, postprandial hyperlipidemia with accumulation of atherogenic remnants. These fats defects can consider the main reasons of metabolism diseases and may be related to inflammatory consequences that can originate in the adipose tissue itself and directly affect the endothelium [30]. The symptoms of dyslipidemia in obesity are hypertriglyceridemia which lead to increased hepatic composition of the very low density lipoproteins (VLDL). As a result can raise liver synthesis of very low density lipoproteins (VLDL-c), lead to the fat degradation of chylomicrons at the level of lipoprotein lipase and raise the rest of TG which being transported to the hepatic [31].

In spite of the low consumption of lipid and saturated fat in the last years, there is an increasing intake of calories and carbohydrates. The consumed of special diet such as soft drinks and sugars has also risen [29]. The main factors of tends toward energy dense food are changes in diet processing, raising portion sizes and marketing pricing. Energy-rich diets (i.e., sugars, breads, and pastas), which have attractive to a person with limited incomes due to low cost. It is suggested that rising of prepackaged diets lead to increase the intake of energy-rich diets [32].

Obesity raises the inflammation-associated hematological parameters and related with chronic inflammation [33, 34]. Hence, ferritin concentrations are directly increased in obese individuals who have inflammations.

During inflammation, there is an elevated in ferritin as an acute phase protein. Therefore, ferritin concentrations below fifteen is considered as iron deficiency (non-inflammatory state) and values less than thirty will be interpreted as iron deficiency since ferritin concentrations will be increased (inflammation and infection) [35].

However, according to our results, ferritin level was not elevated in obesity or thyroid dysfunctions these finding may due to, we excluded any cases with infection from the study, so our patient had low ferritin levels due to iron deficiencies [36].

The results of this study are similar to the results of previous studies on Iranian and Chinese population [37]. Also, an american study noticed a good relation between iron deficiency and BMI in both genders and in all ages and mail intake [38]. Tussing *et al.* found a decrease in iron availability with raising lipid storage amount in adolescents [39].

On the contrary, study by Sanad *et al.* [40] in Egypt found that, in non-obese kids, serum hepcidin was decreased significantly with iron deficiency anemia and significantly increased in obese kids with iron deficiency anemia, other study in mildly overweight adolescents without severely obese subjects suggested that raise ferritin levels and transferrin saturation associated with raising BMI in adult persons [41]. It is to be stated that the results of our study were according to the expectations of the authors.

Raised serum ferritin is associated with many reasons which firstly included iron overload, following the raise of transferrin saturation, and severe hepatic necrosis. Additionally, inflammation considered the main cause of ferritin rose which acts as acute phase protein, like in infectious, rheumatologic, and tumors. [42-48].

Ford *et al.* [49] studied a case-control in Europe, suggesting that persons with high ferritin levels had a higher chance of developing type 2 Diabetic. Furthermore, Salonen *et al.* [50] and Kim *et al*. [51] concluded that raised ferritin

concentrations associated with diabetes disease. As well as, another study obtained that raised ferritin concentrations were related with abdominal obesity [52], hypertension [53], and dyslipidemia [54]. Moreover, Iwasaki *et al.* [55] demonstrated a relation between ferritin levels, visceral fat and subcutaneous adiposity and expected use ferritin as a marker of lipid ferritin level may be a useful marker of lipid presence and degree of IR. Alam *et al.* [56] concluded that high ferritin levels were associated with obesity attributing high levels of ferritin to pro- inflammation.

In a population-based study, Ellervik *et al.* cleared that noticeably raised ferritin levels act as a forecaster indicator of mortality in a dose-dependent manner [57].

As a result of the stopping menstrual periods, ferritin concentrations rise in postmenopausal women. Studies have reported that raised ferritin concentrations are related to main health complications in postmenopausal women [58]. Iron is expected to have effect in wide diseases, such as cardiovascular diseases (CVD), infection, IR, diabetes mellitus (DM), and cancer [59]. Iron Deficiency (ID) with or without anemia is common in obese people and has certain mechanisms involved in its pathogenesis mainly a state of subclinical inflammation. The low iron levels in overweight and obese subjects are most probably caused by the inflammatory events that arrest iron in the reticuloendothelial tissue by releasing different inflammatory mediators like cytokines [60-61].

Conclusions

It is concluded from this study that there is association among hyperferittinemia as index of inflammation, hyperlipidemia hyperglycemia and hypouremia, hypouricemia in both obese genders with the increased of blood pressure and BMI. Increased BMI and ferritin levels are more frequent in the female as compared to the male obese patients which are important risk factor for the obesity complications.

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