Serum Cortisol and BMI in Chronic Diseases and Increased Early Cardiovascular Diseases

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Abstract:

The purpose of this study was to examine the role of cortisol, and it is related to BMI in the chronic diseases which may increase early cardiovascular disease (CVD) in old Iraqi. The subjects were 116 adults, aged 51-71 years. Body Mass Index (BMI), Waist Circumferences (WC) and Waist Hip Ratio (WHR) were used as a measure of adiposity. Investigation showed highly significant difference between patients in BMI ranges, most of male were in an obese weight range (48.5%), as well in women. There were no significant correlations between serum cortisol concentration and age both gender groups. While there were highly significant correlations between cortisol level and BMI, waist, and WHR (except in female subjects), also there were highly significant correlations between cortisol level and SBP,DBP (mmHg)only in male. In both groups, total cholesterol concentration, FBS, and A1C were significantly correlated with serum cortisol. Negatively correlated has been observed between serum cortisol and HDL-C in men but not in women. In men, the results of cortisol with CV risk factors (dyslipidemia, D.M, hypertension, at least 2 risk factors and three risk factors) show significant differences (p>0.0).

In summary, there is a major association between cortisol levels, obese, and chronic diseases. These conclusions promote the hypothesis that the opposing effect of adiposity on the chronic diseases might be mediated by cortisol. This association could cause early development of cardiovascular diseases even in males.

Key words: Cortisol, Body Mass Index, Chronic Diseases, Cardiovascular Disease.

Introduction

Obesity is the main major factor that is associated with other illnesses such as heart disease, diabetes mellitus, and high BP, which are considered the top global health issues. Unnecessary accumulation of body fat can characterize obesity, which is a multifaceted pathophysiological condition. Because of two combination factors; environmental and genetic, obesity remains a chronic disorder. These factors are determined balance

between caloric intake and spending. A major increased risk's factor of illness and mortality is associated with excess body fat [1]. In addition, regardless of weight, high body fat is correlated with a high occur of CVD and its factors of risk [2]. Even if body fat assessments are available currently, the optimal body fat limits which replicate obesity-associated CVD are ambiguous [3- 7]. Many studies have discovered that cortisol high levels' are one causal factor to storage, "visceral" abdominal body fat, of fat. Particularly, fat is unhealthy for heart disease [8]. Besides, the relation between obesity and plasma cortisol are more complicated, because cortisol increased metabolic clearance rate's which is associated with obesity, that tends to lower the levels plasma cortisol in spite of enhanced rate of cortisol production. A study shows that effects in predicting risk factors of cardiovascular of raised plasma cortisol and obesity in people with chronic diseases are additive and independent [9,10] Metabolic syndrome, hypertension, and diabetes are examples of obesity-related disorder, where the major causal factor is obesity [11]. We will not consider metabolic syndrome from the CVD factors in this study, since it has several definitions, unclear pathophysiology and remain a source of controversy in medical research [12]. The current study was to answer if elevated cortisol is associated with increased BMI and early CVD in Iraqi adults.

Materials and Methods:

This study has been carried out at the consultative clinic in Baquba, for the period November 2014. The study included (90) patients (40 females and 50 males) with age range (51-70) year.26 Iraqi control subjects comparable to patients in respect to age (55-70 year) and gender (12 females and 14 males), were included in the study.

Assessment of Cardiovascular Risk Factors

Waist and hip circumferences were measured by using a tape measure, to assess the fat distribution. A waist circumference was measured at the level of umbilicus while hip circumferences were measured at the maximum protuberance of the buttocks [13]. The waist hip ratio was calculated by dividing waist circumference in centimeters by the hip circumference in centimeters [14]. The cutoff value for acceptable WHR that is used as an indicator of central obesity in male and female were 0.95 and 0.80 respectively [15,16]. Body mass index was calculated for each subject using the following equation: BMI = Weight (Kg) / height ^{2} (m²), and blood pressure was measured indirectly by auscultation (listening to sounds) described in 1902 by Russian physician N.S.Korotkoff, using a stethoscope and sphygmomanometer (SK-MINIATUR300B- Germany) consisting of a blood pressure cuff and a mercury column pressure gauge. Both systolic and diastolic blood pressure were recorded in mm Hg. Hypertension was defined as a systolic blood pressure_140 mm Hg, a diastolic blood pressure _90 mm Hg, or treatment of hypertension [17].An 8-hrs fasting blood sample was collected from each subject and prepared for diagnosis of dyslipidemia and diabetes mellitus. Total cholesterol (TC) and triglyceride concentrations were measured by using enzymatic methods. HDL cholesterol was measured after precipitation of apolipoprotein B–containing lipoproteins with sodium phosphor tungstate and magnesium chloride. LDL-cholesterol concentrations were calculated by using the Friedewald formula. Fasting serum glucose (FSG) was measured by using the glucose oxidase method. Glycated hemoglobin (HbA1C) was measured by liquid

chromatography. Dyslipidemia was defined as TC >240 mg/dL and/or HDL cholesterol<40 mg/dL and/or triglyceride>150 mg/dL or treatment of dyslipidemia [18,19]. Diabetes mellitus was defined as FSG >126 mg/dL and Hb A1C >6.5% or treatment of the disease [19,20].An individual was considered a patient when they had _1 of 3 CVD risk factors, such as hypertension ,dyslipidemia, and type 2 diabetes mellitus.

Statistical Analysis

Data were analyzed using the computer facility with available statistical packages of SPSS 11.5 (statistical packages for social sciences-version 11.5). The statistical significance of difference in mean of a normally distributed quantitative variable between 2 groups was assessed by independent samples t-test. In a first analysis, we compared male and female patient groups with different biochemical parameters (plasma glucose, HbA1c, total cholesterol, HDL-cholesterol, systolic and diastolic blood pressures,), with additional covariates [age, gender, body mass index (BMI), WC, and WHR] and in a second analysis we studied the distribution of patients according to BMI. Then we measured the concentration of serum cortisol in different patients depending on BMI, and compared it with healthy men. Also we measured the concentration of serum cortisol in different patients depending on BMI, A level of 0.05, 0.01 and 0.001

was used to determine the statistical significance.

Results and Discussion:

The commonness risk factors of cardiovascular, including high cholesterol, smoking, and untreated hypertension, have fallen significantly since the 1960s, however, prevalence of overweight and particularly obesity continues to rise and become new risk factor. Obesity may become the most common health problem of the 21st century.It is major driving force responsible for the increased prevalence of cardiovascular disease in the developed world. This chronic noncommunicable disease is therefore a major contributor to the global burden of disease and disability associated with numerous conditions such as heart disease, stroke, hypertension, dyslipidemia, type 2 diabetes mellitus, and numerous cancers (endometrial, breast, prostate, and colon). Table (1) shows the clinical characteristics of the study patients. We found that the clinical characteristic of 68 males were similar to female in terms of A_1C, DBP(mmHg), BMI SBP(mmHg) , Tri , FBS , TC, HDL-C, VLDL-C, LDL-C, and age. However, compering between male and female by main waist, we observed that male had elevated main WC and WHR than female and there was a significant difference. Our investigation agrees with the World Health Organization and the International Diabetes Federation [22].

Table (1): Characteristics of study subjects

Variable	whole	male	Female	P value
n	90	50	40	
Age (years)	59.2±9.9	60.8±9.5	57.6±10.4	0.12
Obesity measure				
BMI	30.3±4.4	30.3±5.9	29.4±5.6	NS
Waist	101.1±13.4	105.8±12.3	96.4±14.6	P<0.001
WHR	0.892	0.946	0.84	P<0.001
cardiovascular risk factors measure				
1-Hypertension				
SBP(mmHg)	132.7±10.7	133.3±10.5	132.0±10.7	0.36
DBP(mmHg)	76.4±8.05	76.0±7.3	74.8±8.8	0.53
2- dyslipidemia				
TC	228.05 ± 51.45	228.8 ± 54.7	227.3 ± 48.2	NS
HDL-C		45.4 ± 21.1	46.9 ± 15	NS
LDL-C		144.2 ± 49.3	144.6 ± 46.8	NS
VLDL-C		41.62 ± 40.1	41.42 ± 32.2	NS
Tri		208.1 ± 20.1	207.1 ± 16.1	NS
3-Diabetes mellitus				
FBS		155.2 ± 35	160.7 ± 38.8	
A$_1$C		7.35± 3.2	7.72± 2.1	NS

Significant difference using student's t-test for comparing between two independent means at 0.001levels of significances.

In Table (2) we notice that there was a highly significant difference (P<0.01) between patients in BMI ranges, most of male were in obese weight range (48.5%). Also Table 2 show that there were significant difference (P<0.01) between women in BMI range. Our results are agree with the National Health and Nutrition Examination Survey, which points out that roughly 30% of adults were overweight in 2011-2012 and in compering to19.3% in 2001. For example in 10 years, obesity is approximately increased to 30%, which is major risk factor for heart disease, Type-2 diabetes, cancer, and stroke [23].

Table (2): Distribution of Patients According BMI (Kg/m^2)

BMI	N	%	Comparison of significant by Kruskal-Wallis Test
Men			
18.5-24.9	7	10.3%	
25-29.9	16	29.4%	
30–34.9	21	48.5%	P<0.01
35–39.9	6	11.8%	
total	50	100	
Women			
18.5-24.9	4	8.3	
25-29.9	10	31.3	
30–34.9	23	54.2	P<0.01
35–39.9	3	6.2	
total	40	100	

In Table (3) there were no significant correlations between serum cortisol concentration and age in both gender groups (r=0.217, p >0.05), (r= 0.103, p>0.05) respectively. Though there were highly significant correlations between cortisol level and BMI (r=0.882, p<0.001), WC(r= 0.659, p<0.05) , and WHR (r= 0.734,p<0.05) also there were highly significant correlations between cortisol level and SBP(r = 0.386, p<0.05), DBP(mmHg) (r= 0.392, p<0.001) only in male. Our study has same result as Fraser study [23]. Moreover, Filipovsky reported that morning plasma cortisol concentration to be lower in normotensive, mainly in lean hypertensive subjects, than in hypertensive subject [24].

In the same way, Litchfield found that hypertensive patients have higher urinary free cortisol excretion rates. The rates were higher with high salt intake and higher in men than women [25].In both groups, FBS and A$_1$C were significantly correlated with serum cortisol, because serum cortisol with smaller increases might contribute to anomalous glucose metabolism recognized to happen in metabolic abnormalities and subsequently type 2 diabetes" [26]. In addition, we got positive correlation between serum cortisol and cholesterol. Also, we got negative correlation between serum

cortisol and HDL-C (r= -0.480 p<0.05) in men but not in women. A study done by Sadiqa et al shows that HDL cholesterol and cortisol had inverse relationship which survived stepwise multiple regression analysis and was significant in both women and men. Therefore, cortisol can affect peripheral cholesterol metabolism to change HDL cholesterol formation. Since, cardiovascular risk is intensely associated with lower level of HDL [27].

Table (3): Correlations between Serum Cortisol Concentration and Variable

Variable	Cortisol (ng/ml)	
	Male	Female
Age (years)	0.217	0.133
BMI	0.882**	0.442
Waist	0.659**	0.258
WHR	0.734**	0.227
SBP(mmHg)	0.386*	0.272
DBP(mmHg)	0.392*	0.187
TC	0.381*	0.140*
HDL-C	-0.480*	0.137
FBS	0.416193**	0.481*
A_1C	0.303292*	0.386*

*Correlation is significant at the 0.05 level
** Correlation is significant at the 0.01 level

The results of cortisol with CV risk factors (dyslipidema, D.M, hypertension, At least 2 risk factors and three risk factors) are shown in figures 1.Significant differences (p>0.01) were obtained in BMI among any of the studied groups. A study by Reynolds reported that BMI had significant differences for people who have dyslipidemia or DM2. Which is same as our conclusion. There is a study showed that they got significant positive difference between BMI and hypertension [25], which is the same as our result. Also, we obtained that people, who have at least two risk factors (dyslipidema, DM2), have significant differences with BMI and this obtaining agrees with Oltmanns study [26]. Insulin resistance (IR) is enhanced by body fat accumulation and hyperlipidemia via impairing insulin signaling, increasing free fatty acid in portal blood vessels on one hand, "and by inhibiting key signaling proteins, indicating disturbances in glucose and lipid metabolism , and lead to cortisol secretion on the other hand" [27].

Also, we obtained that people, who have at least three risk factors (dyslipidema, DM2, and hypertention), have significant differences with BMI. Moreover, there is increasing proof that cardiovascular risk is contributed by cortisol, which is not only in Cushing syndrome, but more commonly, in male. Hypertension, dyslipidemia, obesity, insulinresistance, and hyperglycemia are all significant in this respect.
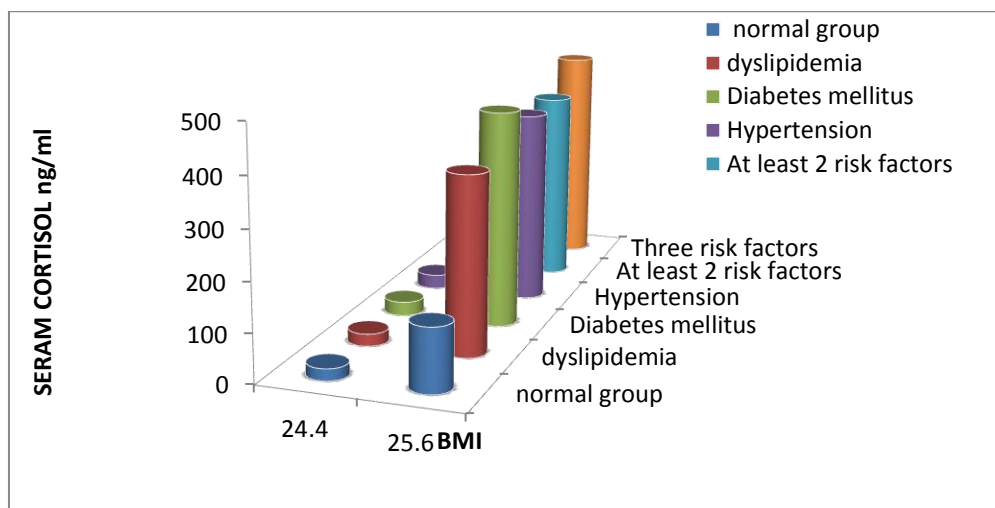

Fig. (1): mean distribution (cortisol & BMI) in CV risk factors (dyslipidema, DM2, hypertension, At least 2 risk factors and three risk factors) patients.

Conclusion:

In summary, there as a major association between cortisol levels, obese, and chronic diseases. These conclusions promote the hypothesis that the opposing effect of adiposity on the chronic diseases might be mediated by cortisol. This association could cause early development of cardiovascular diseases even in males.

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ارتباط الكورتيزول و كتلة الجسم للمرضى المتزايده بالامراض المزمنة و امراض الاوعية القلبية المبكر

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الخلاصة:

الهدف من هذا البحث هو اختبار دور الكورتيزول المتعلق بكتلة الجسم في الامراض المزمنة يؤدي الى زيادة امراض الاوعية القلبيةتضمن البحث اخذ 116 بالغاً،اعمارهم تتراوحبين 51-71 عام. كتلة الجسم ومحيط الخصر ونسبة محيط الخصر الى محيط الورك تم حسابها كدالة للشحوم. مرضى الضغط واختلال الدهون و السكري من النوع الثاني كاشخاص مصابين بامراض مزمنة. مستوى الكورتيزول قيس في الصباح الباكر. البحث بين اختلاف معنوي عالي بين المرضى في دالة كتلة الجسم،اغلبية الذكور(45%) كانوا ضمن مدى السمنة. وكذلك النساء كانت النسبة الكبيرة منهم ضمن مدى السمنة.كذلك لاتوجد أي علاقة بين الكورتيزول والعمر في كلا الجنسين بينما لاحظنا وجود علاقة معنوية عالية بين مستويات الكورتيزول ودالة كتلة الجسم ومحيط الخصر ونسبة محيط الخصر الى الورك في الذكور.كذلك علاقة معنوية عالية بين مستويات الكورتيزول وضغط الدم في الذكور.في كلا المجموعتين لاحظنا وجود علاقة معنوية بين (الكليسترول الكلي ،سكر الدم للصائم ،خضاب الدم) و الكورتيزول.ووجود علاقة معنوية سلبية بين (الدهون الحميدة والكورتيزول) في الذكور فقط وليس في النساء . في الذكور النتائج بينت وجود اختلاف معنوي بين(الكورتيزول ،عوامل زيادة مخاطر تلف الاوعية القلبية) كدالة للكتلة الجسمفي أي مجموعة درست.واستنتجناوجد ارتباط رئيسي بين مستويات الكورتيزول،السمنة والامراض المزمنة.هذا الاستنتاج يشجع على تقدير تاثير الشحوم في الامراض المزمنة الذي يرفع مستوى الكورتيزول. هذا الارتباط يسبب زيادة تطورتلف الاوعية القلبية في الذكور

الكلمات المفتاحية : الكورتيزول، دالة كتلة الجسم ،الامراض المزمنة ، تلف الاوعية القلبية.