Evaluation of Some Biochemical Parameters in Patients With Metabolic Syndrome

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Abstract

Background: Metabolic syndrome is the medical term for a cluster of metabolic abnormalities that increases in individuals risk of diabetic mellitus type 2 (T2DM) and cardiovascular diseases(CVD). _ENREF_1 The components of MS are glucose intolerance, obesity, hypertension and dyslipidemia.An insulin resistance is the key phase of metabolic syndrome constitutes the major risk factor for the development of diabetes mellitus.

Objectives: The present study aimed to comprise insulin resistance values among three study groups.

Subjects: The present study included 50 metabolic syndrome patients, 50 cases who suffered at least one of the metabolic syndrome symptoms as pathological control, finally 50 individuals as healthy control.

Methods: Fasting insulin, hemoglobin A_{1C} (HbA_{1C}), fasting blood glucose and the lipid profile includedtotal cholesterol TC, triglyceride TG and high density lipoprotein cholesterol HDL- and low density lipoprotein cholesterol LDL-C concentrations were determined in present study using a different available kits.

Results:current work showed a highly significant variations among study groups, no significant differences were shown when the comparison was carried out between two genders of the same subgroups.

Keywords:*Metabolic syndrome, insulin resistance, glucose intolerance, hypertension, lipid profile.*

Introduction

The original description of the metabolic syndrome by Reaven[1] consisted of obesity, insulin resistance, hypertension, impaired glucose tolerance or diabetes, hyperinsulinemia and dyslipidemia characterized by elevated triglyceride, and low HDL concentrations[2-4]. All of the features described above are risk factors for atherosclerosis, and thus, metabolic syndrome constituted a significant risk for coronary heart disease. The features of obesity/overweight and insulin resistance also provided a significant risk for developing type 2 diabetes[5, 6]. The risks for coronary heart disease and diabetes with metabolic syndrome are greater than those for simple obesity alone[7].

Metabolic syndrome is quite common. Approximately 32% of the population in the U.S. has metabolic syndrome, and about 85% of those with type 2 diabetes have metabolic syndrome[8, 9] _ENREF_8. Around 25% of adults in Europe and Latin America are estimated to have the condition, and rates are rising in developing East Asian [9].Genetics and the environment both play important roles in the development of the metabolic syndrome, genetic factors influence each individual component of the syndrome, and the syndrome itself. A family history that includes type 2 diabetes, hypertension, and early heart disease greatly increases the chance that an individual will develop the metabolic syndrome[10]. Environmental issues such as low activity level, sedentary lifestyle[11], and

progressive weight gain byeating an excessively high carbohydrate diet also contribute significantly to the risk of developing the metabolic syndrome[12], additionally others factor include: Post-menopausal women and Smoking[13].

Metabolic syndrome is associated with fat accumulation in the liver (fatty liver)resulting in inflammation and the potential forcirrhosis[14]. The kidneys can also be affected, as there is an association with microalbuminuria(the leaking of protein into the urine), a subtle but clear indication of kidney damage[15].Other problems associated with metabolic syndrome include obstructive sleep apnea[16], polycystic ovary syndrome[17], increased risk of dementia with aging, and cognitive decline in the elderly[18].

Insulin resistance is a key step of metabolic syndrome, which is constitutes the main riskfactor for the development of diabetes mellitus[13, 19-21]. Thus , hyperinsulinemia, glucose intolerance , type2 diabetes , hypertriglyceridemia , and low HDL concentration could be accounted for by resistance to the action of insulin on carbohydrate and lipid metabolism[2, 5, 21].

Subjects and Design

During six months ago 50 patients (59.04 years with age range 38) with metabolic syndrome ,50 pathological control (52.06years with age range 34) and 50 healthy controls (52.39years with age range33) were enrolled in the present study. Groups of the present research were classified in to two groups according to their gender.The participated patients were collected from Diabetes Glands Deaf Center in Al-SadderMedical City in Al- Najaf Al-Ashraf governorate, Iraq.

Initial diagnosis was performed by specialist physicians who depended ondefinition of metabolic syndrome requiring the presence of five criteria elevated fasting glucose (≥ 100mg/dL), elevated blood pressure (systolic ≥130 mmHg and/ or diastolic ≥ 85 mmHg), reduced HDL-cholesterol (<40mg/dL), elevated triglycerides (≥ 150 mg/dL) and elevated body mass index (BMI)> 30[22] and through several of clinical and laboratory tests specialist for metabolic syndrome.The individuals as pathological controls suffered at least one of metabolic syndrome symptoms. Selection of healthy individual as a control group based on several criteria; included: an absence of major medical or surgical illness in the previous 5 years, no hospital admissions, no current medication, and a subjective perception of good health as determined by health questionnaire, additionally women who not pregnant or breast feeding.

More than, control group might at approximate age range with the patients group, no smoking, no alcohol drinking with similar food style to patients group. Body mass index (BMI) was calculated as theratio of weight (Kilogram) to the square of height (meters).Obesity and overweight were classified according to WHO criteria[23] [13]. A person was considered obese if the BMI value was ≥30 kg/m2, overweight if BMI ≥25 Kg/$m^2$and <30 Kg/m^2.Blood pressure was measured using an automatic BP device.

Samples Collection

Five milliliters of venous blood samples were collected from the patients and healthy individuals, after fasting period more than eight hours. Samples were allowed to clot at lab temperature, centrifuged at 5000xg for 5 minutes. Sera were collected and stored at -18°C until used.

Methods

Fasting insulin was measured using Sandwich-ELISA kit of Calbiotech[24] company,USA.

Determination of hemoglobin A_{1C} (HbA_{1C}) values by using kits of Stanbiolaboratory company, USA[25, 26]. Colorimetric method was applied for estimating fasting blood glucose using a kit of

Spinract, Spain[27]. The lipid profile includedtotal cholesterol TC, triglyceride TG and high density lipoprotein cholesterol HDL- and low density lipoprotein cholesterol LDL-C concentrations were determined using a commercial available kits of Bilbao company, France.

Statistical Analysis

The statistical analysis of the result obtained in the present study was carried out using the 22th edition of the statistical package for the social science (SPSS). The result were expressed in terms of Mean ± Standard Deviation (Mean±S.D.). The analysis of variance (ANOVA) was used to compare the results of the three groups included in the study, as well the subgroups based on gender differences. Comparison between among studied parameters were done using persons correlation test. The result were statistically significant at 5% probability ($p<0.05$).

Result and Discussion

The current study included 150 individuals classified in three groups including: 50 patients suffered from metabolic syndrome (the first group). The second group included 50 pathological control persons, and the last group included the healthy individuals who were selected to participate in the current study as a control group based on the strict criteria established in the questionnaire which prepared by specialist.The current study aims for comparison the changes of insulin resistance values in patients with metabolic syndrome, pathological and healthy control taking into account differences in age, gender, and body mass index (BMI), as well as the relationship between insulin resistance values and other metabolic disorders in metabolic syndrome.

In order to investigate the most age–matched cases of metabolic syndrome in both genders,the study samples were classified based on their gender.

The present study showed the absence of the difference between females and males in healthy and pathological control groups, but there are significant variation($p=0.033$) between male and female in metabolic syndrome group was recorded, as illustrated in**table 1**.The present finding agreed with the study which mentioned to fact thatthe prevalence of the metabolic syndrome rise with age, reaching peak levels in the sixth decade for men and the seventh decade for women[28]. It suggested that the prevalence of the metabolic syndrome for Mexican American men was significantly higher at 40, 50, 60, and 80 years or older. Occurrence of overweight and obesity are key related factors in the development of visceral adiposity, insulin resistance**,** dyslipidemias, high blood pressure, and impaired glucose metabolism. In addition, aging is associated with evolution of insulin resistance, other hormonal alterations, and increases in visceral adipose tissue,[29] all of which are important in the pathogenesis of the metabolic syndrome.

Table 1: The age (year) in study groups according to their gender

Subjects (n)	Gender (n)	Age (Year) Mean ± SD	Min–Max Age (Year)	Age Range (Year)	p-value
Healthy Control 50	Female 24	52.71± 9.594	43-70	27	0.902For1vs2 0.931For 1vs3 0.115For 1vs5 0.679For 2vs4 0.000For 2vs6 0.651For 3vs4 0.086For 3vs5 0.000For 4vs6 0.033For 5vs6
	Male 26	52.3±10.116	38-73	35	
Pathological Control 50	Female 27	52.48±8.107	40-70	30	
	Male 23	51.57±10.693	36-69	33	
MS Patients 50	Female 30	56.73±7.683	44-81	37	
	Male 20	62.50±9.512	38-71	33	

1: healthy female control. 2: healthy male control, 3:female pathologicalcontrol, 4:male pathological control, 5:female metabolic syndrome, and 4:male metabolic syndrome. The mean difference is significant at 0.05 level

Almost of the participants with MS were obese (BMI ≥ 30) as compared to healthy control(BMI ≤25) with a large waist circumferencecharacteristic accumulation of the lipid layer in the abdomen (apple pattern), meaning they were classified as obese individuals.

The outcomes showed significantdifferences (p=0.000) of BMI between both genders (male and female) in the same groups of pathological control and MS, excepting control group (p= 0.960).A statistically significant variation (p<0.05) was observed when both genders in MS group were compared with their peers in the subgroups of healthy and pathological controls, excepting male in pathological control group who did not exhibit significant elevation when compared with their corsponding in healthy control.

Central obesity as a marker of body fat, which canestimated by measuring body mass index (BMI) and waist circumference (WC) that in turn might effectively predict therisk of MS[30, 31].Obesity seems to be predominant underlying risk factor not only for the development of MS but also other cardiovascularrisk factors[32].Results of many studies indicated forincreasing in body weight and BMI associatedwith the elevation of ischemic heart disease in severalpopulations [31, 33, 34], but this finding has not been reported anapproximate 2-fold increase in the 10-year risk of coronaryartery disease in subjects with a BMI of 30 Kg/m^2or more compared with those with BMI less than 21 Kg/m^2 after adjustment for age[35]. On the other hand, the results of the prospective cardiovascular study indicated thatBMI did not independently contribute to cardiovascularrisk in multiple logistic regression analysis[36].

Table 2: BMI (Kg/m^2)of the Study Subgroups

Subjects (n)	Gender (n)	BMI (Kg/m^2) Mean ± SD	Min–max BMI(Kg/m^2)	BMI Range (Year)	p-value
Healthy Control 50	Female 24	27.316±2.093	23.833-30.637	6.804	0.960 For1vs2 0.000For 1vs3 0.000For 1vs5 0.114For 2vs4 0.000 For 2vs6 0.000For 3vs4 0.000For 3vs5 0.000For 4vs6 0.000For 5vs6
	Male 26	27.268±2.362	21.847-30.628	8.781	
Pathological Control 50	Female 27	32.775±4.880	47.000-25.951	21.049	
	Male 23	28.771±2.766	25.000-36.198	11.198	
MS Patients 50	Female 30	38.512±3.998	31.500-45.000	13.500	
	Male 20	34.957±2.351	32.000-40.000	8.000	

1: healthy female control. 2: healthy male control, 3:female pathological control, 4:male pathological control, 5:female metabolic syndrome, and 4:male metabolic syndrome. The mean difference is significant at 0.05 level

Results of the present study showed significantly (p<0.05) different when the patients groups compared with the healthy control using ANOVA test.Thestudy created a set of individual observations, included: **(1)**A significant increase in blood sugar levels in MS patients and pathological control subjects comparing with healthy control subjects, while did not show significant differences between MS group and pathological group as shown in **table 3**. **(2)**Fasting insulin level seemed to be significantly elevation (p=0.000) in the samples of MS patients and pathological control comparison to healthy individuals, additionally there were significant variation between MS patients and pathological control, as shown in **table 3**.**(3)**The current study recognize arise in the level of HbA1c in the samples of study patients compared to their corresponding values

in the group of healthy individuals, as well asthere were significant changes between MS patients and pathological control.**(4)**The study reported a significant increasing in the levels of cholesterol and very low density lipoproteins binding cholesterol(vLDL-C) in the sera of MS patients comparison to healthy and pathological control, while no such results were noted when the levels of cholesterol and vLDL-C (p=0.234 and p=0.111; respectively) weretestedin healthy and pathological controls.**(5)Table 3** shows highly significant increase in the levelstriglycerides (TGs), high density lipoprotein binding cholesterol(HDL-C), and low density lipoproteins binding cholesterol(LDL-C) in the sera of patients with metabolic syndrome and pathological control subjects comparison to healthy individuals group**.**

Table 3: Levels (Mean±SD) of Sugar Concentration (mg/dL), Insulin Secretion (mIU/L), HbA1c%, and Lipid Profile in Sera of Study Groups

	Subjects (n)			
Parameters	Healthy Control 50 Mean ± SD Min–Max Range	PathologicalControl 50 Mean ± SD Min–Max Range	Ms Patients 50 Mean ± SD Min–Max Range	p-value
Blood Glucose mg/dL	**107.605±15.593** **70.402-129.572** **59.170**	**241.582±81.129** **89.000-421.015** **332.015**	**250.639±81.235** **136.415-442.000** **305.585**	0.000 For 1vs2 0.000For 1vs3 0.542 For 2vs3
Insulin (mIU/L)	**12.223±6.593** **0.068-25.291** **25.223**	**28.379±16.824** **5.864-75.917** **70.053**	**37.935±21.893** **6.291-86.436** **80.145**	0.000For 1vs2 0.000For 1vs3 0.011For 2vs3
HbA1c%	**4.544±0.647** **3.500-5.600** **2.100**	**8.742±1.671** **4.525-12.000** **7.475**	**9.403±1.462** **5.900-12.000** **6.100**	0.000For 1vs2 0.000For 1vs3 0.032For 2vs3
Cholesterol mg/dL	**184.042±38.448** **79.829-266.826** **186.997**	**198.392±50.607** **120.000-325.157** **205.157**	**225.806±42.038** **154.581-340.015** **185.434**	0.243For 1vs2 0.000For 1vs3 0.002For 2vs3
Triglyceride mg/dL	**143.330±40.237** **74.870-215.520** **140.650**	**179.919±84.007** **60.969-350.541** **289.572**	**283.756±90.106** **118.920-598.110** **479.190**	0.016For 1vs2 0.000For 1vs3 0.000For 2vs3
HDL-C mg/dL	**88.250±22.888** **43.910-133.035** **89.125**	**53.673±18.585** **23.245-88.000** **64.755**	**34.3917±7.49752** **20.000-62.620** **42.620**	0.000For 1vs2 0.000For 1vs3 0.000For 2vs3
LDL-C mg/dL	**71.615±33.189** **25.532-126.492** **100.960**	**111.065±50.810** **22.912-236.526** **213.614**	**135.312±44.970** **62.547-248.695** **186.148**	0.001For 1vs2 0.000For 1vs3 0.008For 2vs3
vLDL-C mg/dL	**28.398±7.799** **16.483-43.103** **26.620**	**35.395±16.498** **12.193-70.108** **57.915**	**56.606±18.031** **23.784-119.621** **95.837**	0.111For 1vs2 0.000For 1vs3 0.000For 2vs3
Systolic blood pressure (mmHg)	**114.130±24.915** **110-135** **124**	**133.54±19.560** **100-183** **83**	**153.92±23.839** **180-190** **172**	0.001For 1vs2 0.000For 1vs3 0.000For 2vs3
Diastolic blood pressure (mmHg)	**76.87±5.057** **65-85** **20**	**81.92±11.911** **68-112** **44**	**92.70±13.815** **12-110** **98**	0.119For 1vs2 0.000For 1vs3 0.000For 2vs3

1: healthy female control. 2: healthy male control, 3:female pathological control, 4:male pathological control, 5:female metabolic syndrome, and 4:male metabolic syndrome. The mean difference is significant at 0.05 level

Metabolic syndrome is characterized by a low HDL in association with an elevated triglyceride concentration. This is believed to be a result of anincreased triglyceride load in the HDL particle that is acted on by hepatic lipase, which hydrolyzes the triglyceride. The loss of the triglyceride

results in a small HDL particle that is filtered by the kidney, resulting in adecrease in apolipoprotein (Apo) A and HDL concentrations. Apart from an increase in the loss of apoA, there are data demonstrating that insulin may promote apoA gene transcription[37]. Therefore, insulin resistance states may be associated with diminished apoA biosynthesis[38].

Table 4:Comparison The Levels of HOMA-IR and FIGR Among The Study Groups

	Subjects (n)			
Parameters	**Healthy Control** **50** **Mean ± SD** **Min–Max** **Range**	**Pathological Control** **50** **Mean ± SD** **Min–Max** **Range**	**Ms Patients** **50** **Mean ± SD** **Min–Max** **Range**	**p-value**
HOMA- IR	**3.009±1.566** **0.76-7.78** **7.02**	**16.978±12.398** **2.580-50.56** **47.98**	**23.154±17.616** **2.900-67.363** **64.463**	**0.000 For 1vs2** **0.000For 1vs3** **0.014For 2vs3**
Insulin /Glucose Ratio	**0.114±0.061** **0.033-0.26** **0.227**	**0.131±0.0792** **0.015-0.344** **0.329**	**0.158±0.106** **0.034-0.518** **0.484**	**0.298For 1vs2** **0.009For 1vs3** **0.110For 2vs3**

1: healthy control, 2:pathologicalcontrol, 3:metabolic syndrome. The mean difference is significant at 0.05 level

The insulin resistance level was represented by the HOMA-IR andfasting insulin/glucose ratio(FIGR). The HOMA-IR values in the metabolic syndrome, pathological control,and healthy control groups were 23.154±17.616, 16.978±12.398,and 3.009±1.566; respectively. Independent ANOVA test results showed that IR in the MSgroup was higher than those in pathological control and healthycontrol group, and the differences were statistically significant($p<0.05$) demonstrated in **table 4.**

Outcomes of the current parameter showed there weren't significant differences ($p>0.05$) between the two genders in the same group when HOMA IRwere tested in the six study subgroups, as demonstrated in **table 5**, on the other side; significant increases ($p=0.000$) were recorded when two genders of patients (male and female)were comparedto their matching genders in the healthy group. Additionally significant variations ($p< 0.05$) were observed when the individuals with same genders (healthy male with pathological control male, and healthy female with pathological control female) in the two groups compared together.Levels of HOMA IR of men in the MS group were not statistically different ($p=0.269$) from those in the pathological control group, while levels of HOMAIR were seemed to be statistically high ($p=0.018$)in the MS female comparison to female in pathological control group, as shown **table 5**.Insulin is the central regulator of glucose and lipid homeostasis,it decreased blood glucose concentrations by reducing hepatic gluconeogenesis and glycogenolysisand by enhancing glucose uptake into striated muscles and adipocytes, also,it enhances triglyceridesynthesis in liver and adipose tissues,additionally increases the breakdown of circulating lipoproteins by stimulating lipoprotein lipase activity in adipose tissues, and suppresses lipolysis both in adipose tissues and in muscles[39, 40].

The insulin resistance occurs when adipose, muscle, and liver cells do not response appropriately to insulin, and circulating glucose levels remain high, which leads to pathology and deregulation of feedback mechanism.Insulin resistance is a powerful predicator of T2DM and the hyper-insulinemia is a compensate marker for insulin resistance[41].Insulin resistance is recognized as a component of several Common disorders such as the metabolic syndrome, hypertension,

hyperlipidemia, coronary artery disease and the polycystic ovary syndrome[42]. Metabolic syndrome establish on the basis of resistance to the metabolic actions of insulin. Thus, hyperinsulinemia, glucose intolerance, type 2 diabetes, hypertriglyceridemia, and low HDL concentrations could be accounted for by resistance to the actions of insulin on carbohydrate and lipid metabolism[43].

Table 5:HOMA-IR Levels in The Different Study Subgroups

Subjects	Gender (n)	HOMA-IR Mean ± SD	Min–Max HOMA-IR	Range HOMA-IR	p-value
Healthy Control 50	Female 24	2.693±1.397	0.758-5.711	4.953	0.864For 1vs2 0.001For 1vs3 0.000For 1vs5 0.000For 2vs4 0.000 For 2vs6 0.196For 3vs4 0.018For 3vs5 0.269For 4vs6 0.794For 5vs6
	Male 26	3.300±1.681	0.896-7.780	6.884	
Pathological Control 50	Female 27	14.853±10.662	2.580-49.404	46.824	
	Male 23	19.472±13.998	3.640-50.560	46.920	
MS Patients 50	Female 30	22.777±18.947	2.900-67.363	64.463	
	Male 20	23.720±15.869	5.500-60.900	55.400	

1: healthy female control. 2: healthy male control, 3:female pathological control, 4:male pathological control, 5:female metabolic syndrome, and 4:male metabolic syndrome. The mean difference is significant at 0.05 level

Fasting insulin: glucose ratio(FIGR) levels were observed to be non-significant higher ($p< 0.05$) in patient and pathological control groups than in those in healthy subjects group, as demonstrated in table 4. When the participate individuals in the present study were comparing based on their genders, ANOVA test results showed there are no significantvariation among study subgroups when the FIGR were compared whether in the same group (male with female in the same group) or between same gender subgroups, as illustrates in **table 6.**

Table 6:Levels of FIGR in the Various Study Groups

Subjects	Gender (n)	FIGR Mean ± SD	Min–Max	Range	p-value
Healthy Control 50	Female 24	0.103± 0.553	0.029-0.194	0.165	0.380For 1vs2 0.387For 1vs3 0.054For 1vs5 0.485For 2vs4 0.045For 2vs6 0.468For 3vs4 0.277For 3vs5 0.193For 4vs6 0.274For 5vs6
	Male 26	0.124±0.066	0.030-0.260	0.230	
Pathological Control 50	Female 27	0.123±0.070	0.03-0.31	0.278	
	Male 23	0.141±0.086	0.020-0.344	0.329	
MS Patients 50	Female 30	0.148±0.996	0.034-0.420	0.386	
	Male 20	0.175±0.115	0.050-0.520	0.470	

1: healthy female control. 2: healthy male control, 3:female pathological control, 4:male pathological control, 5:female metabolic syndrome, and 4:male metabolic syndrome. The mean difference is significant at 0.05 level

One of the observations recorded in present study was the significant increase of HOMA IR in patients with Metabolicsyndrome when compared to the healthy and pathological control groups, this indicates the pathogenic effect of insulin resistance, especially when all the combined strains of the syndrome are combined in one person. In addition, it was observed that HOMA IR was more

accurate and acceptable than FIGR to measure the sensitivity of insulin, as the FIGR did not produce significant and acceptable results when comparing study groups, present finding agreed with the study which revealed to fact that HOMA is more appropriate for large epidemiologic studies and is more reliable than FGIR as a measure of insulin resistance among children and adolescents. The use of HOMA is simpler, cheaper, less labor-intensive, less time-consuming, and more acceptable to young people than clamp studies[44].

Conclusion

The metabolic syndrome (visceral obesity, dyslipidemia, hyperglycemia, and hypertension), has become one of the major public- health challenges worldwide[45]. The current study revealed there were significant combined between symptoms of metabolic syndrome,as well as that insulin resistance is the central component of this syndrome and have pathogenic effect on the other components such as hyperlipidemia, hypertension, hyperglycemia and obesity.

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