Metabolic Syndrome and Insulin Resistance in Obese Patients

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Abstract

Background: Metabolic syndrome (MS), diabetes mellitus (DM), and cardiovascular disease (CVD) have been linked to insulin resistance (IR) and its metabolic abnormalities in both young and old people. Today, more young people are diagnosed with MS.

Objectives: to evaluate the hemostasis model of assessment (HOMA) of IR in diagnosing MS in obese patients.

Patients and methods: A case-control study was conducted at the Clinical Pathology and Internal Medicine Departments and Clinic at Qena University Hospital, Egypt, from 1/1/2022 to 1/7/2022. The study involved 110 subjects divided into 2 groups: 90 MS obese cases with a body mass index (BMI) of > 30 kg/m^2, and 20 age- and sex-matched healthy controls. All were clinically evaluated and investigated for serum fasting glucose, fasting insulin, and lipid profile [total cholesterol, LDL, HDL, and triglycerides]. HOMA IR was estimated.

Results: hypertension and diabetes have been associated with MS (P =002). MS patients were significantly older with higher weight, waist circumference (WC), midarm circumference (MAC), BMI (p<0.0001), triglyceride, VLDL (P<0.005), uric acid (P=0.009), fasting glucose (P=0.0002), insulin (P=0.007), HOMA-IR (P=0.0201), and a significant decrease in HDL levels (p<0.0001). HOMA-IR was positively correlated with BMI (r=0.266; 0.007), triglycerides (r=0.216 P=0.031), and VLDL (r=0.216; P=0.031), but negatively correlated with HDL (r=-0.205; P=0.040). Central obesity (WC >100cm) is the main independent predictor of MS.

Conclusion: HOMA-IR is significantly associated with the MS risk factors in obese adults. BMI is the most effective anthropometric indicator of IR, and central obesity significantly increases the risk of MS.

Keywords: Insulin resistance; Metabolic syndrome; Obesity.

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Introduction

Metabolic syndrome (MS) involves clinical and metabolic abnormalities like abdominal obesity, hypertension (HTN), insulin resistance (IR), impaired glucose tolerance, hypertriglyceridemia, and low high-density lipoprotein (HDL) levels **(Wang et al., 2020)**, It affects both young and elderly, with an increasing rates of childhood obesity and IR risk **(Gupta et al., 2012).** MS promotes the development of cardiovascular diseases (CVD) and diabetes, and often linked to visceral obesity **(Gluvic et al., 2017).**

Obesity, a global health concern, causes MS, HTN, DM, stroke, CVD, hyperlipidemia, gallbladder disease, osteoarthritis, some cancers, and sleep apnea **(Hassen et al., 2022).** IR reduces the sensitivity to insulin-regulated metabolic processes, such as glucose clearance and hepatic glucose synthesis. T2DM often results in IR. Insulin sensitivity and resistance can be measured using hyperinsulinemic-euglycemic glucose clamping and insulin suppression tests**.** Homeostatic model assessment of IR (HOMA-IR) is effective in measuring IR in children and adolescents (**Muniyappa et al., 2008**).

IR occurs when insulin production and release increase, but glucose tolerance remains unaffected, affecting glucose consumption **(Lain and Catalano, 2007**).

IR affects general population health, affecting children and teenagers; association between body composition indicators and MS components is crucial **(Nasreddine et al., 2019).** Obesity may impact metabolic alterations in MS, influencing hypertension, dyslipidemia, and insulin resistance,
leading to higher prevalence of certain diseases and a pathophysiological function similar to IR **(Rochlani et al., 2017**).

Patients and methods

A case-control study included 110 subjects, divided into 2 groups, cases group (N= 90) and control group (N=20) conducted to Clinical pathology, internal medicine departments, and clinic at Qena university hospital in Egypt from 1/1/2022 to 1/7/2022.

Inclusion criteria: All cases documented to be obese with BMI more than 30 with metabolic syndrome (condition that is characterized by a congregation of risk factors, including abdominal obesity (AO), based on waist circumference, increased blood pressure, low high-density lipoprotein-cholesterol (HDL-C), and elevated glucose and triglyceride levels, The MS is diagnosed when at least three of the previous five conditions are found in patients **(Gharakhanlou et al., 2012**). and age- and sex-matched healthy controls (Control group participants should have lifestyle factors similar to those of the obese patients. This includes factors such as physical activity levels, dietary habits, smoking status , Similar Socioeconomic Status, lack of pre-existing conditions, absence of MS, IR, or any other significant underlying health conditions and had a BMI less than 30) attended the hospital over 6 months and accepted to participate in the study.

Exclusion criteria: Patients obese without metabolic syndrome.

Ethical consideration: The study protocol was approved by the local institutional Ethical Research Committee of the Qena Faculty of Medicine, and written informed consent was obtained from all patients. **Ethical code:** SVU/ MED /CCP031/1/2022 /1/314

Methods

A) Complete history of the study's patients and controls: Personal data (name, age, sex, occupation and address), history of previous interventions, medical and past history.

B) Careful clinical examination: vital signs (temperature, respiratory rate, blood pressure, and heart rate), pallor, cyanosis, jaundice, lymph node enlargement, and IR skin tags or acanthosis nigricans.

C) Blood sample: After fasting for 12 h, 5 ml venous blood was collected in plain tube under aseptic conditions, clotted for 30 min, centrifuged at 3000 rpm for 10 min, and the serum was separated and assessed for:

- Lipogram: total cholesterol, low-density lipoprotein cholesterol (LDL-cholesterol),

high-density lipoprotein cholesterol (HDL-cholesterol), and triglycerides using Beckman Coulter AU 480-CA-USA by quantitative turbidimetric method (Cat No. OSR6147). Low-density lipoprotein-cholesterol (LDL-C) concentration was calculated by the Friedewald formula. Normal values are total cholesterol < 200 mg/dl, LDL-Cholesterol<100 mg/dl, HDL-Cholesterol> 40 mg/dl, and triglycerides <150 mg/dl.

- Fasting blood glucose: using Beckman Coulter AU 480-CA-USA by quantitative turbidimetric method (Cat No. OSR6147). Normal values 70 - 100 mg/dl.
- Serum uric acid by Beckman Coulter AU 480-CA-USA by quantitative turbidimetric method (Cat No. OSR6147). The adult reference ranges male: 4.0-8.5 mg/dL, female: 2.7-7.3 mg/dl.
- Fasting serum insulin: using automated enzyme immunoassay system (TOSOH AIA-360) by kinetic fluorescence immunoassay. Normal values 5-15 µU/ml.
- Calculation of HOMA-IR [glucose (mg/dl) × insulin (mIU/ml)] ÷ 405. Healthy range: 1.0 (0.5-1.4); Less than 1.0: Insulin-sensitive (optimal); Above 1.9: Early IR; Above 2.9: significant IR **(Matthews et al., 1985).**

Statistical analysis

Data analysis was performed using the Statistical Package for Social (SPSS) version 26. Shapiro-Walk test used to test data normality. The qualitative variables were recorded as number and percentages and assessed with Chi-square. The Student's t-test was used to compare means ± SD for quantitative measures in normally distributed data and Mann-Whitney U test in non-symmetrically distributed data. Pearson's correlation and binary logistic regression analysis was used to evaluate the association between HOMA-IR and MS. The probability (P-value) <0.05 was considered significant.

Results

Cases with MS having a significantly higher mean age of 49.86 ± 15.83 years (range 17-85 years), compared to the control group 32.5 ± 9.48 years (ranged 19-53 years), (P<0.0001). There were 23 male (25.56%) and 67 female (74.44%). However, controls were 5(25%) males and females 15(75%). There were insignificant difference between cases and controls concerning sex (P >0.05)**.** Cases with MS having a significantly higher weight with (p<0.0001), waist circumference with (p <0.0001), MAC (p =0.00048), and BMI with (p <0.0001), (**Table.1).**

Table 1. Demographic data in the studied group

Demographic data	Cases (N = 90)		Controls (N = 20)	P-value
Age (years)^				
Mean ± SD	49.86 ± 15.83		32.5 ± 9.48	<0.0001*
Median (Range)	48 (17-85)		29 (19-53)	
Gender#				
Male	23 (25.56%)		5(25%)	0.959
Female	67 (74.44%)		15(75%)	
WC (cm)^	Mean ± SD	104.73 ± 11.45	82.3 ± 10.45	<0.0001*
	Median (Range)	103 (80-145)	81.5 (64-103)	
Weight (kg)^	Mean ± SD	83.44 ± 11.93	61 ± 10.29	<0.0001*
	Median (Range)	81 (67.5-150)	61.5 (45-77)	
MAC (cm)^	Mean ± SD	32.08 ± 6.09	26.78 ± 5.32	0.0005*
	Median (Range)	32 (22-56)	27 (18-37.5)	
Height (cm)^	Mean ± SD	159.5 ± 7.11	161.43 ± 8.82	0.29643
	Median (Range)	160 (143-183)	160 (150-181.5)	
BMI (kg/m^2)^	Mean ± SD	32.71 ± 3.08	23.4 ± 3.43	<0.0001*
	Median (Range)	31.58 (27.34-46.3)	23.34 (15.12-28.13)	

*: significant; #: Chi-square; ^: student t-test; BMI: body mass index; MAC: mid arm circumference, Waist Circumference

Compared with controls, in MS, 45 (50%) patients were hypertensive and 2 (10 %) controls were hypertensive (P =0.0009). There were 43 (47.78%) patients had diabetes (P =0.0001) and 15 patients had both diabetes and hypertension (P =002), (**Table .2).** Compared with controls, MS patients had significantly higher triglyceride (P =0.005), VLDL (P = 0.005), significantly lower HDL (p <0.0001), (**Table .3).**

Table 2.Associated comorbidity in the studied group

Comorbidity N (%)	**Cases (N = 90)**	**Controls (N = 20)**	**P-value**
HTN	45 (50%)	2 (10%)	0.0009*
DM	43 (47.78%)	0 (0%)	0.00005*
DM & HTN	15	0	0.002*

*: significant; #: Chi-square; DM: diabetes mellitus; HTN: hypertension.

Table 3.Lipid profile in the studied groups

Variables	**Case (N=90)**			**Control (N=20)**			**P-value**
	Median	**Mean**	**SD**	**Median**	**Mean**	**SD**	
Cholesterol (mg/dl)	180.5 (82-367)	189.43	63.51	185(63-236)	172.94	43.61	0.273
Triglyceride (mg/dl)	160.5(66-476)	173.68	78.74	94.5(43-270)	119.64	65.32	0.005*
HDL (mg/dl)	20(3-51)	21.44	10.89	39.5(6-81)	38.45	23.41	<0.0001*
VLDL (mg/dl)	32.1(13.2-95.2)	34.74	15.75	18.9(8.6-54)	23.93	13.06	0.005*
LDL (mg/dl)	84(16-187)	86.9	32.8	72.5(16-135)	74.9	30.48	0.137

*: significant; student t-test; **HDL:** high density lipoprotein, **VLDL**: very low density lipoprotein; **LDL**: low density lipoprotein

Compared with controls, MS patients had significantly higher serum uric acid (P=0.009), serum fasting insulin (P=0.007), fasting blood glucose (p=0.0002), and HOMA-IR (p=0.0201), (**Table .4).**

Table 4. Laboratory finding in the studied groups

Variables	**Case (N=90)**	**Control (N=20)**	**P value**
	Median	**Median**	
Uric Acid (mg/dl)	5 (1-15.5)	3.35(2-7)	0.009*
Fasting glucose (mg/dl)	149.5 (75-680)	87.5 (52-146)	0.0002*
Fasting insulin (µU/ml)	11.6 (1-151.9)	2.7 (0.9-20.4)	0.007*
HOMA IR	3.69 (0.23-102.42)	0.64 (0.13-4.63)	0.020*

Mann-Whitney U test; *: significant; HOMA IR**:** hemostatic model assessment for insulin resistance

Pearson's correlation showed that HOMA IR had significant positive correlation with fasting insulin and BMI), however, no significant correlation with patients age, serum cholesterol and LDL levels. HOMA IR showed significant negative correlation with serum TG level, HDL and VLDL, (**Table .5).** Pearson's correlation shows no significant correlation between fasting insulin and fasting glucose levels, (**Table .6)**

Table 5. Correlation between HOMAR-IR test and (fasting insulin level, BMI, age and lipid profile tests)

Variables	HOMAR-IR	
	r	P- value
Age (years)	0.081	0.424
BMI (kg/m^2)^	0.266	0.007*
Cholesterol (mg/dl)	0.061	0.544
Triglyceride (mg/dl)	0.216	0.031*
HDL (mg/dl)	-0.205	0.040*
VLDL (mg/dl)	0.216	0.031*
LDL (mg/dl)	0.126	0.210
fasting insulin (µU/ml)	0.841	<0.001*

*: significant

Table 6. Correlation between fasting blood glucose level and fasting insulin

Variables	Fasting blood glucose	
	r	P- value
fasting insulin (µU/ml)	0.117	0.247

The binary logistic regression analysis for the predictors of MS reveals that central obesity (waist circumference >100cm) is the main independent predictor of MS in obese persons, (**Table .7)**

Table 7. Binary logistic regression analysis for predictors of metabolic syndrome

Variables	B	S.E.	Wald	P-value	OD	95% CI for EXP(B)	
						Lower	Upper
WC >100cm	-2.369	0.690	11.809	0.001*	0.094	0.024	0.361
MAC >30cm	0.552	0.562	0.961	0.327	1.736	0.576	5.228
BMI >30 (kg/m^2)	-0.174	0.628	0.077	0.781	0.840	0.245	2.877
Cholesterol >200mg/dl	0.983	0.578	2.886	0.089	2.671	0.860	8.300
TG >150 mg/dl	-0.176	0.541	0.106	0.744	0.838	0.290	2.420
VLDL >40mg/dl	0.505	0.681	0.550	0.459	1.656	0.436	6.291
VLDL >100mg/dl	-0.987	0.534	3.419	0.064	0.373	0.131	1.061

*: significant

Discussion

In our study, we examined the association between IR and MS in obese subjects. We found that MS patients have significantly correlated with associated comorbidities, especially hypertension and diabetes (P =002); this was in agreement with **Lejawa et al. (2021)** who studied the correlation between obesity, diabetes, and adipokines in metabolically healthy and unhealthy obesity in young males and revealed that they had comorbidities with higher SBP, DBP, and HbA1c (%) that differed significantly across groups (p <0.0001).

In our study, we found that MS patients were significantly older with higher WC, MAC, weight, and BMI (P <0.0001). This was in line with **Pekgor et al. (2019)**.

Our study showed a significant increase in cases compared to controls in triglycerides and VLDL (p =.005). Uric acid (P= 0.009), fasting glucose (P= 0.0002), insulin (P= 0.007), HOMA-IR (P= 0.0201) and with a significant decrease in HDL levels (p <0.0001). This was in agreement with **Cătoi et al., (2018)** reported that the metabolically unhealthy morbidly obese (MUHMO) with MS MUHMO group had

greater triglycerides, whereas the metabolically healthy morbidly obese (MHMO) had significantly higher HDL-C (P = 0.003). However, the two groups had similar TC (P = 0.984) and LDL-C (P = 0.982). Also, this was in line with the findings of (**Pekgor et al., 2019; Baveicy et al., 2020; Lejawa et al., 2021**).

In our study, we found a significantly higher increase in uric acid (P = 0.009), fasting glucose (P= 0.0002), fasting insulin (P = 0.007), and HOMA IR (P = 0.007) in the case group than in the control group. This was in agreement with (**Monzavi et al., 2006; Ferreira et al., 2018; Gobato et al., 2018; Pekgor et al., 2019).**

Assumpção et al. (2010) reported that there was a significantly higher increase in DBP (mm Hg), and SBP (mm Hg) in the case group than in the control group. Also, they reported that there was a statistically significant increase in insulin (µUI/mL) (p <0.0001) in the case group compared to the control group. Also, **Pekgor et al., (2019)** found that there was a significantly higher increase in SBP and obese DBP in the case group than in the control group.

In our study, we found that HOMA-IR was positively correlated with BMI (r = 0.266; P = 0.007), triglyceride (r = 0.216 P = 0.031), HDL (r = -0.205; P = 0.040) and VLDL (r = -0.216; P = 0.031). The regression analysis revealed that central obesity with a WC >100cm is the main independent predictor of MS.

Conclusion

IR is significantly associated with the MS risk factors in obese adult. BMI is the most effective anthropometric indicator of IR, and central obesity significantly increases the risk of MS.

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