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Adiponectin/Homa-IR ratio as biomarker of metabolic syndrome in Basrah

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Abstract
Adiponectin is a protein hormone secreted predominantly by adipocytes (fat cells). It plays a crucial role in regulating glucose levels, lipid metabolism, and insulin sensitivity. It has been studied for its association with metabolic syndrome components and insulin resistance. The research involved 120 individuals diagnosed with Metabolic Syndrome, comprising 55 males and 65 females, and a control group of 40 males and 40 females ages 18 to 78. We aim to evaluate the adiponectin/HOMA-IR ratio as a reliable biomarker of metabolic syndrome in the Iraq/Basra population. The highest proportion of patients with MetS and controls were from 41 to 50 years of age. Hypertension was present in 74.2% of patients with MetS, and DM was present in 68.3% of patients with MetS. The parameter analysis showed that fasting blood sugar (FBS), total cholesterol, triglyceride levels, VLDL levels, High-sensitivity C-reactive protein (hs-CRP), and HOMA-IR levels were significantly higher ($p \leq 0.001$). Significantly lower ($p \leq 0.001$) in HDL-C, Adiponectin, and Adiponectin/HOMA-IR ratio levels in Metabolic Syndrome patients compared to the control subjects. The adiponectin/HOMA-IR ratio had a significant inverse correlation weak with WC, SBP, DBP, FBS, TG, and VLDL, and a strong correlation with insulin and HOMA-IR. Metabolic syndrome is a common health issue that increases the risk for several serious illnesses, such as Type 2 Diabetes Miletus (DM), Hypertension (HT), and coronary artery disease (CAD). Patients with MetS had significantly decreased adiponectin/HOMA-IR ratio, correlated with various components of MetS. The adiponectin/HOMA-IR ratio could serve as a simple, noninvasive, and cost-effective tool to aid healthcare providers in diagnosing and managing metabolic syndrome.

Keywords: Adiponectin, metabolic syndrome, insulin resistance, obesity

Introduction
Metabolic syndrome is a serious issue worldwide. It is characterized by at least three metabolic risk factors: abdominal obesity, hypertension, hyperglycemia, high serum triglyceride levels, and low serum HDL. The co-occurrence of these factors increases the risk for type 2 diabetes and cardiovascular diseases due to underlying insulin resistance [1].
Unfortunately, no laboratory parameter reliably detects metabolic syndrome, and estimating insulin resistance is tedious. A biomarker that can accurately diagnose metabolic syndrome and insulin-resistant states is needed. Chronic low-grade inflammation is a key factor in insulin resistance and all its components [2].
Adiponectin is a polypeptide hormone secreted predominantly by adipocytes and plays a vital role in regulating glucose levels, lipid metabolism, and insulin sensitivity. Researchers have studied adiponectin for its association with metabolic syndrome components and insulin resistance [3].
This case-control study aimed to Investigate the plasma Adiponectin/HOMA-IR ratio associated with metabolic syndrome in the Basrah general population to Examine whether age and gender impact the Adiponectin/HOMA-IR ratio in MetS patients, Whether Adiponectin/HOMA-IR ratio correlates the with severity of metabolic syndrome and study the possibility of correlating this parameter with the Adiponectin/HOMA-IR ratio

Participants and Methods
This prospective case-control study was performed on patients presenting to the diabetic

center in Al Fayha Hospital from November 2023 to August 2024 after obtaining permission from the institutional ethics committee. Patients aged more than 18 years with Metabolic Syndrome were enrolled as cases (n=120) after voluntary informed consent. MS was defined as per the American Heart Association \National Heart, Lung, and Blood Institute (AHA/NHLBI) consensus 2009 as participants having increased waist circumference (cutoff ≥ 40inch for men and ≥35inch for women) plus any two of the following: Triglycerides ≥ 150 mg/dl or treatment for triglycerides; HDL cholesterol < 40 mg/dl in men and < 50 mg/dl in women or treatment for HDL; Systolic BP > 140 or diastolic BP >90 mm Hg or treatment for hypertension; Fasting plasma glucose ≥100 mg/dl, or treatment for type 2 diabetes.

Results

Table 1 displays the distribution of patients with Metabolic Syndrome and control subjects based on socio-demographic variables. The age range of the subjects was between 18 to 80 years, and the majority of patients with MetS and controls were between the ages of 17 to 54, with frequencies of 74.2% and 73.7%, respectively. However, the age group (54-80 yrs.) had the lowest proportion, with comparative frequencies of 25.8% and 26.3%, respectively.

Table 1: Sociodemographic characteristics of the studied population.

		Subject		Total	p-value
		Control (n=80)	Study (n=120)		
Gender	Male	40 (50.0%)	55 (45.8%)	95 (47.5%)	> 0.05
	Female	40 (50.0%)	65 (54.2%)	105 (52.5%)	
Age group	17-54 yrs.	59 (73.7%)	89 (74.2%)	26 (13.0%)	> 0.05
	54-80 yrs.	21 (26.3%)	31 (25.8%)	(46 23.0%)	
BMI	20-24.9	40 (51.3%)	3 (2.5%)	43 (21.8%)	<0.01*
	25-29.9	38 (48.7%)	19 (16.0%)	57 (28.9%)	
	30-34.9	0 (0.0%)	57 (47.9%)	57 (47.9%)	
	≥35	0 (0.0%)	40 (33.6%)	40 (33.6%)	
T2DM	NO	80 (100.0%)	38 (31.7%)	118 (59.0%)	<0.01*
	yes	0 (0.0%)	82 (68.3%)	82 (41.0%)	
HT	NO	80 (100.0%)	31 (25.8%)	111 (55.5%)	<0.01*
	yes	0 (0.0%)	89 (74.2%)	89 (44.5%)	
Smoking	non smoker	54 (67.5%)	42 (35.0%)	96 (48.0%)	<0.01*
	ex-smoker	0 (0.0%)	7 (5.8%)	7 (3.5%)	
	smoker	26 (32.5%)	71 (59.2%)	97 (48.5%)	
Family history	negative	1 (1.3%)	9 (7.6%)	10 (5.0%)	<0.05**
	HT	2 (2.5%)	30 (25.2%)	32 (16.1%)	
	T2DM	77 (96.3%)	67 (56.3%)	144 (72.4%)	
	CVA	0 (0.0%)	13 (10.9%)	13 (6.5%)	
Total		80 (100.0%)	120 (100.0%)	200 (100.0%)	

(BMI: Body mass index, n: number, T2DM: Type 2 diabetes mellitus, HT: Hypertension, CVA: Cardio Vascular Accident)
*The mean difference is significant at the ≤ 0.01 level between Patients and Controls.
**The mean difference is significant at the ≤ 0.05 level between Patients and Controls.
> 0.05 no significant differences

Patients with Metabolic Syndrome (MetS) were found to have a higher Body Mass Index (BMI) than control subjects, with a significant difference (p<0.001). Patients with MetS also had higher Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) compared to control subjects (p<0.001). Waist Circumference (WC) was also higher among patients with MetS in both genders compared to control subjects (p<0.001) Table 2.

Table 2: Anthropometric measures of the studied group.

	Control (n=80)		Study (n=120)		P-value
	Mean ± SD	SE	Mean ± SD	SE	
Age (year)	45.71±12.284	1.373	45.35±14.176	1.294	> 0.05
BMI	24.67±1.575	0.176	35.11±7.099	0.64	<0.01*
W.C	34.92±2.675	0.299	47.11±6.47	0.590	<0.01*
S. BP	120.575±5.862	0.655	138.53±18.119	1.654	<0.01*
D.BP	76.07±5.336	0.596	83.43±13.359	1.219	<0.01*

(BMI: Body mass index, n: number, W.C: wrist circumference, S.BP: Systolic blood pressure, D.BP: Diastolic Blood pressure)
*The mean difference is significant at the ≤ 0.01 level between Patients and Controls.
p>0.05 no significant differences.

Table 3 shows a highly statically significant increase in the mean of FBS, HbA1c, VLDL, DBP, HDL, and Adiponectin (p<0.01) and a statically significant increase in the mean of S. total cholesterol (p<0.05), while no statically significantly differences in LDL-C, ALP, AST, and ALT in patients' group in compared to the control subjects (p>0.05).

Table 3: Comparison of all biochemical markers in patients and control groups.

Biochemical markers	Control (n=80)	Study (n=120)	P-value
	Mean ± SD	Mean ± SD	
FBS mg/dL	89.3±6.1	149.8±50.3	<0.01*
A1c%	5.1±0.5	7.5±1.8	<0.01*
Total cholesterol mg/dL	166.5±36.9	182.3±41.5	<0.05**
Triglyceride mg/dL	99.9±29.5	218.1±62.1	<0.01*
LDL-C mg/dL	104.3±30.9	107.8±36.8	> 0.05
VLDL mg/dL	19.1±5.9	41.1±7.4	<0.01*
HDL-C mg/dL	45.6±10.5	38.7±10.5	<0.01*
Serum Insulin µU/ml	12.1±5.3	49.1±28.6	<0.01*
Adiponectin ug/L	27.3±7.8	22.4±6.3	<0.01*
HOMA-IR	2.7±1.2	19.1±14.9	<0.01*
hsCRP nmol/L	1.2±0.8	7.1±17.3	<0.01*
Adiponectin/HOMA-IR ratio	12.1±5.9	2.3±2.3	<0.01*
ALP U/L	86.9±29.4	84.7±28.1	> 0.05
AST U/L	21.4±9.1	21.8±15.2	> 0.05
ALT U/L	21.1±12.2	18.9±7.7	> 0.05

(FBS: Fasting Blood Sugar, A1c%: glycosylated hemoglobin, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol, VLDL: Very Low-density lipoprotein, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, hsCRP: high sensitive c reactive protein, HOMA-IR: Homeostasis Model Assessment-Insulin Resistance, ALP: alkaline phosphatases)
***The mean difference is significant at the ≤ 0.01 level between Patients and Controls.
****The mean difference is significant at the ≤ 0.05 level between Patients and Controls.
> 0.05 no significant differences.

Adiponectin/HOMA-IR ratio had significant inverse very weak correlation with WC, SBP while weak inverse correlation with DBP, FBS, TG and VLDL while strong inverse correlation with S. insulin and HOMA-IR, Table 4.

Table 4: Linear regression analysis of studied biomarkers in patients group only.

		Adiponectin/HOMA-IR ratio
BMI	Linear regression R	-0.16
	P-value	>0.05
W.C	Linear regression R	-0.19*
	P-value	<0.05*
S. BP	Linear regression R	-0.185*
	P-value	<0.05*
D.BP	Linear regression R	-0.20*
	P-value	<0.05*
FBS	Linear regression R	-0.25*
	P-value	<0.01**
A1c	Linear regression R	-0.14
	P-value	>0.05
T. cholesterol	Linear regression R	-0.03
	P-value	>0.05
Triglyceride	Linear regression R	-0.24*
	P-value	<0.01**
LDL-C	Linear regression R	0.08
	P-value	>0.05
VLDL	Linear regression R	-0.24
	P-value	<0.01**
HDL-C	Linear regression R	0.01
	P-value	>0.05
S. Insulin	Linear regression R	-0.68
	P-value	<0.01**
Adiponectin	Linear regression R	0.20
	P-value	<0.05*
HOMA-IR	Linear regression R	-0.62
	P-value	<0.01**
hsCRP	Linear regression R	-0.01
	P-value	>0.05

(BMI: Body mass index, W.C: wrist circumference, S.BP: Systolic blood pressure, D.BP: Diastolic Blood pressure FBS: Fasting Blood Sugar, A1c%: glycosylated hemoglobin, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, VLDL: Very Low-density lipoprotein, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, hsCRP: high sensitive c reactive protein, HOMA-IR: Homeostasis Model Assessment-Insulin Resistance, ALP: alkaline phosphatases)
**Correlation is highly significant at the ≤0.01 level (P-value).
*Correlation is significant at the ≤0.05 level (P-value).
>0.05 no significant Correlation

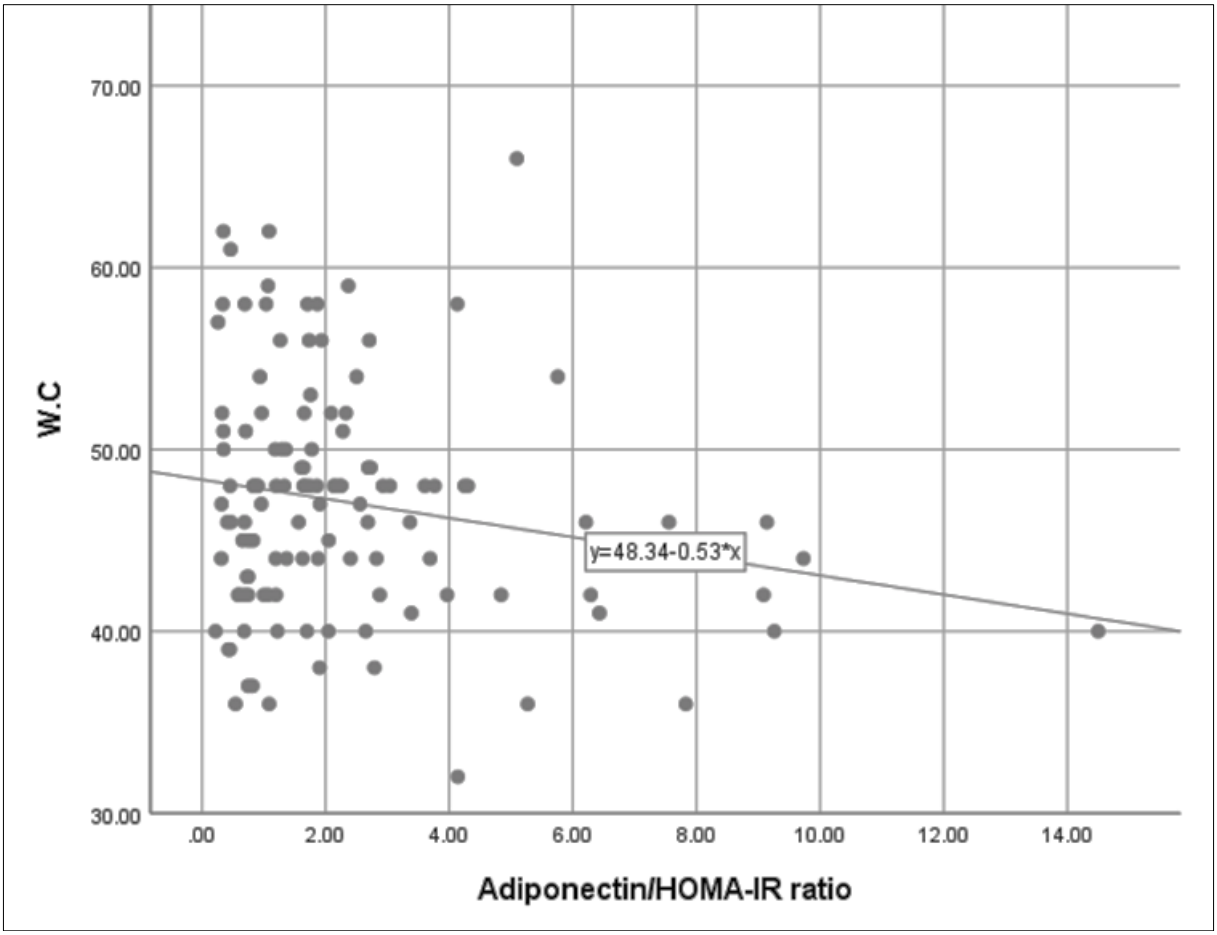

Fig 1: Correlation between adiponectin/HOMA-IR ratio with WC in patients' group.

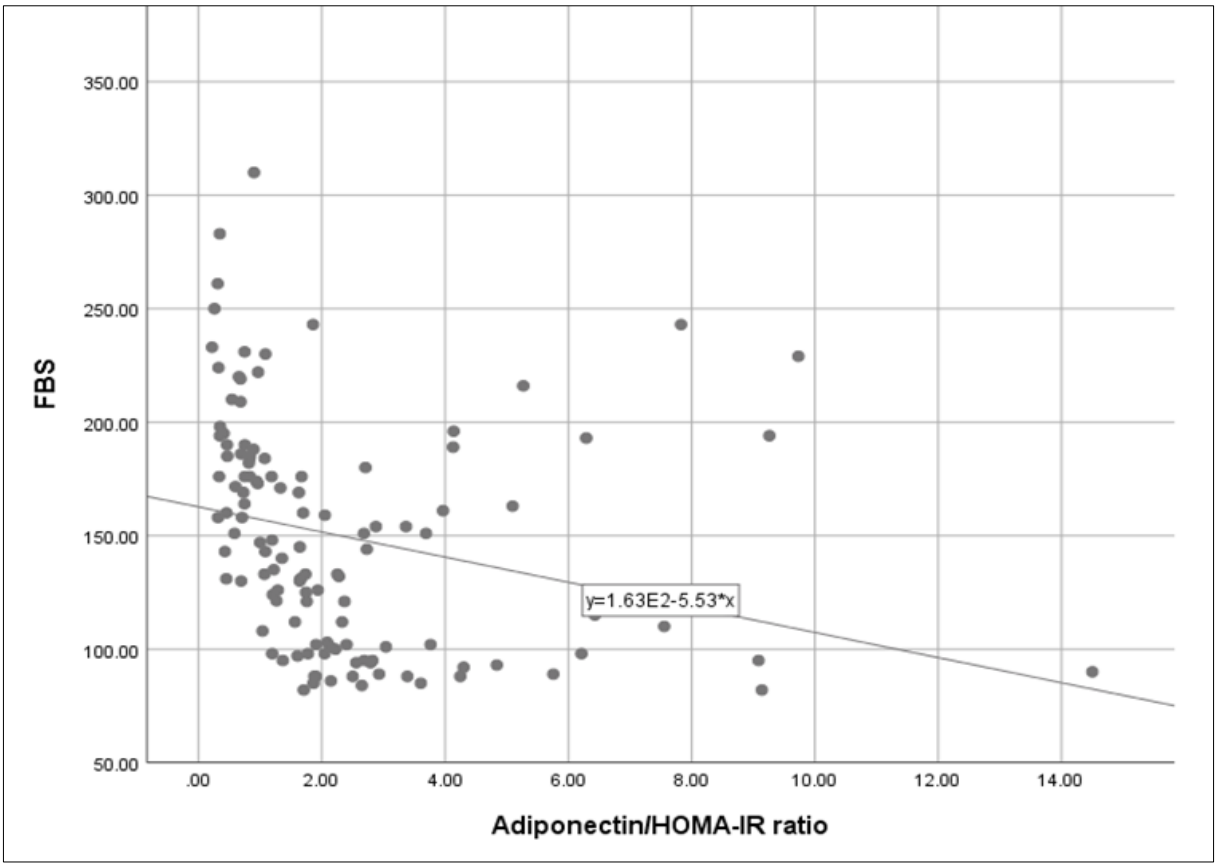

Fig 2: Correlation between adiponectin/HOMA-IR ratio with FBS in patients' group.

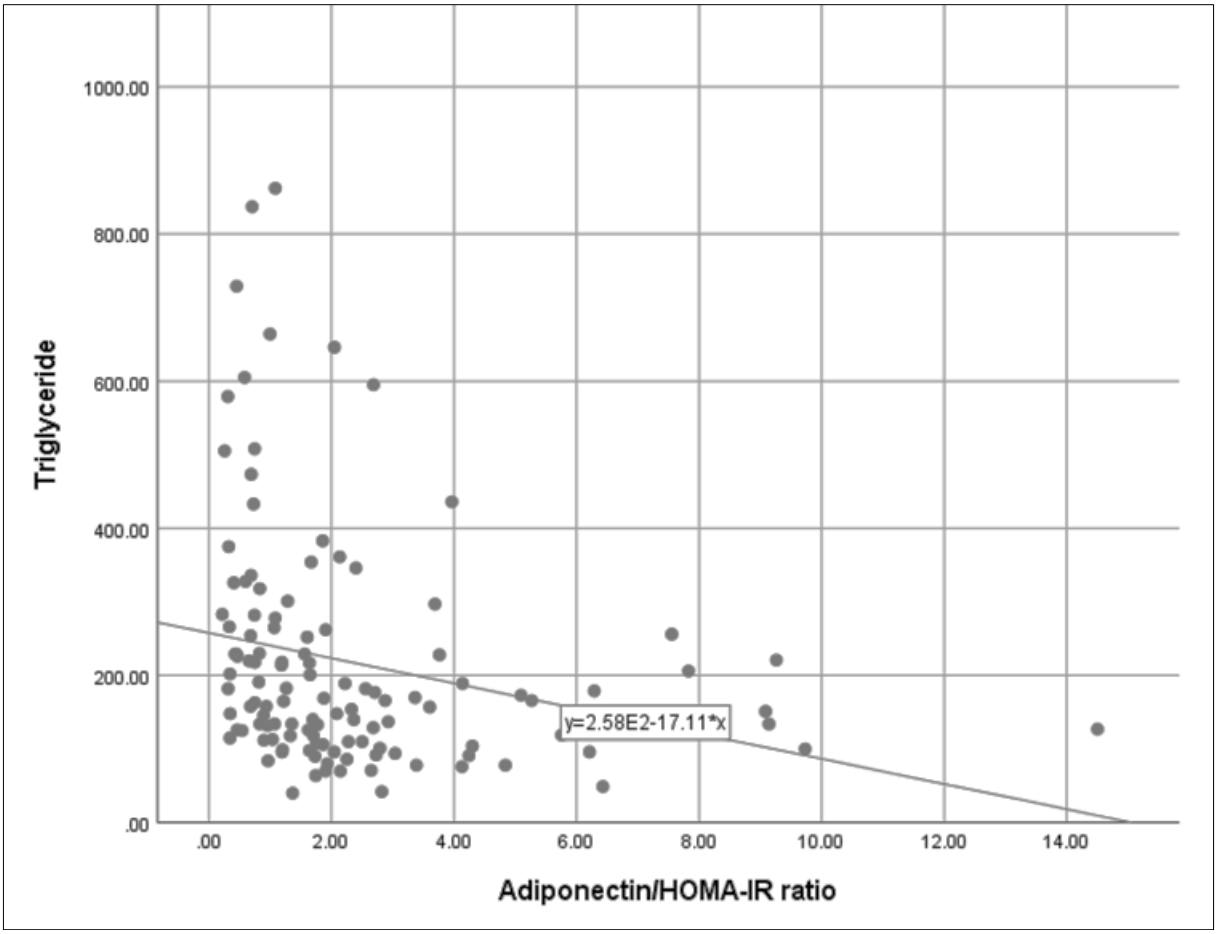

Fig 3: Correlation between adiponectin/HOMA-IR ratio with TG in patients' group.

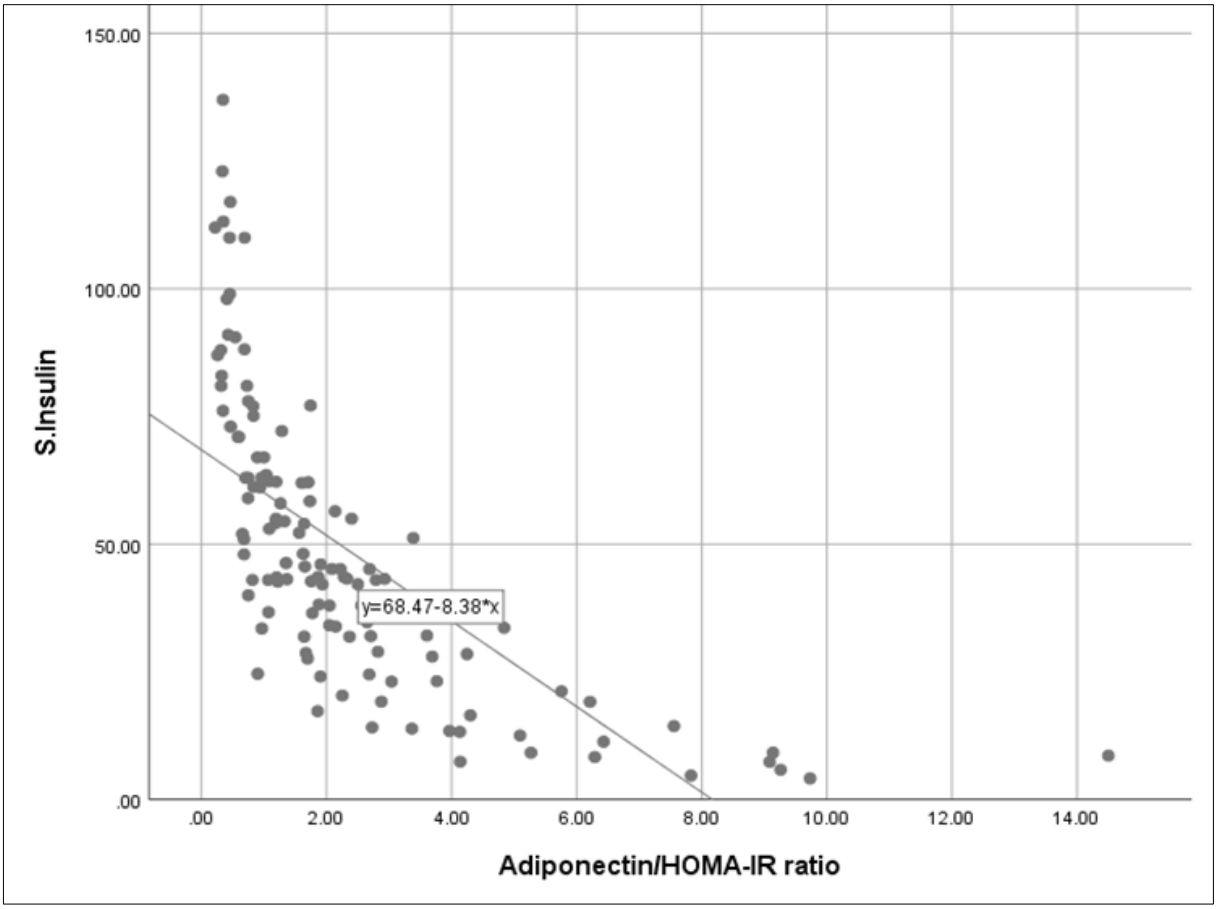

Fig 4: Correlation between adiponectin/HOMA-IR ratio with S. insulin in patients' group.

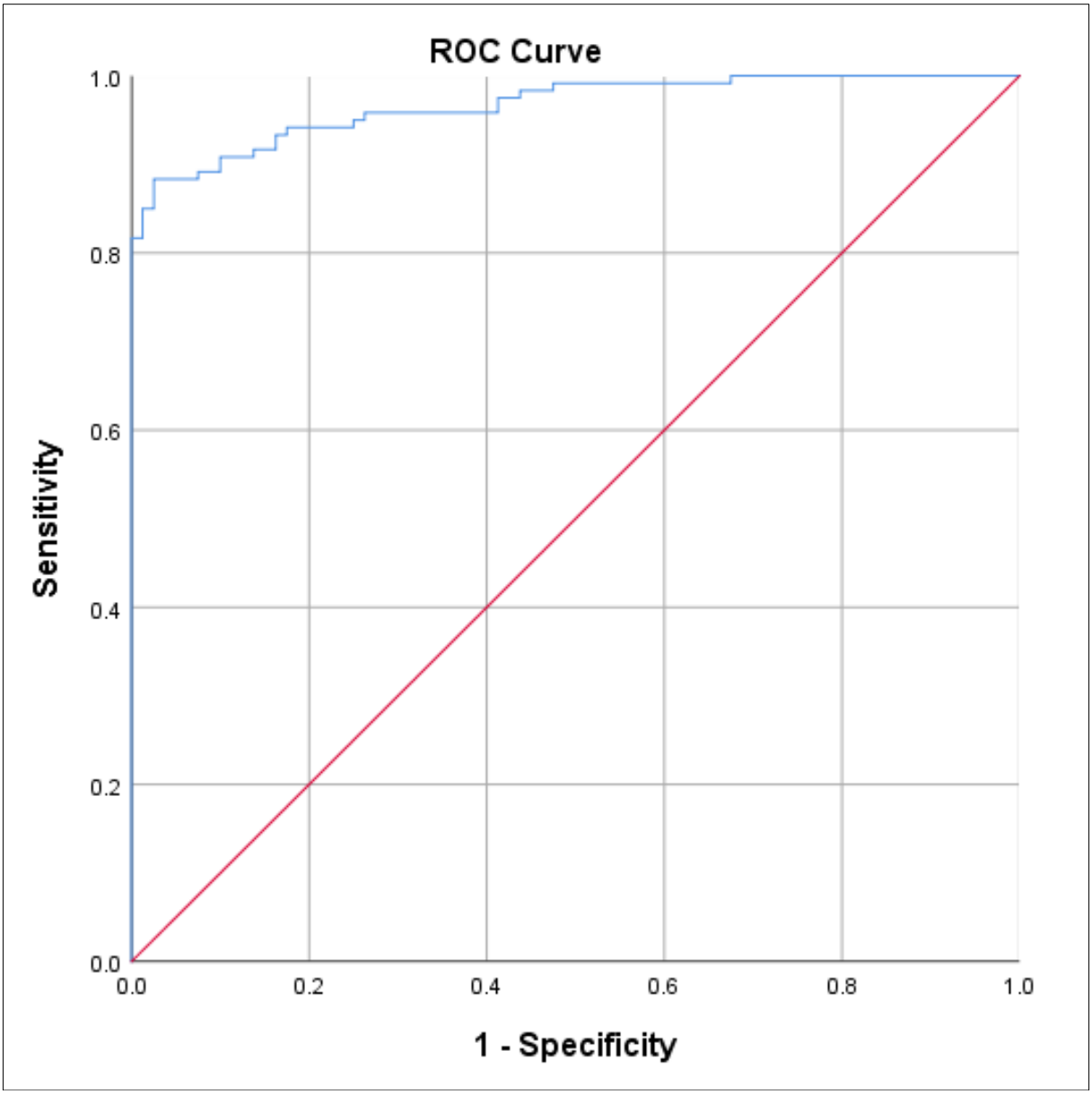

Fig 5: ROC figure of Adiponectin/HOMA-IR ratio

Discussion

Several metabolic and cardiovascular risk factors, including abdominal obesity, insulin resistance, atherogenic dyslipidemia, and hypertension, are combined to form the metabolic syndrome. Insulin resistance is the common pathophysiology of the metabolic syndrome, even though definitions of the illness vary. The cardiovascular risk factors raise the risk of cardiovascular disease by two times and the chance of acquiring type 2 diabetes mellitus by three times, which is partly why metabolic syndrome is essential. [4].

These results are more significant than research on populations with type 2 diabetes mellitus in Ethiopia [5], Egypt [6], and India [7] (53.2%, 55%, 65%, respectively), and another study indicated the prevalence of metabolic syndrome to be as high as 34.2% in the US population [8]. However, the outcomes are consistent with research on Saudi patients with type 2 diabetes, which discovered that 85.8% of them had metabolic syndrome [9].

A strong association between Hypertension and metabolic syndrome is present through the pathophysiology related to obesity. Nonetheless, it is the primary risk factor driving up cardiovascular death and morbidity. In the current study, about 74.2% of metabolic syndrome patients were hypertensive, lower than reported by the Katsimardou *et al*. study (80% of metabolic syndrome patients had HT) [10]. Higher number of patients with HT in metabolic group is related to the fact that presence of HT in addition to other health issues are the leading cause of metabolic syndrome. A significant association between smoking and metabolic syndrome was observed; 59.2% were smokers, in line with a prior study that found smokers to be 2.4 times more likely than non-smokers to develop metabolic syndrome (95% confidence interval [CI], 1.43-3.96) [11].

In the current study, Patients with metabolic syndrome had a higher proportion of obesity (81.5% vs. 0.0%) compared to the control group. Additionally, metabolic syndrome patients had a higher mean BMI in comparison to the control

Systolic and diastolic BP were significantly higher in patients compared to control groups, this can be explained by that presence of hypertension is a key component of metabolic syndrome, consistent with studies by Ali N *et al*. [12]. and Ntougou Assoumou *et al*. [13].

In the current study, the most prevalent metabolic abnormalities among the Mets components were reduced HDL C, higher TG, and higher HbA1c, which were observed in the Mets patients than in the non-Mets subjects.

The higher HbA1c levels in the MetS group could be due to insulin resistance; the cause of reduced HDL C and elevated TG levels might be due to insulin resistance and chronic low-grade inflammation, which is associated with MetS, which can impact lipid metabolism and raise total cholesterol levels.

Those findings aligned with a study from Basrah by Ali Turki [14]. Those results can be explained by the fact that to make an MetS diagnosis, it is necessary to verify the presence of at least three of the following five criteria: abdominal obesity, high TG, low HDL, hypertension, and irregularities in fasting glucose. IR and hyperinsulinemia are the main contributors to the development of MetS.

Consistent with previous research, patients with metabolic syndrome had substantially higher blood insulin and HOMA-IR) [15, 16]. In contrast, serum Adiponectin was significantly lower [17, 18]. Adipose tissue is crucial for preserving glucose and lipid homeostasis. In obesity, however, adipocytes malfunction and secrete an excessive amount of pro-inflammatory adipocytokines, exacerbating the inflammatory response over time and speeding up the development of metabolic and cardiovascular problems.

These adipocytokines include, among other things, proteins that alter insulin sensitivity (adiponectin). Adiponectin has a clear correlation with alterations in lipid profiles, insulin sensitivity, and abdominal obesity, which are essential for metabolic syndrome development [19].

The Adiponectin/HOMA-IR ratio had a higher sensitivity of 90.8% and a specificity of 90% to detect metabolic syndrome with the cut of value <5.3. Those findings support the suggestion of earlier studies about the usefulness of the ratio in determining metabolic syndrome in comparison to the other markers used before [20, 21].

In 2011, it was discovered that the A/H ratio was a potent indicator of each MetS component [21]. Ding *et al*. found that in healthy Chinese participants, the A/H ratio was a more accurate diagnostic marker of MetS than Adiponectin or HOMA-IR combined [22] Previous studies reported that the Adiponectin/HOMA-IR ratio in metabolic syndrome patients was significantly lower than in controls [16].

Linear regression analysis shows that Adiponectin/HOMA-IR ratio was inversely correlated with waist circumference, systolic and diastolic BP, fasting blood glucose, triglycerides level, and VLDL (weak correlation), moderate correlation with insulin and HOMA-IR. similar to the observation of De Abreu VG *et al*. study [16] Biochemical markers such as reduced HDL, elevated triglycerides, and HbA1c were prominent in MetS patients.

The Adiponectin/HOMA-IR ratio proved a highly sensitive and specific diagnostic tool, offering better predictive value than traditional markers.

These insights highlight the importance of comprehensive metabolic assessments in managing MetS effectively.

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