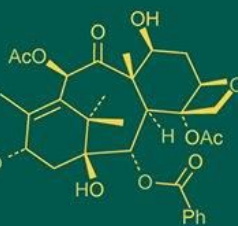
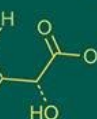


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Adiponectin/HOMA-IR ratio as a predictive biomarker of metabolic syndrome in men and women of Basrah: A step toward gender-specific risk assessment

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Abstract

Metabolic syndrome (MetS) is a complex and increasingly common health issue in Basrah, characterized by a combination of central obesity, insulin resistance, dyslipidemia, and hypertension, which together heighten the risk of cardiovascular diseases and type 2 diabetes. Identifying reliable and early biomarkers is crucial for effective prevention and management. Adiponectin, known for its insulin-sensitizing and anti-inflammatory properties, along with HOMA-IR, a recognized marker of insulin resistance, have both shown strong associations with MetS. This study aims to evaluate the adiponectin/HOMA-IR ratio as a predictive biomarker for metabolic syndrome and to explore its potential role in gender-specific risk assessment among men and women in Basrah. The study (Nov 2023-June 2024) included 200 participants (120 with metabolic syndrome, 80 controls) from Faiha Center, Basrah. Ages ranged 18-75 years. Fasting blood samples were analyzed for insulin, glucose, lipids, adiponectin, and HbA1c. Anthropometric data and blood pressure were recorded. Diagnosis followed updated guidelines, considering clinical history and genetic factors. The study found no significant differences in age or gender distribution between groups ($p > 0.05$). However, BMI, waist circumference, and blood pressure were significantly higher in the metabolic syndrome group ($p < 0.01$). Obesity (class I and II), type II diabetes, and hypertension were also more prevalent in this group, indicating a strong association with metabolic syndrome. No significant gender-based differences were observed in biochemical parameters within the control group, including FBS. The study confirms that obesity, hypertension, and insulin resistance significantly contribute to metabolic syndrome, likely through chronic inflammation and metabolic imbalance. The adiponectin/HOMA-IR ratio shows promise as an early predictive marker, supporting targeted, gender-specific risk assessment.

Keywords: Metabolic syndrome, adiponectin, HOMA-IR ratio, insulin resistance, obesity, gender-specific risk

Introduction

Metabolic syndrome (MetS) is a heterogeneous and polygenic disorder marked by a clustering of component pathologies, including abdominal obesity, metabolic dysregulation (eg, insulin resistance), atherogenic dyslipidemia, and hypertension, which together increase the risk for cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) [1]. The global burden of MetS is alarmingly increasing, with almost a fourth of the adult population being affected globally. Another study conducted in Basrah, southern Iraq, has shown that rapid urbanization, sedentary occupations, unhealthy food habits and poor public health strategies have all contributed to the high prevalence of metabolic syndrome in the region, making it a major concern for clinical management and public health policy. Due to the significant health consequences and economic costs of MetS, early detection and risk stratification are critical to mitigate its consequences [2]. Adiponectin is an adipocyte-derived cytokine that has developed as an important biomarker of metabolic status. Most adipokines are proinflammatory and insulin-resistant; however, adiponectin has insulin-sensitizing, anti-inflammatory, and anti-atherogenic effects. Low circulating levels of adiponectin are consistently associated with an increased risk of insulin resistance, the metabolic syndrome and cardiovascular disease.

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Adiponectin has promising effects on increasing hepatic insulin sensitivity, enhancing fatty acid oxidation in skeletal muscles, and suppressing hepatic gluconeogenesis [3]. As a result, it has a protective association with MetS occurrence. Yet, the response of adiponectin is not the only parameter that describes the metabolic alterations of the body, so the study of more integrative biomarkers is required [4]. The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) is a well-established method of estimating insulin resistance by measuring fasting plasma glucose and insulin. High HOMA-IR levels indicate poor insulin sensitivity and have been linked independently to the components of metabolic syndrome. The ratio of adiponectin/HOMA-IR, which combines both adiponectin levels and HOMA-IR, was proposed as a more reliable and absolute indicator of insulin sensitivity and metabolic risk than either parameter alone [5]. This Hareesh: this ratio accounts for the balance of pro-inflammatory versus anti-inflammatory factors in the adipose tissue and may have greater predictive value for MetS than existing framingham risk scores, particularly in populations with differing exposures and genotypes [6]. Iso, the differences in the pathophysiology leading to MetS have received increasing interest concerning sex in the past years. From the data point that men and women have distinct fat distribution, hormonal profiles and adipokine secretion their predisposition to metabolic imperfections occurs low divergent. For example, premenopausal women have higher adiponectin and better lipids than men, which may provide some cardiometabolic protection [6]. But these benefits gradually decrease with age and hormonal changes. Thus, examining sex differences in the adiponectin/HOMA-IR ratio might bring useful information regarding risk stratification and individual therapeutic approach [7]. Although the adiponectin/HOMA-IR ratio has clinical potential, there have been few studies performed in Middle Eastern cohorts, and none in Basrah, a geographical location where metabolic health may be influenced by cultural, environmental and genetic factors. Additionally, little data exist on risk assessment by gender in this setting. This is vital information for creating prevention and management strategies that are specific to Basrah and recognize sex-related differences in health [8, 9]. This study aimed to assess the predictive ability of the adiponectin/HOMA-IR ratio in metabolic syndrome among men and women living in Basrah. We investigate the relationship of this ratio to various metabolic parameters to assess its potential role in the early identification and classification of HTM. The study will also help clarify possible gender differences in metabolic risk profiles, aligning with increasing evidence for gender-specific strategies in treating metabolic disease. This study may indicate important findings and approaches to clinical practice and public health that may contribute to the decrease of MetS prevalence and its complications in Basrah and similar populations.

Methodology

The study was conducted between November 2023 and June 2024, involving 200 individuals (120 patients with metabolic syndrome and 80 controls) recruited from the Faiha Specialized Diabetes, Metabolism Center in Basrah, Iraq. Participants' ages ranged from 18 to 75 years, and the diagnoses were made by qualified endocrinologists. Blood samples were collected after a minimum of 8 hours of

fasting. Instruments like the COBAS INTEGRA 400 plus and COBAS e 411 were used to measure various biochemical parameters such as insulin, glucose, triglycerides, cholesterol, HDL, LDL, along with adiponectin and HbA1c using ELISA and automated methods. Waist circumference, weight, and height were measured to calculate the body mass index (BMI), and blood pressure was measured using an automatic device. The diagnostic criteria for metabolic syndrome were based on updated medical guidelines, considering medical history and genetic factors.

Statistical analysis

Data analysis was conducted using SPSS "Statistical Package for Social Sciences" version 28. Results were expressed as Standard Deviation±Mean, with a P-value of <0.05 considered statistically significant. P-value ≤0.001 was considered statistically highly significant. To compare continuous data between the two groups, we utilized the independent t-test. To compare variables among three or more groups, we employed the one-way analysis of variance. ROC (Receiver Operating Characteristic) was used to assist the overall diagnostic performance of S. insulin, HOMA-IR, and Adiponectin /HOMA-IR ratio.

Ethical approval

The study was approved by the human ethics committee of Department of Biochemistry, Faculty of Medicine, University of Basrah, Basrah, Iraq.

Results

Sociodemographic and Clinical Characteristics of the Study Population

The results showed that the gender and age distribution between the study and control groups was close, with no statistically significant differences ($p>0.05$). Males comprised approximately 47.5% of the total sample and females 52.5%, with the majority of participants falling within the 17-54 age group (74%). Significant differences were observed in body mass index (BMI), with overweight and obesity rates significantly higher in the study group than in the control group ($p<0.01$), with both class I and II obesity being significantly more prevalent in the study group. The results also showed a higher prevalence of type II diabetes and hypertension in the study group compared to the control group, with statistically significant differences ($p<0.01$), indicating a clear association between these factors and metabolic syndrome in the study population.

Comparison of Anthropometric and Hemodynamic Parameters between Control and Study Groups

The study results showed no significant differences in mean age between the control and study groups ($p>0.05$), reflecting the homogeneity of the sample in terms of age group. However, significant differences were observed in obesity indicators and hemodynamic parameters, with the study group recording significantly higher rates in both body mass index (BMI) and waist circumference (W.C), with a mean of 35.1 versus 24.7 and 47.1 versus 34.9, respectively ($p<0.01$). Systolic and diastolic blood pressure rates were also higher in the study group compared to the control group (138.5 versus 120.6 and 83.4 versus 76.1 mmHg, respectively), with statistically significant differences ($p<0.01$), indicating an association between these indicators and metabolic syndrome in the studied sample.

Table 1: Comparison between Control and Study Groups in Terms of Gender, Age, BMI, T2DM, and Hypertension

		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%)	

Table 2: Analysis of Age, BMI, Waist Circumference, and Blood Pressure Measurements

	Control (n=80)		Study (n=120)		P-value
	Mean ± SD	SE	Mean ± SD	SE	
Age (year)	45.7±12.3	1.8	45.4±14.2	1.3	> 0.05
BMI	24.7±1.6	0.2	35.1±7.1	0.6	<0.01*
W.C	34.9±2.7	0.3	47.1±6.5	0.6	<0.01*
S. BP	120.6±5.9	0.7	138.5±18.1	1.7	<0.01*
D.BP	76.1±5.3	0.6	83.4±13.4	1.2	<0.01*

Gender-Based Comparison of Biochemical Parameters in Control and Study Groups

Biochemical analysis results showed no significant differences between males and females in the control group across all measured parameters, including fasting blood sugar (FBS), glycated hemoglobin (HbA1c), and lipid profile. In the study group, both males and females had higher FBS and HbA1c levels compared to the control group, although the gender differences within the group

were not statistically significant. Regarding the lipid profile, males in the study group had significantly higher levels of triglycerides (268.2 vs. 175.7 mg/dL, $p<0.05$) and very low-density lipoprotein (VLDL) than females (48.6 vs. 34.7 mg/dL, $p<0.05$). These findings reflect the existence of gender-related differences in some lipid parameters in individuals with metabolic syndrome, which may indicate differences in metabolic response between men and women.

Table 3: Evaluation of Glycemic Control and Lipid Profile in Male and Female Subjects

	(Control) (n=80)		P-value	(Study) (n=120)		p-value
	Male(n=40)	Female(n=40)		Male(n=55)	Female(n=65)	
FBS mg/dL	89.4±6.5	89.3±5.6	> 0.05	151.5±48.1	148.4±52.4	> 0.05
A1c %	5.1±0.4	5.1±0.5	> 0.05	7.4±1.7	7.6±1.9	> 0.05
Total cholesterol mg/dL	161.4±34.6	171.7±38.9	> 0.05	188.9±43.7	176.7±39.1	> 0.05
Triglyceride mg/dL	99.6±28.9	100.2±30.5	> 0.05	268.2±184.8	175.7±126.7	<0.05**
LDL-C mg/dL	101.9±29.9	106.7±32.1	> 0.05	112.7±40.1	103.7±33.6	> 0.05
VLDL mg/dL	19.2±5.7	18.9±6.3	> 0.05	48.6±27.9	34.7±25.5	<0.05**
HDL-Cmg/dL	41.9±9.9	49.3±9.8	<0.05**	35.7±8.6	41.2±11.3	<0.05**
Serum Insulin µU/ml	11.4±4.1	12.8±6.3	> 0.05	50.3±31.9	48.1±25.7	> 0.05
Adiponectin ug/L	27.7±7.8	26.9±7.9	> 0.05	21.5±6.1	23.2±6.4	> 0.05
HOMA-IR	2.5±0.9	2.8±1.4	> 0.05	19.7±16.3	18.4±13.7	> 0.05
hsCRP nmol/L	1.1±0.9	1.19±0.8	> 0.05	3.9±4.6	9.6±22.9	> 0.05
Adiponectin/HOMA-IR ratio	12.2±5.2	12.1±6.6	> 0.05	2.4±2.7	2.2±1.9	> 0.05
ALP U/L	94.4±35.9	79.6±18.6	> 0.05	86.9±30.4	82.±25.9	> 0.05
AST U/L	21.1±6.4	21.7±11.2	> 0.05	20.4±8.7	22.9±19.1	> 0.05
ALT U/L	21.5±8.3	20.6±15.1	> 0.05	17.9±5.6	19.7±8.9	> 0.05

Discussion

Age and gender distribution analyses showed no significant differences between the control and study groups ($p>0.05$). With equal numbers of male and female subjects, this study

contributes significantly to the validity of the intended gender-specific assessment. Nonetheless, BMI categories showed statistically significant differences, most notably higher rates of palpably higher rates of obesity (BMI ≥ 30

kg/m²) in the study group, and even more strikingly, the prevalence of type 2 diabetes mellitus (T2DM) and hypertension (HT), both $p < 0.01$. These results are in keeping with previous reports implicating obesity as playing a central role in the pathogenesis of metabolic syndrome [10, 11]. Several studies from the Middle East, including Iraq, have extensively shown a significant relationship between increased BMI and unfavorably high rates of MetS parameters, especially in females [12]. Moreover, the prevalence of hypertension and diabetes in our study group is in line with global trends that identify these as key components of metabolic syndrome [13]. On the other hand, some regional studies have reported low levels of MetS components in young populations, indicating that age-specific factors could modulate risk profiles [14, 15]. The results showed that subjects in the study group had significantly higher BMI, W.C., S.BP, and D.BP than controls (all $p < 0.01$). These results highlight an aggregation of cardiovascular risk factors in persons with metabolic syndrome [16]. Adiposity is the principal driver of metabolic disease, and increased waist circumference in particular evidences visceral adiposity, a well-validated driver of insulin resistance and cardiometabolic risk [17, 18]. Similar findings were reported by Al-Saeed *et al.*, who showed a positive relationship between central obesity and high blood pressure in Iraqi adults [19]. In addition, even slight increases in waist circumference highly increase the risk for hypertension and insulin resistance according to a meta-analysis [20]. On the other hand, a Turkish cohort study showed lower rates of hypertension among MetS individuals that could have been attributed to genetic background and lifestyle differences. These discrepancies highlight the importance of ethnic and regional variability when interpreting metabolic risk factors [21]. Biochemical study shows metabolic derangements in study group. Regardless of gender, the MetS group had significantly higher fasting blood sugar (FBS) and glycated hemoglobin (HbA1c) levels [22]. Lipid profiles were higher in males compared to females, significantly higher in TG and VLDL in males ($p < 0.05$), and females had better control of lipid parameters [23, 24]. These results align with earlier studies that highlight the differences in lipid metabolism between men and women with MetS. For example, Mohammed *et al.* showed that men with metabolic syndrome have more severe hypertriglyceridemia than women, possibly due to hormonal influence and pattern of fat distribution [25]. In addition, the increased HbA1c levels noticed are consistent with well-known relationship between insulin resistance and poor glycemic control in MetS population [26]. In contrast, certain studies among Western populations have demonstrated less pronounced gender differences in lipid profiles, indicating that these effects could be moderated by cultural, dietary, and genetic factors [27]. Interestingly, we found that HDL-C was lower for both genders in the MetS group (characteristic dyslipidemia pattern commonly found in states of insulin-resistance [28, 29]).

Conclusion

The study concludes that elevated BMI, waist circumference, and blood pressure are strongly associated with metabolic syndrome, likely due to increased insulin resistance and chronic low-grade inflammation. These factors contribute to metabolic dysregulation, particularly in individuals with obesity and hypertension. The

adiponectin/HOMA-IR ratio may thus serve as a valuable biomarker for early detection and gender-specific risk assessment.

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