Egyptian Journal of Medical Research

Print ISSN: 2682-4396 / Online ISSN: 2682-440X

Original article

Relation between insulin resistance and coronary artery disease in acute coronary syndrome patients

Samiha Mohamed,MSc[1], Khaled Ahmed El-khashab, MD, Mahmoud Elmallawany,MD ,Noha Khalifa MD , Haitham Soliman,MD [1]

[1] *Department of Cardiology, Fayoum University Hospital, Fayoum, Egypt.*

Article Info

Article history:

Received 7 November 2024

Accepted 15 January 2025

Corresponding Author:

Samiha Mohamed

sms12@fayoum.edu.eg

Keywords

Insulin resistance

ACS incidence

HOMA -IR

Abstract:

Background: Coronary artery diseases are among the most prevalent causes of mortality worldwide. Multiple investigations indicate that coronary artery disease is related to insulin resistance in both diabetic and non-diabetic cases. **The aim of the study is to assess the relationship between insulin resistance (IR) and coronary artery disease incidence and the** severity of lesions. **Methods:** A cross-sectional investigation included 100 cases admitted with acute coronary syndrome to coronary care unit then Coronary angiography was done at cardiology department in 2022. blood samples were taken, and laboratory tests levels were done done. The homeostatic model assessment index of IR (HOMA-IR) has been utilized for determining IR. The HOMA-IR has been determined utilizing the following formula: Baseline serum insulin concentration (milliunit per liter) x Baseline plasma glucose (milligrams per deciliters)/405. The TYG index has been estimated utilizing the following formula: Ln (Fasting triglycerides (milligrams per deciliters) x Fasting blood glucose (mg per deciliters)/2). Finally, coronary angiography has been performed.

Results: 83% of study group show high level of HOMA-IR level however only 34% of cases where diabetics all cases show high level of TyG index which is another index for insulin resistance. mean fasting insulin was (22.5±22.6). The mean level of HOMA-IR was (12.6±20.1) and the mean level of TyG index was (10±50.2) **Conclusions:** The study showed a significant correlation betweeen coronary heart disease incidence and resistance of insulin in diabetic and non-diabetic cases.

1. Introduction:

Coronary artery disease has been one of the leading reasons of mortality around the globe, frequently related to comorbidities like abnormal lipid profiles, insulin resistance and obesity**(1)**.

Insulin is a critical hormone that regulates metabolism of cells in numerous tissues throughout the human body.

Insulin resistance can be identified as a reduction in the response of tissue to insulin stimulation. Obesity, sedentary lifestyle, certain drugs, family history of diabetes, diabetes, and numerous health conditions are all risk factors for insulin resistance. Insulin resistance is regarded as one of the components of metabolic syndrome **(2).**

Insulin resistance can result in an imbalance in the metabolism of glucose, which results in chronic hyperglycemia. This, in turn, initiates oxidative stress and an inflammatory response, which in turn causes damage to cells. Additionally, insulin resistance may change the systemic metabolism of lipids, which in turn results into the development of dyslipidemia (**3)**

Insulin resistance has been recognized as a distinct risk factor for atherosclerosis and has been shown to raise the possibility of coronary artery disease among both diabetics and non-diabetics **(4)**.

Insulin resistance may be measured through a variety of methods, as the Homeostasis Model Assessment of Insulin Resistance formula: baseline insulin concentration (milliunit per liter) x baseline glucose concentration (milligrams per deciliters) / 405 **(5).** and the TyG index is determined as Ln (fasting triglycerides (mg per deciliters l) *fasting blood glucose (mg per deciliters)/2 **(6).**

2. Patients and methods:

The ethical committee approved the research with approval number (D 232)

The cross-sectional investigation comprised one hundred cases who were admitted with acute coronary syndrome. Coronary angiography has been performed at the cardiology department of Fayoum University. Cases with a history of myocardial infarction, revascularization with PCI or prior cardiac operation, heart failure, insufficient medical history or steroid use, chronic kidney disease GFR less than sixty ml/min/1.73 m2; **(Canadian Society of Nephrology. 2014)** and chronic liver disease (Platelet count < 160,000, Albumin less than 3.8 milligram per deciliters, AST > ALT (in non-alcoholic etiologies), INR > 1.2, Bilirubin greater than 1.5 milligrams per deciliters) were excluded **(7)**

Patients have been subjected to Full medical history, general examination including assessment of body mass index (BMI) ,12 lead electrocardiogram., Trans thoracic echocardiography, Renal and liver function tests**,** Lipid profile (, LDL, Total cholesterol, HDL triglycerides and cholesterol).

HOMA-IR

A blood sample has been obtained following an overnight fast of at least eight hours. Plasma glucose and fasting insulin levels have been assessed, and the following scores have been assigned in accordance with the published literature and the clinical data collected by Monobind: Adult (Not Diabetic) 0.7-9micU/ml-Diabetic0.7-25micU/ml.

A Homeostasis Model Assessment of Insulin Resistance has been utilized to assess insulin resistance and has been determined with the following formula: Baseline serum insulin concentration (milliunit per litter) multiplied by baseline plasma glucose (milligrams per deciliters) divided by 405.

TyG index

The following formula has been used to calculate the Ln: Ln (Fasting triglycerides (mg per deciliters) x Fasting blood glucose (mg per deciliters)/2).

Coronary angiography

All these data were collected, and statistical analysis was performed for these variants.

- Data analysis was conducted on Windows 7 utilizing the Statistical Package of Social Science (SPSS) software version 22 (SPSS Inc., Chicago, IL, the states). A simple descriptive analysis that is presented in the form of percentages and numbers for qualitative data, as well as arithmetic means for measuring central tendency and standard deviations for the purpose of determining the degree of dispersion

- for quantitative parametric data. The quantitative data incorporated into the investigation were initially examined for normality utilizing the One-Sample Kolmogorov-Smirnov test in each group under investigation. Subsequently, inferential statistic tests have been chosen.

- **For quantitative nonparametric data**

  - **The kruskalWallis** test utilized to compare more than 2 **independent** groups.
  - **The Mann-Whitney test** utilized to compare 2 **independent** groups.

- **For qualitative data**

  - **Chi square** test utilized to compare among two of more than two qualitative groups.

- **Bivariate Sperman correlation test** to test the correlation among parameters

- The **P-valueless than 0.05** has been considered as statistically significant.

3. Results:

The investigation included 100 patients presented with acute coronary syndrome admitted for coronary angiography.

Table (1): Description of demographic characteristics among group under investigation.

The table illustrated that the mean age among group under investigation was (56.8±7.7) years old ranged between (40 and 76) years and mean BMI of (30.4±4.02) kilogram per square meter with 70% were males versus 30% were females.

Variables	**Number** (number=one hundred)	
Age (years)		
Mean ± SD	56.8±7.7	
Range	40-76	
BMI (kilogram per square meter)		
Mean ± SD	30.4±4.02	
Range	20-40	
Sex		
Men	70	70%
Women	30	30%

Table (2): Risk factors among study group.

As shown here 53% were smokers, 34% has diabetes mellitus, 44.1% were on insulin treatment, and 55.9% on oral hypoglycemic treatment. As regards hypertension it represents 57% of cases

Variables (n=100)	Frequency	
	Number	%
Smoking		
Smokers	**53**	**53%**
Non-smoker	**47**	**47%**
DM		
Yes	**34**	**34%**
No	**66**	**66%**
Type of treatment		
Insulin	**15**	**44.1%**
OHT	**19**	**55.9%**
Hypertension		
Yes	**57**	**57%**
No	**43**	**43%**

Table (3): Description of laboratory investigations among group under investigation.

The table illustrated that as regards lipid profile the mean LDL was (121.9±47.3), mean HDL was (40.6±6.3), mean cholesterol level was (193.1±49.9) and mean triglyceride was (152.8±79.01). For glucose profile the mean fasting glucoses was (170.5±96.9), mean fasting insulin was (22.5±22.6). The mean level of HOMA-IR was (12.6±20.1) and the mean level of TyG index was (10±50.2).

Variables	Mean ±SD	Median /IQR	Range
Lipid profile			
LDL	121.9±47.3	117/65	26-252
HDL	40.6±6.3	40/11	22-76
Cholesterol	193.1±49.9	185.5/80	83-318
Triglyceride	152.8±79.01	140.5/67	59-700
Glucose profile			
Fasting glucose	170.5±96.9	132.5/109	75-491
Fasting insulin (mlU/L)	22.5±22.6	13.8/22.7	2.8-137.5
HOMA-IR	12.6±20.1	4.5/11.5	0.56-101.2
TyG index	10±50.2	4.9/0.41	4.4-507

Table (4): Frequency of different HOMA-IR and TyG index levels among group under investigation.

The table illustrated that 83% of study group show high level of HOMA-IR level, versus all cases show high level of TyG index.

Variables (n=100)	Frequency	
	Number	%
HOMA-IR		
Normal (< 2)	17	17%
High (≥2)	83	83%
TyG index		
Normal (< 4)	0	0%
High (≥4)	100	100%

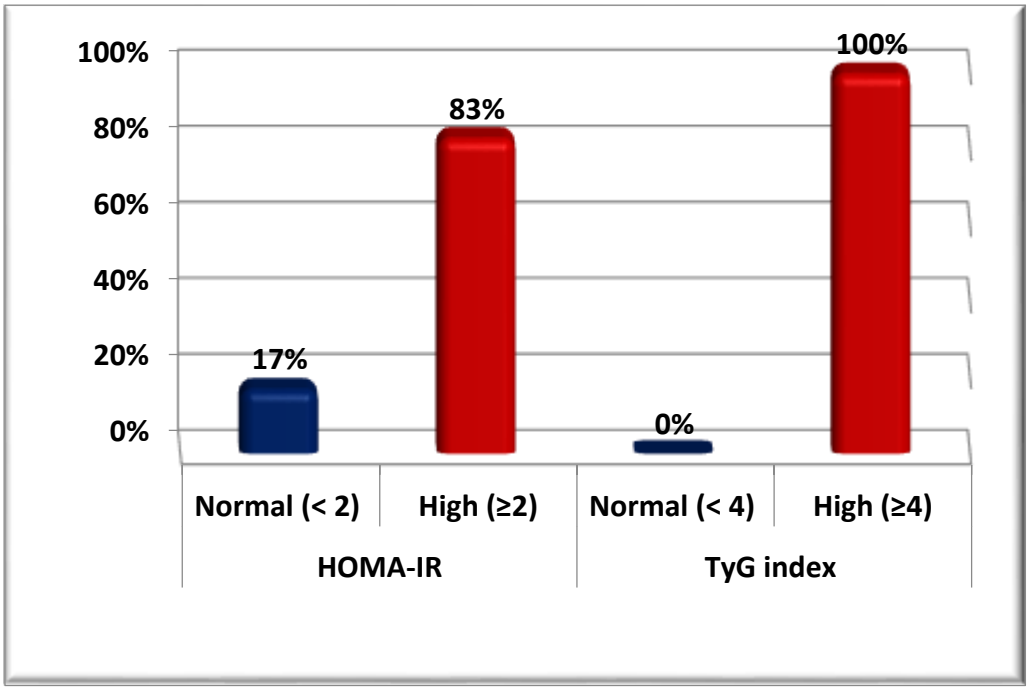
100%
80%
60%
40%
20%
0%
17%
83%
0%
100%
Normal (< 2)
High (≥2)
Normal (< 4)
High (≥4)
HOMA-IR
TyG index

Figure: 1

Table (5): Comparisons of HOMA-IR in different patients' history among cases.

The table illustrated that there was a statistically significant higher median of HOMA-IR with p-value lower than 0.001 among patients with diabetes mellitus, and hypertension. On the other hand, a statistically insignificant variance has been deteted with p-value greater than 0.05 in terms of gender, smoking, types of diabetes treatment and different presented diagnoses.

Variables	HOMA-IR		P-value	Sig.
	Median	IQR		
Sex				
Male	4.25	9.6	0.6	NS
Female	4.58	13.1		
Smoking				
Smokers	3.9	7.1	0.2	NS
Non-smoker	4.8	16.8		
DM				
Yes	20.1	36.4	**<0.001**	**HS**
No	2.9	3.04		
Type of treatment				
Insulin	13.9	34.7	0.5	NS
OHT	22.3	45.1		
Hypertension				
Yes	5.6	20.1	**<0.001**	**HS**
No	2.9	3.8		

Table (6): Comparisons of TyG index in different patients' risk factors.

The table illustrated a statistically significant higher median of TyG index with p-value lower than 0.001 between cases with diabetes mellitus and hypertension. On the other hand, a statistically insignificant variance has been detected with p-value greater than 0.05 in terms of sex, smoking, and types of diabetes treatment

Variables	TyG index		P-value	Sig.
	Median	IQR		
Sex				
Male	4.9	0.42	0.08	NS
Female	5.1	0.47		
Smoking				
Smokers	4.9	0.39	0.2	NS
Non-smoker	4.9	0.50		
DM				
Yes	5.3	0.54	**<0.001**	**HS**
No	4.8	0.29		
Type of treatment				
Insulin	5.3	0.95	0.8	NS
OHT	5.3	0.35		
Hypertension				
Yes	5.1	0.53	**<0.001**	**HS**
No	4.8	0.29		

Table (7): Correlation between HOMA-IR and other study variables among study group.

The table illustrated that a statistically significant **positive** association with p-value less than 0.001has ben detected between level of HOMA-IR and each of triglyceride, fasting glucoses, fasting insulin concentration and TyG index. An **increase** in triglyceride, fasting glucoses, fasting insulin levels and TyG index will correlates with **elevation** in HOMA-IR level. Conversely, there was statistically insignificant association with p-value greater than 0.05 with other variables.

Variables	**HOMA-IR**		
	R	**P-value**	**Sig.**
Age (years)	0.05	0.6	NS
BMI (kg/m^2)	-0.03	0.7	NS
Lipid profile			
LDL	0.09	0.4	NS
HDL	-0.08	0.4	NS
Cholesterol	0.16	0.1	NS
Triglyceride	**0.27**	**0.007**	**HS**
Glucose profile			
Fasting glucose	**0.64**	**<0.001**	**HS**
Fasting insulin (mlU/L)	**0.95**	**<0.001**	**HS**
TyG index	**0.58**	**<0.001***	**HS**

Table (8): Correlation between TyG index with other investigation variables among study group.

The table illustrated that a statistically significant positive association with p-value 0.01, 0.001, <0.001, <0.001 and <0.001 has been detected between level of TyG index and each of LDL, cholesterol, triglyceride, fasting glucoses, and fasting insulin concentration. In addition, a significant negative association among TyG index and HDL concentration has been detected with p-value 0.01. An increase in LDL, cholesterol, triglyceride, fasting glucoses, and fasting insulin levels and decrease in HDL will correlates with elevation in TyG index level. O Conversely, there was statistically insignificant association with p-value greater than 0.05 with other variables.

Variables	**TyG index**		
	R	**P-value**	**Sig.**
Age (years)	-0.03	0.7	NS
BMI (kg/m^2)	-0.01	0.9	NS
Lipid profile			
LDL	0.25	**0.01**	**S**
HDL	-0.24	**0.01**	**S**
Cholesterol	0.33	**0.001**	**HS**
Triglyceride	0.75	**<0.001**	**HS**
Glucose profile			
Fasting glucose	0.72	**<0.001**	**HS**
Fasting insulin (mlU/L)	0.43	**<0.001**	**HS**

4. Discussion:

Coronary heart disease is an important cause of mortality globally, and numerous investigations have illustrated that IR is a strong predictor of atherosclerotic cardiovascular illness.

This investigation has been designed to ascertain the relation between insulin resistance as a risk factor, occurrence, and severity of coronary artery disease in cases who presented with the acute coronary syndrome, given the strong correlation among coronary artery disease and insulin resistance in insulin-resistant states such as impaired tolerance to glucose, early T2DM and obesity. Hyperinsulinemia may speed up the atherosclerotic process through a variety of mechanisms, like the stimulation of lipogenesis and raised very LDL synthesis/secretion, proliferation and growth of vascular smooth muscle cell, and activation of genes related to inflammation and improved LDL cholesterol transport into arterial smooth muscle cells.

In an insulin-resistant state, obesity is the 1^{ry} contributor to the present epidemic of diabetes and is a major risk factor for cardiovascular disease (CVD). In cases that presented with acute coronary syndrome, the mean body mass index (BMI) has been found to be (30.4±4.02) kg/m2. Only 34% of these cases were diabetics. The mean LDL was found to be (121.9±47.3), the mean HDL was found to be (40.6±6.3), the mean cholesterol level was found to be (193.1±49.9), and the mean triglyceride level was (152.8±79.01).

83% of study group show high level of HOMA-IR level however only 34% of cases were people with diabetes this means insulin resistance is an independent risk factor even in non-diabetic cases, all cases show high level of TyG index which is another index for insulin resistance. The mean fasting insulin was 22.5±22.6. The mean level of HOMA-IR was (12.6±20.1), and the mean concentration of TyG index was (10±50.2). **Hanley AJ at 2002** discovered that insulin resistance, as measured by HOMA-IR, was independently and significantly correlated with a higher probability of cardiovascular findings in a large population of Mexican Americans and non-Hispanic whites who did not have T2DM at baseline. insulin resistance is an independent risk factor for coronary artery disease (CAD) severity in cases with impaired tolerance to glucose and metabolic syndrome, according to an investigation conducted by **Metwally et al. in 2020**. The strong correlation between IR and adverse cardiovascular fundings in nondiabetic individuals and individuals suffering from type 2 diabetes mellitus has been summarized in numerous meta-

analyses. In the meta-analysis conducted by **Gast et al,** the probability of coronary heart disease in nondiabetic individuals raised by forty-six percent for a one-standard deviation rise in HOMA-IR. **(10).**

According to **Young-Rak Cho et al.** in 2019, the IR parameters, particularly the TyG index, are independently related to obstructive coronary artery disease and CAD in non-diabetics. Conversely, the occurrence and severity of coronary artery disease, as determined by the percentage of lumen occlusion with CCTA, are more closely associated with glycemic status rather than IR in cases with established diabetes.

Bonora et al., stated that insulin resistance has been found to be related to symptomatic coronary artery disease (CAD) that occurred later, regardless of the usual cardiovascular risk factors, in the general population.

A greater median of HOMA-IR and TYG index with a p-value less than 0.001 is observed among patients of diabetes mellitus and hypertension. This is probably because cases with diabetes and hypertension have an elevated incidence of obesity and dyslipidemia, which is a component of metabolic syndrome. **Pilar Gayoso-Diz et al in 2013** conducted a 2^{ry} analysis of data from a survey of the Spanish general adult population (EPIRCE) and discovered that diabetic individuals had lower cut-off values of Homeostasis Model Assessment of Insulin Resistance than nondiabetic individuals (1.60 vs. 2.05). **José G. González-González et al,2022**conducted a meta-analysis of thirty-eight investigations and discovered that a greater HOMA-IR value had a significant impact on the probability of developing T2DM, hypertension, and presenting non-fatal MACE.

Additionally, a statistically significant positive association (p-value less than 0.001) has been detected between the HOMA-IR level and the triglyceride, fasting glucose, and fasting insulin concentration. A rise in HOMA-IR level is related to a rise in fasting glucose, fasting insulin, and triglycerides concentration in the blood. On the other hand, there was statistically insignificant association with additional parameters, such as the remainder of the lipid profile and BMI, at a p-value greater than 0.05. Nevertheless, a statistically significant positive association has been observed between the level of TyG index and each of the following: LDL, cholesterol, triglycerides, fasting glucose, and fasting insulin levels (p-value lees than 0.001). A significant negative relation among the TyG index and HDL concentration has been additionally recognized, with a p-value of 0.01. The rise in the TyG index concentration has

been correlated with a decrease in HDL and a rise in LDL, cholesterol, triglyceride, fasting glucoses, and fasting insulin concentration. a statistically insignificant association between BMI and p-value greater 0.05. This renders the TYG index more sensitive and predictive of alterations in the lipid profile. **Da-Hye Son et al. (2021)** conducted an investigation to compare the predictive powers of the TyG index and Homeostasis Model Assessment of Insulin Resistance for the incidence and occurrence of MetS in a large community-based prospective cohort over a twelve - year follow-up. The TyG index demonstrated a greater predictive power for common MetS compared to the HOMA-IR (0.837 vs. 0.680, p-value lower than 0.001). In an investigation conducted by **Jamshid Vafaeimanesh,** insulin resistance (HOMA-IR> 2.5) was positive in 49.3 percent of cases and negative in 50.7 percent of cases. As a result, the association between insulin resistance and CAD was statistically insignificant.

Study limitations:

- The sample was small, bigger size of sample will be better.
- A large section of the study population was hypertensive or on angina treatment taking BB, statins and diuretics which may influence glucose and insulin levels.

5. Conclusion:

- Insulin resistance increases the possibility of coronary artery disease in both non-diabetics and diabetics and has been identified as a separate risk factor for atherosclerosis
- HOMA IR and TYG index are simple tests for prediction of insulin resistance.
- Positive correlation between HOMA IR, TYG index and concentration of lipoproteins, triglycerides, glucose and insulin levels.

6. References:

1-Vafaeimanesh, J., Parham, M., Norouzi, S. Insulin resistance and coronary artery disease in non-diabetic patients: Is there any correlation? Caspian Journal of Internal Medicine.2018, 9(2), 121–126. https://doi.org/10.22088/cjim.9.2.121

2-Cho, Y. R., Ann, S. H., Won. Association between insulin resistance, hyperglycemia, and coronary artery disease according to the presence of diabetes. Scientific Reports.2019, 9(1). https://doi.org/10.1038/s41598-019-42700-1

3-King, G. L., Park, K., & Li, Q. Selective insulin resistance and the development of cardiovascular diseases in diabetes: The 2015 Edwin Bierman Award Lecture. In Diabetes 2016 (Vol. 65, Issue 6, pp. 1462–

1471). American Diabetes Association Inc. https://doi.org/10.2337/db16-0152

4-Muniyappa, R., & Sowers, J. R. Role of insulin resistance in endothelial dysfunction. In Reviews in Endocrine and Metabolic Disorders .2013 (Vol. 14, Issue 1, pp. 5–12). https://doi.org/10.1007/s11154-012-9229-1

5-Rewers, M., Zaccaro, D., Agostino, R. D. Insulin Sensitivity, Insulinemia, and Coronary Artery Disease The Insulin Resistance Atherosclerosis Study FOR THE INSULIN RESISTANCE ATHEROSCLEROSIS STUDY INVESTIGATORS.2004. http://diabetesjournals.org/care/article pdf/27/3/781/648616/zdc00304000781.pdf.

6-Hanley AJ, Williams K, Stern MP. Homeostasis model assessment of insulin resistance in relation to the incidence of cardiovascular disease: the San Antonio Heart Study. Diabetes Care. 2002;25(7):1177–1184.

7-Metwally, Y.G., Sedrak, H.K. & Shaltout, I.F. The relationship between coronary artery severity and insulin resistance in patients with impaired glucose tolerance and metabolic syndrome. *Egypt J Intern Med* **32**, 21 (2020). https://doi.org/10.1186/s43162-020-00022-z.

8-**Bonora, E.** Insulin resistance as estimated by homeostasis model assessment predicts incident symptomatic cardiovascular disease in caucasian subjects from the general population: the Bruneck study. *Diabetes Care 2007;* **30**, 318–324.

9-Gast KB, Tjeerdema N, Stijnen T. Insulin resistance and risk of incident cardiovascular events in adults without diabetes: meta-analysis. PLoS One. 2012;7(12):e52036.

10- **Cho, YR., Ann, S.H., Won, KB.** Association between insulin resistance, hyperglycemia, and coronary artery disease according to the presence of diabetes. *Sci Rep* **9**, 6129 (2019). https://doi.org/10.1038/s41598-019-42700-1

11-Gayoso-Diz, P., Otero-González, A., Rodriguez-Alvarez, M.X. Insulin resistance (HOMA-IR) cut-off values and the metabolic syndrome in a general adult population: effect of gender and age: EPIRCE cross-sectional study. *BMC Endocr Disord* **13**, 47 (2013). https://doi.org/10.1186/1472-6823-13-47

12-Da-Hye Son, Hye Sun Lee, Yong-Jae Lee. Comparison of triglyceride-glucose index and HOMA-IR for predicting prevalence and incidence of metabolic

syndrome, Nutrition, Metabolism and Cardiovascular Diseases, Volume 32, Issue 3,2022,Pages 596-604,ISSN 0939-4753,https://doi.org/10.1016/j.numecd.2021.11.017.

13-**Vafaeimanesh J, Parham M, Norouzi S.** Insulin resistance and coronary artery disease in non-diabetic patients: Is there any correlation? Caspian J Intern Med. 2018 Spring;9(2):121-126. doi: 10.22088/cjim.9.2.121. PMID: 29732028; PMCID: PMC5912218.