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Original Article

Survey of HOMA1-IR and HOMA2-IR indexes in first-diagnosed type 2 diabetes patients

Minh Hoang Thi [1], Tinh Hoang Thi [2], Diep Pham Thao [3], Loan Pham Thanh [4], Ha Do Thi Hoang [5], Tuan Quoc Lê [6], Thuan Huynh Quang [1] *

[1] Department of Biochemistry, Military Hospital 103, Ha Noi City, Vietnam
[2] Department of Laboratory and Pathology, Military Institute of Traditional Medicine, Ha Noi City, Vietnam
[3] Department of Biochemistry, Viet Duc University Hospital, Ha Noi City, Vietnam
[4] Department of Biochemistry & Microbiology, A Thai Nguyen Hospital, Thai Nguyen City, Vietnam
[5] Department of Laboratory, Vinmec Hai Phong International Hospital, Hai Phong City, Vietnam
[6] Department of Physiology-Pathophysiology-Immunology, Faculty of Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam

* Correspondence to: Thuan Huynh Quang, Department of Biochemistry, Military Hospital 103 No. 261, Phung Hung Street, Phuc La Ward, Ha Dong District, Hanoi City, Vietnam. Phone: +84904175342; E-mail: huynhquangthuan@vmmu.edu.vn

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Abstract

Insulin resistance is the primary pathogenesis leading to type 2 diabetes. The HOMA model is widely used to assess insulin resistance. This study aims to examine the HOMA1-IR and HOMA2-IR indices in patients with type 2 diabetes diagnosed for the first time. A comparative cross-sectional study including two groups: the patient group was patients with type 2 diabetes diagnosed for the first time (n=101), and the control group was healthy people (n=98). Statistical analysis was performed using SPSS 22.0 software. The study showed that patients with type 2 diabetes had an average value of HOMA1-IR of 3.79 and HOMA2-IR of 1.79, significantly higher than that of healthy people. With a cutoff value of 1.96, the sensitivity and specificity of HOMA1-IR to distinguish between disease and non-disease were 91.1% and 96.9%, respectively. For HOMA2-IR with a cutoff of 0.96, the sensitivity and specificity were 62.4% and 86.7%, respectively. Patients with type 2 diabetes diagnosed for the first time had higher HOMA1-IR and HOMA2-IR than healthy people; HOMA1-IR and HOMA2-IR were higher in type 2 diabetic patients with dyslipidemia than in type 2 diabetic patients without dyslipidemia. HOMA1-IR had higher sensitivity and specificity than HOMA2-IR in distinguishing type 2 diabetes from healthy people.

Keywords: diabetes melitus, HOMA1-IR, HOMA2-IR.

Introduction

Diabetes mellitus (DM) is a common metabolic disorder characterized by chronic hyperglycemia. According to statistics published by the International Diabetes Federation (IDF), in 2021, there were approximately 537 million adults worldwide with DM; it is predicted that by 2030, there will be 643 million people, and by 2045, 783 million people will be living with DM [1]. Type 2 DM accounts for approximately 90% of people with DM. The occurrence of the disease is due to the interaction between genetic factors, environment, obesity, insulin resistance, and abnormalities of pancreatic islet cells [2, 3]. Insulin resistance causes a compensatory reaction that increases blood insulin, causing long-term damage to pancreatic islet β cells, leading to disorders in maintaining blood glucose balance and developing into type 2 diabetes [4].

To assess insulin resistance in patients with type 2 diabetes, the Homeostasis Model Assessment (HOMA) model is commonly used. This model considers the interaction between insulin and glucose kinetics. The classic

HOMA model (HOMA1-IR) is widely used because of its simplicity. However, the limitation of this model is that it does not consider factors such as renal glucose loss, glucose utilization in the brain, and differences between hepatic and peripheral tissue insulin resistance. HOMA2 (HOMA2-IR) is an experimentally derived model that overcomes the disadvantages of the HOMA1 model [5]. HOMA1-IR and HOMA2-IR are calculated based on fasting plasma glucose and insulin concentrations. To eliminate treatment-related factors that cause errors in the results, we examined the HOMA1-IR and HOMA2-IR indices in patients with type 2 diabetes diagnosed for the first time, thereby providing threshold values of these indices to distinguish between type 2 diabetes and non-diabetes.

Material and methods

Subjects

A cross-sectional, controlled study was conducted on 101 patients with type 2 diabetes diagnosed for the first time and 98 ordinary people of similar age to the disease group, with no pathology detected after routine health check-ups.

The newly diagnosed T2DM patients were chosen according to the ADA 2019 criteria [6]. Exclude from the study if the patient has one of the following factors: The patient does not meet the selection criteria. The patient is using drugs that affect blood glucose levels, such as thiazide diuretics, corticosteroids, beta-blockers, and estrogen-containing contraceptives. Type 2 diabetes patients with cirrhosis, kidney failure, nephrotic syndrome, pyelonephritis, myocardial infarction, and cancer. The control group contained healthy people who were similar in age and gender to the T2DM group, ranging in BMI from 18 to 22 and having no disease. No other comorbidities.

Clinical examination and testing

All patients were asked about their medical history, such as the onset of symptoms, hypertension, medication history etc. Clinical examination detected associated diseases, measured height and weight, calculated BMI, and measured waist circumference, pulse, and blood pressure. Blood samples were taken according to a uniform procedure. Patients were required to fast for at least 8 hours to take blood samples.

Biochemical indices were analyzed on the AU5800 automated testing system of Beckman, USA). %HbA1c was quantified by high-performance liquid chromatography on the PREMIER9210 machine of Beckman, USA. Trinity Biotech, USA. Plasma insulin was quantified by chemiluminescence on the DXI 800 system of Beckman, USA.

HOMA 1 – IR Index calculated by formula [7]:

$$\text{HOMA-IR}=[\text{FPG (mmol/L)} \times \text{Fasting IRI (μU/L)}]/22.5$$

HOMA2-IR values were calculated using the HOMA Calculator software.

Statistical analysis

The data were statistical using Microsoft Office Excel 2019 and SPSS22.0. Normally distributed variables were expressed as mean (±) and standard deviation (SD). Correlation and linear regression within variables

Table 1: General characteristics of the study subjects.

Characteristic	Control group (n=98)	Patient group (n=101)	p
Male	59 (60.2%)	64 (63.4%)	>0.05*
Female	39 (39.8%)	37 (36.6%)	
Age (years)	50.71±6.36	52.36±9.26	>0.05**
Systolic blood pressure	116.38±5.2	127.28±12.36	<0.001**
Diastolic blood pressure	71.22±6.05	79.4±10.2	<0.001**
BMI	21.58±0.84	23.43±1.18	<0.001**
Fasting blood glucose (mmol/l)	4.94±0.38	12.59±3.39	<0.001**
HbA1C (%)	4.98±0.36	9.74±2.16	<0.001**
Total cholesterol (mmol/L)	4.67±0.34	5.57±1.24	<0.001**

Table 1: Continued.

Characteristic	Control group (n=98)	Patient group (n=101)	p
HDL-C (mmol/L)	1.31±0.20	1.11±0.2	<0.001**
LDL-C (mmol/L)	2.22±0.21	3.4±1.07	<0.001**
Triglyceride (mmol/L)	1.18±0.29	3.52±3.03	<0.001**
Insulin (mIU/L)	5.79±1.71	6.86±3.0	<0.05**

Note: * – Chi-square test; ** – Independent – Samples T-test.

were analyzed using Pearson or Spearman analysis. p<0.05 was considered to be statistically significant.

Ethical consideration

All participants were dispensed with written informed consent. The protocol was approved by the Ethical Review Committee of Vietnam Military Hospital 103 (Reference No.176/2021/MH103-IRB issued 28/07/2021). The study was also conducted using good clinical practice following the Declaration of Helsinki.

Results

There was no difference in mean age and gender ratio between the two groups. There was a statistically significant difference in blood pressure, BMI, fasting blood glucose, HbA1C, blood lipids, and fasting blood insulin between the case and control groups (P<0.05) (Table 1).

In patients with a first-time diagnosis of type 2 diabetes, the mean value of HOMA1-IR was 3.79, and that of HOMA2-IR was 1.29. The HOMA1-IR index in both the case and control groups was statistically significantly higher than that of HOMA2-IR (Table 2).

The analysis showed a statistically significant difference in the HOMA1-IR and HOMA2-IR indices between the control group and the first-time diagnosed diabetes group. Specifically, the HOMA1-IR and HOMA2-IR of the control group were statistically significantly lower than those of the diabetes group (p<0.001) (Figure 1).

ROC curve analysis of the HOMA1-IR index between the diabetic and control groups showed AUC=0.967, p<0.0001; HOAM2-IR had AUC=0.785, p<0.0001 (Figure 2).

The diagnostic sensitivity and specificity of HOMA-IR index ≥1.92 were very high, 91.1% and 96.9%, respectively; those of HOMA2-IR index ≥0.96 were 62.4% and 86.7%, respectively, lower than HOMA1-IR (Table 3).

In patients with a first-time diagnosis of type 2 diabetes with dyslipidemia, HOMA1-IR and HOMA2-IR were statistically significantly higher than in patients without dyslipidemia (Table 4).

Table 2: Characteristics of HOMA1-IR and HOMA2-IR indices in the study subjects.

Value	Patient group (n=101)		Control group (n=98)	
	HOMA1-IR	HOMA2-IR	HOMA1-IR	HOMA2-IR
Mean	3.79	1.29	1.27	0.75
Median	3.52	1.11	1.32	0.77
SD	1.80	1.50	0.39	0.22
Minimum value	1.02	0.46	0.61	0.40
Maximum value	11.72	15.38	2.48	1.41
Quartile 1	2.51	0.80	0.91	0.55
Quartile 3	4.54	1.36	1.57	0.90
p*	<0.0001		<0.0001	

Note: * – Mann Whitney U test.

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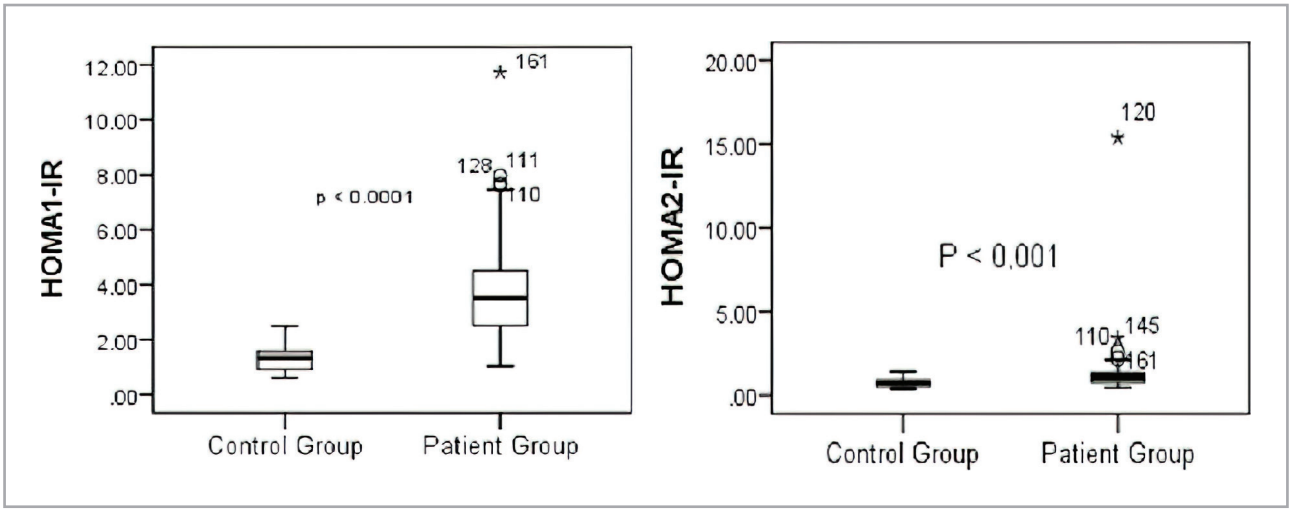

Figure 1: Comparison of HOMA1-IR and HOMA2-IR indexes between study groups. p – Mann Whitney U test.

Discussion

Insulin and glucose concentrations are essential to calculate insulin resistance indexes [8]. Increased fasting blood insulin concentration directly reflects the increased insulin secretion of pancreatic β cells and indirectly reflects insulin resistance [9]. The results in Table 1 show that the fasting blood insulin concentration in the patient group had a median value of 6.86 µU/L, which was statistically higher than that of the control group with p<0.05. Thus, there was an apparent increase in blood insulin concentration in the type 2 diabetes group compared to the control group. The difference between the two groups in our study is similar to the results of Azadi S.M. *et al.* (2023); the average blood insulin concentration of type 2 diabetes patients was 10.07±3.55 µU/mL, statistically higher than that of the control group with p<0.05 [10].

There are many methods and evaluation indexes to assess insulin resistance. The method considered the most accurate or "gold standard" is the "glucose clamp" method. However, this method is very complicated and difficult to perform, so it is rarely applied in epidemiological research and clinical practice. The endogenous assessment method (HOMA- Hemostatic model assessment) is the most popular because it is

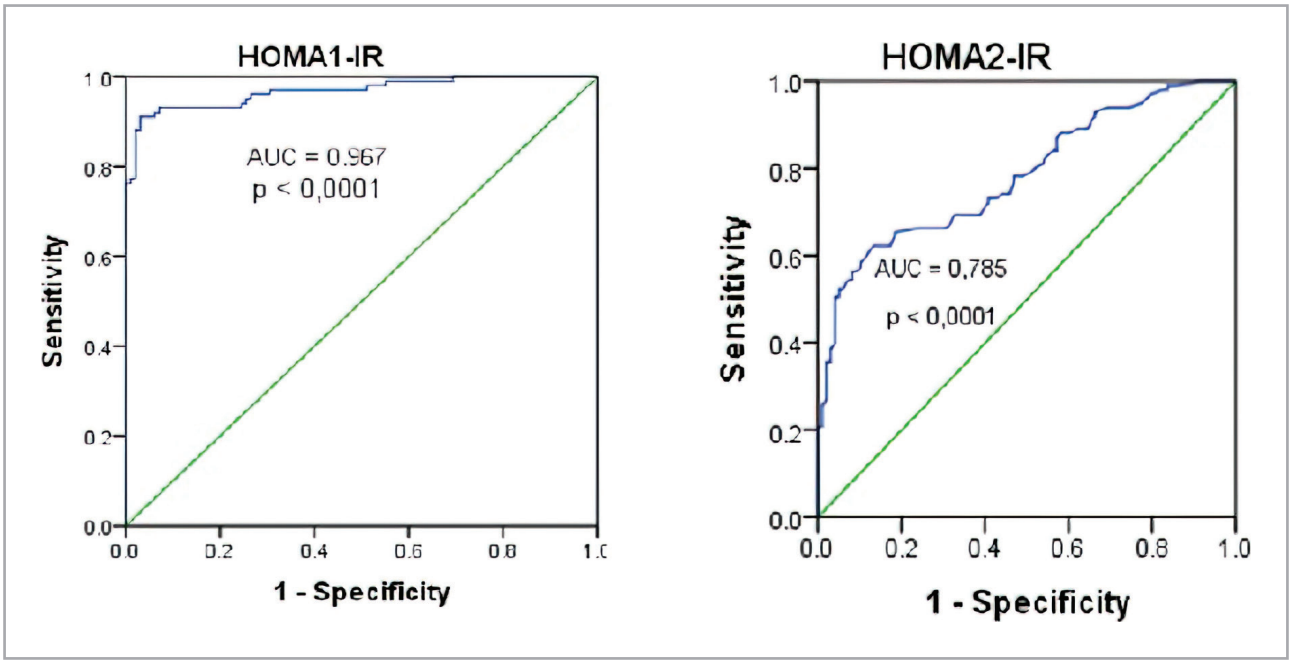

Figure 2: ROC curve analysis of HOAM1-IR and HOMA2-IR in discriminating between diabetes and healthy people.

Table 3: Sensitivity and specificity of HOMA1-IR, HOMA2-IR in discriminating between diabetes and healthy.

Index	Cutoff	Sensitivity (%)	Specificity (%)
HOMA1-IR	1.92	91.1	96.9
HOMA2-IR	0.96	62.4	86.7

simple, easy to perform, and reasonably accurate compared to the method "clip glucose" [8, 9]. Since both HOMA1-IR and HOMA2-IR indices are calculated based on fasting plasma glucose and insulin concentrations, we chose to study patients with type 2 diabetes diagnosed for the first time who had not been treated. With this subject, treatment factors affecting the concentration of substances were eliminated, thereby obtaining more accurate and objective HOMA indices. The results of our study showed that in patients with type 2 diabetes diagnosed for the first time, the mean value of the HOMA1-IR index was 3.79, higher than HOMA2-IR was 1.29, and both were statistically significantly higher than the control group with p<0.0001. The study by Azadi S.M. *et al.* showed that the HOMA1-IR index of the type 2 diabetes group was 3.93±1.53, statistically significantly higher than the control group at 0.68±0.4 with p<0.05 [10]. Author Aliusef.M. H *et al.* also concluded that the average value of HOMA1-IR was statistically significantly higher than the average value of HOMA-IR [11]. The above data confirm that there is very clear insulin resistance in patients with type 2 diabetes. The mean HOMA-1 IR value is significantly higher than the mean HOMA-2 IR value, so determining insulin resistance status by HOMA-1 IR alone may miss some patients.

The HOMA1-IR index differentiated the diabetic group from the non-diabetic group with AUC=0.967, p<0.0001, cutoff threshold of 1.92, with sensitivity and specificity for diagnosing diabetes of 91.1% and 96.9%. The HOMA2-IR index differentiated the diabetic group from the non-diabetic group with AUC=0.765, p<0.001, and a cutoff threshold of 0.96, with sensitivity and specificity of 62.4% and 86.7%, respectively. In a study comparing the values of HOMA1-IR and HOMA2-IR in assessing glucose tolerance, Meshra. B. *et al.* concluded that HOMA1-IR correlated better with fasting and postprandial plasma glucose and measures of obesity than HOMA2-IR. Therefore, HOMA1-IR should be preferred over HOMA2-IR for predicting glucose intolerance [12].

Diabetes is a non-communicable disease that is increasing rapidly worldwide. The disease causes many burdens in terms of labor loss, treatment and control costs, complications and mortality. One of the many causes of treatment failure and loss of control is insulin resistance [13, 14]. When insulin resistance occurs, blood sugar is difficult to control and thus promotes many serious complications. Dyslipidemia is a factor that promotes the progression of diabetes [15]. Our study showed an increased trend of HOMA1-IR and HOMA2-IR in the group of type 2 diabetic patients with dyslipidemia compared with the group without dys-

Table 4: Relationship between HOMA1-IR and HOMA2-IR with dyslipidemia in type 2 diabetes patients.

Value	HOMA1-IR		HOMA2-IR	
	Non dyslipidemia (n=25)	Dyslipidemia (n=76)	Non dyslipidemia (n=25)	Dyslipidemia (n=76)
Mean	3.2	3.98	1.0	1.38
Median	2.6	3.67	0.85	1.13
SD	1.7	1.78	0.45	1.69
Minimum value	1.02	1.19	0.46	0.48
Maximum value	7.69	11.71	2.11	15.38
Quartile 1	2.2	2.77	0.65	0.88
Quartile 3	4.02	4.65	1.21	1.37
p*	<0.05		<0.05	

Note: * – Mann Whitney U test.

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lipidemia (Table 4). Bautista. F. P. *et al*. also gave similar research results when evaluating insulin resistance in newly diagnosed overweight and obese diabetic patients [16]. This suggests a relationship between lipid disorders and insulin resistance and supports previous data that insulin resistance was significantly increased in overweight/obese T2DM patients.

Conclusion

The study showed that patients with type 2 diabetes at the first diagnosis had a mean HOMA1-IR index value of 3.79 and HOMA2-IR of 1.79, which was statistically significantly higher than that of healthy people. With a cutoff value of 1.96, the sensitivity and specificity of HOMA1-IR to distinguish between disease and non-disease were 91.1% and 96.9%, respectively. For HOMA2-IR with a cutoff of 0.96, the sensitivity and specificity were 62.4% and 86.7%, respectively. HOMA1-IR and HOMA2-IR were higher in type 2 diabetic patients with dyslipidemia than in type 2 diabetic patients without dyslipidemia.

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Conflict of interest

The authors declare no conflict of interest.

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