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Original Research Article

Visceral Adiposity Index and Insulin Resistance in Diabetes Mellitus Type 2

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Abstract

Background: Central obesity due to visceral fat can cause insulin resistance, risking type 2 diabetes mellitus (DM) with many complications, including coronary heart disease (CHD). The visceral adiposity index (VAI) was developed as a new indicator of visceral fat dysfunction. The gold standard for assessing insulin resistance is the hyperinsulinemia-euglycemia (HEC) clamp. This method is invasive and expensive, so homeostasis model assessment-insulin resistance (HOMA-IR) and quantitative insulin sensitivity check index (QUICKI) are more accessible, practical, and less invasive measurement methods. This study not only analyzed the relationship between VAI and HOMA-IR but also with QUICKI as a marker of insulin resistance.

Objective: To determine the correlation between visceral adiposity index and insulin resistance (HOMA IR and QUICKI) in patients with type 2 diabetes mellitus.

Methods: A cross-sectional study on 70 adult outpatients with diabetes mellitus in the Diponegoro National Hospital Semarang was performed. Fasting glucose was examined using the hexokinase method, while HDL-C and TG used the colorimetric enzymatic method with an automated clinical chemistry device. Fasting insulin was tested using the Enzyme-Linked Immuno Sorbent Assay (ELISA) method. Weight and height measurement by Tanita body composition scales. VAI, HOMA IR, and QUICKI were calculated manually. Data analysis was performed using the Pearson test ($p< 0.05$).

Results: There was a moderate positive correlation between VAI and HOMA-IR ($r=0.480$; $p=<0.001$). There was moderate negative correlation between VAI and QUICKI ($r=-0.475$; $p=<0.001$).

Conclusion: This study shows that the higher the VAI value, the higher the HOMA IR value. Conversely, the higher the VAI value, the lower the QUICKI value. These results indicate that the higher the VAI value, the more severe the insulin resistance in DM patients. Severe insulin resistance can lead to more serious complications in DM.

Keywords: *Diabetes Mellitus; central obesity; Insulin resistance*
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INTRODUCTION

In the last few decades, the prevalence of type 2 diabetes mellitus (DM-T2) has increased throughout the world. In 2015, Indonesia was ranked seventh in the world for the highest prevalence of DM. According to the 2018 Indonesian Ministry of Health Health Research Study, Central Java province has the highest prevalence of type 2 DM.[1]

Diabetes mellitus is a significant risk factor for premature death, and an enormous social and economic burden. Central obesity is closely related to the high prevalence of T2DM, including acute and chronic complications.[2] High visceral fat in obesity is associated with various systemic diseases including NAFLD, PCOS, hypertension and others.

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Table 1. Data characteristics of research subjects

Variable	Mean ± SD	Median (min – max)
Age (year)	56.91 ± 10.16	
WC (cm)		91.50 (66 – 120)
BMI (kg/m$^{2)}$		25.55 (16.40 – 39.70)
Cholesterol (mg/dL)		200.50 (122 – 346)
LDL-C (mg/dL)	130.04 ± 52.07	
HDL-C (mg/dL)	43.9 ± 13.78	
Triglycerides (mg/dL)	158.15± 74.69	
FBS (mg/dL)	155.30 ± 77.55	
Insulin (IU)	24.05 ± 37.80	
VAI	9.51 ± 16.93	
HOMA-IR	0.30 ± 0.04	
QUICKI	6.50 ± 3.92	

WC, waist circumference; BMI, body mass index; HDL, high-density lipoprotein- cholesterol; FBS fasting blood sugar; HOMA–IR, homeostasis assessment of insulin resistance; QUICKI, quantitative insulin sensitivity assessment index; VAI, visceral adiposity index; SD(standard deviation); min (minimum); max (maximum).

Individuals with high visceral fat are at increased risk of insulin resistance. A further consequence is that the risk of developing T2DM is also greater.[3] Insulin resistance is a metabolic disorder characterized by the failure of fatstorage into subcutaneous adipose tissue, leading to ectopic fat deposition into visceral fat tissue and insulin-sensitive tissues such as liver and skeletal muscle. These tissues progress to lipotoxicity status, interfering with insulin signaling and action, resulting in insulin resistance.[4] The state of insulin resistance in DM patients will cause an increase in further complications such as CHD.[5]

The best measurement of insulin resistance of insulin resistance is using a hyperinsulinemic-euglycemic clamp (HEC), but this method is invasive, time-consuming, and expensive to implement in clinical practice. Current assessment of insulin resistance using the homeostatic model (HOMA-IR) and quantitative insulin sensitivity check index (QUICKI) are more straightforward, practical, and minimally invasive measurement methods. HOMA-IR and QUICKI can be calculated using fasting blood glucose (GDP) and insulin levels.[6] Apart from that, not all laboratories provide parameters for insulin level measurement.

Magnetic resonance imaging (MRI) and computerized tomography scans (CT) can be used to examine visceral fat, which is essential in the mechanism of insulin resistance. However, these techniques are costly, have radiation side effects, and are unavailable in every healthservice. There is a need for a simple alternative parameter to measure visceral fat.[7]The visceral adiposity index (VAI) was developed as a new visceral adipose tissue dysfunction indicator. A previous study reported that VAI can be used to replace visceral CT scan examination as a marker of visceral adiposity. The visceral adiposity index itself is an indirect measurement method based on gender that measures a combination of anthropometric examinations based on waist circumference (WC), body mass index (BMI), triglyceride (TG) levels, and high-density lipoprotein (HDL) cholesterol levels.[7,8] The laboratory's parameters for determining the VAI value are easy and cheap. Almost all laboratories measure all of these parameters. Previous study reported a correlation between VAI and homeostatic model assessment of insulin resistance (HOMA-IR) in participants with normal weight.[8] Another study showed an increase in VAI and HOMA-IR values in type2 DM patients than control group.[3] The quantitative insulin sensitivity check index is an empirical math-transformed calculation of fasting glucose and plasma insulin levels that has been shown to provide better predictive power consistently and precisely. QUICKI is a variation of the HOMA equation, according to Gutch et al. QUICKI has a better correlation in patients with diabetes and obesity.[6] A cut-off value of HOMA-IR > 2.5 indicates insulin resistance while QUICKI <0.328.[10]

Based on the explanation above, we want to analyze the correlation between VAI and insulin resistance assessed by the HOMA-IR and QUICKI methods in patients with type 2 diabetes mellitus. Previous studies only analyzed VAI and HOMA-IR in DM groups and healthy controls. The difference between this study and several previous studies is that this study not only analyzed the relationship between VAI and HOMA-IR but also with QUICKI as a marker of insulin resistance.

MATERIALS AND METHODS

A Cross-sectional study on 70 adult diabetes mellitus patients in outpatient care at Diponegoro National Hospital from March to April 2022. Subjects with a history of hepatic, renal, and thyroid disease were excluded from this study. Ethical clearance was obtained from the Health Research Ethics Commission (KEPK) of the Faculty of Medicine, Universitas Diponegoro, with No: 62/EC/KEPK/FK-UNDIP/III/2022.

All subjects agreed to participate in this study by signing an informed consent form. Venous blood was drawn for fasting glucose levels, lipid profiles (cholesterol, HDL, LDL, triglycerides), and insulin levels. They were also subjected to anthropometric examination, including height and weight. A nutritionist took measurements of the height and weight of the study subjects using the Tanita BC tool using Tanita body composition monitor (Tanita Health Equipment H.K. Ltd).

Consecutive sampling will be done according to the research criteria until the number of samples is met. Fasting glucose was examined using the hexokinase method, while HDL-C and TG used the colorimetric enzymatic method with an automated clinical chemistry device (Indiko TM, Thermo Fisher Scientific, Waltham, MA USA). Fasting insulin was tested using the Enzyme-Linked Immuno Sorbent Assay (ELISA) method. Body mass index (BMI) examination calculates of body weight in kg divided by height in meters squared (kg/m2). VAI was calculated based on the combination of (WC), (BMI), triglyceride (TG), and (HDL) examinations with the formula[8]:

$$Male: VAI = \left(\frac{WC}{(39.58 + (1.886 * BMI))}\right) * \left(\frac{TG}{1.03}\right) * (\frac{1.31}{HDL})$$

$$Famale\ VAI = \left(\frac{WC}{(36.58 + (1.896 * BMI))}\right) * \left(\frac{TG}{0.81}\right) * (\frac{1.52}{HDL})$$

$$HOMA - IR = \frac{glucose\ mg/dL * insulin\ \mu U/L}{405}$$

$$\text{QUICKI} = \frac{1}{[\log(Insulin\ \mu U/mL) + \log(\text{Glucose mg/dL})]}$$

Numerical data is displayed as mean±SD if the data distribution is normal or median(min-max) if the data distribution is not normal. Test the relationship between VAI with HOMA-IR and QUICKI using the Pearson test ($p<0.05$).

RESULT

A total of 70 patients who met the criteria participated in the study. Seventy samples were obtained, consisting of 36 (51,4%) men and 34 (48,6%) women. The distribution of subject characteristics is presented in Table 1. Variables with normal data distributions are shown with the mean±SD, while variables with abnormal data distributions are shown with the median (min-max).

The results of data analysis with the Pearson test showed a moderate positive correlation between the number of VAI and HOMA-IR (p=<0.001; r=0.480) and a moderate negative correlation between VAI and QUICKI (p=<0.001; r=-0.475) can be seen in table 2.

Table 2. Correlation test results of VAI between HOMA-IR and QUICKI

Variable	VAI	
	p	**r**
HOMA-IR	<0.001	0.480
QUICKI	<0.001	-0.475

The distribution of VAI data with HOMA-IR and QUICKI can be seen in Figure 1 and 2.

DISCUSSION

There was a positive correlation between VAI and HOMA-IR and a negative correlation between VAI and QUICKI. The correlation between VAI and HOMA-IR is in line with previous research which shows that VAI is closely related to HOMA-IR. This condition can be used as an independent risk factor influencing the increase in HOMA-IR rates in both male and female groups.[9]

VAI is considered a fat indicator and is essential in managing fat loss. Conventional ways to reduce fat are lifestyle interventions or using medication. This research also showed that obesity is strongly associated with insulin resistance. Those in the BMI >30kg/m2 group will experience four times more insulin resistance. Increasing TG levels is associated with decreased insulin sensitivity. The lower the HDL-C levels, the more insulin resistance occurs.[11]

Another study on 528 subjects with suspected obstructive sleep apnea with and without obesity and metabolic syndrome, reported that increased VAI was associated with insulin resistance.[12] Study of 439 Bangladeshi population, reported VAI had a positive correlation withHOMA-IR in patients with Type 2 DM but did not show a significant correlation in controls.[3]

A previous study showed that visceral fat has a link with insulin resistance calculated by HOMA IR and QUICKI and metabolic syndrome, which has a better correlation in pre-diabetic women and patients with type 2 DM population.[13] Another study by Vizzuso et al. reported a significant correlation between VAI, HOMA-IR, and QUICKI in a population of Caucasian children aged 8-15 years with metabolic syndrome.[14] Another study concluded a moderate correlation between VAI, HOMA- IR, and QUICKI in 396 obese children in Mexico.[15]

Previous studies have demonstrated the correlation between visceral adipose tissue and insulin resistance. A meta-analysis study by Zhang et al. reporteda significant positive association between adipose tissue build-up and insulinresistance as measured by HOMA-IR. The visceral fat mass is closely correlated with HOMA-IR, followed by total fat mass, BMI, and WC.[7]

Sun et al. said there is a correlation between visceral fat in several measurement methods and the risk of diabetes and insulin resistance.[3] Borel et al. showed that changes in visceral adipose tissue were associated with improved insulin sensitivity after one year of lifestyle intervention.[15] The increase influenced the increase in VAI values in WC, BMI, and TG levels. This condition supports the theory that increased fat, especially visceral fat and dyslipidemia, increases glucose blood levels due to insulin resistance. An increased risk of diabetes may result from excess visceral fat. Visceral fat has more excellentendocrine activity than subcutaneous fat and is a marker of adipose tissue dysfunction and ectopic fat deposition. These circumstances cause lipotoxicity and insulin resistance in muscle cells, liver, and pancreatic cells that inhibit glucose uptake. Therefore, visceral fat contributes as one of the risk factors for diabetes.[13]

Insulin resistance measurement with HOMA-IR was done more than 15 years ago.[5] HOMA-IR has been observed to have a linear correlation with glucoseclamp and minimal model in estimating insulin sensitivity/resistance in various studies in different populations. In contrast, QUICKI is the logarithm of HOMA- IR, which explains its almost perfect correlation with HOMA.[17] This is consistent with this study, where a very strong correlation was found between HOMA-IR and QUICKI. Katz et al., in their study, also mentioned that

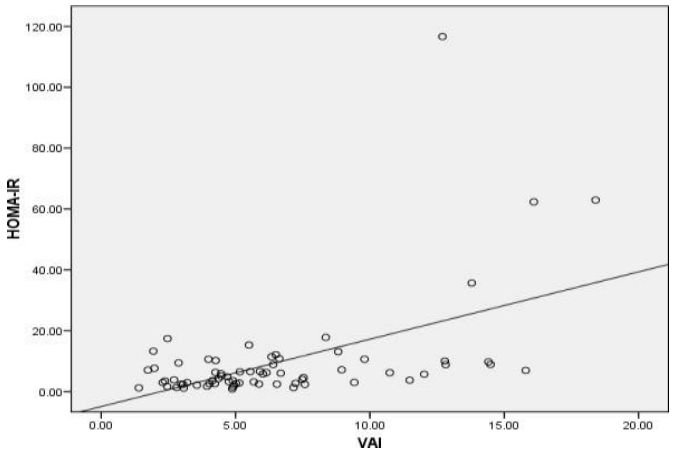

Figure 1. Scatter plot graph of Correlation VAI and HOMA-IR

Figure 1 shows the scatter plot of the VAI and HOMA IR relationship. The line in the figure shows a positive correlation between VAI and HOMA IR, i.e., the higher the VAI value, the higher the HOMA IR value. The higher the VAI value, the more severe the state of insulin resistance

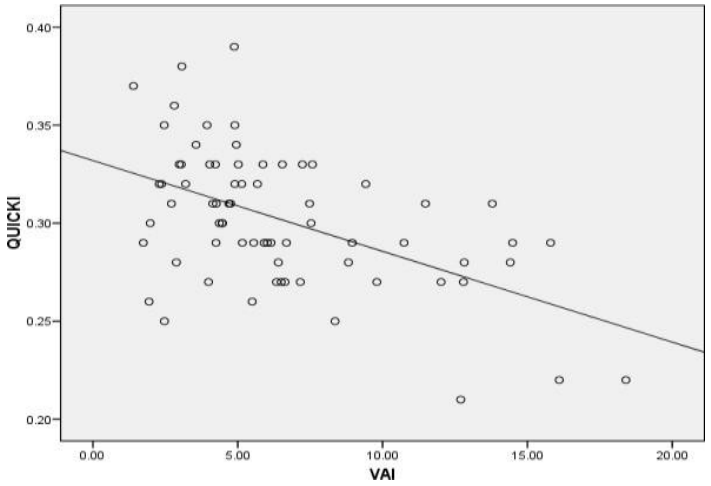

Figure 2. Scatter plot graph of VAI correlation with QUICKI

Figure 2 shows the scatter plot of the relationship between VAI and QUICKI. The line in the figure shows a negative correlation between VAI and QUICKI, i.e., the higher the VAI value, the lower the QUICKI value. The higher the VAI value, the more severe the state of insulin resistance.

HOMA-IR and QUICKI have a better correlation than HOMA-IR with glucose clamp.[18]

Insulin resistance occurs due to impaired insulin action in metabolically active tissues and organs, including skeletal muscle, liver, and fat tissue.[13] In insulin resistance, the effect on adipose tissue is an increased hepatic free fatty acid flow that tends to increase hepatic very low-density lipoprotein (VLDL) production. At the same time, ketogenesis remains suppressed due to compensatory hyperinsulinemia.[9] Fat-induced insulin resistance, where there is decreased fat storage capacity within the subcutaneous adipose tissue, will lead to ectopic fat deposition into visceral fat tissue and insulin-sensitive tissues such as liver and skeletal muscle. These tissues will progressively develop to lipotoxicity status, disrupt insulin signaling and action, and cause insulin resistance and decreased glucose tolerance. Insulin resistance increases as BMI, WC, and especially waist-hip ratio increases. This reflects an increase in adiposity and incredibly visceral adipose tissue.[2,19]

The visceral adiposity index was developed as a novel indicator of visceral adipose tissue dysfunction that proved to be a good indicator of endocrine dysfunction and low-grade inflammation of adipose tissue in a state referred to as adipose tissue dysregulation.[20] Adipose tissue dysregulation altered fat distribution and function and is believed to be a cornerstone in the pathogenesis of insulin resistance through altered adipocytokine production, increased lipolytic activity, and inflammation.[21] Other studies have shown a relationship between obesity parameters and lipid profiles in the form of lipid accumulation products, inflammatory conditions, and glucose levels.[22]

The results of this study indicate that VAI values obtained from examining lipid profile levels (triglycerides and HDL-cholesterol) can be used to assess the state of insulin resistance. This parameter makes it easier for

patients to control further insulin-resistant states. This study did not analyze the length of time the subject suffered from DM. Further research is needed on DM patients and on the period of time after the patient is diagnosed with DM.

CONCLUSION

This study has a positive correlation between the number of VAI and HOMA-IR and a negative correlation between VAI and QUICKI. The higher VAI value indicates a more severe insulin-resistant state, as seen from the increasing HOMA IR and decreasing QUIKI. The higher the VAI value, the more severe the state of insulin resistance, which can increase complications in DM. Further studies linking VAI and insulin resistance to DM complication parameters are needed.

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