



Prevalence and Association of Insulin Resistance in Non-Diabetic Hemodialysis Patients: A Descriptive-Analytic Cross-Sectional Study in Vietnam

Abstract

Background: Patients with chronic kidney disease (CKD) experience high mortality rates from cardiovascular disease (CVD). Insulin resistance (IR) is a frequent complication of CKD and is associated with poorer cardiovascular outcomes. This study investigates the prevalence and associations of IR in hemodialysis (HD) patients. **Materials and Methods:** A descriptive-analytic cross-sectional study was conducted on 103 HD patients. We used the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) and the Quantitative Insulin Sensitivity Check Index (QUICKI) to measure IR. We examined potential associations between IR and the following factors: age, gender, etiology of kidney failure, BMI, waist circumference, blood lipids, hemoglobin concentration, uric acid, and duration of HD. **Results:** The prevalence of IR, as measured by HOMA-IR, was 61.2%, and by QUICKI, it was 48.5%. Age, gender, etiology of kidney failure and increased waist circumference did not significantly influence IR. A significant associations were observed between IR and higher BMI, anemia, dyslipidemia, and longer duration of HD therapy. Interestingly, the HOMA-IR and QUICKI indices correlated for most factors except total cholesterol, LDL-C, and uric acid. **Conclusion:** This study found a high prevalence of IR in HD patients, with 61.2% identified by HOMA-IR and 48.5% by QUICKI. We confirmed significant associations between IR and BMI, anemia, dyslipidemia, and duration of HD therapy in this population.

Keywords: HOMA-IR, Insulin resistance, Kidney failure, QUICKI

Introduction

Majority of patients with chronic kidney disease (CKD) succumb to cardiovascular complications before developing kidney failure. Compared to the general population, their risk of death from cardiovascular disease (CVD) is 10–20 times higher, after accounting for factors like age, gender, race, and diabetes.¹

Traditional CVD risk factors like age, gender, race, hypertension, diabetes, and smoking do not fully explain the increased CVD mortality in this group. This has led researchers to explore the role of inflammation and metabolic disorders. Insulin resistance (IR) has been identified as an independent predictor of mortality in non-diabetic kidney failure patients, even beyond factors like inflammation and BMI.^{2,3} IR is one of the common complications of CKD and is associated with poorer cardiovascular outcomes.⁴⁻⁷

The relationship between IR and cardiovascular risk factors in Vietnamese CKD patients has received limited domestic attention. Addressing this gap, our study investigates the prevalence and association of IR in non-diabetic hemodialysis patients.

Materials and Methods

This descriptive-analytic cross-sectional study was approved by the Hue University of Medicine and Pharmacy's Research and Ethical Committees for human subject research. We obtained approval from the Board of Directors of Quang Nam General Hospital, following informed consent procedures with participating patients.

The study was conducted at the Dialysis Department of Quang Nam General Hospital, Vietnam, from March 2014 to June 2015. All eligible maintenance hemodialysis (MHD) patients were surveyed during this period.

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The study included only patients who met the following inclusion criteria: Non-diabetic kidney failure receiving MHD treatment, aged 18 years or older, provided informed consent. All patients were treated with MHD at least 2 months before inclusion in the study. Patients had to meet the following criteria for at least 2 months before inclusion: stable clinical condition, no recent hospitalizations, traumas, or surgeries. All MHD sessions used arteriovenous fistula access, occurred three times weekly for three hours each, and employed polysulfone high-flux dialyzers with bicarbonate-based dialysate. Patients with the following conditions were excluded as they could influence the research variables: pregnant patients, history of diabetes, nephrotic syndrome, acute illness, liver failure, concomitant endocrine diseases, patients on drugs such as corticosteroids, hormonal contraceptives, beta-blockers, etc.

A control group was recruited from patients undergoing routine health checkups at Quang Nam Provincial General Hospital. These individuals were confirmed healthy through a comprehensive clinical examination and tests and provided informed consent for participation. The researchers matched at least one control subject per case in the patient group based on sex, age, and BMI. Blood samples were collected from the control group only once.

Patients underwent the following assessments: full medical history and complete physical examination. Paraclinical evaluations: fasting blood glucose (G0); hemoglobin (Hb); uric acid; blood lipids: total cholesterol, HDL-C (high density lipoprotein cholesterol), LDL-C (low density lipoprotein cholesterol) and triglyceride levels; blood urea. Serum fasting insulin (I0) was measured using the electrochemiluminescence immunoassay (ECLIA).

IR was calculated using two indices: HOMA-IR (Homeostasis model assessment for insulin resistance) = $I0 (\mu\text{U/mL}) \times G0 (\text{mmol/L}) / 22.5$ and QUICKI (quantitative insulin sensitivity check index) = $1 / [\log I0 (\mu\text{U/mL}) + \log G0 (\text{mg/dL})]$. IR when HOMA > highest quartile of control group or QUICKI < $\bar{X} - 2\text{SD}$ of control group (according to WHO regulations).^{8,9}

Venous blood samples were collected in the morning after an overnight fast, before dialysis. The following analyzers were used: Cobas 6000 for quantifying chemobiological indices (insulin, total cholesterol, triglyceride, HDL-C, LDL-C, urea, glucose, uric acid), Sysmex XS 800i for Hb.

Body mass index (BMI) and waist circumference (WC) were evaluated based on WHO standards for Asian adults.¹⁰ The BMI was calculated by dividing the dry weight (in kg) by the square of the height (in m²). The patients were then classified into the following categories: < 23, ≥ 23. The WC

was measured at the midpoint between the rib cage and the iliac crest. Abdominal obesity was defined as WC ≥ 90 cm in men and ≥ 80 cm in women.

Diagnosis of dyslipidemia was made according to the NCEP-ATP III model guideline,¹¹ anemia according to Kidney Disease: Improving Global Outcomes (KDIGO) 2012.¹²

Statistical analysis

SPSS version 16.0 was used for all statistical analyses. Data were presented according to their distribution: continuous variables with a normal distribution, the values are mean ± standard deviation; continuous variables with a skewed distribution, the values are median (interquartile range); and categorical variables, the values are number (percentage). The Student's t-test and chi-square test were used to compare continuous and categorical data, respectively. The median difference was compared using the Mann-Whitney U test. Variations with $p < 0.05$ or $p < 0.01$ were deemed statistically noteworthy. Between IR and the other measured variables, Pearson correlation coefficients were computed.

Results

Table 1 summarizes the baseline characteristics of the study groups. There were no significant differences between the hemodialysis (HD) patients and the control group in terms of age, gender (predominantly male), and BMI. HD patients exhibited significantly higher levels of HOMA-IR, QUICKI, and serum fasting insulin compared to the control subjects.

HD patients displayed significantly higher HOMA-IR and QUICKI values compared to the control group [Table 2]. Notably, 61.2% and 48.5% of HD patients were identified with IR based on the HOMA-IR and QUICKI indices, respectively.

Table 1: Baseline characteristics of HD patients and control group

Variable	Patients (n = 103)	Control (n = 105)	p
Age (years)	50.1 ± 16.8	51.1 ± 15.9	>0.05
Gender male, n (%)	64 (62.1)	70 (66.7)	>0.05
BMI (kg/m ²)	20.81 ± 2.25	20.93 ± 2.27	>0.05
Insulin levels (mIU/L), Median (25 th –75 th)	13.5 (9.53–19.54)	6.9 (4.35–9.20)	<0.01
HOMA-IR, Median (25 th –75 th)	3.24 (2.11–5.11)	1.99 (1.30–2.64)	<0.01
QUICKI, Median (25 th –75 th)	0.321 (0.302–0.341)	0.364 (0.350–0.381)	<0.01

BMI: Body mass index, HOMA-IR: Homeostasis model assessment for insulin resistance, QUICKI: Quantitative insulin sensitivity check index, HD: Hemodialysis

Table 2: Comparison of IR percentage between patients and control groups

Insulin resistant	Patients (n = 103)	Control (n = 105)	p
HOMA-IR (> 2.64), n (%)	63 (61.2)	26 (24.76)	<0.0001
QUICKI (< 0.319), n (%)	50 (48.5)	12 (11.42)	<0.0001

As mentioned above, IR was noted when HOMA > highest quartile of control group (2.64) or QUICKI < \bar{x} -2SD of control group (0.319) HOMA-IR: Homeostasis model assessment for insulin resistance, QUICKI: Quantitative insulin sensitivity check index, IR: Insulin resistance.

Table 3: Characteristics of insulin resistant patients on HD

Variable	Insulin resistant			
	HOMA-IR n (%)	p	QUICKI n (%)	p
Age (years)				
>60 (n = 28)	21 (75.0)	>0.05	16 (57.1)	>0.05
≤ 60 (n = 75)	42 (56.0)		34 (45.3)	
Gender				
Male (n = 64)	39 (60.9)	>0.05	32 (50.0)	>0.05
Female (n = 39)	24 (61.5)		18 (46.2)	
Etiology of kidney failure				
Chronic glomerulonephritis	22 (57.9)	>0.05	20 (52.6)	>0.05
Chronic pyelonephritis	32 (66.7)		22 (45.8)	
Renal vascular disease	5 (55.6)		5 (55.6)	
Unknown	4 (50.0)		3 (37.5)	
BMI (kg/m ²)				
≥ 23 (n = 11)	10 (90.9)	<0.05	10 (90.9)	<0.01
< 23 (n = 92)	53 (57.6)		40 (43.5)	
Abdominal obesity				
Yes (n = 40)	23 (57.5)	>0.05	18 (45.0)	>0.05
No (n = 63)	40 (63.5)		32 (50.8)	
Anemia				
Yes (n = 91)	61 (66.3)	<0.01	48 (52.2)	<0.05
No (n = 12)	2 (18.2)		2 (18.2)	
Dyslipidemia				
Yes (n = 43)	33 (76.7)	<0.01	32 (74.4)	<0.01
No (n = 60)	30 (50.0)		18 (30.0)	
Duration of HD				
≤ 12 months (n = 59)	25 (42.4)	<0.01	23 (39.0)	<0.05
> 12 months (n = 44)	38 (86.4)		27 (61.4)	

BMI: Body mass index, HOMA-IR: Homeostasis model assessment for insulin resistance, QUICKI: Quantitative insulin sensitivity check index, HD: Hemodialysis

It is evident that there was little effect of age, gender, the cause of kidney failure, or abdominal obesity on insulin resistance. Regarding insulin resistance, BMI, anemia, dyslipidemia, and the length of HD all demonstrated a substantial influence [Table 3].

Table 4 presented the relationship correlation coefficient (r) between IR and some factors in HD patients. Apart from uric acid, LDL-C concentrations, and total cholesterol,

Table 4: Correlation coefficient (r) between IR and selected clinical and laboratory parameters in patients on HD

Variable	Insulin resistant			
	HOMA-IR		QUICKI	
	r	p	r	p
BMI	0.519	<0.01	-0.527	<0.01
Hb	-0.310	<0.01	0.418	<0.01
Total cholesterol	0.044	>0.05	-0.085	>0.05
Triglyceride	0.514	<0.01	-0.569	<0.01
HDL-C	-0.674	<0.01	0.620	<0.01
LDL-C	0.008	>0.05	-0.096	>0.05
Uric acid	-0.063	>0.05	0.079	>0.05
Duration of HD	0.254	<0.05	-0.308	<0.01

BMI: Body mass index, HOMA-IR: Homeostasis model assessment for insulin resistance, QUICKI: Quantitative insulin sensitivity check index, HD: Hemodialysis, IR: Insulin resistance, HDL-C: High density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol

these two indices (HOMA-IR and QUICKI) were correlated with most of the factors.

Discussion

Dynamic tests, which provide a direct and precise measurement, are very useful for physiological or pharmacological studies. However, their broad usage in HD patients is limited by the technical aspects of its implementation. Static tests that measure fasting glucose and insulin concentrations are employed in these circumstances. HOMA-IR and QUICKI both use fasting insulin and glucose levels to calculate insulin resistance and both correlate reasonably with the clamp technique.¹³ HOMA-IR primarily reflects hepatic IR, not IR at peripheral tissues. Subjects with impaired fasting glycemia, who have hepatic IR, can be detected by HOMA-IR. However, subjects with impaired glucose tolerance, who have peripheral IR, might be missed.¹⁴ These limitations also apply to QUICKI, leading to the possibility of missing subjects with impaired glucose tolerance. Therefore, we concluded that using a single formula is insufficient for diagnosing insulin resistance.

We found that, in comparison to control subjects, the value of HOMA-IR was significantly higher in HD patients. This aligns with previous studies.¹⁵⁻¹⁷ Interestingly, the QUICKI index exhibited an opposite trend in CKD patients. Their QUICKI values were significantly lower compared to the healthy control group (0.321 vs. 0.364; p < 0.01). This finding is consistent with the work of Hung AM.¹⁵ In conclusion, while both HOMA-IR and QUICKI indexes may vary in CKD patients, they generally show a pattern of being higher and lower, respectively, compared to the control group.

61.2% and 48.5% of patients were classified as insulin resistant based on HOMA-IR and QUICKI index measurements, respectively. This disparity might be due

to HOMA's greater sensitivity to insulin variations, possibly because of the lower capacity of normalization by the constant denominator used in HOMA compared with the log transformation used in QUICKI.¹⁸

A similar finding was reported in the study performed on 25,868 patients with CKD in stages 3–4 indicating the prevalence of 60% of metabolic syndrome.¹⁹ Hemodialysis patients had a 31.6% IR prevalence according to the HOMA-IR, as demonstrated by Sit D *et al.* (2005).²⁰ IR was found in 48, 42, and 48% of cases in different investigations based on oral glucose tests, QUICKI index, or HOMA-IR in CKD patients.^{21–23} HOMA-IR and QUICKI cut-off values were used to define the IR rate in the community of Vietnamese patients with heart failure who did not have diabetes, obesity, or hypertension (55.3% and 56.3%, respectively).²⁴ Variations in research subjects, thresholds for defining IR, methodologies used to evaluate IR, and ethnicity likely contribute to the observed differences in IR prevalence across these studies.

This study found no significant influence of age or gender on insulin resistance (IR). These results align with previous research.²⁵ In contrast, BMI was associated with IR. We observed a negative correlation between the QUICKI index and BMI, indicating greater insulin sensitivity with lower BMI. Conversely, the HOMA-IR index showed a positive correlation with BMI, suggesting worsening insulin resistance with increasing BMI. This aligns with the findings of Mirzaalian *et al.*²⁶ Our study confirms that overweight and obese patients (BMI \geq 23 kg/m²) have higher IR indices compared to normal weight patients (BMI < 23 kg/m²). This highlights the importance of BMI in managing and monitoring IR in clinical settings.

Our study also identified a link between IR and anemia in HD patients. This finding aligns with previous research demonstrating how short-term erythropoietin therapy can significantly improve insulin sensitivity (lower HOMA-IR values) in this population.²⁵ Furthermore, we observed a relationship between IR, triglyceride levels, and HDL-C levels. Similar associations between elevated triglycerides, decreased HDL-C, and IR have been reported in studies before the diagnosis of CKD.^{15,16} This highlights the importance of managing dyslipidemia to potentially reduce factors that worsen CKD, lower IR, and ultimately, decrease cardiovascular complications in CKD patients.

Chronic kidney failure involves oxidative stress and inflammation, which contribute to IR.²⁷ Our study found a positive correlation between IR and the duration of HD therapy. This might be explained by the link between inflammation and the prolonged course of the disease. The duration of dialysis and a patient's inflammatory state are likely two significant factors influencing oxidative stress in HD patients.^{28,29}

This study has some limitations. First, we employed static tests to measure insulin resistance. Second, data on long-term hemodialysis adequacy was not available. Finally, the study did not explore the potential relationships between IR and physical activity levels or acidosis in these patients.

This study found a high prevalence of insulin resistance (IR) in hemodialysis (HD) patients, with 61.2% identified by HOMA-IR and 48.5% by QUICKI. Our findings demonstrate significant associations between IR and several clinical characteristics in HD patients, including higher BMI, anemia, dyslipidemia, and longer duration of HD therapy. These findings highlight the importance of managing these factors to potentially improve outcomes in HD patients.

Conflicts of interest: There are no conflicts of interest.

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