

Assessment of Insulin Resistance and its Correlation with 25-OH Vitamin D in Chronic Kidney Disease

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ABSTRACT

Introduction: Insulin resistance is more frequent at progressively declining glomerular filtration rate levels and is almost universal in end-stage kidney failure. Multiple studies have also demonstrated that 1,25(OH)₂D administration improves glucose metabolism in patients with chronic kidney disease (CKD). The present study was carried out with an aim to assess insulin resistance and to find an association between eGFR, insulin resistance, and vitamin D levels in patients with chronic kidney disease.

Material and Methods: This Cross-sectional study was conducted in a tertiary care academic hospital. Subjects with age ≥ 18 years; and estimated GFR < 60 mL/min/1.73m² were recruited. CKD was characterized as an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73m² using a Cockcroft-Gault equation. Insulin Resistance was assessed using the HOMA: HOMA-IR. Quantitative measurement of 25-OH vitamin D in serum and plasma samples was done using Chemiflex.

Results: Among sixty-four enrolled subjects, 53.1% had insulin resistance. Insulin resistance showed an inverse relationship with eGFR ($r = -0.50$, $p < 0.001$), and metabolic acidosis ($r = -0.39$, $p < 0.001$) while, it has no relation with vitamin D levels ($r = -0.01$, $p < 0.90$). The study also shows that BMI (OR 1.43, 95% CI 0.99-2.07, $p = 0.05$), waist circumference (OR 1.37, 95% CI 1.10-1.72, $p = 0.005$), and metabolic acidosis (OR 5.71, 95% CI 1.85-17.61, $p = 0.002$) were independently related to insulin resistance.

Conclusion: The present study shows that eGFR and metabolic acidosis has an inverse association with insulin resistance in CKD patients. The study also shows that BMI, waist circumference, and metabolic acidosis were independently related to insulin resistance.

Keywords: Chronic Kidney Disease, Vitamin D, Insulin Resistance

resistance, and vitamin D levels in patients with chronic kidney disease.

MATERIAL AND METHODS

Study subjects were recruited from the outpatient departments or inpatient department of a tertiary care center from February 2016 to August 2017. The study was approved by the Institutional ethical committee, and all participants provided written informed consent.

Inclusion criteria included age ≥ 18 years; estimated GFR < 60 mL/min/1.73m². After obtaining demographic information the patients were subjected to laboratory investigations including fasting insulin, and vitamin D levels.

CKD was characterized as an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73m² using a Cockcroft-Gault equation $[(40 - \text{age}) \times \text{weight}] / (72 \times \text{serum creatinine}) \times 0.85$ (if female)]. Fasting insulin was measured using a microparticle enzyme immunoassay. Insulin Resistance was assessed using the HOMA: HOMA-IR. fasting glucose (mmol/L) $3 \times \text{fasting insulin (IU/mL)} / 22.5$.⁸ HOMA-IR value > 5 is considered a high insulin resistance. Quantitative measurement of 25-OH vitamin D in serum and plasma samples was done using Chemiluminescent Microparticle Immunoassay (CMIA) technology with flexible assay protocol, referred to as Chemiflex.

STATISTICAL ANALYSIS

The statistical analysis was done using Statistical Package for Social Sciences Version 25.0 (SPSS Inc., Chicago, IL, USA). Data were presented as mean \pm SD or n (%). The results of comparing the correlation between two continuous

INTRODUCTION

Insulin Resistance (IR) is common and develops early in chronic kidney disease (CKD), even when the glomerular filtration rate (GFR) is still within the normal range.¹ IR is increasingly more frequent at progressively lower GFR levels and is almost universal in end-stage kidney failure.² In some studies, but not all, the severity of IR was correlated with glomerular filtration rate (GFR).^{3,4} Multiple studies have also demonstrated that 1,25(OH)₂D administration improves glucose metabolism in patients with CKD.^{5,6,7} Therefore, the present study was carried out with an aim to assess insulin resistance and to find an association between eGFR, insulin

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variables were indicated by the correlation coefficient (r) using correlation analysis. The logistic regression test was performed to evaluate the contribution of independent factors. A result was deemed statistically significant when $p < 0.05$

RESULTS

Sixty-four patients with CKD were enrolled in the present study. Table 1 shows the baseline characteristic of all patients. Mean age was 59.64 ± 8.85 years; 64% of the patients were male and male to female ratio was 1.7:1.

Among 64 patients, 22 (34.38%) had Stage 5, 18 (28.13%) had Stage 4, 15 (23.44%) had Stage 3, and 9 (14.06%) had Stage 2 CKD. Their overall mean BMI and eGFR was 24.07 ± 2.74 (kg/m^2) and 25.6 ± 17 ml/min per 1.73 m^2 respectively.

Vitamin D level below the normal range (< 20 ng/ml) was observed in 39.06% of patients. Twenty-six (40%) patients in all had metabolic acidosis and all them were in CKD stage 4-5.

We observed insulin resistance in 53.1% of patients. Majority of these patients were in CKD stage 4 and 5 and had metabolic acidosis, higher age, BMI, waist circumference, serum cholesterol, and serum triglyceride. (Table/Fig-1)

A comparison of the baseline characteristics and physiological variables between patients with CKD stage 2, 3 and CKD stage 4, 5 showed that mean BMI (kg/m^2) (24.37 ± 3.12) and HOMA IR (6.92 ± 2.48) of patients with CKD Stage 4 and 5 was higher as compared to CKD Stage 2 and 3 (23.56 ± 1.89) (5.30 ± 2.52), while mean vitamin D levels were higher in stage 4 and 5 (22.57 ± 4.05) as comparison to CKD stage 2 and 3 (23.62 ± 6.4). However, the differences in the mean BMI, HOMA-IR, and vitamin D levels of both the groups was not found to be statistically significant.

We analyzed the correlation between HOMA-IR, eGFR levels, metabolic acidosis, and vitamin D levels in the study cohort. IR showed an inverse relationship with eGFR ($r = -0.50$, $p < 0.001$), and metabolic acidosis ($r = -0.39$, $p < 0.001$) while, it has no relation with vitamin D levels ($r = -0.01$, $p < 0.90$). (Table/Fig-2)

Logistic regression analysis was performed to determine the independent predictors of IR. eGFR showed independent relationship to IR (OR 0.84, 95% CI 0.75-0.96, $p = 0.008$). Also, BMI (odd ratio (OR) 1.43, 95% CI 0.99-2.07, $p = 0.05$), waist circumference (OR 1.37, 95% CI 1.10-1.72, $p = 0.005$), and metabolic acidosis (OR 5.71, 95% CI 1.85-17.61, $p = 0.002$), showed independent associated with IR in CKD. (Table/Fig-2).

DISCUSSION

Several observational and prospective studies have suggested a relationship between insulin resistance and CKD. Previous studies have demonstrated that IR is associated with an increased risk for developing CKD and vice versa.^{9,10,11}

The prevalence of insulin resistance among CKD patients in different series has been reported to range from 17% to 100%.^{12,13,14,15} The overall prevalence of insulin resistance in

patients of CKD in our study was 53.1%. This wide variability in the prevalence of IR in previous studies depends probably on the patient characteristic and population type.

Our findings of an inverse association between eGFR and IR are consistent with some, but not all, previous studies.^{3,4,16} Defronzo et al. demonstrated that nondiabetic patients with ESRD are insulin resistant.¹⁷ In a cross-sectional analysis of nondiabetic adults, Chen et al. found that insulin resistance is independently associated with moderate CKD.¹⁸ Furthermore, in the Health, Aging and Body Composition study, kidney function was found to be independently associated with insulin resistance assessed as upper quartile of HOMA.¹⁹ However, lack of relationship between the eGFR and insulin sensitivity was noted in a Korean study and Chinese surveys.^{20,21,22,23} A recent study reported that insulin sensitivity was unrelated to the eGFR and suggested that IR across the spectrum of CKD is primarily determined by body composition rather than by the eGFR per se.^{1,24} Although 39% of patients in the present study had vitamin D levels much below the normal range, we found no significant association between Vitamin D levels and IR. As far as the association of IR and vitamin D levels is concerned it seems to be controversial with some studies endorsing its existence while some deny this in some specific group of patients.

Few studies have demonstrated that vitamin D supplementation does not improve glucose metabolism in non-diabetic patients with stage 3-4 CKD.^{25,26} Whereas, a systematic review and meta-analysis in patients on dialysis has shown that short-term vitamin D therapy improves insulin secretion and insulin sensitivity.²⁷

Logistic regression analysis to determine the independent predictors of IR revealed that BMI, waist circumference, and metabolic acidosis were independently related to IR. Although IR is associated with central obesity, some studies have shown that IR is more closely associated with visceral fat, while others have shown the association to be stronger with subcutaneous fat.^{28,29,30,31,32} The causal role of acidosis in IR in CKD is supported by two clinical trials showing an improvement in IR by bicarbonate administration.^{33,34}

CONCLUSION

The present study shows that eGFR and metabolic acidosis has an inverse association with IR in CKD patients. The study also shows that BMI, waist circumference, and metabolic acidosis were independently related to IR.

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