Association of serum adiponectin and leptin levels with renal function in kidney transplant recipients with or without new-onset diabetes after transplantation

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Abstract

Purpose: To evaluate serum adiponectin and leptin concentration in new-onset diabetes after transplantation (NODAT) and non-NODAT patients and association with renal function in kidney transplant recipients (KTRs).

Patients and methods: A study of 314 consecutive adults KTRs divided into four groups: 236 individuals without NODAT who had renal insufficiency (RI; n = 56) or normal renal function (n = 180) and 78 patients with NODAT who had RI (n = 17) or normal renal function (n = 61). NODAT was diagnosed based on venous fasting blood glucose or HbA1c with the criteria of the American Diabetes Association. Renal insufficiency was defined according to KDOQI 2002 guidelines.

Results: In the NODAT group, the median level of serum adiponectin was lower than that of non-NODAT one (30 µg/ml vs 37.15 µg/ml, p < 0.001); in contrast, the median leptin concentration was higher (4.27 ng/ml vs 4.05 ng/ml, p = 0.024). In the RI group, both median serum adiponectin and leptin levels were higher than those of non-RI one (Adiponectin: 40.01 µg/ml vs 33.7 µg/ml; Leptin: 4.51 ng/ml vs 3.91 ng/ml, p < 0.001 both). We found that BMI was related to both adiponectin and leptin levels in both NODAT, non-NODAT, and all subject groups, based on univariate and multivariate linear regression analysis.

Conclusion: New-onset diabetes after transplantation, BMI, and renal insufficiency were affected to the serum level of adiponectin and leptin in KTRs.

KEYWORDS
adipokines, kidney transplant recipients, NODAT, renal insufficiency
INTRODUCTION

Adipokines are peptides that signal the functional status of adipose tissue to targets in the brain, liver, pancreas, immune system, vasculature, muscle, and other tissues. Secretion of adipokines, including leptin, adiponectin, vaspin, apelin, and progranulin..., is altered in adipose tissue dysfunction and may contribute to a spectrum of obesity-associated diseases. Concomitant with the global increase in obesity prevalence in recent decades, there has been an increase in the prevalence of type 2 diabetes mellitus (T2DM). Furthermore, obesity is a significant risk factor for T2DM and closely related to metabolic disturbances in the adipose tissue that primarily functions as a fat reservoir. New-onset diabetes mellitus after transplantation (NODAT) is a frequent complication in kidney allograft recipients. NODAT and T2DM share a common pathophysiology with abnormalities in both insulin sensitivity and insulin secretion. The most worrying complication of NODAT is major adverse cardiovascular events, which represent a leading cause of morbidity and mortality in transplanted patients. It is also associated with the risk of graft failure. As in T2DM patients, adipokines including adiponectin and leptin have a role in the pathogenesis of NODAT and cardiovascular events in NODAT kidney recipients. Thus, it was interesting to ask whether serum adiponectin and leptin levels are related to renal insufficiency in renal transplant recipients with or without NODAT or not? We measured serum adiponectin and leptin levels in kidney transplant recipients with normal renal function and renal insufficiency with or without NODAT.

PATIENTS AND METHODS

Subjects

We included 518 end-stage renal disease patients due to chronic glomerulonephritis (CGN), who transplanted kidney from living donation at Department of Nephrology and Hemodialysis, Military Hospital 103, Ha Noi, Viet Nam during the last 10 years (from January 2010 to December 2020). We excluded patients younger than 18 years at the time of transplantation, those with DM before transplantation. The remaining 314 kidney transplanted patients were provided written informed consent before participating in our study. We also collected all data of clinical characteristics and laboratory parameters at the baseline time of the study.

To find serum adiponectin and leptin levels are related to renal insufficiency in kidney transplant recipients with NODAT, 314 patients were divided into four groups: 236 individuals without NODAT who had RI (n = 56) or normal renal function (n = 180) and 78 patients with NODAT who had RI (n = 17) or normal renal function (n = 61).

Serum adiponectin and leptin were measured by ELISA assay in all the patients using the blood samples, quantified by biochemical indices. Blood samples were centrifuged at 1000 g for 10 min. Plasma specimens were then frozen and stored at −80°C until analysis. Human Adiponectin ELISA kit (Invitrogen, United States) and Human Leptin Instant ELISA kit (Invitrogen, United States) plasma levels were measured commercially available ELISAs.

Definition

New-onset diabetes after transplantation was detected and diagnosed after kidney transplantation for more than 45 days, based on the criteria of the American Diabetes Association. NODAT was diagnosed when HbA1c was above 6.5% or had fasting hyperglycemia above 7.0 mmol/L (126 mg%). For patients with fasting blood glucose levels between 5.6 and 6.9 mmol/L, fasting oral glucose tolerance will be tested. After 2 h, if the glucose concentration is more than 11.1 mmol/L, the patient is also diagnosed with diabetes.

Renal function evaluation

Renal function was assessed by the estimated creatinine clearance (CrCl) derived from Cockroft-Gault formula, where CrCl (ml/min) = [(140 – age (years)) × weight (kg)]/(0.814 × serum creatinine (μmol/L)), corrected in women by a factor of 0.85. A calculated CrCl <60 ml/min was defined as renal insufficiency (RI), according to KDOQI 2002 guidelines.

Statistical analysis

All the normal distribution and continuous data were represented by mean and standard deviation and were analyzed by the Student t test, one-way ANOVA, and post hoc Bonferroni test. All the skewed distributions were represented by median (25 percentile–75 percentile), analyzed by the Mann–Whitney U test and Kruskal–Wallis test. Categorical data were presented by the frequency with percentage and were analyzed using the chi-square test or Friedman Test. To evaluate the correlation between serum adiponectin and leptin levels with other variables such as age, BMI, creatinine, eGFR, CRP..., univariate and multivariate linear regressions were performed. Statistical analysis was done using Statistical Package for Social Science (SPSS) version 20.0. A p-value < 0.05 was considered significant.

RESULTS

The baseline demographic and laboratory characteristics in patients were shown in Table 1. In both groups NODAT and non-NODAT, eGFR, level of hemoglobin was lower, the concentration of serum adiponectin and leptin in RI group was higher than non-RI one, p < 0.001.

Table 2 showed that serum adiponectin level was lower, but serum leptin was higher in NODAT than those of non-NODAT, p < 0.001 and = 0.024. However, serum adiponectin and leptin...
| Characteristics | NODAT (n = 78) | Non-NODAT (n = 61) | p  | Non-NODAT, (n = 236) | Non-RI (n = 180) | p   |
|-----------------|----------------|-------------------|----|---------------------|-----------------|-----|
| Ages (Average)  | 48.94 ± 10.74  | 43.91 ± 11.2      | 0.105 | 40.73 ± 10.89      | 39.52 ± 9.58    | 0.426 |
| Gender (n, %)   |                |                   |     |                     |                 |     |
| Male | 12 (70.6) | 41 (67.2) | 0.792 | 43 (76.8) | 124 (68.9) | 0.257 |
| Female | 5 (29.4) | 20 (32.8) | | 13 (23.2) | 56 (31.1) | |
| Pretransplant Tx (n, %) | | | | | | |
| MHD | 16 (94.1) | 49 (80.3) | 0.277 | 47 (83.9) | 153 (85) | 0.846 |
| PD | 0 (0) | 3 (4.9) | N/A | 3 (5.4) | 6 (3.3) | 0.446 |
| Non-dialysis | 1 (5.9) | 11 (18) | 0.446 | 9 (16.1) | 25 (13.9) | 0.685 |
| Hepatitis virus infection (n, %) | | | | | | |
| None infection | 15 (88.2) | 39 (63.9) | 0.264 | 42 (75) | 133 (73.9) | 1.000 |
| HBV | 1 (5.9) | 4 (6.6) | | 5 (8.9) | 15 (8.3) | |
| HCV | 1 (5.9) | 14 (23) | | 7 (12.5) | 25 (13.9) | |
| HBV + HCV | 0 (0) | 0 (0) | | 2 (3.6) | 7 (3.9) | |
| HLA matching (n, %) | | | | | | |
| 0 | 0 (0) | 2 (3.3) | 0.474 | 2 (3.6) | 6 (3.3) | 0.205 |
| 1 | 2 (11.8) | 7 (11.5) | | 6 (10.7) | 15 (8.3) | |
| 2 | 7 (41.2) | 15 (24.6) | | 10 (17.9) | 50 (27.8) | |
| 3 | 4 (23.5) | 26 (42.6) | | 21 (37.5) | 79 (43.9) | |
| 4 | 4 (23.5) | 8 (13.1) | | 12 (21.4) | 22 (12.2) | |
| 5 | 0 (0) | 3 (4.9) | | 4 (7.1) | 4 (2.2) | |
| 6 | 0 (0) | 0 (0) | | 1 (1.8) | 4 (2.2) | |
| PRA | | | | | | |
| Positive (n, %) | 1 (5.9) | 7 (11.5) | 0.678 | 3 (5.4) | 15 (8.3) | 0.575 |
| Negative (n, %) | 16 (94.1) | 54 (88.5) | | 53 (94.6) | 165 (91.7) | |
| Transplantation duration (month) | 21.2 (6.68–80.96) | 15.6 | 0.387 | 28.45 (9.01–82.00) | 17.23 (8.62–29.44) | 0.009 |
| BMI (kg/cm²) | | | | | | |
| <18.5 | 3 (17.6) | 6 (9.8) | 0.85 | 7 (12.5) | 37 (20.6) | 0.431 |
| 18.5–22.9 | 8 (47.1) | 31 (50.8) | | 37 (66.1) | 115 (63.9) | |
| 23–<25 | 3 (17.6) | 12 (19.7) | | 8 (14.3) | 16 (8.9) | |
| ≥25 | 3 (17.6) | 12 (19.7) | | 4 (7.1) | 12 (6.7) | |
| Average | 22.65 ± 5.11 | 22.42 ± 2.87 | 0.809 | 21.49 ± 2.65 | 20.81 ± 2.59 | 0.09 |
| Hypertension | | | | | | |
| Yes (n, %) | 17 (100) | 43 (70.5) | 0.008 | 46 (82.1) | 136 (75.6) | 0.305 |
| Non (n, %) | 0 (0) | 18 (29.5) | | 10 (17.9) | 44 (24.4) | |
| Glucose (mmol/L) | 6.22 ± 1.47 | 6.17 ± 1.82 | 0.915 | 5.05 ± 0.64 | 5.17 ± 0.53 | 0.176 |
| Urea (mmol/L) | 8.44 ± 3.38 | 5.73 ± 1.42 | 0.005 | 9.12 ± 3.19 | 5.9 ± 1.62 | <0.001 |
| Creatinine (µmol/L) | 133.2 (124.05–150.9) | 90.4 (78.7–103.55) | <0.001 | 141.05 (122.55–175.75) | 96.55 (81.37–110.97) | <0.001 |
| eGFR (ml/min) | 50 (42–54.5) | 82 (73–90) | <0.001 | 48 (42–56) | 76 (68–86.75) | <0.001 |
| Protein (g/L) | 70.02 ± 2.79 | 72.48 ± 4.34 | 0.031 | 72.7 ± 5.45 | 72.32 ± 4.68 | 0.607 |
| Albumin (g/L) | 39.88 ± 2.43 | 41.5 ± 3.19 | 0.057 | 41.09 ± 2.78 | 41.78 ± 3.1 | 0.135 |
| CRP (mg/L) | 1.74 (1.02–4.27) | 1.18 (0.69–2.31) | 0.12 | 1.02 (0.5–2.41) | 1.0 (0.4–1.79) | 0.234 |

(Continues)
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TABLE 3  Single univariate and multivariate linear regression of factors associated with serum adiponectin levels

| Characteristic            | NODAT group |                                        |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
|---------------------------|-------------|----------------------------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|
|                           |             | Single univariate linear               |                  |                  |                  | Multivariate linear |                  |                  |                  |                  |                  |                  |                  |                  |                  |
|                           |             | r                                      | p                | R                | Adjusted R²       | p ANOVA          | p                |                  |                  |                  |                  |                  |                  |                  |                  |
| Age                       | 0.168       | 0.141                                  | 0.607            | 0.203            | 0.013            | 0.828            |                  |                  |                  |                  |                  |                  |                  |                  |
| BMI                       | −0.307      | 0.006                                  |                  |                  |                  | 0.009            |                  |                  |                  |                  |                  |                  |                  |                  |
| Transplantation duration  | 0.059       | 0.605                                  | 0.989            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Urea                      | 0.277       | 0.014                                  | 0.462            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Creatinine                | 0.246       | 0.03                                   | 0.694            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| eGFR                      | −0.288      | 0.01                                   | 0.172            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Protein                   | −0.184      | 0.106                                  | 0.843            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Albumin                   | −0.235      | 0.039                                  | 0.183            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| CRP                       | −0.218      | 0.055                                  | 0.022            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Uric acid                 | 0.245       | 0.031                                  | 0.256            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Cholesterol               | −0.034      | 0.766                                  | 0.045            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Triglyceride              | −0.152      | 0.183                                  | 0.022            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| HDL-C                     | 0.104       | 0.367                                  | 0.083            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| LDL-C                     | −0.037      | 0.747                                  | 0.062            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Hemoglobin                | −0.034      | 0.765                                  | 0.933            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Leptin                    | 0.16        | 0.16                                   | 0.18             |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |

| Non-NODAT group           |             |                                        |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
|                           |             | Single univariate linear               |                  |                  |                  | Multivariate linear |                  |                  |                  |                  |                  |                  |                  |                  |                  |
|                           |             | r                                      | p                | R                | Adjusted R²       | p ANOVA          | p                |                  |                  |                  |                  |                  |                  |                  |                  |
| Age                       | −0.078      | 0.232                                  | 0.346            | 0.055            | 0.026            | 0.331            |                  |                  |                  |                  |                  |                  |                  |                  |
| BMI                       | −0.153      | 0.018                                  | 0.004            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Transplantation duration  | 0.161       | 0.013                                  | 0.078            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Urea                      | 0.157       | 0.016                                  | 0.482            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Creatinine                | 0.162       | 0.013                                  | 0.686            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| eGFR                      | −0.16       | 0.014                                  | 0.35             |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Protein                   | −0.016      | 0.811                                  | 0.608            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Albumin                   | −0.054      | 0.413                                  | 0.657            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| CRP                       | −0.123      | 0.06                                   | 0.136            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Uric acid                 | 0.105       | 0.109                                  | 0.529            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Cholesterol               | 0.028       | 0.667                                  | 0.27             |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Triglyceride              | 0.023       | 0.728                                  | 0.387            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| HDL-C                     | −0.015      | 0.819                                  | 0.52             |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| LDL-C                     | 0.01        | 0.88                                   | 0.379            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Hemoglobin                | −0.144      | 0.027                                  | 0.728            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Leptin                    | 0.024       | 0.719                                  | 0.176            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |

| All subjects              |             |                                        |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |
|                           |             | Single univariate linear               |                  |                  |                  | Multivariate linear |                  |                  |                  |                  |                  |                  |                  |                  |                  |
|                           |             | r                                      | p                | R                | Adjusted R²       | p ANOVA          | p                |                  |                  |                  |                  |                  |                  |                  |                  |
| Age                       | −0.055      | 0.331                                  | 0.45             | 0.159            | <0.001           | 0.345            |                  |                  |                  |                  |                  |                  |                  |                  |
| BMI                       | −0.25       | <0.001                                 |                  |                  |                  | <0.001           |                  |                  |                  |                  |                  |                  |                  |                  |
| Transplantation duration  | 0.128       | 0.024                                  | 0.171            |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |

(Continues)
Multivariate linear analysis demonstrated elevated leptin serum concentration in the NODAT group was significantly higher than in the non-NODAT group (Median level: 4.27 ng/ml versus 4.04 ng/ml), p = 0.024 (Table 2). Kagan et al.\textsuperscript{29} demonstrated elevated leptin serum concentrations in kidney transplant recipients. These authors suggested that increased leptin in post-renal transplant patients is related to leptin overproduction rather than the shortage of leptin degradation. Circulating leptin has a role in predicting patient outcomes after kidney transplantation: low concentrations predict loss of transplant kidney function and predict all-cause mortality.\textsuperscript{30} Elevated leptin levels are associated with insulin resistance and T2DM as well as NODAT development.\textsuperscript{31,32} There is evidence linking high leptin levels with the presence, severity, and/or prognosis of coronary heart disease, stroke, peripheral artery disease, carotid artery disease, and T2DM.\textsuperscript{33} The above-mentioned associations of leptin with the above conditions may be explained by the pathophysiological mechanisms affected by leptin that predispose to these diseases, including vascular inflammation, oxidative stress, endothelial dysfunction, cardiac remodeling, and insulin resistance.\textsuperscript{33}

Interestingly, we found a positive correlation between leptin concentration and BMI and LDL-C concentration in patients after kidney transplantation in both NODAT and non-NODAT groups, p < 0.05 (Table 4). The association between obesity, LDL-C, and leptin synthesis has also been mentioned previously.\textsuperscript{34,35} Houde et al.\textsuperscript{34} reported an association between LDL-C concentration and leptin DNA methylation level in obese men and women, suggesting that LDL-C might regulate their epigenetic profiles in adipose tissues.
4.2 | Association between serum adiponectin, leptin, and renal function

In post-renal transplant patients (both NODAT and non-NODAT), circulating adiponectin and leptin concentrations were related to renal function. The concentration of adiponectin and leptin in the RI patients was higher than in the group of the non-RI ones, \( p < 0.001 \) (Table 2). A negative correlation between adiponectin, leptin, and eGFR was detected in both NODAT and non-NODAT groups, \( p < 0.05 \) (Tables 3 and 4). Leptin and adiponectin are significantly positively associated with the severity of chronic kidney disease (CKD) measured by eGFR.36 Increased synthesis and

| Characteristic      | NODAT group Single univariate linear | Multivariate linear |
|---------------------|--------------------------------------|---------------------|
|                     | \( r \) | \( p \) | \( R \) | Adjusted \( R^2 \) | \( p \) ANOVA | \( p \) |
| Age                 | 0.04   | 0.731 | 0.688 | 0.336 | <0.001 | 0.539 |
| BMI                 | 0.336  | 0.003 | 0.005 | 0.65 | 0.001  |
| Transplantation duration | 0.103  | 0.37  | 0.402 |
| Urea                | 0.235  | 0.039 | 0.059 |
| Creatinine          | 0.258  | 0.022 | 0.665 |
| eGFR                | −0.312 | 0.005 | 0.216 |
| Protein             | −0.016 | 0.89  | 0.533 |
| Albumin             | −0.031 | 0.785 | 0.673 |
| CRP                 | −0.041 | 0.722 | 0.902 |
| Uric acid           | 0.23   | 0.043 | 0.306 |
| Cholesterol         | 0.186  | <0.001| <0.001|
| Triglyceride        | 0.054  | 0.64  | 0.467 |
| HDL-C               | 0.028  | 0.809 | 0.233 |
| LDL-C               | 0.246  | 0.03  | 0.165 |
| Hemoglobin          | −0.188 | 0.1   | 0.4   |
| Adiponectin         | 0.16   | 0.16  | 0.18  |

| Characteristic      | Non-NODAT group Single univariate linear | Multivariate linear |
|---------------------|------------------------------------------|---------------------|
|                     | \( r \) | \( p \) | \( R \) | Adjusted \( R^2 \) | \( p \) ANOVA | \( p \) |
| Age                 | 0.13   | 0.047 | 0.573 | 0.279 | <0.001 | 0.793 |
| BMI                 | 0.518  | <0.001| <0.001|      |        |
| Transplantation duration | 0.04   | 0.538 | 0.19  |
| Urea                | 0.198  | 0.002 | 0.557 |
| Creatinine          | 0.153  | 0.019 | 0.666 |
| eGFR                | −0.214 | 0.001 | 0.558 |
| Protein             | 0.057  | 0.384 | 0.398 |
| Albumin             | −0.063 | 0.338 | 0.166 |
| CRP                 | 0.006  | 0.926 | 0.084 |
| Uric acid           | 0.115  | 0.078 | 0.261 |
| Cholesterol         | 0.169  | 0.009 | 0.249 |
| Triglyceride        | 0.117  | 0.074 | 0.36  |
| HDL-C               | −0.068 | 0.302 | 0.547 |
| LDL-C               | 0.176  | 0.007 | 0.165 |
| Hemoglobin          | −0.076 | 0.249 | 0.755 |
| Adiponectin         | 0.024  | 0.719 | 0.176 |

(Continues)
decreased excretion are the two leading causes of increased circulating adiponectin and leptin levels in CKD patients with and without decreased GFR, as well as diabetic nephropathy. Despite a negative metabolic status, patients with end-stage renal disease have two to three times higher serum adiponectin levels than subjects with normal kidney function. Adamczak et al. pointed out that factors contributing to lower adiponectin secretion are oxidative stress and sympathetic nervous activity, common in chronic kidney disease. Adiponectin is considered a marker of kidney injury and risk of disease progression, and it was a multipotential protein with anti-inflammatory, metabolic, anti-atherogenic, and reactive oxygen species protective actions. Adiponectin presumably has a protective role in cardiovascular diseases’ pathogenesis, the leading cause of morbidity and mortality among kidney transplant recipients (KTRs). An inverse correlation between adiponectin, inflammation, and nutrition in KTRs was also announced. Serum leptin concentrations are elevated in CKD patients and correlate with C-reactive protein levels suggesting that inflammation is an essential factor that contributes to hyperleptinemia in CKD. Hyperleptinemia may be necessary for the pathogenesis of inflammation-associated cachexia in CKD. However, observational studies have not found an association between leptin and inflammation in KTRs, which is once again confirmed in our research results (Table 4).

Our study had a good performance point with a relatively large sample size of both KTRs with and without NODAT, but there are still limitations. Firstly, adiponectin and leptin levels were examined only at a single point in time. Secondly, the study has not been performed in the above adipokines of healthy control group, so multivariate analysis and the influence of factors such as age, sex, BMI, and eGFR on adipokines levels were not confirmed. Thirdly, the study has not evaluated the role of these adipokines in the prognosis of CVD events occurring in patients after kidney transplantation.

5 | CONCLUSION

Both NODAT and renal insufficiency were affected to the serum level of adiponectin and leptin, in which the concentration of adiponectin was lower, while leptin was higher in NODAT patients than in non-NODAT ones ($p < 0.001$ and $= 0.024$; separately). Both adiponectin and leptin concentrations increased in the patients with renal insufficiency compared with those without renal insufficiency in kidney transplant recipients, $p < 0.001$.

6 | SUMMARY POINTS

- The median adiponectin concentration was lower, while the median leptin concentration was higher in the NODAT group than in the non-NODAT group.

**TABLE 3 (Continued)**

| All subjects | Single univariate linear | Multivariate linear | Adjusted $R^2$ | $p$ ANOVA | $p$ |
|----------|-----------------------|-------------------|---------------|---------|------|
|          | $r$       | $p$     | $R$       |          |       |
| Age      | 0.128     | 0.024  | 0.548     | 0.262    | $<0.001$ | 0.664 |
| BMI      | 0.46      | $<0.001$ | 0.292     |          |       |
| Transplantation duration | 0.06     | 0.292  |          |          |       |
| Urea     | 0.184     | 0.001  |          |          |       |
| Creatinine | 0.162   | 0.004  |          |          |       |
| eGFR     | $-0.225$  | $<0.001$ |          |          |       |
| Protein  | 0.022     | 0.693  |          |          |       |
| Albumin  | $-0.061$  | 0.285  |          |          |       |
| CRP      | 0.003     | 0.951  |          |          |       |
| Uric acid| 0.119     | 0.035  |          |          |       |
| Cholesterol | 0.204   | $<0.001$ |          |          |       |
| Triglyceride | 0.115  | 0.042  |          |          |       |
| HDL-C    | $-0.009$  | 0.87   |          |          |       |
| LDL-C    | 0.218     | $<0.001$ |          |          |       |
| Hemoglobin | $-0.119$ | 0.036  |          |          |       |
| Adiponectin | 0.014   | 0.81   |          |          |       |

Abbreviations: BMI, body mass index; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NODAT, new-onset diabetes after transplantation.

Italic values are significant with $p < 0.05$. 

Both NODAT and renal insufficiency were affected to the serum level of adiponectin and leptin, in which the concentration of adiponectin was lower, while leptin was higher in NODAT patients than in non-NODAT ones ($p < 0.001$ and $= 0.024$; separately). Both adiponectin and leptin concentrations increased in the patients with renal insufficiency compared with those without renal insufficiency in kidney transplant recipients, $p < 0.001$.

6 | SUMMARY POINTS

- The median adiponectin concentration was lower, while the median leptin concentration was higher in the NODAT group than in the non-NODAT group.

5 | CONCLUSION

Both NODAT and renal insufficiency were affected to the serum level of adiponectin and leptin, in which the concentration of adiponectin was lower, while leptin was higher in NODAT patients than in non-NODAT ones ($p < 0.001$ and $= 0.024$; separately). Both adiponectin and leptin concentrations increased in the patients with renal insufficiency compared with those without renal insufficiency in kidney transplant recipients, $p < 0.001$. 

6 | SUMMARY POINTS

- The median adiponectin concentration was lower, while the median leptin concentration was higher in the NODAT group than in the non-NODAT group.
• Both adiponectin and leptin concentrations were higher in the patients with renal insufficiency than those without renal insufficiency.
• Both NODAT and renal insufficiency were related to the serum level of adiponectin and leptin.

CONFLICT OF INTEREST
The authors declare no conflict of interest, financial, or otherwise.

HUMAN AND ANIMAL RIGHTS
Animals did not participate in this research. All human research procedures followed the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2008.

CONSENTS FOR PUBLICATION
Informed consent was obtained from all participants.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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How to cite this article: Pham Vu T, Can Van M, Dang Thanh C, et al. Association of serum adiponectin and leptin levels with renal function in kidney transplant recipients with or without new-onset diabetes after transplantation. J Clin Lab Anal. 2021;35:e24000. https://doi.org/10.1002/jcla.24000