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**Original Research Article**

# Assessment of obesity and visceral fat in diabetic nephropathy patients

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## ABSTRACT

**Background:** Diabetic nephropathy is one of the most common diabetic microvascular complication that typically develops after 10 years of diabetes diagnosis. The primary aim of this study was to evaluate the prevalence of obesity and visceral fat in Type 2 Diabetes (T2D) cases with nephropathy and without-nephropathy complication.
**Methods:** In this cross-sectional study, diabetic nephropathy was diagnosed on the basis of biochemical tests of urine albumin, serum creatinine, eGFR, BP, and clinical assessment in patients with T2D. The prevalence of diabetic nephropathy estimated and the association between adiposity and diabetic nephropathy in patients T2D was evaluated. Measures of adiposity included body weight, Body Mass Index (BMI), Waist Circumference (WC), body fat percentage, muscle mass percentage and visceral fat percentage. Analysis of variance indicate difference in the various fat analysis parameters in presence and absence of nephropathy. PROC GLM procedure in the SAS Software was used for statistical calculations.
**Results:** A total of 247 patients with type 2 diabetes (mean age 53.46±11.62 years; 39.5% females) were enrolled in this study. The participants were grouped as with Diabetic Nephropathy (DN) 41.60% (N=99) and without Diabetic Nephropathy (NDN) 58.40% (N=139). The comparison of DN and Non-DN groups showed no significant difference in the BMI, body and visceral fat, muscle mass percentage.
**Conclusions:** Irrespective of the nephropathy status the body fat and visceral fat percentage is increased, and the muscle mass percentage is decreased in diabetes patients. As both obesity and diabetes contribute to the development and progression of renal disease, measures should to taken to reduce the body fat.

**Keywords:** Adiposity, Diabetes, Fat, Nephropathy, Obesity, Visceral

## INTRODUCTION

The epidemic of obesity (body mass index, BMI ≥30 kg/m$^2$) is equally evident in both developed and developing countries. It is posing a major health burden worldwide.[1,2] Growing evidence suggests that obesity is closely related to the augmented incidence of many chronic diseases, including T2D, hypertension, Cardiovascular Disease (CVD) and Chronic Kidney Disease (CKD). Again, the T2D, CVD and CKD are interdependent.[3,4] Obesity initiates a series of disorders including hypertension, diabetes, atherosclerosis, CVD and CKD. Moreover, obesity, T2D, hypertension and CVD are all risk factors for CKD and End-Stage Renal Disease (ESRD).[5,6,7] Presence of multiple risk factors increases the overall threat for development and progression of nephropathy. Obesity in itself is an independent the risk factor for nephropathy.[8,9]

Several cross-sectional studies have demonstrated a higher prevalence of CKD, defined by an eGFR<60 ml/min per

1.73 $m^2$, in presence of higher levels of Body Mass Index (BMI). Longitudinal studies too demonstrated higher levels of obesity associated with incident CKD and development of ESRD.[6,10,11] Even though increased BMI is frequently linked with development of CKD, it may not be the ideal measure of obesity. Some studies have showed that Waist-to-Hip Ratio (WHR) has etiological association to both cardiovascular events and progression of CKD than BMI of the subject.[6,11,12]

BMI is not an ideal marker of obesity in CKD, owing to regular presence of sarcopenia in CKD patients. These patients can have lower BMI either due to reduced visceral fat or reduced muscle mass. The latter is a marker of both malnutrition and inflammation. Similar results are reported in older adults whose WHR is more closely associated with all-cause mortality than BMI.[13] Waist Circumference (WC), but not BMI has been associated with Kidney Function (KF) decline.[14] It is hypothesized that WHR and WC may be better measures of risk of these chronic conditions as they reflect central obesity and visceral fat. Visceral fat is a main regulator of several adipokines and cytokines.[15] It has also been associated with insulin resistance, metabolic syndrome, and diabetes which further lead to development of CKD.[16,17] Intermuscular Adipose Tissue (IMAT) is associated with both muscle and mobility dysfunction in elderly persons. It is also involved in metabolic dysfunction such as insulin resistance.

Diabetic Nephropathy (DN) in T2D is the leading contributor of CKD worldwide. It accounts for almost one out of every two patients of ESRD in the United States.[18] Current treatment strategies to slow the development of DN are not satisfactory.[18] Considerable economic burden and side effects often limit their use.[19,20]

Generally, obesity precedes and is strongly associated with diabetes which in turn is responsible for nephropathy. Weight reduction may reduce albuminuria, a major clinical disease indicator. Moderation of obesity impart significant beneficial effects on DN, though in more advanced cases the evidence of effect is inadequate.[21] Therefore, it is necessary to take measure to prevent obesity and encourage weight loss to combat T2D and nephropathy.[22]

However, the exact mechanisms by which obesity independently, or in combination with T2D and hypertension leads to nephropathy are not clear. Here, author investigated body fat distribution, i.e. visceral fat in nephropathy and non-nephropathy patients with type 2 diabetes. The study also measures various parameters of obesity and compare them in diabetic patients with and without Diabetic Nephropathy (DN).

## METHODS

This was a hospital-based prospective, cross-sectional study at Dr. Chandra's Diabetes and Heart Clinic, Gomatinagar, Lucknow, India. Patients with following inclusion criteria were enrolled in the study: both males and females, aged 20 years and above, clinically diagnosed with DM-2 and willing to participate voluntarily. Patients undergoing dialysis, renal transplantation, and having other serious complications were excluded from the study. As per the Helsinki declaration written informed consent was obtained from all participants prior to inclusion in the study.[23] The participants were completely explained about the risk and benefits associated with the study. They were also informed about their rights to refuse participation and to withdraw their participation during the course of study.

A patient case record form was designed for recording the study parameter. Data were collected from patient's clinical and biochemical records, anthropometric measurements, clinical examination, case record form and checklist. In order to determine the risk factors, thorough medical history was obtained and recorded in case record form. Body Mass Index (BMI) was calculated by using the formula of weight (Kg)/height ($m^2$). High BMI was defined as 25 or more and less than 30. Poor diabetic control was defined as HbA1c level of >8%.

During detailed clinical examination, measurements and investigations were performed. DN was diagnosed on the basis of biochemical tests of urine albumin, serum creatinine, eGFR, and BP. The data on socio-demographic indicators (age, sex, occupation, smoking, alcohol, tobacco intake, and education), systolic and diastolic BP, weight, height, and Body Mass Index (BMI) were obtained. HbA1c, serum creatinine, and urinary albumin were recorded. The duration of diabetes, hypertension and DN, patient's medication history and co-morbidities were obtained from clinical records. Blood pressure was recorded two times in the sitting position at an interval to 10 min to the nearest 2 mm Hg, with the help of mercury sphygmomanometer. Blood pressure was also measured in supine position after a rest of 15 minutes in clinic in comfortable ambient temperature. The average of the two readings was taken. Hypertension was defined as systolic pressure ≥140 mmHg or diastolic pressure ≥90 mmHg or patients on anti-hypertensive medication.[24] Patients were weighed in light clothes, without shoes, and height was recorded using a clinical height scale.

HbA1c was measured by High Performance Liquid Chromatography (HPLC) method. Fasting Glucose was measured in plasma Hexokinase Spectrophotometry method. Serum creatinine and urine creatinine was measured by Spectrophotometry and Jaffe-Kinetic method whereas, total cholesterol by spectrophotometry and CHOD-POD method. Triglyceride was measured by Spectrophotometry, GPO-POD method and HDL was measured by Spectrophotometry, direct enzymatic method. LDL and non-HDL were calculated. Urine microalbumin was measured by immunoturbidimetry method. Routine urine examination included Dipstrix method and microscopic examination of centrifuged urinary sediment.

Body weight, body fat and BMI were measured using Omeron HBF 212 machine. Vibration sensation was

measured by Biothesiometer; Kodys Biothezi-VPT. Patients with DN were enrolled in the study. DN was defined as patients having albuminuria (urinary albumin to creatinine ratio ≥30 mg/g) and an eventual decline in the estimated glomerular filtration rate (Egfr <60 ml/min/1.73 $m^2$).[25]

***Statistical analysis***

Statistical analysis was carried out using SPSS software. Data are presented as Mean±SD or geometric mean with 95 % Confidence Interval (CI) as appropriate according to data distribution. Differences among the two cohort groups were tested with a one-way ANOVA (continuous variables) or Chi square test (categorical variables) followed by Tukey-Kramer methods for the post hoc analyses. Linear regression analysis with a stepwise procedure was used to assess the cross-sectional association of each manifestation of abdominal (VFA) and subcutaneous (SFA) fat accumulation with carotid atherosclerosis. Analysis of variance has been conducted to know the association of visceral fat and body fat with that of clinical factors using PROC GLM in SAS software. The analysis states that if P-value is less than 0.05 (p-value >0.05), then the parameter has a significant effect in the outcome of the primary analysis variable.

## RESULTS

A total of 247 patients with type 2 diabetes (mean age 53.46±11.62 years; 39.5% females) were enrolled in this study. The participants were classified as those with Diabetic Nephropathy (DN) 41.60% (N=99) and No Diabetic Nephropathy (NDN) 58.40% (N=139). The mean duration of diabetes in DN and NDN groups were 8.273±6.282 and 7.496±5.821 years respectively. The clinical characteristic of the two groups are summarized in (Table 1).

**Table 1: Clinical characteristic of patients with diabetic nephropathy and no diabetic nephropathy**

| Parameters | Nephropathy | Non-Nephropathy | p value for trend |
|---|---|---|---|
| N | 99(41.60%) | 139(58.40%) | - |
| Age (years) | 53.465±11.623 | 54.230±9.759 | 0.9008 |
| Body weight | 70.907±15.54) | 72.491±12.550 | 0.3881 |
| Height (cm) | 160.092±9.762 | 161.178±9.430 | 0.0115 |
| BMI (kg/$m^2$) | 27.716(5.739) | 27.987(4.453) | 0.6837 |
| Waist Circumference | 101.949±12.827 | 102.052±9.860 | 0.2017 |
| Hip Circumference | 104.337±13.889 | 103.859±9.907 | 0.1729 |
| Duration of diabetes (years) | 8.273±6.282 | 7.496±5.821 | 0.4177 |
| Pulse (/min) | 94.235±14.211 | 92.911±11.875 | 0.3525 |
| Systolic blood pressure (mmHg) | 147.612±20.496 | 137.185±17.832 | 0.0004 |
| Diastolic blood pressure (mmHg) | 84.020±8.760 | 83.259±14.942 | 0.0404 |
| Random blood sugar (RBS) | 292.052±230.065 | 213.311±84.755 | 0.6610 |

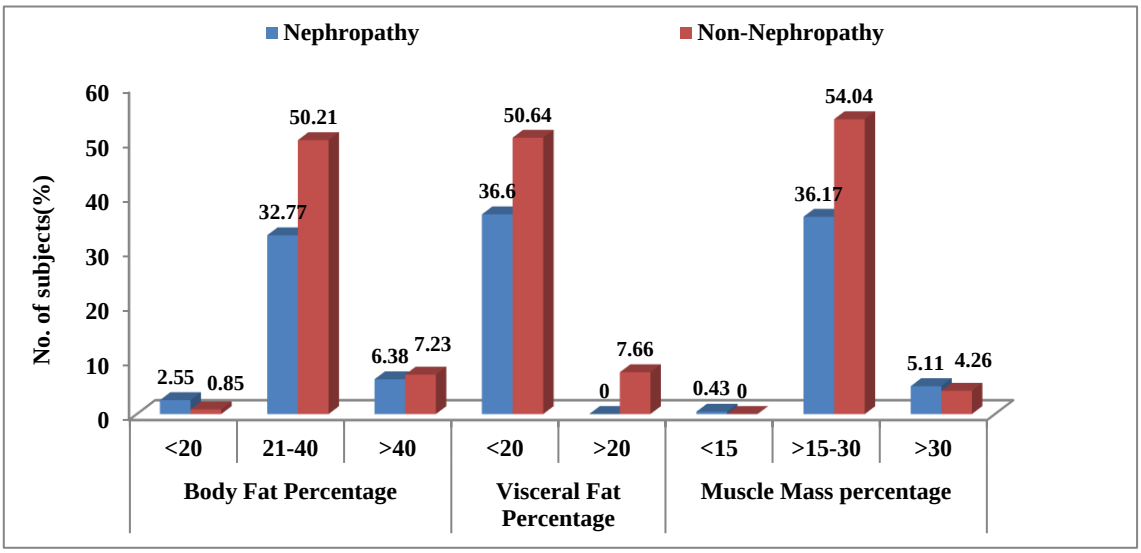


**Figure 1: The frequency distribution of body fat, visceral fat and muscle mass percentage.**

The Systolic blood pressure in the DN group was 147.612±20.496 mmHg and in NDN 137.185±17.832, which was significantly different (p=0.0004). There was also significant differed in the diastolic blood pressure

(mm Hg) between the DN group (84.020±8.760 mm Hg) and NDN group (83.259±14.94) (p=0.0404).

Normal BMI was found in 25(10.59%) patients in DN group and 38(16.10%) in the non-DN group. High BMI was found in 69(29.24%) patients in DN group and 99(41.95%) patients in the non-DN group whereas low BMI was found in 5(2.12%) patients in DN group. There were no patients with low BMI in the non-DN group. Maximum number of patients had weight in the range of 50 to 100 kg that is DN group 89(37.71%) patients and non-DN group 133(56.36%) patients. The frequency distribution of body fat, visceral fat and muscle mass percentage is shown in (Figure 1).

High percentages of body as well as visceral fat were observed in both DN and Non-DN groups. In both DN and Non-DN cohorts, the muscle mass percentage was low in majority of the patients. Analysis of variance did not show any association of visceral fat and body fat with various clinical factors such as habit, signs and symptoms or diabetic complications (Table 2). Comparison of fat and muscle mass analysis parameters between nephropathy and non-nephropathy patients with type 2 diabetes is summarized in (Table 3).

**Table 2: Association of visceral fat with various clinical factors such as habit, signs and symptoms or diabetic complications.**

| | Source | p-value |
|---|---|---|
| Habits | Alcohol | 0.5978 |
| | Smoking | 0.9717 |
| | Tobacco | 0.0748 |
| Signs and Symptom | Excessive urination | 0.1550 |
| | Excessive appetite | 0.6677 |
| | Excessive thirst | 0.2660 |
| | Weight Loss | 0.0003 |
| | Tingling numbness LL | 0.7367 |
| | Swelling in feet | 0.0039 |
| | Shortness of breath | 0.9009 |
| Microvascular Complications | Retinopathy | 0.4633 |
| | Neuropathy | 0.5498 |
| | Nephropathy | 0.7942 |
| Macrovascular complication | CAD | 0.5521 |
| | CVD | 0.7116 |
| | Stroke | 0.9713 |
| | Foot deformity | 0.4640 |
| | Loss of protective sensation | 0.0606 |

**Table 3: Comparison of fat and muscle mass analysis parameters between nephropathy and non-nephropathy patients with type 2 diabetes.**

| Parameter | Nephropathy (N= 99) | Non-Nephropathy (N= 137) | 95% CI | p value* |
|---|---|---|---|---|
| Body Fat percentage | 33.221(7.073) | 34.472(5.735) | -2.899 to 0.398 | 0.1364 |
| Muscle Mass percentage | 25.516(4.306) | 25.147(3.194) | -0.594 to 1.333 | 0.4507 |
| Visceral Fat Percentage | 13.010(7.411) | 13.112(6.860) | -1.951 to 1.747 | 0.9134 |

Data are expressed as Mean±SD, geometric mean (95% CI) or percentage

## DISCUSSION

The exact mechanisms of development and progression of DN are still being investigated. DN develops secondary to prolonged hyperglycemia and hyperinsulinemia/insulin resistance. Production of advanced glycation end products lead to intraglomerular and systemic hypertension, intrarenal oxidative stress and inflammation. The possible contributory factors related to obesity are fatty infiltration and altered adipokine production.[4,26,27]

Obesity paves the way to T2D and is closely associated to T2D in the most cases. The idea of managing DN by weight reduction is an intriguing and attractive option, as it develops after prolonged exposure to the diabetic milieu.

Anti-diabetic treatment target one of several putative downstream pathophysiologic pathways involved in the development of DN. Weight reduction helps in decreasing obesity, the starting and provocative factor the root cause of all the pathways.[28] Recent epidemiologic data suggest that obesity is an independent risk factor for CKD.[10]

Diabetic patients are vulnerable to accelerated aging process and affected by early loss of muscle mass and strength. In this study the muscle mass percentage was similar in diabetes and diabetic nephropathy group. Similarly, in study by Celiker et al, frequency of sarcopenia was similar in diabetes and diabetic nephropathy group.[29]

In this study the BMI was low in relatively higher number of patients with diabetic nephropathy patients as compared to non-nephropathy. The causative role of either reduced visceral fat or reduced muscle mass is supported by of this finding.[30] This study has lower visceral fat percentage or muscle mass percentage in the DN patients. Visceral fat accretion might be a risk factor responsible for deterioration of renal function in non-obese CKD patients, but such effect is not observed among obese CKD patients. There could be an association between visceral fat

accretion and obesity in kidney function decline among CKD patients.

In the Framingham Heart Study, it was found that obesity is associated with increased risk of developing stage 3 CKD, which was no longer significant after adjustment for known CVD risk factors. The relationship between obesity and stage 3 CKD may be mediated through CVD risk factors.[5]

The study finding demonstrated no association between any measure of fat and diabetic nephropathy. Similarly, Madero et al, did not find any association between measure of obesity and kidney outcomes when creatinine values at years 3 and 10 were used to estimate changes in eGFR.[31]

It was observed that visceral adiposity is a risk factor for nephropathy only in patients without baseline CKD. But in case of obese CKD patients, obesity is no longer a risk factor for CKD progression.[31-33] These observations may be the result of the presence of other dominant challenging risk factors for CKD progression such as hypertension, T2M, and proteinuria.

There are a few limitations in this study. First, it is difficult to assess causality since it is cross-sectional design. Second, the study cohort was small and did not include a control group. Third, author evaluated visceral fat percentage and body fat percentage therefore, fat accumulation in other locations of fat depots such as thighs and legs were not evaluated. Finally, as the study was hospital-based, study population was culturally and socially homogeneous; therefore, generalization of this results might have limitations.

## CONCLUSION

It can be concluded irrespective of the nephropathy status the body fat and visceral fat percentage is increased and the muscle mass percentage is decreased in diabetes patients. As both obesity and diabetes contribute to the development and progression of renal disease measures should to taken to reduce the body fat.

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