Original Article

DOI: 10.7860/JCDR/2022/57489.17158

# Serum Adiponectin as a Diagnostic Marker of Nephropathy among Patients with Type 2 Diabetes Mellitus: A Cross-sectional Study

Biochemistry Section

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## ABSTRACT

**Introduction:** Diabetic Nephropathy (DN) is the leading cause of End-Stage Renal Disease (ESRD) among Type 2 Diabetes Mellitus (T2DM) patients and it is diagnosed by laboratory investigation like albuminuria. Albuminuria is a conventional and not a sensitive, specific marker for diagnosis of nephropathy. Additionally some of the patients shows advanced renal pathological changes without albuminuria and some of the patients with microalbuminuria revert back to normoalbuminuria. However, there is need for early detection, sensitive and specific marker for nephropathy. Serum adiponectin is an adipocytokine synthesised from adipose tissue, liver, kidney, heart, salivary glands. This has physiological properties like antidiabetic, antioxidative and anti-inflammatory properties beneficial for particularly in patient with T2DM. Adiponectin activates Adenosine Mono Phosphate (AMP) Kinase and Nicotinamide Adenine Dinucleotide Phosphate (NADPH) pathways results in improved insulin sensitivity and prevent albumin excretion in urine. Increased adiponectin levels are beneficial to patients with T2DM and its complications.

**Aim:** To determine serum adiponectin levels for the prediction of early onset of nephropathy in patients with T2DM.

**Materials and Methods:** This cross-sectional study was conducted from March 2018 to May 2019 at the Department of Biochemistry and Endocrine at the Basaveshwara Medical University Hospital and Research Centre in Karnataka, India, with a total of 120 subjects. Out of the 120 subjects, 80 were T2DM subjects and 40 were age, gender and Body Mass Index (BMI) matched controls (group 1). Eighty T2DM subjects were further categorised into two groups based on urinary Albumin-to-Creatinine Ratio (ACR) levels, such as 40 T2DM with normoalbuminuria [(Group 2), Urine ACR: <30 mg/g], and 40 T2DM with microalbuminuria, [(Group 3) urinary ACR: 30-299 mg/g]. Comparisons were made between groups based on socio-demographic and clinical parameters. Pearson's correlation was used to test the relationship between estimated Glomerular Filtration Rates (eGFR), Glycated Haemoglobin (HbA1c), urine ACR, and serum adiponectin. The Receiver Operating Characteristic (ROC) curve was used to test the sensitivity and specificity of a marker for nephropathy. The Statistical Package for the Social Sciences (SPSS) version 20.0 and Medcalc Software were used to analyse data.

**Results:** The mean values of serum adiponectin were significantly higher in patients with T2DM 11.92±3.86 mg/dL when compared to controls 3.84±1.98 mg/dL. The serum adiponectin had a significantly very high positive correlation with HbA1c, urinary ACR r=0.726, 0.642, p-value=0.0001 and also a significantly very high negative correlation with estimated glomerular filtration rate, r=-0.399, p-value=0.0001 was observed. In ROC analysis serum adiponectin was found to be proportionately elevated in T2DM with normoalbuminuria and it was statistically significant, with a sensitivity of 92.5% and specificity of 87.50, p-value=0.0001. The urinary ACR also has shown significance with low sensitivity of 62.5% and specificity of 80%, p-value=0.0250.

**Conclusion:** The serum adiponectin might be a sensitive and specific marker to predict the early onset of nephropathy in T2DM patients and therefore can be used as a diagnostic marker for DN. These concentrations were positively correlated with urinary ACR and negatively correlated with eGFR.

**Keywords:** Albumin creatinine ratio, Diabetic nephropathy, Estimated glomerular filtration rate, Glycated haemoglobin

## INTRODUCTION

The T2DM is a chronic metabolic disease characterised by hyperglycaemia due to both deficiency of insulin from the pancreatic beta cells and inactivation of insulin [1]. The prevalence of T2DM was 415 million people worldwide by 2015 and is expected to raise upto 650 million people by 2030. In India, 65 million people were affected in 2013 and are expected to raise to 103 million by 2030 [2,3]. The DN is considered a major healthcare issue and is listed first cause of kidney damage across the world, which is the common clinical manifestation, characterised by persistent albuminuria, reduced eGFR, and increased cardiovascular morbidity and mortality due to damage to the kidney caused by chronic hyperglycaemia and hypertension [4].

Chronic hyperglycaemia in the blood and the skeletal muscles leads to the production of Advanced Glycation End Products (AGEs) by the glycosylation of amino acids, these compounds will trigger the generation of hormones, free radicals, and infiltration of inflammatory cytokines resulting in vascular damage of podocytes, glomerulus, and tubules of the kidney [5]. Along with that excess mobilisation of lipids and proteins leads to increased generation of reactive oxygen species and decreased antioxidants accelerate renal impairment in patients with T2DM [6,7]. Albuminuria was considered a gold standard declining marker kidney function in patients with T2DM. Albuminuria is the mainspring for early detection of renal impairment, some of the patients showed kidney dysfunction without excretion of protein. Despite being a conventional marker, even though albuminuria is detected, it could be too late to prevent developing nephropathy. It is also elevated in other pathological conditions such as hypertension, urinary tract infections, cardiovascular diseases, and other types of kidney disorders [8]. Hence there is a need for other markers which may be sensitive, specific, and early predictable markers for the diagnosis of nephropathy in patients with T2DM.

Adiponectin is considered a protein that has 244 amino acids produced majorly from white adipose tissue, as well as the kidney, liver, bones, skeletal muscles, salivary glands, and other organs

[9,10]. Its three receptors, ADIPO R1, ADIPO R2, and T-cadherin, are highly active in organs like liver, kidney, and skeletal muscles, and their physiological properties like antidiabetic, antioxidative, and anti-inflammatory which are beneficial to patients with T2DM [11-13]. It acts as an antidiabetic through its ADIPO R1 receptor, by activation of AMP kinase is a transmembrane protein in the tissues that results in insulin sensitivity, glucose uptake, and fatty acid activation [14]. The ADIPO R2 triggers the hypothalamus and enhances food intake, whereas the AMP kinases activated by high molecular weight protein results in glucose uptake in the tissues and lipolysis [15]. Albuminuria is prevented by adiponectin's renoprotective activities, which are mediated through AMP kinase and NADPH activation [16]. In T2DM patients, fluctuating levels of serum adiponectin cause various metabolic disorders, especially nephropathy. For this reason, the measurement of serum adiponectin is more sensitive and specific than albuminuria for the assessment of nephropathy. Thus, the present study aimed to evaluate serum adiponectin as an early diagnostic marker of nephropathy and to determine the correlation between eGFR, urinary ACR, and serum adiponectin in T2DM patients.

## MATERIALS AND METHODS

This cross-sectional study was conducted from March 2018 to May 2019 at the Department of Biochemistry and Endocrinology at the Basaveshwara Medical College Hospital and Research Centre in Karnataka, India, with a total of 120 subjects. After obtaining the approval by Basaveshwara Medical College Hospital and Research Centre, Institutional Ethics Committee (IEC) with reference number (BMC&H/IEC/2018-2019/07) the study was conducted.

**Sample size calculation:** The sample size was determined based on the mean and standard deviation of adiponectin levels, with 80% power and a 95% of confidence interval. Out of the 120 subjects, 80 were T2DM subjects and 40 were healthy controls (group 1). Eighty T2DM subjects were further categorised into two groups based on urinary ACR levels, such as 40 T2DM with normoalbuminuria [(group 2), Urine ACR: <30 mg/g], and 40 T2DM with microalbuminuria, [(group 3) urinary ACR: 30-299 mg/g].

**Inclusion criteria:** All of the subjects were between 30-70 years old. This study includes patients who were diagnosed with T2DM according to the American Diabetes Association (ADA) criteria and the Kidney Disease Improving Global Outcomes (KDIGO) criteria [17,18].

**Exclusion criteria:** Patients with smoking, alcoholism, type 1 diabetes mellitus, arterial hypertension, liver disease, thyroid disease, cardiovascular disease, cerebrovascular disease, and peripheral vascular lesions, as well as persons with T2DM treated with thiazolidine, and anti-inflammatory drugs, were excluded from the study.

### Study Procedure

Blood samples were collected after an overnight fast and 3 mL of postprandial venous blood samples were collected under strict aseptic precautions. A 3 mL of blood was transferred to a sodium fluoride vacutainer for estimation of Fasting Blood Glucose (FBS), Post Prandial Blood Glucose (PPBS), and 3 mL to Ethylene Diamine Tetraacetic Acid (EDTA) vacuole for HbA1c estimation. The remaining 4 mL was transferred for serum urea, creatinine, and adiponectin. Ordinary red capped vacuum blood collection tubes for measurement. In addition to blood samples, on-site urine samples were collected for urine ACR analysis. The FBS, PPBS and HbA1c were estimated using the Glucose Oxidase and Peroxidase (GOD POD) method on the Erba 200, Transasia automated analyser, and serum urea and creatinine were estimated using the glutamate dehydrogenase method on the Erba 200, Transasia automated analyser was analysed using modified Jaffe's kinetic method [19]. HbA1c is fully automated and measured by latex immunoturbidimetry [20]. The eGFR were calculated using the Epidemiological Collaboration for Chronic Kidney Disease (CKD-EPI) formula, and for measurement of urine, ACR was calculated by urinary protein/urinary creatinine×1000 formula (urinary protein measured by immunoturbidometric method and urinary creatinine by Modified Jaffe's rate kinetic method) [21,22]. Serum adiponectin was analysed using an enzyme linked immunosorbent assay (Euro immune Analyser I-2p ELISA Kit obtained from Genxbio health sciences Pvt. Ltd. Noida, India).

## STATISTICAL ANALYSIS

The SPSS version 20.0 and Medcalc Software were used to analyse the data. Descriptive statistical measures were employed to summarise the data. Normal distribution by the Kolmogorov-Smirnov test and the data were presented as the mean±standard deviation, data comparison was performed by a one way Analysis of Variance (ANOVA) followed by a Tukey posthoc test to analyse the statistical significance difference between the groups. A Pearson correlation analysis was performed between serum adiponectin and HbA1c, urinary ACR and eGFR. The ROC curves were constructed to investigate the diagnostic accuracy of identifying markers of diabetic nephropathy in T2DM patients with normoalbuminuria compared to controls. The statistical significance was defined as $p<0.05$.

## RESULTS

In this current study, 120 people were included, of whom 40 subjects T2DM with normoalbuminuria (group 2) and 40 subjects T2DM with microalbuminuria (group 3), respectively. The controls were involved in group 1. The comparison of mean±SD of the anthropometric, biochemical, urinary ACR and serum adiponectin data were analysed among T2DM patients and controls. The FBS, PPBS, creatinine, serum urea, HbA1c, urinary ACR, and serum adiponectin had a statistically significant difference between cases and controls with p-value=0.0001. Patients with T2DM showed no statistically significant difference of height, weight and eGFR when compared to controls p-value=0.433, 0.295 and 0.096. The other two parameters of age and BMI were statistically significant, with p-value=0.003 and p-value=0.01, respectively [Table/Fig-1].

| Parameters | Healthy controls (n=40) | T2DM patients (n=80) | p-value |
|---|---|---|---|
| Age (years) | 48.80±12.89 | 49.68±7.88 | 0.003* |
| Height (feet) | 3.60±0.61 | 3.41±0.53 | 0.433† |
| Weight (kg) | 73.20±11.65 | 83.11±13.68 | 0.295† |
| BMI (kg/m$^2$) | 20.55±2.66 | 24.65±4.59 | 0.01* |
| FBS (mg/dL) | 97.22±8.86 | 148.93±36.47 | 0.0001** |
| PPBS (mg/dL) | 119.72±21.20 | 223.43±85.76 | 0.0001** |
| Serum urea (mg/dL) | 24.60±9.73 | 46.70±24.47 | 0.0001** |
| Serum creatinine (mg/dL) | 1.13±0.22 | 3.66±2.78 | 0.0001** |
| HbA1c (%) | 4.34±0.72 | 7.12±1.99 | 0.0001** |
| eGFR (mL/min) | 111.89±36.20 | 79.98±27.37 | 0.096† |
| Urinary ACR (mg/g) | 3.41±2.64 | 78.80±27.43 | 0.0001** |
| Serum adiponectin (mg/L) | 3.84±1.98 | 11.92±3.86 | 0.0001** |

**[Table/Fig-1]:** Comparison of means of the anthropometric, biochemical, urinary ACR and serum adiponectin data among T2DM patients and controls.
**Highly significant at the 0.05 probability level; *significant; †NS- Not significant at the 0.05 probability level. BMI: Body mass index; FBS: Fasting blood sugar; PPBS: Post prandial blood sugar; HbA1c: Glycosylated haemoglobin; Urinary ACR: Urinary albumin creatinine ratio; eGFR: Estimated glomerular filtration rate

The comparison of the anthropometric, routine biochemical parameters, urinary ACR, and serum adiponectin biomarkers

in the different study groups were analysed using ANOVA. There was a significantly very high levels of FBS, PPBS, urinary ACR and serum adiponectin, respectively p-value=0.0001 and there were no significant difference of serum urea, creatinine and HbA1c were observed in group 2 when compared to group 1. In group 3 subjects showed a highly significant increased levels of PPBS, urea, creatinine, HbA1c, urinary ACR and serum adiponectin p=0.0001** and reduced levels of e GFR were observed when compared with group 1 and group 2, p-value=0.0001 [Table/Fig-2,3].

The Pearson's correlation between HbA1c, eGFR, and urinary ACR with serum adiponectin among study group is shown in [Table/Fig-4].

| Parameters | Group 1 (n=40) | Group 2 (n=40) | Group 3 (n=40) | p-value |
|---|---|---|---|---|
| Age (years) | 48.80±12.89 | 46.10±6.16 | 53.28±7.84 | 0.004* |
| Height (feet) | 3.60±0.61 | 3.40±0.52 | 3.43±0.54 | 0.242† |
| Weight (kg) | 73.20±11.65 | 77.18±13.49 | 89.05±11.17 | 0.0001** |
| BMI (kg/m$^2$) | 20.55±2.66 | 22.75±2.76 | 26.56±5.26 | 0.0001** |
| FBS (mg/dL) | 97.22±8.86 | 147.58±42.66 | 150.30±29.51 | 0.0001** |
| PPBS (mg/dL) | 119.72±21.20 | 157±27.09 | 289.18±72.82 | 0.0001** |
| Serum urea (mg/dL) | 24.60±9.73 | 26.70±9.10 | 66.70±17.61 | 0.0001** |
| Serum creatinine (mg/dL) | 1.13±0.22 | 1.10±0.30 | 6.23±1.46 | 0.0001** |
| HbA1c (%) | 4.34±0.72 | 6.71±0.81 | 7.90±1.13 | 0.0001** |
| eGFR (mL/min) | 111.89±36.20 | 88.63±23.00 | 71.35±28.91 | 0.0001** |
| Urinary ACR (mg/g) | 3.41±2.64 | 10.27±8.95 | 147.60±75.49 | 0.0001** |
| Serum adiponectin (mg/L) | 3.84±1.98 | 9.22±3.29 | 14.62±2.12 | 0.0001** |

**[Table/Fig-2]:** Comparison of the anthropometric, routine biochemical parameters and urinary ACR and serum adiponectin biomarkers across the study groups by ANOVA.
Group 1; controls, Group 2; T2DM patients with normoalbuminuria, Group 3; T2DM with microalbuminuria, *Significant at the 0.05 probability level, **Highly significant, †NS- Not significant at the 0.05 probability level

| Parameters | Group 1 vs Group 2 | Group 1 vs Group 3 | Group 2 vs Group 3 |
|---|---|---|---|
| FBS (mg/dL) | 0.0001** | 0.0001** | 0.983† |
| PPBS (mg/dL) | 0.0001** | 0.0001** | 0.0001** |
| Serum urea (mg/dL) | 0.688† | 0.0001** | 0.0001** |
| Serum Creatinine (mg/dL) | 0.920† | 0.0001** | 0.0001** |
| HbA1c (%) | 0.556† | 0.0001** | 0.0001** |
| eGFR (mL/min) | 0.003* | 0.0001** | 0.012* |
| Urinary ACR (mg/g) | 0.0001** | 0.0001** | 0.0001** |
| Serum adiponectin (mg/L) | 0.0001** | 0.0001** | 0.0001** |

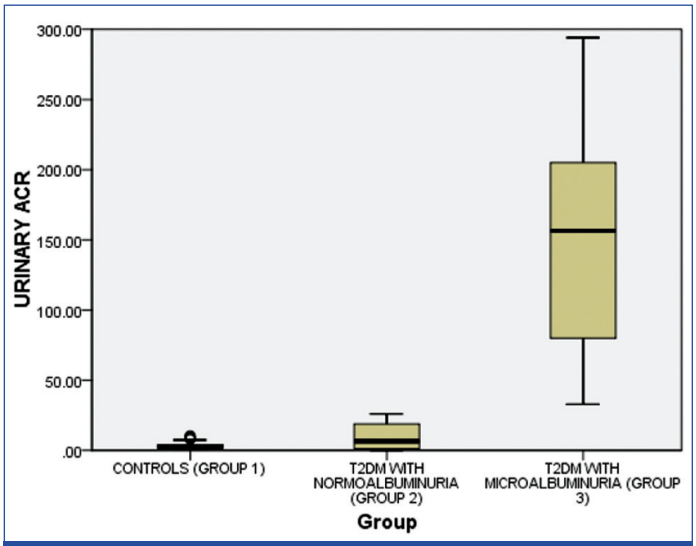
**[Table/Fig-3]:** Comparison of biochemical, clinical and serum adiponectin among the study subjects by posthoc analysis.
Group 1: controls, Group 2: T2DM with normoalbuminuria, Group 3: T2DM with microalbuminuria. *Significant at the 0.05 probability level, **Highly significant, †NS- Not significant at the 0.05 probability level

| Parameters | Values | HbA1c | Urinary ACR | eGFR |
|---|---|---|---|---|
| Serum adiponectin | r value | 0.726 | 0.642 | -0.399 |
| | p-value | 0.0001** | 0.0001** | 0.0001** |

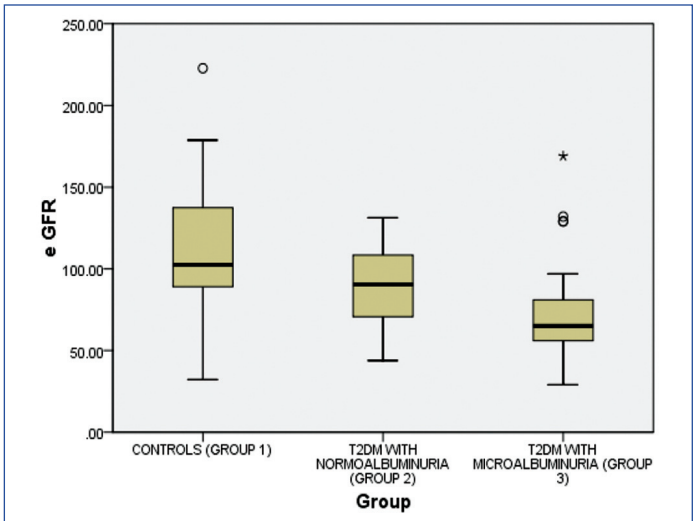
**[Table/Fig-4]:** Correlation between serum adiponectin and HbA1c, eGFR, urinary ACR.
Pearson correlation test **significant at the level of 0.05, r: rho factor

The distribution of urinary ACR levels in all three groups of study subjects is graphically represented. There were significantly elevated levels in group 3 subjects when compared to group 1 and group 3 [Table/Fig-5]. In the graphical representation of eGFR levels in different groups of study subjects, statistically decreased levels were observed in T2DM patients with microalbuminuria when compared with T2DM with normoalbuminuria and healthy controls [Table/Fig-6].

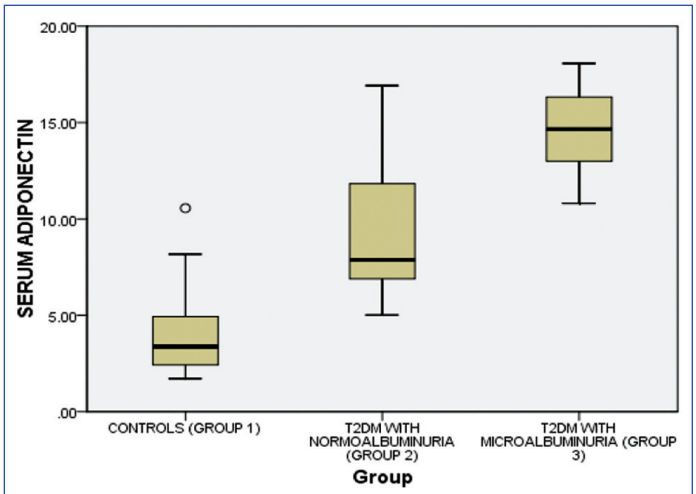
The serum adiponectin was significantly elevated in T2DM with normoalbuminuria and microalbuminuria when compared to healthy individuals; the data distribution was represented graphically [Table/Fig-7].




**[Table/Fig-5]:** Distribution of urinary ACR levels among the study subjects.




**[Table/Fig-6]:** Comparison of estimated glomerular filtration rate levels in three groups of study subjects.

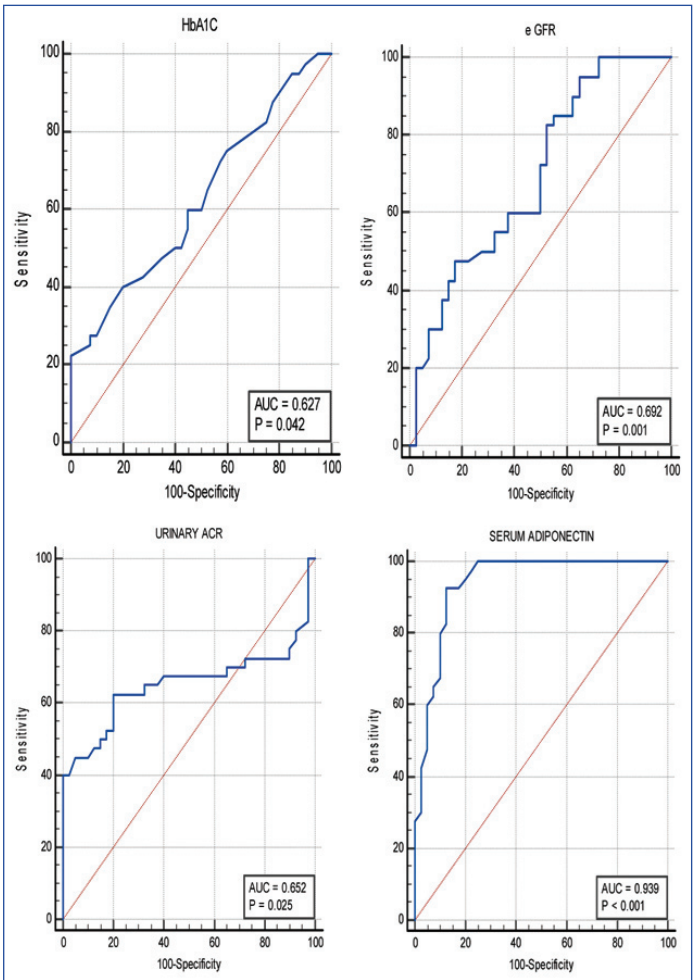



**[Table/Fig-7]:** Comparison of serum adiponectin concentrations in two groups of T2DM patients and healthy individuals.

There was no significant area under the curve with sensitivity ranging from 62.50-22.50 and specificity ranging from 100-80.00 for HbA1c and urinary ACR with p-value <0.0420 and p=0.0250, respectively. The eGFR and serum adiponectin showed a statistically significant area under the curve with sensitivity ranging from 85.00-92.50 and specificity from 45.00-87.50 and p-value <0.001 and p-value <0.0001, respectively [Table/Fig-8,9].

| Parameters | AUC | 95% CI for AUC | Sensitivity (%) 95%CI | Specificity (%) 95%CI | p-value |
|---|---|---|---|---|---|
| HbA1c (%) | 0.627 | 0.512-0.733 | 22.50 | 100 | 0.042 |
| eGFR (mL/min) | 0.692 | 0.579-0.791 | 85.00 | 45.00 | <0.001* |
| Urinary ACR (mg/g) | 0.652 | 0.537-0.755 | 62.50 | 80.00 | 0.025 |
| Serum adiponectin (mg/L) | 0.939 | 0.862-0.980 | 92.50 | 87.50 | <0.0001** |

**[Table/Fig-8]:** Receiver Operating Curves (ROC) curve analysis of Serum Adiponectin, urinary ACR and e GFR.
ROC curve analysis was done in T2DM patients with normoalbuminuria and controls, **highly significant, †Not Significant, AUC: Area under the curve; CI: Confidence interval




**[Table/Fig-9]:** ROC curves of HbA1c, eGFR, urinary ACR and serum adiponectin in type 2 diabetes mellitus patients with normoalbuminuria and healthy individuals.

## DISCUSSION

The T2DM patients were more likely to develop kidney diseases characterised by the occurrence of persistent albuminuria, reduced kidney function, hypertension, and an increased risk of cardiovascular morbidity and mortality [23]. Various factors have contributed to an increase in its pathophysiology and available treatment modalities. This develops as a result of complex interactions between metabolism, haemodynamic, inflammation, oxidant-antioxidant, and other pathways that ultimately affect glomerular cells as well as tubulointerstitial tissue via signalling pathways that involve nuclear factor kappa B (NF-κB) and protein kinase C activation [24]. The key pathological events in Glomerular Basement Membrane (GBM) result from proteinuria in diabetic nephropathy; persistent development of albuminuria is a critical event since intervention at this stage prevents further progression of nephropathy because of the reduction of albuminuria using therapeutic interventions was shown to preserve renal function.

Albuminuria is a currently used clinical investigation for the diagnosis of nephropathy in patients with T2DM. According to these studies, this is a conventional marker and it's not a golden standard, specific and sensitive marker for early prediction of nephropathy because it is elevated in other diseased conditions like obesity, hypertension, and other types of kidney diseases, along with that some of the T2DM patients with microalbuminuria revert back to normoalbuminuria [25,26]. Because of the limitations of urine ACR, there is a need for other markers to early predict nephropathy in T2DM patients. It shows that hyperglycaemia, AGEs, mean arterial blood pressure, HbA1c, aldosterone, and atrial natriuretic peptide cause protein excretion in urine, and the authors also observed that some T2DM patients with microalbuminuria revert to a normoalbuminuric stage [27-29].

In the present study, it was also found that there were statistically highly significant elevated levels of FBS, PPBS, urea, creatinine, HbA1c, urinary ACR, serum adiponectin, and reduced levels of eGFR also observed in T2DM patients (not significant) with microalbuminuria when compared to T2DM with normoalbuminuria and healthy controls. Similarly, another recent study reported that elevated levels of serum adiponectin might be useful for predicting the early onset of nephropathy [30]. A cross-sectional study done with the 60 T2DM patients found elevated FBS, PPBS, HbA1c and serum adiponectin levels, the adiponectin was positively correlated with urinary ACR and HbA1c, and they reported that adiponectin measurement might be useful for early detection of nephropathy in patients with T2DM [31]. Furthermore another recent research studies discovered that adiponectin, rather than urinary albuminuria, is used for the early prediction and progression of nephropathy in patients with T2DM [32,33]. Adiponectin is an adipocytokine produced by the white adipose tissue. The beneficial effects of this improved insulin sensitivity by its antidiabetic property, protect the tissue from damage by reactive oxygen species by inhibiting NADPH oxidase activity by its antioxidative property, and decrease the adverse effects of inflammatory cytokines by its anti-inflammatory properties [34,35]. There is a conflict with serum adiponectin; either it is a sensitive, specific, and accurate marker to predict early renal impairments in patients with T2DM.

In the present study also, the ELISA method was used for the quantification of serum adiponectin in patients with T2DM compared to healthy controls. It is particularly important that authors found a statistically significant difference in the concentration of serum adiponectin in T2DM patients with normoalbuminuria compared with healthy individuals. These results indicate that before the appearance of microalbuminuria, in addition to that, the present study found statistically significant elevated levels of serum adiponectin in T2DM patients with microalbuminuria, and the glomerular filtration rate was found to be lower in comparison to normal eGFR. Similarly another cross-sectional study also found similar results, where significantly elevated levels of serum adiponectin positively correlated with microalbumin and negatively correlated with eGFR and also they suggested adiponectin measurement can be useful for early onset of nephropathy in T2DM [36]. Previous studies have also found elevated levels of adiponectin in T2DM patients with Chronic Kidney Disease (CKD) and ESRD [37,38]. Other studies found that serum adiponectin was negatively correlated with urinary albumin and that adiponectin deficiency was directly associated with renal dysfunction; it could be one of the triggering factors that increases protein kinase activation, protects podocytes from damage, and prevents albuminuria all at the same

time [39]. Furthermore, in this study, serum adiponectin strongly correlated with HbA1c and urinary ACR and negatively correlated with eGFR, indicating that serum adiponectin is a marker of renal impairment. Similarly, previous studies reported that the serum adiponectin levels were inversely proportional to the eGFR levels and also reported that ADIPO R1 enhances the AMPK pathways and inhibits the free radicals, which simultaneously protects the development of albuminuria [28,40].

The eGFR and serum adiponectin showed a statistically significant area under the curve with sensitivity ranging from 85.00-92.50 and specificity from 45.00-87.50 and $p<0.001$ and $p<0.0001$, respectively. According to the current study findings, serum adiponectin is the best marker for early prediction of Diabetic Nephropathy than urinary ACR in patients with T2DM because, before excretion of albuminuria, these serum adiponectin levels were significantly elevated in T2DM patients with normoalbuminuria.

### Limitation(s)

Limitations of the present study were small sample size as well as authors didn't follow-up the T2DM cases with different stages of nephropathy. Secondly, statistically significant difference was found for age and BMI among both the groups (T2DM and controls). Moreover, it was a single centre study. Further longitudinal and follow-up studies are required to prove that adiponectin can be used for early prediction and progression of nephropathy in T2DM patients.

## CONCLUSION(S)

According to the study findings, serum adiponectin levels are proportionately elevated in T2DM patients with normoalbuminuria to microalbuminuria and also positively correlated with urinary ACR and negatively correlated with eGFR. The ROC curve analysis revealed that serum adiponectin had higher diagnostic accuracy, sensitivity, and specificity in T2DM patients with normoalbuminuria than urinary ACR. Hence, serum adiponectin might be a sensitive and specific marker to predict the early onset of nephropathy in T2DM patients and therefore can be used as a diagnostic marker for DN.

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**PLAGIARISM CHECKING METHODS:** [Jain H et al.]
- Plagiarism X-checker: May 06, 2022
- Manual Googling: Aug 06, 2022
- iThenticate Software: Sep 16, 2022 (21%)

**ETYMOLOGY:** Author Origin

**AUTHOR DECLARATION:**
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **May 01, 2022**
Date of Peer Review: **Jul 19, 2022**
Date of Acceptance: **Sep 20, 2022**
Date of Publishing: **Nov 01, 2022**