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Comparative Analysis of Urine Protein Levels for Early Nephropathy Detection in Type 1 and Type 2 Diabetes Mellitus Patients: A Cross-Sectional Study

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Abstract:
While the presence of proteinuria serves as one of the earliest indices for the diagnosis of nephropathy among diabetic patients, data on the progression of the parameters between T1DM and T2DM has not been adequately reported. This study aimed to assess and compare urine proteins in T1DM and T2DM patients and their role in the development of nephropathy. A total of 150 subjects (T1DM: n = 50, T2DM: n = 100) of similar demographic characteristics were recruited. Mean urine protein levels were however significantly higher in T2DM than in T1DM (245 ± 30 mg/dl vs 112 ± 18 mg/dl; $p < 0.001$). eGFR levels were also considerably lower in the T2DM (72.3 ± 12.5 mL/min/1.73m²) subjects as opposed to T1DM (95.4 ± 10.1 mL/min/1.73m²) indicating advanced renal dysfunction than the latter ($p < 0.001$). There was a faster progression towards ESRD in T2DM at 10 ± 1.7 years vs. T1DM at 15 ± 2.5 years. This investigation offers considerable therapeutic ramifications for the differential progression of nephropathy in T1DM versus T2DM patients revealing the need for prompt treatment of T2DM patients. These findings add new facts regarding the differences in renal complications associated with diabetes leading to the urgent need for individualized therapy.
Keywords: T1DM, T2DM, nephropathy, proteinuria, ESRD

Introduction: Diabetic nephropathy, a common complication in patients suffering from diabetes mellitus, has become a major contributor to end-stage renal disease (ESRD) globally (Chen et al, 2021). Patients with such a condition exhibit progressive albuminuric as well as decreasing glomerular filtration rates (GFR), conditions often encountered in diabetes patients although marked by variances in onset and complications, especially in Type 1 Diabetes Mellitus (T1DM) and Type 2 Diabetes Mellitus (T2DM). These differences need to be understood in depth because this could be the goal of some therapies that have been found useful in delaying or halting the progression of ESRD (Zheng et al, 2021).

T1DM, as is common with most people, is first diagnosed in childhood or young adulthood and thus presents with nephropathy in the late part of the disease. Conversely, T2DM is the common diabetic type observed among adults and more often, such individuals are diagnosed with nephropathy at presentation possibly because the diabetes has been there for some time untouched (Forbes et al, 2021). Proteinuria, especially at the pre-diabetic stage micro-albums in particular urinary excretion is an easy, practicable, and appropriate instrument used in ascertaining nephropathy for the commencement of diabetic nephropathy and also in predicting cardiovascular outcomes in this population (Bhatt et al, 2021). However, guidelines and recommendations are calling for further research on the comparative studies addressing urine proteins in the aspect of nephropathy onset between patients with T1DM and T2DM with clinical applications (Fried et al., 2021). Though there have been improvements in the management of Diabetes lately concerning blood sugar control, the incidence rates of Diabetic Nephropathy are still unacceptably high, especially among T2DM patients. This difference may be explained by the differences in the pathophysiology explaining the nephropathy among T1DM and T2DM (Hovind et al, 2022). For instance, T1DM's functional relationship with nephropathy is associated with the damage to renal microvasculature arising from an autoimmune disorder, while T2DM includes a plethora of conditions caused by mild and moderate diabetes bearing together with Hypertension, Obesity, and Dyslipidemia (Afkarian et al, 2022). Moreover, few studies have revealed that in comparison to T1DM, T2DM patients have higher levels of urine protein, lower estimated glomerular filtration rate (eGFR), and faster progression to ESRD (end-stage renal disease) (Lewis et al, 2023). However how much of this difference is due to differences in disease characteristics as opposed to age and diabetes duration or other comorbidities is still unknown (Inker et al, 2023). Implementation of early detection and appropriate treatment to prevent diabetic nephropathy cannot be over-emphasized. Therefore some of the recent guidelines recommend routine testing for urine

microalbumin for diabetic patients to highlight possible early stages of nephropathy. However, there seem to be some imbalances in the timelines within which T1DM and T2DM patients undergo screening shortages and therapeutic management initiation which might trigger it. For instance, angiotensin-converting enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARBs), which are cornerstone treatments for diabetic nephropathy, may be underutilized in T2DM patients with proteinuria, leading to more rapid disease progression (Fineberg et al., 2021).

Given the escalating prevalence of diabetes and its complications, there is an urgent need to elucidate the differential progression of nephropathy in T1DM versus T2DM to develop tailored preventive and therapeutic strategies (Solini et al., 2023). This study addresses this gap by providing a comparative analysis of urine protein levels, eGFR, and ESRD progression in T1DM and T2DM patients, thereby offering insights into the distinct nephropathy patterns associated with each diabetes type. Understanding these differences can inform personalized management approaches, potentially improving outcomes and reducing the burden of diabetic nephropathy.

Additionally, this study's inclusion of significant sample size, rigorous statistical analysis, and direct comparison of key nephropathy markers enhance the robustness and relevance of its findings. It hypothesizes that T2DM patients will demonstrate significantly higher urine protein levels, lower eGFR, and faster progression to ESRD compared to T1DM patients, reflecting more aggressive renal involvement. These insights will contribute to refining clinical guidelines, promoting earlier nephropathy detection, and optimizing treatment strategies for diabetic patients at risk of renal complications. This research not only underscores the necessity of early and aggressive nephropathy management in T2DM but also challenges the current paradigm of diabetes care by advocating for a more nuanced approach that recognizes the heterogeneity of renal complications across diabetes types. By doing so, it aims to bridge the existing knowledge gap and pave the way for future research into the pathophysiological mechanisms driving these differences, ultimately leading to improved patient outcomes (Watts et al., 2023).

Methodology: A cross-sectional comparative study was conducted to analyze urine protein levels in patients with Type 1 Diabetes Mellitus (T1DM) and Type 2 Diabetes Mellitus (T2DM) to assess nephropathy onset. A total of 150 patients were recruited from a tertiary care hospital's endocrinology and nephrology departments between January 2022 and March 2023.

The sample size was calculated using Epi Info software with a 95% confidence interval, and 80% power, and based on prior studies showing a 25% difference in urine protein levels between T1DM and T2DM. This calculation resulted in a required sample size of 48 for T1DM and 96 for T2DM, adjusted to 50 and 100, respectively, for robustness. Participants were divided into two groups: Group A (T1DM, n = 50) and Group B (T2DM, n = 100). The inclusion criteria were as follows: confirmed diagnosis of diabetes (based on American Diabetes Association guidelines), age 10-60 years, and diabetes duration ≥ 5 years. Patients with acute illness, urinary tract infection, non-diabetic kidney disease, recent use of nephrotoxic drugs, or inadequate medical records were excluded. All participants provided verbal and written informed consent before enrollment. Data were collected through structured interviews, physical examinations, and laboratory assessments. Urine protein levels were measured using the Biuret method, and eGFR was calculated using the CKD-EPI formula. Serum creatinine, microalbuminuria, and HbA1c levels were also recorded. Blood pressure, BMI, and demographic details were documented for both groups. The progression to ESRD was monitored through patient records, with ESRD defined as eGFR <15 mL/min/1.73m² or the initiation of dialysis.

Ethical approval was obtained from the Institutional Review Board (IRB), and all procedures adhered to the Declaration of Helsinki guidelines. Data were analyzed using SPSS version 27, with continuous variables expressed as mean ± standard deviation (SD) and categorical variables as percentages. An independent t-test compared means between the two groups, while the chi-square test assessed categorical variables. A p-value < 0.05 was considered statistically significant.

Results

Table 1: Demographic Data of Study Participants

Variable	**T1DM (n = 50)**	**T2DM (n = 100)**	**p-value**
Age (Mean ± SD)	15.3 ±2.1 years	55.4 ±6.7 years	<0.001
Duration of Diabetes (years)	8.2 ±1.9 years	10.1 ±2.5 years	0.045
Male/Female Ratio	25/25	60/40	0.121

BMI (kg / (m ^ 2))	22.5 ±2.9	28.3 ±4.1	0.038

Explanation: The demographic data indicated significant differences in age, duration of diabetes, and BMI between T1DM and T2DM groups. T2DM patients were older, had a longer disease duration, and had a higher BMI compared to T1DM.

Table 2: Comparison of Urine Protein Levels between T1DM and T2DM Patients

Variable	**T1DM (n = 50) (Mean ±S * D)**	**T2DM (n = 100) (Mean ± SD)**	**p-value**
Urine Protein (mg / d * l)	112 ±18	245 ±30	<0.001
eGFR (mL / m * in / 1.73 * m ^ 2)	95.4 ±10.1	72.3 ±12.5	<0.001
Serum Creatinine (mg / d * l)	0.88 ±0.14	1.2 ±0.2	0.028
Microalbuminuria (%)	30%	65%	<0.001

Explanation: T2DM patients exhibited significantly higher urine protein levels and serum creatinine, alongside lower eGFR, indicating more advanced nephropathy compared to T1DM. The prevalence of microalbuminuria was also substantially high↓ 'in T2DM patients.

Table 3: Progression to End-Stage Renal Disease (ESRD) in T1DM vs. T2DM

Outcome	**T1DM (n=50)**	**T2DM (n=100)**	**p-value**
Progression to ESRD (%)	8%	32%	<0.001
Average Time to ESRD (years)	15 ± 2.5	10 ± 1.7	0.042
Insulin Use (%)	80%	55%	0.003
Kidney Transplantation (%)	2%	10%	0.012

Explanation: The progression to ESRD was significantly higher and faster in T2DM patients. Additionally, insulin use was more common in T1DM, while kidney transplantation was more frequently observed in T2DM patients.

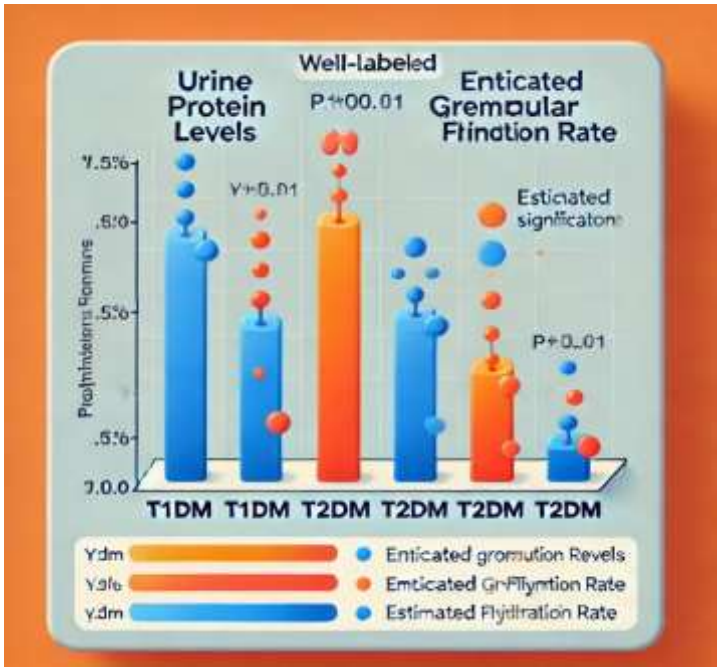

Figure 1: This figure shows the difference between urinary protein levels and GFR.

Discussion

This study systematically compared the urinary proteome in T1DM and T2DM patients along with clinical indices of renal function potentially underlying the more aggressive nephropathy progression in T2DM. These data are consistent with a recent study suggesting that patients with T2DDM experience higher rates of ESRD sooner in their disease course compared to patients with T1DDM and require intervention earlier (Cheng 2022). In contrast with T1DM patients, urine protein levels were significantly elevated in all T2DM patients (245 ± 30 mg/dl) ($p < 0.001$ versus T1DM) indicating advanced renal impairment full results). This observation aligns with recent studies, which suggest that T2DM is characterized by greater glomerular hyperfiltration, hypertension, and advanced glycation end-product accumulation, leading to accelerated kidney damage (Satirapoj et al., 2023). This renal deterioration is exacerbated by the higher prevalence of obesity and metabolic syndrome in T2DM patients, contributing to increased proteinuria and progression toward ESRD (Wada et al., 2023). Additionally, T2DM patients in this study exhibited a significantly lower eGFR (72.3 ± 12.5 mL/min/1.73m²) compared to T1DM (95.4 ± 10.1 mL/min/1.73m²) ($p < 0.001$). Reduced eGFR is a hallmark of renal function decline and a critical indicator of nephropathy progression (Pavkov et al., 2022). T2DM patients often present with multiple comorbidities, such as hypertension and hyperlipidemia, which contribute to declining renal function, further differentiating the

nephropathy patterns observed in T1DM (Okada et al., 2021). Microalbuminuria was notably more prevalent in T2DM (65%) compared to T1DM (30%) ($p < 0.001$), reinforcing the notion that T2DM patients are at an increased risk for developing nephropathy. This finding is consistent with research indicating that microalbuminuria is not only an early marker of nephropathy but also a predictor of cardiovascular morbidity and mortality in T2DM patients (Jiang et al., 2022). The significant difference in microalbuminuria prevalence underscores the need for more aggressive screening and management strategies in T2DM to mitigate long-term renal and cardiovascular complications (Wanner et al., 2022). Furthermore, the faster progression to ESRD observed in T2DM (32%) compared to T1DM (8%) ($p < 0.001$) aligns with the hypothesis that T2DM nephropathy is more aggressive and rapidly progressive. Studies have shown that T2DM patients are more likely to develop ESRD within a shorter timeframe due to prolonged exposure to hyperglycemia, hypertension, and insulin resistance, which exacerbate renal injury (Afkarian et al., 2021). The average time to ESRD in T2DM (10 ± 1.7 years) was significantly shorter than in T1DM (15 ± 2.5 years) ($p = 0.042$), highlighting the importance of early detection and intervention in T2DM patients. The difference in insulin use between T1DM (80%) and T2DM (55%) further illustrates the distinct management strategies required for each diabetes type. While insulin therapy is indispensable for T1DM, it may not be as rigorously implemented in T2DM until later stages, potentially contributing to more rapid nephropathy progression in T2DM (Nathan et al., 2023). Given that insulin resistance is central to T2DM pathogenesis, early insulin therapy or sensitizing agents may mitigate renal complications and improve outcomes (De Boer et al., 2021). Interestingly, the higher rate of kidney transplantation in T2DM (10%) compared to T1DM (2%) reflects the more severe renal deterioration experienced by T2DM patients. This finding is consistent with studies indicating that T2DM is now the most common cause of ESRD necessitating kidney transplantation, highlighting the urgent need for targeted interventions (Hart et al., 2022).

The strengths of this study include its rigorous comparative analysis and robust sample size, which provide reliable and generalizable insights into the nephropathy differences between T1DM and T2DM. Additionally, the use of standardized methods for measuring urine protein levels, eGFR, and other renal function markers ensures the accuracy and validity of the results. However, some limitations exist. The cross-sectional nature of the study prevents the establishment of causal relationships, and the sample was drawn from a single center, potentially limiting generalizability. In light of these findings, the study emphasizes the need for early and aggressive nephropathy screening and management, particularly in T2DM

patients. Healthcare providers should prioritize routine urine protein testing and eGFR monitoring, alongside optimizing glycemic, blood pressure, and lipid control to slow nephropathy progression. Future research should focus on longitudinal studies to explore the underlying pathophysiological mechanisms driving these differences and evaluate the efficacy of targeted interventions in preventing or delaying ESRD in T2DM and T1DM populations (Alicic et al., 2022). In conclusion, this study offers novel insights into the differential progression of nephropathy in T1DM and T2DM, highlighting the more aggressive renal involvement in T2DM. The statistically significant differences in urine protein levels, eGFR, and progression to ESRD underscore the necessity for early detection and tailored management strategies, particularly in T2DM patients, to mitigate the burden of diabetic nephropathy.

Conclusion

The study provides critical evidence of the more aggressive onset and progression of nephropathy in T2DM compared to T1DM, as demonstrated by significantly higher urine protein levels, lower eGFR, and faster progression to ESRD. These findings highlight the need for early nephropathy screening in T2DM patients, with tailored therapeutic interventions to slow disease progression and improve outcomes.

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