

The diagnostic utility of urinary Transferrin excretion rate as predictor for micro albuminuria in patients with Type 2 Diabetes Mellitus among Karbala province

Zahraa Abduladheem Almaialy^{1,*}, Rabab Salman Baidah², Hosam A.A. Al-Issawi³ and Muna Ali Hussein⁴

¹University of Karbala/ College of Dentistry, Karbala, Iraq

²University of Karbala/College of Dentistry, Karbala, Iraq

³University of Karbala/College of Dentistry, Department of Basic science, Karbala, Iraq

⁴University of Karbala, College of Medicine, Department of Biochemistry, Karbala, Iraq

Abstract

One of the factors responsible of end-stage renal disease and chronic kidney disease is diabetic nephropathy. Microalbuminuria itself is regarded as the initial indication of diabetic nephropathy, and it affects 20% to 40% of patients with diabetes mellitus. Because of the limited accuracy and precision of microalbuminuria, more susceptible markers may be developed to more accurately identify diabetic nephropathy early on. The purpose of this research was to ascertain whether urine transferrin could be used as a marker for diabetic nephropathy. In our research, 80 subjects with type 2 diabetes were divided into two categories: 10 healthy controls and group 1 (normoalbuminuric, with albumin excretion up to 30 mg/d) and group 2 (microalbuminuric, with albumin excretion between 30 and 300 mg/d). all subjects was over the age of 18, had diabetes for further than a year, and had a glomerular filtration rate greater than 60 mL/min/1.73 m². The concentration of transferrin, serum creatinine, and glycosylated hemoglobin (HbA1c) in both spot urine and 24-hour urine samples were assessed using a super accurate sandwich enzyme - linked immunosorbent assay kit. subjects with microalbuminuria had substantially greater urinary transferrin levels than both normoalbuminuric and healthy control participants. We discovered a significantly positive correlation $r = 0.584$ ($p < 0.001$) when we compared these categories based on the urinary transferrin concentration. Urinary transferrin levels did not correlate with glycoregulation, and neither did transferrin levels and the length of diabetes. Urinary transferrin levels may be utilized as an important indicator of diabetic nephropathy, according to the findings of the research.

Key words: Diabetes mellitus; Diabetic nephropathies; Albuminuria; Biomarkers; Transferrin.

Introduction

The predominance and development of diabetes mellitus (DM), a serious illness, are steadily rising. Approximately 415 million individuals globally have diabetes, and by 2040, that number is expected to rise to 642 million, with 10% predominance, according to the "International Diabetes Federation" (Forouhi, N. G., & Wareham, N. J. (2019).

The prevalence of diabetic abnormalities, such as "diabetic kidney disease ", is rising among diabetic patients; those who have primarily type 2 diabetes (90%) Cole, J. B., & Florez, J. C. (2020).

"End-stage renal disease (ESRD) and chronic kidney disease (CKD)" are thought to be primarily caused by diabetes. Diagnosis and management "diabetic nephropathy" quickly as humanly possible is essential because the approach to treating patients with DKD is very high, particularly after they develop "end-stage renal disease (ESRD)." (Sagoo, M. K., & Gnudi, L. (2020).

Initially identified in the 1960s, "microalbuminuria (MA)" is widely regarded as the first non-invasive indicator of renal disease.(Hsu, C. C.,*et al* ., 2011)

"Micro albuminuria ", which is characterized by a continuous increase in albumin levels in the urine of 30 to 300 mg per day, is widely regarded as the first non - invasive indicator of "diabetic nephropathy (DN)", despite the limited precision and accuracy of MA.(Basi, S., et al ., 2008) Even when albuminuria levels are within the average limits, some patients with diabetes mellitus develop DN, suggesting that albuminuria is not the ideal indicator for the timely identification of DN.(MacIsaac, R. J.,*et al*., 2014)

According to latest research, certain pertinent screening tests linked to DN have been identified and may one day be used to forecast DN or the course of the illness (Gross, J. L., et al.,2005) .

Numerous indicators of renal injury were examined in order to identify DN earlier than usual and initiate treatment as soon as feasible.(Sagoo, M. K., & Gnudi, L. (2020).

In individuals with diabetes, "urinary transferrin" is thought to be an excellent indicator of nephron damage. It is a protein with a particle size of 76.5 kDa, which is comparatively higher than that of" albumin". Its ionic force and low molecular weight allow it to pass through the" glomerular membrane "with simplicity.(Mackinnon, B.,*et al* ., 2003)

According to certain earlier research, normoalbuminuric patients with DM type 2 may exhibit elevated urine transferrin efflux prior to MA. Urinary transferrin is therefore thought to be a more significant indicator of nephron injury in individuals with diabetes.(Casanova, A. G.,*et al* ., 2020)

The purpose of this investigation was to ascertain whether urine transferrin falls under the category of initial DN biological markers.

Methods

Studying the relationship between MA and "urine transferrin in DN" was the goal of this "cross-sectional study", which was conducted between October 2023 and November 2024.

Al-Husain Medical Academy's Ethics Committee in Kerbela, Iraq, ethical approval was obtained, and each patient gave their permission to conduct the study.

The research project involved 80 patients with "type 2 diabetes mellitus (DM2)" who had been ill for a year or longer, had "estimated glomerular filtration rates" greater than 60 mL/min/1.73 m², and did not have "albuminuria".

The chosen patients underwent a thorough health assessment, which included kidney ultrasonography. Additionally recorded were age, gender, blood pressure, height, weight, smoking habits, and the length of time that the patient had diabetes mellitus.

Using the formula based on the patients' height and weight, the body mass index (BMI) was determined. Following a minimum of eight hours of fasting, blood samples were obtained, and the blood levels of "glycated hemoglobin (HbA1C), urea, creatinine, and glucose" were measured. Glomerular filtration rate (GFR) was calculated based on the CKD-EPI formula.

A "spot urine sample" taken in the early hours was used to measure the "transferrin concentration (ng/mL) and the transferrin to creatinine ratio (mg/g of creatinine)". A "24-hour urine sample" taken the next day was used to measure "albuminuria" (30 mg/day or higher). "Elabscience Biotechnology Co., Ltd.'s commercially available ELISA kits" were used to measure the levels of "urine transferrin".

Results

The research consisted of 80 individuals with type 2 diabetes, with an average age of 58.47 ± 7.29 years (range 39–75 years), comprising 44 (55%) males and 36 (45%) females.

The presence of normoalbuminuria was 57.65% (47 subjects) and MA was 40.15% (33 subjects). The mean "eGFR" was 84.76 ± 13.28 , and the disease duration was 12.39 ± 6.59 years.

The investigated teams' base-line clinical features did not differ significantly from one another (Table 1).

Table 1: Base - line clinical features of individuals with type 2 diabetes based on urinary albumin levels

Features	All subjects (n=80)	Normo-albuminuric (n= 47)	Micro-albuminuric (n=33)	Healthy (n=10)	p-value
Gender (M/F)	44/36	27/20	17/16	10	0.12
Ages (years)	59.85±8.871	60.49±8.73	58.94±9.13	54±10.59	0.014
Duration (years)	13.29±7.69	13.34± 7.74	13.21± 7.73	n/a	0.942
BMI (kg/m2)	27.36±4.42	26.64± 3.56	28.38± 5.31	25.73±4.77	0.325
S.creatinine (µmol/L)	75.38±15.04	76.64±15.97	73.58±13.64	73.6 ± 7.6	0.360
GFR (mL/min /1.73 m2),	86.86± 14.18	85.78 ± 13.55	88.39 ± 15.12	92.84 ± 9.06	0.430
HbA1c (%)	7.59 ± 1.34	7.25 ± 1.15	8.07 ± 1.45	4.93 ± 0.3	0.074

BMI – body mass index; HbA1c – hemoglobin A1c; GFR – glomerular filtration rate

Urinary transferrin levels were $85.07 \pm 56.54 \mu\text{g/gCr}$ for MA subjects and $25.63 \pm 29.85 \mu\text{g/gCr}$ for normoalbuminuric subjects. Between these two groups, we discovered a statistically significant correlation in the transferrin concentration (Table 2).

Table 2: Transferrinuria and microalbuminuria correlation

Transferrin conc. (µg/gCr)	Microalbuminuric (≥ 30 mg/24h)	Normoalbuminuric (< 30 mg/24h)	Perason's <i>r</i>	<i>p</i>
Transferrin conc. 24h urine	91.76 ± 68.45	22.56 ± 31.46	0.489	< 0.001
Transferrin conc. spot urine	85.07 ± 56.54	25.63 ± 29.85	0.354	< 0.001

Cr – creatinine; Pearson's test, *r* – correlation coefficient

Table 3 displays the correlation coefficient between the concentration of urine transferrin and explanatory parameters .

We only discovered a significant correlation with MA out of all the parameters (Table 3).

Variables	All subjects n=80	<i>Pearson's r</i>
Age (years)	59.85 ± 8.87	0.003
BMI (kg/m ²)	27.3 ± 4.42	0.053
HbA1c (%)	7.59 ± 1.34	0.132
Duration of DM (years)	13.29 ± 7.69	0.127
Microalbuminuria	40.42 ± 40.89	0.584

Pearson's test, *r* – correlation coefficient ; BMI – body mass index; HbA1c – hemoglobin A1c; DM – diabetes mellitus.

Discussion

"Albuminuria" is thought to be the first typical sign of the existence of DN and an indicator of kidney injury. It remains a medically valuable tool for risk prediction and treatment response controlling currently. (Grauer, G. F. (2007)

One important aspect of albuminuria's diagnostic value is the variance between its presence and the deterioration of renal function. It is not required for all patients with decreased GFR to have albuminuria. According to (Perkins et al., 2010) patients with type 1 diabetes introduced advanced chronic kidney disease (CKD) (GFR < 60 mL/min 1.73 m²) without concurrently developing albuminuria. Matching multiple studies from 1977 to the present, (Chen et al. 2017) demonstrated that some diabetic patients with normoalbuminuria also had nonalbuminuric DN, a accelerated drop in renal function.

HbA1c and retinopathy were not linked to nonalbuminuric renal insufficiency; however, some research indicated a linkage between nonalbuminuric renal insufficiency and gender. Therefore, in order to detect DN sooner and predict the advancement to ESRD more appropriately, we require a new marker with greater accuracy and precision. Thus, in nonalbuminuric diabetic patients, we examined urine transferrin as a diagnostic marker of nephron injury linked to the initial phases of DN.

Our research findings indicated that subjects with MA had elevated amounts of "urinary transferrin excretions" compared to subjects with "normoalbuminuric type 2 diabetes". We observed a "statistically significant correlation" between MA and "urine transferrin concentration".

This is consistent with the findings of (Narita et al., 2005), who found that elevated urinary transferrin in people with diabetes, regardless of microalbuminuria, could also indicate the onset of MA in populations with normoalbuminuria (DM2).

According to (Kazumi T., et al., 1999) 1 year follow-up research with DM2 population, 31% of subjects with starting point "transferrinuria" began developing MA, while only 7% of subjects without "transferrin excretion" did so. They came to the realization that elevated "urine transferrin excretion" may suggest the onset of MA in people with type 2 diabetes who do not have the disease.

(Kanauchi M, et al., 1995) discovered the same outcomes in a sample of 60 DM2 subjects. They demonstrated a strong relationship between albumin and transferrin excretion in the urine. Their results suggest that urinary transferrin could be important in the initial detection of DN.

Conclusion

DM2 subjects with MA had significantly higher "urinary transferrin" levels. It was unaffected by glycemic control or the length of diabetes. Our findings suggest that the amount of transferrin excreted in the urine may serve as an early indicator of diabetic nephropathy.

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