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URINARY BIOMARKERS IN DIABETIC NEPHROPATHY: CORRELATION BETWEEN UREA AND CREATININE LEVELS

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Abstract

Diabetic nephropathy (DN) is one of the most common complications that can result in chronic kidney disease and end-stage kidney failure all over the world and it remains very important to identify DN at the early stages. This study aimed to assess the connection of urinary urea, urinary creatinine and urinary urea-to-creatinine ratio (UCR) in diabetic nephropathy patients with the healthy controls as well as its role as a biomarker in renal impairment. Two hundred subjects were recruited, 100 of which were patients diagnosed with DN and 100 healthy control subjects. Demographic and clinical factors such as age, gender, body mass index (BMI), blood pressure and glycated hemoglobin (HbA1c) were noted down. Serum and urinary urea and creatinine concentrations were determined and UCR calculated. Patients with DN had significantly higher BMI, systolic and diastolic blood pressure, HbA1c, serum urea, serum creatinine, and UCR when compared to controls ($p < 0.001$). Pearson correlation analysis indicated a strong positive association between urinary urea and creatinine in DN patients ($r=0.74$, $p<0.001$) and the correlation was moderate with control group ($r=0.52$, $p<0.001$). On Multivariate logistic regression, urinary urea, urinary creatinine, UCR and HbA1c are independent predictors of DN after adjusting for confounding factors ($p < 0.01$). Although urinary urea and creatinine showed a positive correlation with each other, logistic regression indicated that higher urinary urea and UCR are associated with DN whereas lower urinary creatinine was associated with disease severity. These results confirm the use of urinary biomarkers as valuable tests of the presence of diabetic nephropathy. The combination of urinary urea and UCR tests with the customary clinical radiological and biochemical tests may help to detect renal dysfunction among diabetics earlier. Therefore, early disease identification and early intervention can delay disease progression, achieve better patient outcomes and prevent the health care long-term burden of diabetic kidney disease.

INTRODUCTION

Diabetic nephropathy (DN) is a cumulative disease involving the kidney that develops because of long-term hyperglycemia, and it is among the biggest causes of chronic kidney disease (CKD) all over the world. It presents itself through albuminuria, worsening of the

glomerular filtration rate (GFR), as well as an increased chance of cardiovascular deaths (Zhang et al., 2021). In both type 1 and type 2 diabetes mellitus, DN develops in patients with long-standing hyperglycemia, and research has shown that 30-50 percent of diabetics develop some kind of kidney impairment (Chen et al., 2020). The disease typically progresses through five stages, with initial stages being hyperfiltration, and in later stages, the patients will require a kidney transplant or dialysis (Thomas et al., 2019). Notwithstanding these advancements, DN has been one of the clinical challenges because its pathophysiology is not that straightforward, and patients do not respond uniformly to interventions. The recent development in precision medicine has brought forward new treatment targets of DN. Considering the rising burden of DN, there is increasing need to implement better early detection methods and personalized treatment methods. Some of the earliest structural changes in diabetic nephropathy are glomerular hypertrophy and thickening of the basement membrane. Chronic glucose stimulation of mesangial cells triggers proliferation of mesangial cells and production of extracellular matrix, which results in mesangial expansion and the accumulation of glomerulosclerosis (Forbes & Cooper, 2013). Such changes decrease the kidney's filtration ability, resulting in progressive albuminuria and loss in the rate of glomerular filtration (GFR). The other major event in the pathogenesis of DN is the injury of podocyte cells, which have an important role in ensuring the glomerular filtration barrier remains intact. The loss of podocytes is observed during apoptotic events or their detachment which leads to higher protein leakage and progressive kidney dysfunction (Reidy et al., 2014). The induced inflammatory mediators enhance permeability and glomerular-fibrosis and interstitial inflammation which causes kidney damage that is irreversible. Researchers have proved that low-grade chronic inflammation worsens kidney damage by promoting apoptosis or fibrosis, which accelerates the conversion process of the mild renal dysfunction to ESRD (Eirin et al., 2017). The contribution of oxidative stress to diabetic nephropathy is not in doubt. Hyperglycemia results in excessive generation of reactive oxygen species, which activate mitochondrial malfunctioning, lipid peroxidation and DNA destruction, in the renal cells (Brownlee, 2005). Accumulation of oxidative stress impairs the normal functioning of the cell, increases inflammation, and leads to renal fibrosis. In diabetic patients, the antioxidant defense mechanisms are usually incapacitated, which further increases the development rate of kidney disease (Aminzadeh-Gohari et al., 2021). The other characteristic of diabetic nephropathy is tubulointerstitial damage. Alongside the issue of glomerular damage, in the case of diabetes, the severe changes in renal tubules also occur, namely, the development of tubular atrophy, interstitial fibrosis, and inflammation (Vallon & Thomson, 2020). The proximal tubules are critical in the reabsorption of the glucose molecules, and their overload would result in increased metabolic burden and apoptosis of the tubule cells (Heerspink et al., 2021). Hyperglycemia-induced vasodilation increases renal blood flow, leading to glomerular hypertension and subsequent renal damage. (Pavkov et al., 2018). Microalbuminuria (30-300 mg/day) is used as an early indicator of kidney damage and macroalbuminuria (>300 mg/day) is used as a sign of severe glomerular damage (Perkins et al., 2003). Although albuminuria is clinically significant, this parameter has shortcomings because not all patients that demonstrate a deterioration of kidney function progression show an elevated urinary albumin level (Matsushita et al., 2020). Estimated glomerular filtration rate (eGFR) is one of the most recognized parameters which touch on the use of serum creatinine to approximate the kidney capacity. As opposed to serum creatinine alone, the eGFR presents a more detailed picture of the kidney work because, in addition to age, sex, and ethnicity, there are variables (Inker et al., 2021). When creatinine clearance is determined via urine sampling and subsequently compared to the prevailing condition of kidney disease, it provides a decisive response concerning the

effectiveness of kidney filtering, and this leads to the overall assessment of kidney diseases having increased accuracy. Most of the developments in the nephrology field in recent years have been based on the introduction of the newer biomarkers, cystatin C and neutrophil gelatinase-associated lipocalin (NGAL), along with older biomarkers, in order to increase the strength of the early signals and risk stratification (Stevens et al., 2018). Recently, Urinary urea-to-creatinine ratio (UCR) has been proposed as an effective indicator in collection of information regarding kidney health and the development of end-stage kidney diseases. UCR is considered as the body tradeoff between protein metabolism and effectiveness of kidney excretion; hence, is a valuable indicator of renal dysfunction (Martin-Cleary et al., 2021). Both increase in UCR and reduction in the ratio can be signs of prerenal process (e.g., dehydration or congestive heart failure) and intrinsic renal disease or failure to reabsorb solutes into the tubules (Vanholder et al., 2018). The research has made a few insights on predictive quality of diabetic nephropathy of UCR. Researchers discovered that declining UCR is linked to develop progressive kidney dysfunction and risk of ESRD in diabetics. It has already been observed that the UCR can also be applied to differentiate between those causes of the acute kidney injury that are prerenal or intrinsic renal, and provide clinicians with a more specific example of a diagnostic resource. Moreover, UCR can potentially anticipate the onset of kidney dysfunction at an early stage despite the fact that serum creatinine or eGFR alterations do not necessarily happen yet. It is a great assistance in diabetic nephropathy as early treatment is vital in lowering progression levels. Urinary Urea-to-Creatinine Ratio (UCR) has been proposed as one of the helpful indices that can quantify the kidney functions and disease progression in diabetics (Zhang et al., 2021). Several studies have stated that there is a strong association between the urinary urea and creatinine concentrations and the occurrence of DN. It has been revealed that an increment in the level of urea in the urine is associated with a protein breakdown and a reducing speed of kidney clearance, whereas the reduction in urine creatinine excretion, in turn, signifies a poor kidney functioning (Dabla, 2010). It is proved that the level of urinary creatinine is less with DN patients than healthy controls, which presents with decreasing eGFR values. In the same line of thought, another systematic review by (Zhang et al. 2021) affirmed that UCR is indeed an accurate indicator of the progression of CKD, as it has been proved to precede the onset of DN severity. A number of clinical advantages exist with monitoring of urinary urea and creatinine. An increase in the urinary urea and a decrease in the urinary creatinine level may be the first sign of renal dysfunction before the increase in serum creatinine level is seen thus giving a chance to have an intervention early (Levey et al., 2009). This UCR assessment capability can be used to optimize risk levels of DN patients and therefore clinicians can formulate treatment strategies depending on the severity of the disease (Fiseha, 2015). Therapeutic monitoring can also be facilitated by the measurement of urinary biomarkers carried out on a regular basis to monitor treatment progress and to make appropriate adjustments to the treatment sessions, resulting to eventual superior outcomes of the patients (Dabla, 2010).

Diabetic nephropathy is a leading cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD) worldwide, making early detection and intervention vital to prevent progression and improve patient outcomes. Conventional biomarkers such as serum creatinine and albuminuria are widely used to evaluate renal function, but they often lack the sensitivity to detect kidney damage in its early stages. Urinary urea and creatinine levels have been suggested as potential alternative biomarkers; however, their correlation with disease severity and diagnostic efficacy in diabetic nephropathy remain inadequately studied. This research therefore aims to investigate the urinary concentrations of urea and creatinine in patients with diabetic nephropathy compared to healthy individuals, and to determine their relationship with disease progression, particularly towards ESRD. It also assesses how clinical parameters

such as age, sex, glycemic control, and hypertension influence these biomarkers, and evaluate the feasibility of using urinary urea and creatinine as non-invasive, reliable indicators of early kidney dysfunction.

Materials and Methods

3.1 Design of the study

This study was designed as an observational cross-sectional study whose purpose was to identify the correlation between the levels of urinary urea and creatinine in patients with diabetic nephropathy. The patients with diabetic nephropathy were the first group (Group 1), and healthy individuals constituted the second group (Group 2). The study was carried out in the hospitals and diagnostic laboratories in the area of Okara district as it was easier to reach the varied kinds of people. A variety of healthcare facilities in the community were considered, including both governmental and private healthcare facilities.

3.2 Participants

Two hundred participants were recruited who were put into two groups. Group 1 comprised 100 patients with the diagnosis of diabetic nephropathy among the local hospitals and outpatient clinics specializing in care of the diabetic patients. Patients included in this group had previously been diagnosed with Type 1 or Type 2 diabetes mellitus and showed signs of nephropathy; participants displayed either abnormal urine albumin levels (albuminuria) or had a slow glomerular filtration rate (GFR). Group 2 consisted of 100 healthy controls with no diabetes, hypertension or any known renal diseases that were matched in terms of age, gender and other demographic variables. The healthy controls, either recruited through the same hospitals or general community in Okara, had no history of kidney disease or diabetes.

3.3 Inclusion and Exclusion Criteria

Participants diagnosed with Type 1 or Type 2 diabetes mellitus and indicators of the diabetic nephropathy via albuminuria or a low GFR were studied. Participants had to be aged 40 to 70 years. People were not included in case of acute kidney injury, history of serious renal diseases, including polycystic kidney disease or glomerulonephritis, pregnancy and lactation, the presence of active infections and inflammatory diseases, as well as refusal to participate in the study. Excluding patients with other major forms of kidney diseases ensured that the study was specific on the effect of diabetic nephropathy and not any other factor as this would present a confound which would affect the study of it.

3.4 Sample Size Calculation

The sample size was calculated using a confidence level of 95% and statistical power of 80% to detect a moderate correlation effect size. The specific parameters were selected as they will help identify a medium effect size in correlation between the urinary urea and creatinine levels among patients with diabetic nephropathy. The size of the population was 200 subjects (100 subjects of each group) to ensure statistically reliable results.

3.5 Data Collection

Data were obtained through clinical evaluation and laboratory examinations that were conducted at the local hospitals and diagnostic labs in the city of Okara.

3.6 Clinical Assessment

Structured interviews and medical history questionnaires were used to gather demographic and clinical information related to each participant. The data obtained was age, sex, the time/length of diabetes (in case of diabetic patients) blood pressure figures, and related health history as well as comorbid structures, including hypertension and cardiovascular disorders. Along with that the anthropometric measures took place to get the body mass index (BMI) measured in height, weight, and waist circumference. These measures were employed in evaluating how this can affect the kidney as obesity is a major contributor to both diabetes and nephropathy.

3.6.1 Collection of the Urine Sample

Urinary concentration of urea and creatinine was measured by a 24-hour urine collection technique. This approach was chosen because it is reliable in the measurement of biomarkers of renal function in consideration of changes of urine production over a 24-hour period (Levey et al., 2015). The people were given adequate guidelines concerning the collection of urine samples within the required period of 24 hours. The samples acquired were preserved in the clean containers containing preservatives and taken to the laboratory where they were subjected to biochemical testing.

3.6.2 Sample Collection of Blood

All participants submitted fasting blood samples in the morning before breakfast. Serum levels of urea and creatinine were determined in these samples and other biomarkers of glycated hemoglobin (HbA1c), fasting blood glucose (FBG), and lipid profile. These assessments were performed in hospital laboratories by standard biochemical methods. Automated clinical chemistry analyzers were used to administer tests of blood urea nitrogen (BUN) and serum creatinine, with available directions and protocols of medical laboratory testing. Outcomes of these tests were employed to evaluate kidney functioning as well as comparing them with the urinary levels of urea and creatinine.

3.6.3 Anthropometric Measurements

Anthropometric measures with the data of weight, height, and waist circumference were measured on all participants. BMI was computed and the classification into normal, overweight, and obese was done. The information may be utilized to understand the potential role of body composition to kidney functions particularly among diabetic nephropathies patients as obesity poses a risk in such patients.

3.6.4 Laboratory Methods for Analyzing Urea and Creatinine

The amount of urea and creatinine in the urine was diagnosed using colorimetric test and spectrophotometry method which is a precise and highly reliable analytical procedure to detect renal indicators (Levey et al., 2015). Renal activity was analyzed by calculating urinary urea to creatinine ratio (UCR). UCR was an essential test of identifying minimal renal damages among the patients with diabetic nephropathy and an elevated score in UCR was a factor of augmented kidney harm. Serum urea and creatinine were investigated in the laboratory with the assistance of automated clinical chemistry analyzers. The tests provided valid details on assessment of renal functioning and potential malfunction due to diabetic nephropathy.

3.7 Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS). Descriptive statistics were used to detail the characteristics of participants in regard to age, sex, BMI and clinical indices.

3.7.1 Correlation Analysis

The relationship between the urinary urea level and the urinary creatinine in the two groups was considered by utilizing Pearson or Spearman correlation coefficient. They have been analyzed by means of statistical examinations carried out in IBM SPSS Statistics version 26.0. Other correlations of 0.7 or greater were regarded to be strong correlations.

3.7.2 Comparative Analysis

Urinary urea-to-creatinine ratios (UCR) or other clinical data were compared by independent t-tests to compare diabetics with nephropathy and healthy controls.

3.7.3 Multivariate Regression Analysis

The coverage of confounding factors was carried out by multivariate regression analysis that was used to adjust the age, gender, BMI, blood pressure, and HbA1c levels. This analysis was used to assess the relationship persisting between the variables urinary urea and creatinine and diabetic nephropathy even when these variables were included.

3.7.4 Ethical Approval Statement

Ethical approval was obtained from the Institutional Ethical Review Committee of the University of Okara and written informed consent was obtained from all participants.

Results

4.1 Participant Characteristics

Table 1: Demographic and Clinical Characteristics of Participants

The data presented in Table 1 suggest that age and gender distribution were comparable between the two groups with the resulting non-significant p-values of age and gender distributions.

Variable	Diabetic Nephropathy (n=100)	Healthy Controls (n=100)	p-value
Age (years, mean ± SD)	57.4 ± 6.8	56.9 ± 6.5	0.62
Male n (%)	54%	52%	0.84
BMI (kg/m², mean ± SD)	28.6 ± 3.5	24.2 ± 2.8	<0.001
Systolic BP (mmHg)	146.3 ± 12.4	121.5 ± 10.6	<0.001
Diastolic BP (mmHg)	88.5 ± 8.7	77.1 ± 7.4	<0.001
Duration of Diabetes (years)	11.2 ± 4.1	–	–
HbA1c (%)	8.3 ± 1.1	5.2 ± 0.6	<0.001

This is an indication that age and sex differences will have less effect in any clinical outcome disparities. But, significant differences were observed in some of the important health indicators. BMI levels were significantly higher in our diabetic nephropathy group, which shows that a higher number of such subjects were overweight and even obese than in the healthy ones. Also, the patient group has shown high systolic and diastolic blood pressure, which is indicative of a greater degree of hypertension, which is a recognized kidney damage risk factor.

The levels of HbA1c were also quite significantly higher in patients with diabetic nephropathy, which indicates inadequate glycemic control over a longer period of time. The average duration of diabetes in the patient group was more than ten years and this corresponds to the progressive development of the diabetic nephropathy. Overall, these results point out those diabetic nephropathy individuals cannot only be identified by their impaired kidney functioning but also by a clustering of metabolic and cardiovascular risk factors to a greater extent, in comparison to those who are healthy.

4.2 Urinary and Serum Biomarkers

Table 2: Comparison of Urinary and Serum Biomarkers

The ratio of urea to creatinine as measured in urinary (UCR) increased significantly in patients with diabetic nephropathy than in healthy controls which indicated high impairment of renal functions among the patient population.

Parameter	Diabetic Nephropathy (n=100)	Healthy Controls (n=100)	p-value
Urinary Urea (mmol/L)	312.4 ± 58.6	245.7 ± 51.3	<0.001
Urinary Creatinine (mmol/L)	5.2 ± 1.1	8.1 ± 1.47	<0.001
UCR (mmol/mmol)	60.1 ± 9.4	30.3 ± 6.7	<0.001
Serum Urea (mmol/L)	9.8 ± 1.7	5.6 ± 1.3	<0.001
Serum Creatinine	152.3 ± 18.5	88.4 ± 15.2	<0.001

(µmol/L)			

This increase demonstrates a distorted protein metabolism and loss of renal clearance capacity, which are both typical phenomena of kidney damage as it is presented with diabetic nephropathy.

4.3 Correlation Analysis

The analysis of Pearson correlation revealed a strong positive correlation between levels of urinary urea and urinary creatinine in the group of diabetic nephropathy ($r = 0.74$, $p < 0.001$), which means that the higher the urinary urea levels were the more likely the urinary creatinine levels to increase respectively among this group of patients. Conversely, the figure recorded a moderate positive correlation with the healthy control group ($r = 0.52$, $p < 0.001$), implying a lesser and statistically significant association between the two parameters. The results suggest that the interaction between urinary urea and creatinine is more accentuated in persons with diabetic nephropathy, which could be representing the pathology-condition changes in the renal activity and the nitrogen balance.

4.4 Comparative Analysis

The independent t -test results showed that in relation to the healthy control group, diabetic nephropathy patients were statistically different in urinary urea-to-creatinine ratio (UCR), serum urea and serum creatinine values ($p < 0.001$). These findings imply that patients with diabetic nephropathy had considerably significant findings of these indicators of kidney function as opposed to the healthy population. The high levels recorded among the patient group indicate severe deficit in the functioning of the kidney in accordance with the pathophysiological phenomena associated with diabetic nephropathy.

4.5 The Multivariate Regression Analysis

Table 3: Multivariate Logistic Regression Predicting Diabetic Nephropathy

The results of the multivariate logistic regression analysis (Table 3) demonstrate that urinary urea, urinary creatinine, urinary urea-to-creatinine ratio (UCR), and HbA1c were all significant predictors of diabetic nephropathy. Urinary urea ($\beta = 0.045$, $p = 0.001$) and UCR ($\beta = 0.089$, $p < 0.001$) were positively associated with diabetic nephropathy, whereas urinary creatinine showed an inverse association with the disease.

Predictor	β Coefficient	Standard Error	p-value
Urinary Urea	0.045	0.012	0.001
Urinary Creatinine	-0.067	0.021	0.003
UCR	0.089	0.017	<0.001
HbA1c	0.310	0.098	0.002

A positive β coefficient for urinary urea ($\beta = 0.045$, $p = 0.001$) and UCR ($\beta = 0.089$, $p < 0.001$) indicates that higher values of these parameters were associated with an increased likelihood of having diabetic nephropathy. Conversely, the negative β coefficient for urinary creatinine ($\beta = -0.067$, $p = 0.003$) suggests that lower urinary creatinine levels were linked to a higher probability of the disease, reflecting reduced renal clearance. HbA1c ($\beta = 0.310$, $p = 0.002$) was positively associated with diabetic nephropathy, reinforcing the role of poor long-term glycemic control in its development. These findings highlight that both urinary biomarkers and glycemic status serve as independent and significant predictors of diabetic nephropathy.

Discussion

This study was conducted to assess the correlation of the urinary urea level and creatinine in patients with diabetic nephropathy as well as assess whether these indicators can be considered as a reliable indicator of renal dysfunction alongside the urinary urea to

creatinine ratio (UCR). This study attempted to fill a clinically significant gap in the early diagnosis and detection of the damage to the kidney in diabetes mellitus patients. The findings indicated that the diabetic nephropathy group and the healthy control group showed significant biochemical and clinical variations that assisted in offering valuable information regarding the metabolic and renal changes present in such a condition. As shown in the demographic analysis, there was no statistically significant age and gender distribution between the two groups. This comparability is methodologically important and it reduces confounding by demographic factors and increases the likelihood that observed differences in parameters of biochemical investigations are likely to be the effect related to the presence or absence of the disease but not to characteristics of the population. The detected finding is crucial specifically due to the consideration that both age and sex were found to affect renal physiology and the levels of biomarkers (Glassock & Rule, 2012). Nevertheless, regardless of the fact that the demographics were similar, there were significant differences in essential clinical parameters. The diabetic nephropathy group had mean body mass index (BMI) that was significantly increased, systolic and diastolic blood pressure that was also increased and glycated hemoglobin (HbA1c) increased notably, when compared to the healthy controls. The variations are similar to known risk factors of diabetic nephropathy, which are recorded in long-term longitudinal prospective cohort studies (Gross et al., 2005; Alicic et al., 2017). The high BMI has been linked to high intraglomerular pressure and hyperfiltration, which speed up the renal damage in persons with diabetes. Similarly, uncontrolled hypertension is a notorious source of glomerular damage via a number of processes, including rising shear pressure and renin-angiotensin-aldosterone system (RAAS) activation (Bakris et al., 2020). There is also poor glycemic control seen in increased levels of HbA1c which in addition worsen the renal injury through a process of generating advanced glycation end-products (AGEs), oxidative stress and inflammatory cascades. Analysis of urinary biomarkers showed a well-established increase in UCR in the diabetic nephropathy group as opposed to their healthy controls. This finding confirms the results of previous research (Levey et al., 2015) which showed higher UCR as the preliminary indicator of impaired total protein metabolism and decreased renal clearance ability of people. The ratio combines 2 complementary components urea a byproduct of protein catabolism which is excreted mostly through the kidneys and creatinine, a degradation end product of muscle metabolism which is excreted at a comparatively fixed rate. Hypothetically, a high UCR implies uneven urea accumulation or an imbalance in its clearance compared to creatinine, probably because of glomerular injury, tubular illness or catabolic stress in connection to the chronic hyperglycemia. The rising levels of serum urea and creatinine point toward diabetic nephropathy among the patients in the group with the use of serum creatinine confirming low glomerular filtration rate (GFR). It is in accord with the pathophysiological characteristic of diabetic nephropathy that the regressive stage in nephron functions leads to decreased nitrogenous waste filtration (Mogensen et al., 1983). Serum creatinine as a marker of chronic kidney disease (CKD) is still widely used in diagnosis although the inclusion of urinary parameters can enable a further resolution of renal function dealing with excretion of waste metabolites. The correlation analysis revealed there was a strong positive correlation between urinary urea and urinary creatinine that was statistically significant within the diabetic nephropathy group ($r = 0.74$, $p < 0.001$) as compared to a moderate correlation within the healthy controls ($r = 0.52$, $p < 0.001$). In diabetic nephropathy, the insidious decrease in nephron population and symmetrical decline in filtration might, however, cause their excretion to become statistically more highly correlated as they are coordinated in time. Multivariate logit regression showed that all the indicators of urinary urea, urinary creatinine, UCR, and HbA1c were independent predictors of diabetic nephropathy

despite correcting possible confounding factors like age, gender, BMI, and blood pressure.

In diabetic nephropathy, the progressive decline in nephron number and filtration capacity may cause these metabolites to be excreted in a more coordinated manner.

Although urinary creatinine levels were lower in DN patients overall, the positive correlation with urinary urea suggests that both biomarkers still vary proportionally within the patient group due to shared renal excretion mechanisms.

The positive correlation between the urinary urea (0.045, P = 0.001), and UCR (0.089, P<0.001) with the disease status reveals that the greater the quantity the more probably the individual will be affected with diabetic nephropathy. The inverse relationship between urinary creatinine (p = 0.003) and the disease is also logically fitting since smaller amounts of creatinine excretion indicate insufficient renal filtration activity. The robust nature of the positive correlation of HbA1c (β = 0.310, p = 0.002) supports the centrality of the chronic hyperglycemia in the prevention and sequencing of nephropathy. This is in line with the Diabetes Control and Complications Trial (DCCT, 1993) and the UK Prospective Diabetes Study (UKPDS, 1998) who found that intense glucose control significantly decreases risks of microvascular complications such as kidney disease. These are the biochemical patterns that may be accounted through the interaction between the metabolic stress caused by hyperglycemia and structural damage of the kidney vasculature. The persistent elevation of blood glucose results in hyperplasia of renal plasma flow and hyperfiltration of glomeruli which are manifested at initial stages after which the nephrons proceed to apoptosis and sclerosis.

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