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Original Research Article

DIABETIC NEPHROPATHY: SPECTRUM AND CLINICAL OUTCOMES IMPACT OF GLYCEMIC CONTROL ON PROGRESSION TO ESRD

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Abstract: ***Background:*** Numerous conditions that affect people worldwide, including diabetic nephropathy, are among the leading contributors to the development of chronic kidney disease and end-stage renal disease. The condition has a gradual continuum consisting of increments of microalbuminuria and leading to advanced kidney failure. HbA1c values that indicate glycemic control and long-term clinical prognosis are the most vital of the factors that can be controlled that will affect the decline of renal function among diabetic patients. ***Objectives:*** To assess the range of manifestations of diabetic nephropathy and examine the influence of glycemic control on the progression of the condition and the development of end-stage renal disease in diabetic patients. ***Methodology:*** One hundred patients with diabetic nephropathy who are users of a tertiary care centre were the subject of the observational study. Based on diabetes management, clinical information, plus HbA1c values, serum creatinine, and the glomerular filtration rate were documented. Using SPSS 24 and relevant statistical tests for the study, with $p<0.05$ considered statistically significant, the renal outcomes were examined. ***Results:*** One hundred patients signed up to study with ages averaging to 54.2 with an 11.8-year standard deviation. Poorly controlled patients experienced mean eGFR and progression of disease at an elevated rate than their counterparts who exhibited better clinical control. The loss of renal function between groups of glycemic control was different at a significant rate ($p=0.01$). ***Conclusion:*** Uncontrollable symptoms of diabetes cause a large spectrum of diabetic nephropathy cases, having different symptoms and results depending on how well blood sugar levels are controlled. Poorly controlled blood sugar levels of diabetic patients fast pass the process of healthy functioning kidneys becoming diseased and eventually terminally diseased.

Keywords: Diabetic nephropathy; Glycemic control; Chronic kidney disease; ESRD

INTRODUCTION

Diabetic nephropathy (DN) is one of the most prevalent microvascular complications of diabetes mellitus. It is also the most common cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD) worldwide. While diabetes is increasing worldwide, kidney sequelae also affect most healthcare systems, especially in poorer countries,

which are often marketed as low and middle-income. DN sequelae encompass a broad range of complications (comorbidities) such as chronic ailments, premature death, diminished well-being, and substantial economic drain for the healthcare system as a result of long-term renal replacement therapy [1,2]. Clinically, diabetic nephropathy has a long-term and complex spectrum. The initial stages involve microalbuminuria and maintained renal function, while the later stages result in major proteinuria, hypertension, anaemia, and ultimately ESRD. There is a wide variability in the progression rate among individuals, suggesting the impact of both modifiable and non-modifiable risk factors. The modifiable risk factors, in particular, are those for which the identification of patients is most likely to produce the greatest benefit in terms of timely intervention that leads to a wide range of favourable effects [3,4]. Of the modifiable factors, the most important one is glycemic control, which is of central importance in the pathogenesis and progression of DN. A state of chronic hyperglycemia triggers a range of structural and functional changes to the kidney, such as glomerular hyperfiltration, oxidative stress, the formation of advanced glycation end products, and silencing of the inflammatory and fibrotic pathways [5]. A longitudinal clinical study has found that the above adaptations are responsible for glomerulosclerosis and tubulointerstitial scarring, which ultimately lead to irreparable organ damage (citation needed) [6]. Numerous cornerstone clinical studies have shown that the incidence of microalbuminuria and diabetic kidney disease can be postponed by maintaining stringent diabetes control. In contrast, the impact of maintaining control of type 2 diabetes on the rate of already established diabetic kidney disease progressing to end-stage renal disease (ESRD) remains vague, and has been even more poorly defined in applied clinical studies [7]. Additionally, most of the existing studies have come from developed countries, with an almost complete absence of information from the developing world (citation needed). The need to optimise the clinical approach to the diabetic nephropathy and/or chronic kidney disease (CKD) continuum, in particular with respect to diabetes control, is more pressing than ever [8]. The focus of practice on these coordinates is expected to fine-tune the strategy by setting more suitable diabetes complexity goals, increasing follow-up frequency in the most vulnerable, and integrating early protective kidney medications as needed. The current study intends to characterise the nephropathy associated with diabetes in a tertiary care environment and evaluate how the control of glucose levels affects the rate of decline of renal function and clinical outcome of ESRD. The exploration of the connection between levels of HbA1c and the decline of renal function will add credence to the need for ongoing and continuous glycemic control to mitigate adverse endpoints for renal function [9].

Study Objectives:
To assess how diabetic nephropathy develops its clinical spectrum, and how retention of optimal glycemic control would influence the progression of the disease, the risk of developing end-stage renal disease will also be assessed.

MATERIALS AND METHODS

Study Design and Setting:
This observational study was conducted at Department of Nephrology Prime Teaching Hospital Peshawar from jan 2025 to june 2025.

Participants:
The subject of the study consists of 100 adult patients suffering from diabetes mellitus and nephropathy diabetes. Their diabetes nephropathy based on clinical laboratory was evaluated and diagnosed based on clinical laboratory results. Patients had to meet the eligibility criteria of having documented albuminuria and/or diminished eGFR due to diabetes and at least three months of clinical follow-up data.

Sample Size Calculation:
One hundred patients were chosen via pragmatic sampling theory due to their availability and based on similar studies conducted in the past. This sample size would be sufficient to determine differences in renal outcomes across the various categories pertaining to glycemic control and to detect differences across those categories.

Inclusion Criteria:
• Individuals aged 18 and older
• Confirmed diagnosis of diabetes mellitus
• Presence of diabetic nephropathy (albuminuria and/or decreased eGFR)
• Availability of HbA1c and renal function data

Exclusion Criteria:
• Kidney disease without diabetes
• Acute renal trauma
• Current UTI
• Obstructive sleep apnea
• Autoimmune or systemic vascular renal disease

Diagnostic and Management Strategy:
Albuminuria and/or decreased eGFR were observed among the diabetic patients, which confirmed a diabetic nephropathy diagnosis. Treatment followed institutional guidelines for standard glycemic control, blood pressure management, and RAS blockade.

Statistical Analysis:
Data were analysed with SPSS version 24.0. Means and standard deviations were used to describe continuous variables; frequencies and percentages

were used to present categorical variables. The right statistical tests were used to compare groups, and a p-value of less than 0.05 was considered statistically significant.

RESULTS

There were 100 participants that had diabetic nephropathy were recruited into the study. The mean age was 54.2 ± 11.8 years, and most were in the middle-aged and older cohorts. Stratification of participants was in accordance toHbA1c levels into good and poor control. Participants within the poor control group had significantly lower mean eGFR and greater disease progressions than those that were moderate control. There was a statistically significant adverse correlation of eGFR and HbA1c within the diabetic nephropathy population (p = 0.01). Among the population there was a greater advanced stage of diabetic nephropathy in those with greater and persistent poor control. Greater rates of diabetic nephropathy also were seen with progressively lower eGFR and lower HbA1c levels. Renal results demonstrated an overwhelming correlation to the degree of glycemic control.

Intervention Outcomes:

Patients who attain better control of their glycemic levels experience a more gradual decline in their renal function and a slower progression to more serious levels of diabetic nephropathy. Renal function was better in patients who had higher levels of HbA1c, which resulted in a beneficial impact from the continuous improvement of glycemic levels on the degree of ESRD progression.

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants (n = 100)

Variable	Value
Age (years), mean ± SD	54.2 ± 11.8
Male sex, n (%)	58 (58%)
Female sex, n (%)	42 (42%)
Duration of diabetes (years), mean ± SD	10.6 ± 4.9
HbA1c (%), mean ± SD	8.7 ± 1.6
Systolic BP (mmHg), mean ± SD	138 ± 16
Diastolic BP (mmHg), mean ± SD	84 ± 10
Serum creatinine (mg/dL), mean ± SD	2.1 ± 0.9
eGFR (ml/min/1.73 m²), mean ± SD	48.6 ± 18.4
ACEi/ARB use, n (%)	72 (72%)

This table summarizes baseline demographic, glycemic, and renal characteristics of the study population. Data are expressed as mean ± standard deviation or frequency (percentage).

Table 2. Distribution of Diabetic Nephropathy Spectrum According to CKD Stage

CKD Stage	eGFR Range (ml/min/1.73 m²)	n (%)
Stage 1	≥90	6 (6%)
Stage 2	60–89	18 (18%)
Stage 3a	45–59	26 (26%)
Stage 3b	30–44	22 (22%)
Stage 4	15–29	18 (18%)
Stage 5	<15	10 (10%)

Patients were classified according to KDIGO chronic kidney disease staging based on estimated glomerular filtration rate, illustrating the clinical spectrum of diabetic nephropathy.

Table 3. Comparison of Renal Outcomes by Glycemic Control Status

Parameter	Good Control (HbA1c <7%)	Poor Control (HbA1c ≥9%)	p-value
Number of patients, n	38	42	—
Mean eGFR (ml/min/1.73 m²)	56.8 ± 15.9	41.2 ± 17.6	0.01
CKD stage progression, n (%)	8 (21.1%)	19 (45.2%)	0.02
ESRD progression, n (%)	4 (10.5%)	14 (33.3%)	0.01

Comparison of renal outcomes between patients with good and poor glycemic control. Poor glycemic control was significantly associated with lower eGFR, higher CKD progression, and increased risk of ESRD.

Table 4. Factors Associated with Progression to End-Stage Renal Disease

Variable	Odds Ratio (OR)	95% Confidence Interval	p-value
HbA1c ≥9%	3.4	1.4–8.1	0.006
Baseline eGFR <45 ml/min	4.1	1.8–9.2	0.001
Diabetes duration >10 years	2.6	1.1–6.0	0.03
Hypertension	2.2	1.0–4.9	0.04
ACEi/ARB non-use	1.9	0.8–4.4	0.09

Multivariable logistic regression analysis identifying predictors of progression to end-stage renal disease. Poor glycemic control and reduced baseline renal function were the strongest independent predictors.

DISCUSSION

The study assessed the spectrum of clinical diabetic nephropathy and evaluated the effects of glycemic control on the progression of diabetic renal disease and end-stage renal disease (ESRD). The results showed that due to poor glycemic control and higher HbA1c levels, the accelerated decline of renal function, advancement in stage of chronic kidney disease (CKD) and higher ESRD risk are correlated. Thus, there are significant findings that underscore the importance of sustained glycemic control on adverse renal outcomes in patients with diabetic nephropathy [10]. The average age of the patients in this study was in line with previously documented cohorts, where diabetic nephropathy develops in middle-aged to older individuals with longstanding diabetes [11]. The stage of CKD that was documented was in line with the spectrum of diabetic nephropathy, showing that patients may present with different CKD stages. The findings highlight the heterogeneous spectrum of diabetic nephropathy. This relationship has also been documented in recent studies, both in high- and low-resource settings [12]. Our results show that patients with poor glycemic control (HbA1c ≥9%) also had significantly lower mean eGFR and higher frequencies of advancing CKD stages relative to those with adequate glycemic control [13]. This corresponds to recent cohort studies, which document higher levels of HbA1c as an independent factor associated with an increase in the rate of eGFR decline and increased kidney-related morbidity [14]. A comprehensive meta-analysis conducted within the last five years has also documented that every increase of 1% in HbA1c significantly increases the risk of an individual advancing in CKD and ESRD, therefore supporting the biological rationale of our results [15,16]. The association of glycemic control and advancement to ESRD, as demonstrated in the current study, corroborates current findings. Numerous longitudinal studies have confirmed that poor glycemic control continues to be a powerful predictor of ESRD even when accounting for initial renal function, blood pressure, and albuminuria [17]. Our multivariable analysis also pinpointed an elevated HbA1c and a lower baseline eGFR as cardinal predictors of ESRD, emphasising the principal role of hyperglycemia and even more so with renal impairment [18]. The most recent neurocognitive interventions and real-life studies have underscored the need for integrated restraint approaches that target glycemic control, blood pressure, and renin–angiotensin system blockade to be able to slow the progression of diabetic nephropathy [19]. Although Reno's protective effects have been proven in the recent glucose-lowering drugs, mainly SGLT2 inhibitors and GLP-1 receptor antagonists, poor glycemic control remains more prevalent in the everyday clinical practice of many resource-limited settings [20]. This might in part explain the greater burden of advanced CKD and ESRD that such populations have [21]. The current study enriches the body of literature with real-world evidence from a tertiary care setup, depicting routine clinical practice, as opposed to ideal situations encountered in clinical trials. This increases the external validity of the findings and reinforces the validity of the current guideline recommendations advocating for individualised and stringent glycemic control for renal protective effect [22]. Like any other study, this one also has some limitations, like, for instance, its observational design and somewhat small sample size, which may restrict the ability to draw causal conclusions. Nevertheless, the consistency of the findings with other recent large and extensive studies only adds to the confidence of the conclusions [23].

Limitations:

This study has faults related to an observational design, which provides an inability to draw strong relations among associations. The small sample size, coupled with a single centre, may limit its external validity, i.e. generalizability. The lack of long-term follow-up, as well as missing time-averaged HbA1c measurements, impacts the estimation of the progression of the renal disease.

CONCLUSION

The condition of diabetic nephropathy has a very broad range of clinical characteristics, and these characteristics are heavily affected by how well a patient maintains glycemic control. Those who maintain poor glycemic control are even more likely to experience a decline in renal function and progression to end-stage renal disease. If high-risk patients are identified early and glycemic control is sustained and optimised, it is possible to mitigate their negative renal outcomes in the long term.

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