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ASSOCIATION BETWEEN HbA1c AND RENAL FUNCTION IMPAIRMENT IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A CROSS-SECTIONAL STUDY

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Abstract

Introduction: Type 2 Diabetes Mellitus (T2DM) represents a profound global public health crisis, with a disproportionately high burden in South Asia, including Pakistan. Glycated hemoglobin (HbA1c) is the cornerstone for assessing long-term glycemic control, while renal function tests (RFTs), including serum creatinine and urea, are fundamental for detecting kidney impairment. This study aimed to evaluate the correlation between HbA1c and RFT in a cohort of T2DM patients in Peshawar, Pakistan.

Methodology: A hospital-based, descriptive cross-sectional study was conducted from June to November 2024 at the Endocrinology Ward of Hayatabad Medical Complex,

Peshawar. A total of 290 participants (145 T2DM patients and 145 age-matched non-diabetic controls) were enrolled via non-probability convenience sampling. Fasting venous blood samples were analyzed for HbA1c, serum creatinine, and serum urea using a Cobas c503 automated chemistry analyzer. Statistical analysis was performed using SPSS, employing independent samples t-tests and descriptive statistics.

Results: The study population had a mean age of 49.73 ± 10.12 years. Gender distribution was comparable. The mean HbA1c level was significantly elevated in the diabetic group (9.44% ± 2.43) compared to controls (4.43% ± 0.54), with a p-value of <0.001. Renal function markers were also significantly higher in diabetics: serum creatinine (0.91 ± 0.32 mg/dL vs. 0.73 ± 0.19 mg/dL, p=0.001) and serum urea (32.07 ± 18.82 mg/dL vs. 26.44 ± 8.09 mg/dL, p<0.001). The standard deviations for urea were notably larger in the diabetic group, indicating greater variability.

Conclusion: This study confirms a strong and significant association between poor glycemic control, as indicated by elevated HbA1c, and impaired renal function in T2DM patients in Peshawar. The findings underscore the critical need for stringent glycemic management and regular, integrated monitoring of both metabolic and renal parameters to prevent or delay the onset of diabetic nephropathy in this high-risk population.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a complex, chronic metabolic disorder characterized by persistent hyperglycemia resulting from a combination of insulin resistance and progressive pancreatic beta-cell dysfunction [1]. Its global prevalence has reached epidemic proportions, with an estimated 537 million adults living with diabetes in 2021, a number projected to rise to 643 million by 2030 [2]. South Asia, including Pakistan, is a

major epicenter of this epidemic, driven by rapid urbanization, nutritional transitions, genetic predisposition, and increasingly sedentary lifestyles [3].

In Pakistan, the situation is particularly alarming. The International Diabetes Federation ranks Pakistan third globally in the number of adults with diabetes, with a national prevalence estimated at 26.7%, one of the highest in the world [2]. This high prevalence translates into a massive burden of diabetes-related complications, placing an immense strain on the country's healthcare infrastructure [4]. Among the most devastating of these complications is diabetic nephropathy (DN), which is the leading cause of end-stage renal disease (ESRD) globally, accounting for nearly 40-50% of all ESRD cases in developed countries, with similar trends emerging in developing nations [5, 6].

The pathogenesis of DN is multifactorial, with chronic hyperglycemia serving as the primary initiating and perpetuating factor. Sustained high blood glucose levels trigger a cascade of pathological processes, including the formation of advanced glycation end-products (AGEs), activation of protein kinase C, increased polyol pathway flux, and induction of oxidative stress and chronic inflammation [7]. These mechanisms collectively lead to glomerular hypertrophy, basement membrane thickening, mesangial expansion, podocyte injury, and ultimately, glomerulosclerosis. This structural damage manifests functionally as albuminuria (initially microalbuminuria) and a progressive decline in the glomerular filtration rate (GFR) [8].

Glycated hemoglobin (HbA1c) has been the gold-standard biomarker for assessing long-term glycemic control for decades. It reflects the average plasma glucose concentration over the preceding 8-12 weeks and is strongly correlated with the risk of developing diabetes-related complications [9]. Major clinical guidelines, including those

from the American Diabetes Association (ADA), recommend maintaining an HbA1c level below 7% for most non-pregnant adults to reduce the risk of microvascular complications [10].

Renal function tests (RFTs) are essential tools for screening and monitoring kidney health. Serum creatinine, a breakdown product of muscle creatine phosphate, is a key marker. Its concentration is inversely related to the GFR; rising levels indicate declining kidney function [11]. Serum urea (or blood urea nitrogen, BUN) is another nitrogenous waste product. While more susceptible to non-renal influences like diet, hydration, and catabolic state, elevated levels often accompany impaired renal filtration [12]. Together, these parameters provide a fundamental, albeit not early, assessment of renal status.

A robust body of international literature confirms the association between elevated HbA1c levels and the onset/progression of DN [13, 14]. However, epidemiological and clinical patterns can exhibit regional variations influenced by genetic, environmental, and healthcare-access factors. While studies from other parts of Pakistan and South Asia exist [15, 16], there is a paucity of recent data specifically from the Khyber Pakhtunkhwa province, particularly Peshawar. This study, therefore, aimed to investigate the correlation between HbA1c levels and conventional renal function markers (serum creatinine and urea) in patients with T2DM attending a major tertiary care hospital in Peshawar. The findings are intended to reinforce the importance of integrated metabolic-renal care and provide locally relevant data to inform clinical practice and public health strategy.

Methodology

A hospital-based, descriptive cross-sectional study was conducted at the Endocrinology Ward of Hayatabad Medical Complex (HMC), Peshawar, over six months from June to November 2024. Ethical approval was obtained from the Clinical Research Ethics

Committee of the School of Health Sciences (SHS), Peshawar, and administrative permission was secured from HMC. Written informed consent was obtained from all participants before enrollment.

A total of 290 participants were finally enrolled: 145 patients with a confirmed diagnosis of T2DM (based on ADA criteria or physician diagnosis on treatment) and 145 age-matched non-diabetic individuals as a control group. Non-probability convenience sampling was employed for recruitment.

Inclusion criteria for the diabetic group were age >30 years, diagnosis of T2DM, and willingness to participate. The control group comprised apparently healthy individuals or non-diabetic patients attending for minor complaints, matched for age. Exclusion criteria applied to both groups included known cardiac failure, systemic inflammatory diseases, history of kidney transplants, recent blood transfusion (within 3 months), active malignancy, and pregnancy.

Data collection involved a two-step process. First, demographic information (age, gender) and clinical history were recorded on a structured proforma. Subsequently, a 5 mL venous blood sample was drawn from each fasting participant under aseptic conditions. Samples were collected in appropriate vacutainers: EDTA tubes for HbA1c analysis and plain serum separator tubes for renal function tests. All biochemical analyses were performed on the same day in the hospital's central laboratory using a fully automated chemistry analyzer (Cobas c503, Roche Diagnostics, Switzerland) following standardized protocols. HbA1c was measured via a turbidimetric inhibition immunoassay, while serum creatinine and urea were determined by enzymatic methods.

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 28.0. Continuous variables were presented as mean ± standard deviation (SD). The

normality of data distribution was assessed using the Shapiro-Wilk test. Differences in means between the diabetic and non-diabetic groups for HbA1c, serum creatinine, and serum urea were analyzed using independent samples t-tests. A two-tailed p-value of less than 0.05 was considered statistically significant throughout the analysis.

Results

The study comprised a total of 290 participants with a mean (±SD) age of 49.73 ± 10.12 years. The demographic composition is detailed in Table 1. The diabetic group consisted of 70 males (48.3%) and 75 females (51.7%). The non-diabetic control group had 56 males (38.6%) and 89 females (61.4%). The overall cohort included 126 males (43.4%) and 164 females (56.6%), showing a higher proportion of female participants.

Table 1: Gender-wise Distribution of Study Participants

Patient Group	Gender	Frequency (n)	Percentage (%)
Diabetic (n=145)	Male	70	48.3
	Female	75	51.7
Non-Diabetic (n=145)	Male	56	38.6
	Female	89	61.4
Total (N=290)	**Male**	126	43.4
	Female	164	56.6

The comparative analysis of biochemical parameters revealed stark and statistically significant differences between the diabetic and non-diabetic groups, as summarized in Table 2.

Table 2: Comparative Analysis of HbA1c and Renal Function Tests

Variable	Non-Diabetic Group (Mean ± SD)	Diabetic Group (Mean ± SD)	p-value
HbA1c (%)	4.43 ± 0.54	9.44 ± 2.43	< 0.001
Serum Creatinine (mg/dL)	0.73 ± 0.19	0.91 ± 0.32	0.001
Serum Urea (mg/dL)	26.44 ± 8.09	32.07 ± 18.82	< 0.001

The mean HbA1c level in the diabetic cohort was 9.44%, which is more than double the mean value in the control group (4.43%) and substantially higher than the recommended therapeutic target of <7.0%. The variability (SD=2.43) in the diabetic group also indicates a wide range of glycemic control among patients.

Regarding renal function, the mean serum creatinine level was 0.91 mg/dL in diabetics compared to 0.73 mg/dL in controls (p=0.001). More pronounced was the difference in serum urea levels, with a mean of 32.07 mg/dL in the diabetic group versus 26.44 mg/dL in the non-diabetic group (p<0.001). It is noteworthy that the standard deviation for serum urea was markedly larger in the diabetic group (18.82) compared to the control group (8.09), suggesting greater heterogeneity and potentially the influence of factors like hydration status, dietary protein intake, or catabolism in poorly controlled diabetes.

Discussion

The findings of this cross-sectional study unequivocally demonstrate a significant correlation between elevated HbA1c levels and impaired renal function, as indicated by

increased serum creatinine and urea, in T2DM patients attending a tertiary care center in Peshawar, Pakistan.

The mean HbA1c of 9.44% observed in our diabetic cohort is critically high and aligns with other reports from Pakistan highlighting suboptimal glycemic control at the population level [4, 17]. This level far exceeds the ADA's recommended target and is firmly within the range associated with a substantially elevated risk for microvascular complications, including nephropathy [10, 13]. The significant elevation of both serum creatinine and urea in the same group provides direct evidence of concomitant renal dysfunction. This triad of findings, high HbA1c, high creatinine, and high urea, paints a concerning picture of the metabolic and renal health status of the studied T2DM population.

Our results are consistent with a vast body of international evidence. Landmark trials like the UK Prospective Diabetes Study (UKPDS) and the Epidemiology of Diabetes Interventions and Complications (EDIC) follow-up of the Diabetes Control and Complications Trial (DCCT) established that intensive glycemic control significantly reduces the risk of developing microalbuminuria and overt nephropathy in both type 1 and type 2 diabetes [13, 18]. More recent large-scale observational studies continue to affirm this relationship. A Swedish national registry study found that HbA1c levels above 7% were strongly associated with increased risks of hospitalization for heart failure, stroke, and mortality, with renal disease being a key mediator [19].

The regional context is crucial. Studies from across South Asia, including India, Bangladesh, and other parts of Pakistan, consistently report similar associations. For instance, research from North India found that HbA1c >8.5% was an independent predictor of diabetic kidney disease [15]. Another study from Karachi, Pakistan, reported a significant positive correlation between HbA1c and serum creatinine, mirroring our

findings [16]. Our study adds granular, location-specific data from Khyber Pakhtunkhwa, confirming that this pattern holds true in this demographic and healthcare setting.

The notably larger standard deviation for serum urea in the diabetic group warrants discussion. While creatinine is a more specific marker for GFR, urea is influenced by extra-renal factors such as high protein intake, gastrointestinal bleeding, dehydration, and a hypercatabolic state [12]. Poorly controlled diabetes can often involve catabolism and fluctuating hydration, which may explain the greater variability in urea levels observed. This suggests that while serum creatinine is a more reliable standalone marker for renal function, urea levels can provide adjunctive information about the patient's overall metabolic and hydration state.

Several limitations of this study must be acknowledged. The cross-sectional design establishes association but not causation. We did not measure urinary albumin excretion (microalbuminuria) or calculate estimated GFR (eGFR), which are more sensitive and earlier indicators of diabetic kidney damage than serum creatinine alone [20]. The use of convenient sampling may introduce selection bias, as patients attending a tertiary hospital may have more advanced disease than the general diabetic population. Furthermore, we did not adjust for potential confounders such as diabetes duration, specific antihyperglycemic and antihypertensive medications (especially ACE inhibitors/ARBs), body mass index, or blood pressure control, all of which influence renal outcomes [21].

Despite these limitations, the clinical and public health implications are significant. The high prevalence of poor glycemic control, coupled with signs of renal impairment, calls for urgent action. It underscores the necessity for healthcare providers to implement rigorous, protocol-driven monitoring that integrates HbA1c assessment with comprehensive renal evaluation (including urine ACR and eGFR calculation). Early

identification of at-risk patients, those with elevated HbA1c and early signs of renal stress, should trigger a multifactorial intervention strategy.

Conclusion

This study confirms a strong, statistically significant association between poor long-term glycemic control (high HbA1c) and derangements in standard renal function markers among T2DM patients in Peshawar, Pakistan. The alarmingly high mean HbA1c and the concomitant rise in serum creatinine and urea highlight a critical gap in effective diabetes management and a substantial risk for progressive diabetic nephropathy in this population.

Conflict of Interest

The authors declare no conflict of interest.

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