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Clinical Association of Early Morning Serum Cortisol Levels with Glycemic Control and Severity of Diabetic Nephropathy in Type 2 Diabetes Mellitus: A Cross-sectional Study

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Abstract

Diabetic nephropathy (DN) is one of the leading causes of chronic kidney disease and end-stage renal failure in patients with Type 2 Diabetes Mellitus (T2DM). This study evaluated the relationship between fasting serum cortisol levels and the severity of nephropathy and glycemic control in T2DM patients. A cross-sectional observational study was conducted over 18 months at a tertiary care center in Northern India. Among 500 screened patients, 100 individuals with T2DM and nephropathy (urinary albumin-creatinine ratio [UACR] ≥30 mg/g) were enrolled. Early morning fasting serum cortisol levels were measured using chemiluminescence immunoassay. Statistical analysis was performed using SPSS version 26. The mean age of participants was 60.7±11.25 years and 93% had diabetes for more than five years. Serum cortisol levels were significantly higher in patients with poor glycemic control (HbA1c >10%) compared with those having HbA1c 6.5–8% (24.05±3.43 vs. 22.46±2.12 µg/dL; p=0.019). Patients with macroalbuminuria showed significantly higher cortisol levels than those with microalbuminuria (24.45±3.02 vs. 21.47±1.84 µg/dL; p=0.001). Cortisol demonstrated positive correlations with UACR (r=0.425), diabetes duration (r=0.412) and HbA1c (r=0.385) (all p<0.001). Higher cortisol levels were also associated with diabetic retinopathy and neuropathy. Elevated serum cortisol levels are associated with poor glycemic control, increasing albuminuria and microvascular complications in T2DM. Serum cortisol may serve as a useful biomarker for identifying patients at risk of progressive diabetic nephropathy.

Keywords: Albuminuria, Diabetic Nephropathy, Glycemic Control, Serum Cortisol, Type 2 Diabetes Mellitus.

Introduction

Type 2 Diabetes Mellitus (T2DM) is one of the most significant global public health challenges, accounting for more than 90% of all diabetes cases worldwide (1). The prevalence of T2DM continues to increase because of population ageing, urbanization, obesity, sedentary lifestyles and unhealthy dietary habits. According to the International Diabetes Federation, more than 537 million adults were living with diabetes in 2021 and this number is expected to increase to approximately 783 million by 2045, with the greatest burden occurring in low- and middle-income countries (2, 3). India is among the countries most affected by T2DM and experiences a substantial burden of diabetes-related complications that contribute significantly to morbidity, mortality and healthcare expenditure. Persistent hyperglycaemia initiates a cascade of metabolic disturbances, including oxidative stress, chronic inflammation, endothelial dysfunction and activation of multiple biochemical pathways, ultimately leading to progressive vascular damage involving several organ systems (2-4). Diabetic nephropathy (DN) is one of the most common and debilitating microvascular complications of T2DM and remains the leading cause of chronic kidney disease (CKD) and end-stage kidney disease worldwide. Approximately 30–40% of patients with T2DM develop diabetic kidney disease during the course of their illness, making it a major contributor to cardiovascular morbidity, renal replacement therapy and premature mortality (5, 6). The pathological process involves glomerular hyperfiltration, mesangial expansion, thickening of the glomerular basement membrane, podocyte injury, progressive albuminuria and declining glomerular filtration rate (7). Since these structural changes often occur before the appearance of overt clinical manifestations, early identification of patients at risk remains essential.

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Although urinary albumin-to-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR) are routinely used for diagnosis and monitoring, these parameters may be influenced by transient physiological and pathological factors and may not completely reflect ongoing renal injury (2, 3). Consequently, there is increasing interest in identifying complementary biomarkers that may improve early detection and risk stratification (5, 7).

Growing evidence indicates that dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis may contribute to the pathogenesis of diabetic complications. Cortisol, the principal glucocorticoid hormone, plays a central role in glucose homeostasis, lipid metabolism, immune regulation and the physiological response to stress. Chronic activation of the HPA axis results in sustained elevations of circulating cortisol, promoting hepatic gluconeogenesis, insulin resistance, impaired pancreatic β-cell function, oxidative stress, endothelial dysfunction and activation of the renin–angiotensin–aldosterone system, all of which may accelerate renal injury and fibrosis. These biological mechanisms support the hypothesis that serum cortisol may serve as a useful biomarker reflecting both metabolic dysregulation and the progression of diabetic nephropathy (8, 9).

Several clinical studies have demonstrated an association between elevated serum cortisol concentrations and diabetic complications. Previous investigations have reported significant associations between increased cortisol levels and microalbuminuria, greater severity of albuminuria, poor glycaemic control, prolonged duration of diabetes, diabetic retinopathy, peripheral neuropathy and impaired glucose metabolism. Collectively, these findings suggest that chronic hypercortisolaemia may contribute to progressive microvascular damage and could serve as a marker of cumulative metabolic stress in patients with T2DM (10, 11).

Despite these observations, important gaps remain in the existing literature. Most previous studies evaluated serum cortisol in relation to isolated clinical outcomes such as glycaemic control or individual diabetic complications without comprehensively assessing its relationship with nephropathy severity and other microvascular manifestations. Differences in study populations, cortisol assay methods, sampling protocols and inclusion criteria have also contributed to variability among published findings. Furthermore, relatively few studies have simultaneously examined fasting morning serum cortisol, albuminuria severity, duration of diabetes, glycaemic status and associated diabetic complications within a single clinical cohort. Consequently, the role of serum cortisol in routine clinical risk stratification for diabetic nephropathy has not yet been clearly established (10, 12, 13).

Evidence from the Indian population remains limited despite the country's high burden of T2DM and diabetic kidney disease (3, 4). Regional differences in genetic susceptibility, environmental exposures, dietary habits and healthcare accessibility may influence both cortisol physiology and disease progression. Therefore, additional evidence from Indian patients is required to determine whether fasting early morning serum cortisol may provide clinically useful information beyond conventional renal biomarkers.

Accordingly, the present study was undertaken to evaluate the association between fasting early morning serum cortisol levels and the severity of diabetic nephropathy in patients with Type 2 Diabetes Mellitus. The specific objectives were to compare serum cortisol concentrations between patients with microalbuminuria and macroalbuminuria, assess their relationship with glycaemic control and duration of diabetes and determine their association with diabetic retinopathy and peripheral neuropathy. The novelty of this study lies in the simultaneous evaluation of serum cortisol, nephropathy severity, glycaemic status and diabetic microvascular complications within a single Indian tertiary-care cohort, thereby providing clinically relevant evidence regarding the potential role of serum cortisol as an adjunctive biomarker for early risk stratification in diabetic nephropathy.

Methodology

Study Design and Setting

A hospital-based, cross-sectional observational study was conducted in the Department of Medicine, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar, Punjab, India, over an 18-month period from July 2024 to December 2025. The study aimed to evaluate the

association between fasting early morning serum cortisol levels, glycaemic control and the severity of diabetic nephropathy among patients with Type 2 Diabetes Mellitus (T2DM).

Study Population and Participant Selection

Adult patients (≥18 years) with a confirmed diagnosis of T2DM attending the outpatient and inpatient services of the Department of Medicine during the study period were screened using a consecutive sampling technique. A total of 500 patients were assessed for eligibility. Patients with diabetic nephropathy, defined by a urinary albumin-to-creatinine ratio (UACR) of ≥30 mg/g, were considered for enrolment.

Patients were excluded if they had Cushing's disease or Cushing's syndrome, were receiving systemic corticosteroid therapy, had undergone chemotherapy, radiotherapy, or immunosuppressive treatment within the preceding three months, or had a known history of malignancy. Following application of the eligibility criteria, 100 participants were enrolled and included in the final analysis.

Diagnostic Criteria and Clinical Assessment

The diagnosis of T2DM was established according to the American Diabetes Association (ADA) diagnostic criteria, including glycated haemoglobin (HbA1c) ≥6.5%, fasting plasma glucose ≥126 mg/dL, or random plasma glucose ≥200 mg/dL in the presence of classical symptoms of hyperglycaemia.

Diabetic nephropathy was diagnosed using the urinary albumin-to-creatinine ratio obtained from an overnight urine sample. Participants with UACR values between 30 and 300 mg/g were classified as having microalbuminuria, whereas those with UACR >300 mg/g were categorized as having macroalbuminuria.

A detailed clinical evaluation was performed for all participants. Demographic characteristics, duration of diabetes, treatment history, hypertension status and the presence of diabetic microvascular complications, including retinopathy and peripheral neuropathy, were documented. Physical examination included measurement of blood pressure and assessment for clinical features suggestive of renal involvement, including peripheral oedema and fluid overload.

Laboratory Investigations

Following an overnight fast of 8–10 hours, peripheral venous blood samples were collected between 08:00 and 09:00 hours to minimize the influence of physiological diurnal variation in serum cortisol secretion. Blood samples for serum cortisol estimation were collected in plain yellow-top vacutainer tubes, while EDTA vacutainers were used for HbA1c analysis.

Fasting serum cortisol concentrations were measured using a chemiluminescence immunoassay (CLIA), following the manufacturer's recommended protocol. The laboratory reference range for fasting morning serum cortisol was 3.7–19.4 µg/dL.

Renal function was assessed using urinary albumin-to-creatinine ratio (UACR), serum creatinine, blood urea and estimated glomerular filtration rate (eGFR). Glycaemic status was evaluated using glycated haemoglobin (HbA1c).

Variables

The primary outcome variable was fasting early morning serum cortisol concentration. Independent variables included glycaemic control (HbA1c), urinary albumin-to-creatinine ratio, duration of diabetes, diabetic retinopathy, peripheral neuropathy, serum creatinine, blood urea and estimated glomerular filtration rate.

Bias Reduction

To minimize potential measurement bias, all blood samples were collected under standardized fasting conditions during the same morning time period. Laboratory investigations were performed using standardized protocols in the institutional central laboratory. Uniform inclusion and exclusion criteria were applied to all participants to reduce selection bias and potential confounding.

Study Size

The study included all eligible patients fulfilling the predefined inclusion and exclusion criteria during the study period. Of the 500 patients screened consecutively, 100 participants satisfied the eligibility criteria and were included in the final analysis.

Statistical Analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), whereas categorical variables were

presented as frequencies and percentages. Comparisons between two groups were performed using the independent Student's *t*-test. Differences among more than two groups were analysed using one-way analysis of variance (ANOVA). Associations between categorical variables were evaluated using the Chi-square test. All statistical tests were two-tailed and a p-value <0.05 was considered statistically significant.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee of Sri Guru Ram Das Institute of Medical Sciences and Research (Approval No. SGRD/IEC/2024-366). Written informed consent was obtained from all participants before enrolment after explaining the study objectives in their preferred language. Participant confidentiality and data privacy were maintained throughout the study in accordance with institutional ethical standards and the principles of the Declaration of Helsinki.

Results

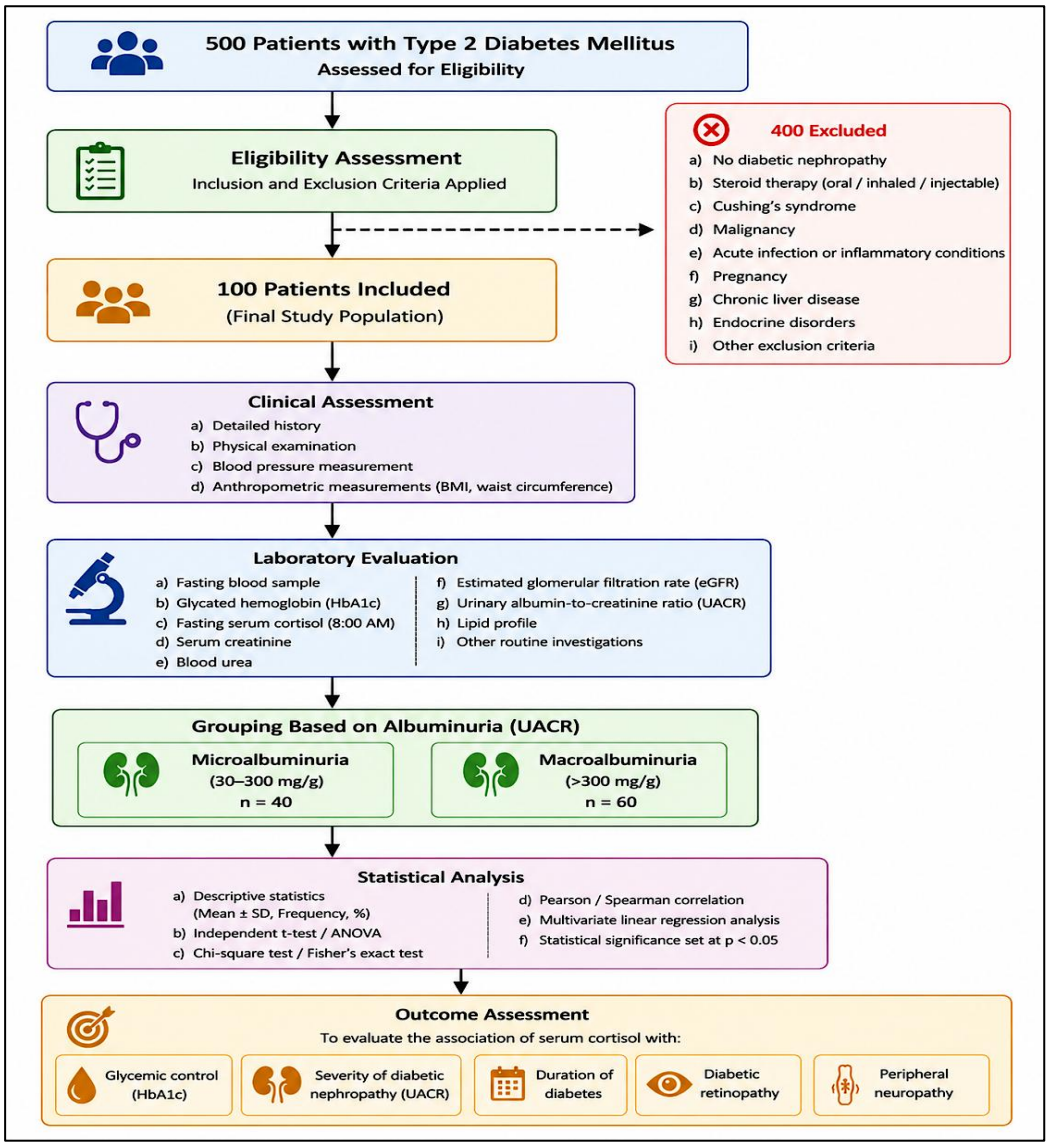

Figure 1: Schematic Representation of the Study Design and Methodological Workflow

Figure 1 illustrates the overall study methodology, including participant screening, eligibility assessment, application of inclusion and exclusion criteria, enrolment of the final study population, clinical and laboratory evaluations, classification based on albuminuria severity, statistical analyses

performed and assessment of the association between fasting serum cortisol and diabetic nephropathy-related clinical outcomes.

The study cohort in Table 1 represents a high-risk population characterized by advanced age and established metabolic syndrome, with 85% of participants aged 51 years or older and a nearly equal gender distribution. Clinical chronicity is evident, as 93% of the patients have a disease duration exceeding five years, significantly predisposing them to microvascular injury. The metabolic burden is further underscored by a 90% prevalence of central obesity and a 65% incidence of advanced hypertension (Stages 1 and 2), which likely act as synergistic drivers for renal decline. Furthermore, the high frequency of cutaneous markers such as Acanthosis Nigricans (67%) and skin tags (46%) serves as a visible surrogate for profound insulin resistance, providing a robust clinical context for the investigation of systemic cortisol as a biomarker of chronic metabolic stress.

Table 1: Baseline Demographic and Clinical Profile of the Study Population (n=100)

Variable	Category	Frequency (n)	Percentage (%)
Age Group (Years)	< 40	5	5.0
	41–50	10	10.0
	51–60	34	34.0
	61–70	25	25.0
	> 70	26	26.0
Gender	Female	51	51.0
	Male	49	49.0
Diabetes Duration	< 5 Years	7	7.0
	5–10 Years	50	50.0
	> 10 Years	43	43.0
Hypertension (AHA)	Normal (<120/80)	15	15.0
	Pre-hypertension	20	20.0
	Stage 1	39	39.0
	Stage 2	26	26.0
Waist-Hip Ratio	Normal	10	10.0
	Abnormal	90	90.0
Cutaneous Markers	Acanthosis Nigricans	67	67.0
	Skin Tags	46	46.0

The biochemical profile reveals in Table 2 with severe metabolic dysregulation and established renal impairment. Glycemic control is notably poor, with 81% of patients exceeding an HbA1c of 8.0%, including a majority (52%) with extreme hyperglycemia (>10%). This is mirrored by advanced nephropathy, where 60% of the participants have progressed to macroalbuminuria and 55% demonstrate a decline in glomerular health (eGFR <90 ml/min/1.73m^2). The systemic impact of this metabolic stress is underscored by a near-universal elevation in serum cortisol levels (96%), alongside significant increases in serum creatinine (63%) and blood urea nitrogen (70%). Collectively, these markers indicate that the study population is characterized by a high burden of uncontrolled diabetes and significant secondary renal deterioration.

Table 2: Biochemical Parameters and Renal Function Metrics

Biochemical Marker	Category/Range	Frequency (n)	Percentage (%)
Glycemic Control (HbA1c)	6.5%–8.0%	19	19.0
	> 8.0%–10.0%	29	29.0
	> 10%	52	52.0
Renal Function (UACR)	Microalbuminuria (30–300 mg/g)	40	40.0
	Macroalbuminuria (> 300 mg/g)	60	60.0
Glomerular Health (eGFR)	> 90 ml/min/1.73m^2	45	45.0
	60–89 ml/min/1.73m^2	31	31.0
	45–59 ml/min/1.73m^2	20	20.0

	< 45 ml/min/1.73m²	4	4.0
Serum Cortisol	Normal (3.7–19.4 µg/dL)	4	4.0
	Elevated (>19.4 µg/dL)	96	96.0
Other Renal Markers	Elevated Creatinine (>1.02 mg/dL)	63	63.0
	Elevated BUN (>17 mg/dL)	70	70.0

The inferential analysis in Table 3 demonstrates that serum cortisol serves as a sensitive indicator of disease progression and metabolic instability in Type 2 Diabetes Mellitus. Statistically significant elevations in cortisol were observed as HbA1c exceeded 10% (p=0.019) and as the duration of diabetes surpassed 10 years (p=0.002), underscoring the impact of chronic glycemic stress on HPA-axis activity. Furthermore, cortisol levels were markedly higher in patients with advanced complications, specifically showing a robust association with macroalbuminuria (p=0.001) and the presence of neuropathy (p=0.001) and retinopathy (p=0.005). These findings confirm that hypercortisolemia is not merely a byproduct of hyperglycemia but is inextricably linked to the severity of microvascular damage and end-organ renal impairment.

Table 3: Inferential Analysis – factors Associated with Serum Cortisol Levels

Independent Variable	Sub-category	Mean Cortisol (±SD)	Statistical Test	p-value
HbA1c Levels	6.5%–8.0%	22.46±2.12	F = 4.116	0.019
	8.0%–10.0%	22.34±2.20		
	>10%	24.05±3.43		
Duration of T2DM	< 5 Years	20.80±1.66	F = 6.380	0.002
	5–10 Years	22.71±2.14		
	> 10 Years	24.29±3.59		
UACR Severity	Microalbuminuria	21.47±1.84	t = 3.40	0.001
	Macroalbuminuria	24.45±3.02		
Retinopathy	Present	24.05±2.98	t = 2.87	0.005
	Absent	22.39±2.78		
Neuropathy	Present	24.29±2.27	t = 5.89	0.001
	Absent	20.86±2.91		

The correlation analysis in Table 4 reveals a statistically significant positive relationship between early morning serum cortisol and all primary markers of metabolic and renal distress. The strongest association was observed with the Urinary Albumin-Creatinine Ratio (r = 0.425, p<0.001) and Duration of Diabetes (r=0.412, p<0.001), indicating that as renal injury progresses and disease chronicity increases, cortisol levels rise proportionately. Furthermore, cortisol exhibited a robust link with glycemic instability (HbA1c: r = 0.385, p<0.001) and a significant, though more moderate, correlation with Blood Urea Nitrogen (r=0.200, p=0.046). Collectively, these results suggest that hypercortisolemia is inextricably linked to the severity of diabetic nephropathy and may serve as a systemic indicator of advanced microvascular damage.

Table 4: Correlation Matrix of Serum Cortisol with Metabolic and Renal Variables

Variable	Correlation Coefficient (r)	p-value
UACR (> 30 mg/g)	0.425	< 0.001
Duration of Diabetes	0.412	< 0.001
HbA1c (> 6.5%)	0.385	< 0.001
Blood Urea Nitrogen	0.200	0.046

Discussion

Cortisol, one of the most important human glucocorticoids, is a powerful modulator of physiological systems, including the central nervous system. When initially discovered in the 1950s, it was applied to rheumatic patients with remarkable results (14). Subsequent experiments expanded the scope and validated powerful effects in anti-inflammation, anti-allergy and anti-shock.

Our observation that cortisol levels were significantly higher in patients with macroalbuminuria than in those with microalbuminuria (24.45±3.02 vs. 21.47±1.84 μg/dL, p=0.001) is consistent with previous studies reporting significantly higher morning and afternoon cortisol levels in patients with microalbuminuria compared with normoalbuminuric controls (11). Furthermore, a dose–response relationship has been demonstrated between cortisol levels and the severity of albuminuria, with higher cortisol concentrations being positively associated with increasing albuminuria and conferring a 3.39-fold and 8.40-fold higher risk of microalbuminuria and macroalbuminuria, respectively, in the highest cortisol quartile (10).

The biological plausibility of these findings is supported by the multifactorial effects of cortisol on renal physiology. Persistent hypercortisolemia promotes insulin resistance, oxidative stress, endothelial dysfunction and activation of the renin–angiotensin–aldosterone system, all of which contribute to glomerular hyperfiltration, podocyte injury and progressive disruption of the glomerular filtration barrier. These pathophysiological alterations facilitate urinary albumin leakage and accelerate the transition from early to advanced diabetic nephropathy. Therefore, elevated serum cortisol may represent not only a marker of physiological stress but also an active participant in the progression of diabetic kidney disease (15).

The positive correlation observed between cortisol and HbA1c (r=0.385) is consistent with previous findings demonstrating that higher serum cortisol is associated with lower Time in Range (TIR) and is negatively correlated with pancreatic function indicators, including HOMA-β and the insulinogenic index (12). This metabolic dysregulation is further supported by evidence showing that increased cortisol levels are associated with higher fasting plasma glucose and HbA1c in patients with diabetes. Additionally, higher cortisol quartiles have been associated with a 1.26-fold increase in the odds of prevalent Type 2 Diabetes, reinforcing the role of cortisol in the development and progression of metabolic syndrome (16).

Cortisol-induced impairment of glucose metabolism provides a plausible explanation for this association. Sustained elevations in cortisol stimulate hepatic gluconeogenesis, suppress peripheral glucose uptake and reduce pancreatic β-cell function, thereby aggravating chronic hyperglycaemia. Persistent exposure to hyperglycaemia subsequently enhances oxidative stress, advanced glycation end-product formation and low-grade inflammation, creating a vicious cycle that further worsens metabolic control and promotes diabetic microvascular injury (10).

Our study identified significantly elevated cortisol levels in patients with retinopathy (24.05±2.98 μg/dL) and neuropathy (24.29±2.27 μg/dL), which is consistent with previous studies reporting an increased risk of both non-proliferative and proliferative diabetic retinopathy among patients with elevated cortisol levels (10). Furthermore, a significant association between the total number of diabetic complications, mean 24-hour cortisol levels and diabetes duration has been reported previously, supporting our finding that cortisol levels increase with longer disease duration and may reflect the cumulative physiological stress associated with long-standing diabetes (17).

The association between elevated cortisol and diabetic microvascular complications observed in the present study further suggests that HPA-axis dysregulation may reflect the cumulative burden of chronic metabolic stress rather than isolated disturbances in glucose homeostasis. Since diabetic retinopathy, neuropathy and nephropathy share common pathogenic mechanisms involving endothelial dysfunction, chronic inflammation and microvascular ischemia, increasing cortisol concentrations may serve as an integrated indicator of widespread microvascular damage across multiple organ systems (18).

Collectively, these studies validate our results by demonstrating that hypercortisolemia is inextricably linked to poor glycemic control, prolonged disease duration and the progression of microvascular complications. The evidence provided by different researchers confirms that

even cortisol levels within the upper-normal range can be predictive of renal deterioration, supporting our conclusion that serum cortisol is a valuable biomarker for risk stratification in diabetic nephropathy (11, 12, 17).

An important observation in the present study is that serum cortisol demonstrated significant associations with several independent indicators of disease severity, including albuminuria, duration of diabetes, glycaemic status, retinopathy and neuropathy. Unlike conventional renal biomarkers that primarily reflect established kidney injury, cortisol may provide additional information regarding the systemic neuroendocrine response accompanying chronic metabolic stress. Consequently, assessment of fasting morning serum cortisol could complement routine biochemical investigations and assist clinicians in identifying patients who may benefit from intensified surveillance and early therapeutic intervention (10).

The majority of studies found no statistically significant difference in early morning blood cortisol between CKD patients and healthy controls (19-21).

However, a significant subset of studies reported a negative correlation between eGFR and morning cortisol, meaning cortisol levels rose as kidney function declined (22-25). High morning cortisol was more frequently observed when CKD co-existed with other stressors like heart failure or hypertension (13, 24, 25). Although cortisol measurement is not currently incorporated into routine diabetic nephropathy assessment, the present findings suggest that it may have potential value as an adjunctive biomarker when interpreted alongside HbA1c, UACR and eGFR. Because serum cortisol estimation is widely available and relatively inexpensive in most tertiary-care laboratories, its incorporation into future risk-prediction models deserves further investigation. Longitudinal studies are warranted to determine whether persistent elevations in cortisol precede deterioration in renal function or simply reflect established disease severity. Ultimately, our findings suggest that the HPA axis may serve as a crucial mediator in the vicious cycle of metabolic and renal decline. Rather than viewing cortisol solely as a stress-response hormone, clinical practice should begin to recognize its potential as a predictive biomarker for microvascular vulnerability in Type 2 Diabetes.

Conclusion

The present study demonstrates that elevated fasting early morning serum cortisol levels are significantly associated with poor glycaemic control and greater severity of diabetic nephropathy in patients with Type 2 Diabetes Mellitus. Higher cortisol concentrations were observed in patients with macroalbuminuria, prolonged duration of diabetes, diabetic retinopathy and peripheral neuropathy, suggesting that activation of the hypothalamic–pituitary–adrenal axis is closely linked with progressive metabolic dysfunction and microvascular complications. Furthermore, the significant positive correlations between serum cortisol, urinary albumin-to-creatinine ratio, glycated haemoglobin and duration of diabetes indicate that serum cortisol may serve as a useful adjunctive biomarker for identifying patients at increased risk of renal disease progression.

The findings of this study support the potential clinical utility of fasting morning serum cortisol as an additional marker for risk assessment when interpreted alongside established indicators such as urinary albumin excretion and renal function parameters. Early identification of patients with increased cortisol levels may facilitate closer monitoring, individualized management strategies and timely interventions aimed at slowing the progression of diabetic kidney disease and reducing the burden of long-term complications.

Nevertheless, these findings should be interpreted in light of certain limitations. The cross-sectional design does not permit causal inference between elevated cortisol levels and the development or progression of diabetic nephropathy. In addition, the study was conducted at a single tertiary care centre with a relatively small sample size, which may limit the generalizability of the findings to populations with different ethnic, socioeconomic and healthcare backgrounds. Serum cortisol was measured only once in the early morning and therefore diurnal variations in cortisol secretion were not assessed. Moreover, although stringent eligibility criteria were applied, the influence of residual confounding factors such as psychological stress, sleep disturbances, lifestyle factors and

other endocrine variables cannot be completely excluded.

Future multicentre prospective studies involving larger and more diverse populations are needed to validate these findings and determine whether serial assessment of serum cortisol improves prediction of diabetic nephropathy beyond conventional renal biomarkers. Overall, the present study provides evidence that fasting early morning serum cortisol is associated with the severity of diabetic nephropathy and supports its potential role as a complementary biomarker for risk stratification in patients with Type 2 Diabetes Mellitus.

Abbreviations

eGFR: Estimated Glomerular Filtration Rate, ESRD: End-Stage Renal Disease, HbA1c: Glycated Hemoglobin, HOMA-β: Homeostatic Model Assessment of Beta-Cell Function, HPA Axis: Hypothalamic-Pituitary-Adrenal Axis, SPSS: Statistical Package for the Social Sciences, T2DM: Type 2 Diabetes Mellitus, TIR:Time in Range, UACR: Urinary Albumin-to-Creatinine Ratio

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Author Contributions

Akash Bawa, Prabhjot Kaur Gill: Conceived and Designed the Study, Interpreted the Data, Drafted the Manuscript, Aneesha Chhibber, Sahil Attri: Data Collection, Data Management, Raman Kumar Sharma, Jasmine Kaur: Critically Reviewed the Manuscript for Important Intellectual Content, Approved the Final Version for Publication. All authors read and approved the final manuscript.

Conflict of Interest

The authors declare that they have no financial or personal relationships that could inappropriately influence or bias the results and conclusions presented in this work.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration of Artificial Intelligence (AI) Assistance

AI tools were used only for minor language editing. All research content is the authors' own. The authors used OpenAI's ChatGPT (GPT-5.5) to assist in preparing the graphical layout and wording of Figure 1. The scientific content, study design, data interpretation and final version of the figure were carefully reviewed, verified and approved by the authors, who take full responsibility for its accuracy.

Ethics Approval

Ethical clearance for this study was formally granted by the Institutional Ethics Committee of SGRDIMSR (SGRD/IEC/2024-366) on 29 July 2024. Written informed consent was obtained from all participants prior to their enrolment in the study.

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