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A STUDY ON THE CORRELATION OF DIABETIC RETINOPATHY AND NEPHROPATHY WITH GLYCEMIC STATUS

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ABSTRACT

Background: Diabetes mellitus is a global epidemic with a projected prevalence of over 783 million people by 2045. Microvascular complications, such as diabetic retinopathy (DR) and nephropathy (DN), are significant contributors to the disease burden, leading to vision loss and end-stage renal disease. Chronic hyperglycemia plays a key role in their pathogenesis by triggering vascular damage, oxidative stress, and inflammation. Glycemic control, as measured by HbA1c, is a pivotal determinant of DR and DN progression, yet the complex interplay between these complications and glycemic status warrants further investigation. **Methods:** This cross-sectional study was conducted at a tertiary care hospital over three months, including 25 diabetes patients aged ≥18 years. Exclusion criteria included hypertension, renal replacement therapy, and pregnancy. DR severity was classified via fundus examination, while DN was assessed using urine protein-creatinine ratio (PCR) and estimated glomerular filtration rate (eGFR). HbA1c was used to categorize glycemic status into good (<7%), moderate (7–8%), and poor control (>8%). Descriptive statistics, correlation analysis, and multivariate logistic regression were performed to evaluate associations between glycemic control, DR, and DN. **Results:** The mean age was 55.4 years, with 60% females. Mean HbA1c was 10.48% (SD ± 2.58), indicating poor glycemic control. DR was present in 60% of participants, predominantly in mild to moderate stages. Albuminuria (PCR ≥0.2) was noted in 92%, and 72% were in CKD stages 3–5. A weak correlation was found between HbA1c and CKD stage (r=0.08). Urine PCR showed a weak negative correlation with CKD stage (r=-0.217). **Conclusion:** The study highlights a high prevalence of diabetic retinopathy and nephropathy in individuals with poor glycemic control. Although glycemic control plays a central role, weak correlations suggest other contributing factors such as hypertension and systemic inflammation. Early detection and integrated management are essential to mitigate the burden of these complications.

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INTRODUCTION

Diabetes mellitus, a chronic metabolic disorder characterized by hyperglycemia, is a leading cause of morbidity and mortality globally. The International Diabetes Federation estimates that by 2045, over 783 million people will be living with diabetes, reflecting a concerning rise in disease prevalence worldwide [(1)]. Among the myriad complications associated with diabetes, microvascular complications such as diabetic retinopathy (DR) and diabetic nephropathy (DN) are significant contributors to the burden of disease. These complications result from prolonged hyperglycemia and are pivotal in diminishing the quality of life in affected individuals [(2)].

Diabetic retinopathy is a progressive disorder of the retina, leading to vision impairment and eventual blindness if left untreated. It arises from damage to retinal microvasculature due to chronic hyperglycemia, causing increased vascular permeability, capillary occlusion, and neovascularization [(3)]. Similarly, diabetic nephropathy, characterized by albuminuria, reduced glomerular filtration rate, and progressive kidney damage, is a leading cause of end-stage renal disease globally. Persistent hyperglycemia in diabetes triggers glomerular hyperfiltration, oxidative stress, and inflammatory pathways, which exacerbate renal damage [(4)].

The role of glycemic control, often measured by glycated hemoglobin (HbA1c), in the pathogenesis and progression of DR and DN is well established. Studies demonstrate a strong correlation between suboptimal glycemic status and the risk of developing microvascular complications. The Diabetes Control and Complications Trial (DCCT) and its follow-up, the Epidemiology of Diabetes Interventions and Complications (EDIC) study, show the importance of achieving and maintaining near-normal glycemic levels to mitigate these complications [(5)]. Despite this, the prevalence of DR and DN remains high, even in individuals with moderate glycemic control, indicating a complex interplay of factors in disease progression [(5)]. Understanding the correlation between glycemic status and the development of DR and DN is critical for optimizing management strategies in diabetic patients. While the association between hyperglycemia and microvascular complications has been extensively studied, variations in the progression and severity of DR and DN across individuals with similar glycemic levels highlight the need for further investigation. Comprehensive studies assessing glycemic control in relation to the concurrent occurrence of these complications are limited [(6)], and the mechanistic pathways linking hyperglycemia to simultaneous retinal and renal damage warrant exploration. This study highlights the relationship between glycemic control and microvascular complications.

This study aims to elucidate the correlation between glycemic status and the prevalence of diabetic retinopathy and nephropathy. By identifying the patterns and strength of these associations, this research will provide valuable insights into the interplay between systemic glycemic control and the microvascular complications of diabetes. The findings have the potential to inform clinical practice, emphasizing tailored interventions for glycemic management to prevent or mitigate these debilitating complications.

AIM

- To evaluate the presence of nephropathy and retinopathy in patients with long-standing diabetes mellitus
- To correlate the severity of retinopathy to that of diabetic nephropathy with the glycemic status of the patient.

MATERIALS AND METHODS

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This cross-sectional study was conducted in a tertiary care hospital to evaluate the correlation between diabetic retinopathy, diabetic nephropathy, and glycemic status. The study included 25 diagnosed cases of diabetes mellitus of either sex, who consulted the general medicine outpatient clinic during the study period. Data collection was performed between August 2024 and October 2024.

Inclusion and Exclusion Criteria

The inclusion criteria for participation were as follows:

1. Patients with a confirmed diagnosis of diabetes mellitus.
2. Adults aged 18 years and above.
3. Patients who provided informed written consent for the study.

Exclusion criteria included:

1. Patients under 18 years of age.
2. Pregnant females, to eliminate confounding factors associated with pregnancy-induced changes in glycemic and vascular physiology.
3. Patients diagnosed with hypertension, as it could independently influence microvascular complications.
4. Patients undergoing renal replacement therapy (e.g., dialysis), as advanced renal disease could obscure the correlation between glycemic control and diabetic nephropathy.
5. Individuals who declined to participate or did not provide informed consent.

Procedures and Assessments

Ophthalmic Examination for Diabetic Retinopathy

A comprehensive ophthalmic evaluation was performed for all participants. This included:

1. **Visual acuity assessment** using Snellen's chart.
2. **Fundus examination** via direct and indirect ophthalmoscopy and, when indicated, fundus photography to identify and classify diabetic retinopathy.
3. Diabetic retinopathy was categorized based on standardized fundoscopic findings, as per the International Clinical Diabetic Retinopathy Disease Severity Scale. The classification included mild non-proliferative diabetic retinopathy (NPDR), moderate NPDR, severe NPDR, and proliferative diabetic retinopathy (PDR).

Diagnosis of Diabetic Nephropathy

The presence of diabetic nephropathy was evaluated using biochemical markers, specifically:

1. **Urine protein-creatinine ratio (PCR):** Measured to assess albuminuria, a hallmark of diabetic nephropathy. PCR values were interpreted in accordance with clinical guidelines for diagnosing albuminuria.
2. **Estimated glomerular filtration rate (eGFR):** Calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, based on serum creatinine levels. A reduced eGFR (<60 mL/min/1.73 m^2) was indicative of impaired renal function.

Glycemic Status Evaluation

Glycemic control was assessed using the glycated hemoglobin (HbA1c) levels, which reflect the average blood glucose levels over the previous three months. HbA1c levels were categorized as follows:

- <7%: Good glycemic control.
- 7–8%: Moderate glycemic control.
- >8%: Poor glycemic control.

Data Collection and Analysis

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The statistical analysis evaluated the correlation between glycemic status (HbA1c levels), diabetic retinopathy (DR), and diabetic nephropathy (DN). Glycemic status was categorized into good (<7%), moderate (7–8%), and poor control (>8%). DR severity was classified using the International Clinical Diabetic Retinopathy Disease Severity Scale, while DN was identified through urine protein-creatinine ratio and eGFR (<60 mL/min/1.73 m^2). Descriptive statistics summarized data, with means or medians used for continuous variables and frequencies for categorical variables. Correlation analysis (Pearson or Spearman) assessed the relationship between HbA1c levels and DR/DN severity. ANOVA or Kruskal-Wallis tests compared HbA1c across DR severity groups, and chi-square tests analyzed associations between glycemic status and DR/DN. Multivariate logistic regression determined the independent effect of glycemic status on DR/DN, adjusting for confounders. Odds ratios (ORs) and 95% confidence intervals (CIs) were reported, with a p-value <0.05 considered statistically significant. Statistical analyses were performed using SPSS version 26.0

RESULTS

The study included a total of 25 participants, with an average age of 55.4 years (SD ± 11.23). Of these, 40% were male (n=10), and 60% were female (n=15). The mean HbA1c level among the participants was 10.48% (SD ± 2.58), indicating generally poor glycemic control across the study population. These results highlight the predominance of female participants and the high prevalence of poor glycemic control, which may contribute to the development of diabetic complications.

Table 1: Demographic Characteristics

PARAMETER	NO OF SUBJECTS n=25	PERCENTAGE (%)
Age in years (Mean (SD))	55.4 (11.23)	
Male	10	40
Female	15	60
HbA1c (Mean (SD))	10.48 (2.58)	

Diabetic retinopathy was absent in 40% of participants (n=10), while 40% (n=10) had mild non-proliferative diabetic retinopathy (NPDR). Moderate NPDR was observed in 12% (n=3), and severe NPDR in 8% (n=2). No participants had proliferative diabetic retinopathy (PDR). These findings suggest that while diabetic retinopathy was prevalent in 60% of participants, most cases were in the early stages (mild to moderate NPDR), with fewer severe cases observed.

Table 2: Prevalence of Diabetic Retinopathy

DIABETIC RETINOPATHY	NO OF SUBJECTS n=25	PERCENTAGE (%)
ABSENT	10	40
MILD NPDR	10	40
MODERATE NPDR	3	12
SEVERE NPDR	2	8
PDR	0	0

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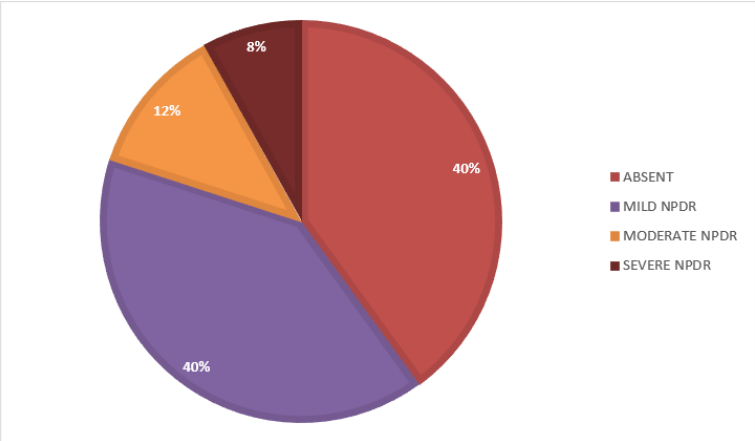
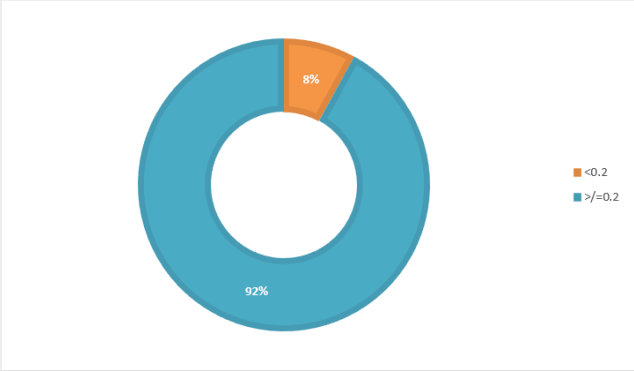


Figure

The majority of participants (92%, n=23) had a urine PCR of ≥0.2, indicating significant albuminuria, while only 8% (n=2) had a PCR <0.2. This suggests a high prevalence of renal impairment in the study cohort, aligning with the expected burden of diabetic nephropathy in poorly controlled diabetes.

Table 3: Urine Spot Protein-Creatinine Ratio (PCR)

URINE SPOT PCR	NO OF SUBJECTS n=25	PERCENTAGE (%)
<0.2	2	8
>/=0.2	23	92



Figure

The distribution of CKD stages showed that 8% of participants (n=2) were in stage 1, 12% (n=3) in stage 2, 40% (n=10) in stage 3, 32% (n=8) in stage 4, and 8% (n=2) in stage 5. This indicates that a majority of participants had moderate-to-severe CKD (stages 3–5), reflecting significant renal involvement likely exacerbated by poor glycemic control and advanced diabetic nephropathy.

Table 4: Distribution of Chronic Kidney Disease (CKD) Stages

CKD STAGE	NO OF SUBJECTS n=25	PERCENTAGE (%)
1	2	8
2	3	12
3	10	40
4	8	32
5	2	8

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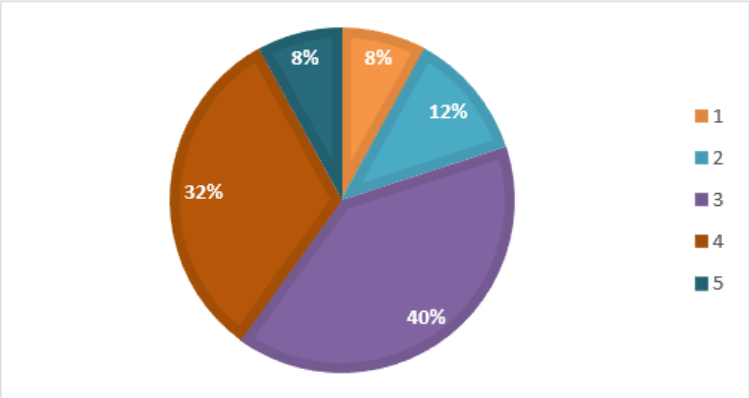

Figure

Correlation analysis revealed a weak positive correlation between HbA1c and CKD stage (r=0.08), suggesting minimal direct association between glycemic status and renal impairment in this cohort. Similarly, HbA1c and urine PCR showed a negligible correlation (r=0.011). Interestingly, a weak negative correlation was observed between urine PCR and CKD stage (r=-0.217), indicating that higher albuminuria levels may not directly correspond with CKD progression.

Table 5: Correlation Analysis

	Correlation	**P-Value**
HbA1c-Urine PCR	0.011	0.958
HbA1c-CKD Stage	0.08	0.704
Urine PCR-CKD Stage	-0.217	0.297

Fundus (DR severity) and Urine PCR (Albuminuria): Correlation = 0.48 This indicates a moderate positive correlation between diabetic retinopathy severity and albuminuria, suggesting that more severe DR is associated with higher urine protein levels. Fundus (DR severity) and CKD Stage: Correlation = 0.80. This represents a strong positive correlation, indicating that more severe DR is closely associated with advanced CKD stages (more severe diabetic nephropathy). Urine PCR and CKD Stage: Correlation = 0.15. This shows a weak positive correlation, implying that albuminuria levels are not strongly tied to CKD stage progression in this dataset.

Table 6: Correlation Between DR (Fundus) and DN Indicators

Variable 1	**Variable 2**	**r Value**	**p Value**
Fundus (DR Severity)	Urine PCR	0.479	0.136
Fundus (DR Severity)	CKD STAGE	0.8	**0.003**
Urine PCR	CKD STAGE	0.148	0.663

DISCUSSION

The findings of this study highlight the substantial burden of microvascular complications, including diabetic retinopathy (DR) and nephropathy, in a cohort of patients with poorly controlled diabetes mellitus. The results demonstrate that poor glycemic control, reflected by a mean HbA1c of 10.48% (SD ± 2.58), plays a critical role in the prevalence of these complications, albeit with varying degrees of severity and progression.

Diabetic retinopathy was present in 60% of the study participants, with most cases being in the mild to moderate non-proliferative stage (52%). Severe NPDR was observed in a smaller

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proportion (8%), and no cases of proliferative diabetic retinopathy (PDR) were noted. These findings are consistent with earlier studies. For example, the UK Prospective Diabetes Study (UKPDS) demonstrated a 35% prevalence of retinopathy in newly diagnosed diabetes patients, which increased significantly with rising HbA1c levels over time [(6)]. Similarly, the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) showed that patients with poor glycemic control (HbA1c >10%) had an approximately 60% likelihood of developing DR within a decade of diabetes diagnosis [(7)]. The absence of PDR in this cohort may suggest shorter diabetes duration or adequate management of associated risk factors in some patients, consistent with findings from the DCCT, which reported delayed progression of DR with intensive glycemic control [(5)].

The prevalence of nephropathy was marked by significant albuminuria, with 92% of participants exhibiting a urine protein-creatinine ratio (PCR) of ≥0.2. This finding reflects widespread renal impairment, aligning with the ADVANCE study, which found a strong association between poor glycemic control (mean HbA1c of 8.3%) and increased albuminuria (8). Similarly, in the United States National Health and Nutrition Examination Survey (NHANES), nearly 40% of patients with diabetes exhibited evidence of diabetic nephropathy, with microalbuminuria being the most common feature (9). The CKD stage distribution in this study revealed that a majority of participants (72%) were in moderate-to-severe stages (stages 3–5), suggesting advanced renal dysfunction. These findings parallel the findings of the Chronic Renal Insufficiency Cohort (CRIC) study, which demonstrated that the combination of poor glycemic control and elevated albuminuria is associated with faster progression to end-stage renal disease (ESRD)[(10)].

Interestingly, the correlation analysis revealed a weak positive correlation between HbA1c and CKD stage (r=0.08) and a negligible correlation between HbA1c and urine PCR (r=0.011). These findings are consistent with studies suggesting that hyperglycemia alone may not fully account for nephropathy progression. For instance, in the Joslin Diabetes Center's 50-year Medalist Study, a subgroup of patients maintained normoalbuminuria despite decades of poorly controlled diabetes, suggesting that genetic, inflammatory, or vascular factors may play a role [(11)]. Similarly, the weak negative correlation between urine PCR and CKD stage (r=-0.217) observed in this study reflects findings from the RIACE (Renal Insufficiency And Cardiovascular Events) study, which found that CKD progression was not always proportional to albuminuria levels in patients with diabetes [(12)]. The strong correlation between DR severity (Fundus) and CKD stage suggests that these complications may progress together in severity, likely influenced by shared pathophysiological mechanisms such as vascular damage and inflammation. The moderate correlation between DR severity and albuminuria (Urine PCR) further supports the interconnectedness of these microvascular complications. The weak correlation between Urine PCR and CKD stage aligns with findings that albuminuria does not always predict CKD progression, reinforcing the multifactorial nature of diabetic nephropathy.

Several large-scale studies have reported similar trends in microvascular complications. The DCCT/EDIC trials emphasized the critical role of intensive glycemic control in delaying the onset and progression of both DR and DN, but highlighted residual risks even with well-controlled HbA1c, indicating the influence of other factors such as systemic inflammation and endothelial dysfunction [(5)]. Furthermore, the ACCORD Eye study noted that for every 1% reduction in HbA1c, there was a 13% reduction in the risk of developing DR, reinforcing the importance of glycemic control while also suggesting the need for multifactorial interventions, including lipid and blood pressure management [(13)].

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The results emphasize the need for an integrated approach to managing diabetes, focusing not only on glycemic control but also on regular screening and early detection of microvascular complications. Comprehensive ophthalmic evaluations and urine PCR measurements should be routine in diabetic care to identify retinopathy and nephropathy in their early stages. Furthermore, the weak correlation between HbA1c and microvascular complications in this study suggests that individualized management strategies, addressing factors such as blood pressure control and lipid management, are equally crucial for preventing disease progression. This study was limited by its small sample size (n=25), which may have reduced the statistical power to detect stronger associations between glycemic control and complications. Additionally, other confounding factors, such as duration of diabetes, comorbidities (e.g., hypertension), and medication use, were not accounted for, which may have influenced the outcomes. Future studies with larger, more diverse cohorts and detailed clinical profiling are needed to validate these findings and explore additional factors contributing to diabetic complications. This study reveal the high prevalence of diabetic retinopathy and nephropathy in patients with poor glycemic control, with most cases occurring in the early to moderate stages. The weak correlations between HbA1c and microvascular complications highlight the multifactorial nature of these conditions and the need for comprehensive management strategies. Early detection, regular monitoring, and individualized treatment approaches are essential to mitigate the burden of diabetes-related microvascular complications and improve patient outcomes.

CONCLUSION

This study highlights the significant burden of diabetic retinopathy (DR) and nephropathy (DN) in patients with poor glycemic control. The prevalence of DR, observed in 60% of participants, predominantly in the mild to moderate stages, highlights the importance of early ophthalmic screening to prevent vision-threatening complications. Similarly, the high prevalence of albuminuria (92%) and advanced CKD stages (72% in stages 3–5) points to widespread renal involvement, emphasizing the critical need for regular renal function monitoring in diabetic patients. The weak correlations between glycemic control (HbA1c) and the progression of DR and DN suggest that while hyperglycemia is a major risk factor, other factors such as hypertension, inflammation, and genetic predisposition also contribute significantly to microvascular disease. These findings support the necessity of a multifactorial approach to diabetes management, incorporating glycemic, blood pressure, and lipid control along with early screening and individualized care plans. Given the study's limitations, including a small sample size and lack of data on diabetes duration and comorbidities, further research with larger cohorts is needed to validate these findings and explore additional risk factors influencing microvascular complications. Nevertheless, the study reinforces the need for proactive and comprehensive diabetes management to mitigate the substantial burden of diabetic complications and improve patient outcomes.

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