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Original Article

A Cross-Sectional Study to Evaluate the Relationship of Diabetic Retinopathy with Chronic Kidney Disease in Diabetic Patients in a Tertiary Care Hospital

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ABSTRACT

Introduction: *Diabetes mellitus (DM) and chronic kidney disease (CKD) are common chronic diseases globally and in Bangladesh. Diabetic retinopathy worsens with CKD. This study examines their relationship in diabetic patients at a tertiary hospital.* ***Methods & Materials:*** *This is a cross-sectional observational study conducted at the Department of Ophthalmology, Dhaka Medical College Hospital from Aug 2017 to Oct 2018. A total of 100 diabetic patients were included in the study. Following informed written consent, a physical examination, and relevant investigations were done. In all cases, ethical issues were maintained properly, and collected data were analyzed by SPSS 23.* ***Result:*** *Among 100 participants, the mean±SD age was 57.3±11.1 years (Range 35-85 years) 74% were male and 26% were female. Mean±SD value of HbA1c was (7.4 ±1.8), eGFR was 42.2 ± 32.3mmol/L. Out of 100 patients, 66 had diabetic retinopathy, among them 42 had NPDR and 24 had PDR. Among them 39 CKD patients and 27 0f non CKD patients had DR. CKD patients were found 8 in stage 3B, 10 in stage IV and 32 in stage V. Stage IIIB, stage IV, and stage V had 2, 6, and 31 diabetic retinopathy respectively. Diabetic retinopathy had a positive correlation with low eGFR and CKD stages (p-value <0.001).* ***Conclusion:*** *This study finds that diabetic retinopathy is linked to CKD severity, increasing from stage IIIB to V. While age and sex showed no significant differences, hemoglobin, blood sugar levels, HbA1c, serum creatinine, and eGFR varied significantly with retinopathy.*

Keywords: *Diabetic Retinopathy, Chronic Kidney Disease, Diabetes mellitus, eGFR*

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INTRODUCTION

Chronic kidney disease (CKD), previously termed chronic renal failure, refers to an irreversible decline in renal function that progresses over the years. When renal replacement therapy (RRT) becomes essential for survival (CKD stage 5), it is termed end-stage renal disease (ESRD). CKD poses significant social and economic burdens, with CKD stage 3–5 (eGFR < 60) affecting approximately 5–7% of the population, predominantly those aged 65 and older. The prevalence is higher in individuals with hypertension, diabetes, and vascular disease, warranting targeted screening [1]. Diabetic retinopathy (DR), a leading cause of blindness, is prevalent in around 40% of diabetics, with sight-threatening forms affecting up to 10%. It is more common in type 1 diabetes, where up to 90% of patients develop proliferative DR (PDR) after 30 years [2]. CKD and DR share risk factors like poor glycemic control and hypertension, and both conditions exhibit similar microvascular lesions in the glomerular and retinal vessels. Clinical markers such as urine albumin-to-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR) help assess renal function. CKD is often associated with DR, with some studies indicating that albuminuria is a stronger predictor of DR than eGFR alone [3]. High UACR, a marker of endothelial dysfunction, affects both kidney and retinal microvasculature. Some studies have linked increased UACR levels to DR, while others suggest CKD is associated with DR primarily in the presence of albuminuria [4,5]. Satchell and Tooke highlighted that UACR is not only a key marker for

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CKD but also closely linked to DR progression [6]. The relationship between eGFR and DR remains debated, though some reports indicate that lower eGFR is associated with DR severity [7]. A study by Chen et al. found both elevated UACR and reduced eGFR predict DR, with UACR having a greater impact [8]. DR is a growing global health issue, particularly in emerging Asian nations such as India and China [9,10]. CKD has also become a major public health concern, contributing to premature morbidity and mortality [11]. The severity of CKD correlates with the presence of retinopathy, as retinal microvascular disease reflects renal microvascular pathology, independent of diabetes [12]. The Atherosclerosis Risk in Communities (ARIC) study supported this association [13]. Diabetes mellitus and hypertension are the primary risk factors for CKD and DR, with disease duration influencing progression. Regular monitoring of CKD patients with DR is essential for timely intervention, and improving quality of life [14]. CKD-related microvascular defects, exacerbated by hypertension and diabetes, manifest as severe hypertensive retinopathy due to nitrogenous waste accumulation [12]. Impaired vision in CKD patients increases fall risk, hampers daily activities, and contributes to sleep disorders and depression. Visual rehabilitation can enhance their quality of life. The renal-retinal microvascular link has been recognized for over 50 years. Pathologic, clinical, and epidemiologic studies confirm shared mechanisms between renal and retinal disease, particularly in diabetes and hypertension [15]. Retinal microvascular abnormalities, increasingly prevalent with age, correlate with renal function decline and CKD onset, both contributing to cardiovascular complications [16]. Early detection and preventive strategies are essential given the severe outcomes of CKD and DR, including ESRD and blindness. Retinal microvasculature is easily accessible for non-invasive assessment, offering potential for early CKD detection. Some longitudinal studies have explored associations between retinal vessel caliber and CKD incidence, though results vary [12]. Many studies focus on diabetic populations with limited ethnic diversity and lack concurrent renal-retinal data or albuminuria measures [17].

METHODS & MATERIALS

This cross-sectional study was conducted at the Department of Ophthalmology, Dhaka Medical College, Hospital, Dhaka, from August 2017 to October 2018. Male and female DM patients of OPD and indoor DMCH were considered as the study population. A total of 100 patients were selected as study subjects by non-probability purposive sampling. Subjects were screened through history, clinical examination, and laboratory investigations and diagnosed as having chronic kidney disease and diabetic retinopathy. Data was collected in a questionnaire after completion of history, and physical examination. A blood sample was sent for fasting glucose, 2HABF blood glucose, HbA1C, and Serum creatinine and then the patient was sent for a color fundus photograph of both eyes. Statistical analyses were carried out by using the Statistical Package for Social Sciences version 23.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. The chi-square test, fisher exact test, and Bonferroni test were used to analyze the categorical variables, shown with cross-tabulation. ANOVA test was used to analyze the continuous variables, shown with mean and standard deviation. Spearman's correlation coefficients were used to test the relationship between the groups. P values <0.05 were considered statistically significant. The research protocol was approved by the "Research Review Committee" & the "Ethical Committee" of DMCH, Dhaka.

Inclusion criteria:

- Known cases of diabetes mellitus (male and female)
  a. DM with CKD
  b. DM without CKD

Exclusion criteria:

- Nondiabetic patient
- Active infection
- Dense Cataract patient
- Pregnant women
- Cases of reversible renal failure.

RESULTS

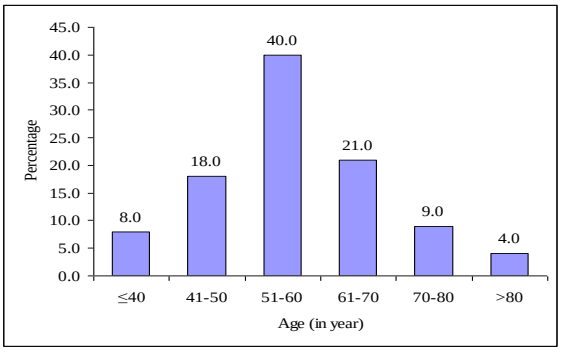

Figure – 1: The bar diagram shows the age distribution of the study patients (*n*=100)

The bar diagram shows that the majority (40.0%) of patients belonged to age 51-60 years. The mean age was found 57.3±11.1 years with a range from 35 to 85 years.

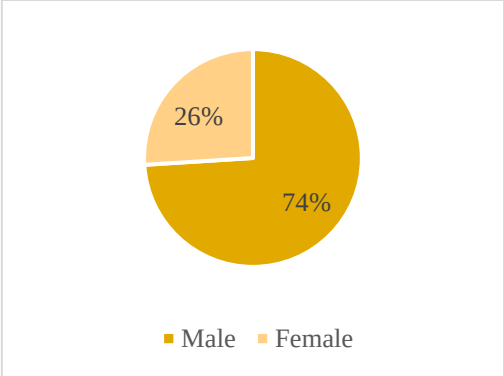

Figure – 2: Pie chart shows the sex distribution of the study patients (*n*=100)

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The pie chart shows that almost three-fourths (74.0%) of patients were male and 26(26.0%) patients were female. Male female ratio was 2.8:1.

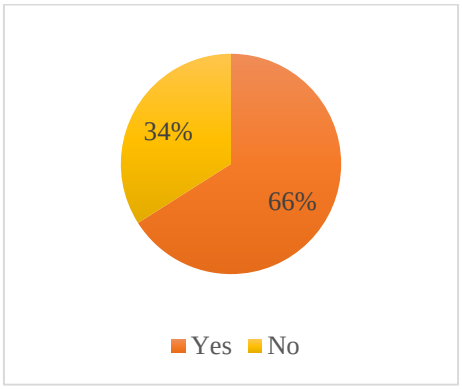

Figure – 3: Pie chart shows diabetic retinopathy of the study patients (*n*=100)

The pie chart shows that 66(66.0%) patients had diabetic retinopathy and 34(34.0%) had not diabetic retinopathy.

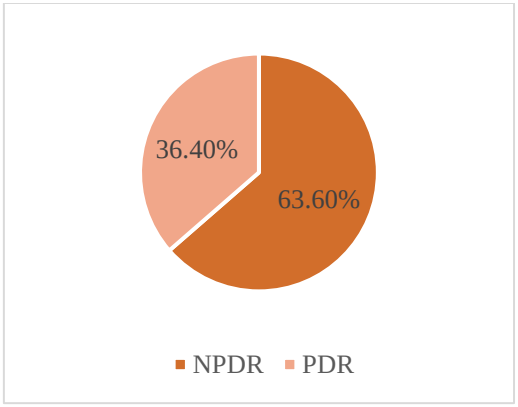

Figure – 4: Pie chart shows PDR and NPDR of the study patients (*n*=66)

The pie chart shows that 42(63.6%) patients were found NPDR and 24(36.4%) were PDR.

Table – I: Association between diabetic retinopathy with CKD (*n*=100)

Diabetic retinopathy	CKD (n=50)		Non-CKD (n=50)		p-value
	n	%	n	%	
Yes	39	78.0	27	54.0	0.011[s]
No	11	22.0	23	46.0	

s= significant
p-value reached from the chi-square test

Table I shows that 39(78.0%) patients were found with diabetic retinopathy in CKD and 27(54.0%) in non-CKD. The difference was statistically significant (p<0.05) between the two groups.

Table – II: Relation between PDR and NPDR with CKD (*n*=66)

Diabetic retinopathy	CKD (n=39)		Non-CKD (n=27)		p-value
	n	%	n	%	
PDR	13	33.3	11	40.7	0.539[ns]
NPDR	26	66.7	16	59.3	

ns= not significant
p-value reached from the chi-square test

Table II shows no significant relationship between PDR and NPDR among the group.

Table – III: Relationship of age with diabetic retinopathy in CKD and non-CKD patients (*n*=100)

	CKD		Non CKD		p value
	DR (n=39)	No DR (n=11)	DR (n=27)	No DR (n=23)	
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Age (years)	57.9±9.7	56.5±6.8	60.5±14.3	52.7±8.7	0.085[ns]

ns= not significant
p-value reached from ANOVA t-test

Table III shows DR has no significant relationship with age between the two groups.

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Table – IV: Relation of sex with diabetic retinopathy in CKD and non-CKD patients (*n*=100)

Sex	CKD				Non-CKD				p-value
	DR (n=39)		No DR (n=11)		DR (n=27)		No DR (n=23)		
	n	%	n	%	n	%	n	%	
Male	33	84.6	9	81.8	19	70.4	13	56.5	0.091[ns]
Female	6	15.4	2	18.2	8	29.6	10	43.5	

ns= not significant
p-value reached from the Fisher exact test

Table IV Shows no significant relationship between DR with sex among the group.

Table – V: Relationship of smoking and anemia with diabetic retinopathy in CKD and non-CKD patients (*n*=100)

	Diabetic retinopathy					p-value
	Yes (n=66)			No (n=34)		
	N	n	%	n	%	
Smoker						
CKD	18	13	76.5	5	29.4	0.583[ns]
Non CKD	13	9	64.3	4	28.6	
Anaemia						
CKD	46	38	82.6	8	17.4	0.040[s]
Non CKD	19	11	57.9	8	42.1	

s= significant, ns= not significant
p-value reached from the chi-square test

Table V shows that 76.5% of the smokers among the CKD patients developed DR. Smoking was not statistically significant to develop DR among the group. 82.6% of patients with CKD who had anemia developed DR and anemia had a significant relationship to develop DR among the groups.

Table – VI: relationship of duration of diabetes mellitus with diabetic retinopathy in CKD and non-CKD patients (*n*=100)

	CKD		Non CKD		p value
	DR (n=39)	No DR (n=11)	DR (n=27)	No DR (n=23)	
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Duration of diabetes mellitus (years)	17.8±7.0	13.1±5.9	19.3±4.7	7.5±6.1	0.001[s]

s= significant
p-value reached from ANOVA t-test

Table VI shows a significant relationship between DR with duration of diabetes among the group.

Table – VII: Relationship of laboratory report with diabetic retinopathy in CKD and non-CKD patients (*n*=100)

Laboratory report	CKD		Non-CKD		p-value
	DR (n=39)	No DR (n=11)	DR (n=27)	No DR (n=23)	
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Hemoglobin (gm/dl)	9.5±1.7	11.3±2.0	12.1±1.5	12.4±1.9	0.001[s]
Fasting blood glucose (mmol/l)	9.1±3.3	5.9±0.8	7.0±2.2	5.9±1.4	0.001[s]
Blood sugar 2 hours after breakfast (mmol/l)	14.3±5.1	9.4±1.8	10.9±4.3	9.3±3.4	0.001[s]
HbA1C (%)	8.1±2.0	6.6±0.3	7.5±1.5	6.3±1.6	0.001[s]
Serum creatinine (mg/dl)	6.6±4.3	5.4±3.6	1.1±0.4	1.6±1.8	0.001[s]
eGFR (ml/min/1.73m^2)	11.9±8.7	11.5±4.4	73.5±26.3	78.6±29.1	0.001[s]

s= significant
p-value reached from ANOVA t-test

Table VII shows a significant relationship of DR with hemoglobin%, fasting blood glucose, blood sugar 2 hours after breakfast, HbA1C, serum creatinine, and eGFR.

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Table – VIII: Laboratory report and duration of diabetes mellitus with diabetic retinopathy in CKD and non-CKD patients (Bonferroni test)

	CKD DR vs CKD no DR	CKD DR vs non CKD DR	CKD DR vs non CKD no DR	Non CKD DR vs non CKD no DR
Hemoglobin (gm/dl)	1.000^{ns}	0.001^{s}	0.001^{s}	1.000^{ns}
Fasting blood glucose (mmol/l)	0.049^{ns}	0.402^{ns}	0.001^{s}	0.046^{s}
Blood sugar 2 hours after breakfast (mmol/l)	0.341^{ns}	1.000^{ns}	0.025^{s}	0.338^{ns}
HbA1C (%)	1.000^{ns}	1.000^{ns}	0.109^{ns}	0.018^{s}
Serum creatinine (mg/dl)	1.000^{ns}	0.001^{s}	0.001^{s}	0.150^{ns}
eGFR (ml/min/1.73m^2)	1.000^{ns}	0.001^{s}	0.001^{s}	1.000^{ns}

s= significant, ns= not significant
p-value reached from the Bonferroni test

Table – IX: Association between diabetic retinopathy with CKD stage (*n*=50)

CKD stage	Diabetic retinopathy				p-value
	Yes (n=39)		No (n=11)		
	N	%	N	%	
Stage 3B	2	5.1	6	54.5	
Stage 4	6	15.4	4	36.4	0.001^{s}
Stage 5	31	79.5	1	9.1	

s= significant
p-value reached from the chi-square test

Table IX shows that 31(79.5%) patients were found with CKD stage 5 in diabetic retinopathy and 1(9.1%) without diabetic retinopathy. The difference was statistically significant (p<0.05) between the two groups.

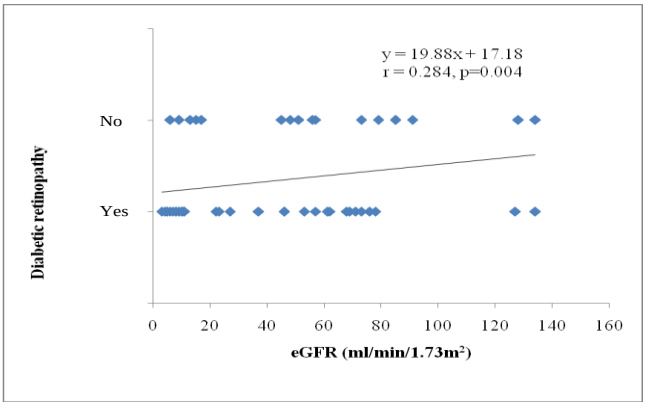

Figure – 5: Scatter diagram showing the relation between eGFR and diabetic retinopathy

Scatter diagram showing positive correlation (r=0.284; p=0.004) between eGFR and diabetic retinopathy.

DISCUSSION

The present study observed that 66(66.0%) patients were found with diabetic retinopathy among 100 patients. Rouf et al. found 68% of the respondent population had some form of retinopathy [18]. The present study shows that 34.4% of patients had proliferative retinopathy and 63.6% of patients had nonproliferative diabetic retinopathy. Rouf et al. found 63.7% found nonproliferative diabetic retinopathy and 31.8% found proliferative diabetic retinopathy in the respondent population [18]. Bansal et al. showed out of the 500 diabetics 28.12% (45/160) had proliferative diabetes retinopathy and 71.88% (115/160) had nonproliferative diabetes retinopathy which is almost similar to our study [19]. The current study observed that 39(78.0%) patients were found with diabetic retinopathy in CKD and 27(54.0%) in non-CKD. The difference was statistically significant (p<0.05) between the two groups. Alghaythi et al. observed that the overall prevalence of diabetes in patients with chronic kidney disease is 69% as indicated, among them 73% with retinopathy [20]. Liew et al. showed there was a significant trend for stronger associations of retinopathy with increasing severity of CKD [21]. Lee et al. showed a direct association between DR and CKD [22]. Mathew et al. (2016) showed in CKD patients 50.9% had NPDR and 19% had PDR. There was a statistically significant relationship between CKD with DR. Present study shows CKD patients who had DR age mean±SD was 57.9±9.7 years, whereas it was 56.5±6.8 years who had no DR. Non-CKD patients who had DR age mean±SD was 60.5±14.3 years, whereas it was 52.7±8.7 years who had no DR. So age has no significant relation to developing DR among the groups. Bansal et al. showed that the mean age of the patients without DR was 54 years while the mean age of the patients having DR was found to be 66 years [19]. In this study mean±SD duration of development of diabetic retinopathy in CKD patients was 17.8±7.0 years, whereas in CKD patients it was 19.3±6.1 years. There was a significant relation of duration to development of DR in both the group. Bansal et al. showed an increasing prevalence of DR with increasing duration of DM [19]. The prevalence of DR was seen to be 9.44% when the duration of diabetes detected was less than 5 years and was 76.47% in patients with diabetes of more than 20 to 25 years. There is an increasing prevalence of

DR with an increase in the duration of DM. All patients having diabetes of more than 25 years were found to have retinopathy. This study observed that the mean hemoglobin was found to mean±SD, 9.5±1.7 gm/dl in CKD patients who had DR. In non-CKD patients who developed DR mean±SD, 12.1±1.5 gm/dl which was statistically significant. Behar et al. showed the mean hemoglobin level in case and control group was 12.15±1.50 gm/dl and 12.73±1.38 gm/dl, respectively (p<0.001) was significant [23]. The mean fasting blood glucose was found 9.1±3.3 mmol/l who had DR whereas in non CKD patient it was 7.0±2.2 mmol/l. In between the group Hb% had a significant relationship to develop DR. The mean blood sugar 2 hour after breakfast found in CKD patient was 14.3±5.1 mmol/l who had DR whereas in non CKD patient it was 10.9±4.3 mmol/l. In both groups of patients there was a significant relationship to the development of DR. Solomon et al. showed in a large and consistent set of observational studies and clinical trials documented the association of poor glucose control and retinopathy [24]. In this study HbA1c mean was 8.1±2.0% in CKD patients and the mean was 7.5±1.5% in CKD patients who had DR and these relations were significant in both groups. Zhang et al. showed that the prevalence of DR increased markedly from less than 1.6% to 8.3% and 7.8%, with minimum levels of 7.03 mmol/L for FPG and 6.4% for HbA1c ($p < 0.01$) which is similar in our study [25]. In the non-CKD group mean serum creatinine was 1.1±0.4 mg/dl and in the CKD group mean serum creatinine was 6.6±4.3 mg/dl who had developed DR. eGFR was calculated in the CKD group to classify the stages of CKD. Mean eGFR was found 11.9±8.7ml/min/1.73m^2 in the CKD patient who had DR. Mean eGFR was found 1.1±0.4ml/min/1.73m^2 in the non CKD patient who had DR. Serum creatinine and eGFR had statistically significant relationship to develop DR among the group. Bello et al. study showed the median eGFR in patients with retinopathy was 32.4 mL/min/1.73 m^2 compared to 34.7 mL/min/1.73 m^2 in patients without retinopathy (p<0.001) [26]. Grunwald et al. study showed 188(39.0%) patients were found eGFR ≤29 ml/min per 1.73m^2 and eGFR had a significant relationship to develop DR. Man et al. also showed a significant relationship between eGFR with DR [7, 27]. In this study 31(79.5%) patients were found diabetic retinopathy in stage 5 and 1(9.1%) in without diabetic retinopathy. Again 6 people were found without retinopathy while 2(5.1%) were found with retinopathy in stage 3B CKD. The difference was statistically significant (p<0.05) between the two groups. Man et al. showed when eGFR was analyzed categorically, impaired renal function and CKD were associated with the presence of DR when compared to normal renal function in multivariable models with 95% confidence [7]. In DR severity analyses, CKD showed significant associations with moderate and severe DR (P = 0.04). These associations persisted when eGFR was analyzed continuously (P = 0.04). Our results suggest that lower levels of eGFR were associated with the presence and severity of DR. Alghaythi et al. study showed that diabetic patients were associated with more advanced stage of CKD (p value <0.05) [20]. Rodríguez-Poncelas et al. showed CKD was associated with a higher rate of DR 95% [CI] [2]. This association was lower in patients with eGFR levels 44 to 30 mL/min/1.73m2 [OR], 95% confidence interval [CI]. Grunwald et al. showed greater severity of retinopathy was associated with lower estimated glomerular filtration rate (eGFR) after adjustment for traditional and non-traditional risk factors [27].

Limitations of The Study

This study was conducted in a single hospital in Dhaka, limiting the generalizability of the findings to the entire country. Most patients were referred from various medical specialties such as Endocrinology, Nephrology, and Internal Medicine for ophthalmological evaluation in suspected cases, which may lead to variations compared to a population-based randomized study. Additionally, the short study duration and relatively small sample size make it challenging to capture the true epidemiology.

CONCLUSION

This study concludes that diabetic retinopathy is associated with chronic kidney disease, with its severity and prevalence increasing as CKD progresses from stage IIIB to stage V. No statistically significant difference was observed between the two groups in terms of age and sex distribution of diabetic retinopathy. However, significant differences were found between the groups concerning hemoglobin levels, fasting blood sugar, postprandial blood sugar (2 hours after breakfast), HbA1c, serum creatinine, and eGFR concerning diabetic retinopathy. However, in the absence of large randomized controlled trials, these findings must not be inferred from the general population.

RECOMMENDATION

A larger prospective cohort study with an extended follow-up period is recommended to strengthen the findings. This study serves as an eye-opener for healthcare professionals managing CKD and DM patients, as well as for policymakers in Bangladesh, emphasizing the need for improved diagnostic facilities and nationwide DR treatment strategies. Implementing an early inpatient risk detection protocol requires proper training and assignment of doctors to ensure adherence. Additionally, establishing a locally tailored clinical practice guideline for early detection and timely treatment of DR is crucial. The results of this study can also serve as a valuable reference for future research assessing the impact of such measures on patient outcomes in the Nephrology and Endocrinology departments.

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