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Original Research Article

Urinary Albumin Excretion Rate and Retinopathy in Adults with Prediabetes: A Prospective Observational Study

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Abstract

Background: Microvascular injury may begin before type 2 diabetes is diagnosed, but the relationship between early renal albumin leak and retinal abnormalities in prediabetes is poorly defined.

Aim: To evaluate urinary albumin excretion (UAE), retinopathy prevalence, and the renal–retinal association in adults with prediabetes.

Methods: In this prospective observational real-world study, 107 adults with prediabetes underwent standardized clinical and biochemical assessment, two 24-hour urine collections for UAE, and dilated retinal evaluation. Mean UAE was categorized as normal (<30 mg/24 h) or moderately increased (30–299 mg/24 h); an exploratory three-stratum analysis used <15, 15–29.9, and ≥30 mg/24 h. Logistic regression examined retinopathy in relation to UAE, HbA1c, systolic blood pressure, and age.

Results: Mean age was 48.1 ± 9.9 years and 48.6% were men. Moderately increased UAE was present in 20 (18.7%) and retinopathy in 14 (13.1%); 11 cases were mild NPDR and 3 moderate NPDR. Median UAE was 37.8 mg/24 h in participants with retinopathy versus 13.9 mg/24 h without retinopathy (P<0.001). Retinopathy prevalence increased from 1.7% at UAE <15 mg/24 h to 17.9% at 15–29.9 mg/24 h and 40.0% at ≥30 mg/24 h (P for trend <0.001). Retinopathy occurred in 40.0% with moderately increased UAE versus 6.9% with UAE <30 mg/24 h (unadjusted OR 9.00, 95% CI 2.66–30.48). After adjustment, moderately increased UAE remained associated with retinopathy (adjusted OR 10.39, 95% CI 2.39–45.18; P=0.002); a sensitivity model yielded an adjusted OR of 5.39 per doubling of UAE.

Conclusion: Prediabetes was accompanied by a measurable burden of early renal and retinal microvascular abnormalities, with a strong graded association between UAE and retinopathy. UAE may help identify a higher-risk prediabetes phenotype warranting closer vascular risk assessment and prospective validation.

Keywords: Prediabetes; Urinary Albumin Excretion; Microalbuminuria; Retinopathy; Microvascular Disease; HbA1c; Renal–Retinal Association.

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Introduction

Prediabetes is increasingly recognized as a clinically meaningful intermediate state of dysglycaemia rather than a metabolically neutral interval between normal glucose regulation and diabetes. The American Diabetes Association currently defines prediabetes by a fasting plasma glucose of 100–125 mg/dL, a 2-hour plasma glucose of 140–199 mg/dL during a 75-g oral glucose tolerance test, or glycated haemoglobin (HbA1c) of 5.7–6.4%, provided diagnostic criteria for diabetes are not met [1]. These categories identify heterogeneous phenotypes that differ in insulin resistance, beta-cell dysfunction, hepatic glucose production, postprandial glucose handling, adiposity, and cardiovascular risk. Longitudinal evidence has shown that prediabetes confers a substantial probability of progression to type 2 diabetes, but also that regression to normoglycaemia occurs in a meaningful proportion of individuals, emphasizing that the biological state is dynamic [2]. The conventional clinical focus has therefore been prevention of overt diabetes.

However, accumulating evidence indicates that tissue injury attributed to chronic hyperglycaemia may begin below the diagnostic glucose thresholds used to label diabetes.

The microcirculation may be particularly vulnerable during this transition. Endothelial dysfunction, oxidative stress, impaired nitric oxide bioavailability, low-grade inflammation, advanced glycation, altered autoregulation, and capillary rarefaction have all been described in persons with prediabetes [3]. Importantly, these processes are systemic rather than organ specific. In the Maastricht Study, prediabetes was associated with generalized microvascular dysfunction assessed in distinct vascular beds, supporting the concept that the prediabetic state can be accompanied by measurable microvascular abnormalities before diabetes is formally diagnosed [4]. Such observations challenge a simple threshold model in which microvascular complications appear only after glucose crosses a diagnostic boundary. Instead, risk appears to rise along a continuum influenced by cumulative glycaemic exposure, blood pressure, adiposity, lipid abnormalities, smoking, and individual susceptibility.

The retina provides a unique opportunity to observe microvascular injury directly. Retinal microaneurysms, haemorrhages, and other diabetic-retinopathy-like lesions have been reported among adults with impaired glucose regulation. In the Diabetes Prevention Program, retinopathy was identified in 7.9% of participants who had impaired glucose tolerance but had not developed diabetes, compared with 12.6% among those who had progressed to diabetes by the time of retinal assessment [5]. Indian data are particularly relevant because of the high cardiometabolic burden and relatively early onset of dysglycaemia in South Asian populations. In a study of Asian Indians with prediabetes, Rajalakshmi and colleagues reported retinopathy in 6.3%; most lesions were mild non-proliferative diabetic retinopathy (NPDR), and higher HbA1c was associated with greater retinopathy risk [6].

A systematic review including 24 studies and 8,759 participants with prediabetes found reported retinopathy prevalence ranging from 0.3% to 14.1%, with a median of 7.1%, and concluded that the available evidence supports an excess retinal-lesion burden in prediabetes despite considerable methodological heterogeneity [7]. A subsequent meta-analysis also found greater retinal disease burden in prediabetes or hyperglycaemia than in normoglycaemic controls, although estimates varied according to retinal outcome definitions and study design [8]. Most recently, a 2025 systematic review and meta-analysis of microvascular complications in prediabetes reinforced that retinal abnormalities are demonstrable within the ADA-defined HbA1c range and highlighted the need to reconsider the assumption that microvascular screening is relevant only after diabetes develops [9].

The kidney represents another vascular bed in which early injury may be detectable before overt diabetes. Urinary albumin excretion (UAE), whether measured as timed albumin excretion or approximated by a urinary albumin-to-creatinine ratio, reflects glomerular barrier permeability and is also influenced by systemic endothelial function and haemodynamic stress. Population-based evidence from the KORA F4 Study demonstrated associations between prediabetes and microalbuminuria, reduced kidney function, and chronic kidney disease phenotypes even in persons without known diabetes [10]. Prospective data from the RENIS cohort further showed that prediabetes predicted glomerular hyperfiltration and higher urinary albumin excretion over follow-up, suggesting that glomerular haemodynamic changes may be initiated during the prediabetic period [11]. In an Indian longitudinal cohort, urinary albumin-to-creatinine ratio was also associated with subsequent progression from prediabetes to diabetes and with the likelihood of reversal to normoglycaemia, linking low-grade albuminuria to the broader metabolic trajectory [12]. Collectively, these data indicate that albumin excretion should not be viewed exclusively as a late manifestation of established diabetic kidney disease.

The clinically important unanswered question is whether early renal and retinal abnormalities cluster in the same individuals with prediabetes. In established diabetes, albuminuria and retinopathy frequently coexist because both reflect cumulative microvascular injury; however, the strength of this renal–retinal relationship during prediabetes is far less clearly characterized. Demonstrating concordance at this stage could have practical value. A simple renal marker such as UAE might help identify a subgroup with a broader microvascular phenotype who could benefit from more intensive cardiovascular risk-factor management and selective retinal assessment. Conversely, absence of such an association would argue against extrapolating diabetes-stage screening paradigms backward into prediabetes. The present prospective observational study therefore evaluated urinary albumin excretion and retinal findings in adults with prediabetes treated in a real-world tertiary-care setting in Jaipur, India. The primary objective was to determine the prevalence of moderately increased UAE and retinopathy and to quantify their association. Secondary objectives were to examine the gradient of retinopathy across UAE strata and to assess whether any observed relationship persisted after

accounting for glycaemia, systolic blood pressure, and age.

Materials and Methods

This prospective observational real-world study was conducted in the Department of General Medicine, National Institute of Medical Sciences & Research, Jaipur, Rajasthan, India, and included 107 consecutive adults with prediabetes enrolled during the predefined recruitment period. Adults aged 30–70 years were eligible when they had no previous diagnosis of diabetes and fulfilled at least one current biochemical criterion for prediabetes: fasting plasma glucose 100–125 mg/dL, 2-hour plasma glucose 140–199 mg/dL following a 75-g oral glucose tolerance test, or HbA1c 5.7–6.4%; participants meeting diagnostic criteria for diabetes on study testing were excluded. Additional exclusions were known chronic kidney disease with estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m², urinary albumin excretion ≥300 mg/24 h, active urinary tract infection, fever or acute systemic illness, decompensated heart failure, pregnancy, known primary glomerular disease, gross haematuria, and circumstances expected to cause transient albuminuria such as strenuous exercise immediately before urine collection.

Demographic characteristics, smoking status, family history of diabetes, anthropometry, and medication history were recorded at enrolment. Height and weight were measured without shoes and body mass index was calculated as kg/m²; waist circumference was measured midway between the lowest rib and iliac crest. Blood pressure was recorded after at least 5 minutes of seated rest, and the average of two measurements was used. Fasting venous samples were analysed for plasma glucose, HbA1c, serum creatinine, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides using routine standardized laboratory methods. eGFR was calculated from serum creatinine using a contemporary creatinine-based equation. Each participant completed two 24-hour urine collections separated by a short interval under written collection instructions; urinary albumin was quantified by an immunochemical method and the arithmetic mean of the two valid collections was used as the participant's UAE. UAE <30 mg/24 h was classified as normal and 30–299 mg/24 h as moderately increased, consistent with the clinically established albuminuria range used in contemporary kidney-risk guidance [13].

For exploratory dose-response analysis, UAE was additionally divided into <15, 15–29.9, and 30–299 mg/24 h. Retinal assessment was performed after pharmacological pupillary dilatation by an ophthalmologist, using dilated fundus examination supplemented by fundus photography when required for documentation. Retinopathy was graded according to the International Clinical Diabetic Retinopathy Disease Severity Scale as no apparent retinopathy, mild NPDR, moderate NPDR, severe NPDR, or proliferative diabetic retinopathy [14]. The principal outcome was the presence of any retinopathy in relation to UAE; secondary outcomes included retinopathy severity and the UAE–retinopathy dose-response pattern. Continuous variables were examined for distributional form and are presented as mean ± standard deviation when approximately symmetric and median with interquartile range (IQR) when skewed; categorical variables are presented as number and percentage. Between-group comparisons used Welch's t test for approximately normally distributed continuous variables, the Mann–Whitney U test for skewed variables, and Fisher's exact test for categorical variables. Spearman correlation quantified the relationship between UAE and HbA1c. Unadjusted odds ratios (ORs) with 95% confidence intervals (CIs) were estimated for retinal outcomes across UAE strata. A multivariable logistic regression model was fitted with retinopathy as the dependent variable and clinically selected covariates consisting of moderately increased UAE, HbA1c expressed per 0.1% increment, systolic blood pressure per 10-mmHg increment, and age per 10-year increment. Because only 14 retinal events were observed, this model was considered exploratory, no automated variable selection was used, and coefficient precision was interpreted from the width of the 95% CIs rather than from P values alone. A sensitivity model replaced the binary albuminuria term with log2-transformed continuous UAE so that its OR represented the change in odds of retinopathy per doubling of UAE. Model discrimination was summarized by the area under the receiver-operating-characteristic curve. All tests were two-sided and $P<0.05$ was considered statistically significant.

Results

All 107 participants were included in the analysis. Mean age was 48.1 ± 9.9 years and 52 (48.6%) were men. Mean HbA1c was 6.05 ± 0.19%, mean systolic blood pressure was 129.3 ± 12.3 mmHg, and mean eGFR was 104.0 ± 9.7 mL/min/1.73 m². Moderately increased UAE was present in 20 participants (18.7%). Retinopathy was identified in 14 (13.1%): 11 had mild NPDR and 3 had moderate NPDR; no severe NPDR or proliferative retinopathy was observed. Participants with retinopathy had higher HbA1c and substantially higher UAE than those without retinopathy, whereas age, body mass index, fasting glucose, 2-hour glucose, and eGFR did not differ significantly (Table 1). Median UAE was 37.8 mg/24 h (IQR 28.8–65.7) in participants with retinopathy

compared with 13.9 mg/24 h (IQR 10.2–17.2) in those without retinopathy (P<0.001). UAE correlated modestly with HbA1c (Spearman ρ=0.284, P=0.003).

Table 1: Clinical and biochemical characteristics according to retinopathy status

Variable	Overall (n=107)	No retinopathy (n=93)	Retinopathy (n=14)	P value
Age, years	48.1 ± 9.9	47.6 ± 9.8	51.6 ± 10.0	0.175
Male sex, n (%)	52 (48.6%)	44 (47.3%)	8 (57.1%)	0.573
BMI, kg/m²	27.0 ± 3.3	26.8 ± 3.1	28.5 ± 4.0	0.139
Systolic blood pressure, mmHg	129.3 ± 12.3	128.6 ± 12.3	133.8 ± 11.4	0.135
Hypertension, n (%)	32 (29.9%)	27 (29.0%)	5 (35.7%)	0.755
Fasting plasma glucose, mg/dL	105.7 ± 11.9	105.9 ± 11.9	104.2 ± 12.1	0.615
2-h plasma glucose, mg/dL	148.7 ± 27.7	148.3 ± 27.4	151.9 ± 30.5	0.682
HbA1c, %	6.05 ± 0.19	6.03 ± 0.18	6.20 ± 0.14	<0.001
eGFR, mL/min/1.73 m²	104.0 ± 9.7	104.4 ± 9.3	101.5 ± 11.9	0.405
Mean 24-h UAE, mg/24 h	14.4 (11.1–21.5)	13.9 (10.2–17.2)	37.8 (28.8–65.7)	<0.001
Moderately increased UAE, n (%)	20 (18.7%)	12 (12.9%)	8 (57.1%)	<0.001
Triglycerides, mg/dL	160.8 (133.0–188.6)	160.8 (133.7–185.3)	171.9 (136.2–214.9)	0.483

Values are mean ± SD, median (IQR), or n (%). P values were obtained with Welch's t test, Mann–Whitney U test, or Fisher's exact test as appropriate.

A clear graded relationship was observed between albumin excretion and retinal abnormalities. Retinopathy was present in 1 of 59 participants (1.7%) with UAE <15 mg/24 h, 5 of 28 (17.9%) with UAE 15–29.9 mg/24 h, and 8 of 20 (40.0%) with UAE 30–299 mg/24 h (P for ordinal trend <0.001; Table 2 and Figure 1). Using the clinical albuminuria threshold, retinopathy occurred in 8/20 (40.0%) participants with moderately increased UAE versus 6/87 (6.9%) among those with UAE <30 mg/24 h, corresponding to an unadjusted OR of 9.00 (95% CI 2.66–30.48; P<0.001). All three cases of moderate NPDR occurred in the moderately increased UAE group.

Table 2: Retinopathy prevalence and severity across urinary albumin excretion strata

UAE stratum	n	Any retinopathy, n (%)	Mild NPDR	Moderate NPDR	OR vs <15 mg/24 h (95% CI)	P value
<15 mg/24 h	59	1 (1.7%)	1	0	Reference	
15–29.9 mg/24 h	28	5 (17.9%)	5	0	12.61 (1.40–113.88)	0.012
30–299 mg/24 h	20	8 (40.0%)	5	3	38.67 (4.42–338.60)	<0.001

Clinical threshold analysis (30–299 vs <30 mg/24 h): OR 9.00 (95% CI 2.66–30.48), P<0.001. Ordinal trend across UAE strata: OR 5.12 per stratum (95% CI 2.21–11.87), P<0.001.

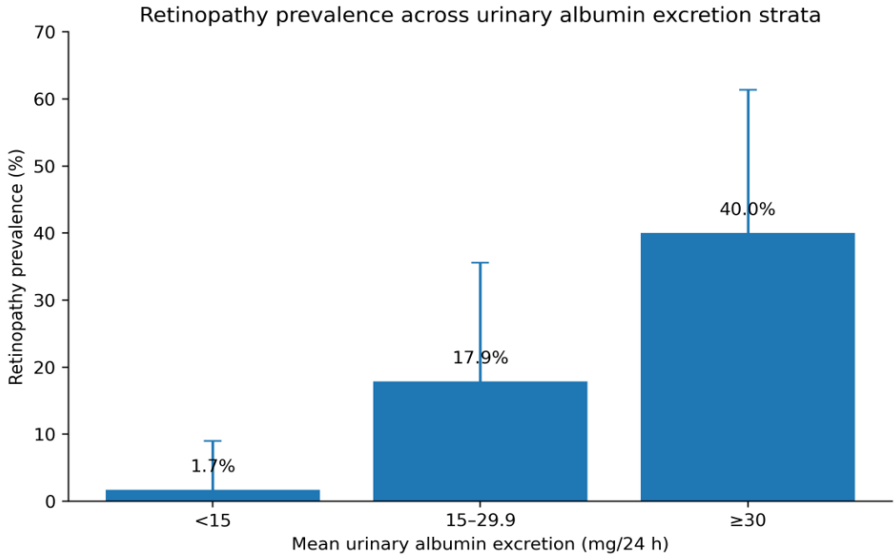


Figure 1: Retinopathy prevalence across mean 24-hour urinary albumin excretion strata. Error bars show Wilson 95% confidence intervals

In exploratory multivariable logistic regression, moderately increased UAE remained strongly associated with retinopathy after adjustment for HbA1c, systolic blood pressure, and age (adjusted OR 10.39, 95% CI 2.39–45.18; P=0.002). HbA1c was independently associated with retinopathy (adjusted OR 2.08 per 0.1% increase, 95% CI 1.29–3.36; P=0.003), as was systolic blood pressure (adjusted OR 1.96 per 10 mmHg, 95% CI 1.04–3.69; P=0.037); age was not independently significant (Table 3 and Figure 2).

The adjusted model had an AUC of 0.839. In the prespecified sensitivity model, each doubling of continuous UAE was associated with an adjusted OR of 5.39 (95% CI 2.20–13.21; P<0.001), with an AUC of 0.894, supporting a graded rather than purely threshold-based relationship.

Table 3: Exploratory logistic regression for presence of retinopathy

Predictor	Unit	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted P value
Moderately increased UAE (30–299 vs <30 mg/24 h)	binary	9.00 (2.66–30.48)	10.39 (2.39–45.18)	0.002
HbA1c	per 0.1%	1.77 (1.22–2.59)	2.08 (1.29–3.36)	0.003
Systolic blood pressure	per 10 mmHg	1.41 (0.89–2.25)	1.96 (1.04–3.69)	0.037
Age	per 10 years	1.53 (0.85–2.76)	1.34 (0.66–2.72)	0.423

Adjusted model included the four prespecified variables shown. AUC=0.839. Sensitivity analysis with log2 UAE: adjusted OR 5.39 per doubling (95% CI 2.20–13.21), P<0.001; AUC=0.894. Estimates are exploratory because only 14 retinal events were available.

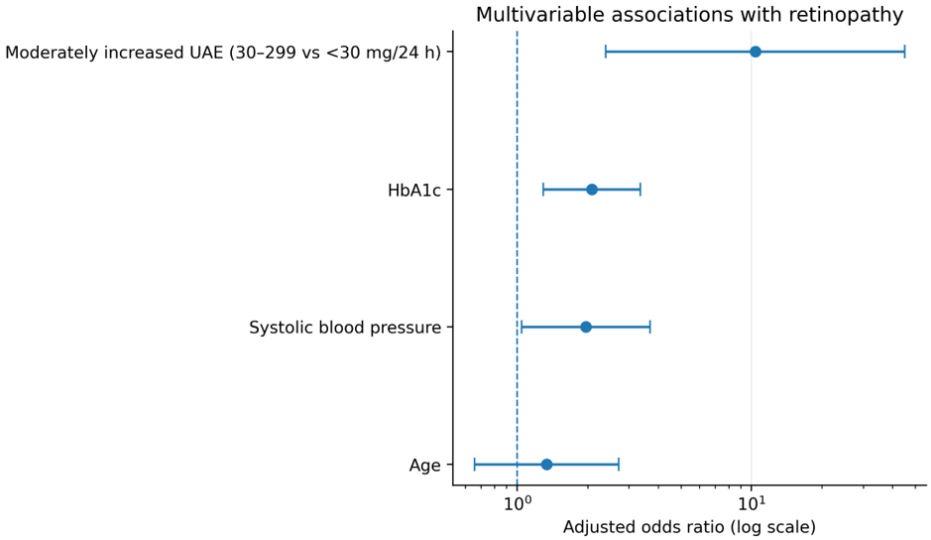


Figure 2: Adjusted odds ratios and 95% confidence intervals for retinopathy in the exploratory multivariable model. The x-axis is logarithmic; the dashed vertical line indicates OR=1

Discussion

The present study identified a clinically important clustering of renal and retinal microvascular abnormalities among adults with prediabetes. Three findings deserve emphasis. First, retinopathy was present in 13.1% of the cohort and was confined to mild or moderate NPDR, indicating that retinal microvascular lesions may be detectable before conventional diagnostic criteria for diabetes are reached. Second, moderately increased UAE was present in 18.7%, and UAE was substantially higher in participants with retinopathy. Third, the association was graded: retinopathy prevalence rose from 1.7% at UAE <15 mg/24 h to 17.9% at 15–29.9 mg/24 h and 40.0% at 30–299 mg/24 h. The renal–retinal relationship persisted in exploratory multivariable analysis after accounting for HbA1c, systolic blood pressure, and age, and a sensitivity analysis using UAE as a continuous log2-transformed variable yielded a similarly strong signal. Taken together, these observations support the concept of a shared microvascular phenotype in a subset of adults with prediabetes rather than two unrelated organ-specific abnormalities.

The observed 13.1% prevalence of retinopathy lies near the upper end of previously reported estimates, but it remains biologically and epidemiologically plausible. In the original Diabetes Prevention Program retinal assessment, retinopathy was found in 7.9% of participants who still had impaired glucose tolerance and in 12.6% of those who had

developed diabetes [5]. In the Asian Indian study by Rajalakshmi et al., retinopathy was documented in 6.3% of 192 individuals with prediabetes; the distribution was predominantly mild NPDR, with a smaller proportion of moderate NPDR and no sight-threatening disease [6]. That severity pattern closely resembles the present findings, although our prevalence was higher. Kirthi et al. reported a median retinopathy prevalence of 7.1% across 24 studies, with estimates ranging from 0.3% to 14.1%, demonstrating substantial heterogeneity related to population selection, glycaemic definitions, retinal imaging methods, and lesion grading [7]. Longer-term Diabetes Prevention Program Outcomes Study data are also informative: approximately two decades after randomization, retinopathy was present in 14% of participants who had not developed diabetes and 24% of those who had developed type 2 diabetes [15]. Thus, our estimate is higher than that reported in some cross-sectional prediabetes cohorts but comparable with the upper range of systematic-review estimates and the long-term burden seen in high-risk individuals. A tertiary-care referral setting, enrichment for cardiometabolic risk, and the use of dilated retinal assessment may all contribute to this difference.

The prevalence of moderately increased UAE was also notable. The 2025 systematic review and meta-analysis of microvascular complications in prediabetes reported nephropathy or albuminuria estimates that varied substantially and generally ranged from approximately 1% to 15%, while emphasizing the scarcity of robust renal studies specifically within prediabetic populations [9]. Our 18.7% prevalence is therefore somewhat higher than the range synthesized in that review. This may reflect the use of timed 24-hour UAE, repeated collections, and a tertiary-care population with a mean systolic blood pressure near 130 mmHg rather than a community-screened cohort. The direction of the finding, however, is consistent with several independent studies. KORA F4 showed that prediabetes was associated with microalbuminuria and kidney dysfunction phenotypes in the general population [10], while Melsom et al. demonstrated prospectively that prediabetes predicted hyperfiltration and higher urinary albumin excretion even among adults who did not have diabetes at baseline [11]. Indian data from Shilpasree et al. similarly documented renal functional abnormalities and albuminuria in prediabetes [16], and Dutta et al. showed that urinary albumin-to-creatinine ratio carried prognostic information for progression from prediabetes to diabetes as well as reversal to normoglycaemia [12]. These converging data make it increasingly difficult to regard low-grade albuminuria in prediabetes as an incidental laboratory finding.

The central contribution of the present analysis is the strength and graded nature of the renal–retinal association. Retinopathy was six times more prevalent in absolute terms among participants with UAE ≥30 mg/24 h than among those below that threshold, and all moderate NPDR cases clustered in the elevated-UAE group. More importantly, the relationship was not restricted to the conventional 30-mg threshold: participants with UAE 15–29.9 mg/24 h already showed a higher retinal-lesion prevalence than those below 15 mg/24 h. This pattern is consistent with recent evidence that microvascular autoregulation may be altered before overt diabetes. In the 2026 Maastricht Study analysis, blood-pressure associations with urinary albumin excretion and retinal arteriolar characteristics were modified by glucose-metabolism status, providing population-level support for coupled glomerular and retinal vascular vulnerability in prediabetes [17]. Although that study evaluated retinal vessel calibre rather than clinical retinopathy, the underlying implication is relevant: the retinal and glomerular circulations may respond abnormally to haemodynamic stress during prediabetes.

Several mechanisms could explain such concordance. Low-grade hyperglycaemia promotes oxidative stress, endothelial activation, inflammatory signalling, and non-enzymatic glycation. In the glomerulus, endothelial glycocalyx injury and disruption of the filtration barrier increase albumin passage; Satchell and Tooke proposed glomerular endothelial dysfunction as a key initiating mechanism linking microalbuminuria with generalized vascular injury [18]. The retinal circulation is likewise dependent on intact endothelial function and autoregulation. Blood-pressure elevation can therefore amplify metabolic injury in both beds, particularly when autoregulatory reserve is impaired. This framework is compatible with our finding that systolic blood pressure retained an independent association with retinopathy and that UAE rose modestly with HbA1c. Importantly, albumin excretion should be interpreted as a continuous vascular-risk marker rather than a binary disease label. In the PREVEND study, progression and regression of UAE occurred in the nondiabetic population and were influenced by cardiovascular and metabolic risk factors [19]. Similarly, the broader diabetes literature emphasizes that microalbuminuria is a risk marker with prognostic meaning but does not, by itself, prove irreversible structural kidney disease when filtration is preserved [20].

The association between albuminuria and retinopathy is well established after diabetes develops, which strengthens the biological plausibility of the present prediabetes findings while also providing a caution against direct

extrapolation. In a real-world cohort of 3,090 adults with type 2 diabetes, Chawla et al. observed a close relationship between diabetic retinopathy and microalbuminuria alongside other modifiable risk factors [21]. Ajoy Mohan et al. also found microalbuminuria to be strongly associated with the occurrence and increasing severity of diabetic retinopathy in type 2 diabetes [22]. Our study extends that renal–retinal concept backward along the glycaemic continuum, but the lesions in prediabetes are milder and less specific. A retinal microaneurysm in a person with prediabetes may reflect glycaemic exposure, hypertension, aging, or another vascular process. The appropriate inference is therefore not that every lesion represents classic diabetic retinopathy in the same etiologic sense as long-standing diabetes, but that the co-occurrence of retinal lesions with rising UAE may identify systemic microvascular susceptibility.

HbA1c provided additional information independent of albuminuria. The adjusted odds of retinopathy increased approximately twofold for each 0.1% rise in HbA1c in this small cohort, an estimate that should be interpreted cautiously because of its magnitude and the limited number of events. Nevertheless, the direction is consistent with prior work. Rajalakshmi et al. found approximately twice the retinopathy risk among Asian Indians with prediabetes and HbA1c ≥6.0% compared with lower HbA1c values [6]. In DPPOS, average HbA1c across long-term follow-up was one of the strongest metabolic correlates of retinopathy across the continuum from prediabetes to diabetes [15]. The independent systolic blood-pressure association is similarly coherent with the Maastricht data [17] and reinforces a practical point: early microvascular risk is not purely glycaemic. Blood pressure, adiposity, lipid exposure, smoking, and duration of metabolic disturbance likely modify the effect of modest hyperglycaemia.

The clinical implications should be framed as risk stratification rather than a recommendation for universal retinal screening of all adults with prediabetes. Current diabetes retinopathy guidance is directed primarily toward people with established diabetes, in whom the benefit and timing of screening are well defined [23].

Evidence in prediabetes is not yet sufficient to mandate an equivalent population-wide program. However, our findings suggest a testable, low-cost strategy: adults with prediabetes who have persistent or reproducible elevation of urinary albumin excretion, particularly when accompanied by higher HbA1c or systolic blood pressure, may represent a subgroup in whom a baseline retinal examination has higher yield than in unselected prediabetes. This concept aligns with the growing recognition that prediabetes can coexist with early kidney injury and chronic kidney disease risk [24]. It would also integrate microvascular assessment with the broader goal of aggressive risk-factor modification rather than treating UAE or retinal lesions in isolation.

This study has several strengths. Participants underwent paired renal and retinal assessment within the same clinical framework; UAE was based on two 24-hour collections rather than a single unconfirmed measurement; retinopathy was graded using an internationally recognized clinical scale; and the analysis examined both a conventional albuminuria threshold and a continuous dose-response relationship. The sensitivity analysis showing increased retinopathy odds per doubling of UAE supports the internal coherence of the principal finding. At the same time, several limitations are important. The study was single-centre and hospital based, limiting generalizability to community populations. Only 14 retinal events occurred; consequently, multivariable estimates have wide confidence intervals and the regression model is exploratory and susceptible to small-sample instability. There was no normoglycaemic control group, so the study cannot quantify excess risk attributable specifically to prediabetes. Although repeated 24-hour urine collections reduce random variation, timed urine remains vulnerable to incomplete collection and day-to-day haemodynamic effects. Retinal lesions were clinically graded, but more sensitive imaging such as optical coherence tomography angiography or quantitative retinal vascular analysis was not incorporated. Hypertension-related and age-related microvascular lesions can resemble early diabetic changes, creating potential phenotypic misclassification. Finally, the prospective recruitment design does not establish temporal direction between albuminuria and retinal lesions because the primary renal and retinal measurements were assessed contemporaneously. Larger multicentre cohorts with normoglycaemic comparators, standardized retinal photography, repeated UAE or UACR confirmation, and longitudinal follow-up are needed to determine whether the renal–retinal phenotype predicts progression to diabetes, worsening retinopathy, chronic kidney disease, or cardiovascular events.

Conclusion

In this cohort of adults with prediabetes, moderately increased urinary albumin excretion and early retinopathy were both common, and retinal abnormalities increased markedly across progressively higher UAE strata. Elevated UAE remained associated with retinopathy after adjustment for glycaemia, systolic blood pressure, and age, while continuous UAE analysis supported a graded relationship. These findings suggest that renal albumin leak may identify a subgroup of

people with prediabetes who already have broader microvascular vulnerability. Confirmation in larger longitudinal cohorts is required before selective retinal screening based on UAE can be recommended routinely.

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