Review Article

Interrelationship between Serum FGF21, GDF15, and Microalbuminuria as Predictive Biomarkers for Early Detection of Diabetic Retinopathy in Type 2 Diabetes Mellitus

Mustakin, M.Kes, Sp.PK[1*]

[1]*Department of Clinical Pathology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia*

Article Info

**Corresponding Author:*
Mustakin, M.Kes, Sp.PK
Department of Clinical Pathology, Faculty of Medicine
Hasanuddin University, Makassar, Indonesia
E-mail: mustakimduharing@ymail.com

Keywords

FGF21, GDF15, Microalbuminuria, Diabetic retinopathy, Biomarkers, Mitochondrial stress, Endothelial dysfunction, Type 2 diabetes mellitus

Abstract

Diabetic retinopathy (DR) is a leading cause of preventable visual loss in type 2 diabetes mellitus (T2DM), yet current screening largely detects disease after microvascular damage has occurred. This review synthesizes emerging evidence that three measurable biomarkers - fibroblast growth factor-21 (FGF21), growth differentiation factor-15 (GDF15), and microalbuminuria -capture complementary dimensions of early DR pathobiology. FGF21 reflects hepatometabolic stress and adaptive signaling via the β-Klotho–FGFR1 axis; GDF15 mirrors mitochondrial/integrated-stress-response activation with systemic effects through the glial cell-derived neurotrophic factor family receptor-α-like (GFRAL) REarranged during Transfection (RET); and microalbuminuria indicates systemic endothelial dysfunction and increased microvascular permeability. We narratively integrate cross-sectional, cohort, and meta-analytic studies in human T2DM populations (excluding type 1 diabetes and animal experiments) and map these signals onto a unified metabolic–renal–retinal framework. Across studies, higher circulating FGF21 and GDF15 associate with DR presence and severity, while microalbuminuria correlates with DR grade and predicts progression independent of glycemic control. We propose a tri-biomarker model in which chronic lipotoxicity and oxidative stress elevate FGF21/GDF15, drive endothelial injury detectable as microalbuminuria, and together forecast early retinal microangiopathy. Translational implications include risk stratification before funduscopic changes, therapy monitoring for metabolic/mitochondrial targets, and development of multimarker algorithms alongside OCTA imaging. To our knowledge, this is the first review to integrate FGF21, GDF15, and microalbuminuria as a coherent predictive axis for early DR in T2DM, highlighting priorities for longitudinal validation and population-specific cut-offs.

Background and Rationale

Diabetic retinopathy (DR) is a leading cause of preventable blindness among patients with type 2 diabetes mellitus (T2DM). Despite advances in retinal screening technologies, most cases of DR are still detected only after clinically apparent microvascular damage has occurred [1,2].

DR is not solely the result of chronic hyperglycemia; rather, it involves a complex pathophysiological process characterized by metabolic stress, mitochondrial dysfunction, neurovascular unit impairment, inflammation, and systemic endothelial injury [3–5,6].

Among circulating biomarkers, fibroblast growth factor-21 (FGF21) and growth differentiation factor-15 (GDF15) have emerged as key indicators of metabolic and mitochondrial stress in T2DM. Elevated FGF21 levels have been associated with the presence and severity of DR [6–10], whereas increased GDF15 concentrations have been consistently observed in patients with T2DM exhibiting microvascular complications, including DR [11–14]. Both biomarkers rise in response to lipotoxicity, oxidative stress, and activation of the integrated stress response (ISR) pathway.

In parallel, microalbuminuria - reflected by an increased urinary albumin-to-creatinine ratio (UACR) - serves as an established marker of systemic endothelial injury and enhanced microvascular permeability. Numerous studies have demonstrated strong associations between albuminuria and both the presence and progression of DR [15–18].

Molecular Basis of Fibroblast Growth Factor-21 (FGF21) in Retinal Microangiopathy

Fibroblast growth factor-21 (FGF21) is a hepatokine that increases in response to fasting, lipotoxic stress, and chronic hyperglycemia, functioning to regulate glucose and lipid metabolism through the β-Klotho–fibroblast growth factor receptor-1 (FGFR1) complex. Under conditions of chronic metabolic stress, elevated reactive oxygen species stimulate FGF21 expression as a compensatory mechanism to maintain mitochondrial homeostasis [6–9].

Consistent elevations in circulating FGF21 have been reported in patients with T2DM across various stages of diabetic retinopathy [6–10]. Mechanistically, FGF21 exhibits a dual role. In the early phase, it acts as a metabolic protector by enhancing insulin sensitivity, increasing adiponectin secretion, and reducing the formation of reactive oxygen species. However, during prolonged metabolic overload, FGF21 resistance develops - characterized by impaired β-Klotho–FGFR1 signaling and paradoxically elevated FGF21 concentrations [9]. This maladaptive state parallels retinal hypoxia, endothelial dysfunction, and oxidative imbalance, which represent hallmark features of early retinal microangiopathy.

Recent meta-analyses strengthen this association. Basir et al. reported that higher circulating FGF21 levels were significantly linked to the risk and severity of diabetic retinopathy, a finding further confirmed by another meta-analysis demonstrating consistent FGF21 elevation across multiple disease stages [11,12]. Biologically, FGF21 is involved in retinal lipid regulation via activation of peroxisome proliferator-activatedreceptor-α (PPAR-α), modulation of oxidative pathways, and suppression of apoptosis related to endoplasmic reticulum stress. Overall, FGF21 reflects both compensatory and maladaptive processes in systemic and retinal microvascular metabolism, underscoring its potential as an early biomarker to identify individuals at increased risk for diabetic retinopathy.

Growth Differentiation Factor-15 (GDF15) and Mitochondrial Stress Signaling in Retinopathy

Growth differentiation factor-15 (GDF15) is a member of the transforming growth factor-β (TGF-β) superfamily and functions as a mitochondrial distress signal. Its expression increases through the integrated stress response (ISR) pathway, primarily via activation of CCAAT/enhancer-binding protein homologous protein (CHOP), activating transcription factor-4 (ATF4), and p53 during oxidative stress or endoplasmic reticulum stress [13–15]. Several clinical studies have consistently reported elevated serum GDF15 levels in patients with T2DM who have diabetic retinopathy [13–15].

Unlike fibroblast growth factor-21 (FGF21), which acts predominantly in peripheral tissues, GDF15 exerts systemic effects through the glial cell-derived neurotrophic factor family receptor-α-like (GFRAL) and REarranged during Transfection (RET) receptor complex located in the brainstem. Activation of the GFRAL–RET pathway modulates inflammation, energy metabolism, and systemic stress responses. High circulating GDF15 levels in patients with T2DM reflect mitochondrial stress and chronic endothelial injury, both of which contribute to retinal microvascular degeneration [16].

At the molecular level, GDF15 helps suppress excessive production of reactive oxygen species (ROS); however, its sustained elevation indicates failure of cellular adaptive mechanisms in the face of prolonged metabolic stress. This positions GDF15 within an adaptive–maladaptive continuum, whereby simultaneous increases in GDF15 and FGF21 occur as the system transitions from metabolic compensation toward progressive vascular injury.

Recent evidence also highlights the involvement of GDF15 in renal microangiopathy, with elevated GDF15 levels observed in T2DM patients exhibiting microalbuminuria. This finding aligns with data showing higher GDF15 concentrations in patients who present with both diabetic retinopathy and impaired renal function [17,18]. Collectively, this dual expression pattern across retinal and renal tissues reinforces the role of GDF15 as a systemic biomarker reflecting microvascular dysfunction in type 2 diabetes.

Microalbuminuria as a Systemic Marker of Endothelial Injury

Microalbuminuria, defined as urinary albumin excretion of 30–300 mg/day, is one of the earliest markers of microvascular dysfunction in T2DM [19]. This condition reflects increased permeability of the glomerular capillary wall and indicates the presence of systemic endothelial injury. Numerous cross-sectional and cohort studies have demonstrated that even mild elevations in albuminuria are significantly associated with both the presence and severity of diabetic retinopathy (DR) [19–21].

Pathophysiologically, chronic hyperglycemia, the accumulation of advanced glycation end-products (AGEs), and oxidative stress lead to disruption of the endothelial glycocalyx and neurovascular unit dysfunction, resulting in vascular injury that affects both the renal glomerulus and the retinal microcirculation [22]. Large population-based studies further strengthen this association. The Singapore Malay Eye Study reported that microalbuminuria independently increases the risk of any-stage DR [22], whereas the Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study (SN-DREAMS) demonstrated that albuminuria predicts proliferative DR even after adjustment for glycemic control and blood pressure [21]. Therefore, albuminuria is not merely a renal manifestation butfunctions as a systemic vascular biomarker integrating metabolic, inflammatory, and hemodynamic stress.

In recent years, the relationship among fibroblast growth factor-21 (FGF21), growth differentiation factor-15 (GDF15), microalbuminuria, and diabetic retinopathy has been increasingly explored across diverse study designs. Consistently, elevated FGF21 and GDF15 reflect metabolic stress and mitochondrial dysfunction, whereas microalbuminuria indicates systemic endothelial injury. Although inter-study variations exist in methodology and population characteristics, the majority of findings report positive associations between these biomarkers and the presence or progression of DR. Collectively, this evidence supports their roles as early indicators of metabolic–microvascular dysregulation preceding clinically detectable retinal damage.

Table 1: summarizes the key clinical and meta-analytic studies evaluating the associations between serum FGF21, GDF15, and microalbuminuria with the presence and severity of diabetic retinopathy in patients with type 2 diabetes mellitus.

Author (Year)	Sample size / Study design	Biomarker(s) assessed	Main findings	Ref
Jin S et al. (2021)	312 T2DM patients / cross-sectional	Serum FGF21	Elevated FGF21 significantly associated with sight-threatening diabetic retinopathy.	[1]
Heidari Z, Hasanpour M (2021)	210 T2DM patients / case–control	Serum FGF21	FGF21 positively correlated with DR severity, independent of HbA1c and lipid profile.	[2]
Jung CH et al. (2017)	1,110 T2DM subjects / cohort	Serum FGF21	U-shaped association between FGF21 levels and microvascular complications, including DR.	[3]
Esteghamati A et al. (2016)	140 T2DM patients / case–control	Serum FGF21	Circulating FGF21 levels significantly higher in DR compared with non-DR patients.	[4]
Lee CH et al. (2023)	438 T2DM patients / prospective	FGF21, AFABP, PEDF	Elevated FGF21 predicts progression to sight-threatening diabetic retinopathy.	[5]
Basir H et al. (2024)	Meta-analysis (10 studies; n≈3,400)	Serum FGF21	Meta-analysis demonstrates a strong association between elevated FGF21 levels and DR risk.	[6]
Jiang Y et al. (2024)	Meta-analysis (9 studies)	FGF21, Klotho	Higher FGF21 and lower Klotho levels associated with increased DR severity.	[7]
Niu Y et al. (2021)	402 T2DM patients / cross-sectional	Serum GDF15	GDF15 significantly elevated in patients with DR and correlates with disease severity.	[11]

Author (Year)	Sample size / Study design	Biomarker(s) assessed	Main findings	Ref
Chung JO et al. (2020)	312 T2DM patients / cross-sectional	Plasma GDF15	Higher plasma GDF15 levels associated with presence and severity of DR.	[12]
Billeson K et al. (2024)	214 diabetic subjects / case–control	Serum GDF15, MMP-3	GDF15 levels associated with diabetic microvascular complications, including retinopathy.	[13]
Feng N et al. (2026)	3369 adults diabetes / cross-sectional	UACR	Higher urinary albu-min-to-creatinine ratio positively associated with DR and may serve an early predictive DR	[18]
Paterson N et al. (2021)	1,883 subjects T2DM / cross-sectional case control(UK Biobank)	Microalbuminuria	Albuminuria is associated with alterations in retinal microvas-cular parameters.	[19]
Dash S et al. (2022)	250 T2DM patients / cross-sectional	Albuminuria	Severity of albuminuria positively correlates with the grade of diabetic retinopathy.	[20]
Rani PK et al. (2011)	1,411 T2DM patients / cohort (SN-DREAMS)	Albuminuria	Albuminuria predicts proliferative DR inde-pendent of HbA1c and blood pressure.	[21]
Shahrir NF et al. (2022)	343 T2DM patients / cross-sectional study	Microalbuminuria	Microalbuminuria inde-pendently associated with diabetic retinopathy in Malay population.	[22]

Integrative Mechanism

The Metabolic–Renal–Retinal Axis

The interplay among fibroblast growth factor-21 (FGF21), growth differentiation factor-15 (GDF15), and microalbuminuria represents a unified pathophysiological pathway that bridges hepatic metabolism, mitochondrial stress, and endothelial integrity in *type 2 diabetes mellitus (T2DM)* [6,13,19]. This biological framework is conceptualized as the Metabolic–Renal–Retinal Axis (Figure 1).

Metabolic Overload

Chronic lipotoxicity and excessive fatty acid flux activate peroxisome proliferator-activated receptor-α (PPAR-α) and mitochondrial stress pathways, leading to the upregulation of FGF21 and GDF15 as adaptive metabolic hormones [6,12].

Mitochondrial Stress and the Integrated Stress Response (ISR)

Impaired oxidative phosphorylation and reactive oxygen species accumulation trigger the integrated stress response, involving CHOP, ATF4, and p53 activation, which in turn induces systemic elevation of GDF15 as a mitochondrial distress signal [13–15].

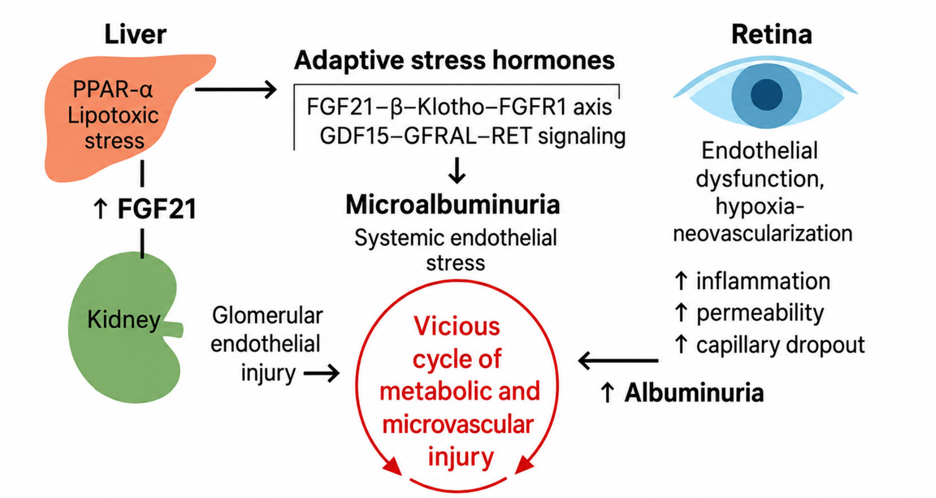
Endothelial Dysfunction

Oxidative and inflammatory insults disrupt the endothelial glycocalyx and tight junctions, causing urinary albumin leakage and increased retinal microvascular fragility. This shared mechanism underlies the parallel emergence of microalbuminuria and early diabetic retinopathy lesions [19–22].

Feed-Forward Loop

Elevated FGF21 and GDF15 further modulate inflammation, vascular permeability, and metabolic stress responses, creating a self-reinforcing cycle that accelerates microvascular injury in both renal and retinal tissues [11,16]. Collectively, this integrative framework illustrates how metabolic overload stimulates hepatic FGF21 secretion, mitochondrial stress drives GDF15 upregulation, and endothelial damage manifests as microalbuminuria. Together, these interlinked pathways form a feed-forward loop that amplifies systemic inflammation, oxidative stress, and microvascular permeability. This mechanistic model provides the biological foundation for a multi-biomarker strategy aimed at early prediction and detection of diabetic retinopathy in individuals with T2DM.

Figure 1: The Metabolic–Renal–Retinal Axis.



Source: Created by the authors using BioRender (www.biorender.com), adapted and synthesized from previously published studies [11,12,18,22].

This Figure illustrates the integrated roles of fibroblast growth factor-21 (FGF21) and growth differentiation factor-15 (GDF15) as circulating metabolic stress hormones, and microalbuminuria as a systemic marker of endothelial dysfunction. Chronic lipotoxicity and oxidative stress promote hepatic FGF21 secretion and systemic GDF15 elevation, which converge to impair endothelial integrity within renal and retinal microcirculation. These mechanisms generate a feed-forward loop that amplifies metabolic stress, vascular permeability, and microvascular injury in type 2 diabetes mellitus.

Clinical and Translational Implications

The combined assessment of fibroblast growth factor-21 (FGF21), growth differentiation factor-15 (GDF15), and microalbuminuria offers a promising approach for enhancing the early detection of diabetic retinopathy (DR). As a non-invasive, low-cost biomarker triad, these markers capture complementary aspects of metabolic stress, mitochondrial dysfunction, and endothelial injury, providing a more sensitive reflection of microvascular risk than glycemic indices alone [11,13,19]. Diabetic retinopathy remains one of the leading causes of vision impairment worldwide and represents a complex microvascular complication driven by chronic metabolic dysregulation in diabetes mellitus [24].

From a clinical perspective, this integrative biomarker framework may provide several practical applications for improving risk assessment and management in patients with type 2 diabetes mellitus. Early identification of individuals at risk of developing diabetic retinopathy is essential for preventing irreversible retinal damage. Biomarker-based profiling using FGF21, GDF15, and microalbuminuria may help identify patients experiencing early systemic microvascular stress before the appearance of overt retinal lesions. This approach may complement established international classification systems used to stage diabetic retinopathy severity and guide clinical monitoring strategies [25]. Recent advances in screening programs emphasize the need for combining systemic biomarkers with retinal imaging technologies to enhance early detection of retinal microvascular damage. Novel screening frameworks incorporate digital retinal photography and emerging imaging modalities such as optical coherence tomography angiography (OCTA) to improve diagnostic sensitivity and population-based screening efficiency [26]. Understanding the biological mechanisms underlying diabetic retinopathy is critical for improving prevention strategies. Chronic hyperglycemia induces metabolic stress, oxidative damage, and endothelial dysfunction that contribute to progressive retinal microvascular injury. These mechanisms have long been recognized as key contributors to the development and progression of diabetic retinopathy [27]. Circulating levels of FGF21 and GDF15 may provide insights into systemic metabolic stress and mitochondrial dysfunction during treatment interventions targeting insulin resistance or lipid metabolism. Experimental studies suggest that GDF15 may also play regulatory roles in inflammation, cellular stress signaling, and tissue remodeling processes associated with metabolic disease [28]. Microalbuminuria represents a widely recognized marker of endothelial dysfunction and systemic microvascular injury in diabetes. Several studies have demonstrated that increased urinary albumin excretion correlates with the presence and severity of diabetic microvascular complications, including diabetic retinopathy [29]. Retinal vascular endothelial cell damage and neuroretinal degeneration are increasingly recognized as central mechanisms contributing to diabetic retinopathy progression. Endothelial dysfunction disrupts retinal microvascular integrity and promotes inflammatory and neurodegenerative processes within the retina [30]. Microalbuminuria has also been proposed as an early clinical indicator of systemic vascular injury in patients with type 2 diabetes mellitus and may precede the development of overt diabetic complications. Emerging therapeutics targeting thesepathways, including FGF21 analogs and GDF15–GFRAL axis modulators, demonstrate potential in reducing systemic metabolic stress and inflammation. However, their application in DR remains exploratory, and longitudinal validation is required to determine whether modifying these biomarkers translates into reduced microvascular injury [12,16,22].

Taken together, these translational insights highlight the potential of multi-biomarker models to complement current screening tools and advance personalized approaches to the prevention of diabetic retinopathy.

Future Prospects and Conclusion

Microalbuminuria, fibroblast growth factor-21 (FGF21), and growth differentiation factor-15 (GDF15) collectively reflect the metabolic, mitochondrial, and endothelial stress underpinning microvascular injury in type 2 diabetes mellitus (T2DM). Their combined assessment may substantially improve early diagnosis and prediction of diabetic retinopathy (DR), especially during subclinical stages when conventional ophthalmic screening has limited sensitivity [11,13,19].

Future research should prioritize large-scale longitudinal studies to establish standardized cut-off values for each biomarker, determine temporal trajectories in relation to DR progression, and examine gene - environment interactions influencing biomarker expression. Population-based studies across diverse ethnic groups - including Indonesia's Bugis-Makassar population - are particularly important to account for genetic variation, metabolic phenotypes, and differing susceptibilities to microvascular complications.

To the best of current knowledge, the present review is the first to integrate FGF21, GDF15, and microalbuminuria into a unified Metabolic–Renal–Retinal Axis, offering a comprehensive biological model that links metabolic overload, mitochondrial stress, and endothelial dysfunction to early retinal microangiopathy. This tri-biomarker framework provides mechanistic insights that extend beyond glycemic control and may complement existing screening strategies by identifying high-risk individuals earlier.

Further translational research is required to validate this integrative model, define population-specific thresholds, and evaluate whether modifying these biomarkers - through metabolic, mitochondrial, or vascular-targeted therapies - can reduce microvascular injury and ultimately prevent vision-threatening diabetic retinopathy.

Acknowledgments

The authors express sincere appreciation to the Department of Clinical Pathology and Laboratory Medicine, Faculty of Medicine, Universitas Hasanuddin, for academic and technical support.

Funding Statement

No external funding was received for this review.

Conflict of Interest

The authors declare no conflict of interest related to this manuscript.

Ethics Statement

No ethical approval was required for this review article as it did not involve direct patient participation or identifiable human data.

Artificial Intelligence Assistance Declaration

Artificial intelligence assistance was utilized in the preparation of this manuscript exclusively for non-creative technical tasks, including language polishing, structural refinement, and reference formatting. The AI model used was OpenAI's ChatGPT(GPT-5 model), accessed through a subscription-based interface. No content generation, data interpretation, or scientific conclusion was made autonomously by the AI. All critical analyses, conceptual frameworks, and interpretations were independently developed, reviewed, and validated by the authors. The use of AI tools complied with the journal's ethical standards and current COPE guidelines on responsible use of generative language models in scientific writing.

References

1. Jin S, Xia N, Han L. Association between serum fibroblast growth factor 21 level and sight-threatening diabetic retinopathy in Chinese patients with type 2 diabetes. BMJ Open Diabetes Research & Care. 2021;9(1):e002126. https://doi.org/10.1136/bmjdrc-2021-002126
2. Heidari Z, Hasanpour M. The serum fibroblast growth factor 21 is correlated with retinopathy in patients with type 2 diabetes mellitus. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2021;15(6):102296. https://doi.org/10.1016/j.dsx.2021.102296
3. Jung CH, Jung SH, Kim BY, Kim CH, Kang SK, Mok JO. The U-shaped relationship between fibroblast growth factor 21 and microvascular complication in type 2 diabetes mellitus. Journal of Diabetes and its Complications. 2017;31(1):134. https://doi.org/10.1016/j.jdiacomp.2016.10.017
4. Esteghamati A, Momeni A, Abdollahi A, Khandan A, Afarideh M, Noshad S, et al. Dosage sérique du facteur de croissance des fibroblastes 21 chez les patients atteints de rétinopathie diabétique de type 2. Annales d'Endocrinologie. 2016;77(5):586. https://doi.org/10.1016/j.ando.2016.01.005
5. Lee CH, Lui DTW, Cheung CY, Fong CHY, Yuen MMA, Woo YC, et al. Circulating AFABP, FGF21, and PEDF levels as prognostic biomarkers of sight-threatening diabetic retinopathy. Journal of Clinical Endocrinology and Metabolism. 2023;108(9):E799. https://doi.org/10.1210/CLINEM/DGAD112
6. Basir H, Nugrahani ASD, Aman AM, Bakri S, Rasyid H, Umar H, et al. The association between fibroblast growth factor 21 with diabetic retinopathy among type 2 diabetes mellitus patients: a systematic review, meta-analysis, and meta-regression. PeerJ. 2024;12(12). https://doi.org/10.7717/PEERJ.18308
7. Jiang Y, Zhang W, Xu Y, Zeng X, Sun X. Relationship of fibroblast growth factor 21, Klotho, and diabetic retinopathy: a meta-analysis. Frontiers in Endocrinology. 2024;15. https://doi.org/10.3389/FENDO.2024.1390035
8. Wei L, Sun X, Fan C, Li R, Zhou S, Yu H. The pathophysiological mechanisms underlying diabetic retinopathy. Frontiers in Cell and Developmental Biology. 2022;10:963615. https://doi.org/10.3389/fcell.2022.963615

9. Shakthiya T, Chand L, Annamalai R. A recent update on candidate biomarkers in the pathogenesis of diabetic retinopathy. The Open Biomarkers Journal. 2025;15(1). https://doi.org/10.2174/0118753183372247250213110930
10. Niu Y, Ding X, Yang Z, Han Y, Zhang H, Zhang X, et al. The relationship between circulating growth differentiation factor-15 levels and diabetic retinopathy in patients with type 2 diabetes. Frontiers in Endocrinology. 2021;12:627395. https://doi.org/10.3389/fendo.2021.627395
11. Chung JO, Park SY, Cho DH, Chung DJ, Chung MY.
12. Relationship between plasma growth differentiation factor-15 levels and diabetic retinopathy in individuals with type 2 diabetes.Scientific Reports. 2020;10:20568. https://doi.org/10.1038/s41598-020-77584-z
13. Billeson K, Baldimtsi E, Wahlberg J, Whiss PA. Growth Differentiation Factor 15 and Matrix Metalloproteinase 3 in Plasma as Biomarkers for Neuropathy and Nephropathy in Type 1 Diabetes. Int J Mol Sci. 2024;25(13):7328. https://doi.org/10.3390/ijms25137328
14. Berezin AE. Diabetes mellitus related biomarker: The predictive role of growth-differentiation factor-15. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2016;10(1):S154. https://doi.org/10.1016/j.dsx.2015.09.016
15. Torm MEW, Dorweiler TF, Fickweiler W, et al. Frontiers in diabetic retinal disease. Journal of Diabetes and its Complications. 2023;37(2):108386. https://doi.org/10.1016/j.jdiacomp.2022.108386
16. Soelistijo SA, Ardiany D, Adiwinoto RD, Pranoto A, Widjaja SA.Albuminuria as a risk factor for diabetic retinopathy in Indonesian type 2 diabetes mellitus patients.
17. Rom J Diabetes Nutr Metab Dis. 2024;31(2):170–175. https://doi.org/10.46389/rjd-2024-1446
18. Supraja P, Hemalatha K, Suneetha P.Correlation of microalbuminuria and diabetic retinopathy: a retrospective study.Int J Res Med Sci. 2024;12(11):4185–4192. https://doi.org/10.18203/2320-6012.ijrms20243370
19. Antwi-Boasiako C, Obeng KA, Amissah-Arthur KN, Musah L, Abaidoo B, Awuviri HW, et al. Association between albuminuria and retinal microvascular dysfunction in type 2 diabetes with and without hypertension. Diabetes Epidemiology and Management. 2023;11:100139. https://doi.org/10.1016/j.deman.2023.100139
20. Feng N, Wang YX, Tian XJ, Zhao SF, Du LJ, Feng BQ, et al. Positive association between urinary albumin-to-creatinine ratio and diabetic retinopathy in American adults: a cross-sectional study. Medicine (Baltimore). 2026;105:e47439. https://doi.org/10.1097/MD.0000000000047439
21. Paterson EN, Cardwell CR, MacGillivray TJ, Trucco E, Doney ASF, Foster PJ, et al. Investigation of associations between retinal microvascular parameters and albuminuria in UK Biobank: a cross-sectional case-control study. BMC Nephrol. 2021;22:72. https://doi.org/10.1186/s12882-021-02273-6
22. Dash S, Chougule A, Mohanty S. Correlation of albuminuria and diabetic retinopathy in type-II diabetes mellitus patients. Cureus. 2022;14(2):e21927. https://doi.org/10.7759/cureus.21927
23. Rani PK, Raman R, Gupta A, Pal SS, Kulothungan V, Sharma T. Albuminuria and diabetic retinopathy in type 2 diabetes mellitus: Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study (SN-DREAMS, Report 12). Diabetol Metab Syndr. 2011;3:9. https://doi.org/10.1186/1758-5996-3-9
24. Shahrir NF, Aziz NRAA, Ahmad FL, Muzaid NA, Samat F, Syed Ghazaili SNA, et al. Determinants of microalbuminuria among type 2 diabetes mellitus patients in Kuala Selangor district: A cross-sectional study. Malays Fam Physician. 2022;17(3):53–63. https://doi.org/10.51866/oa.122
25. Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. The Lancet. 2010;376(9735):124. https://doi.org/10.1016/S0140-6736(09)62124-3
26. Wilkinson CP, Ferris FL, Klein RE, Lee PP, Agardh CD, Davis M, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology. 2003;110(9):1677. https://doi.org/10.1016/S0161-6420(03)00475-5
27. Vujosevic S, Aldington SJ, Silva P, Hernández C, Scanlon P, Peto T, et al. Screening for diabetic retinopathy: new perspectives and challenges. The Lancet Diabetes and Endocrinology. 2020;8(4):337. https://doi.org/10.1016/S2213-8587(19)30411-5
28. Aiello LM. Perspectives on diabetic retinopathy. American Journal of Ophthalmology. 2003;136(1):122. https://doi.org/10.1016/S0002-9394(03)00219-8
29. Sawant H, Borthakur A. Disease-specific novel role of growth differentiation factor 15 in organ fibrosis. International Journal of Molecular Sciences. 2025;26(12):5713. https://doi.org/10.3390/ijms26125713
30. Yadav S, Singhal S, Shashwat K, Saklani A, Mittal S, Anand H. Study of correlation of urine albumin creatinine ratio with diabetic retinopathy in type 2 diabetes mellitus patients. International Journal of Scientific Development and Research. 2024;9(11): Available from https://www.ijsdr.org/papers/IJSDR2411003.pdf
31. Mrugacz M, Bryl A, Zorena K. Retinal vascular endothelial cell dysfunction and neuroretinal degeneration in diabetic patients. Journal of Clinical Medicine. 2021;10(3):458. https://doi.org/10.3390/jcm10030458
32. Asghar S, Asghar S, Mahmood T, Bukhari SMH, Mumtaz MH, Rasheed A. Microalbuminuria as the Tip of Iceberg in Type 2 Diabetes Mellitus: Prevalence, Risk Factors, and Associated Diabetic Complications. Cureus. 2023;15(8):e43190. https://doi.org/10.7759/cureus.43190