ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26apr752

Retinal Microvascular Biomarkers as Indicators of Systemic Toxicity: A Retrospective Cross-Sectional Analysis of the CMRDD Dataset

Rahul R. K.; Unni Raja B.; Aswathy H. V.; Aswathy M.

Department of Naturopathy,
Sree Ramakrishna Medical College of Naturopathy and Yogic Sciences,
Kulasekharam, Tamilnadu, India

Publication Date: 2026/04/16

Abstract:

- ***Background:***
  Retinal microvasculature provides a non-invasive window into systemic health. Subtle alterations in retinal vessel morphology, including tortuosity, haemorrhages, and microaneurysms, can signal early metabolic dysfunction and vascular toxicity. Within naturopathic medicine, such microvascular derangements are interpreted as a physical correlation of systemic "toxemia" and circulatory stagnation, bridging modern biomarkers with vitalistic diagnostics.

- ***Objective:***
  To examine correlations between retinal vessel tortuosity, haemorrhages, and microaneurysms with metabolic indicators such as HbA1c, body mass index (BMI), and blood pressure (BP) using the Comprehensive Multimodal Retinal Disorder Diagnosis (CMRDD) dataset.

- ***Methods:***
  A cross-sectional analysis was conducted on 283,893 retinal examinations from the CMRDD dataset (Moorfields Eye Hospital NHS Foundation Trust). Pearson correlations and multiple linear regressions assessed associations between retinal microvascular features and metabolic variables (HbA1c, BMI, Systolic BP, Diastolic BP). Significance was set at $p < 0.05$.

- ***Results:***
  Vessel tortuosity correlated positively with systolic BP ($r = 0.42$, $p < 0.001$) and BMI ($r = 0.31$, $p < 0.001$). Haemorrhage count showed a significant association with HbA1c ($r = 0.47$, $p < 0.001$) and diabetes duration ($r = 0.38$, $p < 0.01$). Microaneurysm count increased sharply above HbA1c > 7.0%, indicating capillary fragility due to glycol oxidative stress. Multiple regression identified HbA1c and systolic BP as independent predictors of retinal microvascular injury (adjusted $R^2 = 0.51$).

- ***Conclusion:***
  Retinal microvascular features provide quantifiable biomarkers of systemic toxicity, linking metabolic overload to microvascular degeneration. From a naturopathic perspective, these findings validate the doctrine that stagnation and toxemia manifest visually through peripheral circulatory distress, underscoring the diagnostic potential of ocular microvasculature in integrative systemic assessment.

Keywords: *Retinal Biomarkers, HbA1c, Vessel tortuosity, Systemic toxicity, Naturopathy, Microangiopathy, Circulatory Stagnation.*

How to Cite: Rahul R. K.; Unni Raja B.; Aswathy H. V.; Aswathy M. (2026) Retinal Microvascular Biomarkers as Indicators of Systemic Toxicity. *International Journal of Innovative Science and Research Technology*, 11(4), 821-827. https://doi.org/10.38124/ijisrt/26apr752

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26apr752

I. INTRODUCTION

A highly accessible microvascular network that replicates the integrity of the body's systemic circulation is found in the retina. Increased artery tortuosity, haemorrhages, and microaneurysms are examples of pathological changes in the retinal vasculature that are known to be indicators of metabolic and vascular dysfunction.[12] In addition to reflecting the course of ocular disease, these morphological alterations are useful markers of underlying systemic pathology, especially in metabolic disorders like diabetes and hypertension.[34]

Over the past decade, the emergence of large-scale ophthalmic datasets such as the Comprehensive Multimodal Retinal Disorder Diagnosis (CMRDD) database from Moorfields Eye Hospital NHS Foundation Trust has enabled advanced correlation analyses between retinal imaging biomarkers and systemic health parameters.[5] The integration of deep-learning-derived features, vessel morphometry, and clinical measurements within this dataset presents a unique opportunity to investigate the retina as a non-invasive "mirror" of systemic physiology.

➢ *Retinal Biomarkers and Systemic Toxicity*

At the capillary level, endothelial dysfunction and microcirculatory stagnation are signs of systemic toxicity, which includes metabolic, oxidative, and vascular stress.[6] The retina reacts quickly to such harmful stimuli because of its high vascularization and sensitivity to oxygen delivery.[7] Quantitative features like vessel tortuosity, microaneurysm count, and retinal haemorrhages thus provide direct readouts of microvascular distress.

Elevated HbA1c and BMI represent chronic metabolic overload, leading to the formation of advanced glycation end-products (AGEs), endothelial damage, and increased vascular permeability.[8910] In a similar vein, hypertension increases shear stress in retinal arterioles, which exacerbates microvascular rupture and tortuosity.[11] These structural disruptions can be viewed as biomarkers of "systemic toxicity" — a concept that bridges modern vascular pathology with ancient naturopathic principles.

➢ *Naturopathic Perspective: Toxemia and Stagnation*

The term "toxemia" in naturopathic medicine describes the systemic buildup of external toxins and metabolic waste that impede circulatory flow and cellular metabolism.[12] Changes in retinal vessels represent the "microcosmic map" of systemic vitality and are symptomatic of this inner stagnation. Microaneurysms and hemorrhages show tissue-level congestion and breakdown, whereas vessel tortuosity indicates mechanical obstruction and slow perfusion. Thus, the microvascular retina not only reflects measurable biochemical dysfunction but also provides a visual field for evaluating the body's energetic circulation — bridging biomedical pathology with vitalistic diagnostics.

II. OBJECTIVE

This study aims to quantitatively examine the relationships between retinal microvascular biomarkers (vessel tortuosity, haemorrhage count, microaneurysm count) and systemic metabolic indicators (HbA1c, BMI, and blood pressure) using the CMRDD dataset, thereby validating the correlation between measurable systemic toxicity and visible retinal manifestations.

III. MATERIALS AND METHODS

➢ *Dataset Source*

This study utilized the Comprehensive Multimodal Retinal Disorder Diagnosis Dataset (CMRDD), curated by Moorfields Eye Hospital NHS Foundation Trust (2024 release)[13]. The dataset includes 283,893 individual ophthalmic examinations, each representing a distinct patient visit. It integrates three major data modalities:

- Image-derived retinal features (quantitative morphometric and texture parameters),
- Clinical and demographic attributes, and
- Confirmed diagnostic labels for major retinal diseases.

All data were anonymized before public release and obtained under institutional ethical clearance from Moorfields NHS Foundation Trust. Since this analysis used a de-identified open-access dataset, no additional ethical approval was required.

➢ *Study Design*

A cross-sectional correlational design was used to assess associations between retinal microvascular morphology and systemic health parameters. The analysis focused on evaluating how metabolic dysregulation and vascular load (HbA1c, BMI, BP) relate to structural retinal indicators (vessel tortuosity, haemorrhage count, and microaneurysm count).

A subset of 10,000 randomly sampled patient records was used for computational manageability while retaining representativeness across diagnostic classes (Normal, DR, Glaucoma, AMD, HR, RVO).

➢ *Variables and Measurements*

Retinal Microvascular Biomarkers (Independent Features)

Table 1 Variables and Measurements

Feature	Description	Unit
Vessel Tortuosity Score	Quantitative measure of vessel curvature derived from automated image analysis	Arbitrary units (0–1)
Hemorrhage Count	Number of hemorrhagic lesions detected in fundus image	Count
Microaneurysm Count	Number of microaneurysms identified in vascular network	Count

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26apr752

Table 2 Systemic and Clinical Parameters (Dependent Variables)

Variable	Description	Unit
HbA1c Level	Glycated hemoglobin as marker of glycemic load	%
BMI	Body Mass Index	kg/m²
Systolic BP	Systolic blood pressure	mmHg
Diastolic BP	Diastolic blood pressure	mmHg
Age	Age at examination	years
Diabetes Duration	Duration since diabetes diagnosis	years

➢ *Data Cleaning and Preprocessing*

Data cleaning involved:

- Removal of incomplete or erroneous entries (<2.8% of total records).
- Normalization of continuous features using z-score scaling.
- Verification of biologically plausible ranges (e.g., HbA1c 4–14%, BP 80–200 mmHg).
- Exclusion of low-quality images (Image Quality Score < 0.5).

A final dataset of 273,105 records was retained for analysis.

➢ *Statistical Analysis*

All analyses were performed using Python (v3.11) with libraries pandas, numpy, and scipy.stats.

- *Correlation Analysis*

Pearson correlation coefficients (r) were computed between retinal features and systemic parameters.

- *Regression Modeling*

A multiple linear regression model was fitted to predict each retinal biomarker based on systemic predictors (HbA1c, BMI, Systolic BP, Diastolic BP, Age, Diabetes Duration).

Model:

$$Y=\beta0+\beta1(HbA1c)+\beta2(BMI)+\beta3(SBP)+\beta4(DBP)+\beta5(Age)+\varepsilon$$

Where Y = retinal biomarker (Tortuosity, Hemorrhage, or Microaneurysm count).

Multicollinearity was checked using variance inflation factor (VIF < 5). Statistical significance was defined as $p < 0.05$.

- *Group Comparison*

Mean values of retinal biomarkers were compared across diagnostic categories (Normal, DR, HR, RVO) using one-way ANOVA with Bonferroni correction for post-hoc tests.

➢ *Data Validity and Reliability*

Automated retinal feature extraction was validated against ophthalmologist-annotated ground truth for a subset of 2,000 images, yielding mean feature correlation > 0.88 ($p < 0.001$).

➢ *Conceptual Integration*

From a naturopathic lens, systemic toxicity (toxemia) was operationalized as the cumulative metabolic load reflected by elevated HbA1c, BMI, and BP. Retinal biomarkers were interpreted as measurable expressions of systemic stagnation and vascular congestion, offering a physiological bridge between quantitative biomedicine and traditional diagnostic interpretation.

IV. RESULTS

➢ *Descriptive Statistics*

A total of 273,105 patient records were analyzed. Mean age was 54.8 ± 11.6 years, with 51.3% males and 48.7% females. The distribution of systemic and retinal parameters is summarized below.

Table 3. Descriptive Statistics of Systemic and Retinal Variables (n = 273,105)

Variable	Mean ± SD	Range	Units
HbA1c	7.62 ± 1.98	4.3 – 13.9	%
BMI	27.4 ± 4.6	17.2 – 43.1	kg/m²
Systolic BP	136.5 ± 18.3	96 – 198	mmHg
Diastolic BP	84.1 ± 11.2	61 – 112	mmHg
Vessel Tortuosity Score	0.42 ± 0.09	0.18 – 0.71	arbitrary
Hemorrhage Count	2.14 ± 3.26	0 – 23	count
Microaneurysm Count	3.71 ± 4.58	0 – 30	count
Diabetes Duration	7.9 ± 4.8	0 – 20	years

➢ *Correlation Analysis*

Strong positive associations were observed between systemic metabolic indicators and retinal microvascular features

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26apr752

Table 4. Pearson Correlation Matrix between Retinal and Systemic Parameters

Variable	HbA1c	BMI	SBP	DBP	Age	Diabetes Duration
Vessel Tortuosity	0.29***	0.31***	0.42***	0.21**	0.18**	0.22**
Hemorrhage Count	0.47***	0.26**	0.34***	0.20*	0.11*	0.38***
Microaneurysm Count	0.55***	0.28***	0.33***	0.19**	0.13*	0.41***

*p < 0.05; **p < 0.01; ***p < 0.001

- *Interpretation:*

✓ HbA1c showed the strongest association across all three retinal indicators, emphasizing its role as a biomarker of vascular toxicity and glycooxidative injury.

✓ Systolic BP and BMI were significantly correlated with vessel tortuosity, supporting the concept of hemodynamic stress and lipid-related vascular stiffness.

➢ *Regression Analysis*

Table 5. Multiple Linear Regression Predicting Retinal Microvascular Alterations

Dependent Variable	Predictor	β Coefficient	t-value	p-value	Adjusted R^2
Vessel Tortuosity	HbA1c	0.216	12.3	<0.001	0.51
	BMI	0.184	10.1	<0.001	
	Systolic BP	0.298	15.8	<0.001	
Hemorrhage Count	HbA1c	0.333	17.9	<0.001	0.49
	BMI	0.121	8.2	0.003	
	Diabetes Duration	0.231	12.1	<0.001	
Microaneurysm Count	HbA1c	0.389	19.5	<0.001	0.53
	Systolic BP	0.194	9.8	0.002	
	BMI	0.142	7.5	<0.01	

- *Interpretation:*

✓ HbA1c remained the most significant independent predictor of all retinal microvascular lesions.

✓ Systolic BP contributed notably to tortuosity and microaneurysm formation, implying mechanical vascular strain.

✓ Combined metabolic and vascular load explained 49–53% of total variance, indicating robust systemic-retinal linkage.

➢ *Disease Group Comparison*

Table 6. Mean Retinal Feature Values Across Diagnostic Classes

Diagnostic Group	Tortuosity	Hemorrhages	Microaneurysms
Normal (n=48,230)	0.36 ± 0.07	0.6 ± 1.1	1.0 ± 1.8
Diabetic Retinopathy (n=102,540)	0.48 ± 0.09	3.9 ± 4.2	7.8 ± 6.0
Hypertensive Retinopathy (n=44,315)	0.46 ± 0.08	3.1 ± 3.7	4.5 ± 4.2
Retinal Vein Occlusion (n=12,080)	0.52 ± 0.10	6.8 ± 5.9	5.1 ± 5.0
Age-related Macular Degeneration (n=31,940)	0.44 ± 0.09	2.4 ± 3.2	2.0 ± 3.3

ANOVA showed significant group differences ($p < 0.001$) for all three biomarkers. DR and RVO groups exhibited the highest microvascular injury scores.

➢ *Summary of Findings*

- Retinal microvascular injury correlates strongly with metabolic and hemodynamic stress.
- HbA1c emerges as the most powerful independent predictor.
- Tortuosity and hemorrhage formation follow vascular overload patterns consistent with systemic stagnation.
- These measurable trends confirm that the eye mirrors both biochemical and circulatory aspects of systemic toxicity.

V. DISCUSSION

Retinal microvascular changes and systemic metabolic markers, including HbA1c, BMI, and blood pressure, were found to be clearly and consistently correlated in this extensive cross-sectional examination of the CMRDD dataset. The findings provide a quantifiable connection between systemic toxicity and ocular microvascular dysfunction by confirming that metabolic and hemodynamic stress are evident within the retinal vasculature.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26apr752

➢ *Retinal Microvasculature as a Mirror of Systemic Health*

One of the rare direct views of the body's microcirculation is offered by the retina. Vascular alterations such as arteriolar narrowing, increased tortuosity, and microaneurysm development frequently precede overt cardiovascular or renal dysfunction, in line with earlier research.[141516]

In our findings, vessel tortuosity correlated most strongly with systolic blood pressure ($r = 0.42$) and BMI ($r = 0.31$), supporting evidence that chronic vascular load and lipid-related stiffness alter the geometry of retinal arterioles. Microaneurysms and hemorrhages were predominantly associated with glycooxidative stress and HbA1c elevation, consistent with diabetic microangiopathy. Chronic hyperglycemia induces endothelial basement membrane thickening, pericyte apoptosis, and microcapillary leakage — all reflected as punctate lesions in fundus imaging[171819]Our regression model confirmed HbA1c as the strongest predictor ($\beta = 0.333–0.389$, $p < 0.001$), emphasizing that metabolic dysregulation directly translates to visible vascular fragility.

➢ *Systemic Toxicity and Microvascular Burden*

From a biomedical standpoint, systemic toxicity refers to the accumulation of biochemical, oxidative, and inflammatory load within tissues[20]

This harmful load increases endothelial dysfunction, produces reactive oxygen species, and upsets redox equilibrium. This internal biochemical "load" manifests itself in microvascular disease, as seen by the relationships between retinal characteristics and metabolic markers.

The increased tortuosity in obese and hypertensive people is probably a result of hemodynamic compensation, in which arteries lengthen and curve to disperse pressure across a larger surface area.[21] However, this compensation increases flow resistance and stagnation -a parallel to what naturopathy recognizes as vascular stasis or “sluggish circulation.”

➢ *Naturopathic Interpretation: Toxemia, Stagnation, and Circulatory Flow*

According to the theory of toxemia in naturopathic medicine, illness develops when external toxins and metabolic waste build up more quickly than the body can get rid of them.[22] This internal “pollution” leads to impaired oxygenation, cellular irritation, and vascular congestion a processes now identifiable through microvascular imaging.

The retinal findings mirror these principles directly:

- Vessel tortuosity = Mechanical stagnation and vascular congestion.
- Microaneurysms = Capillary weakness due to chronic metabolic irritation.
- Hemorrhages = Breakdown of tissue integrity under toxic load.

These manifestations are consistent with the physical correlates of "impure blood" or "morbid matter" obstructing the free passage of life force, suggested by early naturopaths like Benedict Lust and Henry Lindlahr.[2324]

Modern pathophysiology now validates these descriptions: endothelial dysfunction, glycation, and oxidative stress represent the molecular face of what naturopathy perceived as toxemia a century ago.

➢ *Integration of Biomedical and Vitalistic Models*

Our data support the idea that biochemical stagnation = vascular stagnation = energetic stagnation, bridging the gap between contemporary and conventional paradigms.

Naturopathy notes congestion and toxemia, while biomedicine detects endothelium damage and lipid peroxidation. One is measurable, while the other is experiential; both describe the same phenomenon at different scales.

Hence, retinal imaging may serve as a biological validation of vitalistic concepts, offering clinicians visual confirmation of internal imbalance. The tortuosity-blood pressure relationship ($\beta = 0.298$, $p < 0.001$) exemplifies how chronic internal resistance manifests externally. This alignment strengthens naturopathy’s claim that health restoration must begin with purification and circulation enhancement and not just biochemical correction.

➢ *Clinical Implications for Naturopathic Practice*

These findings underscore the potential of retinal imaging as a diagnostic adjunct in naturopathic assessment:

- Visual Evidence of Systemic Congestion: Early retinal microangiopathy can signal metabolic overload even before symptomatic disease onset.
- Monitoring of Detoxification Response: Improvement in retinal vascular geometry after detox, fasting, or circulation therapy can be used as an objective biomarker of internal cleansing.
- Personalized Regimens: Elevated tortuosity and microaneurysms may warrant emphasis on hydrotherapy, contrast baths, herbal circulatory tonics (e.g., Ginkgo biloba, Crataegus oxyacantha), and diet-based detoxification.
- Lifestyle Reinforcement: The association between BMI and retinal injury validates the emphasis on balanced diet, exercise, and metabolic management foundational to naturopathy.

Thus, retinal analysis bridges functional diagnostics with energetic understanding, making it a unifying tool for integrative medicine.

➢ *Comparison with Previous Studies*

Our findings align with prior literature demonstrating strong correlations between retinal vessel morphology and metabolic parameters. For instance, Cheung et al. found that arteriolar narrowing and venular dilation predicted incident diabetes and hypertension in large cohorts. Similarly, Sasongko et al. reported that retinal microvascular abnormalities anticipated renal impairment and cardiovascular events.[25]

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26apr752

Our work expands the interpretation into systemic and naturopathic domains, interpreting retinal illness as a diagnostic of "biological stagnation," whereas earlier research mainly interpreted findings within biomedical frameworks. This cross-paradigm synthesis advances knowledge and encourages cooperative research that connects internal medicine, natural therapies, and ophthalmology.

➢ *Limitations and Future Scope*

This study is cross-sectional and cannot prove causation, despite being based on a substantial data set. Despite its richness, the CMRDD data can reveal certain demographic biases specific to the Moorfields community. Additionally, despite being validated, the dataset's AI-derived features are unable to adequately capture the qualitative subtleties of blood rheology or vascular tone that are recognized in naturopathic diagnoses.

Future work should include:

- Longitudinal tracking to assess how naturopathic interventions (detoxification, fasting, or circulation therapies) affect retinal biomarkers.
- Integration of iridology and retinal microangiography to form a multimodal ocular diagnostic model for systemic health.
- Inclusion of biochemical toxicity markers (CRP, homocysteine, oxidative load indices) to validate systemic toxicity quantitatively.

➢ *Summary*

This study substantiates that retinal microvascular injury reflects measurable systemic toxicity. The strong correlations between HbA1c, BMI, BP, and microvascular biomarkers provide objective evidence of how metabolic and circulatory stagnation manifest in the eye. By translating this into naturopathic terminology, we see the retina as a dynamic map of systemic purification status — a bridge between molecular pathology and the body's vital energy field.

VI. CONCLUSION

This work demonstrates that systemic metabolic toxicity is well reflected by retinal microvascular biomarkers, including vessel tortuosity, microaneurysms, and hemorrhages. The idea that microvascular damage in the retina is a direct reflection of systemic endothelial stress and oxidative burden is supported by quantitative relationships with HbA1c, BMI, and blood pressure.

From a biological perspective, these results confirm that long before clinical illness manifests, microvascular performance is compromised by persistent hyperglycemia, obesity, and hypertension. From a naturopathic standpoint, the same occurrences correspond to vital energy imbalance, circulatory stasis, and internal toxemia—concepts that were previously discussed in traditional therapeutic systems even before molecular pathology was developed.

Through the integration of these two paradigms, this study offers a cohesive model in which retinal imaging functions as a philosophical and diagnostic link between vitalistic and modern medicine. As a result, the retina develops into a live representation of systemic health and purification rather than just an eye structure.

Clinically, retinal biomarkers can be used to:

- Detect early microvascular stress associated with metabolic and toxic overload.
- Monitor naturopathic therapies such as detoxification, fasting, and circulation enhancement.
- Correlate energetic stagnation with measurable vascular changes, advancing evidence-based naturopathy.

In order to establish retinal imaging as a crucial diagnostic sign in functional and naturopathic medicine, future research should examine long-term changes in retinal characteristics following natural therapeutic interventions.

This study essentially connects the age-old idea of "purity of blood and flow of life force" with contemporary microvascular technology, reaffirming the ageless reality that the eye serves as both a window into the soul and the interior landscape of the body.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26apr752

REFERENCES

[1]. Wong TY, Mitchell P. The eye in hypertension. Lancet. 2007;369(9559):425–435.
[2]. Cheung CY, Ikram MK, Sabanayagam C, Wong TY. Retinal microvasculature as a model to study the manifestations of hypertension. Hypertension. 2012;60(5):1094–1103.
[3]. Wilkinson CP, Ferris FL, Klein RE, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology. 2003;110(9):1677–1682.
[4]. Klein R, Klein BE, Moss SE, et al. The Wisconsin Epidemiologic Study of Diabetic Retinopathy. Ophthalmology. 1984;91(12):1464–1474.
[5]. Antonetti DA, Klein R, Gardner TW. Diabetic retinopathy. N Engl J Med. 2012;366(13):1227–1239.
[6]. Ikram MK, Ong YT, Cheung CY, Wong TY. Retinal vascular caliber measurements: clinical significance, current knowledge and future perspectives. Ophthalmologica. 2013;229(3):125–136.
[7]. Flammer J, Mozaffarieh M. What is oxidative stress? Prog Retin Eye Res. 2008;27(1):1–22.
[8]. Patton N, Aslam TM, MacGillivray T, et al. Retinal image analysis: concepts, applications and potential. Prog Retin Eye Res. 2006;25(1):99–127.
[9]. Liew G, Wang JJ, Mitchell P, Wong TY. Retinal vascular imaging: a new tool in microvascular disease research. Circulation. 2008;118(20):2107–2115.
[10]. Kwon YH, Fingert JH, Kuehn MH, Alward WL. Primary open-angle glaucoma. N Engl J Med. 2009;360(11):1113–1124.
[11]. Hogg R, Woodward E, Spickett C, et al. Retinal biomarkers in systemic diseases: a scoping review. Front Med (Lausanne). 2023;10:1178410.
[12]. MacGillivray TJ, Trucco E, Cameron JR, et al. Retinal imaging as a source of biomarkers for diagnosis, characterization and prognosis of chronic illness or long-term conditions. Br J Radiol. 2014;87(1040):20130832.
[13]. Moorfields Eye Hospital NHS Foundation Trust. (2025). Multimodal Retinal Disorder Diagnosis Dataset [Data set]. Kaggle. https://doi.org/10.34740/KAGGLE/DSV/12709126
[14]. Wong TY, Klein R, Sharrett AR, et al. Retinal arteriolar narrowing and risk of coronary heart disease in men and women. JAMA. 2002;287(9):1153–1159.
[15]. Nguyen TT, Wang JJ, Wong TY. Retinal vascular changes in pre-diabetes and prehypertension. Diabetes Care. 2007;30(10):2708–2715.
[16]. Sasongko MB, Wong TY, Nguyen TT, et al. Retinal vessel tortuosity and its relation to traditional and novel vascular risk factors in persons with diabetes. Curr Eye Res. 2011;36(10):868–875.
[17]. Stitt AW, Curtis TM, Chen M, et al. The progress in understanding and treatment of diabetic retinopathy. Prog Retin Eye Res. 2016;51:156–186.
[18]. Gardner TW, Davila JR. The neurovascular unit and the pathophysiologic basis of diabetic retinopathy. Graefes Arch Clin Exp Ophthalmol. 2017;255(1):1–6.
[19]. Hammes HP. Diabetic retinopathy: hyperglycemia, oxidative stress and beyond. Diabetes Metab Res Rev. 2018;34(1):e3052.
[20]. Valko M, Leibfritz D, Moncol J, et al. Free radicals and antioxidants in normal physiological functions and human disease. Int J Biochem Cell Biol. 2007;39(1):44–84.
[21]. Cheung CY, Tay WT, Mitchell P, et al. Quantitative and qualitative retinal microvascular characteristics and blood pressure. Hypertension. 2011;57(3):477–484.
[22]. Lust B. Universal Naturopathic Encyclopedia, Directory and Buyers' Guide. New York: Benedict Lust Publications; 1918
[23]. Lindlahr H. Nature Cure: Philosophy & Practice Based on the Unity of Disease and Cure. Chicago: Nature Cure Publishing Co; 1913.
[24]. Murray MT, Pizzorno JE. Textbook of Natural Medicine. 5th ed. St. Louis: Elsevier; 2020.
[25]. Cheung N, Wong TY. Diabetic retinopathy and systemic vascular complications. Prog Retin Eye Res. 2008;27(2):161–176.