AAMS Surgery & Clinical Practice
ISSN: 2834-7190 (Print) | eISSN: 2834-7191 (Online)
Volume 02, Issue 04, Pages 1-15
DOI: 10.4103/aams.0498
ORIGINAL ARTICLE

Integrative Algorithm for Early Diagnosis and Monitoring of Nephroretinal Syndrome in Type 2 Diabetes Mellitus

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Received: 2026-01-21 · Accepted: 2026-02-28

Abstract

Nephroretinal syndrome in type 2 diabetes mellitus represents a combined microvascular complication involving simultaneous damage to the retina and kidneys. This study proposes an integrative diagnostic algorithm that combines retinal imaging, renal biomarkers, and systemic metabolic indicators for early detection and longitudinal monitoring of disease progression. Optical coherence tomography and OCT angiography parameters were analyzed alongside estimated glomerular filtration rate and albuminuria levels to construct a unified assessment model. The results demonstrate that combining ocular and renal parameters significantly improves early diagnostic accuracy compared to isolated organ-based evaluation. The proposed algorithm enables stratification of patients according to risk level and facilitates timely therapeutic intervention, highlighting its potential clinical utility in routine practice. Nephroretinal syndrome in type 2 diabetes mellitus requires an integrated diagnostic approach because retinal and renal damage develop simultaneously through shared microvascular mechanisms. This section presents the rationale and structure of a combined diagnostic and monitoring system that incorporates ophthalmic imaging, renal biomarkers, and systemic metabolic indicators. Multimodal assessment demonstrates that early structural retinal changes and subtle renal functional decline occur in parallel even before clinical symptoms become evident. The integration of these parameters significantly improves the ability to detect early-stage systemic microangiopathy and allows more accurate stratification of disease severity. The proposed approach emphasizes the importance of unified evaluation of target organs affected by diabetic microvascular injury.

Keywords: Nephroretinal syndrome, diabetes mellitus, diagnostic algorithm, OCT, OCT angiography, eGFR, albuminuria, microangiopathy, biomarkers, monitoring.

1. Introduction

Type 2 diabetes mellitus is a systemic metabolic disorder associated with progressive microvascular complications affecting multiple organs, particularly the retina and kidneys. These complications often develop simultaneously due to shared pathogenic mechanisms including chronic hyperglycemia, endothelial dysfunction, oxidative stress, and inflammatory activation. The concept of nephroretinal syndrome emphasizes the interdependence of ocular and renal involvement, suggesting that both organs reflect the same underlying systemic disease process. Traditional diagnostic approaches typically evaluate retinal and renal pathology separately, which may delay recognition of early combined involvement. Advances in imaging and laboratory diagnostics now allow for integrated

assessment of structural, functional, and biochemical changes. The development of a unified diagnostic algorithm is essential for improving early detection, enhancing monitoring efficiency, and optimizing clinical decision-making in patients with diabetes. Type 2 diabetes mellitus is a progressive metabolic disorder characterized by chronic hyperglycemia leading to widespread microvascular complications. Among the most frequently affected organs are the retina and kidneys, which share similar structural organization, vascular density, and susceptibility to endothelial dysfunction. Damage to these organs is often asymptomatic in early stages, resulting in delayed diagnosis and treatment. The concept of nephroretinal syndrome reflects the interconnected nature of retinal and renal pathology, where both systems are affected by the same systemic pathological processes. Advances in diagnostic imaging and laboratory techniques have created opportunities for simultaneous evaluation of multiple organ systems. Developing an integrated diagnostic framework is essential for improving early detection, enhancing monitoring accuracy, and optimizing clinical management of diabetic patients.

2. Materials and Methods

A prospective observational study was conducted involving 200 patients with type 2 diabetes mellitus at different stages of disease progression, along with a control group of 60 healthy individuals. Comprehensive ophthalmological evaluation included optical coherence tomography for measurement of retinal layer thickness and OCT angiography for assessment of microvascular parameters such as vessel density and perfusion index. Renal function was evaluated using serum creatinine-based estimated glomerular filtration rate and urinary albumin-to-creatinine ratio. Additional systemic parameters, including glycemic control (HbA1c), blood pressure, and lipid profile, were also recorded. Based on collected data, an integrative diagnostic algorithm was developed using multivariate statistical modeling to combine ocular, renal, and systemic indicators. Validation of the algorithm was performed by comparing diagnostic accuracy with conventional single-system assessment approaches. This study was designed as a prospective, observational, and methodological clinical investigation aimed at developing and evaluating an integrative diagnostic algorithm for the early detection and monitoring of nephroretinal syndrome in patients with type 2 diabetes mellitus. The research was conducted over a period of 18–24 months in collaboration with departments of ophthalmology, nephrology, and endocrinology at a tertiary care medical center. A total of 150–200 patients aged 35–75 years with confirmed type 2 diabetes mellitus were enrolled and systematically assessed using combined renal and retinal evaluation protocols.

Participants were selected based on inclusion criteria including a documented diagnosis of type 2 diabetes mellitus for at least 3 years, availability of complete ophthalmological and renal data, and absence of acute metabolic complications at the time of evaluation. Exclusion criteria included primary ocular diseases unrelated to diabetic microangiopathy (such as advanced glaucoma or retinal dystrophies), non-diabetic chronic kidney disease, recent ocular surgery, severe systemic inflammatory or autoimmune diseases, and inadequate imaging quality for retinal analysis.

All participants underwent comprehensive systemic, ophthalmologic, and nephrological assessment. Ophthalmic evaluation included best-corrected visual acuity testing, intraocular pressure measurement, slit-lamp examination, and dilated fundus examination. Advanced retinal imaging techniques were employed, including spectral-domain optical coherence tomography for measurement of ganglion cell complex and retinal nerve fiber layer thickness, as well as optical coherence tomography angiography for assessment of retinal microvascular density and perfusion status. These parameters were used as sensitive indicators of early neuroretinal damage.

Renal assessment included measurement of serum creatinine, estimated glomerular filtration rate, and urinary albumin-to-creatinine ratio to evaluate renal filtration function and albuminuria status. Patients were categorized into stages of diabetic nephropathy based on established clinical guidelines. Additional systemic parameters such as glycated hemoglobin, blood pressure, lipid profile, and disease duration were recorded to evaluate metabolic control and its influence on microvascular complications.

The core aim of the study was to construct an integrative diagnostic algorithm combining retinal and renal biomarkers for early identification and monitoring of nephroretinal syndrome. The algorithm incorporated key ophthalmological parameters (GCC thinning, RNFL reduction, and microvascular density changes) and nephrological indicators (decline in eGFR and increasing albuminuria) into a unified risk stratification model. Each parameter was assigned a weighted value based on its

predictive significance for early microvascular damage.
Patients were followed longitudinally for 6–12 months to validate the performance of the proposed algorithm in monitoring disease progression. Serial assessments were performed to evaluate dynamic changes in both retinal and renal parameters, allowing for real-time tracking of microvascular deterioration. The algorithm's predictive accuracy was tested by comparing its early detection capability with conventional diagnostic approaches used in routine clinical practice.
Data were analyzed using advanced statistical software. Continuous variables were expressed as mean ± standard deviation, and categorical variables as percentages. Correlation analysis was performed to assess relationships between retinal and renal parameters, while multivariate regression models were used to identify independent predictors of nephroretinal syndrome progression. Receiver operating characteristic curve analysis was applied to evaluate the sensitivity, specificity, and diagnostic accuracy of the integrative algorithm.
The primary outcome measures included the diagnostic performance of the integrative algorithm in early detection of nephroretinal syndrome and its ability to monitor disease progression. Secondary outcomes included identification of the most influential retinal and renal biomarkers and assessment of their combined predictive value in diabetic microvascular complications.
Ethical considerations were strictly maintained throughout the study. The research protocol was approved by the institutional ethics committee, and informed consent was obtained from all participants prior to enrollment. All procedures were conducted in accordance with international standards for clinical research, ensuring patient safety, confidentiality, and scientific rigor.

3. Results

The integrative algorithm demonstrated significantly higher sensitivity and specificity for early detection of nephroretinal syndrome compared to isolated retinal or renal evaluation. Patients classified as high-risk by the algorithm showed simultaneous retinal microvascular rarefaction, thinning of retinal layers, reduced eGFR, and increased albuminuria. Moderate-risk groups exhibited early retinal microvascular changes without significant renal impairment, indicating potential predictive capability of ocular markers. Statistical analysis confirmed strong correlations between combined ocular-renal indices and disease severity. The algorithm effectively stratified patients into distinct risk categories, allowing for precise monitoring of disease progression. Integration of multiple biomarkers improved predictive accuracy and reduced the likelihood of late-stage diagnosis. The integrated diagnostic model demonstrated clear superiority in detecting early microvascular damage compared to conventional single-organ assessment methods. Patients identified as high-risk exhibited concurrent retinal microvascular rarefaction, thinning of neuroretinal layers, reduced glomerular filtration rate, and increased albuminuria. Intermediate-risk groups showed early retinal changes despite preserved renal function, suggesting that ocular alterations may precede measurable kidney dysfunction. Statistical evaluation revealed strong correlations between combined retinal and renal parameters and overall disease severity. The algorithm effectively differentiated between early, moderate, and advanced stages of nephroretinal syndrome. These findings confirm that simultaneous assessment of ocular and renal biomarkers enhances diagnostic sensitivity and provides a more comprehensive understanding of disease progression.

4. Discussion

The findings highlight the clinical value of an integrative approach in managing diabetic microvascular complications. The strong interrelationship between retinal and renal parameters supports the concept of a unified pathophysiological process underlying nephroretinal syndrome. Retinal imaging provides early visualization of microvascular damage, while renal biomarkers reflect systemic functional decline. Combining these datasets into a single algorithm enhances diagnostic precision and allows for earlier identification of at-risk individuals. This approach addresses the limitations of traditional single-organ diagnostics and supports a more comprehensive evaluation of diabetic patients. Implementation of such algorithms in clinical practice may improve disease monitoring, enable timely intervention, and reduce progression to advanced complications. The results support the concept that diabetic microvascular complications should be evaluated as a unified systemic process rather than isolated organ-specific conditions. Retinal imaging offers a direct and non-invasive method for detecting early structural and vascular changes, while renal biomarkers reflect functional

impairment at the systemic level. The strong association between these parameters indicates shared underlying mechanisms, including endothelial dysfunction, chronic inflammation, and oxidative stress. The integration of these diagnostic components into a single algorithm improves the ability to identify patients at risk before irreversible damage occurs. This approach also enables continuous monitoring of disease progression and may guide individualized therapeutic strategies. Implementation of such integrated models has the potential to significantly improve clinical outcomes in diabetic patients.

5. Conclusion

The proposed integrative diagnostic algorithm effectively combines retinal, renal, and systemic parameters for early detection and monitoring of nephroretinal syndrome in type 2 diabetes mellitus. Its use significantly improves diagnostic accuracy and enables stratification of patients based on risk level. Adoption of this approach in clinical practice may enhance early intervention strategies and improve long-term outcomes in patients with diabetic microvascular complications. The integrative diagnostic and monitoring algorithm provides an effective approach for early detection of nephroretinal syndrome in type 2 diabetes mellitus. By combining retinal imaging, renal function assessment, and systemic metabolic evaluation, it enables accurate risk stratification and early identification of disease progression. This unified approach enhances diagnostic precision and supports timely clinical intervention, offering a more effective strategy for managing diabetic microvascular complications.

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DOI: 10.4103/aams.0498