LUMEN ET VIRTUS
ISSN: 2177-2789

PAPILLEDEMA: CORRELATION BETWEEN OPHTHALMOLOGICAL FINDINGS AND NEUROLOGICAL CAUSES — A SYSTEMATIC REVIEW

PAPILEDEMA: CORRELAÇÃO ENTRE ACHADOS OFTALMOLÓGICOS E CAUSAS NEUROLÓGICAS — UMA REVISÃO SISTEMÁTICA

PAPILEDEMA: CORRELACIÓN ENTRE HALLAZGOS OFTALMOLÓGICOS Y CAUSAS NEUROLÓGICAS — UNA REVISIÓN SISTEMÁTICA

https://doi.org/10.56238/levv17n57-067

Submitted on: 01/21/2026 **Publication date:** 02/21/2026

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ABSTRACT

Introduction: Papilledema represents a neuro-ophthalmological manifestation of elevated intracranial pressure and requires urgent differentiation from other causes of optic disc swelling.

Objective: To systematically analyze contemporary evidence correlating ophthalmological findings with the spectrum of neurological causes underlying papilledema, with emphasis on structural imaging, functional impairment, and neuroimaging markers.

Methods: A systematic review was conducted according to PRISMA guidelines. Searches were performed in PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, ICTRP, and Google Scholar. Studies published within the last five years were prioritized and evaluated using RoB 2, ROBINS-I, and QUADAS-2 tools, with certainty of evidence assessed using the GRADE framework.

Results and Discussion: Twenty-five studies were included in the qualitative synthesis. Structural optical coherence tomography parameters, particularly peripapillary retinal nerve fiber layer thickness and ganglion cell-inner plexiform layer metrics, demonstrated consistent correlation with papilledema severity and treatment response. Magnetic resonance imaging markers such as posterior globe flattening and perioptic subarachnoid space distension enhanced etiological identification.

Conclusion: Papilledema requires a multidisciplinary diagnostic approach integrating quantitative ophthalmological imaging and standardized neuroimaging criteria. Early detection and objective monitoring are fundamental to preventing irreversible visual

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impairment. Harmonized imaging protocols and prospective multicenter validation studies are necessary to optimize clinical algorithms.

Keywords: Papilledema. Intracranial Hypertension. Optical Coherence Tomography. Magnetic Resonance Imaging.

RESUMO

Introdução: O papiledema representa uma manifestação neuro-oftalmológica da hipertensão intracraniana e requer diferenciação urgente de outras causas de edema de disco óptico.

Objetivo: Analisar sistematicamente as evidências contemporâneas que correlacionam achados oftalmológicos com o espectro de causas neurológicas subjacentes ao papiledema, com ênfase em imagem estrutural, comprometimento funcional e marcadores de neuroimagem.

Métodos: Foi realizada uma revisão sistemática de acordo com as diretrizes PRISMA. As buscas foram conduzidas nas bases PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, ICTRP e Google Scholar. Estudos publicados nos últimos cinco anos foram priorizados e avaliados utilizando as ferramentas RoB 2, ROBINS-I e QUADAS-2, com a certeza da evidência avaliada pelo sistema GRADE.

Resultados e Discussão: Vinte e cinco estudos foram incluídos na síntese qualitativa. Parâmetros estruturais de tomografia de coerência óptica, particularmente a espessura da camada de fibras nervosas da retina peripapilar e as métricas da camada de células ganglionares-camada plexiforme interna, demonstraram correlação consistente com a gravidade do papiledema e a resposta ao tratamento. Marcadores de ressonância magnética, como o achatamento do globo posterior e a distensão do espaço subaracnoideo peri-óptico, aprimoraram a identificação etiológica.

Conclusão: O papiledema requer uma abordagem diagnóstica multidisciplinar que integre imagem oftalmológica quantitativa e critérios padronizados de neuroimagem. A detecção precoce e o monitoramento objetivo são fundamentais para prevenir comprometimento visual irreversível. Protocolos de imagem harmonizados e estudos prospectivos multicêntricos de validação são necessários para otimizar os algoritmos clínicos.

Palavras-chave: Papiledema. Hipertensão Intracraniana. Tomografia de Coerência Óptica. Ressonância Magnética.

RESUMEN

Introducción: El papiledema representa una manifestación neurooftalmológica de la hipertensión intracraneal y requiere una diferenciación urgente de otras causas de edema del disco óptico.

Objetivo: Analizar sistemáticamente la evidencia contemporánea que correlaciona los hallazgos oftalmológicos con el espectro de causas neurológicas subyacentes al papiledema, con énfasis en la imagen estructural, el deterioro funcional y los marcadores de neuroimagen.

Métodos: Se realizó una revisión sistemática de acuerdo con las directrices PRISMA. Las búsquedas se efectuaron en PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, ICTRP y Google Scholar. Se priorizaron los estudios publicados en los últimos cinco años y fueron evaluados mediante las herramientas RoB 2, ROBINS-I y QUADAS-2, con la certeza de la evidencia valorada utilizando el sistema GRADE.

Resultados y Discusión: Se incluyeron veinticinco estudios en la síntesis cualitativa. Los parámetros estructurales de tomografía de coherencia óptica, particularmente el grosor de la capa de fibras nerviosas retinianas peripapilares y las métricas de la capa de células ganglionares-capa plexiforme interna, demostraron una correlación consistente con la gravedad del papiledema y la respuesta al tratamiento. Los marcadores de resonancia magnética, como el aplanamiento del globo posterior y la distensión del espacio subaracnoideo perioptic, mejoraron la identificación etiológica.

Conclusión: El papiledema requiere un enfoque diagnóstico multidisciplinario que integre la imagen oftalmológica cuantitativa y criterios estandarizados de neuroimagen. La detección temprana y el monitoreo objetivo son fundamentales para prevenir el deterioro visual irreversible. Son necesarios protocolos de imagen armonizados y estudios prospectivos multicéntricos de validación para optimizar los algoritmos clínicos.

Palabras clave: Papiledema. Hipertensión Intracraneal. Tomografía de Coherencia Óptica. Resonancia Magnética.

1 INTRODUCTION

Papilledema represents a critical neuro-ophthalmological sign reflecting elevated intracranial pressure and remains a diagnostic challenge requiring prompt recognition and etiological clarification[1]. The presence of optic disc edema secondary to intracranial hypertension necessitates immediate differentiation from other causes of optic nerve head swelling to prevent irreversible visual impairment[1]. Recent epidemiological data demonstrate a rising incidence of referrals for suspected papilledema, particularly in the context of increasing obesity and idiopathic intracranial hypertension prevalence[1].

Advances in neuroimaging and ocular imaging have substantially refined the diagnostic pathway for papilledema over the last decade[2]. Magnetic resonance imaging and magnetic resonance venography have become indispensable in excluding secondary causes such as mass lesions or venous sinus thrombosis[2]. Concurrently, optical coherence tomography has emerged as a quantitative tool capable of objectively measuring peripapillary retinal nerve fiber layer thickness and monitoring structural progression[2].

The correlation between ophthalmological findings and underlying neurological pathology is complex and often multifactorial[3]. Fundoscopic features such as hyperemia, obscuration of vessels, hemorrhages, and cotton wool spots may vary according to the severity and chronicity of intracranial pressure elevation[3]. These clinical signs must be interpreted alongside neuroimaging findings to establish a comprehensive etiological diagnosis[3].

Idiopathic intracranial hypertension constitutes the most common cause of papilledema in young women of childbearing age, but secondary etiologies remain clinically significant[4]. Intracranial tumors, hydrocephalus, cerebral venous sinus thrombosis, and intracranial hemorrhage are critical differential diagnoses that demand exclusion[4]. Failure to identify secondary causes may lead to delayed treatment and adverse neurological outcomes[4].

Optical coherence tomography provides high-resolution cross-sectional imaging of the optic nerve head and has become integral in differentiating true papilledema from pseudopapilledema[5]. Enhanced depth imaging and ganglion cell layer analysis contribute to distinguishing optic disc drusen and other structural anomalies from pressure-induced swelling[5]. Quantitative monitoring of retinal nerve fiber layer thickness also allows longitudinal assessment of treatment response[5].

Magnetic resonance imaging signs associated with intracranial hypertension include flattening of the posterior globe, distension of the perioptic subarachnoid space, and empty sella configuration[6]. These radiological markers have been increasingly validated as supportive criteria for idiopathic intracranial hypertension[6]. The integration of radiological and ophthalmological findings strengthens diagnostic confidence and reduces misclassification[6].

Visual field testing remains a cornerstone in evaluating functional impairment associated with papilledema[7]. Enlarged blind spots and peripheral constriction may precede subjective visual complaints and serve as early indicators of optic nerve compromise[7]. Correlating structural OCT metrics with functional perimetry results enhances risk stratification and prognostic evaluation[7].

The severity of papilledema does not always correlate linearly with intracranial pressure values, underscoring the need for comprehensive assessment[8]. Lumbar puncture measurements provide essential diagnostic confirmation but must be interpreted in conjunction with clinical and imaging findings[8]. Isolated intracranial pressure elevation without corresponding disc edema may occur in certain scenarios, complicating diagnostic algorithms[8].

Chronic papilledema may progress to optic atrophy if intracranial hypertension persists untreated[9]. Progressive axonal loss can be objectively documented by ganglion cell complex thinning on optical coherence tomography[9]. Early recognition and multidisciplinary intervention are therefore essential to preserve visual function[9].

Given the evolving landscape of diagnostic technologies and the heterogeneity of neurological causes, a systematic synthesis of current evidence is warranted[10]. Understanding the interplay between ophthalmological findings and underlying neurological pathology is fundamental for timely intervention[10]. This systematic review aims to critically analyze contemporary evidence correlating structural ocular findings with diverse neurological etiologies of papilledema[10].

2 OBJECTIVES

2.1 PRIMARY OBJECTIVE

The primary objective of this systematic review is to critically evaluate the correlation between ophthalmological findings and the spectrum of neurological causes underlying papilledema, with particular emphasis on integrating structural ocular imaging, functional visual assessment, and neuroimaging markers to improve diagnostic accuracy and clinical decision-making.

2.2 SECONDARY OBJECTIVES

The secondary objectives are: to assess the diagnostic value of optical coherence tomography parameters, including peripapillary retinal nerve fiber layer thickness and ganglion cell complex analysis, in differentiating papilledema from pseudopapilledema; to analyze the contribution of magnetic resonance imaging and magnetic resonance venography findings in identifying secondary causes of intracranial hypertension; to compare structural ocular findings with functional visual field alterations and clinical severity grading; to examine the epidemiological and etiological distribution of neurological conditions associated with papilledema, including idiopathic intracranial hypertension, intracranial neoplasms, cerebral venous sinus thrombosis, and obstructive hydrocephalus; to evaluate the role of lumbar puncture and cerebrospinal fluid pressure measurement in diagnostic confirmation; and to synthesize evidence supporting multidisciplinary and individualized management strategies aimed at preventing irreversible visual loss.

3 METHODOLOGY

A systematic review was conducted in accordance with PRISMA guidelines. Electronic searches were performed in PubMed (MEDLINE), Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, ICTRP, and Google Scholar using combinations of terms related to papilledema, intracranial hypertension, optical coherence tomography, neuroimaging, and associated neurological causes. Reference lists of included articles were manually screened to identify additional relevant studies.

Studies published within the last five years were prioritized to ensure contemporary relevance, with possible expansion to ten years if insufficient eligible data were available. Randomized controlled trials, cohort studies, case-control studies, cross-sectional diagnostic accuracy studies, and large case series were included. Single case reports, narrative opinions, non-peer-reviewed materials, and studies without extractable ophthalmological or neuroimaging outcomes were excluded. No language restrictions were applied.

Study selection was performed independently by two reviewers through title and abstract screening followed by full-text evaluation, with disagreements resolved by consensus. Data extraction included study design, sample characteristics, neurological etiology, ophthalmological findings, optical coherence tomography parameters, visual field outcomes, neuroimaging markers, lumbar puncture results, management strategies, and clinical outcomes. Studies were categorized thematically for structured qualitative synthesis.

Risk of bias was assessed using RoB 2 for randomized trials, ROBINS-I for non-randomized studies, and QUADAS-2 for diagnostic accuracy studies. Certainty of evidence was evaluated using the GRADE approach. The choice of a systematic review methodology was justified by the heterogeneity of available data and the need for structured synthesis to inform multidisciplinary clinical practice.

Table 1

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Torres et al., 2021	Adults with idiopathic intracranial hypertension (IIH) underwent optical coherence tomography angiography (OCTA) and were compared across papilledema grades using standard grading systems.	The study assessed peripapillary capillary network metrics on OCTA and their correlations with papilledema grade, retinal nerve fiber layer (RNFL) thickness, and ganglion cell layer (GCL) measures.	Peripapillary OCTA vascular metrics correlated with papilledema severity and structural OCT parameters, supporting OCTA as a quantitative adjunct for phenotyping papilledema in IIH.
Dağdelen et al., 2022	Adults with IIH and healthy controls underwent standardized ultrasonographic optic nerve sheath diameter (ONSD) measurement using a high-frequency probe.	The study evaluated ONSD diagnostic accuracy for IIH and quantified sensitivity, specificity, and optimal cut-offs using receiver operating characteristic analyses.	Ultrasonographic ONSD discriminated IIH from controls with clinically useful accuracy, supporting ONSD as a practical noninvasive biomarker of intracranial hypertension in appropriate settings.
Banerjee et al., 2022	Patients with IIH underwent structural OCT of the optic nerve head and macula alongside functional testing, and imaging-functional relationships were analyzed.	The study measured OCT features of papilledema and correlated these with functional parameters including visual function metrics used in neuro-ophthalmic follow-up.	Structural OCT parameters demonstrated meaningful correlations with functional impairment in IIH, supporting OCT-based phenotyping for risk stratification and longitudinal monitoring.
Yu et al., 2023	Patients evaluated for elevated intracranial pressure underwent transorbital ultrasound measuring optic disc height (ODH) and ONSD, with comparisons across ICP status.	The study assessed the association of ultrasonic ODH and ONSD with elevated intracranial pressure and evaluated combined diagnostic performance.	Combining ultrasonic ODH with ONSD improved noninvasive detection of elevated intracranial pressure compared with single-parameter approaches in the studied cohort.
Kaplan et al., 2023	Children referred for suspected papilledema were classified as papilledema or pseudopapilledema and compared with healthy controls using multimodal ophthalmic assessment including OCT.	The study assessed differences in OCT-derived optic nerve and retinal parameters and related these to clinical classification and diagnostic certainty.	Pediatric papilledema and pseudopapilledema showed distinguishable OCT profiles at the group level, supporting OCT as a high-yield adjunct in pediatric diagnostic pathways.
Bassi et al., 2023	Eyes diagnosed with pseudopapilledema underwent enhanced-depth imaging spectral-domain OCT to characterize optic nerve head drusen and related structural markers.	The study quantified the frequency of optic nerve head drusen and OCT biomarkers such as peripapillary hyperreflective ovoid mass-like structures in pseudopapilledema.	Specific OCT biomarkers were prevalent in pseudopapilledema and can support differentiation from true papilledema when interpreted within a structured clinical framework.
Beier et al., 2024	A cohort of patients with IIH and controls underwent brain magnetic resonance imaging (MRI) with systematic assessment of imaging signs associated with intracranial hypertension.	The study evaluated an evidence-based MRI score and its association with papilledema presence compared with existing diagnostic criteria performance.	An MRI score integrating selected neuroimaging signs estimated papilledema presence more accurately than current criteria, supporting refined imaging-based risk estimation in IIH workups.
Macher et al., 2024	Patients assessed for IIH underwent MRI evaluation in the context of proposed diagnostic criteria integrating cerebrospinal fluid opening pressure, papilledema, and neuroimaging signs.	The study measured external validation performance of MRI-augmented criteria and quantified additive diagnostic value in real-world cohorts.	Incorporating standardized MRI criteria added diagnostic value for identifying IIH, supporting multimodal diagnostic frameworks that integrate ophthalmic and neuroimaging data.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Majmudar et al., 2024	Children with papilledema undergoing follow-up were monitored with multiple OCT-derived optic nerve head measures to evaluate sensitivity to early resolution.	The study compared which OCT measures change earliest during resolving papilledema relative to standard OCT parameters.	Selected OCT optic nerve head metrics detected resolving papilledema earlier than conventional thickness measures, supporting targeted OCT endpoints for pediatric monitoring.
Remolí-Sargues et al., 2024	Patients with intracranial hypertension, including IIH, were evaluated after papilledema regression using OCT and OCTA to quantify residual structural and microvascular changes.	The study assessed relationships between optic nerve and retinal structural measures and peripapillary microvasculature metrics on OCTA.	Microvascular OCTA changes were associated with structural alterations after papilledema regression, suggesting persistent neurovascular remodeling relevant to long-term follow-up strategies.
Pahuja et al., 2024	Patients with IIH and papilledema at different stages underwent OCT and OCTA at baseline and follow-up, with comparisons across early, chronic, and atrophic phenotypes.	The study evaluated peripapillary RNFL and macular ganglion cell-inner plexiform layer measures and OCTA perfusion across retinal and choriocapillaris layers.	Structural OCT and OCTA perfusion patterns differed by papilledema stage, supporting combined structure-perfusion profiling for staging and prognostication in IIH-related papilledema.
Aghdam et al., 2024	Healthy subjects and patients with optic disc drusen, active papilledema, and acute nonarteritic anterior ischemic optic neuropathy were compared using OCTA of optic disc microvasculature.	The study quantified optic disc microvascular parameters and compared patterns across true disc swelling, pseudopapilledema, and ischemic optic neuropathy.	OCTA microvascular signatures differed across true and pseudo-optic disc swelling etiologies, supporting OCTA as an adjunct for differential diagnosis in complex disc edema presentations.
Shemesh et al., 2024	Patients with IIH were followed longitudinally with OCT to characterize temporal dynamics of RNFL and ganglion cell complex (GCC) changes and their clinical correlates.	The study assessed timing to RNFL nadir, magnitude of RNFL and GCC thinning, and associations with disease severity and visual function metrics.	Longitudinal OCT trajectories revealed clinically meaningful timing and magnitude of structural loss, supporting OCT-based prognostic modeling in IIH-related papilledema.
Toro et al., 2024	Patients with clinical parameters suggestive of IIH underwent OCT assessment of optic nerve head and retinal structure, with associations tested against clinical features.	The study evaluated optic nerve and macular OCT parameters and their relationships with clinical indicators of intracranial hypertension.	OCT detected noninvasive optic nerve and retinal alterations associated with IIH clinical parameters, supporting OCT integration into multidisciplinary diagnostic and monitoring pathways.
Bassi et al., 2024	Patients with optic disc edema secondary to raised intracranial pressure underwent OCT characterization of optic nerve head features with correlation to intracranial pressure measurements.	The study assessed RNFL thickness, ganglion cell-inner plexiform layer thickness, and enhanced depth imaging optic nerve head features against intracranial pressure.	Quantitative OCT features correlated with intracranial pressure and can complement fundus grading to improve objective assessment and follow-up of papilledema.
Biousse et al., 2024	Nonmydriatic fundus photographs from emergency and non-ophthalmic settings were analyzed by a deep learning system and compared against reference clinical diagnoses.	The study evaluated diagnostic performance for identifying papilledema and normal optic discs in real-world image acquisition conditions.	A deep learning system reliably identified papilledema on nonmydriatic photographs, supporting AI-assisted triage where ophthalmic expertise or timely neuroimaging access is limited.
Huang-Link et al., 2025	Patients with active and chronic IIH and healthy controls underwent OCT and	The study assessed how OCT-derived RNFL measurements relate to	OCT structural metrics showed strong clinical utility for monitoring IIH and may outperform or complement

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
	fundus imaging, with relationships tested among RNFL thickness, papilledema grade, and intracranial pressure.	papilledema grade and intracranial pressure across IIH phenotypes.	subjective grading and pressure-centric monitoring in selected contexts.
Phillips et al., 2025	Pediatric neuro-ophthalmologists independently classified optic disc photographs of children with papilledema and pseudopapilledema, and agreement and accuracy were quantified.	The study measured inter-expert agreement, rates of disagreement in low-grade disease, and classification accuracy relative to reference diagnoses.	Expert agreement on pediatric optic disc photographs was limited, reinforcing the need for multimodal evaluation, ancillary testing, and structured pathways for suspected papilledema.
Molander et al., 2025	Patients with IIH were assessed for patterns of retinal damage across papilledema severities using structural retinal imaging and visual function outcomes over time.	The study evaluated predictors of persistent visual impairment, including papilledema severity and macular structural disruption, and proposed a visual outcome score.	Distinct structural damage patterns were associated with long-term functional outcomes, highlighting papilledema severity and macular integrity as key determinants of prognosis.
El-Gendy et al., 2025	Patients with IIH underwent optic nerve sheath evaluation and Frisen classification, with comparisons to cerebrospinal fluid opening pressure and chronic papilledema grading.	The study assessed correlations among optic nerve sheath parameters, intracranial pressure estimates, and clinical papilledema staging.	Optic nerve sheath assessment complemented clinical grading and pressure measures, supporting combined ophthalmic and neurodiagnostic stratification for chronic papilledema management.
Valsecchi et al., 2025	Eyes with papilledema secondary to IIH were compared with pseudopapilledema due to optic disc drusen using peripapillary choroidal vascularity index derived via a deep learning approach.	The study evaluated discriminatory performance of peripapillary choroidal metrics for differentiating true papilledema from pseudopapilledema.	Peripapillary choroidal vascularity metrics provided diagnostic separation between papilledema and optic disc drusen-related pseudopapilledema, supporting novel quantitative imaging features for challenging cases.

4 RESULTS AND DISCUSSION

The contemporary evidence demonstrates that papilledema remains most frequently associated with idiopathic intracranial hypertension, although secondary etiologies such as venous sinus thrombosis, intracranial tumors, and obstructive hydrocephalus continue to represent clinically significant causes[11]. Across the included studies, structural ophthalmological findings were consistently correlated with neuroimaging markers of raised intracranial pressure, reinforcing the need for multimodal diagnostic assessment[11]. The convergence of clinical examination, optical coherence tomography, and magnetic resonance imaging findings enhances etiological discrimination and minimizes misclassification in patients with optic disc swelling[11].

Structural optical coherence tomography parameters, particularly peripapillary retinal nerve fiber layer thickness and ganglion cell-inner plexiform layer metrics, demonstrated robust correlations with papilledema severity grading systems[12]. Longitudinal data indicate that dynamic changes in retinal nerve fiber layer thickness mirror intracranial pressure control and therapeutic response, thereby providing an objective monitoring tool[12]. Importantly, several studies revealed that ganglion cell complex thinning may precede overt optic atrophy, suggesting that early macular analysis is critical for prognostic evaluation[12].

Optical coherence tomography angiography has emerged as a complementary modality capable of identifying microvascular alterations associated with active papilledema and chronic structural remodeling[13]. Reduced peripapillary perfusion density and altered choriocapillaris flow patterns were associated with disease stage and structural loss in multiple cohorts[13]. These findings suggest that microvascular assessment may refine staging algorithms and contribute to early detection of irreversible damage[13].

Neuroimaging findings remain fundamental in establishing causality, particularly when differentiating idiopathic intracranial hypertension from secondary intracranial processes[14]. Magnetic resonance imaging signs such as posterior globe flattening, distension of the perioptic subarachnoid space, and empty sella configuration were repeatedly validated as supportive indicators of intracranial hypertension[14]. Evidence-based MRI scoring systems demonstrated improved diagnostic performance compared with isolated imaging markers, highlighting the value of composite radiological frameworks[14].

Ultrasonographic measurement of optic nerve sheath diameter has been evaluated as a rapid bedside screening tool for intracranial hypertension[15]. The included studies demonstrated moderate to high diagnostic accuracy when standardized protocols were applied, particularly in acute care settings[15]. Nevertheless, variability in cut-off thresholds and operator dependence limits its use as a standalone diagnostic modality[15].

The differentiation between true papilledema and pseudopapilledema remains a critical diagnostic challenge in neuro-ophthalmology[16]. Enhanced depth imaging optical coherence tomography and peripapillary structural biomarkers significantly improved identification of optic disc drusen and other mimicking conditions[16]. Additionally, choroidal vascularity metrics derived from advanced imaging algorithms provided further discriminatory capacity in equivocal cases[16].

Pediatric populations pose unique diagnostic complexities due to anatomical variability and lower interobserver agreement in fundus photograph interpretation[17]. Studies assessing expert classification revealed substantial variability in grading low-grade disc edema, underscoring the importance of objective imaging adjuncts[17]. Multimodal assessment strategies, including OCT and neuroimaging, are therefore essential in pediatric diagnostic pathways[17].

The relationship between structural findings and functional impairment was consistently demonstrated across longitudinal cohorts[18]. Enlargement of the blind spot and progressive visual field constriction correlated with structural retinal nerve fiber layer and ganglion cell thinning[18]. These structure–function relationships support integrated monitoring approaches rather than reliance on single-modality assessment[18].

Chronic papilledema was associated with distinct patterns of neuroretinal damage that predicted long-term visual prognosis[19]. Studies identified macular structural disruption and advanced papilledema grade as independent predictors of persistent visual impairment[19]. These findings emphasize the necessity of early intervention to prevent irreversible axonal loss[19].

Artificial intelligence applications in fundus photograph analysis demonstrated promising diagnostic accuracy for papilledema detection in non-specialist settings[20]. Deep learning systems trained on nonmydriatic images achieved clinically meaningful sensitivity and specificity in real-world acquisition environments[20]. Such technologies may facilitate triage in resource-limited settings where immediate neuroimaging is unavailable[20].

Lumbar puncture remains indispensable for confirming elevated intracranial pressure and for cerebrospinal fluid analysis in suspected secondary etiologies[21]. However, multiple studies underscored that opening pressure values must be interpreted in conjunction with clinical and imaging findings to avoid diagnostic errors[21]. Isolated pressure measurements without structural correlation may fail to capture the dynamic spectrum of papilledema evolution[21].

Heterogeneity among included studies was primarily attributable to variations in imaging protocols, papilledema grading systems, and follow-up duration[22]. Differences in OCT device algorithms and segmentation methods also contributed to variability in reported retinal thickness values[22]. Despite these methodological differences, overall trends consistently supported strong correlations between structural ocular findings and neurological disease mechanisms[22].

Risk of bias assessment revealed moderate limitations in retrospective cohorts, particularly related to selection bias and incomplete longitudinal follow-up[23]. Diagnostic accuracy studies generally demonstrated lower risk of bias when predefined imaging thresholds and masked evaluators were employed[23]. The certainty of evidence was rated moderate for imaging–structure associations and low to moderate for long-term prognostic conclusions according to GRADE criteria[23].

When compared with existing clinical guidelines, the synthesized evidence supports expanding the role of quantitative OCT and standardized MRI scoring systems in routine practice[24]. The integration of multimodal imaging aligns with contemporary recommendations for comprehensive evaluation of suspected intracranial hypertension[24]. These findings reinforce the transition from subjective fundoscopic grading alone to objective, reproducible structural metrics[24].

Collectively, the evidence indicates that papilledema should be approached as a multidisciplinary diagnostic entity requiring coordinated ophthalmological and neurological evaluation[25]. Structural imaging biomarkers provide early detection of damage and facilitate treatment monitoring across diverse etiologies[25]. Future research should focus on harmonizing imaging protocols, validating composite diagnostic scores, and establishing standardized longitudinal outcome metrics to optimize patient care[25].

5 CONCLUSION

The present systematic review demonstrates that papilledema represents a complex neuro-ophthalmological manifestation strongly linked to diverse neurological conditions, most prominently idiopathic intracranial hypertension but also including intracranial tumors, venous sinus thrombosis, and hydrocephalus. Contemporary evidence consistently supports the integration of structural optical coherence tomography parameters and standardized magnetic resonance imaging markers to improve diagnostic accuracy. The convergence of ophthalmological and neuroimaging findings enhances etiological clarification and allows earlier detection of vision-threatening progression.

From a clinical perspective, quantitative imaging tools such as retinal nerve fiber layer analysis, ganglion cell complex assessment, and evidence-based MRI scoring systems have transformed the evaluation and monitoring of papilledema. These modalities reduce reliance on subjective grading and facilitate longitudinal assessment of therapeutic response. Incorporating multimodal imaging into routine practice improves risk stratification and supports individualized treatment strategies aimed at preventing irreversible optic nerve damage.

Despite these advances, the literature remains heterogeneous, with variability in imaging protocols, grading scales, and follow-up duration. Many studies are limited by retrospective design, small sample sizes, or incomplete long-term outcome reporting. Furthermore, differences in optical coherence tomography devices and segmentation algorithms introduce methodological variability that may influence comparability across cohorts.

Future research should prioritize multicenter prospective studies using standardized imaging protocols and harmonized outcome definitions. The validation of composite diagnostic models integrating structural, functional, and radiological metrics is essential to refine clinical decision-making algorithms. Additionally, further investigation into artificial intelligence–assisted diagnostics and microvascular imaging biomarkers may expand early detection capabilities, particularly in resource-limited settings.

Ultimately, papilledema requires a multidisciplinary, evidence-based approach that integrates ophthalmology, neurology, and neuroradiology. Early recognition, accurate etiological identification, and objective longitudinal monitoring are fundamental to preserving visual function and optimizing neurological outcomes. Individualized management strategies grounded in quantitative imaging and comprehensive clinical assessment represent the current and future standard of care for patients presenting with optic disc edema secondary to intracranial hypertension.

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