Review Article

Grading scales for vitreous haze

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ABSTRACT

Background: Grading scales for vitreous haze are crucial for the diagnosis, monitoring, and management of uveitis. The presence of inflammatory cells within the vitreous cavity is widely recognized as a key indicator of disease activity and severity, offering valuable insights into the underlying inflammatory processes. This mini-review aims to explore the evolution of vitreous haze grading scales systematically, emphasizing conventional grading methods, advances in imaging technologies, and the integration of artificial intelligence (AI) into the grading process.

Methods: The PubMed/MEDLINE database was comprehensively searched for studies published between 1959 and 2024, using keywords such as "AI-based grading systems," "artificial intelligence," "automated grading," "grading scales for vitreous cells," "inflammation," "uveitis," and "vitreous haze." Relevant studies were identified, and additional articles were selected by reviewing the reference lists of the included publications. The selection of articles for inclusion in the mini-review was limited to those written in English.

Results: In the current literature, two grading methods are used: the National Institutes of Health (NIH) scale and the Miami scale. Despite their widespread utilization, both scales entail subjective assessments of vitreous haze, which renders them susceptible to observer bias and interobserver variability. The NIH scale uses six levels, while the Miami scale employs nine levels, both of which require subjective assessments of vitreous haze. Recent advances in objective imaging technologies, namely ultrawide-field fundus photography and advanced optical coherence tomography-based analysis, have given rise to increasingly consistent and standardized grading systems, which may enhance the reliability of these assessments. Innovative techniques have been developed to enhance accuracy and sensitivity, thereby facilitating the early detection and precise monitoring of vitreous inflammation. Despite these advances, challenges remain, including the difficulty of distinguishing subtle variations in vitreous haze and the variability of inflammatory presentations. The incorporation of AI-driven tools and state-of-the-art imaging technologies into the vitreous cell grading signifies a substantial advance in the evaluation and management of uveitis.

Conclusions: The development of more objective, reproducible, and quantitative grading scales is imperative for optimizing uveitis evaluation and grading vitreous haze in clinical settings and clinical trials. These innovations will also provide robust endpoints for clinical studies, ultimately improving patient care. Moreover, objective grading criteria will enhance diagnostic precision, facilitate better management of ocular inflammatory diseases, and promote further advances in uveitis research and treatment.

KEYWORDS

vitreous humor, posterior uveitis, inflammations, uveitides, machine intelligence, intelligence, artificial, automated grading, optical coherence tomography, AI-based grading systems

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INTRODUCTION

Vitreous inflammation, or "vitritis," is a prominent clinical manifestation of uveitis affecting the posterior segment of the eye [1]. Although it is a hallmark of intermediate uveitis, it is also commonly observed in posterior uveitis. This condition is characterized by the infiltration of inflammatory cells and the influx of proteins into the vitreous body [1]. Vitreous transparency is affected to varying degrees, correlating with disease severity [2, 3].

Clinically, the condition presents as vitreous haze, which may obscure the visibility of retinal vessels and the optic nerve. In cases where inflammation control cannot be achieved, the haze may progress, while successful treatment typically leads to its resolution [3-6]. Recognized as a surrogate indicator of disease activity, vitreous haze has been validated as a primary outcome measure in pharmacological trials on uveitis, underlining the necessity for precise and standardized grading in both clinical practice and research [3-6].

Various classification systems for assessing and grading vitritis in patients with uveitis have been proposed over the years [4-9]. These systems are designed to offer a standardized approach for evaluating the severity of vitreous inflammation, thereby enhancing the accuracy of diagnosis, monitoring, and treatment planning in clinical practice [4-9].

This mini-review sought to provide a systematic overview and analysis of the evolution of grading scales for vitreous haze, tracing their development from historical foundations to contemporary advances.

METHODS

A comprehensive search was conducted in the PubMed/MEDLINE database for literature published between 1959 and 2024, utilizing keywords: "artificial intelligence (AI)," "AI-based grading systems," "automated grading," "grading scales for vitreous cells," "inflammation," "uveitis," and "vitreous haze." In addition to the studies identified by the database search, additional articles were identified by a meticulous review of the reference lists of the included studies. Papers included in this review were limited to those published in the English language with no limits on study design.

RESULTS and DISCUSSION

Twenty-one articles were identified in the initial search and by examining the reference lists of the included studies. These publications were assessed by two senior ophthalmologists (O.K., A.O.S.). These studies are discussed below.

The first scale for grading vitreous haze was proposed by Kimura et al. [6] in 1959. The researchers categorized vitreous opacities based on three criteria: size, morphology, and location. They emphasized the diagnostic relevance of these opacities in posterior segment diseases. Opacities were defined as follows: Fine opacities were characterized as small, clumped formations composed of lymphocytes, plasma cells, macrophages, debris, and fibrin. These opacities were typically associated with active inflammation and milder vitreous involvement [6]. In contrast, coarse opacities were characterized by a larger size and irregular morphology, and were comprised of macrophages, fibrin clumps, and tissue fragments. These opacities were indicative of severe posterior segment lesions and extensive damage [6]. Stringy opacities, which are frequently observed in cases of chronic and severe uveitis, were defined as elongated structures resulting from degenerative changes in the vitreous and were often accompanied by both fine and coarse opacities [6]. Finally, snowball opacities were defined as large, spherical, gray formations located in the peripheral posterior vitreous and resembled "mutton-fat" keratic precipitates [6]. The authors introduced a five-tier descriptive scale for evaluating vitreous inflammation using slit-lamp microscopy. Their scale focused primarily on the assessment of fundus clarity, with a particular emphasis on the visualization of key structures, such as the optic nerve head, retinal blood vessels, and the nerve fiber layer [6]. The authors developed a grading system for vitreous opacities, classifying them based on their density and their effect on fundus visualization. They proposed the following system: Grade 0: Absence of opacities with a clear view. Grade 1: Presence of fine and coarse opacities, but with the fundus remaining clearly visible. Grade 2: Presence of scattered fine and coarse opacities that slightly obscure fundus details. Grade 3: Presence of multiple opacities that significantly obscure the fundus. Grade 4: Presence of dense opacities that completely obstruct the view of the fundus [6]. This scale formed the basis for subsequent classification systems [6].

In 1985, Nussenblatt et al. [7] at the National Institutes of Health (NIH) introduced a six-level fundus photographic grading scale for vitreous haze. Their scale was based on the clarity of three key fundus landmarks: the optic nerve head, retinal vessels, and nerve fiber layer [7]. The scale ranged from severe vitreous haze (4+) through various intermediate grades (3+, 2+, 1+, trace) to no detectable haze (0) [7]. Grade 4+: Complete obscuration of the optic nerve head, denoting the most substantial level of vitreous haze [7]. Grade 3+: The optic nerve head is visible, but its borders are significantly blurred [7]. Grade 2+: The retinal vessels are discernible but are moderately blurred [7]. Grade 1+: Both the optic nerve head and the retinal vessels are visible, exhibiting enhanced definition compared to higher grades [7]. Trace: Subtle blurring of the optic nerve head margin is present, and the normal striations and reflexes of the nerve fiber layer are not fully discernible. Grade 0: No vitreous haze is detected, and all fundus landmarks are clearly visible [7]. The Nussenblatt scale is a clinical grading system for vitreous haze that utilizes an indirect ophthalmoscope and a 20-diopter lens. It involves a visual comparison of the degree of haze to a printed reference scale [4]. This scale has gained widespread recognition and, in 2005, was endorsed by the Standardization of Uveitis Nomenclature (SUN) Working Group for grading vitreous haze. Notably, the "trace" grade was subsequently modified to 0.5+, to facilitate mathematical calculations [4].

The NIH scale rapidly gained widespread utilization and was subsequently endorsed by the Food and Drug Administration for clinical trials [8]. While this scale is straightforward and reproducible, it has several limitations. A notable shortcoming is its subjective nature, as evidenced by the modest interobserver agreement, even when the assessment was conducted by experienced uveitis specialists [1, 4, 5]. In a validation study of the NIH scale by Kempen et al. [9], the vitreous haze gradings assigned by two independent, experienced observers were compared. They demonstrated moderate exact agreement (kappa statistics [κ] = 0.53) and strong agreement within one grade (κ = 0.75). These findings highlighted the challenges in achieving consistent and precise grading with this scale [9]. Additionally, the NIH scale's grading system is non-continuous and non-linear, with substantial gaps between grades, which hampers precision. Furthermore, the system lacks sensitivity at low levels of vitreous inflammation, whereas early detection of inflammatory activity is crucial for timely clinical intervention. These limitations underscore the necessity for more refined and objective methods to assess vitreous haze, particularly for detecting subtle inflammation in the early stages of uveitis [1].

In response to the limitations of the original Nussenblatt scale's grading system, Davis et al. [8]. developed the Miami scale in 2010, a more refined nine-level grading system. This scale was designed to be more quantitative in nature, and employed calibrated Bangerter filters to apply varying degrees of blur to fundus photographs of a healthy subject [8]. The gradations of the Miami scale were meticulously aligned with the logarithmic scale of Snellen visual acuity measurements. The scale demonstrated a high degree of consistency in vitreous haze grading, both between different observers and within the same observer, when utilizing color fundus photographs and a 9-point, log-linear scale. The κ values, which averaged 0.91, reflected exceptional reliability of this grading procedure. The Miami scale exhibited superior interobserver reliability as compared to the NIH scale, particularly within controlled settings, such as reading centers. Due to its more refined gradations, it demonstrated comparable performance in clinics [4, 5, 9].

In a study involving 271 eyes from 142 patients, Madow et al. [4] investigated the validation of a photographic vitreous haze grading technique using a nine-step logarithmic scale for clinical trials on uveitis. Evaluation of vitreous haze was conducted by three postgraduate ophthalmologists [4]. The intraclass correlation coefficients for both interobserver and intraobserver agreement were excellent, ranging from 0.84 to 0.93. A moderate correlation ($r = 0.51$, $P < 0.001$) was observed between the photographic and clinical vitreous haze scores [4]. Notably, significant differences in the mean and median photographic haze scores were found for the three lowest clinical grades (0, 1+, and 2+), highlighting the disparity in grading methods for low levels of haze [4]. The Miami scale, with its expanded range of levels and consistent increments of blur, exhibited enhanced discriminatory power, particularly in discerning varying degrees of inflammation. This improvement in vitreous haze grading scale accuracy facilitated more precise patient inclusion in clinical trials, and particularly in terms of cases with minimal haze that might have been overlooked using the NIH scale [5, 7, 8].

In an investigative study, Hornbeak et al. [5] assessed the reliability of clinical vitreous haze grading. They compared a newly developed nine-level ordinal scale with a previously established six-level scale by Nussenblatt et al. [5, 7]. The study revealed a strong correlation between the six-level and nine-level vitreous haze grading scales ($r = 0.84$) [5]. The interobserver agreement was moderate for both scales, with average κ values of 0.46 (range: 0.28–0.81) for the six-level scale and 0.40 (range: 0.15–0.63) for the nine-level scale [5]. The six-level scale demonstrated slightly higher agreement within a grade, yet both scales exhibited excellent agreement (κ = 0.75; range: 0.66–0.96 for the six-level scale and κ = 0.62; range: 0.38–0.87 for the nine-level scale) [5]. The nine-level scale also demonstrated excellent agreement within two grades (κ = 0.85; range: 0.79–0.92). Notably, the nine-level scale identified twice as many cases as being potentially eligible for clinical trials as did the six-level scale ($P < 0.001$) [5]. The findings of that study indicated that both scales yielded adequately reproducible results for clinical and research applications when appropriate thresholds were applied (i.e., ≥ 2-step differences for the six-level scale and ≥ 3-step differences for the nine-level scale) [5]. The findings indicated that the nine-level scale may allow a greater number of eyes to meet eligibility criteria for clinical trials. The authors further noted that the nine-level scale exhibited superior reproducibility when evaluated at a reading center than when applied for clinical grading. This finding suggested that reading center evaluations may be more suitable for utilization in clinical trials [5].

Patient examples illustrating the grading of vitritis using the Nussenblatt vitreous haze scale [7] and the Miami scale [8] in individuals with uveitis of various etiologies are presented in Figures 1, 2, and 3.

The uveitis research community is in broad agreement regarding the necessity for objective methods to quantify the inflammatory activity in sight-threatening uveitis. In recent years, optical coherence tomography (OCT) has emerged as a prominent technique in this field, with a substantial number of publications addressing the topic [11-13]. Some studies have described various methods for measuring optical density [14] and/or signal intensities of the vitreous by using OCT imaging. Indirect measurements of vitreous haze have been obtained by calculating the vitreous/retinal pigment epithelium (RPE) relative density index on posterior segment OCT scans [15-17].

A retrospective observational case–control series was conducted to explore the potential of spectral domain-OCT (SD-OCT) for objectively measuring vitreous inflammation in patients with intermediate uveitis, posterior uveitis, and panuveitis. The study included 30 eyes from 30 patients diagnosed with vitreous haze due to intermediate, posterior, or panuveitis; 12 eyes from 12 patients with uveitis but without evidence of vitreous haze; and 18 eyes from 18 patients without intraocular inflammation or vitreoretinal disease [15].

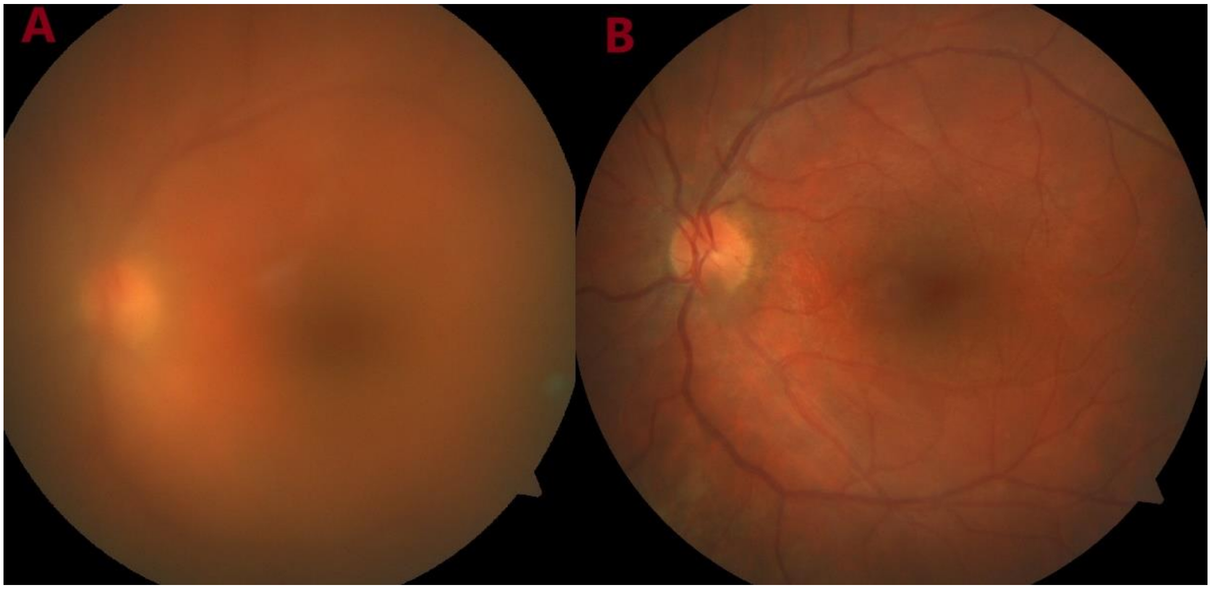

Figure 1. Color fundus photographs of a 40-year-old male patient with intermediate uveitis. The left eye (A), showing severe vitritis, was graded as 3+ on the National Institutes of Health scale [7] and as grade 8 on the Miami scale [8]. Resolution of vitritis was observed (B) following systemic treatment with azathioprine and corticosteroids.

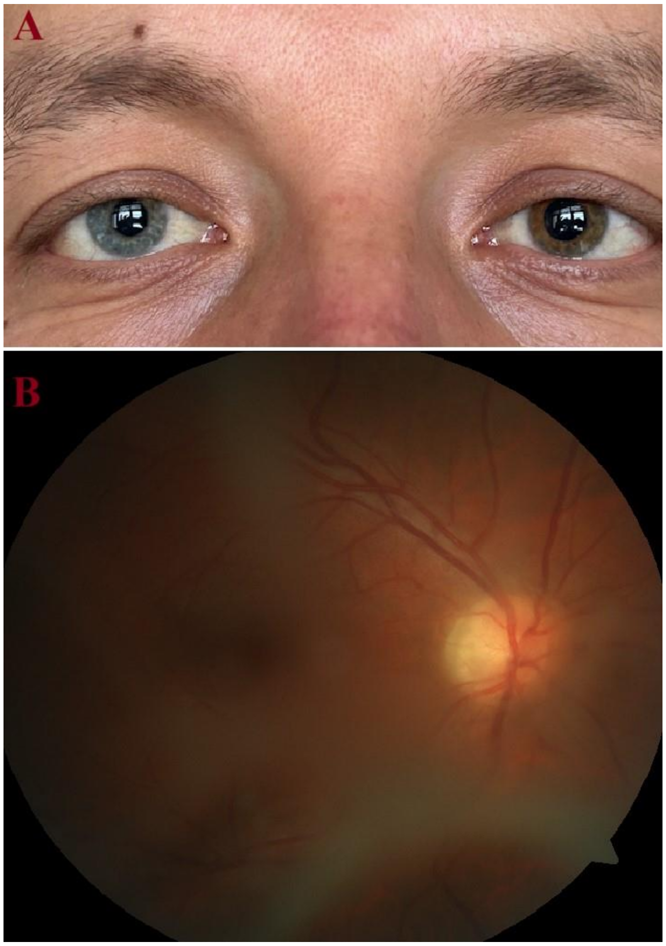

Figure 2. Images of a 45-year-old patient with Fuchs heterochromic iridocyclitis. Hypochromic heterochromia is evident in the patient's right eye (A). A color fundus photograph of the right eye demonstrates moderate vitritis, graded as 2+ on the National Institutes of Health scale [7] and as grade 4 on the Miami scale [8].

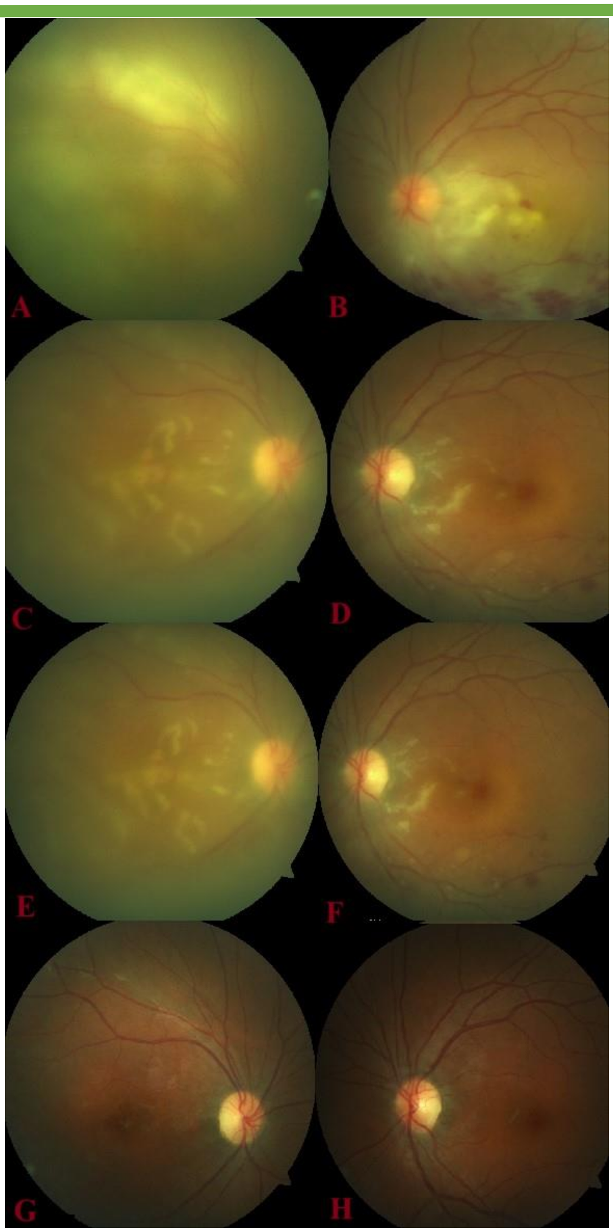

Figure 3. Color fundus photographs of a 20-year-old treatment-naive female with Behcet's disease with bilateral panuveitis. At admission, severe vitritis was observed in the right eye (A), graded as 4+ on the National Institutes of Health (NIH) scale [7] scale and grade 8 on the Miami scale [8], and mild vitritis in the left eye (B), graded as 2+ on the NIH scale [7] and grade 4 on the Miami scale [8]. After 3 days of intravenous pulse methylprednisolone therapy, the vitritis decreased to grade 3+ on the NIH scale [7] and grade 5 on the Miami scale [8] in the right eye(C), and to grade 2+ on the NIH scale [7] and grade 3 on the Miami scale [8] in the left eye (D). By 10 days after the intravenous pulse steroid treatment, vitritis further decreased to grade 2+ on the NIH scale [7] and grade 4 on the Miami scale [8] in the right eye (E), and to grade 1+ on the NIH scale [7] and grade 2 on the Miami scale [8] in the left eye (F). After 10 weeks of gradually tapered oral steroid therapy combined with subcutaneous adalimumab, no vitritis was observed in either eye (G, H).

The presence and severity of vitreous haze in that study were graded based on the NIH scale [7, 15]. SD-OCT images were processed using specialized custom software, which provided an "absolute" quantification of vitreous signal intensity (VIT). This measurement was then compared to the signal intensity of the RPE, and this optical density ratio was expressed in arbitrary units and referred to as the "VIT/RPE-relative intensity" [15]. The authors observed a substantial positive correlation between the VIT/RPE-relative intensity and clinical vitreous haze scores (r = 0.566, P = 0.0001). Furthermore, measurements of the VIT/RPE-relative intensity exhibited high intergrader reproducibility, with 95% limits of agreement ranging from - 0.019 to 0.016. The authors concluded that their findings provided preliminary evidence supporting the potential utility of OCT-derived measurements of VIT as an objective outcome measure in patients with uveitis [15]. Nevertheless, the study had several limitations that should be considered when interpreting the results [15]. First, the small sample size precluded subgroup analyses to evaluate factors such as lens status or previous vitreoretinal surgery. Second, the use of a single SD-OCT device limited generalizability across platforms. Third, the findings were derived from a single cohort analyzed by one team, which underscored the need for replication in independent populations and by different investigators, to validate the method's reliability [15, 16].

To address this, Zarranz-Ventura et al. [16] evaluated the method for objectively measuring vitreous inflammation using SD-OCT in a large cohort of uveitic eyes, including pseudophakic and vitrectomized eyes. Their retrospective observational study included 105 eyes from 105 patients with varying grades of vitreous haze scores, assessed according to standardized protocols, alongside corresponding SD-OCT images [16]. The clinical data collected encompassed the phakic status, vitreoretinal surgery history, and anterior chamber (AC) cell and flare grades. SD-OCT images were analyzed using custom-developed software to obtain absolute signal intensity measurements for the VIT and the RPE. These values were then used to calculate a VIT/RPE-relative intensity. The ratio was subsequently compared with vitreous haze scores [16]. The authors identified a significant positive correlation between VIT/RPE-relative intensity and vitreous haze scores (r = 0.535, $P < 0.001$). This correlation remained significant after adjusting for media clarity factors, such as AC cells, AC flare, and phakic status (R^2-adjusted = 0.424, $P < 0.001$) [16]. Notable differences in the VIT/RPE-relative intensity were observed among the vitreous haze score groups ($P < 0.001$). Preliminary findings revealed no significant differences in the VIT/RPE-relative intensity between phakic and pseudophakic eyes (0.3522 vs. 0.3577, $P = 0.48$) or between non-vitrectomized and vitrectomized eyes (0.3540 vs. 0.3580, $P = 0.52$), both overall and within vitreous haze subgroups [16]. The authors concluded that the VIT/RPE-relative intensity values obtained using SD-OCT provide an objective measurement of vitreous inflammation. The authors further emphasized that phakic status and prior vitrectomy do not appear to influence these values, although further studies are required to validate their findings [16].

In a separate study, Zicarelli et al. [17] sought to quantify the posterior segment inflammation objectively by analyzing the vitreous cells and haze through the OCT scans, comparing OCT-based measurements with clinical judgements. The severity of the vitreous haze was graded by using the NIH scale [7, 17]. Vitreous cell density was measured on OCT images using both the manual and automated methods via a custom-developed algorithm. Additionally, vitreous haze was assessed indirectly by calculating the VIT/RPE-relative intensity, employing both the manual and automated techniques [17]. That study also examined changes in OCT-derived measurements over time and compared these results with the clinical grading of the vitreous haze. The authors analyzed 222 OCT scans from 74 eyes. The study revealed a decline in both vitreous cell density and VIT/RPE-relative intensity over time [17]. These findings indicated a correlation between the cell density and clinical grading, with a notable increase in the cell density observed at each increasing level of the NIH scale. In contrast, while the VIT/RPE-relative intensity exhibited a positive correlation with the clinical grade overall, no significant differences were observed when comparing adjacent grades of the NIH scale [17]. Furthermore, the study observed a positive correlation between infectious uveitis and elevated cell density. The intraclass correlation coefficient was 0.83 for cell density and 0.423 for the VIT/RPE-relative intensity, indicating a substantial agreement between manual and automated assessments. The authors concluded that posterior segment inflammation could be objectively graded using OCT scans [17]. They further pointed out that vitreous cell density, assessed both manually and automatically, showed good agreement and correlated more strongly with the NIH clinical grading than with VIT/RPE-relative intensity [17].

Despite substantial advances in digital imaging and refinement in clinical grading scales, assessment of the vitreous haze remains inherently subjective. Currently, vitreous haze evaluation is performed through ophthalmoscopy by uveitis specialists in clinical settings or via digital fundus photographs by independently trained graders at reading centers [3]. However, the advent of AI-driven vitreous grading systems has revolutionized this process by enabling the precise, automated, and unbiased quantification of vitreous inflammation. These AI algorithms, trained on extensive datasets from imaging modalities, such as OCT and fundus photography, ensure consistent and reliable grading, thereby eliminating the variability introduced by human interpretation. These advances not only enhance the precision of vitreous cell evaluation, but also provide standardized metrics to seamlessly integrated into both clinical practice and research settings [3, 18, 19].

Keane et al. [20] conducted a study aimed at objectively quantifying vitreous signal intensity using macular OCT. The NIH classification system [7, 20] was employed to assess the presence and severity of the vitreous haze. SD-OCT images were analyzed with a customized software program, called VITreous ANalysis ("VITAN"), that performed automated segmentation, thus obviating the need for manual segmentation [20]. The authors introduced the OCT-derived VIT/RPE-relative intensity index [15, 20]. They showed that this ratio was significantly elevated in uveitic eyes with vitreous haze as compared to those without haze and healthy control eyes. The VIT/RPE-relative intensity index exhibited a significant positive correlation with vitreous haze scores using manual segmentation of vitreous and RPE (r = 0.566) [20]. Consequently, the authors proposed a rapid, automated approach for quantifying vitreous signal intensity using OCT, demonstrating a strong correlation with clinical evaluations of vitreous inflammation. The authors emphasized that OCT-based indices could serve as valuable objective markers of vitreous activity, facilitating both routine clinical assessments and providing reliable outcome measures in clinical trials for intermediate, posterior, and panuveitis [20].

Haggag et al. [21] developed an AI-driven computer-aided diagnostic (CAD) system for evaluating vitreous inflammation using macular OCT images. Their methodology involved a two-stage process for automating inflammation evaluation. In the initial stage, the system utilizes a U-net convolutional neural network, which employed three adaptive image descriptors incorporating grayscale images, distance maps, and prior shape data derived from manually segmented examples [21]. In the subsequent stage, a fully connected neural network analyzed cumulative distribution functions of vitreous signal intensities to classify inflammation as grades 0–3. The model's performance was evaluated using 200 OCT scans, resulting in an accuracy of 86% for inflammation grading [21]. While the system demonstrated promise as a reliable and objective instrument, its performance was constrained by the visual similarity of vitreous appearances at different inflammation levels. Nevertheless, the authors concluded that their findings underscore the potential of the CAD system to improve early detection and consistent grading of vitreous inflammation [21].

In a very recent study by Mhibik et al. [19], the authors explored the use of a deep learning algorithm for the automated detection and grading of vitritis using ultrawide-field fundus images. The study incorporated fundus photographs of uveitis patients and implemented the SUN system for grading vitreous haze [10, 19]. The researchers implemented a deep learning framework with TensorFlow and a DenseNet121 convolutional neural network for classification. The model's performance was validated using a dataset comprising 1181 images, and yielded noteworthy outcomes in vitritis detection. The model demonstrated a sensitivity of 91%, specificity of 89%, accuracy of 0.90, and an area under the receiver operating characteristics curve of 0.97 [19]. However, the model's accuracy for classifying vitritis using the comprehensive six-step SUN scale [10, 19] was found to be lower, with a sensitivity of 0.61 and specificity of 0.89. However, when the grading process was simplified into three categories, the accuracy of the model improved to 0.75. The authors concluded that the new deep learning model is an effective tool for detecting vitritis, with a satisfactory performance in classifying it into three severity categories. The authors further noted that enhancing model performance when using the six-step grading system through augmentation of the image dataset could lead to further improvements [19].

In a study, Passaglia et al. [3] sought to formulate a method for evaluating vitreous haze in patients with uveitis that was both objective and quantitative. They developed an image-processing algorithm designed to quantify vitreous haze through high-pass filtering, entropy analysis, and power-spectrum integration. The efficacy of this algorithm was then ascertained by applying it to 120 random fundus images obtained from a uveitis database [3]. These images were then compared against the grades assigned by two trained readers using the NIH [3, 7] and Miami [3, 8] scales, in addition to acutance, which is a measure of image clarity. The findings indicated a substantial correlation between the algorithm's and the reader's assessments, as evidenced by significant exact agreement ($\kappa = 0.61$ and 0.67) and nearly perfect within-one ($\kappa = 0.78$ and 0.82) and within-two ($\kappa = 0.80$ and 0.84) level agreements [3]. The authors concluded that the algorithm provided a reliable and quantitative method for assessing vitreous haze, closely matching the assessments of expert graders [3].

Notwithstanding the advances in AI-based techniques previously enumerated, numerous challenges remain. These challenges encompass variability in inflammatory presentation, the dependence on high-quality imaging, and the difficulty in discerning subtle variations in inflammation severity [18]. This underscores the necessity for persistent refinement and enhancement of AI-driven tools to bolster their accuracy and reliability in clinical applications [18].

This narrative review highlighted the results of relevant studies on vitreous haze, offering a comprehensive examination of currently available grading scales for vitreous haze. A salient strength of this analysis is its broad coverage of both conventional and contemporary grading systems, which provides an extensive perspective on the evolution of these scales. Nevertheless, the review has some limitations. The inherent subjective nature of narrative reviews could lead to the unintended exclusion of pertinent studies, thereby potentially resulting in an overly limited scope. Furthermore, the review is based exclusively on extant published data. As such, research and recent developments that are not yet reflected in the existing literature may not have been included. In contemplating future prospects, the continuous evolution and optimization of AI-driven systems should be acknowledged as a pivotal strategy in addressing the challenges posed by the subtle variations in vitreous haze. The integration of these sophisticated technologies within standard clinical practices holds potential to improve uveitis management markedly. This enhancement can be achieved by facilitating more precise monitoring, expediting early detection, and supporting personalized therapeutic strategies. To substantiate and refine these systems further, prospective research endeavors must concentrate on utilizing extensive, diverse datasets, thereby guaranteeing their relevance, scalability, and dependability in a range of clinical settings and across diverse patient populations.

CONCLUSIONS

The evaluation of vitreous haze is a critical step in the diagnosis and management of uveitis and other ocular conditions characterized by vitreous inflammation. The existing literature delineates two primary grading methods: the NIH scale and the Miami scale. These scales, although widely adopted, entail a subjective assessment of vitreous haze, rendering them susceptible to observer bias and interobserver variability. The NIH scale, which utilizes six levels, and the Miami scale, which uses nine levels, are both widely used; however, both of these scales are influenced by variability between observers. The advent of new objective imaging technologies, including ultrawide-field fundus photography and advanced OCT-based analysis, has led to the emergence of more consistent and standardized grading systems that may offer enhanced reliability. These innovative techniques demonstrate improved accuracy and sensitivity, facilitating the early detection and more effective monitoring of vitreous inflammation. Despite these advances, challenges persist, including the difficulty of distinguishing subtle variations in vitreous opacity and the variability of inflammatory presentations. Consequently, continuous enhancement of both conventional grading systems and AI-driven tools is imperative to attain more precise and reproducible outcomes in clinical practice, thereby enhancing patient care and advancing research into the management of uveitis.

ETHICAL DECLARATIONS

Ethical approval: This narrative review received ethical approval from the department level. The figures presented in this manuscript were derived from the archive of our unit's patient documentation. Patients provided informed consent before including figures in this review.

Conflict of interests: None.

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REFERENCES

1. Liu X, Hui BT, Way C, Beese S, Adriano A, Keane PA, Moore DJ, Denniston AK. Noninvasive Instrument-based Tests for Detecting and Measuring Vitreous Inflammation in Uveitis: A Systematic Review. Ocul Immunol Inflamm. 2022 Jan 2;30(1):137-148. doi: 10.1080/09273948.2020.1799038. Epub 2020 Oct 6. PMID: 33021418; PMCID: PMC8935946.
2. Liu X, Kale AU, Ometto G, Montesano G, Sitch AJ, Capewell N, Radovanovic C, Bucknall N, Beare NAV, Moore DJ, Keane PA, Crabb DP, Denniston AK. OCT Assisted Quantification of Vitreous Inflammation in Uveitis. Transl Vis Sci Technol. 2022 Jan 3;11(1):3. doi: 10.1167/tvst.11.1.3. PMID: 34982094; PMCID: PMC8742534.
3. Passaglia CL, Arvaneh T, Greenberg E, Richards D, Madow B. Automated Method of Grading Vitreous Haze in Patients With Uveitis for Clinical Trials. Transl Vis Sci Technol. 2018 Mar 23;7(2):10. doi: 10.1167/tvst.7.2.10. PMID: 29600118; PMCID: PMC5868860.
4. Madow B, Galor A, Feuer WJ, Altaweel MM, Davis JL. Validation of a photographic vitreous haze grading technique for clinical trials in uveitis. Am J Ophthalmol. 2011 Aug;152(2):170-176.e1. doi: 10.1016/j.ajo.2011.01.058. Epub 2011 Jun 8. PMID: 21652026; PMCID: PMC4556733.
5. Hornbeak DM, Payal A, Pistilli M, Biswas J, Ganesh SK, Gupta V, Rathinam SR, Davis JL, Kempen JH. Interobserver agreement in clinical grading of vitreous haze using alternative grading scales. Ophthalmology. 2014 Aug;121(8):1643-8. doi: 10.1016/j.ophtha.2014.02.018. Epub 2014 Mar 31. PMID: 24697913; PMCID: PMC4122589.
6. KIMURA SJ, THYGESON P, HOGAN MJ. Signs and symptoms of uveitis. II. Classification of the posterior manifestations of uveitis. Am J Ophthalmol. 1959 May;47(5 Pt 2):171-6. doi: 10.1016/s0002-9394(14)78240-6. PMID: 13649856.
7. Nussenblatt RB, Palestine AG, Chan CC, Roberge F. Standardization of vitreal inflammatory activity in intermediate and posterior uveitis. Ophthalmology. 1985 Apr;92(4):467-71. doi: 10.1016/s0161-6420(85)34001-0. PMID: 4000641.
8. Davis JL, Madow B, Cornett J, Stratton R, Hess D, Porciatti V, Feuer WJ. Scale for photographic grading of vitreous haze in uveitis. Am J Ophthalmol. 2010 Nov;150(5):637-641.e1. doi: 10.1016/j.ajo.2010.05.036. Epub 2010 Aug 16. PMID: 20719302; PMCID: PMC3220938.
9. Kempen JH, Ganesh SK, Sangwan VS, Rathinam SR. Interobserver agreement in grading activity and site of inflammation in eyes of patients with uveitis. Am J Ophthalmol. 2008 Dec;146(6):813-8.e1. doi: 10.1016/j.ajo.2008.06.004. Epub 2008 Aug 8. PMID: 18687418.
10. Jabs DA, Nussenblatt RB, Rosenbaum JT; Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. Am J Ophthalmol. 2005 Sep;140(3):509-16. doi: 10.1016/j.ajo.2005.03.057. PMID: 16196117; PMCID: PMC8935739.
11. Pichi F, Carreño E. The Vitreous in Uveitis: Characterizing the Invisible with Optical Coherence Tomography. Ocul Immunol Inflamm. 2022 Apr 3;30(3):690-696. doi: 10.1080/09273948.2022.2075399. PMID: 35901539.
12. Köksaldı S, Kayabaşı M, Mammadov T, Saatci AO. Are intravitreal hyperreflective particles alike in eyes with acute toxoplasma chorioretinitis and non-infectious uveitis? Photodiagnosis Photodyn Ther. 2024 Feb;45:103929. doi: 10.1016/j.pdpdt.2023.103929. Epub 2023 Dec 14. PMID: 38101501.
13. Invernizzi A, Zaffalon C, Manni P, Zicarelli F, Chisari D, Adani C, Mastrofilippo V, Bolletta E, Gozzi F, De Simone L, Staurenghi G, Cimino L. Anterior Vitreous Objective Assessment in Uveitis: An Anterior Segment Swept Source Optical Coherence Tomography Study. Ocul Immunol Inflamm. 2024 Apr 22:1-9. doi: 10.1080/09273948.2024.2339435. Epub ahead of print. PMID: 38648627.
14. Durmaz Engin C, Kayabasi M, Koksaldi S, Ipek SC, Saatci AO. Does Subretinal Fluid Optical Density Ratio Differ Among the Eyes with Acute Central Serous Chorioretinopathy,Vogt Koyanagi Harada Disease and Choroidal Hemangioma: A Cross-sectional Study. Photodiagnosis Photodyn Ther. 2023 Jun;42:103634. doi: 10.1016/j.pdpdt.2023.103634. Epub 2023 May 25. PMID: 37244453.
15. Keane PA, Karampelas M, Sim DA, Sadda SR, Tufail A, Sen HN, Nussenblatt RB, Dick AD, Lee RW, Murray PI, Pavesio CE, Denniston AK. Objective measurement of vitreous inflammation using optical coherence tomography. Ophthalmology. 2014 Sep;121(9):1706-14. doi: 10.1016/j.ophtha.2014.03.006. Epub 2014 May 15. PMID: 24835759; PMCID: PMC4507470.
16. Zarranz-Ventura J, Keane PA, Sim DA, Llorens V, Tufail A, Sadda SR, Dick AD, Lee RW, Pavesio C, Denniston AK, Adan A; EQUATOR Study Group. Evaluation of Objective Vitritis Grading Method Using Optical Coherence Tomography: Influence of Phakic Status and Previous Vitrectomy. Am J Ophthalmol. 2016 Jan;161:172-80.e1-4. doi: 10.1016/j.ajo.2015.10.009. Epub 2015 Oct 23. PMID: 26476212.
17. Zicarelli F, Ometto G, Montesano G, Motta S, De Simone L, Cimino L, Staurenghi G, Agarwal A, Pichi F, Invernizzi A. Objective Quantification of Posterior Segment Inflammation: Measuring Vitreous Cells and Haze Using Optical Coherence Tomography. Am J Ophthalmol. 2023 Jan;245:134-144. doi: 10.1016/j.ajo.2022.08.025. Epub 2022 Sep 7. PMID: 36084686.

18. Murugan SRB, Sanjay S, Somanath A, Mahendradas P, Patil A, Kaur K, Gurnani B. Artificial Intelligence in Uveitis: Innovations in Diagnosis and Therapeutic Strategies. Clin Ophthalmol. 2024 Dec 14;18:3753-3766. doi: 10.2147/OPTH.S495307. PMID: 39703602; PMCID: PMC11656483.

19. Mhibik B, Kouadio D, Jung C, Bchir C, Toutée A, Maestri F, Gulic K, Miere A, Falcione A, Touati M, Monnet D, Bodaghi B, Touhami S. AUTOMATED DETECTION OF VITRITIS USING ULTRAWIDE-FIELD FUNDUS PHOTOGRAPHS AND DEEP LEARNING. Retina. 2024 Jun 1;44(6):1034-1044. doi: 10.1097/IAE.0000000000004049. PMID: 38261816.

20. Keane PA, Balaskas K, Sim DA, Aman K, Denniston AK, Aslam T, And For The Equator Study Group. Automated Analysis of Vitreous Inflammation Using Spectral-Domain Optical Coherence Tomography. Transl Vis Sci Technol. 2015 Sep 16;4(5):4. doi: 10.1167/tvst.4.5.4. PMID: 26396930; PMCID: PMC4572940.

21. Haggag S, Khalifa F, Abdeltawab H, Elnakib A, Ghazal M, Mohamed MA, Sandhu HS, Alghamdi NS, El-Baz A. An Automated CAD System for Accurate Grading of Uveitis Using Optical Coherence Tomography Images. Sensors (Basel). 2021 Aug 13;21(16):5457. doi: 10.3390/s21165457. PMID: 34450898; PMCID: PMC8401645.