Retinal Hemorrhages: Etiologies, Diagnostic Approaches, and Management Strategies for Ocular and Systemic Disorders

Amer Hassan Mohammed Al-Shahri [1*], Ali Mesfer Alkhathami [1], Ali Jamal Faleh Al-Anzi [1], Binselm, Khalid Rashad A [1], Faleh Mohammed Al Dawsar [1], Al Duheem, Bader Sughayir D [1], Ahmad Ayad M Alanzi [1], Naif Munif Aldumayki Alotaibi [1], Saleh Helayyil Saleh Alharbi [1], Rayan Mohammed Mubarak Alotaibi [1]

Abstract

Retinal hemorrhages are pivotal clinical findings that signify a broad range of ocular and systemic pathologies, varying from benign to vision-threatening conditions. This review highlights the etiologies, clinical implications, diagnostic challenges, and emergency management strategies associated with retinal hemorrhages. A systematic analysis of peer-reviewed literature, clinical guidelines, and recent studies was performed, focusing on hemorrhage classification, pathophysiology, diagnostic approaches, and treatment protocols. Findings reveal that hemorrhage location critically influences prognosis and treatment strategies, with systemic diseases such as hypertension, diabetes, and coagulopathies accounting for 70% of adult cases. Nd:YAG laser membranotomy achieves up to 85% visual recovery in subhyaloid hemorrhages, while timely intervention within 7–14 days is crucial for submacular hemorrhages to prevent photoreceptor damage. Multidisciplinary management enhances outcomes in trauma- and abuse-related hemorrhages. Diagnostic imaging modalities like optical coherence tomography (OCT) and fundus fluorescein angiography (FFA), combined with targeted laboratory tests, are essential for accurate diagnosis. Ultimately, tailored management strategies based on anatomical and systemic contexts, coupled with prompt intervention, are critical for preserving vision and addressing underlying systemic disorders.

Keywords: retinal hemorrhage, submacular hemorrhage, vitreous hemorrhage, Terson syndrome, hypertensive retinopathy

Significance | Retinal hemorrhages are critical markers of ocular and systemic disease, requiring timely diagnosis and intervention to preserve vision.

*Correspondence. Amer Hassan Mohammed Al-Shahri, Ministry of National Guard Health Affairs, Prince Mutib Ibn Abdullah Ibn Abdulaziz Rd, Ar Rimayah, Riyadh 11426, Saudi Arabia.
E-mail: Akk29337@gmail.com

Editor Aman Shah Abdul Majid, Ph.D., And accepted by the Editorial Board Aug 15, 2024 (received for review May 30, 2024)

Introduction

Retinal hemorrhages serve as a critical ophthalmological indicator of systemic vascular pathology. These hemorrhages can vary in presentation from minute dot and blot formations to extensive subhyaloid bleeding. The characteristics of the hemorrhage, including its anatomical location, dimensions, and pattern offer valuable diagnostic insights, often revealing systemic conditions such as vascular abnormalities, hematologic diseases, blood dyscrasias, infections, traumatic injury, or hypoxia. In rare cases, retinal hemorrhages may occur without an identifiable cause (idiopathic). Due to their association with systemic disorders, most cases necessitate a comprehensive medical evaluation to determine the underlying etiology. Management of retinal hemorrhages

Author Affiliation.
[1] Ministry of National Guard Health Affairs, Prince Mutib Ibn Abdullah Ibn Abdulaziz Rd, Ar Rimayah, Riyadh 11426, Saudi Arabia.

Please cite this article.
Al-Shahri, A. H. M., Alkhathami, A. M., Al-Anzi, A. J. F., Binselm, A, K. R., Dawsar, F. M. A., Duheem, A., D, B. S., Αναζι, A. A. M., Alotaibi, N. M. A., Alharbi, S. H. S., Alotaibi, R. M. M. (2024). "Revolutionizing Healthcare: The Impact of Business and HR Analytics on Hospital Management, Cost Reduction, and Fraud Prevention", Journal of Angiotherapy, 8(8),1-8,10216

involves a multifaceted approach. Initial strategies typically include careful monitoring, particularly for smaller hemorrhages that may be resolved spontaneously. However, addressing the root systemic cause—whether it be hypertension, diabetes, anemia, or coagulopathy—is essential to prevent recurrence and further complications. In cases where hemorrhages lead to retinal ischemia or neovascularization, intraocular interventions may be required. These treatments aim to mitigate secondary damage, such as laser therapy to reduce abnormal blood vessel growth or intravitreal injections to manage associated edema or bleeding. Given the potential for vision-threatening complications, early detection and appropriate management are crucial. Ophthalmologists often collaborate with internists, hematologists, or other specialists to ensure a holistic approach to treatment. Long-term follow-up may be necessary to monitor for residual effects, such as macular scarring or glaucoma, which can arise from prolonged hemorrhage-related ischemia. Thus, retinal hemorrhages not only signify ocular pathology but also serve as a window into broader systemic health, warranting thorough investigation and coordinated care (Agrawal et al., 2012).

Etiology of Retinal Hemorrhages

Retinal hemorrhages occur in a range of ocular and systemic conditions, with their patterns and severity varying according to the underlying disease stage. Several primary ocular diseases can result in retinal hemorrhages. In age-related macular degeneration (ARMD) and polypoidal choroidal vasculopathy (PCV), hemorrhages arise from abnormal choroidal blood vessel growth, while juxtafoveal telangiectasia leads to localized hemorrhages near the macula. Optic disc hemorrhages are commonly seen in glaucoma and other optic nerve disorders (Agrawal et al., 2012). In diabetic retinopathy, dot and blot hemorrhages predominantly affect the posterior pole, and as the disease advances, retinal neovascularization can cause vitreous hemorrhages. These manifestations are typically bilateral and diffusely distributed, reflecting extensive microvascular injury resulting from chronic hyperglycemia (Binenbaum et al., 2009). In hypertensive retinopathy, flame-shaped hemorrhages occur due to rupture of superficial capillaries, with preretinal hemorrhages sometimes developing in severe cases. These hemorrhages are usually bilateral and focused in the posterior pole, correlating with the severity of systemic hypertension (Czorlich et al., 2015).

Retinal vein occlusions also contribute significantly, with central retinal vein occlusion (CRVO) producing diffuse intraretinal hemorrhages across all quadrants, while branch retinal vein occlusion (BRVO) causes sectoral hemorrhages localized to the area of the affected vein, both stemming from venous congestion and ischemia (Duane, 1972). Trauma induces a wide variety of retinal hemorrhage patterns depending on the mechanism of injury; multilayered hemorrhages involving the intraretinal, subhyaloid, and vitreous spaces can be unilateral or bilateral. Terson syndrome, associated with subarachnoid hemorrhage, and Valsalva retinopathy, triggered by sudden increases in intrathoracic pressure, often result in preretinal hemorrhages. Shaken baby syndrome produces bilateral, diffuse, multilayered hemorrhages in infants, while in neonates, birth trauma is the most common cause (Hochman et al., 1997).

Systemic conditions like severe anemia can give rise to Roth spots (white-centered hemorrhages), multilayered hemorrhages, subhyaloid hemorrhages, and vitreous hemorrhages, which are usually bilateral and widespread due to systemic hypoxia and vascular fragility (Kanukollu & Ahmad, 2023). Similarly, leukemia often presents with a variety of hemorrhages, including preretinal, vitreous, flame-shaped, and intraretinal hemorrhages, along with Roth spots and cotton wool spots; sea-fan neovascularization is also a hallmark feature. These manifestations are bilateral and diffuse, resulting from thrombocytopenia, hyperviscosity, and leukemic infiltration (Kaur & Taylor, 1990). In acute bacterial endocarditis, hemorrhages such as preretinal, vitreous, intraretinal, and flame-shaped types occur, predominantly in the parapapillary region, accompanied by cotton wool spots and Roth spots, resulting from septic emboli and immune complex deposition (Kaur & Taylor, 1992).

In sickle cell retinopathy, particularly in SC and S-Thal variants, characteristic findings include salmon patch hemorrhages, black sunburst lesions, and sea-fan neovascularization, with progression to vitreous hemorrhage due to chronic vascular occlusion and ischemia, typically affecting both eyes (Khawly & Pollock, 1994). Ocular ischemic syndrome, arising from chronic hypoperfusion usually secondary to carotid artery disease, presents with mid-peripheral intraretinal hemorrhages and retinal neovascularization (Kitagawa et al., 2016). Preeclampsia induces bilateral retinal changes such as intraretinal hemorrhages, Elschnig spots (choroidal infarcts), and serous retinal detachment, with severity dependent on blood pressure control (Ling & James, 1998).

Connective tissue disorders, notably systemic lupus erythematosus (SLE), can cause retinal hemorrhages and vascular occlusions in advanced stages due to immune-mediated vasculopathy, usually manifesting bilaterally (Liu et al., 2014). Additionally, exposure to high altitudes can provoke Roth spots, multilayered hemorrhages, and vitreous hemorrhages, resulting bilaterally from hypoxia-induced vascular changes (Loughrey et al., 2015). Retinal hemorrhages thus serve as critical diagnostic indicators for both ocular and systemic diseases, with their location, pattern, and distribution offering essential clues to the underlying etiology. Thorough systemic evaluation is often necessary, and management focuses on treating the primary disease and addressing secondary complications such as retinal ischemia and neovascularization (Loughrey et al., 2015).

Epidemiology of Retinal Hemorrhages

Retinal hemorrhages demonstrate distinct epidemiological patterns across different age groups. In critically ill pediatric patients without trauma or abuse history, retinal hemorrhages occur in approximately 15% of cases. These hemorrhages are typically mild and predominantly affect children under two years of age, with systemic infections, accidental head trauma, and severe coagulopathies being the most common associated conditions. Neonatal retinal hemorrhages show a clear correlation with delivery method, appearing in 25% of vaginally delivered newborns and increasing to 40-50% in instrumental deliveries (forceps or vacuum-assisted births). Child abuse represents a significant epidemiological concern, with retinal hemorrhages present in about 30% of physically abused children, particularly those under six months of age (Czorlich et al., 2015; Duane, 1972). In adult populations, the prevalence of retinal hemorrhages rises substantially after 40 years, primarily due to the increased incidence of systemic disorders such as hypertension, diabetes, and vascular diseases in this age group. The age-related patterns reflect both developmental vulnerabilities in pediatric populations and the cumulative effects of systemic diseases in adults. These epidemiological insights underscore the importance of considering both age-specific risk factors and underlying etiologies when evaluating patients with retinal hemorrhages. The varying prevalence rates across different populations highlight the need for tailored diagnostic approaches in clinical practice (Czorlich et al., 2015; Duane, 1972).

Pathophysiology of Retinal Hemorrhages

Retinal hemorrhages represent an important clinical finding that provides diagnostic information about both ocular and systemic conditions. These hemorrhages are classified based on their anatomical location within the retinal layers, with each type demonstrating distinct morphological characteristics and clinical implications (Hochman et al., 1997). Understanding the pathophysiology requires examination of their classification, appearance, and underlying causes.

Retinal Nerve Fiber Layer (RNFL) hemorrhages occur in the most superficial retinal layer and follow the orientation of nerve fiber bundles. Three distinct types are observed in this layer (Hochman et al., 1997). Flame-shaped hemorrhages appear as diffuse, linear lesions in the posterior pole that typically resolve within 6-12 weeks (Hochman et al., 1997). These occur in conditions affecting the superficial retinal capillary plexus, particularly arterial diseases like hypertension, blood dyscrasias, and anemias. Disc hemorrhages (Drance hemorrhages) present as superficial splinter-shaped lesions near the optic disc margin (Kanukollu & Ahmad, 2023; Kaur & Taylor, 1990). They are oriented perpendicular to the disc margin and are strongly associated with normal-tension glaucoma and primary open-angle glaucoma, though they may also occur in diabetes, anemia, and retinal vascular diseases (Kanukollu & Ahmad, 2023; Kaur & Taylor, 1990). Roth spots are round hemorrhages with white centers resulting from capillary rupture and fibrin-platelet plug formation (Kaur & Taylor, 1992; Khawly & Pollock, 1994; Kitagawa et al., 2016). While classically associated with subacute bacterial endocarditis, they also occur in leukemia, anemia, and other conditions (Kaur & Taylor, 1992; Khawly & Pollock, 1994; Kitagawa et al., 2016).

Intraretinal hemorrhages occur deeper within retinal layers, appearing as dense, dark red lesions with sharp borders (Hochman et al., 1997). They result from disorders affecting the deep capillary layer, including diabetic retinopathy, retinal vein occlusions, and ocular ischemic syndrome (Hochman et al., 1997). Purtscher retinopathy, an occlusive microvasculopathy from trauma, shows intraretinal whitening and hemorrhages (Ling & James, 1998). Similar findings (Purtscher-like retinopathy) occur in systemic conditions like acute pancreatitis and renal failure (Ling & James, 1998).

Subretinal hemorrhages, located between photoreceptors and the retinal pigment epithelium (RPE), appear as deep red lesions with diffuse margins (Hochman et al., 1997; Liu et al., 2014). Common causes include age-related macular degeneration, high myopia, and trauma (Hochman et al., 1997; Liu et al., 2014). Submacular hemorrhages frequently accompany choroidal neovascular membranes in age-related macular degeneration (Liu et al., 2014). Sub-RPE hemorrhages occur between RPE and Bruch's membrane, appearing dark red with sharp borders (Hochman et al., 1997). They are seen in choroidal neovascular membranes, tumors, and traumatic choroidal ruptures (Hochman et al., 1997).

Subhyaloid or preretinal hemorrhages are "boat-shaped" and collect between the vitreous and internal limiting membrane (Loughrey et al., 2015). Causes include Terson syndrome, which is associated with intracranial hemorrhage (Maguire et al., 2009), and Valsalva retinopathy from sudden pressure increases (Mennel, 2007). They also occur in proliferative diabetic retinopathy and retinal vein occlusions (Loughrey et al., 2015).

Vitreous hemorrhage occurs when there is bleeding into the vitreous cavity, appearing as fresh blood clots or diffuse clouding (Mills, 1998). Common causes include proliferative diabetic retinopathy, retinal tears during posterior vitreous detachment, and breakthrough bleeding from subretinal hemorrhages (Mills, 1998). Rare causes include choroidal melanoma and idiopathic polypoidal choroidal vasculopathy (Mills, 1998).

Shaken Baby Syndrome is a form of abusive head trauma characterized by multilayered retinal hemorrhages, intracranial injury, and occult fractures (Miguel et al., 2013). The hemorrhages result from repetitive acceleration-deceleration forces damaging retinal vessels (Miguel et al., 2013).

History and Physical Examination for Retinal Hemorrhages

A comprehensive history and thorough ophthalmic examination are essential for diagnosing the underlying cause of retinal hemorrhages. Clinicians should obtain detailed information regarding the patient's social conditions, medication history (particularly anticoagulants or antiplatelet drugs), and any history of trauma, abuse, or recent Valsalva maneuvers (e.g., heavy lifting, coughing, or vomiting). Symptoms such as sudden flashes, floaters, or transient vision loss should also be documented, as they may indicate vitreous hemorrhage or retinal traction. A complete ophthalmic evaluation includes slit-lamp examination of the anterior segment, measurement of intraocular pressure, and dilated fundus examination to assess the extent and location of hemorrhages. Ancillary imaging techniques, such as optical coherence tomography (OCT), fundus fluorescein angiography (FFA), and fundus photography, help determine the precise depth of hemorrhage and identify associated retinal abnormalities. In pediatric cases, abusive head trauma (shaken baby syndrome) must be suspected if a child under three years of age presents with multilayered retinal hemorrhages and concurrent intracranial injury (Ozturker et al., 2017). The presence of extensive, bilateral hemorrhages—particularly those involving the vitreous, subhyaloid, and intraretinal layers—should raise immediate concern for non-accidental injury, warranting further investigation and multidisciplinary involvement. A systematic approach to history-taking and physical examination ensures accurate diagnosis and timely intervention for both ocular and systemic conditions associated with retinal hemorrhages (Ozturker et al., 2017).

Evaluation of Retinal Hemorrhages: Diagnostic Workup

The evaluation of retinal hemorrhages requires a systematic approach that begins with assessing basic health parameters, including blood pressure, body mass index (BMI), and blood glucose levels, as these factors often contribute to vascular abnormalities that may manifest as retinal bleeding. Following this initial assessment, a targeted diagnostic workup should be performed to identify any underlying systemic disorders that could be responsible for the hemorrhages. For patients with suspected diabetes or metabolic syndrome, laboratory investigations should include a complete blood count (CBC) with platelet assessment to evaluate for thrombocytopenia or hematologic abnormalities. Additionally, inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) may indicate underlying vasculitis or infection. Metabolic screening should include fasting blood glucose, hemoglobin A1c (HbA1c), and a lipid profile to assess dyslipidemia, which is often associated with microvascular damage (Sato et al., 2013).

In cases where hypercoagulable states are suspected, coagulation studies are essential. These should include prothrombin time (PT) and activated partial thromboplastin time (aPTT) to assess clotting function. Further testing for protein C, protein S, factor V Leiden mutation, prothrombin gene mutation, homocysteine levels, antithrombin III activity, and antiphospholipid antibodies can help identify thrombophilic disorders that may predispose to retinal vascular occlusions and subsequent hemorrhages. For patients with suspected autoimmune conditions such as systemic lupus erythematosus (SLE), an autoimmune workup is critical. This includes antinuclear antibody (ANA) testing, anti-double-stranded DNA (anti-dsDNA) antibodies, anti-nRNP antibodies, anti-histone antibodies, and anti-Ro/SS-A and anti-La/SS-B antibodies. These tests help confirm autoimmune-mediated vasculopathy, which can lead to retinal vascular damage and hemorrhage (Sato et al., 2013).

Infectious etiologies must also be considered, particularly in cases of unexplained retinal hemorrhages. Serologic testing for syphilis (FTA-ABS/RPR) and HIV (ELISA) should be performed, as these infections can cause vasculitis and retinal vascular occlusions. When clinical suspicion remains high but initial tests are inconclusive, Lyme disease titers and herpes simplex virus (HSV) serology may be warranted to exclude masquerade syndromes that mimic retinal vascular disease. In patients presenting with both anterior and posterior segment inflammation, HLA-B51 and HLA-B12 testing should be considered to evaluate for Behçet disease, a systemic vasculitis that can lead to retinal vasculitis and hemorrhages. A comprehensive evaluation integrating clinical findings with targeted laboratory testing ensures accurate diagnosis and appropriate management of retinal hemorrhages, addressing both ocular manifestations and underlying systemic conditions (Sato et al., 2013).

Treatment and Management of Retinal Hemorrhages

The management of retinal hemorrhages depends on their type, location, severity, and underlying etiology. While many retinal hemorrhages resolve spontaneously without requiring direct intervention, certain vision-threatening hemorrhages necessitate prompt treatment to prevent permanent visual impairment. The treatment approach should always address both the hemorrhage itself and the systemic condition causing it (Sato et al., 2013).

Observation for Non-Threatening Hemorrhages

Most retinal hemorrhages that do not threaten vision can be managed conservatively with careful observation. Dot and blot hemorrhages, splinter hemorrhages, and flame-shaped hemorrhages typically occur in the posterior pole while sparing the fovea, allowing for monitoring rather than immediate intervention

(Hochman et al., 1997). These hemorrhages commonly appear in conditions like diabetic retinopathy, hypertensive retinopathy, and retinal vein occlusions. While the hemorrhages themselves may not require treatment, the associated retinal edema or subsequent neovascularization often needs management. For example, in retinal vein occlusions, while the intraretinal hemorrhages resolve over time, macular edema or retinal neovascularization that develops later may require laser treatment or intravitreal anti-VEGF injections (Hochman et al., 1997). Roth spots, which are retinal hemorrhages with white centers, are generally asymptomatic and resolve with treatment of the underlying systemic condition such as subacute bacterial endocarditis or hematologic disorders (Kaur & Taylor, 1992; Khawly & Pollock, 1994; Kitagawa et al., 2016).

Management of Subhyaloid Hemorrhages

Subhyaloid hemorrhages, which occur between the posterior hyaloid face and internal limiting membrane, present unique management challenges. These hemorrhages are classically seen in Terson syndrome (associated with intracranial hemorrhage) and Valsalva retinopathy (Maguire et al., 2009; Mennel, 2007). The initial approach is typically conservative observation for 1-3 months to allow for spontaneous resolution (Maguire et al., 2009). However, if the hemorrhage persists or the patient has high visual demands (such as professionals requiring acute central vision), Nd:YAG laser membranotomy can be performed to rupture the posterior hyaloid or internal limiting membrane (Mennel, 2007). This procedure allows the blood to drain into the vitreous cavity, where it settles inferiorly and away from the visual axis, often resulting in rapid visual recovery. For cases where vitreous hemorrhage persists and significantly impairs vision beyond 2-3 months, pars plana vitrectomy (PPV) may be necessary to clear the hemorrhage and restore vision (Mills, 1998).

Treatment of Submacular Hemorrhages

Submacular hemorrhages (SMH) represent one of the most vision-threatening forms of retinal hemorrhage, as the accumulation of blood beneath the macula can lead to irreversible photoreceptor damage (Sato et al., 2013). These hemorrhages most commonly occur secondary to choroidal neovascularization (CNV) associated with conditions such as exudative age-related macular degeneration (ARMD), polypoidal choroidal vasculopathy (PCV), high myopia, and angioid streaks. Clinically, CNV often presents as a dirty grey-green lesion beneath the retina, resulting from retinal pigment epithelium (RPE) hyperplasia, and may be accompanied by subretinal fluid, pigment epithelial detachments, and macular edema (Sato et al., 2013). Treatment strategies for SMH depend largely on the size and duration of the hemorrhage as well as the underlying etiology. Pneumatic displacement, involving intravitreal injection of expansile gases such as sulfur hexafluoride (SF6) or perfluoropropane (C3F8) combined with face-down positioning, aims to mechanically displace submacular blood away from the fovea. This technique can be enhanced by the adjunctive use of tissue plasminogen activator (tPA), which helps to liquefy the blood clot and facilitate displacement (Sato et al., 2013). Pharmacologic clot lysis with intravitreal recombinant tPA alone has also been employed to break down the fibrin matrix within the hemorrhage, promoting resorption. Anti-vascular endothelial growth factor (anti-VEGF) therapy targets the underlying CNV, stabilizing the vasculature and potentially reducing the size of the hemorrhage. In cases where the hemorrhage is large, dense, or longstanding—typically present for more than one to two weeks—pars plana vitrectomy combined with subretinal tPA injection and gas tamponade is often necessary to evacuate the blood and preserve vision (Sato et al., 2013). For patients at risk for CNV, such as those with ARMD, regular vision monitoring using Amsler grids is recommended to detect early metamorphopsia that could indicate new hemorrhage or neovascular activity.

Vitreous hemorrhage (VH), another common and serious retinal hemorrhage, requires a tailored approach based on the cause, severity, and duration of the bleed (Saxena et al., 2003). Initial conservative measures include bed rest with head elevation to facilitate the gravitational settling of blood within the vitreous cavity, bilateral eye patching to minimize ocular movements, and temporary discontinuation of antiplatelet medications where medically appropriate to reduce the risk of rebleeding. If spontaneous clearing does not occur, more definitive treatments are necessary. Laser photocoagulation is often used to treat retinal breaks or sites of neovascularization, simultaneously addressing the source of hemorrhage and preventing retinal detachment. In cases where media opacity prevents adequate visualization for laser treatment, cryotherapy may be employed as an alternative. Pars plana vitrectomy is indicated for dense, non-clearing VH persisting beyond two to three months, or sooner if accompanied by retinal detachment, rubeosis iridis, ghost cell glaucoma, or tractional complications. Ghost cell glaucoma, a potential sequela of long-standing vitreous hemorrhage, occurs when degenerated red blood cells (ghost cells) obstruct the trabecular meshwork, causing elevated intraocular pressure (Saxena et al., 2003). These khaki-colored ghost cells typically appear one to three months after hemorrhage onset, and the condition often requires surgical intervention to prevent permanent optic nerve damage.

Special considerations must be made in pediatric cases, particularly in instances of suspected abusive head trauma, such as shaken baby syndrome. In these situations, a multidisciplinary approach involving ophthalmologists, pediatricians, and child protection teams is essential (Miguel et al., 2013; Ozturker et al., 2017). Retinal hemorrhages in such cases are often multilayered, involving intraretinal, preretinal, and vitreous layers, and are usually bilateral. While most hemorrhages in children resolve spontaneously over several weeks to months, persistent vitreous hemorrhages that continue to obstruct vision may necessitate vitrectomy after a prolonged period of observation (Miguel et al., 2013).

Regardless of the specific type of retinal hemorrhage, systemic management is crucial to prevent recurrence and optimize outcomes. Tight glycemic control is paramount in diabetic retinopathy, while blood pressure regulation is essential in hypertensive retinopathy. In patients with hematologic disorders, careful adjustment of anticoagulation therapy is needed, and in cases of infectious endocarditis, appropriate antibiotic treatment is critical. Immunosuppressive therapy may be necessary for autoimmune vasculitis. Regular follow-up is necessary to monitor the resolution of hemorrhages and identify complications such as retinal neovascularization, tractional retinal detachment, macular edema, ghost cell glaucoma, and epiretinal membrane formation. Follow-up intervals vary according to the severity and location of the hemorrhage, ranging from weekly visits for acute submacular hemorrhages to monthly evaluations for stable intraretinal hemorrhages. The management of retinal hemorrhages demands a nuanced understanding that balances prompt ocular intervention with systemic disease control. While some hemorrhages can be managed conservatively, vision-threatening ones require timely surgical or pharmacologic treatment to preserve visual function. Advances in therapeutic techniques continue to refine management protocols, particularly for challenging cases like submacular hemorrhages, with the overarching goal of maintaining maximal visual potential in affected patients.

Differential Diagnosis of Retinal Hemorrhages by Age Group

The differential diagnosis of retinal hemorrhages varies significantly across different age groups, reflecting distinct underlying etiologies and risk factors. In neonates, retinal hemorrhages most commonly result from birth trauma, with incidence rates directly correlating with delivery method. Spontaneous vaginal delivery produces hemorrhages in approximately 25% of cases, while instrumental deliveries using vacuum extraction or forceps demonstrate higher rates of 40-50% (Binenbaum et al., 2009). The most severe cases occur with combined vacuum-forceps deliveries, emphasizing the mechanical nature of these hemorrhages.

In infants and children, the differential diagnosis expands to include both ocular and systemic conditions. Non-accidental trauma, particularly shaken baby syndrome, represents a critical consideration requiring prompt identification. Other ocular causes include Coats disease, persistent fetal vasculature, retinopathy of prematurity, and retinal dysplasia. Systemic conditions in this age group encompass hematologic disorders such as leukemia and protein C deficiency, cardiovascular abnormalities, and severe infections. Pediatric hypertension, though less common than in adults, can also manifest with retinal hemorrhages (Uhler & Piltz-Seymour, 2008). Adult populations present with a distinct set of differential diagnoses dominated by vascular and systemic disorders. Diabetes mellitus and hypertension rank as the most frequent causes, often presenting with characteristic hemorrhage patterns. Hematologic conditions including leukemia and various blood dyscrasias must be considered, particularly when hemorrhages appear atypical or bilateral. High-altitude exposure, severe hypoxia, and high myopia represent additional potential causes. Posterior vitreous detachment with associated retinal tears or detachment may lead to vitreous hemorrhages, while Roth spots suggest specific systemic conditions (Uhler & Piltz-Seymour, 2008).

The differential diagnosis for Roth spots merits particular attention as these white-centered hemorrhages indicate diverse systemic pathologies. Infectious causes include subacute bacterial endocarditis, while hematologic conditions encompass leukemia and severe anemia. Hypoxic states such as carbon monoxide poisoning, prolonged anesthesia with intubation, and high-altitude exposure can produce similar findings. Pregnancy-related conditions including preeclampsia and complicated deliveries may cause Roth spots in both mothers and neonates. Neurologic conditions such as shaken baby syndrome and intracranial hemorrhage from vascular malformations complete the differential. Iatrogenic causes, particularly acute intraocular pressure reduction following glaucoma surgery, may also produce these characteristic lesions (Uhler & Piltz-Seymour, 2008). This comprehensive differential diagnosis underscores the importance of considering both local ocular pathology and systemic disease when evaluating retinal hemorrhages. The patient's age, medical history, and hemorrhage characteristics guide appropriate diagnostic testing and management, ensuring accurate identification of the underlying condition while preventing vision-threatening complications.

Prognosis of Retinal Hemorrhages

The prognosis of retinal hemorrhages varies significantly depending on their location, underlying cause, and timely management. In neonates and infants, hemorrhages resulting from birth trauma or accidental injury typically demonstrate favorable outcomes, with most resolving spontaneously within 2 to 4 weeks without long-term visual sequelae (Binenbaum et al., 2009). Similarly, hemorrhages associated with metabolic disorders such as diabetes or retinal vein occlusions often improve with proper control of the systemic condition, particularly when detected and managed early. Submacular and subretinal hemorrhages carry a guarded prognosis due to their proximity to the photoreceptor layer. Without prompt intervention, these hemorrhages can lead to

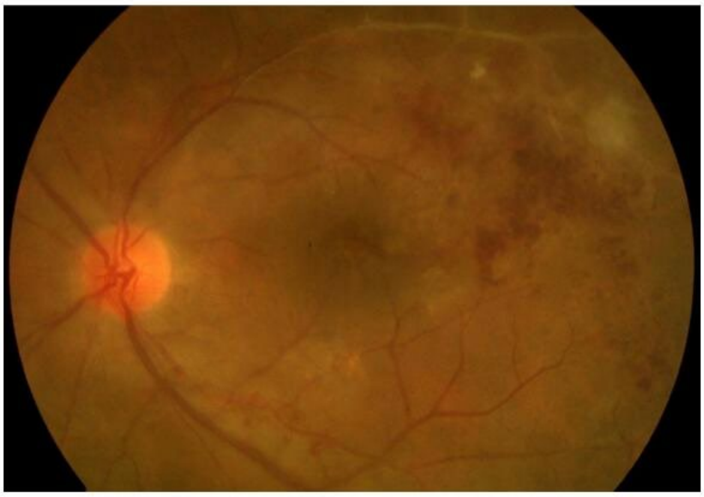

Figure 1. Eales Disease. Tuberculosis-delayed hypersensitivity uveitis (Eales disease) presenting with hemorrhagic ischemic vascular occlusion. Retinal hemorrhages, vascular obliteration, and sheathing temporal to the macula can also be seen.

vision loss demands careful clinical judgment. Sight-threatening hemorrhages, such as dense vitreous hemorrhages and submacular hemorrhages, call for immediate, aggressive intervention. Techniques like pneumatic displacement combined with intravitreal tissue plasminogen activator (tPA) have proven effective, with data indicating significant visual acuity gains when treatment is initiated within a two-week window. Likewise, Nd:YAG laser disruption of subhyaloid hemorrhages and vitrectomy for persistent vitreous hemorrhages are essential tools in the therapeutic arsenal.

However, the treatment of retinal hemorrhages extends far beyond localized ocular therapy. Their presence often signals an underlying systemic disease—hypertension, diabetes, hematologic disorders, or even trauma-related pathology in pediatric populations. Notably, up to 30% of adult patients with retinal hemorrhages may harbor undiagnosed systemic illnesses, while in children, multilayered hemorrhages raise immediate concern for abusive head trauma, necessitating a sensitive, multidisciplinary response. These observations highlight the indispensable role of comprehensive systemic evaluation alongside ophthalmologic treatment.

The growing sophistication of multimodal imaging technologies—particularly optical coherence tomography (OCT) and fundus fluorescein angiography (FFA)—enhances the clinician's ability to assess hemorrhage depth, ischemic burden, and underlying vascular pathology. Targeted laboratory investigations, including hematologic, infectious, and autoimmune panels, further help elucidate systemic contributors. Yet challenges remain. The optimal timing for intervention in submacular hemorrhages continues to provoke debate, as does the safe management of patients on systemic anticoagulation. While emerging therapies such as microplasmin-assisted vitrectomy and next-generation anti-VEGF agents offer exciting potential, their efficacy and safety require validation through robust, randomized clinical trials.

Critical knowledge gaps persist, notably in the standardized management of hemorrhages associated with sickle cell retinopathy and the establishment of evidence-based protocols for pediatric hemorrhages, especially in the context of trauma. In light of these gaps, three principal strategies are recommended. First, risk-stratified management based on hemorrhage location, size, and chronicity should be universally implemented. Second, systemic evaluations must be mandated even when hemorrhages initially appear isolated to the eye. Third, multidisciplinary approaches—encompassing ophthalmology, pediatrics, neurology, hematology, and social services—should be standard practice, especially in trauma and abuse-related cases.

Looking ahead, the integration of artificial intelligence in hemorrhage detection, classification, and risk prediction holds promise for revolutionizing care pathways. Furthermore, future research should prioritize randomized trials comparing early versus delayed interventions for submacular hemorrhages, as well as direct comparisons of surgical and pharmacologic strategies in various clinical scenarios. Ultimately, retinal hemorrhages must be recognized not as isolated ophthalmic findings but as systemic alarms requiring holistic patient-centered management. Their study and treatment demand an interdisciplinary mindset, blending ophthalmologic expertise with broader internal medicine acumen, and their evolving management will increasingly benefit from technological innovation and collaborative research.

Conclusion

Retinal hemorrhages, bridging ophthalmology and systemic medicine, serve as critical diagnostic and prognostic markers. Effective management demands urgent ocular intervention for vision-threatening cases and thorough systemic evaluation to uncover underlying diseases. Proven therapies like pneumatic displacement with tPA, vitrectomy, and Nd:YAG laser, along with advances in imaging and emerging pharmacologic innovations, have expanded treatment possibilities. Nevertheless, challenges such as managing anticoagulated patients and standardizing pediatric protocols persist. Future directions must include risk-based strategies, mandated systemic assessments, and AI-assisted diagnostic support. Recognizing retinal hemorrhages as manifestations of broader health issues ensures comprehensive patient care and optimizes both visual and systemic outcomes.

Author contributions

H.M.A.S. conceived and designed the study. A.M.A., A.J.F.A.A., and B.K.R.A. contributed to data collection and methodology development. F.M.A.-D. and A.D.B.S.D. performed data analysis and interpretation. A.A.M.A. and N.M.A.A. contributed to the statistical analysis and validation. S.H.S.A. and R.M.M.A. assisted in drafting and critically revising the manuscript. All authors reviewed and approved the final version of the manuscript for submission.

Acknowledgment

Not declared

Competing financial interests

The authors have no conflict of interest.

References

Agrawal, S., Peters, M. J., Adams, G. G., & Pierce, C. M. (2012). Prevalence of retinal hemorrhages in critically ill children. Pediatrics, 129(6), e1388–e1396. https://doi.org/10.1542/peds.2011-2772

Binenbaum, G., Mirza-George, N., Christian, C. W., & Forbes, B. J. (2009). Odds of abuse associated with retinal hemorrhages in children suspected of child abuse. Journal of AAPOS, 13(3), 268–272. https://doi.org/10.1016/j.jaapos.2009.03.005

Czorlich, P., Skevas, C., Knospe, V., Vettorazzi, E., Richard, G., Wagenfeld, L., Westphal, M., & Regelsberger, J. (2015). Terson syndrome in subarachnoid hemorrhage, intracerebral hemorrhage, and traumatic brain injury. Neurosurgical Review, 38(1), 129–136. https://doi.org/10.1007/s10143-014-0573-3

Duane, T. D. (1972). Valsalva hemorrhagic retinopathy. Transactions of the American Ophthalmological Society, 70, 298–313.

Hochman, M. A., Seery, C. M., & Zarbin, M. A. (1997). Pathophysiology and management of subretinal hemorrhage. Survey of Ophthalmology, 42(3), 195–213. https://doi.org/10.1016/S0039-6257(97)00086-4

Kanukollu, V. M., & Ahmad, S. S. (2023). Retinal hemorrhage. In StatPearls [Internet]. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK560777/

Kaur, B., & Taylor, D. (1990). Retinal haemorrhages. Archives of Disease in Childhood, 65(12), 1369–1372. https://doi.org/10.1136/adc.65.12.1369

Kaur, B., & Taylor, D. (1992). Fundus hemorrhages in infancy. Survey of Ophthalmology, 37(1), 1–17. https://doi.org/10.1016/0039-6257(92)90002-9

Khawly, J. A., & Pollock, S. C. (1994). Litten's sign (Roth's spots) in bacterial endocarditis. Archives of Ophthalmology, 112(5), 683–684. https://doi.org/10.1001/archopht.1994.01090170129032

Kitagawa, Y., Shimada, H., Mori, R., Tanaka, K., & Yuzawa, M. (2016). Intravitreal tissue plasminogen activator, ranibizumab, and gas injection for submacular hemorrhage in polypoidal choroidal vasculopathy. Ophthalmology, 123(6), 1278–1286. https://doi.org/10.1016/j.ophtha.2016.01.035

Ling, R., & James, B. (1998). White-centred retinal haemorrhages (Roth spots). Postgraduate Medical Journal, 74(876), 581–582. https://doi.org/10.1136/pgmj.74.876.581

Liu, Z., Pan, X., & Bi, H. (2014). Treatment of Valsalva retinopathy. Optometry and Vision Science, 91(11), e278–e281. https://doi.org/10.1097/OPX.0000000000000403

Loughrey, P. B., Armstrong, D., & Lockhart, C. J. (2015). Classical eye signs in bacterial endocarditis. QJM, 108(11), 909–910. https://doi.org/10.1093/qjmed/hcv089

Maguire, S., Pickerd, N., Farewell, D., Mann, M., Tempest, V., & Kemp, A. M. (2009). Which clinical features distinguish inflicted from non-inflicted brain injury? A systematic review. Archives of Disease in Childhood, 94(11), 860–867. https://doi.org/10.1136/adc.2008.150110

Mennel, S. (2007). Subhyaloidal and macular haemorrhage: Localisation and treatment strategies. British Journal of Ophthalmology, 91(7), 850–852. https://doi.org/10.1136/bjo.2006.108571

Miguel, A. I., Henriques, F., Azevedo, L. F., Loureiro, A. J., & Maberley, D. A. (2013). Systematic review of Purtscher's and Purtscher-like retinopathies. Eye, 27(1), 1–13. https://doi.org/10.1038/eye.2012.222

Mills, M. (1998). Funduscopic lesions associated with mortality in shaken baby syndrome. Journal of AAPOS, 2(2), 67–71. https://doi.org/10.1016/S1091-8531(98)90067-1

Ozturker, Z. K., Munro, K., & Gupta, N. (2017). Optic disc hemorrhages in glaucoma and common clinical features. Canadian Journal of Ophthalmology, 52(6), 583–591. https://doi.org/10.1016/j.jcjo.2017.05.015

Sato, T., Morita, S., Bando, H., Sato, S., Ikeda, T., & Emi, K. (2013). Early vitreous hemorrhage after vitrectomy with preoperative intravitreal bevacizumab for proliferative diabetic retinopathy. Middle East African Journal of Ophthalmology, 20(1), 51–55. https://doi.org/10.4103/0974-9233.106388

Saxena, S., Jalali, S., Verma, L., & Pathengay, A. (2003). Management of vitreous haemorrhage. Indian Journal of Ophthalmology, 51(2), 189–196.

Uhler, T. A., & Piltz-Seymour, J. (2008). Optic disc hemorrhages in glaucoma and ocular hypertension: Implications and recommendations. Current Opinion in Ophthalmology, 19(2), 89–94. https://doi.org/10.1097/ICU.0b013e3282f3919b

Watts, P., Maguire, S., Kwok, T., Talabani, B., Mann, M., Wiener, J., Lawson, Z., & Kemp, A. (2013). Newborn retinal hemorrhages: A systematic review. Journal of AAPOS, 17(1), 70–78. https://doi.org/10.1016/j.jaapos.2012.09.009