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BIOMARKERS IN GEOGRAPHIC ATROPHY: PREDICTIVE VALUE AND IMPLICATIONS FOR ADVANCED THERAPEUTIC STRATEGIES IN AMD: A NARRATIVE REVIEW

Urszula Borucińska[1] ✉, ***Hanna Pietruszewska [2]***, ***Oliwia Sędziak[3]***, ***Natalia Kruszewska [4]***, ***Sabina Skrzynecka[5]***, ***Karol Perski [6]***

[1] *Dr. Anna Gostyńska Wolski Hospital, Warsaw, Poland*
[2] *Medical University of Łódź, Poland*
[3] *Faculty of Medicine, University of Opole, Poland*
[4] *Provincial Hospital in Poznan, Poland*
[5] *University Clinical Hospital in Opole, Poland*
[6] *mjkstomatologia.pl Dental Clinic, Warsaw, Poland*

✉ ***ula.borucinska123@gmail.com***

ABSTRACT

Background: Geographic atrophy is an advanced form of age related macular degeneration that causes irreversible loss of retinal structures. Imaging shows structural changes but does not reflect molecular mechanisms, which creates a need for biomarkers that can support earlier detection and guide therapeutic development.

Aims: This review analyses molecular biomarkers associated with geographic atrophy, their links to pathogenic mechanisms and disease progression and their potential use in prediction and targeted therapeutic strategies.

Methods: A structured search of peer reviewed English language literature was performed in PubMed and Google Scholar for publications from 2002 to September 2025. Search terms included geographic atrophy, age related macular degeneration, biomarkers, aqueous humor, tear fluid, proteomics, oxidative stress and complement system. Eligible studies included reviews, clinical and observational studies, case series and clinical guidelines. Preprints and studies without biomarker related data were excluded. Fifty publications were included.

Results: Identified biomarkers in aqueous humor, tear fluid, plasma, urine and retinal tissues reflect oxidative stress, complement activation, inflammatory pathways and lipid dysregulation. These markers show associations with disease activity and may complement imaging by indicating underlying molecular processes. Experimental evidence suggests that modulation of complement activity, oxidative stress and inflammation may influence progression and that biomarker profiles may support patient stratification.

Conclusions: Biomarkers provide insight into mechanisms of geographic atrophy and may assist in prediction, risk assessment and planning of targeted therapies. Further validation and methodological standardization are required to determine their diagnostic and prognostic value.

Keywords: age related macular degeneration, geographic atrophy, biomarkers, aqueous humor, tear fluid, proteomics, complement system, oxidative stress, inflammation, metabolomics, retina

INTRODUCTION

Geographic atrophy (GA) secondary to age-related macular degeneration (AMD) is a progressive and irreversible degenerative disease of the macula for which no effective preventive or restorative treatments currently exist [1]. Several studies have shown that age over 60, genetics, smoking, and dietary factors are additional known risk factors [2]. Age remains the most significant determinant. This condition is the leading cause of blindness in developed countries. The aging of the global population indicates an inevitable surge in the absolute number of AMD patients worldwide, with a projected increase from 196 million in 2020 to 288 million by 2040 [3]. GA is manifested as loss of retinal pigment epithelium (RPE) cells, overlying photoreceptors, and underlying choroidal capillaries, which does not involve blood or serum leakage. Despite recent progress in treatment, effective strategies to prevent photoreceptor loss or halt the GA lesions enlargement are still lacking [4,5]. Progression rates of GA vary substantially between patients and have been estimated to average approximately 1.5 square millimeters per year according to longitudinal imaging studies [27].

Aqueous humor (AH) in the anterior chamber does not come directly in contact with the retina, but retinal proteins may diffuse from the vitreous to the aqueous compartment. Analysis of the aqueous humor proteome could be helpful to offer important perspectives on the mechanisms underlying retinal disease and GA pathogenesis. Since retinal proteins and inflammatory mediators can diffuse from the retina into the aqueous humor and tear fluid, their levels may reflect the ongoing cellular and molecular changes in GA, making them potential predictive biomarkers of disease progression. Moreover, these biomarkers could serve as potential therapeutic targets for the development of precision treatments. Molecular differences have been found between patients with AMD and the control [1,6,7]. Proteomics is a powerful platform for studying both single proteins and complex protein samples. Mass spectrometry (MS) can be used to study biomarkers of AMD [4,5]. Moreover, most existing studies are limited by small sample sizes, lack of standardization and methodological constraints. For example, mass spectrometry based approaches typically detect less than 5% of the total proteome and often fail to identify low-abundance proteins, which could be highly relevant for disease progression [4]. This highlights the need for a comprehensive overview of aqueous humor and tear fluid biomarkers in GA. Diagnosis and monitoring of GA currently rely on clinical examination and retinal imaging modalities, such as optical coherence tomography (OCT) and fundus autofluorescence (FAF) [8,9]. These techniques allow for detailed visualization of atrophic lesions and longitudinal assessment of their progression. These biomarkers provide a molecular perspective on retinal changes, complementing imaging and clarifying the mechanisms behind observed structural damage. Nevertheless, imaging alone cannot fully capture the underlying molecular mechanisms driving disease progression. In this context, fluid biomarkers derived from aqueous humor or tear samples could complement imaging-based approaches, enhancing the prediction of GA progression.

RELEVANCE

Geographic atrophy is a leading cause of irreversible central vision loss in developed countries, and the increasing number of elderly patients makes it a significant public health concern. Despite recent advances with complement inhibitors, no available therapies can halt photoreceptor degeneration. Current monitoring relies primarily on imaging and does not capture the underlying molecular mechanisms that drive disease progression. This creates a clear need to investigate biomarkers in ocular fluids that may reflect local inflammatory and degenerative changes, improve prediction of GA progression, and support the development of personalized therapeutic approaches.

NOVELTY

This review brings together data on biomarkers derived from aqueous humor and tear fluid and relates them to the key pathogenic mechanisms of geographic atrophy. Its distinct contribution lies in integrating proteomic, metabolomic, and immunologic alterations and demonstrating their links to complement activation, oxidative stress, and inflammasome signaling. The article also outlines methodological constraints of current proteomic research and underscores the need for standardization, allowing a critical evaluation of biomarker utility both for prognostication and for advancing targeted therapeutic strategies.

AIM

The aim of this narrative review is to analyse molecular biomarkers associated with geographic atrophy secondary to age related macular degeneration and to evaluate their clinical relevance. The review examines biomarkers detected in aqueous humor and tear fluid as primary sources and also considers complementary biomarkers identified in plasma, urine and retinal tissues when they contribute to understanding pathogenic mechanisms. The aim includes assessment of associations between biomarkers and disease progression, evaluation of their potential predictive value and consideration of how biomarker profiles may inform individualized therapeutic strategies. A further aim is to identify methodological limitations that influence biomarker detection, interpretation and clinical translation.

Research questions

Which molecular biomarkers in aqueous humor and tear fluid are associated with geographic atrophy and what biological processes do they reflect

Which additional biomarker sources such as plasma urine and retinal tissue provide meaningful information for understanding geographic atrophy mechanisms

How consistently do identified biomarkers correlate with the rate or pattern of geographic atrophy progression

Can molecular biomarkers support prediction of disease activity or future lesion enlargement

How may biomarker profiles contribute to patient stratification or guide the selection of emerging targeted therapies

What methodological limitations affect biomarker studies in geographic atrophy including sample handling analytical sensitivity and variability between study protocols

Which areas require standardization to enable reliable validation and clinical application of biomarkers in geographic atrophy

MATERIAL AND METHODS

This narrative review is based on a structured search of peer reviewed literature in PubMed and Google Scholar. The search was limited to publications written in English. Keywords included geographic atrophy, age related macular degeneration, biomarkers, aqueous humor, tear fluid, proteomics, oxidative stress, complement system, retinal pigment epithelium, photoreceptor degeneration and therapeutic strategies.

Inclusion criteria:

- publications written in English
- peer reviewed sources
- studies reporting biomarkers relevant to geographic atrophy or dry age related macular degeneration
- studies addressing diagnostic, prognostic or therapeutic implications of biomarkers
  systematic reviews, meta analyses, randomized and non randomized clinical studies, observational studies, narrative reviews, case series, case reports, clinical guidelines

Exclusion criteria:

- preprints
- publications without biomarker related content
- studies not relevant to geographic atrophy

Reference lists of all included publications were reviewed to identify additional relevant sources. The final reference list contains fifty items.

RESULTS

PATHOPHYSIOLOGY OF AMD AND GEOGRAPHIC ATROPHY

The retinal pigment epithelium nourishes the photoreceptor layer, where rods and cones perform the phototransduction process and also maintains important homeostatic functions of the retina, phagocytosis, and electrolyte balance [10,11].

With aging, the retinal pigment epithelium (RPE) becomes increasingly vulnerable to both intrinsic and extrinsic oxidative stress, as well as environmental factors such as cigarette smoke. The cumulative oxidative damage promotes the development of drusen, which are yellowish extracellular deposits rich in lipids and proteins [12]. These deposits also contain lipofuscin and by-products of photoreceptor outer-segment degradation, such as A2E, as well as other oxidative stress–related compounds, including advanced glycation end products [13]. The appearance and progression of drusen deposits are prognostic features of GA [12]. Drusen accumulation may lead to chronic inflammation via multiple paths, such as complement cascade and the NLRP3 inflammasome [13]. The complement system can be activated through three distinct pathways: the classical, triggered by antigen-antibody complexes; the lectin, activated by microbial polysaccharides; or the alternative, initiated by foreign pathogen cell surfaces [14]. Age- and inflammation-related accumulation of C1q, an initiating component of the classical complement pathway, has been implicated in retinal damage and is considered a major factor in the initiation and progression of GA [15]. Protease complexes, known as C3 and C5 convertases, cleave complement factor C3 into the pro-inflammatory

anaphylatoxin C3a and the opsonin C3b, as well as generate C5a and C5b. In AMD patients, components of the complement system C5, C3, and its fragments were detected in the subretinal space and the drusen particles [16-23]. The C5b leads to formation of MAC (membrane attack complex) and these deposits accumulate within Bruch's membrane- an extracellular matrix located between the retinal pigment epithelium and the choroid- and in the choriocapillaris, with the extent of deposition increasing with age and the presence of AMD. The formation of the membrane attack complex (MAC) in the choriocapillaris and its interaction with choroidal endothelial cells induce cell lysis, which likely contributes to RPE atrophy in both atrophic AMD and neovascular AMD [18-20]. These findings suggest that components of the complement system are essential in maintaining retinal homeostasis and structural integrity during aging. Targeting early complement factors is crucial, as their activation triggers a cascade of events leading to retinal damage; intervening at this initial stage may help prevent or reduce subsequent injury to the retinal tissue. Consequently, the importance of early complement factors should be taken into consideration when developing therapeutic strategies for AMD. Pegcetacoplan, recently approved by the FDA for intravitreal injection for GA secondary to AMD, is a complement inhibitor that binds to complement protein C3 and its activation fragment C3b to regulate the cleavage of C3 and the generation of downstream effectors of complement activation [10,24]. The NLRP3 inflammasome is a multiprotein complex in the cytoplasm that participates in the production of pro-inflammatory cytokines, including caspase-1 and the crucial IL-1β and IL-18, which is believed to play a major role in retinal degeneration [25,26]. Ongoing research aims to elucidate the pathways that activate the NLRP3 inflammasome. One proposed mechanism involves the accumulation of RNA resulting from downregulation of the RNA-processing enzyme DICER1, which in turn triggers cell death through NLRP3 inflammasome activation [27]. Reduced DICER1 expression and the consequent RNA accumulation have been observed in human donor eyes affected by GA. Experimental studies have demonstrated that exposure of cultured RPE cells to individual drusen components, such as A2E—the primary fluorophore of lipofuscin—induces secretion of IL-1β through inflammasome activation. Similarly, in vivo data from mouse models show that intravitreal administration of amyloid-β, another drusen constituent, results in transcriptional upregulation of inflammasome-related genes in the neuroretina, accompanied by elevated levels of IL-1β and IL-18 [25,26]. Experimental evidence indicated that exogenous exposure to complement components, including C3a, C5a, and the membrane attack complex (MAC), can stimulate NLRP3 inflammasome activation. These in vitro findings suggest that complement activation may promote downstream cytokine signaling via IL-1β and IL-18 [13]. Overall, oxidative stress, persistent complement activation, and inflammasome signaling constitute interrelated pathogenic mechanisms that synergistically contribute to RPE degeneration and the progression of GA.

SOURCES OF BIOMARKERS IN AMD

Retinal biomarkers can immensely contribute to the early detection of AMD. Detection of serum biomarkers in AMD may facilitate monitoring of disease progression and therapeutic outcomes. Assessing concentrations of C-reactive protein (CRP), cholesterol, interferon γ, homocysteine, and proinflammatory cytokines such as IL 8 can provide insight into AMD risk and hold potential as screening tools [10]. Biomarkers can be measured in various biological fluids, including aqueous humor, plasma, urine and RPE [1,4]. Visual function, genetic and imaging biomarkers also can be used. Among imaging techniques, Optical Coherence Tomography (OCT) is the most frequently utilized and provides the ability to identify relevant structural biomarkers as drusen volume, hyper-reflective foci, hyper-transmission defects, reticular pseudo drusen, and incomplete RPE and outer retinal atrophy (iRORA) [1,28]. In the management of GA, Fundus autofluorescence (FAF) patterns such as hypo-autofluorescent atrophic areas and hyper-autofluorescent lesions are widely recognized as reliable indicators for delineating atrophic areas and tracking disease progression [29]. Next, we review the main classes of biomarkers, highlighting their potential roles in prediction of GA progression. In GA, the degeneration of the retinal pigment epithelium (RPE) may increase permeability between the choriocapillaris and the retina, enabling blood-derived proteins to enter retinal tissue and subsequently diffuse into the aqueous humor [1]. Table 1 summarizes key biomarker sources in geographic atrophy and explains that each source has specific methodological constraints related to sampling feasibility, tissue specificity and analytical reliability.

Table 1. Biomarker sources and methodological limitations

Biomarker	Source	Methodological limitations
Clusterin, Serpin A4, TF	Aqueous humor	Limited sample volume, lack of standardization
TIMP3, ES8L2, C1R, STMN2	Retinal pigment epithelium (RPE) / retinal tissue	Invasive sampling, limited sample availability

APOC1, APOA1, APOE, HDL	Plasma	Systemic variability, may not fully reflect local retinal processes
SERPINA1, TIMP1, APOA1	Urine	Low eye specificity, influenced by systemic metabolism
GPX3, SOD1, SOD3, CAT, Alpha-1-antitrypsin	Vitreous	Rarely studied, small sample sizes, limited availability
IL-6, IL-1β, IL-18, NLRP3	Aqueous humor / plasma	Differences between local and systemic levels, assay sensitivity

CLASSES OF BIOMARKERS

Biomarkers associated with AMD can be classified according to the source of material from which they are obtained. They may be detected locally in ocular fluids such as aqueous humor, in plasma,urine or through tissue analysis and imaging techniques. This division reflects not only the feasibility of sample collection but also the extent to which the biomarker mirrors local retinal pathology versus systemic processes. Aqueous humor (AH) provides a valuable source for protein biomarkers such as clusterin, Serpin A4 and TF [30]. Transferrins (TFs) function as carriers of iron, delivering it to tissues for storage or metabolic use following absorption or heme degradation. Additionally, serum transferrin may contribute to the stimulation of cell proliferation [31]. Studies have also shown that Transferrin receptor and variability of its gene might also influence AMD risk [32].

RPE represents an important source for tissue inhibitor of metalloproteinases (TIMP3), ES8L2 protein, C1R complement component, Stathmin 2 (STMN2), which are involved in maintaining extracellular matrix integrity, immune response, and cytoskeletal stability [33]. The five proteins exhibiting the highest fold change (FC) between GA patients and controls were ITIH3, RNASE4, Phospholipase A2 Group IIA (PLA2G2A), Secreted Frizzled-Related Protein (5SFRP5), and Apolipoprotein C1 (APOC1), reflect substantial alterations in pathways relevant to AMD pathophysiology, such as lipid metabolism, inflammation, and cellular stress. Other AMD- related proteins showed smaller changes, such as APOE and CFB. Neutrophil elastase and alpha-2-macroglobulin (macrophage- secreted) levels also rose [4].

Plasma constitutes a useful source for NRG4 and sICAM-1 protein [34]. Urine serves as a key source for SERPINA1, TIMP1 and APOA1- one of the major components of high-density lipoprotein (HDL) [35]. Studies have indicated that increased HDL cholesterol levels may play a role in drusen formation during AMD development [36].

There were only 3 studies that examined the vitreous of AMD patients. There were none with GA patients. Alpha-1-antitrypsin reached statistical significance, while transthyretin and apolipoprotein A- 1 (APO A1) showed a nonsignificant increase in untreated neovascular AMD [37]. All 4 oxidative stress related proteins- GPX3 (Glutathione Peroxidase 3), SOD1 (Superoxide Dismutase 1), SOD3 (Superoxide Dismutase 3), and CAT (Catalase)- showed upregulation trends in proteasomics of Vitreous in AMD patients [4]. Analysis of tear film revealed that eight proteins were exclusive to AMD, with 98 unique to dry AMD and 110 specific to neovascular AMD (nvAMD) [38]. SPARC-Related Modular Calcium Binding (SMOC2), one of the top pathophysiological biomarker candidates in aqueous humor, shows increased expression in the macula of AMD donor eyes compared to controls and could be originating from the retina and is a potential biomarker for AMD. In a recent study, IL 6 was identified among the top ten proteins exhibiting the highest fold change between non-AMD controls and GA patients. In geographic atrophy, IL-6 is believed to play a role in sustaining chronic inflammation, which is considered a key factor driving disease progression. Analysis of paired plasma and aqueous humor samples collected on the same day revealed no correlation between systemic and local IL 6 levels, and no significant association with age was observed. These findings indicate that IL 6 in aqueous humor may serve as a potential biomarker for GA progression [1].

Inflammatory and immune-related proteins- NT-proBNP, TNFRSF13B, and CXCL9 - were found to be elevated in patients with geographic atrophy (GA) compared with those with intermediate AMD [1].

Redox regulating proteins- glutathione peroxidase 8 (GPX8) also appeared relevant with glutathione peroxidase 8 (GPX8) identified as a key regulator of oxidative homeostasis. The authors proposed GPX8 as a promising target for future research in AMD progression [39].

Metabolic biomarkers including serum levels of hypoxanthine, 2-furoylglycine, and 1-hexadecyl-2-azelaoyl-sn-glycero-3-phosphocholine showed a gradual increase from non-progressive to progressive stages of AMD, indicating their potential utility as reliable indicators for tracking disease progression and severity as well as for tracking the advancement and intensity of AMD [40]. Although existing studies display some heterogeneity, several proteins have consistently demonstrated significant alterations and have been validated as potential biomarkers for AMD [4]. Notably, aqueous humor biomarkers remain of particular interest, as they may provide direct insight into local retinal

and choroidal processes driving AMD progression.

Table 2 summarizes major biomarker classes in geographic atrophy, illustrating how complement activation, oxidative and inflammatory pathways, lipid metabolism disturbances and extracellular matrix dysregulation contribute to RPE and photoreceptor damage and to AMD progression.

Table 2. Biomarker classes and their biological relevance in geographic atrophy

Biomarker class	Examples of biomarkers	Biological relevance in GA
Complement and immune-related proteins	C1q, C1R, C3, C5, CFB, MAC, NT-proBNP, TNFRSF13B, CXCL9	Complement activation, chronic inflammation, RPE and photoreceptor damage
Oxidative stress / redox-related proteins	GPX3, GPX8, SOD1, SOD3, CAT, A2E, advanced glycation end products (AGEs)	Oxidative damage to RPE and photoreceptors, lipofuscin accumulation
Inflammasome / inflammatory cytokines	IL-1β, IL-18, IL-6, NLRP3	Inflammasome activation, chronic inflammatory response, RPE cell death
Lipid and metabolic biomarkers	APOC1, APOA1, APOE, HDL, 1-hexadecyl-2-azelaoyl-sn-glycero-3-phosphocholine, hypoxanthine, 2-furoylglycine	Lipid metabolism dysregulation, drusen formation, AMD progression
Structural / extracellular matrix (ECM) regulators	TIMP3, ES8L2, STMN2, clusterin, Serpin A4, transferrin (TF)	ECM integrity, RPE homeostasis, regulation of cell proliferation

TREATMENT OF GA AND ONGOING CLINICAL TRIALS

Pegcetacoplan, a C3 inhibitor administered via intravitreal injection, has been shown to significantly reduce GA lesion growth [22,41]. Reported cases of retinal vasculitis following intravitreal pegcetacoplan administration have raised safety concerns regarding complement inhibition therapy. These safety concerns highlight the need for a more detailed understanding of complement inhibition, as it can simultaneously reduce GA lesion progression while potentially increasing the risk of neovascularization. The precise role of complement inhibition in these processes has yet to be elucidated, underscoring the need for further studies to clarify its complex involvement in AMD pathogenesis [22,42]. ACP-Avacincaptad Pegol, another complement inhibitor, demonstrates similar benefits in slowing GA progression in the GATHER1 and GATHER2 trials [43]. ANX007, a C1q inhibitor currently under development, represents a promising therapeutic approach aimed at preserving visual function in patients with geographic atrophy. By blocking C1q activation, ANX007 prevents initiation of the classical complement cascade involving C4, C3, and C5, which has been implicated in retinal tissue damage. Pharmacological inhibition of C1q has been shown to protect photoreceptor cells and maintain their function, even when administered after photooxidative injury has occurred [44]. In the MAHALO study, lampalizumab- a monoclonal antibody directed against complement factor D- was evaluated as a potential therapy for geographic atrophy. Factor D plays a key role in the activation of C3 convertase within the alternative complement pathway. Administered via intravitreal injection, lampalizumab demonstrated a 20% reduction in GA lesion area progression at 18 months in eyes receiving monthly treatment compared to sham controls [45]. AVD-104 is a glycomimetic, sialic acid– coated nanoparticle designed to selectively bind receptors on activated macrophages, promoting their repolarization toward a resting phenotype and thereby suppressing their phagocytic activity. In addition to modulating macrophage function, AVD-104 has been shown to inhibit the complement cascade and mitigate inflammatory damage in preclinical retinal models. Administered via intravitreal injection, this agent is currently being developed by Aviceda Therapeutics as a potential treatment for GA [10]. Beyond complement inhibition, other therapeutic approaches include the use of statins, which lower cholesterol levels and may aid in the clearance of lipid deposits in patients with AMD. In a study involving individuals at high risk of disease progression, treatment with high- dose atorvastatin (80 mg) was associated with a reduction in lipid accumulation, improved visual acuity, and a slower transition to advanced stages of AMD [46,47]. Oxidative damage to polyunsaturated fatty acids within photoreceptor membranes, particularly docosahexaenoic acid (DHA), contributes to retinal degeneration. Deuterated DHA, which exhibits resistance to lipid peroxidation, has demonstrated protective potential against such degenerative processes in the retina [48]. With aging, decreased expression of the ELOVL2 (Elongation of Very Long Chain Fatty Acids-Like 2) gene leads to a reduction in long and very long chain

polyunsaturated fatty acids (PUFAs), a change that has been linked to the pathogenesis of AMD [49]. Subretinal delivery of VGX-0111, carrying an ELOVL2 transgene, is being planned as a treatment for dry AMD. The large Age-Related Eye Disease Study (AREDS) demonstrated that daily supplementation with specific vitamins and minerals reduced drusen formation and lowered the risk of progression to neovascular (wet) AMD and associated vision loss. These formulations, now marketed as AREDS2 supplements, are recommended for patients at high risk of developing AMD. The heterogeneity observed in GA progression underscores the need for personalized therapeutic strategies. Combination approaches, such as complement inhibition together with photobiomodulation or dietary supplementation, may provide synergistic benefits and deserve further investigation [50]. Additionally, photobiomodulation therapy (PBM) and dietary supplementation have been explored as noninvasive alternatives, with some improvements in visual outcomes and slower disease progression, particularly in earlier stages

DISCUSSION

CLINICAL RELEVANCE AND LIMITATIONS

Geographic atrophy remains a condition for which current therapies cannot restore the damaged retinal pigment epithelium or the outer retinal layers. Available evidence indicates that the most promising therapeutic directions target molecular pathways involved in oxidative stress, complement activity, inflammation and neurodegeneration. Several experimental approaches described in the reviewed studies, including oxidative stress modulation, stem cell based interventions and neuroprotective strategies, illustrate the effort to identify mechanisms that could slow the degenerative process.

Interpretation of biomarker studies is limited by methodological constraints. Mass spectrometry based methods detect only a small proportion of the total proteome and have reduced sensitivity for low abundance proteins, while aptamer based assays extend proteome coverage but do not provide absolute quantification. Additional sources of variability arise from differences in protein identification criteria and statistical approaches. Many studies include small cohorts, and sample pooling is sometimes required, introducing selection bias. The origin of total protein content in aqueous humor from patients with geographic atrophy remains unclear, raising questions about the biological relevance of some findings. These limitations indicate the need for larger, well characterized cohorts and standardized analytical procedures to improve reproducibility and interpretability. Despite these constraints, the available evidence contributes to an improved understanding of disease mechanisms and outlines potential avenues for therapeutic development.

FUTURE DIRECTIONS

Future research should prioritize validation of candidate biomarkers in larger and clinically homogeneous cohorts. Standardization of proteomic and metabolomic techniques is required to reduce methodological variability and allow meaningful comparison across studies. Integration of multiomics approaches, including genomics, transcriptomics, proteomics and metabolomics, may provide a more complete representation of pathogenic processes and support the identification of biomarker panels. Longitudinal studies will be necessary to determine the predictive value of biomarkers for disease progression and treatment response. Insights from these investigations may guide the development of personalized therapeutic approaches, including complement inhibition, oxidative stress modulation, neuroprotection and combination strategies aimed at slowing or halting progression and preserving visual function.

CONCLUSION

This review summarizes current evidence on molecular biomarkers associated with geographic atrophy and shows that alterations in oxidative stress, complement activity, inflammatory pathways and lipid metabolism are reflected in the composition of aqueous humor and tear fluid as well as in plasma, urine and retinal tissues. These biomarkers correspond to key pathogenic mechanisms and demonstrate associations with disease activity and progression patterns. Molecular profiles may complement imaging based assessment by clarifying underlying mechanisms of tissue damage and may provide a basis for patient stratification in the context of emerging targeted therapeutic approaches.

Available evidence remains fragmented, and the findings across studies are limited by methodological variability, small cohorts and insufficient standardization of analytical procedures. Larger and clinically homogeneous cohorts together with unified analytical protocols are required to validate the diagnostic and prognostic value of these biomarkers and to enable their integration into clinical practice.

DISCLOSURE

Authors' contributions

Conceptualization: Urszula Borucińska, Hanna Pietruszewska and Oliwia Sędziak;

Methodology: Urszula Borucińska, Hanna Pietruszewska and Oliwia Sędziak;

Investigation: Urszula Borucińska., Hanna Pietruszewska, Natalia Kruszewska. and Oliwia Sędziak;

Writing: Urszula Borucińska, Sabina Skrzynecka, Oliwia Sędziak;., Karol Perski, Natalia Kruszewska and Hanna Pietruszewska;

Supervision: Urszula Borucińska;

Project Administration: Urszula Borucińska, Karol Perski and Oliwia Sędziak;

Conflicts of interest

The authors declare that they have no conflict of interest.

Use of AI

Artificial intelligence tools, such as ChatGPT and other OpenAI systems, were used to support language refinement and structural improvement. All AI-generated contributions were thoroughly reviewed and verified by the authors.

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