Keywords: Alport syndrome, fleck retinopathy, lenticconus, corneal dystrophy, cataracts.

Summary

Alport syndrome (AS) is a hereditary disease that causes hearing impairment, kidney failure, and ocular abnormalities. Because AS is a rare disease, it might remain undetected, meaning impacted individuals and their kin have low chances of being screened and receiving timely genetic counseling. Also, diagnosing AS requires high expertise and complex technology, which are expensive for most patients. These limitations might hinder them from getting the appropriate medical attention and hinders efforts to fight it. Additionally, a standard diagnostic method has not been established, so it is difficult to determine the prevalence accurately. This paper investigates ocular manifestations of AS and the prevalence of the disease.

Introduction

Most ocular abnormalities in AS do not impact vision but are essential in diagnosing the disease and evaluating its inheritance (Savige et al., 2016). Diagnosis is critical since it can predict whether other family members are impacted. Early detection and treatment of AS can delay complications and end-stage kidney failure. For instance, lenticconus often develops in middle-aged years when kidney failure has already developed. Therefore, an early AS diagnosis may save the lives of affected individuals and their family members because it lowers the risk of early renal failure. Savige et al. (2015) argue that the main characteristics of AS are hearing loss, progress failure of the renal system, and ocular problems. When the COL4A3, COL4A4, and COL4A5 (X-linked) genes experience mutations, they cause the loss of collagen IV α3α4α5 network from the basic membranes of the retina, lens capsule, and the cornea, and scientists have noticed that they are associated with anterior lenticconus, corneal opacities, temporal retinal thinning, and fleck retinopathy. Normally, these features have no impact on vision, and the lenticconus is correctable. However, the rarer ophthalmic problems of the posterior polymorphous corneal dystrophy, maculopathy, and giant macular hole might cause blindness. Scientists might use the ophthalmic features to determine the mode of inheritance.

There are no clear statistics about the prevalence of AS across the world. Based on existing estimates, the prevalence varies from 1 in 5,000 to 1 in 53,000 people. Similarly, the situation in Baltic countries remains largely unknown (Savige et al., 2021). The prevalence of AS in Baltic countries can be estimated using data related to renal failure. Alport syndrome is the second largest risk factor for inherited kidney failure (Savige et al., 2021). Patients with ocular manifestations, such as retinopathy, also tend to develop renal failure (Shaw et al., 2007). Baltic countries have a low prevalence of end-stage kidney failure. For instance, the incidence of renal failure in Estonia ranges from 22–85 persons per million (Thurlow et al., 2021). The people treated for end-stage kidney failure in Latvia range from 117–540 persons per million (Thurlow et al., 2021).

Purpose of the Study. This literature review focuses on the prevalence of AS in different countries and its ocular manifestations. The study especially focuses on the prevalence and impact of the disease in the Baltic countries, the US, and the UK.

Research Objectives and Methods

There were three objectives of this study: 1). To determine the prevalence of AS in different countries. 2). To identify the most common ocular manifestations of the AS. 3). To establish the diagnosis of AS.

For the study to accomplish the prevalence of AS in different countries, it reviewed two current journals and information from the National Organization of Rare Disorders (NORD). The study obtained data regarding the prevalence of AS in the US, Sweden, Poland, and other parts of Europe and compared it to know the prevalence of the disease in the two regions. The study identified the flaws in the data collected, given that scientists have problems with diagnosing
AS because there are no standard diagnostic criteria, and the problem is difficult to study because it is rare.

For the study to accomplish the most common ocular manifestations of AS, it obtained information from academic journals and critically analyzed it. The study identified lenticonus, fleck retinography, and corneal dystrophy as the most common ocular abnormalities for people with AS. Other abnormalities identified were lamellar and cataracts. The study explained the prevalence of the abnormalities in males and females, challenges with their diagnosis, and processes involved in developing the abnormalities. An explanation was also provided for the link between the abnormalities and AS.

For the study to accomplish the diagnosis of AS, it collected information from peer-reviewed academic journals, critically reviewed it, and created two tables. The first table shows the abnormalities in the glomerular basement membrane (GBM) alongside the basements of other tissues, including ears and eyes. It also provided the differential diagnosis of various types of AS and other diseases/disorders. The second table highlighted the importance of ocular features in diagnosis, prediction of early-onset renal failure, and identifying the mode of inheritance.

Research results

Prevalence of the Disease in Different Countries. Alport syndrome has been studied widely, but there are no global figures about its incidence, prevalence, and related mortality. The aggregation of valid figures about the prevalence of AS is challenging because of the lack of broadly accepted diagnostic criteria (Hertz, 2009). In 2020, about 47 scientific and medical specialists from different continents held meetings in London to develop unified guidelines for genetic testing of AS in molecular laboratories (Savige et al., 2021). Despite holding two sessions, the scientists and medical specialists did not develop uniform diagnostic criteria. Amidst these challenges, there are sufficient data to predict AS’s prevalence. The disease has been reported in different countries and affects people of different ethnic groups.

The prevalence of AS in the US is 1:5,000. This prevalence was developed following the discovery of 300 cases of AS in a population of 1,500,000 across southern Idaho and Utah (Hertz, 2009). Furthermore, 77 cases of AS were reported in Rhode Island, where the population is approximately 1,000,000 people. Based on these new cases, the prevalence became 1:13,000 (Hertz, 2009). Over time, data on the prevalence of AS in the US have been updated to reflect new reports. The most recent data from the National Organization for Rare Disorders (NORD) estimate that AS affects about 1 in 5,000–10,000 persons in the US, meaning nearly 30,000–60,000 individuals in the US have the disease (Kashtan, 2020). This disease accounts for about 3% of children suffering from kidney disease and 0.2% of adults with end-stage kidney failure in the US (Kashtan, 2020).

The prevalence of the disease might be higher in certain European countries. An examination of 269 patients listed in Poland’s Children’s National Registry for glomerular hematuria showed that 131 patients had X-linked AS (Żurowska et al., 2021). Also, the study identified that 195 adults related to these children were affected by AS (Żurowska et al., 2021). Poland is likely experiencing a high prevalence of AS across all age groups. In Finland, the prevalence is predicted at 1:53,000 people (Heidet & Lennon, 2020), and that of southern Sweden is 1:17,000 (Hertz, 2009). The disease affects about 1.3% of every 1,000 persons who undergo a kidney transplant in Sweden (Hertz, 2009). Across Europe, nearly 0.56% of all dialysis patients are diagnosed with AS (Hertz, 2009). These statistics suggest that AS is not widely prevalent in different countries worldwide. However, the data does not account for diagnostic difficulty, misdiagnosis, or undiagnosed disease. Uniform diagnostic criteria and classification of AS can produce actual data on global prevalence.

Ocular Manifestations. The most common ocular abnormalities in individuals diagnosed with AS include lenticonus, fleck retinopathy, and corneal dystrophy. Vast research has been done on these three ocular abnormalities, revealing their prevalence and manifestations. Additional ocular manifestations that might develop among individuals with Alport syndrome include partial-thickness macular holes or lamellar and cataracts (Zhang & Ding, 2018).

Fleck Retinopathy. Most people diagnosed with autosomal recessive disease and men with X-linked AS suffer from peripheral or mid-peripheral retinopathy (Shaw et al., 2007). Peripheral retinopathy develops in about 33% (3 in 9) of individuals with X-linked AS and is more common than central retinopathy in women with X-linked AS carriers. Peripheral retinopathy can affect the periphery, mid-periphery, or both. Even though these might be sparse and localized, they can affect the entire periphery. Fleck retinopathy can have diverse symptoms or manifestations in affected persons (Figure 1). In their study, Shaw et al. (2007) stated that peripheral retinopathy consisted of diffuse confluent depigmented regions, and mid-peripheral retinopathy consisted of flecks and dots. Nevertheless, the patterns of appearance are likely to differ from one family member to another. According to Fawzi et al. (2009), mid-peripheral or peripheral flecks in the retina are less described in previous studies despite the possibility of being the only symptom among X-linked carriers.

Earlier studies had led to a flawed conclusion that retinopathy manifestations only appear in the inner retina.
because of type IV collagen gene mutations; the collagen prominently forms the internal limiting membrane (Fawzi et al., 2009). However, type IV collagen has also been discovered in Bruch’s membrane (Fawzi et al., 2009). Retinopathy mainly manifests as whitish-yellow flecks or dots and does not impact vision. Importantly, fleck retinopathy does not impact visual acuity, and retinal function tests appear normal or show only minor abnormalities. Although retinopathy is often detected with ophthalmoscopy, it is documented through photographs (Shaw et al., 2007). When eyes are not carefully examined, retinopathy might be missed or mischaracterized.

**Lenticonus.** Lenticonus is the cone-shaped protrusion in the anterior or posterior lens (Bamotra, Meenakshi, & Qayum, 2017). Anterior lenticonus is perhaps the most common manifestation in patients with AS (Figure 2). Zhang and Ding (2018) stated that the anterior lenticonus develops in a quarter to half of the males with X-linked AS and is linked to the early start of kidney failure. The occurrence of lenticonus is strongly linked with AS diagnosis. Slit-lamp examinations by well-trained ophthalmologists are vital to detect lenticonus. If lenticonus is not identified early, it might worsen, leading to visual symptoms (Zhang & Ding, 2018).

Even though anterior lenticonus is prevalent, posterior and anterior might occur simultaneously. Nevertheless, simultaneous posterior and anterior lenticonus is uncommon (Bamotra et al., 2017). Bamotra et al. (2017) reported simultaneous posterior and anterior lenticonus presentation in a woman aged 22 years. The ocular examination resulted in the detection of AS in the 22-year-old woman. The posterior lenticonus is mostly unilateral and linked to Lowe’s syndrome, while the anterior lenticonus is usually bilateral and might be linked to AS. These ocular abnormalities involve the retina and the lens but rarely the cornea (Bamotra et al., 2017).

**Corneal Dystrophy.** Research has not placed a lot of at-

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**Figure 1.** (a) Typical perimacular dots and flecks, (b) peripheral retinopathy, (c) dull macular reflex (lozenge), and (d) red-free photograph demonstrating the dots and flecks in 1c more obviously. (Source: Savige et al., 2009)

**Figure 2.** Anterior lenticonus in the right eye in a patient with Alport syndrome. (Source: Al-Mahmood et al., 2010)

**Figure 3.** Slit-lamp photos of a patient showing diffuse, geographic-shaped, discrete, gray lesions at the level of Descemet’s membrane as seen by direct illumination. (Source: Dahrouj et al., 2015)

**Figure 4.** Fundus photography of the right (a) and left eye (b) showing bilateral full-thickness giant macular holes. (Source: Raimundo et al., 2018)
tention on corneal dystrophy. Corneal dystrophy has not been described widely compared to other ocular abnormalities in AS. According to Zhang and Ding (2018), the corneal disease is rare in individuals with AS. Corneal erosions develop in less than 10% of all patients (Savige et al., 2015). On the contrary, another study indicated that nearly 20% of individuals with AS had experienced corneal erosion, characterized by attacks of blurred vision, lacrimation, acute ocular pain, and photophobia (Zhang & Ding, 2018). Corneal erosions are normally bilateral and frequently develop when Alport mutations are severe.

Erosions occur due to deformed Bowman’s membrane within corneal subepithelial and posterior polymorphous corneal dystrophy because of deformed Descemet’s membrane within the subendothelium (Figure 3). These abnormal membranes are weak, do not have a collagen IV α3α4α5 network, and attach weakly to the underlying stroma, epithelium, and endothelium (Savige et al., 2015).

Erosions might develop before a patient is diagnosed with AS, which usually happens in the teenage years. They normally develop in persons with extrarenal features and early start of kidney failure (Savige et al., 2015). In some cases, erosions can develop in members of the same family, although they are not linked to precise mutations.

Nicklason et al. (2020) designed a study involving both

**Figure 5.** Spectral domain optical coherence tomography showing bilateral full-thickness macular holes (Source: Raimundo et al., 2018).

**Figure 6.** Posterior subcapsular cataract. (Source: Cabán et al., 2008)

**Figure 7.** Glomerular basement membrane showing its lamination with transmission electron microscopy (TEM). (Source: Tecellioglu et al., 2021)
genders from eight families diagnosed with X-linked AS to investigate the manifestation of corneal abnormalities. These family members were subjected to ophthalmological examinations, including corneal endothelial specular microscopy and slit-lamp examination. Based on the results, two males had experienced recurrent corneal erosions, although they did not have a history of posterior polymorphous corneal dystrophy (Nicklason et al., 2020). Furthermore, one woman and her son had experienced corneal erosions. The findings concluded that corneal erosion occurs at the same rate for females and males with X-linked AS.

Even though corneal abnormalities are common in affected women, their correlation with AS might be overlooked (Savige et al., 2016). People experience dry, scratchy eyes that may last several days and even recur.

The characteristics of attacks are tears, acute ocular pain, and photophobia. Attack triggers correlate with a dry ocular surface, including contact lens use, waking up prolonged screen time, and exposure to windy outdoor conditions (Nicklason et al., 2020). Other important precipitants are irritation from wind and computer screens (Savige et al., 2015). Individuals affected by AS usually start experiencing attacks during their teenage years, and an episode can last hours or even days (Nicklason et al., 2020). An examination can reveal red eyes. In some instances, corneal dystrophy progression can lead to vision loss. Supportive measures can help reduce most attack episodes without serious treatment (Savige et al., 2015). Treatments for corneal erosion include lubrication and avoidance of trigger factors. In addition, an occlusive eye patch and occasional anti-inflammatory agents might be used as treatment (Nicklason et al., 2020). These products often produce good results for affected individuals when used appropriately.

Moreover, Zhang and Ding (2018) stated that patients with AS might experience posterior polymorphous corneal dystrophy and corneal clouding. Savige et al. (2016) attested that posterior polymorphous corneal dystrophy differs from some corneal lesions that manifest in certain patients and has not been discovered in females with X-linked AS. This manifestation is more severe than typical erosions. A patient might be asymptomatic, although some individuals report persistent photophobia, watering, and grittiness. Diagnosis is completed using specular microscopy or slit-lamp biomicroscopy (Savige et al., 2015), (Figure 3).

**Macular Holes or Lamellar.** Lamellar is non-prevalent in males suffering from X-linked AS and females and males with the recessive disease. Studies indicate that full-thickness holes are uncommon in all genders (Savige et al., 2015). Shah & Weinberg (2010) argued that cases of macular holes in previous studies were not appropriately correlated to AS. Macular holes develop early in life and are larger than instantaneous holes in individuals who have not been genetically diagnosed with AS. These holes might be unilateral, bilateral, or asymmetric (Savige et al., 2015). The occurrence of macular holes is procedural. It starts with minor defects on the inner limiting membrane and then microcystic fusion.

Studies have presented different pathways through which macular holes develop. Shah and Weinberg (2010) described a case of a patient who presented with a “giant macular hole” and AS diagnosis. The examination showed that many small macular holes emerged after the giant hole had developed. The authors attested that the clinical progression and mechanism of the occurrence of giant macular holes are completely different from the mechanism and progression of idiopathic macular holes (Shah & Weinberg, 2010).

Full-thickness macular holes are caused by abnormalities of collagen IV within Bruch’s membrane, the internal limiting membrane alongside anterior lens capsule rupture, retinal detachment, and anomalous vitreoretinal traction (Savige et al., 2015; Shah & Weinberg, 2010).

Individuals with macular holes experience challenges with metamorphopsia and central vision. Diagnosis of macular holes happens when a patient’s visual impairment fails to improve even after undergoing surgery for lenticonus (Savige et al., 2015). Indeed, lamellar holes do not often improve through surgical treatment. Retinal photographs might fail to show lamellar holes, and ocular coherence tomography (OCT) might be needed for diagnosis (Savige et al., 2015). Serial clinical examination, fundus photographs, and visual acuity can also be used for diagnosis (Figures 4 and 5) (Shah & Weinberg, 2010). An inaccurate diagnosis might confuse lamellar holes with a retinal lozenge.

Macular holes in patients with AS usually lead to permanent visual impairment since they respond poorly to surgical treatments (Zhang & Ding, 2018). Additionally, macular holes increase the chances of vision loss in people with AS. (Figure 4, 5).

**Cataracts.** Cataracts are often associated with lenticonus because they might co-occur in patients with AS. Lenticonus results when the lens bulges, specifically through the weakest and thinnest regions of the eye capsule. Since the capsule lacks the α3α4α5 network, it incurs splits that might rupture (Savige et al., 2015). The healing of these minor instantaneous ruptures results in the development of cataracts. The formation of cataracts blocks the progression of lenticonus. Symptomatic cataracts are usually treated by removing the lens removal and implanting an intraocular lens (Savige et al., 2015). However, cataracts are not often symptomatic, and a patient might experience visual impairment without knowing the cause if an appropriate diagnosis is not made.
One study described a gradual, painless vision loss in males with AS (Santiago-Cabán et al., 2008). Cataracts in this patient were only diagnosed after a comprehensive ocular and history examination. The study also showed that cataracts might develop in patients with diffuse leiomyomatosis (DL) and AS. Careful examination is needed to rule out other potential causes of cataracts in patients. For instance, prolonged use of steroids can eventually lead to the formation of cataracts (Santiago-Cabán et al., 2008). This finding means that patients with AS may develop cataracts because of steroid use rather than the disease.

Literature has delved deep into identifying why certain ocular abnormalities in individuals with AS are usually overlooked. It is imperative to document current guidelines for diagnosing AS (Savige et al., 2015; Savige et al., 2021). For example, fleck retinopathy does not impact a patient’s vision and may be subtle and misdiagnosed for retinal sheen (Zhang & Ding, 2018). Ophthalmologists can detect a small

<table>
<thead>
<tr>
<th>Disorder/Disease</th>
<th>Clinical/Pathological/Genetic features</th>
<th>Diagnostic Tool(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>XLAS Male XLAS with truncating mutation</td>
<td>α5 in Bowman’s capsule and GBM shows weaker/negative staining.</td>
<td>Type IV collagen staining</td>
</tr>
<tr>
<td>Female XLAS</td>
<td>α5 in Bowman’s capsule and GBM shows weaker/negative staining or mosaic expression.</td>
<td>Type IV collagen staining</td>
</tr>
<tr>
<td>ARAS ARAS with homozygous truncating mutation</td>
<td>α5 in Bowman’s capsule shows positive staining. α5 in GBM shows negative/weaker staining.</td>
<td>Type IV collagen staining</td>
</tr>
<tr>
<td>ARAS with compound heterozygous truncating mutation and non-truncating mutation</td>
<td>α5 in Bowman’s capsule shows positive staining. α5 in GBM shows negative/weaker staining or mosaic expression.</td>
<td>Type IV collagen staining</td>
</tr>
<tr>
<td>ARAS with compound heterozygous non-truncating mutation</td>
<td>α5 in Bowman’s capsule shows positive staining. α5 in GBM shows negative/weaker staining or mosaic expression.</td>
<td>Type IV collagen staining</td>
</tr>
<tr>
<td>ADAS ADAS</td>
<td>α5 in Bowman’s capsule shows positive staining. α5 in GBM shows positive staining or mosaic expression. α2 in GBM shows strongly positive staining.</td>
<td>Type IV collagen staining Laminin staining Fibronectin staining</td>
</tr>
<tr>
<td>Early Stage of ADAS / Thin basal membrane nephropathy (TBMN)</td>
<td>α5 in Bowman’s capsule shows positive staining. α5 in GBM shows positive staining or mosaic expression. α2 in GBM shows weakly positive staining.</td>
<td>Type IV collagen staining Laminin staining Fibronectin staining</td>
</tr>
<tr>
<td>Thin basal membrane nephropathy (TBMN)</td>
<td>Several aspects of TBMN are clinically and histopathologically similar to early onset AS. TBMN has diffused thinning of the GBM that can be found through an examination utilizing transmission electron microscopy (TEM) COL4A3/COL4A4 mutations.</td>
<td>Diagnosis could be made with the help of collagen IV immunostaining and genetic studies.</td>
</tr>
<tr>
<td>Immunoglobulin A (IgA) nephropathy or nephritis</td>
<td>IgA nephropathy may cause persistent hematuria that has almost identical features to that of TBMN. Diffuse direct immunofluorescence (DIF) staining in the mesangium is one of the diagnostic markers of IgA nephritis.</td>
<td>The TEM findings could be used, as these findings for IgA nephritis are different from that of AS in that they are not characterized by a change in the GBM. Mesangial electron-dense deposits are commonly found utilizing TEM in the diagnosis of IgA nephritis. Subendothelial electron-dense deposits could also be found in the active lesions.</td>
</tr>
</tbody>
</table>
differential diagnosis in different types of AS and other disorders/diseases based on type IV collagen, fibronectin, and laminin staining (Akihisa et al., 2019; Nozu et al., 2019; Tecellioglu et al., 2021) is presented in Table 1,2.

**Results**

It is difficult to find accurate statistics regarding AS because it is a rare condition with complex diagnostic methods that often lead to misdiagnosis. Developed countries, including Sweden, Poland, and the US, have more data about AS than developing countries because they are more technologically advanced than the latter. Currently, scientists have not created standard diagnostic methods for AS, creating many challenges in its treatment. In the US, approximately 13,000 – 60,000 people suffer from AS, but since diagnostic methods have not been well-developed, the numbers might vary. Poland has a higher proportion of people with AS than the US in all age groups. Only 0.56 percent of European dialysis patients have been diagnosed with AS, which means some countries have fewer cases than others.

The most common ocular manifestations of AS include lenticonus, fleck retinopathy, and corneal dystrophy. Other manifestations are cataracts and lamellar. A higher proportion of men and people with autosomal recessive disease suffer from peripheral and mid-peripheral retinopathy. The patterns of peripheral retinopathy might be different between family members. Scientists use ophthalmoscopy to detect retinopathy, which shows as dots or whitish-yellow flecks that do not affect vision; however, without extra caution, they might

**Table 2. Usefulness of Ocular Features in Diagnosis, Predicting Early Onset Renal Failure, and Identifying Mode of Inheritance**

(Source: Savige et al., 2015)

<table>
<thead>
<tr>
<th>Ocular feature</th>
<th>Diagnostic</th>
<th>Severe Mutations</th>
<th>Early Onset Renal Failure</th>
<th>Distinguish Autosomal Recessive Alport Syndrome from X linked Alport Syndrome in Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior Polymorphous corneal dystrophy</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>?</td>
</tr>
<tr>
<td>Lenticonus</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Central retinopathy</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Retinal thinning</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Giant macular hole</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Peripheral retinopathy</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
mischaracterize or miss to detect retinopathy. Most people with AS manifest anterior lenticonus, which is associated with early kidney failure. In some instances, patients can have both anterior and posterior lenticonus. There has been limited research on corneal dystrophy, and scientists have discovered that it is rare among people with AS. One-fifth of AS suffer from corneal erosion, which causes ocular pain, blurs vision, photophobia, and lacrimation; the erosions occur when people have severe Alport mutations.

In some cases, the erosions occur before people are diagnosed with AS, especially when they are teenagers. Lamellar is less common in males and females suffering recessive AS and males with X-linked AS. Full-thickness macular holes are rare in males and females and can occur in people that have not been genetically diagnosed with AS. The holes differ in size and affect central vision and metamorphopsia. Macular holes likely cause vision impairment or vision loss in patients with AS. Scientists associate cataracts with lenticonus as patients with AS might develop them. When cataracts form, they obstruct the development of the lenticonus; if they are symptomatic, they can be treated surgically, but if they are non-symptomatic, patients might develop visual impairment unknowingly. Diagnosing and treating these five problems requires complex technology and medical procedures, and there is no guarantee that patients can fully recover.

AS is characterized by abnormalities in the GBM and the basements of other membranes, including the ears and eyes. The GBM is a sheet-like extracellular matrix (ECM) that helps prevent blood-related proteins and blood cells from flowing into the urinary space. The ECM comprises four major macromolecules, including laminin and type IV collagen. When people have AS mutations appear in COL4A3, COL4A4, or COL4A5, which cause defects in type IV collagen α3, α4, or α5 chains, respectively. Mutations in COL4A3, COL4A4, or COL4A5 could cause AS, and the condition can be established by studying these mutations. The transmission of AS is related to X-mutations and is sometimes called X-linked Alport syndrome (XLAS). A differential diagnosis can be performed on many diseases and disorders, including AS based on laminin staining, type IV collagen, and fibronectin.

Discussion of the Results. Various countries have reported different numbers of AS patients, with the number being higher in European countries like Poland than in other European countries and the US. The condition is rare, and scientists have conducted minimal research about it. Because they have not conclusively agreed on the diagnostic method, the differences in the number of patients between different countries might result from using different diagnostic methods. The level of technology between countries, especially developing and developed ones, varies, so the number of unidentified cases might be higher than reported. The differences in cases can also be attributed to the level of attention and amount of research that a country has dedicated to AS, with countries with higher attention recording more cases. Genetic factors could contribute to the disparities because the disease is associated with gene mutations that differ between countries.

AS has many characteristics, including lenticonus, fleck retinopathy, corneal dystrophy, cataracts, and lamellar. The diagnosis and treatment of each of these characteristics require a different approach, complicating the treatment of AS. Some of these characteristics can be detected early and treated, while others can be detected after diagnosis with AS. The different requirements of each characteristic negatively impact attempts to diagnose AS. The severity of each characteristic also differs, complicating the treatment of ocular manifestations of AS; thus, AS is a condition with unique demand for technology and resources for diagnosis and treatment.

The diagnosis of AS is more complex than other conditions because it involves complex physical examinations complemented by testing body tissues and fluids. One of the most relied-on examinations is a differential diagnosis of AS and other disorders and conditions based on type IV collagen, laminin staining, and fibronectin. The complex testing process could hinder the study and treatment of the disease in many countries, especially the developing and developed ones that lack enough resources to fund their medical industries.

Conclusion
Alport syndrome is not widely prevalent in Baltic countries, and its global prevalence is low. Despite its low prevalence, the disease is associated with several ocular abnormalities that might or might not affect a patient’s vision. Certain ocular manifestations, such as peripheral retinopathy, lenticonus, and corneal erosions, are common among individuals affected by AS. These ocular manifestations can be used as a confirmation of a positive diagnosis. There are different diagnoses of ocular manifestations, each of which is complex. Early detection of these problems can prevent visual impairment or loss, but in some circumstances, it cannot. On the other hand, less common ocular manifestations are cataracts and macular holes. The identification of these abnormalities can be used to determine the mode of inheritance and prevent early-onset kidney failure through treatment. Because some of these ocular manifestations may be subtle and asymptomatic, ophthalmologists should perform comprehensive examinations when assessing AS patients.
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ALPORTO SINDROMO, PASIREIŠKIANČIO AKIŲ SISTEMOJE, CHARAKTERISTIKOS
J. Daukantaitė, R. Strupaitė-Šileikienė

Raktažodžiai: Alporto sindromas, dėmės retinopatija, lenticokus, ragenos distrofija, katarakta.

Santrauka
Alporto sindromas (AS) yra paveldima liga, kuriai būdingas klausos sutrikimas, inkstų nepakankamumas ir akių sutrikimai. AS yra reta liga, todėl ji gali likti nepastebėta. Mažai tikėtina, jog paveikti asmenys ir jų giminaščiai bus laiku patikrinti ir konsultuojami. Šiame straipsnyje nagrinėjamos AS aprašos akyse ir ligos paplitimas.

Correspondence to: jdaukantaite@outlook.com

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