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Standardized evaluation of quality of life related to health in pediatric and adult patients with congenital aniridia

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Declaration

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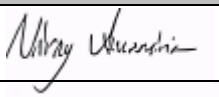
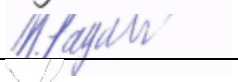
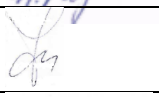
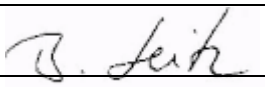
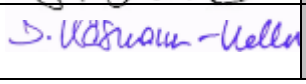
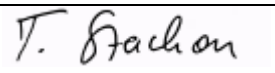
Hoxha Z		**Náray A**	
Fries N F		**Lagali N**	
Hecker D		**Grupcheva C**	
Seitz B		**Szentmáry N**	
Käsmann-Kellner B		**Stachon T**	

Abbreviations

AAK	Aniridia-associated keratopathy
AFS	Anterior fibrosis syndrome
AHDH	Attention deficit hyperactivity disorder
BCVA	Best corrected visual acuity
Chi^2 or χ^2	Chi-square statistic
DCDC1	Doublecortin domain-containing protein 1 gene
DED	Dry eye disease
DPH4	Diphthamide biosynthesis protein gene
ELP4	Elongator acetyltransferase complex, subunit 4, gene
FOXC1	Fork head box C1 gene
IMMP1L	Inner mitochondrial membrane peptidase 1-like gene
IOL	Intraocular lens
ITPR1	Inositol 1,4,5-trisphosphate receptor type 1 gene
Kpro	Keratoprothesis
LSCD	Limbal stem cell deficiency
MRI	Magnetic resonance imaging
OCT	Optical coherence tomography
PAX6	Paired box protein 6
PCO	Posterior capsule opacification
PITX2	Paired-like homeodomain transcription factor 2 gene
PTK	Phototherapeutic keratectomy
QoL	Quality of life
TRIM44	Tripartite motif-containing 44 gene
WAGR	Wilms Tumor or nephroblastoma, Aniridia, Genitourinary anomalies and mental Retardation
ρ	Spearman correlation coefficient
Φ	Phi coefficient

German abstract

Standardisierte Bewertung der gesundheitsbezogenen Lebensqualität bei Patienten mit kongenitaler Aniridie

Einleitung: Die kongenitale Aniridie ist eine panokuläre Erkrankung mit progressivem Verlauf und Sehbeeinträchtigung. Mittels einer Umfrage der COST-Action (CA18116) wurden die Erfahrungen der deutschen Patienten mit ihrer Krankheit und deren Einfluss auf das tägliche Leben erfasst. Diese Erfahrungen wurden dann mit den objektiven Augenbefunde des Homburger Aniridie Zentrums verglichen, um zu verstehen wie sich verschiedene Aspekte der Krankheit auf das tägliche Leben der Patienten auswirken.

Patienten und Methoden: Die deutsche Version der Umfrage umfasste Daten zu Krankheitssymptomen, sehbezogenen Schwierigkeiten im Alltag mit den Schwerpunkten Arbeit, Schule und soziales Leben sowie zur Nutzung von Sehhilfen. Zusätzlich wurde die selbsteingeschätzte Lebensqualität erfragt. Die klinischen Daten umfassten die bestkorrigierte Sehschärfe, das Vorhandensein von Komplikationen wie Aniridie-assoziierte Keratopathie (AAK), Katarakt und Glaukom und deren Behandlungsbedarf.

Ergebnisse: 71 Patienten im Alter von 28,8 ± 20,2 Jahren (6-78 Jahre) nahmen an der Umfrage teil; 27 (38,0%) waren Kinder und 44 (62,0%) Erwachsene. 55 (77,5%) berichteten über *tägliche* Lichtempfindlichkeit, und 34 (47,9%) über *tägliche* trockene Augen. Schwankendes Sehvermögen, Augenschmerzen und tränende Augen waren ebenfalls *tägliche* Beschwerden bei 17 (23,9%), 11 (15,5%) und 5 (7,0%) Patienten, wobei diese Beschwerden mit dem Alter zunahmen ($p \leq 0{,}001$). Die Mehrheit der Patienten war in ihrem Alltag selbstständig: 27 (38,0%) benötigten *nie* Hilfe bei täglichen Verrichtungen, 35 (49,3%) gingen selbständig zur Schule oder Arbeit, und 22 (31,0%) konnten ohne Hilfe an sozialen Aktivitäten teilnehmen. Sehhilfen wurden von 39 (54,9%) *regelmäßig* in der Schule oder bei der Arbeit genutzt, von 24 (33,8%) während sozialer Aktivitäten, und von 32 (45,1%) in der Freizeit. Kinder wiesen eine höhere Lebensqualität auf als Erwachsene ($\rho = 0{,}44$, $p < 0{,}001$). Patienten mit fortgeschrittener AAK hatten eine signifikant niedrigere Lebensqualität ($\rho = 0{,}28$, $p = 0{,}027$), und das Vorhandensein einer Katarakt, eine Kataraktoperation sowie eine Operation in jungen Jahren waren ebenfalls mit einem Rückgang der Lebensqualität verbunden ($p \leq 0{,}01$).

Schlussfolgerungen: Trotz erheblicher Sehbeeinträchtigungen konnten die meisten Patienten mit kongenitaler Aniridie ihren Alltag in Schule, Beruf und sozialen Situationen gut bewältigen. Sehhilfen spielen eine entscheidende Rolle beim Erwachsenwerden. Der ANIRIDIA-NET-Fragebogen zeigte eine effektive Korrelation zwischen den Symptomen der Patienten und den klinischen Befunden, was eine wertvolle Unterstützung bei Nachuntersuchungen bietet.

English abstract

Introduction: Congenital aniridia is a panocular disease with a progressive course and visual impairment. Through a survey conducted by COST Action (CA18116), the experiences of German patients with their disease and its impact on daily life were collected. These experiences were then compared with the objective ocular findings from the Homburg Aniridia Center to understand how different aspects of the disease affect the patients' daily lives.

Patients and methods: The German version of the survey included data on disease symptoms, vision-related difficulties in daily life with a focus on work, school, and social life, as well as the use of visual aids. Additionally, self-assessed quality of life was queried. The clinical data included best-corrected visual acuity, the presence of complications such as aniridia-associated keratopathy (AAK), cataract, and glaucoma, and their need for treatment.

Results: Seventy-one patients aged 28.8 ± 20.2 years (6 - 78 years) participated in the survey; 27 (38.0%) were children and 44 (62.0%) were adults. A total of 55 patients (77.5%) reported *daily* light sensitivity, and 34 (47.9%) reported *daily* dry eyes. Fluctuating vision, eye pain, and watery eyes were also *daily* complaints for 17 (23.9%), 11 (15.5%), and 5 (7.0%) patients, respectively, with these complaints increasing with age ($p \leq 0.001$). The majority of patients were independent in their daily lives: 27 (38.0%) *never* required assistance with daily activities, 35 (49.3%) went to school or work independently, and 22 (31.0%) could participate in social activities without assistance. Visual aids were regularly used by 39 patients (54.9%) at school or work, by 24 (33.8%) during social activities, and by 32 (45.1%) during leisure time. Children reported a higher quality of life than adults ($\rho = 0.44$, $p < 0.001$). Patients with advanced AAK had a significantly lower quality of life ($\rho = 0.28$, $p = 0.027$), and the presence of cataracts, cataract surgery, and surgery at a young age were also associated with a decline in quality of life ($p \leq 0.01$).

Conclusions: Despite significant visual impairments, most patients with congenital aniridia were able to manage their daily lives in school, work, and social situations well. Visual aids play a crucial role in the transition to adulthood. The ANIRIDIA-NET questionnaire demonstrated an effective correlation between the patients' symptoms and clinical findings, providing valuable support for follow-up examinations.

1 Introduction

Congenital aniridia is a panocular disorder characterized by a variable degree of iris hypoplasia or absence, along with other developmental features [38, 58, 88]. Some features, such as iris hypoplasia, anterior polar cataract, foveal hypoplasia, nystagmus, optic disc hypoplasia, and other optic disc abnormalities, are present from birth, leading to reduced visual acuity in almost all patients. Secondary complications such as aniridia-associated keratopathy, cataract, secondary glaucoma and dry eye disease typically manifest in childhood or early adulthood. These complications are often progressive, exacerbating visual impairment and potentially leading to blindness later in life [58]. Mutations in the paired-box gene *PAX6* are responsible for 85-90% of aniridia cases [38].

Congenital aniridia may be part of WAGR and Gillespie syndrome and is often associated with nonocular phenotypic anomalies, leading to its common reference as "aniridia syndrome" or "*PAX6* syndrome" [46]. Patients with *PAX6* syndrome alone may experience obesity, early-onset type II diabetes, hypothyroidism, auditory perceptual deficits, and brain morphological abnormalities such as agenesis of the corpus callosum [1, 58]. The most prevalent comorbidities in congenital aniridia include obesity, diabetes mellitus, hearing impairment, intellectual disability, autism and pituitary hypoplasia [24, 27, 58].

Due to the significant and progressive visual impairment associated with congenital aniridia, the majority of patients require ongoing ophthalmic monitoring and complex conservative and surgical treatments to preserve their vision and alleviate symptoms.

1.1 Epidemiology

Congenital aniridia is classified as a rare disease according to Orphanet, the European consortium for rare diseases (www.orpha.net), and the National Organization for Rare Disorders in the USA. Its estimated incidence ranges from 1 in 64,000 to 1 in 96,000 live births, depending on the population studied [36]. Notably, there is no significant sex or race predilection for the condition [67]. Additionally, research has not found an increased risk of congenital aniridia associated with exposure to medication or environmental factors during pregnancy [59].

1.2 Genetics

85% of patients with congenital aniridia have a *PAX6*-related variant inherited in an autosomal dominant manner [50]. This variant shows complete penetrance but variable expressivity. De novo mutations of the *PAX6* gene account for 13-33% of cases, known as sporadic congenital aniridia [50]. A small percentage of cases (1-3%) are inherited in an autosomal recessive manner and are often associated with cerebellar ataxia and intellectual disability, known as Gillespie syndrome [40, 59].

1.2.1 PAX6

The major gene responsible for congenital aniridia is the paired-box gene *PAX6*, a highly conserved gene found across various species, including roundworms, zebrafish, and quail [31, 59] . Located on chromosome band 11p13, *PAX6* encodes a transcription factor crucial for eye development [76]. It is initially expressed in the optic sulcus, optic stalk, and optic vesicle, with later strong expression in neuroectoderm-derived cells of the optic cup and anterior surface ectoderm. *PAX6* gene exhibits strong dosage sensitivity; thus, haploinsufficiency — loss of one functional gene copy — leads to insufficient *PAX6* transcription factor production [80]. This insufficiency affects the expression of many target genes, impacting cell development, particularly the growth and differentiation of the iris and ciliary body, resulting in their dysgenesis. Additionally, *PAX6* haploinsufficiency influences *PAX2* expression, affecting optic cup and stalk development [82].

The most common *PAX6* mutations include splice, frameshift, and nonsense mutations, with missense mutations being less frequent [34]. Beyond mutations in *PAX6* itself, deletions in downstream genes can also cause aniridia [77]. For instance, mutations in the *ELP4* (elongator acetyltransferase complex, subunit 4), *DCDC1* (doublecortin domain-containing protein 1), *IMMP1L* (inner mitochondrial membrane peptidase 1-like), and DPH4 (diphthamide biosynthesis protein) genes were identified in a large Turkish family with isolated aniridia [59].

1.2.1.1 WAGR Syndrome

Sporadic aniridia arises from de novo gene mutations or deletions. The deletion of the *PAX6* gene often affects the WT1 gene (Willms tumor gene), which is also situated at 11p13 [93]. This leads to WAGR Syndrome (Wilms Tumor or nephroblastoma; aniridia; genitourinary anomalies and mental retardation). A specific subtype of WAGR is WAGRO, which includes obesity too. Approximately 25%-33% of children with sporadic congenital aniridia develop nephroblastoma before 3 years of age [33]. The ocular clinical manifestations are usually more aggressive in WAGR syndrome [55]. Genetic testing of children with congenital aniridia is especially crucial to identify this syndrome and facilitate timely diagnosis of a potential nephroblastoma [18].

1.2.2 *PAX6*-negative Aniridia

Several mutations have been identified in patients with aniridia phenotype but a normal *PAX6*. These were the FOXC1 (fork head box C1) gene mutation, which is involved in eye development, the PITX2 (paired-like homeodomain transcription factor 2) gene mutation, involved in eye development including left-right signaling, and the TRIM44 (tripartite motif-containing 44) gene mutation [4, 96]. FOXC1 and PITX2 may give rise to other conditions mimicking congenital aniridia such as the Axenfeld-Rieger syndrome, which results in anterior segment dysgenesis [4, 40]. The phenotype of *PAX6*-negative patients

with congenital aniridia can range from milder to more severe compared to typical *PAX6*-associated aniridia.

1.3 Clinical overview

Congenital aniridia is often first suspected in children with solid black eyes due to an enlarged pupil from a lack of iris tissue [18]. While the absence of the iris is the hallmark of aniridia, it is somewhat of a misnomer, as some remnant iris tissue is almost always detectable on gonioscopy [67]. Both eyes are affected, though symptom severity and findings can vary between them. Common symptoms in children include light sensitivity, eye pain, dry eyes, and low vision, with reduced visual acuity being almost universal among congenital aniridia patients [58]. A study by Edén et al. reported a mean Snellen visual acuity of 0.19 in a cohort from Sweden and Norway, with a range from no light perception to 0.9 [20]. This reduced visual acuity is primarily due to foveal hypoplasia, but it worsens over time with complications involving the cornea, the lens, and with development or worsening of glaucoma. Additionally, patients often have impaired red-green and yellow-blue vision, though the impact on overall visual function remains unclear [73]. Moreover, 64%-94% of patients experience nystagmus, further contributing to visual impairment.

Family history is particularly important in diagnosing congenital aniridia, as two-third of affected children have a parent with the condition, which can aid in early identification and management.

1.3.1 Ocular findings

1.3.1.1 Iris hypoplasia

Some degree of iris hypoplasia is present in nearly 100% of patients with congenital aniridia. The extent of iris tissue varies significantly between patients, even within families, but some stump iris tissue can typically be visualized using gonioscopy, optical coherence tomography (OCT), ultrasound biomicroscopy, or histology [61]. In cases involving the *PAX6* gene, the level of *PAX6* expression affects the amount of iris tissue present. This does not impact visual acuity, but it can cause photophobia, loss of depth of focus, and cosmetic concerns [88]. Depending on the amount of iris tissue present, the pupil may appear normal, be ectopic, or be entirely absent, leading to the characteristic "black eyes" of aniridia.

Several therapeutic options have been described in the literature, to manage glare and improve cosmetic appearance in congenital aniridia. Nevertheless, these are not used on a routine basis, due to the expected often severe complications. Although colored contact lenses are often used for traumatic aniridia, their use in congenital aniridia must be considered very carefully due to the potential effect of the contact lens on aniridia associated keratopathy. The described, but not often used surgical option is the intraocular implantation of iris prosthesis [40]. Three main types of devices

have been described in the literature are the capsular tension ring-based (CTR) [Morscher GmbH, Stuttgart, Germany], Iris-lens implants [Morscher GmbH, Stuttgart, Germany], and Silicone elastomer iris diaphragm [Artificial*Iris*®, HumanOptics, Erlangen, Germany] [62, 63, 70]. Nevertheless, the insertion of these intraocular devices carries high risk of intraoperative and postoperative complications, such as exacerbation or new onset of secondary glaucoma, aniridia associated keratopathy, or aniridia-associated fibrosis syndrome. These complications may outweigh their benefits, in many cases resulting in complete blindness, therefore, such surgeries are generally contraindicated [88].

1.3.1.2 Dry eye disease

Dry eye disease (DED) affects 56%-95% of patients with congenital aniridia, and its severity surpasses that observed in healthy individuals [44, 84]Klicken oder tippen Sie hier, um Text einzugeben.. Contributing factors include decreased tear production, compromised tear quality with elevated tear osmolarity, and Meibomian gland dysfunction stemming from increased gland atrophy and stenotic orifices [44]. Landsend et al. have demonstrated a close association between dry eye disease and aniridia-associated keratopathy, where DED can either induce or exacerbate keratopathy, and vice versa [57]. Reduced corneal sensitivity further impedes tear production and exacerbates DED [57].

Clinically, patients commonly report symptoms such as dryness, burning, scratching, and a foreign body sensation in both eyes. They often experience difficulties with contact lens wear. During examination, tear film break-up time (the duration until the first dry spot appears on the cornea following a complete blink) is reduced. As described above, Meibomian glands exhibit partial atrophy with stenotic orifices. Frequent use of preservative-free artificial tears throughout the day is typically necessary, while the use of preservatives should be avoided due to their potential to exacerbate or worsen ocular surface disease [57].

1.3.1.3 Cornea

The normal cornea is transparent and free of blood vessels. Its uppermost layer is the corneal epithelium, made of terminal cells that naturally shed and are continuously regenerated by the limbal stem cells [3]. These are a line of pluripotent cells, situated at the periphery of the cornea, act as a barrier between the transparent cornea and the vascularized conjunctiva [79]. If there is a loss or deficiency of these stem cells, the corneal epithelium can no longer renew itself and its barrier function is no longer preserved. This results in recurrent corneal erosions, corneal neovascularisation, and scarring [79]. The cornea may lose its transparency and will be covered by a subepithelial fibrovascular tissue called pannus [87].

Limbal stem cell deficiency (LSCD) is thought to be one of the primary causes of aniridia-associated keratopathy (AAK) [81]. AAK is a progressive disorder characterized by corneal pannus and opacification, typically advancing from the periphery towards the center [40]. The severity of clinical presentation is

believed to be influenced by *PAX6* mutations. Reduced corneal sensitivity due to diminished corneal nerve endings and increased corneal thickness is common [90]. Depending on slit lamp findings, Lagali et al. proposed a grading from 0-4, with Grade 4 being the most advanced form [56]. The different grades are illustrated in **Figure 1**.

AAK typically manifests in early childhood but becomes clinically significant in early adulthood, affecting nearly 90% of patients with congenital aniridia. It poses significant challenges and can lead to blindness later in life, with symptoms including chronic irritation, tearing, eye pain, and visual impairment, which is particularly severe when the corneal pannus affects the visual axis [56].

Management of AAK depends on its grade and the severity of symptoms. Conservative approaches for early stages involve preservative-free artificial tears and autologous serum eye drops [88]. For recurrent erosions, some patients benefit from bandage contact lenses alongside topical antibiotics to prevent infections. Surgical interventions, such as pannectomy, phototherapeutic keratectomy (PTK), keratoplasty, and keratoprosthesis, are reserved for cases where the visual axis is affected [90]. Attempts to restore the limbal stem cell niche include various techniques like amniotic membrane transplantation, limbal allografting, and cultivated limbal epithelial transplantation, but their success is limited [90]. Even after keratoplasty, graft opacification and neovascularization may occur. Due to these factors, these patients need a lifelong monitoring by an ophthalmologist [40, 90].

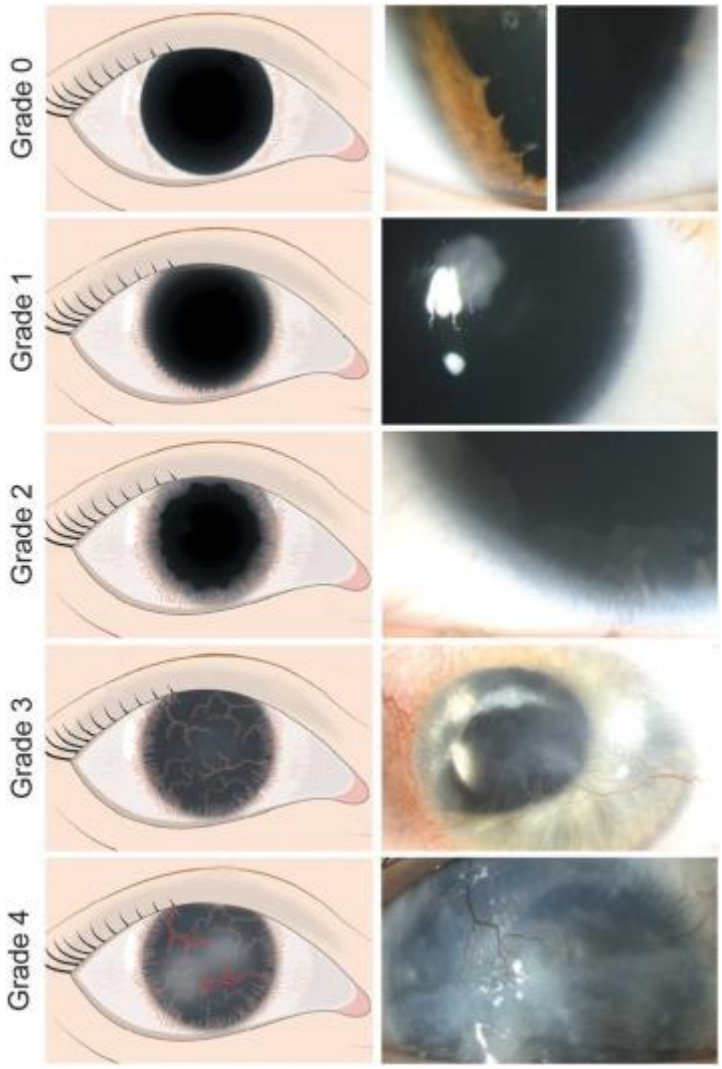


Figure 1. Stages of AAK according to Lagali et al. [56] ***Grade 0 consists of intact limbal border and no corneal lesions; Grade 1 is characterized by partial or complete limbal invasion from vessels and conjunctival tissue, reaching 1 mm from the limbus; Grade 2 consists of conjunctival tissue invading peripheral and mid-peripheral cornea, leaving the central 2-3 mm of cornea transparent; Grade 3 is characterized by a diffuse, translucent, vascularized pannus affecting the entire cornea, including the visual axis; Grade 4 is the most advanced form, with an opaque, thick and irregular pannus covering the entire ocular surface (Figure from van Velthoven et al*** [90]***).***

1.3.1.4 The lens

The most common ocular complication affecting the crystalline lens in patients with congenital aniridia is cataract, characterized by the clouding of the lens and impacting 40%-82% of individuals with this condition. While the median age of onset is around 14 years, cataracts can develop at any age and typically progress over time. A study involving 26 Norwegian subjects revealed that congenital or early-onset cataracts were present in 19.2% of congenital aniridia patients [21]. Common types of cataracts observed in congenital aniridia patients include anterior polar, posterior polar, posterior subcapsular, and mature cataracts [21, 40].

Less frequently encountered lens abnormalities in congenital aniridia patients include lens dislocation with zonular insufficiency, lens coloboma (localized flattening of the lens), microspherophakia (small and spherical lens), and posterior lenticonus (bulging and opacification of the posterior axial zone of the lens) [21].

The early onset of cataracts significantly impacts the already compromised visual acuity in individuals with congenital aniridia, potentially necessitating earlier cataract surgery. The mean age for surgery varies between 25.4 to 29.8 years. However, due to the complex eye anatomy characteristic of aniridia, cataract surgery may be accompanied by various intraoperative and postoperative complications. In addition, cataract surgery may exacerbate AAK or aniridia fibrosis syndrome development [21].

1.3.1.5 Secondary glaucoma

Glaucoma is a progressive optic neuropathy characterized by distinctive morphological changes in the optic nerve head, including cupping, along with the progressive death of retinal ganglion cells, resulting in visual field loss [32]. One modifiable risk factor for glaucoma is elevated intraocular pressure, which stems from an imbalance between aqueous inflow and outflow. In individuals with congenital aniridia, dysgenesis of the anterior chamber and iridocorneal angle becomes increasingly relevant with age, leading to a secondary glaucoma [32]. Two commonly described mechanisms include anterior rotation of the iris stroma leading to trabecular meshwork occlusion, and the formation of irregular fine adhesions (synechiae) covering the angle wall, obstructing outflow, and subsequently increasing intraocular pressure, ultimately leading to glaucomatous optic neuropathy [32]. Prevalence of secondary glaucoma in congenital aniridia ranges from 46-70%, with diagnosis typically occurring around the age of 13.6 years, and prevalence increasing with age [67]. Managing glaucoma in these patients presents significant challenges and resistance to both conservative and surgical treatments. Topical medications containing prostaglandin analogues, beta-blockers, or carbonic anhydrase inhibitors are commonly employed [65]. However, many patients eventually require surgical intervention. Options include goniotomy, trabeculotomy, filtering surgeries with antimetabolites, aqueous drainage devices, and cyclodestruction [66].

A retrospective study examining outcomes of various surgical procedures for aniridic glaucoma revealed that, on average, 28 months postoperatively, 65% of eyes achieved intraocular pressures ≤ 21 mmHg. On average, 2.8 surgeries were performed on these eyes [94].

1.3.1.6 Retina

Foveal hypoplasia is a characteristic feature of congenital aniridia, observed in 81%-91% of patients [58]. Clinical examination reveals hypopigmentation of the retina and macula. Fundus autofluorescence typically demonstrates loss of the foveal reflex, with blood vessels extending into the central fovea, contrary to the avascular zone observed in normal subjects [40]. Both cones and rods, the retinal

photoreceptors, are equally affected in congenital aniridia [59]. These have reduced activity and diminished sensitivity. In addition, the density of cones, which are normally highly concentrated in the fovea, is diminished in individuals with congenital aniridia. These retinal malformations may be a result of *PAX6* mutation or according to some authors to phototoxicity resulting from the iris hypoplasia [73]. Consequently, patients experience reduced visual acuity, impaired color vision and nystagmus [58].

1.3.1.7 Optic nerve head abnormalities

Optic hypoplasia is reported to affect 2%-30% of cases in various studies, with its prominence often associated with more advanced forms of foveal hypoplasia [88]. Additionally, less frequent abnormalities observed in congenital aniridia, apart from glaucomatous neuropathy, include optic nerve aplasia, optic disc pallor, optic disc pit, and morning glory disc [58].

1.3.2 Systemic associations in congenital aniridia

Syndromes

Aniridia can occur as part of syndromes, with the most common being WAGR syndrome. At the Homburg Aniridia Center, its prevalence was found to be 5.4% among 130 aniridia patients [46].

Gillespie syndrome is caused by a mutation in the ITPR1 (inositol 1,4,5-trisphosphate receptor type 1) gene, there is no *PAX6* mutation. Clinically, patients present with bilateral aniridia, cerebral ataxia, and oligophrenia [27]. The prevalence of Gillespie syndrome is approximately 2.2% [20]. Unlike congenital aniridia, in Gillespie syndrome, the iris is hypoplastic and the pupil is dilated. Foveal hypoplasia is less frequent in this syndrome [20].

Other abnormalities

In addition to ocular manifestations, patients with congenital aniridia frequently present with various systemic conditions, including mental retardation and auditory deficits [15]. Brain abnormalities are often detected in magnetic resonance imaging (MRI) [8]. Furthermore, endocrine conditions such as diabetes mellitus, overweight and obesity, pineal gland hypoplasia, and melanin deficiency with associated sleep disturbances have been reported with varying prevalence among these patients [15, 35].

1.4 Quality of life as a health indicator

The quality of life (QoL) has become increasingly important in assessing and managing patient's health [72]. Health-related quality of life measures aim to comprehensively evaluate general health along with social, psychological, and physical functioning. Vision plays a vital role in a person's ability to function, and numerous studies have demonstrated that vision impairment significantly impacts both function and QoL [37, 40]. Visual disability restricts social interactions and independence, affecting daily activities,

emotional well-being, social engagement, and mobility. Interventions that improve visual function, such as cataract surgery, also enhance QoL [51].

Rehabilitation for individuals with permanent visual impairment focuses on acquiring compensatory skills and training in the use of assistive technology. Studies on the impact of low vision care have yielded varied outcomes, ranging from significant positive effects to minimal or no improvement in QoL[51].

However, traditional objective measures such as visual acuity, visual field, and dark adaptation may not fully capture the patient's perspective on the burden of disability in daily activities. Patients with congenital aniridia experience visual impairment that is typically difficult to correct by conventional means such as glasses, contact lenses, or surgery [58]. Furthermore, complications such as aniridia-associated keratopathy, glaucoma, cataracts, and dry eye disease tend to worsen with age and may be exacerbated by surgical interventions. Consequently, patients require lifelong monitoring and treatment by ophthalmologists [14].

Despite these challenges, there are currently no surveys available to assess the subjective limitations and difficulties faced by individuals with congenital aniridia in their daily lives. Such assessments could provide valuable insights into the specific needs and experiences of these patients, ultimately facilitating more targeted interventions and improved QoL outcomes.

2 Purpose

The purpose was to gather comprehensive experiences from German-speaking patients with congenital aniridia using the ANIRIDIA-NET survey. Additionally, we aimed to analyze the correlation between their Quality of Life (QoL) and various clinical data collected at the Homburger Aniridia Center, to better understand how different clinical factors impact their daily lives and overall well-being.

3 Patients and methods

3.1 Study design

This is a retrospective, cross-sectional, descriptive, survey-based study of patients with congenital aniridia at the Homburg Aniridia Centre of Saarland University Medical Center in Homburg/Saar, Germany. It adheres to the principles of the Declaration of Helsinki and was approved by the Ethics Committee of the Medical Council of Saarland under number 132/22. Informed consent was obtained from all participating patients. For minors, their legal guardians provided informed consent.

3.2 Patients

Patients who underwent a comprehensive ophthalmological examination at the Homburg Aniridia Center, Department of Ophthalmology at the Saarland University Medical Center between June 2003 and June 2022, were recruited.

Inclusion criteria:

- Diagnosis of congenital aniridia
- Age 6 years or older, as this age group was considered capable of providing assessments of their daily challenges
- Residence in Germany

Exclusion criteria:

- Patients younger than 6 years.

3.3 Methods

3.3.1 Questionnaire

A questionnaire to investigate patients' subjective problems and their adaptation with daily tasks was developed by the ANIRIDIA-NET, a pan-European network of researchers and interest groups dedicated to congenital aniridia. The questionnaire is available in 13 languages at https://aniridia-net.eu/survey. It is part of a survey conducted by the 'COST Action ANIRIDIA-NET' (European Cooperation in Science and Technology, COST Action CA18116) across multiple European countries, aiming to assess how much assistance from other people and optical devices is required for daily life in patients with congenital aniridia.

The German version of the questionnaire was sent to the subjects in Germany [40]. The questions referred to information regarding demographics of the patients (age and gender), the frequency of eye

complaints; use of electronic devices such as computers or mobile phones and, accordingly, the need for special software for their use; interaction with other people at school, work and in the family; need for visual aid; need for help and/or support from other people during daily activities. In addition to the COST survey, two additional questions were included. These questions evaluated patients' self-assessed QoL (rated as very good, good, satisfactory, poor, or very poor) and whether the patients completed the questionnaire independently or with the assistance of someone else.

Patients were provided with a patient information sheet, a patient consent form, a data privacy statement and a questionnaire in a prepaid envelope via postal mail. Upon receiving a written informed consent from the patients, the subsequently described clinical data were also collected and were stored pseudonymized in a database.

3.3.2 Clinical data

Clinical data were extracted from our electronic medical record system, encompassing ocular findings, systemic diagnoses, genetic mutations, and local and systemic therapies. Ocular findings included parameters such as best corrected visual acuity (BCVA), as well as assessments of the cornea, lens, and glaucoma status. Under therapy, details such as the number and type of eye drops, as well as the use of systemic immunosuppressive medication, were noted (systemic immunosuppression is often required after multiple corneal transplantations). Additionally, the frequency of visits to the ophthalmologist was documented.

3.3.2.1 BCVA

Visual impairment was classified according to the WHO definitions of visual impairment [13]. Thus, logMAR visual acuity under 0.5 was classified as mild or no visual impairment; 1.0-0.5 moderate impairment; 1.3-1.1 severe impairment and above 1.3 blindness. Non-optotype vision was recorded as counting fingers, hand motion, light perception and no light perception and these were approximated as 1.79, 2.20, 2.69, 3.0 logMAR visual acuity, respectively.

3.3.2.2 Slit lamp findings

Cornea: The grade of aniridia-associated keratopathy according to Lagali et al., the necessity for use of eyes drops, therapeutic contact lens usage, and any history of prior corneal surgeries, particularly corneal transplantations, were documented.

Cataract: Details regarding the presence and type of cataract, whether cataract surgery was performed, and the age at which the surgery occurred were documented.

Glaucoma: Information on the presence of aniridic glaucoma, the necessity for conservative antiglaucomatous treatment or surgical intervention, age at first surgery, and the total number of glaucoma surgeries were recorded [40].

3.4 Statistical analysis

Data collection and statistical analysis were conducted using SPSS (IBM SPSS Statistics for Windows, Version 26). Continuous data were presented as mean, standard deviation, minimum and maximum values. For categorical ordinal data, we utilized the Spearman correlation test (ρ). The Chi-square (Chi^2 or χ^2) test for independence was applied to compare ordinal and nominal data, while the Phi test (Φ) was used to evaluate correlations between nominal data. Statistical significance was set at $p < 0.05$.

The flowchart below illustrates the schematic process of data collection and analysis [40].

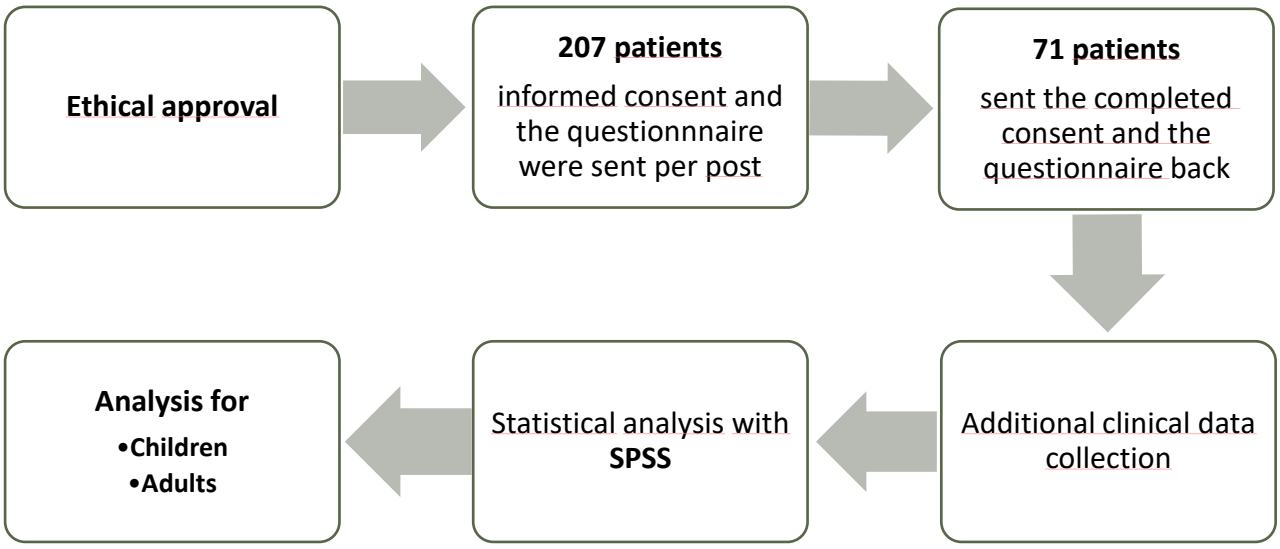


Figure 2. Flowchart of data collection and analysis.

4 Results

4.1 Demographic data

A cohort of 207 patients were initially invited to take part in the study. Of this group, 71 individuals (34.3%) completed the survey. Notably, 41 participants (19.8%) were unreachable due to outdated address details. Among the respondents, 37 (52.1%) were female, 31 (43.7%) male, and 3 (4.2%) diverse (non-binary, gender fluid, agender, or other). The mean age of the participants was 28.8 ± 20.7 years, ranging from 6 to 78 years. Of the total, 27 individuals (38.0%) were children (≤ 18 years), while 44 (62.0%) were adults.

4.2 Questionnaire-based data

4.2.1 Frequency of eye symptoms

In total, 55 patients (77.5%) reported that the most common symptom happening *daily* was light sensitivity. 34 patients (47.9%) reported *daily* dry eye symptoms, 17 (23.9%) fluctuating eyesight, 11 (15.5%) eye pain and 5 (7.0%) had *daily* teary eyes. On the other hand, teary eyes, fluctuating vision and eye pain were not observed in 40.8%, 45.1% and 47.9% of patients, respectively. **Table 1** and regarding children and adults **Figure 3** provide a visual summary of these responses, showing the absolute and percentage frequencies of each symptom.

Light sensitivity was equally present among the participants, showing no age-correlation. However, for the rest of the eye complaints, older patients were significantly more affected than children (Spearman-Rho correlation test, $p \leq 0.03$)[40].

	Daily	**Multiple times a week**	**Once a week**	**Less than once a week**	**Never**
My eyes are sensitive to light	55 (77.5%)	7 (9.9%)	2 (2.8%)	6 (8.5%)	1 (1.4%)
My eyes are gritty/dry	34 (47.9%)	11 (15.5%)	1 (1.4%)	7 (9.9%)	18 (25.4%)
I have pain in my eyes	11 (15.5%)	8 (11.3%)	7 (9.9%)	11 (15.5%)	34 (47.9%)
My vision is fluctuating/not stable	17 (23.9%)	11 (15.5%)	6 (8.5%)	5 (7.0%)	32 (45.1%)
My eyes are watering	5 (7.0%)	13 (18.3%)	9 (12.7%)	15 (21.1%)	29 (40.8%)

Table 1. Frequencies of the most common eye symptoms present in patients with congenital aniridia. The absolute number of patients and the percentage frequency are shown.

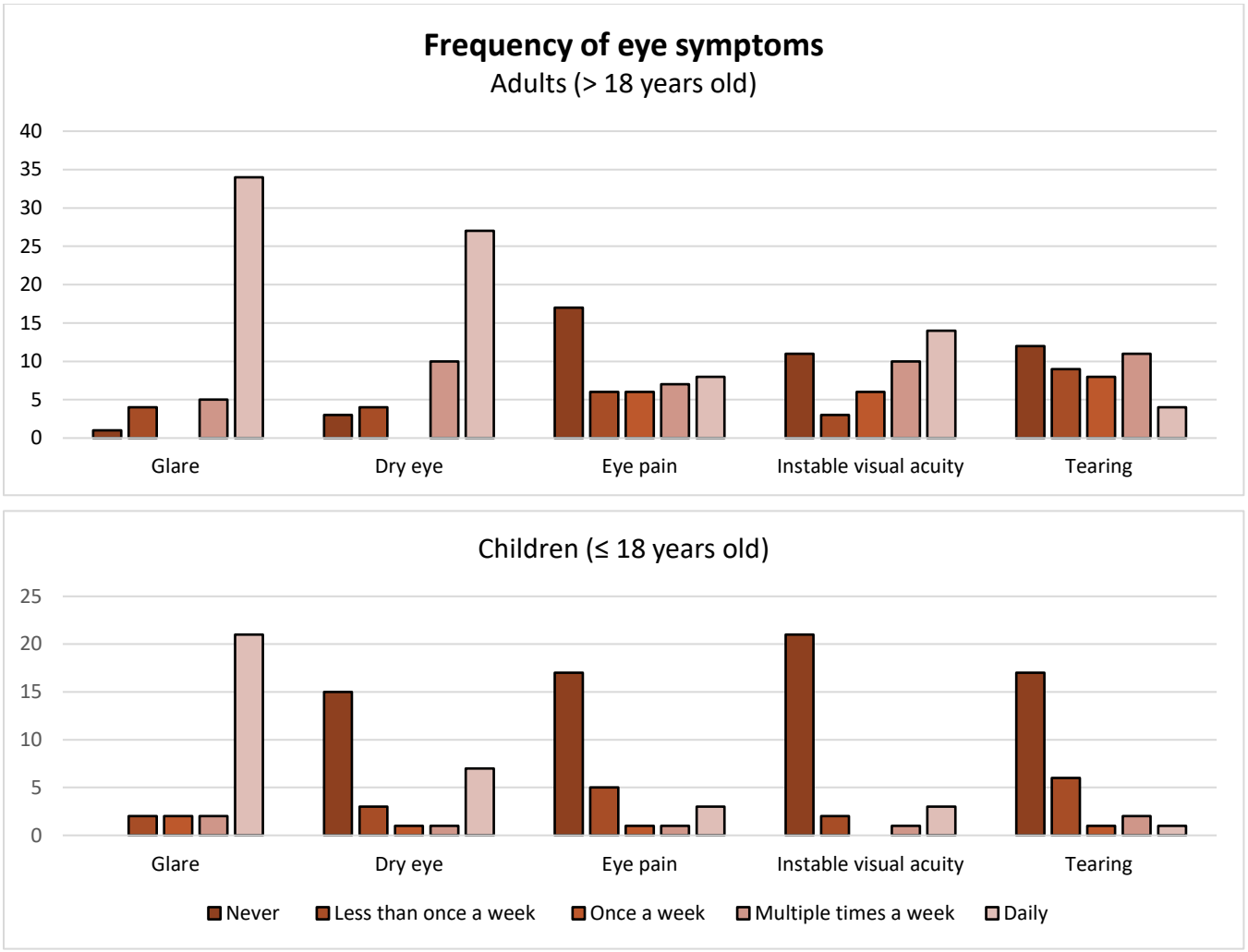


Figure 3. Bar diagrams depicting the frequency of eye symptoms reported by participants, in adults (above) and children (below). The x-axis represents the symptoms, while the y-axis the number of patients who reported them. The columns reflect the frequencies, described as: never, less than once a week, once a week, multiple times a week and daily.

4.2.2 Use of technology among congenital aniridia patients

Among participants, 37 (52.1%) reported using a standard computer without the need for visual aids or special software, while 32 (45.1%) relied on special software to facilitate screen reading and computer use. Interestingly, older patients were more dependent on these technological aids compared to younger individuals (p = 0.02). Additionally, 47 (66.2%) patients reported using special software on their mobile phones, with no observed age sensitivity among mobile phone users (p = 0.08). The most used software and tools included Zoom Text magnifier/reader and Voice Over [40].

4.2.3 Communication

Face to face communication was *never* problematic for 47 (66.2%) of the patients, and *sometimes* for 18 (25.4%) of them. The remaining 6 (8.5%) *always* had problems when communicating face-to-face, in person or online. Conversely, reading and interpreting face expressions was *always* difficult for 28 (39.4%) and *sometimes* for 22 (31.0%) of the participants. Only 20 (28.2%) *never* had problems with recognizing face expressions. None of the aspects were age-sensitive ($p \geq 0.1$).

4.2.4 School and Work

Most participants reported occasional difficulties in understanding and completing their school tasks despite their visual impairment. Only 8 (11.3%) indicated they *never* experienced such challenges, while 10 (14.1%) reported always facing them. Similarly, completing work tasks posed *occasional* challenges for 26 (36.6%) respondents, with 20 (28.2%) stating they *never* encountered such difficulties and only 4 (5.6%) indicating constant struggles. Patients commented that following lectures during their school years was challenging when the boards were too far away. These issues also arose at work, prompting them to develop adaptive strategies to compensate for their visual impairment.

Socializing at both school and work was generally unproblematic for most respondents. Specifically, 25 (35.2%) and 10 (14.1%) reported difficulty socializing at school as '*never*' and '*sometimes'*, respectively. Likewise, 17 (23.9%) *never* experienced issues socializing with colleagues at work, while 19 (26.8%) reported challenges as *sometimes*.

4.2.5 Need for assistance

The need for assistance during daily activities was explored among the patients. The majority reported being mostly independent, with 51 (71.8%) requiring help *never* or *sometimes* for routine activities at home. Similarly, nearly half (49.3%) could attend school without needing assistance. Additionally, most participants indicated they *never* or only *sometimes* needed help to engage in social activities, with 31.0% and 33.8% respectively. These findings are summarized in **Table 2**.

Participants also reported how often they needed assistance for doctor's appointments (**Figure 4**). As expected, children required help more frequently than adults ($\rho = -0.36$, $p = 0.001$) [40].

	Always	Most of the time	Sometimes	Never	Not applicable
I need someone to help me with my daily routine at home	14 (19.7%)	4 (5.6%)	24 (33.8%)	27 (38.0%)	2 (2.8%)
I need someone to help me to go to school/work	19 (26.8%)	4 (5.6%)	9 (12.7%)	35 (49.3%)	4 (5.6%)
I need someone to help me, so I can participate in social activities (shopping, sports, restaurants, events)	21 (29.6%)	3 (4.2%)	24 (33.8%)	22 (31.0%)	1 (1.4%)

Table 2. Distribution of responses to the question 'How much do you need help from friends, relatives, or others during your daily life?' reported by participants. Absolute and percent frequencies are shown.

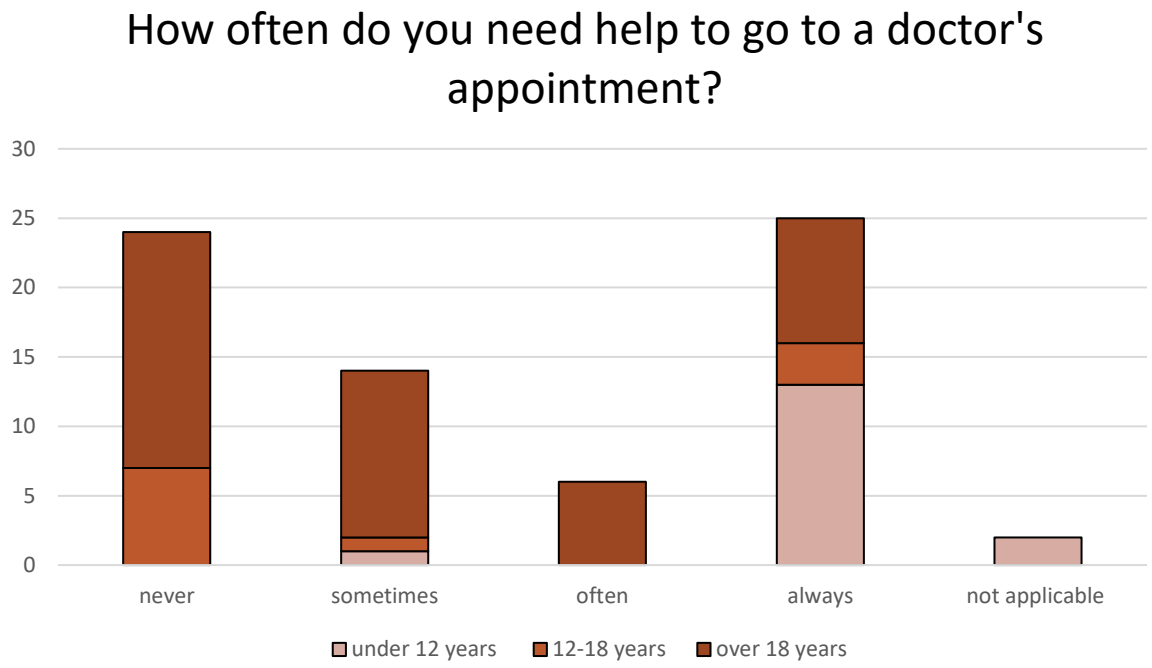


Figure 4. Bar diagram illustrating the frequency with which patients required assistance to attend a doctor's appointment, categorized by age groups. The x-axis shows the frequency of needing help, and the y-axis indicates the number of patients. Different colors represent the three age groups: under 12, 12-18, and over 18 years of age. Not applicable shows the patients who did not answer.

4.2.6 Visual aids

Visual aids significantly enhance patients' ability to navigate daily life. Among the participants, 39 (54.9%) reported *always* using visual aids at work or school, 24 (33.8%) during social activities, and 32 (45.1%) during free time. Conversely, some participants *never* used visual aids for communication (30, 42.3%), social activities (16, 22.5%), traveling (13, 18.3%), or studying/working (7, 9.9%). Their responses regarding children and adults are summarized in the column diagram in **Figure 5** [40].

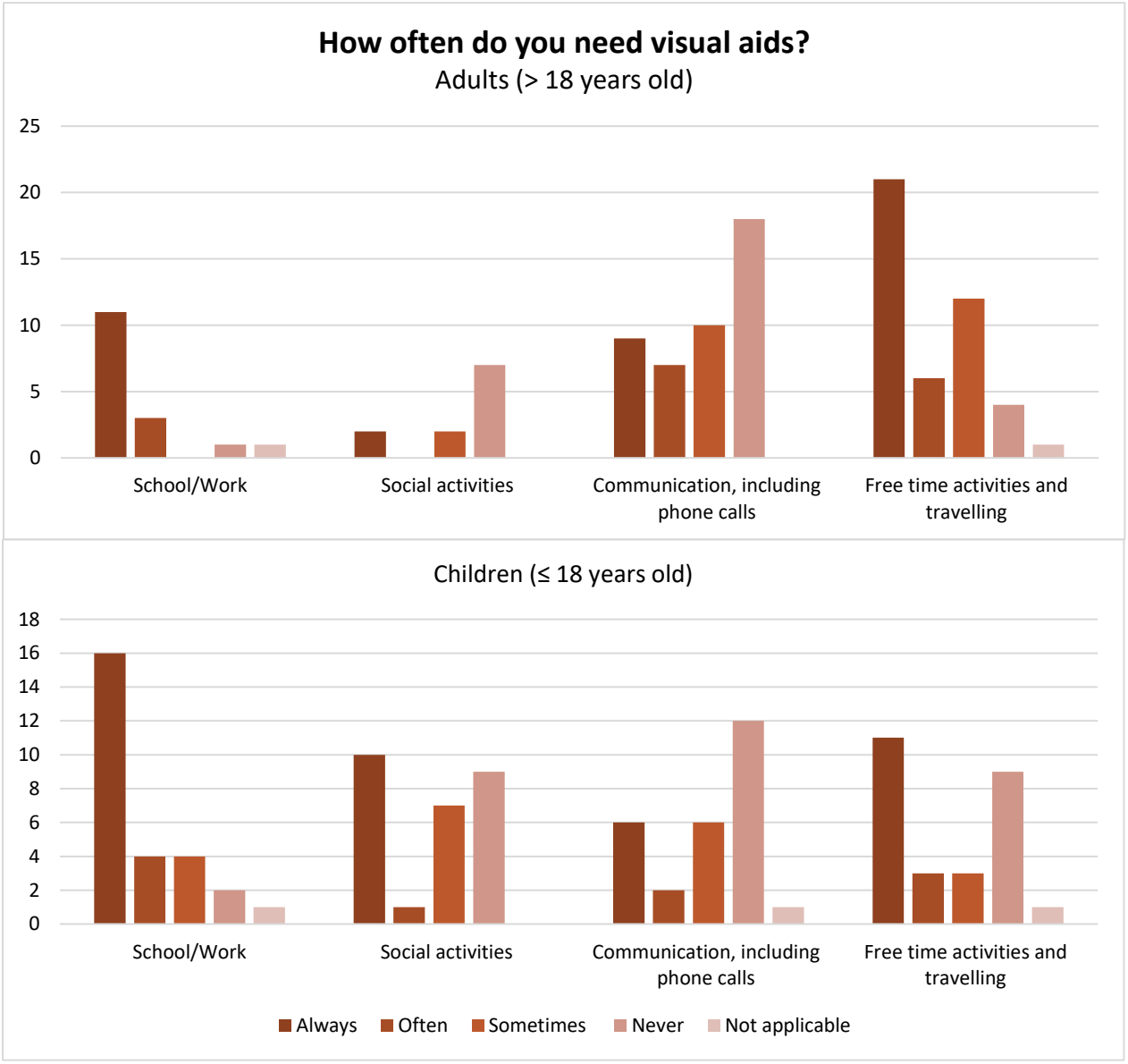


Figure 5. Bar diagrams depicting how often patients need visual aids during school/work, social activities, communication and free time activities, among adults (above) and children (under). The vertical axis shows the number of patients, and the columns reflect the frequencies denoted by categories such as 'always,' 'often,' 'sometimes,' and 'never.' 'Not applicable' shows the patients who did not answer.

Daily activities were mostly managed without help or only with visual aids, despite reduced vision. As shown in **Figure 6** regarding children and adults, most participants completed daily tasks such as eating, dressing, maintaining personal hygiene, choosing items in the kitchen, or finding personal belongings independently. Conversely, when undertaking new activities such as visiting new places or trying new tasks (**Figure 7**), 18.3% *often* needed help, and 31.0% *always* needed help. Adults were just as likely to need assistance, as children ($\rho = 0.04$, $p = 0.70$)[40].

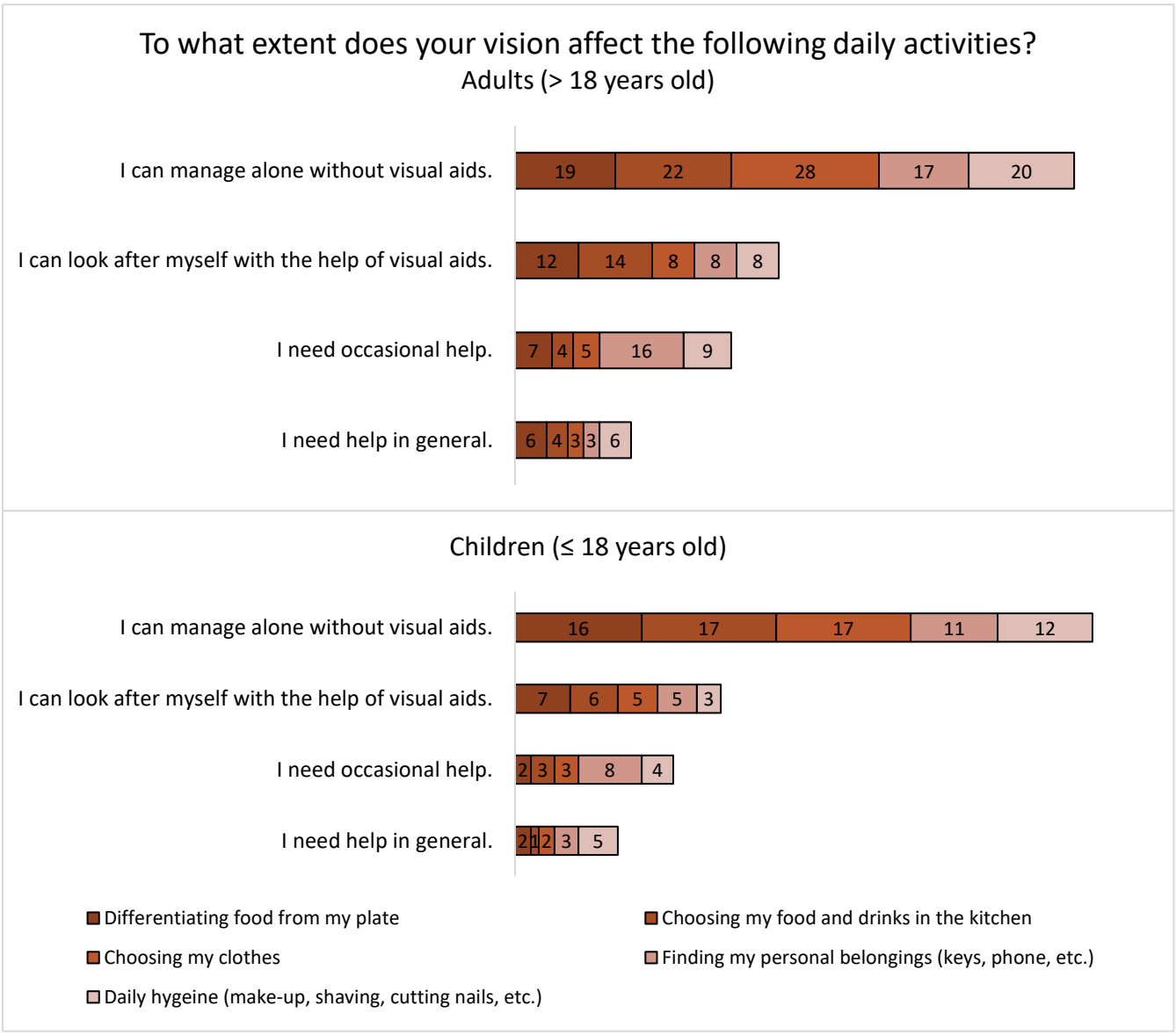


Figure 6. Bar charts showing the impact of visual impairment on daily activities, for adults (above) and children (below). The vertical axis describes the need for help, and the bars indicate various aspects of daily life. The number of patients is indicated within the bars.

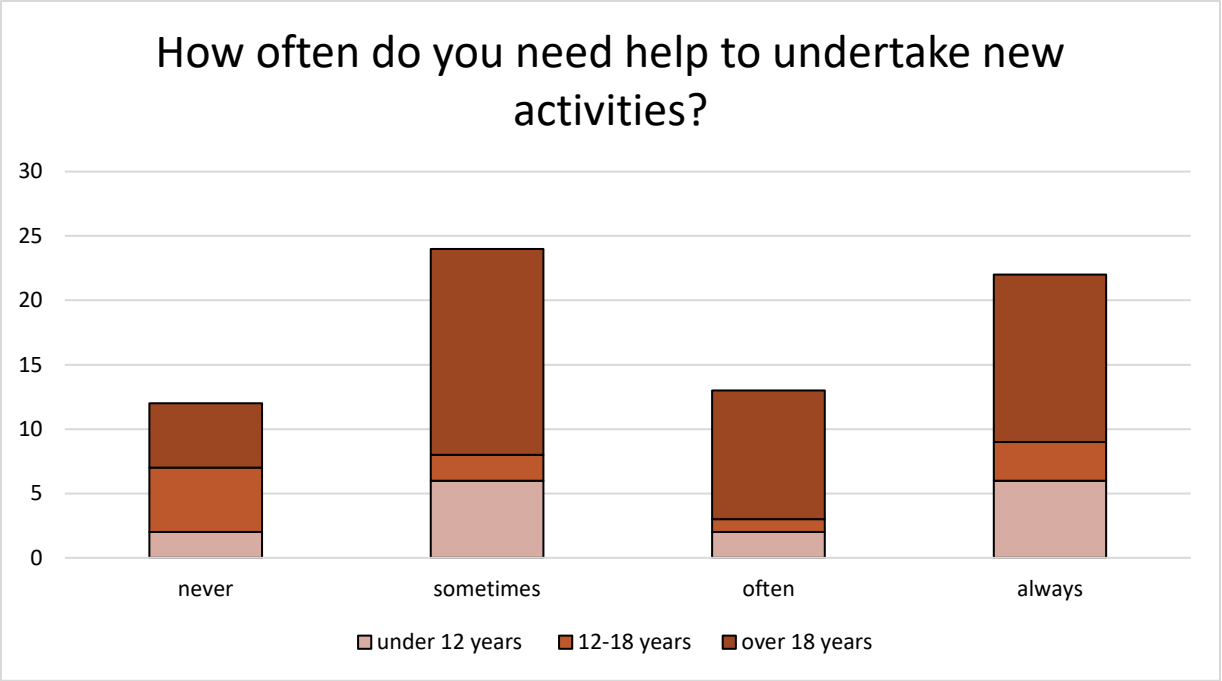


Figure 7. Bar diagram illustrating the frequency with which patients required assistance to undertake a new activity, categorized by age groups. The x-axis shows the frequency of needing help, and the y-axis indicates the number of patients. Different colors represent the three age groups: under 12, 12-18, and over 18 years old.

4.3 Self-assessed quality of life

An analysis of the self-assessed quality of life (QoL) among participants revealed that a majority reported a good QoL (29, 40.8%). Children reported a higher QoL compared to adults ($\rho = 0.44$, $p < 0.001$) (**Figure 8**).

A Spearman's Rho and Chi^2 correlation test was conducted to compare QoL with various clinical findings in congenital aniridia. Factors such as genetic mutation, visual acuity (BCVA), corneal surgery, corneal grafting, presence of glaucoma, glaucoma surgery and its timing, and the total number of surgeries did not show a significant correlation with QoL (**Table 3**). Similarly, the frequency of ophthalmologist visits, the number and type of eye drops, and the use of systemic immunosuppressants (typically given after corneal grafting) did not significantly impact self-reported QoL.

Conversely, patients with more advanced (AAK) exhibited a significantly lower quality of life ($\rho = 0.28$, $p = 0.027$). Additionally, cataract, cataract surgery and cataract surgery earlier in life was associated with a more pronounced decline in QoL. **Table 3** summarizes these correlations, including p values [40].

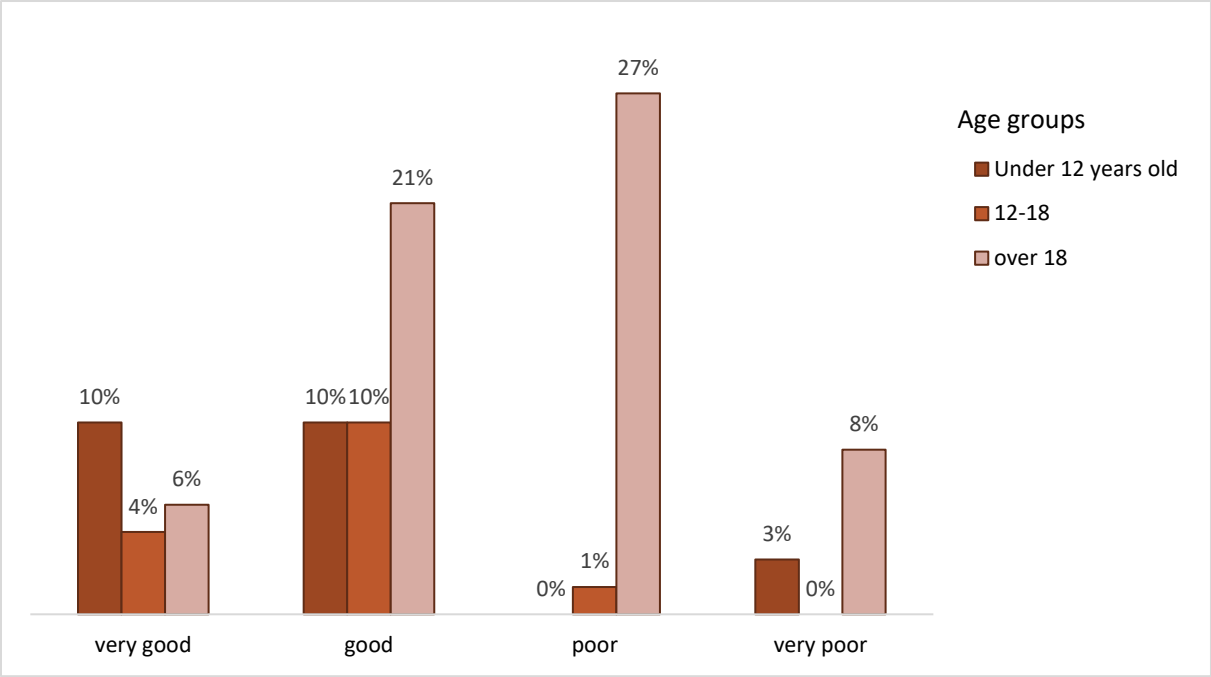


Figure 8. Self-reported quality of life among different age groups is depicted. The x-axis indicates the self-assessed QoL, with the percentage of patients labeled above each bar. The participants are categorized into three groups: children under 12 years old, adolescents between 12 and 18 years old, and adults. A Spearman's rho correlation analysis revealed that children generally report a higher quality of life compared to adults ($\rho = 0.44$, $p < 0.001$, $N = 71$) [40].

Correlation of QoL with clinical findings

	Correlation coefficient	*p-value*
Genetic mutation		
PAX6	11.07**	0.14
WAGR	8.01**	0.12
Other	8.07**	0.24
Not tested	9.33**	0.23
BCVA	0.11*	0.35
Cornea		
AAK Grade	0.28*	**0.02**
Corneal surgery	7.98**	0.24
Corneal graft	7.97**	0.24
Cataract		
Cataract	28.07**	**0.005**
Cataract surgery	15.50**	**0.01**
Age of first surgery	-0.36*	**0.002**
Glaucoma		
Aniridic glaucoma	8.01**	0.23
Glaucoma surgery	5.87**	0.43
Age of first surgery	-0.19*	0.10
Total number of surgeries	0.18*	0.13
Frequency of visits to ophthalmologist	0.11*	0.35
Frequency of eyedrops per day and systemic immunosupression	0.18*	0.12
Artificial tears	11.70**	0.06
Antiglaucomatous eyedrops	8.48**	0.20
Steroid eyedrops	11.97**	0.06
Systemic immunosuppression	9.99**	0.12

Table 3 Correlation between self-reported quality of life and various clinical findings among the patients (N = 71). * (ρ) Spearman correlation coefficient. ** ($\chi 2$) Chi^2 test for independence. Significant correlations are highlighted in bold (p < 0.05).

4.4 Clinical findings

4.4.1 Genetic mutations

An overview of the genetic mutations among the participants revealed that 39 (54.9%) had a *PAX6* mutation. A smaller portion, specifically 4 (5.6%) patients, had a WAGR mutation. Additionally, one patient had Gillespie syndrome, one had ELP4-gene related congenital aniridia, and one patient had no known genetic mutation despite testing. 12 (16.9%) participants had not yet undergone genetic testing [40].

4.4.2 Systemic disease

Systemic diseases were present in 27 (38.0%) of the participants. The most common conditions included obesity, developmental delay and diabetes mellitus.

4.4.3 Visual acuity

Table 4 provides a summary of the visual acuity among the participants. Visual impairment increased with age (ρ = 0.32, p = 0.005).

As expected, all clinical complications of congenital aniridia, such as AAK, cataract, secondary glaucoma and surgeries, as well as the early age of surgery, negatively impacted the BCVA (p = 0.001).

Communication in person or face-to-face was not significantly impacted by BCVA. Similarly, no significant correlation was found between BCVA and how patients completed their tasks or socialized at school and work (p = 0.09 and p = 0.35, respectively). BCVA also did not influence the amount of help which patients needed in their daily lives ($p \geq 0.10$). This suggests that BCVA may not be a sufficient indicator of patients' daily functioning and level of independence.

LogMAR BCVA	**N (%)**	**Descriptive statistics**
Mild or no impairment (<0.5)	17 (23.9%)	
Moderate impairment (0.5-1.0)	26 (36.6%)	**Mean Value** 0.85 ± 0.82 logMAR
Severe impairment (1.3-1.1)	9 (12.7%)	**Minimum** 3.0 logMAR
Blindness (>1.3)	14 (19.7%)	**Maximum** 0.09 logMAR
No data available	5 (7.0%)	

Table 4. Best corrected visual acuity (BCVA) of the participants.

4.4.4 Cornea

Eighteen (25.4%) patients had grade 0 AAK. Grade 3 keratopathy was observed in 20 patients (28.2%), followed by grade 1 in 11 patients (15.5%) and grade 2 in 8 patients (11.3%). 4 patients (5.6%) had severe AAK grade 4. There was no significant correlation between age and severity of AAK (ρ = 0.17, p = 0.15) (**Figure 9**).

Eight (11.3%) patients permanently required therapeutic contact lenses due to persistent corneal erosions, with these lenses typically being replaced every four weeks. Corneal surgeries, including pannectomy, amniotic membrane transplantation, phototherapeutic keratectomy, and penetrating keratoplasty were performed in 21 participants (29.6%), with 18 of them (25.4%) having undergone corneal grafting. This group used significantly more eyedrops (χ^2 = 97.9, p = 0.001)[40]. Eleven of the

patients who had undergone corneal transplantation used systemic immunosuppressants, 15 of them used steroid eyedrops and 3 patients used local steroids despite not having a corneal graft.

As shown above, the severity of AAK negatively impacted perceived quality of life. Additionally, patients with more advanced AAK had more frequent ophthalmologist visits (ρ = 0.46, p = 0.001). However, the severity of AAK did not significantly correlate with the frequency of eye symptoms, communication, performance at school and work, or other practical aspects of daily life indicated above ($p \geq 0.22$).

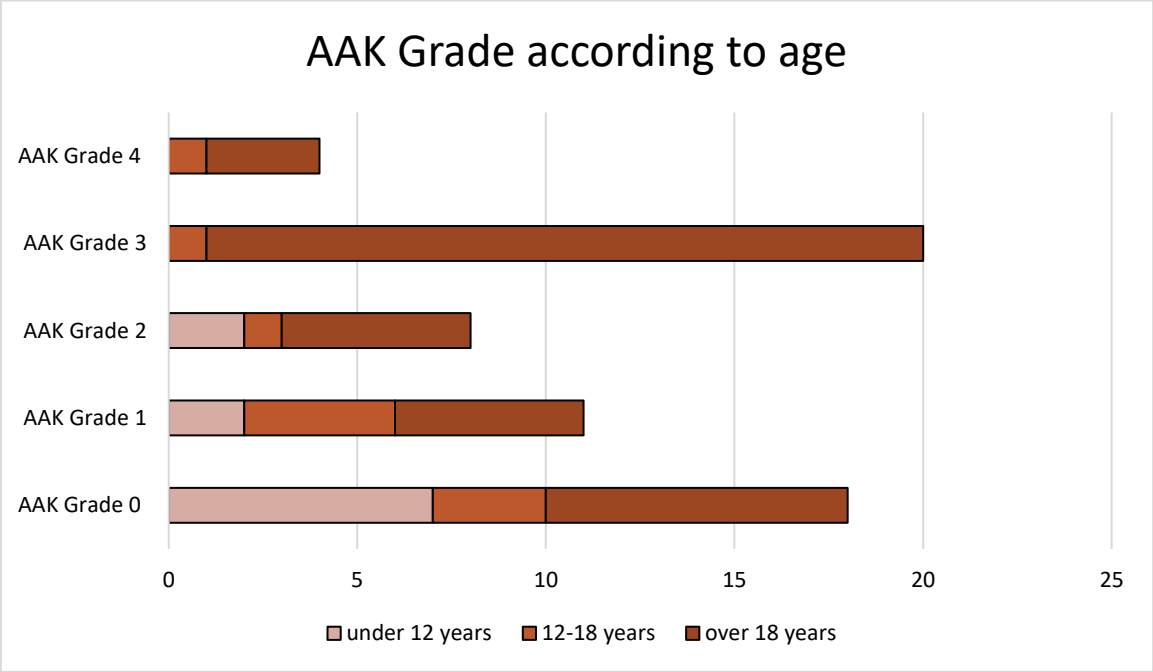


Figure 9. Bar chart showing the AAK grade according to age. The x-axis shows the number of patients, the y-axis the AAK grade and the different bars the age groups.

4.4.5 Cataract

The majority of the participants, specifically 52 (73.2%), had cataracts. The types of cataracts included posterior subcapsular cataract, posterior polar cataract, corticonuclear cataract, and mature cataract. Thirty-five patients (49.3%) had undergone cataract surgery. Most of these surgeries (17 patients, 48.6%) occurred between the ages of 19 and 49. Eleven patients (31.4%) were under 12 years old, 6 patients (17.1%) were between 12 and 18 years old, and one patient was over 50 years old. Earlier cataract surgery was correlated with a lower quality of life (p = 0.002).

Cataract surgery and its early age showed a correlation with dry eye symptoms (p = 0.03 and $p < 0.001$, respectively), but not with other symptoms [40]. Earlier cataract surgery was also correlated with more frequent use of special software for mobile phones (p = 0.03) and tended to correlate with difficulties

in face recognition during communication (p = 0.05). However, it did not significantly correlate with performance and socialization at school and work or with completing daily tasks ($p \geq 0.02$).

Corneal and glaucoma complications were more prominent in patients who had cataract surgery earlier in life. There was a correlation between cataract surgery and severity of AAK (χ^2 = 62.3, p = 0.001), corneal surgery (Φ = 1.41, p = 0.001), and corneal transplantation (Φ = 1.13, p = 0.001). Additionally, an earlier age of cataract surgery correlated with more frequent corneal surgery (χ^2 = 0.37, p = 0.001) and corneal transplantation (χ^2 = 34.3, p = 0.001). The presence of cataract alone did not significantly impact AAK (p = 0.28).

Cataract surgery was correlated with the presence of aniridic glaucoma (Φ = 1.08, p = 0.001), glaucoma surgery (Φ = 1.04, p = 0.001), and earlier glaucoma surgery (ρ = -0.37, p = 0.001). Similarly, earlier cataract surgery was correlated with the presence of aniridic glaucoma (χ^2 = 16.0, p = 0.001) glaucoma surgery (χ^2 = 36.7, p = 0.04) and earlier glaucoma surgery (ρ = 0.58, p = 0.001).

Finally, patients with cataracts, those who had undergone cataract surgery, and those who had cataract surgery at an earlier age had significantly more surgeries overall (χ^2 = 105.8, p = 0.001; χ^2 = 114.5, p = 0.001; and ρ = -0.57, p = 0.001, respectively).

4.4.6 Glaucoma

Forty-five (63.4%) patients had glaucoma, and its presence tended to increase with age (χ^2 = 8.7, p = 0.05). Twenty-four (33.8%) of these patients had undergone at least one glaucoma surgery. Most of these patients (12 (50.0%)) had their first surgery between ages 19 and 49. This was followed by those under 12, who compromised 21.8%. One patient had surgery between 12 and 18, and 2 above 50 years of age. Types of performed surgeries were cyclophotocoagulation, trabeculotomy, trabeculectomy and glaucoma valve implants. Most patients (44 (62.0%)) used antiglaucomatous eyedrops, independent of having had glaucoma surgery. These patients significantly went more often to the ophthalmologist (χ^2 = 79.7, p = 0.001), with 28 (63.6%) of these patients going up to 6 times a year and 13 (28.8%) monthly.

Communication, how patients performed and socialized at school and work, their need for assistance during daily life was not correlated to the presence of glaucoma ($p \geq 0.053$).

As indicated above, the severity of AAK, corneal surgery as well as cataract, its surgery and early age were strongly correlated with the glaucoma surgery ($p \leq 0.001$)[40].

4.4.7 Doctor appointments

Most patients (34, 47.9%) visited the ophthalmologist up to six times a year, while 17 patients (23.9%) had biannual visits. Thirteen patients (18.3%) went up to twelve times a year, and one patient (1.4%) never visited the ophthalmologist. Patients with more severe AAK, aniridic glaucoma, and those who had early cataract surgery visited the doctor significantly more frequently ($p \leq 0.001$).

4.4.8 Treatment

Table 5 summarizes the number of surgeries patients had undergone, the frequency and type of eyedrops used per day, and the use of systemic immunosuppressants. Cataract surgery was the most frequent, with 30 (42.3%) patients having undergone the procedure. This was followed by glaucoma surgery in 22 (31.0%) patients and corneal surgery in 21 (29.6%) patients. Glaucoma and corneal complications were the most common reasons for repeat surgeries. Artificial tears and antiglaucomatous eyedrops were the most frequently used medications [40].

	Frequency	***Percent (%)***
Number of surgeries		
None	29	40.8
Up to 4	16	22.5
Up to 10	10	14.1
More than 10	11	15.5
No data available	5	7.0
Frequency of eye drops per day		
0	14	19.7
Up to 3	27	38.0
Up to 6	22	31.0
Up to 9	3	4.2
No data available	5	7.0
Artificial tears	44	62.0
Antiglaucomatous eyedrops	41	57.7
Steroid eyedrops	18	25.4
Systemic immunosuppressants	11	15.5

Table 5. Overview of the number of surgeries undergone by the patients, the frequency with which they use eyedrops daily, and the types of eyedrops they use, shown in absolute and percentage frequencies.

5 Discussion

This study explored how patients with congenital aniridia navigate their daily lives and how this relates to their degree of visual impairment and syndrome features. The first part of the questionnaire was included in a larger survey from "COST Action ANIRIDIA-NET" (European Cooperation in Science and Technology, COST Action CA18116), which was conducted across several European countries to assess how much assistance from other people and optical devices is required for daily life. Questions concerning the quality of life in patients with congenital aniridia were included in the German version of the questionnaire. In the second part, complications of aniridia were documented for the participants, and the associations between these complications and the patients' daily lives were examined.

According to our findings, patients with congenital aniridia, despite facing pronounced visual impairments, reported a relatively good QoL and manage daily activities effectively. Interestingly, children with this condition often exhibit a better self-reported QoL than adults. This can be attributed to the progressive nature of aniridia, where complications such as aniridia-associated keratopathy (AAK), cataract, and glaucoma tend to worsen with age. Early childhood typically sees fewer severe complications, while adulthood brings increased severity and frequency of these issues, necessitating multiple surgical interventions. The severity of AAK and the prevalence of cataract and glaucoma increases with age, significantly impacting the visual acuity and overall health of patients.

5.1 Quality of life

5.1.1 Effect of age on better QoL

Despite pronounced visual impairment, patients reported an overall good quality of life (QoL) and effective daily life management. Children exhibited a moderately better self-reported QoL than adults ($p = 0.001$). This finding can be attributed to several factors. Firstly, congenital aniridia is a progressive condition, with complications typically emerging in late adolescence and early adulthood. Our study demonstrated that the severity of aniridia-associated keratopathy (AAK), as well as the diagnosis of cataract and glaucoma, increased with age. Fries et al. investigated the age-related ocular surface and tear film status in 45 subjects with congenital aniridia and found that ocular surface damage and tear abnormalities, such as reduced tear production, were present in all patients but only became evident after 10 years of age [25]. They suggested that this window for the onset of dry eye disease could be a potential therapeutic target to delay the progression of AAK. In this context, it is crucial to prescribe only preservative-free eyedrops and to begin using artificial tears in infancy [40].

AAK severity also increases with age. In our study, no patients under 12 years of age had AAK Grade 3 or 4. Lagali et al. found that in a cohort of 37 patients (67 eyes), young subjects under 20 years of age

generally had Grade 1 keratopathy, with significant AAK progression occurring after 20 years of age [56]. It has been postulated that a certain degree of keratopathy is present in all congenital aniridia subjects, regardless of age and mutational status. Slit lamp and in vivo confocal microscopy examinations have revealed an increased density of mature dendritic cells and corneal nerve degeneration in the central cornea, present from early childhood [54, 64]. This leads to increased ocular surface immune activity and reduced corneal sensitivity. Chronic inflammation may result in limbal stem cell deficiency, becoming clinically significant later in life and thus affecting the vision and QoL of older patients.

Furthermore, cataract prevalence increases with age; however, in our study, cataract diagnosis, surgery, and early age of surgery were all associated with a lower QoL. In a cohort of Korean patients aged 0.1 years-52 years, 88.3% had either lens opacities or had undergone cataract surgery [71]. The median age of cataract diagnosis varied between 3-14 years [69, 86]. These findings highlight the importance of age in the progression and management of cataract in patients with congenital aniridia. A further discussion on how cataract surgery may impact on the health of aniridia eyes follows later.

Likewise, aniridic secondary glaucoma diagnosis increases with age, nevertheless was not associated with QoL (see **Table 3**, no significant correlation between glaucoma and QoL, $p = 0.23$). In our group 7 (10.6%) patients with glaucoma were under 12 years old, 9 (13.6%) were between 12-18 and 29 (43.9%) were over 18 years old. There was no information for 5 (7.5%) of the participants. In a cohort of 30 unrelated aniridia patients, the frequency of secondary glaucoma was found to be 15% in the age group of 0 to 9 years [30]. In the following decades, up to the age of 40, an additional 15% of patients were diagnosed with glaucoma per decade [30].

Finally, while children with congenital aniridia initially have less pronounced complications, this changes in adulthood where conservative treatment becomes insufficient, leading to an increase in surgical interventions. Almost all patients eventually undergo cataract surgery, and many require multiple corneal and glaucoma surgeries. As we have shown, all patients who underwent glaucoma surgery continued using antiglaucomatous eyedrops. The combined implications of AAK and glaucoma significantly reduce both BCVA and visual field [95].

Overall, as patients with congenital aniridia age, they experience clinical complications that progressively diminish their visual acuity and visual field, necessitating repeated treatments and surgeries with often limited success. These aspects may contribute to the decline in their quality of life with increasing age [40].

5.1.2 Adaptation effect on QoL

Another argument why children demonstrate a better QoL is early adaptation with their condition. A study on young adults with primary congenital glaucoma indicated a good QoL regardless of their visual

field status, surgical history, and medication use [29]. Contrastingly, studies involving patients with visual impairments from glaucoma, age-related macular degeneration, or senile cataract have shown lower QoL [42, 45, 15]. This suggests that factors beyond clinical measures may influence QoL. These patients had previously experienced normal vision and had to adapt to decreased visual acuity later in life. On the other hand, research by Labiris et al. found that even patients with early-stage keratoconus, who have normal best-corrected visual acuity, report a reduced QoL [53]. Since keratoconus typically affects young and active individuals (with onset usually between 9.2 and 28.0 years), its diagnosis can lead to increased anxiety and stress [85, 52, 48]. Patients with congenital aniridia, however, are born with their condition and develop adaptation strategies that help them complete basic activities in daily life. This early adaptation may contribute to their relatively better perceived QoL.

Furthermore, adult patients often face increased responsibilities, leading to activity limitations, financial and social strain [11]. A three-year cross-sectional study of adults aged 60-96 years found a significant association between visual impairment and greater activity limitations, as well as reduced socioeconomic, social, and psychological resources [11]. Vision impairment frequently creates obstacles to employment opportunities, further contributing to the diminished QoL in adult population [16].

5.1.3 Social interactions

Among our participants, 36.6% of children and 40.9% of adults reported difficulties in socializing. This is consistent with research suggesting that visual impairment can lead to social isolation. For example, a study by Pinquart and Pfeiffer found that children and adolescents with visual impairments often experience higher levels of social exclusion and have fewer friends than their sighted peers [75]. Difficulty interpreting facial cues and expressions was reported by 39.6% of our patients, reflecting the broader challenges that people with visual impairments face with non-verbal communication, which is crucial for effective social interactions. Hurro and Aro found that young people with visual impairment tend to have fewer friends and more feelings of loneliness, but their psychosocial development is similar to that of their sighted peers [41].

Research on older adults with age-related vision loss often highlights reduced social participation, increased feelings of loneliness, and depression [92]. However, these findings cannot be directly applied to people with congenital aniridia, whose experience may be different due to the lifelong nature of their condition. Developing strong friendship networks can significantly improve social inclusion for those with visual impairments. Peer support groups, as well as cognitive behavioral therapy help people with visual impairment build social skills and confidence, facilitating better social integration [40, 75]. Additionally, strong family support systems can mitigate the negative impact of visual impairment on social participation and psychological well-being.

Familiarity with the environment was an important factor influencing patients' independence. Notably, 33.8% of individuals sought occasional assistance, while 31.0% required consistent aid. This dependency on assistance, especially in a familiar environment, could potentially impede their capacity to readily engage in new activities, both within educational settings and workplaces. The rehabilitation of individuals with significant visual impairment encompasses various components, with one key aspect being orientation and mobility training. In Germany, this training is provided by the DBSV (*Deutscher Blinden- und Sehbehindertenverband e.V.*). The primary objective of this training is to enhance individuals' mobility beyond their homes. Through targeted instruction and support, the program assists visually impaired individuals in developing skills to confidently navigate and engage with their external environment. In addition, the DBSV provides access to training in DLA – daily living activities – enabling patients to perform household tasks, cook, and do the washing and ironing without harming themselves.

In conclusion, although people with visual impairment, including those with aniridia, face significant social challenges, various strategies can help to alleviate these problems. Support from family, friends, and peers, together with targeted interventions such as orientation and mobility training, and daily living activities training, can play a crucial role in improving social participation, independence, and overall quality of life.

5.1.4 Visual impairment

The mean visual acuity in the study was 0.14 ± 0.15 (logMAR 0.85 ± 0.79). Edén et al. reported a similar level of acuity in 125 patients in Sweden and Norway, with a Snellen VA of 0.19[20]. According to WHO criteria, a visual acuity threshold of logMAR 1.0 (equivalent to 20/200) in the better-seeing eye is used to define "serious" vision impairment, while logMAR 1.3 is considered legal blindness. In Germany, legal blindness is defined at logMAR 1.69 (equivalent to 1/50), as per the Versorgungsmedizin-Verordnung (Teil A.6.a der Anlage zu § 2 VersMedVO). In this study, 9 patients (12.7%) met the criteria for serious visual impairment by WHO standards, and 14 patients (19.7%) met the criteria for legal blindness. Jacobson found a higher proportion of aniridia patients with legal blindness at presentation (38%) [43].

Despite their low visual acuity, most patients reported being able to independently complete their tasks at school and work, as well as participate in social activities. Additionally, about half of them only occasionally experienced difficulties in completing their work and school tasks. Adaptation skills may play a crucial role in this perceived independence [40]. Bosmann et al. found no significant difference in the reading processes of students with visual impairment compared to their normal-sighted peers [10]. Although the former group was slower, they were equally accurate. According to Gompel et al.,

children with visual impairment relied more on sentence context than on word phonetics [28]. It is essential for children to gain these skills to be employable later in life.

A study in Norway among 574 adults aged 18-67 years with visual impairment found that unemployment rates were higher than in the general population [12]. These patients are restricted in the range of jobs available to them and face impediments in many other jobs [98]. Adjustments in the work and school environment can greatly enhance their ability to perform tasks. Implementing glare reduction, contrast enhancement, improved lighting, and providing desktops with screen reading or magnification software are crucial steps. Additionally, using OCR (optical character recognition) software, larger print materials, and tactile or talking devices has been shown to significantly improve task performance and accessibility [5].

Visual aids play a crucial role in maintaining patients' autonomy, particularly in school, work, and leisure activities. Participants highlighted the use of specific tools and applications on mobile smartphones and computers, such as the Zoom Text magnifier/reader and Voice Over. However, many reported struggling at school due to the small or distant text on blackboards. Providing appropriate optical aids is essential for these patients. Edge filters can enhance contrast sensitivity and control glare. To magnify text and objects, various optical magnifiers, including hand-held and stand magnifiers, simple high-plus spectacles, and telescopic spectacles, can be utilized. For higher magnification needs (greater than 6x), electronic reading devices are typically recommended [2].

There is no one-size-fits-all low vision aid, and these aids are most effective in specific situations, like reading. Custom fitting is necessary to optimize residual vision and reduce the patient's disability, including alleviating symptoms and photophobia, and improving their independence. Since aniridia is a progressive disease, visual acuity-adapted low vision aids are essential, and regular evaluations of the sufficiency of these aids should be conducted [75]

The same survey was used to evaluate the experiences of patients in Hungary who had congenital aniridia, as part of the "COST Action ANIRIDIA-NET" [17]. The assessed group demonstrated a high level of freedom in daily routine activities and very little restriction in personal communication. Furthermore, the research findings indicated a relationship between advanced age and a heightened need for support during tasks, along with an emphasis on using visual aids [40].

5.2 Impact of complications

5.2.1 Aniridia associated keratopathy

In our study, 61 patients (85.9%) were affected by AAK, with a prevalence similar to that reported by Latta et al [61]. Among our patients, 29.6% had undergone corneal surgery and 25.4% had received a corneal transplantation. According to Viberg et al. [92], the improvement in visual acuity after corneal transplantation was modest, and many patients experienced complications such as AAK recurrence in the graft, rejection, and glaucoma. These issues were also a primary reason for more frequent ophthalmologist visits. Collectively, these factors likely contribute to the lower reported quality of life (QoL) among patients with advanced AAK ($p = 0.027$).

AAK exhibits high genetic and phenotypic variability, necessitating individualized treatment for patients. The early stage of AAK, characterized by microscopic changes while the cornea remains clear, is a potential target for future treatments aimed at halting progression [25]. It is crucial for all patients to receive preservative-free artificial tears to optimize the ocular surface. Novel pharmacological options include immunomodulators and gene therapy to potentially optimize *PAX6* levels [91].

However, AAK Grades 3 and 4 usually require surgical treatment, and corneal transplantation remains a challenging procedure with questionable success. At the Homburg Aniridia Center, a combination technique is employed that includes penetrating keratoplasty with simultaneous amniotic membrane patch, bandage contact lens, and temporary tarsorrhaphy, along with postoperative autologous serum eye drops and systemic immunosuppression [23]. This approach aims to accelerate epithelialization of the corneal surface, typically delayed due to LSCI. It is not uncommon for patients to require multiple allografts due to recurrent AAK on the graft [23].

As a last resort in severe AAK, where corneal transplantation has repeatedly failed, the Boston Type I Keratoprosthesis (Kpro) can be considered. This implant features an artificial central part that does not opacify. However, its complications include corneal melting, glaucoma, retrocorneal membrane, and AFS [19, 84]. None of the patients in our study group had a Kpro.

Long-term immunosuppression is crucial for graft survival. All patients receive local corticosteroids like prednisolone, dexamethasone, or loteprednol. Systemic immunosuppression, including tacrolimus, betamethasone, azathioprine, and mycophenolate mofetil, is used to control inflammation and reduce the risk of early allograft rejection [39]. In our transplanted patients, all but one received oral mycophenolate mofetil [40]. These patients need routine monitoring of their blood and liver function and

must be free of infections during treatment. Due to its teratogenic effects, mycophenolate mofetil is not suitable for women or men planning to have children.

AAK is one of the most significant progressive complications of aniridia, requiring various conservative and surgical treatments to preserve vision. Further research is essential to develop better treatment strategies, ultimately enhancing the quality of life for these patients.

5.2.2 Cataract

In our study, cataract emerged as the most impactful complication of congenital aniridia, with 73.3% of patients having cataracts and 49.2% having already undergone cataract surgery. Of those, 17 (23.9%) underwent surgery between the ages of 19 and 49. All three aspects — presence of cataract, cataract surgery, and early age of surgery — were correlated not only with a decline in QoL but also with more advanced AAK, glaucoma, and increased frequency of ocular surgeries. According to Kit et al., cataract surgery is required in about 50%–85% of aniridia patients at a mean age of 30 years [48].

Cataract becomes relevant in patients with congenital aniridia during childhood or early adulthood, significantly compromising their already low visual acuity. While lens opacities that are not visually relevant are common, long-term assessment of visual acuity is crucial to detect when cataracts become clinically significant. Careful preoperative evaluation of the cornea and the grade of AAK is important and possible corneal surgery can be considered. Second, due to typical presence of dry eye disease, preoperative intensive treatment with conservative free artificial tear eyedrops is necessary. Dysregulated intraocular pressure should be adjusted preoperatively [9].

Cataract surgery in aniridia patients is high-risk and should ideally be performed by a highly skilled surgeon [18]. Calculating the correct lens is challenging, especially given the degree of AAK present. Intraoperative challenges include poor visibility through the opacified cornea, a very thin and fragile anterior capsule prone to tears, altered anterior chamber anatomy, and a compromised zonular apparatus [7]. To stabilize the lens during extraction and IOL implantation, a capsular tension ring is preferred. The objective is usually to perform classic phacoemulsification and IOL implantation in the bag.

Iris reconstruction combined with cataract surgery can theoretically improve glare, but it is not routinely recommended, though is extensive complications [78]. If necessary, patients may use colored glasses to control glare. Iris prostheses require larger incisions, increasing intraoperative and postoperative stimulus, which can prolong healing and lead to more postoperative complications like dislocation and exacerbation of glaucoma and AAK and development of aniridia fibrosis syndrome [6, 40].

Postoperative complications such as IOL dislocation, anterior capsule fibrosis, and posterior capsule opacification (PCO) are common due to the patient's young age. While Nd:YAG-capsulotomy is the conventional treatment for PCO, it is challenging in patients with nystagmus. Hence, a simultaneous anterior vitrectomy with surgical capsulotomy during cataract surgery may also be considered [9].

Long-term complications of cataract surgery in patients with aniridia include exacerbation of AAK, glaucoma, and anterior segment fibrosis syndrome (AFS). Intraoperative trauma can lead to corneal decompensation, which may initially be managed with local steroid therapy, osmotic agents, and intensive artificial tears. Additionally, glaucoma exacerbation or the onset of secondary glaucoma can occur due to dysregulation of intraocular pressure following cataract surgery. This can be treated with topical antiglaucomatous eyedrops and systemic acetazolamide [9].

Anterior segment fibrosis syndrome is a rare complication that can arise after any type of ocular surgery in congenital aniridia, including cataract surgery [89]. It is caused by intraoperative manipulation and disruption of blood vessels at the iris remnants, leading to an excessive inflammatory response and the growth of fibrous membranes in the anterior chamber. These membranes can result in lens dislocation, corneal decompensation, retinal detachment, and, if they affect the ciliary body, hypotonia and phthisis bulbi [89].

In conclusion, cataract and cataract surgery are common in patients with congenital aniridia. Due to the significant impact on overall eye and general health, meticulous preoperative and postoperative management is crucial.

5.2.3 Glaucoma

In our study, glaucoma, surgical interventions, and early surgeries did not show a correlation with QoL. However, these factors were common reasons for frequent visits to the ophthalmologist. The prevalence of glaucoma in our cohort was 63.4%, consistent with previous reports [18, 46]. Typically, glaucoma onset occurs around the age of 8 and its incidence tends to increase with age. Given its potential to cause blindness and the difficulties in diagnosis, monitoring, and treatment, especially in young children, aniridic glaucoma can have a significant impact on vision.

Furthermore, 51.4% of patients were using antiglaucomatous drops, and all patients who had undergone glaucoma surgery continued with local medication due to insufficient pressure regulation. Another study from our Homburg Aniridia Center found that among 163 subjects with glaucoma, 45.6% did not use antiglaucomatous eyedrops [25]. Reasons for this included previous successful surgery, pain-free end-stage glaucoma, or noncompliance[40]. Compliance may have been better among our participants since they made the effort to complete and mail the questionnaire. The same study found that patients with quadruple antiglaucomatous therapy or previous glaucoma surgery had the highest

AAK grades. As AAK advances, it becomes increasingly difficult to evaluate the optic nerve head and monitor glaucoma progression through the opacified cornea. Early examination and treatment, along with the use of preservative-free eyedrops, are essential to preserving vision and preventing glaucoma progression [25].

5.2.4 Genetic testing

Twelve (16.9%) patients were not tested for genetic mutations. After a clinical diagnosis of congenital aniridia, it is essential to conduct a family history assessment and at least an eye examination of the parents to identify *PAX6* spectrum anomalies [66]. Establishing the molecular and genetic cause of the disease is crucial, even though there is not always a direct correlation between genotype and phenotype. Patients with the same mutation or within the same family may present with different phenotypes. Identifying specific mutations, such as *PAX6* or others, can influence the prognosis provided to patients. For instance, WAGR Syndrome typically has more aggressive ocular findings compared to *PAX6* mutations. Furthermore, patients may become candidates for future gene therapies aimed at increasing *PAX6* expression in the ocular surface to improve DED and AAK [90]. Discovering other mutations, such as PITX2, CYP1B1, or FOXC1, can indicate the presence of overlapping phenotypes like Peters Syndrome or Rieger Type I Syndrome[38].

Genetic screening is also vital for surveillance among affected individuals and their families. Due to its autosomal dominant inheritance pattern, siblings of an affected patient have a 50% chance of being affected if the parents carry the mutation. In cases of de novo *PAX6* mutations, the offspring of the affected individual are at 50% risk, but not their siblings. This is also applicable to patients with a continuous *PAX6* and WT1 mutation or WAGR Syndrome. Additionally, cases of children with two mutated *PAX6* copies have been reported, presenting with anophthalmia and brain abnormalities. Therefore, molecular genetic testing and eye examinations for the affected patient, their parents, and siblings are recommended. This allows for the identification of individuals who would benefit from early treatment and surveillance of complications [14].

Regardless of mutations, children younger than eight years should be monitored every four to six months for refractive errors and the detection and treatment of incipient or actual amblyopia. Annual eye examinations for all individuals are recommended to detect issues such as corneal changes, raised intraocular pressure, and cataracts [40, 66].

For children with WAGR Syndrome who have congenital aniridia and WT1 deletion, renal ultrasound examinations are necessary every three months, and they should be followed by a pediatric oncologist until they are eight years old. Due to the increased risk of renal impairment in WAGR Syndrome, particularly in those with bilateral Wilms tumor, lifelong evaluation of renal function is recommended.

Regular monitoring of developmental progress and educational needs is also essential. Behavioral assessments for anxiety, ADHD, and aggressive or self-injurious behavior should be conducted as needed [66].

In cases of a known *PAX6* mutation within a family, preimplantation and prenatal genetic testing is possible, allowing for genetic assessment before and during pregnancy, respectively.

5.3 Intervention strategies

Intervention strategies for the improvement of QoL of patients with congenital aniridia can be focused on support measures to facilitate their daily lives, as well as ongoing research for disease treatment and prevention of complications. These medical, therapeutic, and educational interventions should be tailored to the evolving needs of children and adults with congenital aniridia.

Early multidisciplinary care with ophthalmologists, genetics, orthoptists and special education teachers is essential to address visual impairment and complications. Due to the rarity of this condition, there is a lack of information among ophthalmologists and family doctors, which may delay appropriate treatment and create confusion in patients and their relatives [66]. Workshops, publications, and partnerships with rare disease groups can help ophthalmologists recognize and manage congenital aniridia. Social media and referral networks further support early diagnosis and patient care. A non-profit organization to support patients and their relatives is the self-help group for Aniridia and WAGR Syndrome (www.aniridie-wagr.de), active in German-speaking countries [40].

Children with visual impairments, especially with the progressive nature of congenital aniridia, often face complex emotional and social challenges. Providing psychological support, encouraging social inclusion among peers, and supporting families of the affected patients can also positively improve the children's well-being. Furthermore, interventions to allow independence should begin as early as possible. Thus, providing low-vision aids and adjusting them during different disease stages is necessary. These and literacy skills training through technology-assisted reading tools should aim to keep literacy skills in line with their peers [2]. Mobility training should also prepare children and young adults for more autonomy in varied environments, from navigating school corridors to outdoor spaces.

There is a notable lack of high-quality, long-term studies assessing the effectiveness of rehabilitation services on quality of life for children with congenital aniridia [22]. Addressing this gap would help identify the most impactful interventions, enabling healthcare providers to offer targeted, evidence-based support that enhances social, academic, and emotional outcomes for these patients [22].

Effective medical treatment for patients with congenital aniridia should begin with genetic testing to identify the specific genetic mutations, allowing for prompt diagnosis and early identification of conditions like WAGR syndrome [14]. This genetic insight supports timely intervention and enables personalized management strategies and may help determine eligibility for clinical trials [66].

The existence of a preclinical phase in early adulthood presents a crucial opportunity for interventions aimed at delaying or preventing complications [25]. Early preventive measures — such as regular eye examinations, consistent ocular surface lubrication, and intraocular pressure monitoring — can help delay the onset and reduce the severity of symptoms, supporting a higher QoL. Additionally, research into PAX6-related anti-inflammatory treatments holds promise for delaying the progression of AAK and glaucoma [26]. Further investigation is essential to enhance the efficacy of current available treatments.

In Germany, the treatment of patients with congenital aniridia is concentrated in specialized centers. This increases patient safety and promotes continuity of care, research opportunities, and access to the latest treatment innovations [40].

6 Limitations

The study had a relatively low participation rate of 34.3%. 19.8% of the envelopes were returned due to incorrect or changed postal addresses. Several factors might have contributed to the low response rate. Patients with advanced disease, who typically have low visual acuity and limited visual fields, may have struggled to read the questionnaire. Conversely, patients with very mild clinical symptoms who rarely require ophthalmological care may have been less motivated to participate. However, the mean visual acuity and the presence of glaucoma among participants were comparable to those reported in other studies [58].

It's important to note that the study relied on self-reported information, which is subject to individual interpretation of the questions. Moreover, the clinical data was collected from the last examination the patient had in the clinic, which may not necessarily reflect the patient’s condition at the time of completing the questionnaire. Patients with more severe symptoms tend to visit the clinic more frequently, whereas those with milder symptoms may only attend annual check-ups. Additionally, the study lacked a control group with normal vision for comparative analysis.

To gain a more comprehensive understanding of how congenital aniridia impacts patients' daily lives, studies with broader participation rates and longer observation periods are needed [40].

7 Conclusions

This study assessed various aspects of the daily lives of patients with congenital aniridia in Germany as part of the larger European survey COST Action ANIRIDIA-NET. Despite the challenges associated with their condition, patients in Germany demonstrated high levels of autonomy and a good quality of life (QoL). Most patients were able to perform tasks at school and work independently, communicate effectively, and socialize normally. Visual aids and adaptive technologies were widely utilized in these settings, providing significant support for patient autonomy.

The development of individual and social adaptation strategies is essential for maintaining autonomy throughout life, as this condition typically follows a progressive course. Children generally showed better adaptation than adults, with difficulties in communication, task completion, and socializing becoming more apparent with age. This trend aligns with clinical data indicating that complications such as AAK, cataracts, and glaucoma significantly impact daily life and QoL. Particularly, AAK, cataracts, and cataract surgery require careful and continuous evaluation to avoid worsening the condition due to premature interventions. The emergence of these complications in early adulthood represents a critical period for research and potential treatment to delay further clinical deterioration.

The information gathered from the ANIRIDIA-NET questionnaire offers valuable insights into the lives of patients with congenital aniridia and can effectively support follow-up examinations [40].

8 Literature

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Publications

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1. Hoxha Z, Fries FN, Hecker D, Seitz B, Käsman-Kellner B, Náray A, Lagali N, Grupcheva C, Szentmáry N, Stachon T. Standardized assessment of health-related quality of life in patients with congenital aniridia. *Klin Monbl Augenheilkd. 2024;* [accepted for publication].
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Presentations:

Zamira Hoxha, Fabian Norbert Fries, Dietmar Hecker, Berthold Seitz, Barbara Käsmann-Kellner, Annamária Náray, Neil Lagali, Christina Grupcheva, Nóra Szentmáry, Tanja Stachon: **Erfahrungen von Patienten mit kongenitaler Aniridie mit ihrer Sehbehinderung - eine ANIRIDIA-NET-Umfrage im Homburger Aniridie Zentrum.** Congress of the German Ophthalmological Society DOG (28.09.2023 – 01.10.2023, Berlin).

Zamira Hoxha, Elias Flockerzi, Nóra Szentmáry, Fabian Norbert Fries, Berthold Seitz: **Phototherapeutische Keratektomie zur Behandlung einer infektiösen Keratitis bei einer Patientin mit PAX6-assozierter Aniridie.** Congress of the German Ophthalmological Society DOG (28.09.2023 – 01.10.2023, Berlin).

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Curriculum vitae

Aus datenschutzrechtlichen Gründen wird der Lebenslauf in der elektronischen Fassung der Dissertation nicht veröffentlicht.