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Case Report

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Ocular manifestations of familial osteogenesis imperfecta: a three-patient case series with a narrative literature review

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ABSTRACT

Background: Osteogenesis imperfecta (OI) is a genetic disorder affecting primarily connective tissue that may also affect several ocular structures. It has varied ophthalmic manifestations such as thinning of the sclera, predisposition to glaucoma due to increased susceptibility of the optic nerve head to damage, and corneal thinning, that may further complicate the interpretation of intraocular pressure (IOP). We reviewed the published evidence on ocular involvement in OI and described the findings in three affected members of one family.

Methods: A qualitative literature review was conducted using PubMed, after duplicate removal and screening, 34 publications were included. We also retrospectively reviewed the ophthalmic examinations and genetic findings of a mother and her two daughters with confirmed OI.

Results: The literature describes abnormalities involving the sclera, cornea, lens and posterior segment of the eye, including glaucoma and retinal complications. All three family members had blue sclerae and above average central corneal thickness (CCT), with CCT ranging from 449 to 465 μm across the examined eyes. Some measured IOP values were near or above the upper limit of the normal range, while estimates adjusted for corneal thickness were higher. Optical coherence tomography and visual field testing showed no evidence of glaucomatous damage during the reported examinations and genetic testing identified the same pathogenic COL1A1 variant, c.1127delC (p.Pro376fs), in all three women.

Conclusions: Ocular involvement in OI extends beyond blue sclerae. The findings in this family illustrate why IOP should be interpreted alongside corneal thickness, optic nerve structure and visual function. Regular ophthalmic assessment may help identify complications early, although the evidence available to guide screening remains limited.

Keywords: Osteogenesis Imperfecta; Eye Diseases; Ocular manifestations; Glaucoma; Cornea; Corneal Thinning; Intraocular Pressure; COL1A1; Ophthalmic screening.

1. INTRODUCTION

Osteogenesis Imperfecta (OI), also known as brittle bones disease, is a rare group of inherited connective tissue disorders predominantly caused by mutations in the genes encoding the alpha chains of type I collagen – *COL1A1* or *COL1A2*. However, pathogenic variants in other genes have also been implicated in the disease[1–3]. The incidence of OI varies from 1 in 15,000 to 1 in 20,000 live births. [1, 4, 5]. Several clinical types of OI have been described, with disease severity varying widely from almost asymptomatic forms to conditions that are lethal in utero or shortly after birth (Table 1.), [1, 5].

OI type I is the most frequently occurring form of OI with the incidence ranging between 2.35 to 4.7 in 100,000 worldwide [5]. It is typically caused by quantitative defects in type I collagen due to mutations in *COL1A1*, leading to reduced collagen production. Clinically, it represents the mildest phenotype, characterized by bone fragility, blue sclera, and normal or near-normal life expectancy. Extra skeletal manifestations, including hearing loss and ocular abnormalities, are common but usually less severe than in other types [6].

OI type II is the most severe and perinatally lethal form, with an incidence ranging between 1,4 in 100,000 and 1 in 40,000 live births [5]. It is usually caused by structural mutations in *COL1A1* or *COL1A2* that result in abnormal type I collagen formation. The phenotype is characterized by extreme bone fragility, multiple in utero fractures, severe skeletal deformities, and respiratory insufficiency leading to early mortality [6].

OI type III represents the most severe non-lethal form of the disease. It is typically caused by structural defects in type I collagen and is associated with progressive bone deformities, very short stature, and recurrent fractures beginning in early childhood. Patients often develop significant skeletal and extra skeletal complications, including dentinogenesis imperfecta and pronounced scleral discoloration. Life expectancy may be reduced, primarily due to respiratory complications [6].

OI type IV is considered a moderately severe form with variable clinical expression. It is also associated with structural mutations in type I collagen genes. Patients present with bone fragility and deformities of intermediate severity, often without the striking blue sclera typical of type I. Life expectancy is generally near normal, although orthopedic and functional complications are common [6].

OI type V is moderate form of OI caused by mutation in the IFITM5 gene characterized by triad if findings: formation of hyperplastic callus after injury, bone fraction and/or surgery, calcification of the interosseous membrane, and a hyperdense metaphyseal band near the growth plate [5, 7].

Other, rarer forms of OI (types VI–XI) account for less than 5% of cases [5]. Unlike types I–IV, these variants are not caused by mutations in type I collagen genes but rather by defects in proteins involved in collagen post-translational modification, folding, or intracellular processing. Many of these mutations affect components of the collagen 3-hydroxylation complex, which facilitates proper triple-helix assembly. The clinical phenotype varies widely, ranging from moderate to severe skeletal involvement, often accompanied by distinct histological or radiological features [5].

Table 1. Osteogenesis Imperfecta classification.

OI type	Inheritance	Gene/Mutation	Severity	General manifestations	Ocular manifestations	Life expectancy
Type I	Autosomal dominant	COL1A1, COL1A2 (quantitative defect), Rare X-linked variant with mutation in the PLS3 gene	Mild, nondeforming	Bone fragility, generalized osteoporosis hearing loss, short stature	Blue sclera, corneal thinning, myopia, glaucoma	Normal
Type II	Autosomal dominant or autosomal recessive inheritance (mostly de novo)	COL1A1 / COL1A2 (qualitative defect), CRTAP, LEPRE1, PPIB, and BMP1.	Perinatal lethal	Severe skeletal deformities, extreme bone fragility, delayed skull ossification, respiratory failure	Ocular findings rarely assessed	Lethal in utero or shortly after birth
Type III	Autosomal dominant or autosomal recessive	COL1A1, COL1A2, CRTAP, LEPRE1, PPIB, FKBP10, SERPINH1, SERPINF1, and WNT1.	Severe, progressive	Moderate to severe bone deformities, severe growth restriction, fractures	Blue sclera, corneal thinning, high myopia	Reduced
Type IV	Autosomal dominant or autosomal recessive	COL1A1/COL1A2, (both qualitative and quantitative collagen abnormalities) CRTAP, FKBP10, SP7, SERPINF1, WNT1, and TMEM38B	Moderate (greater than type I but less than type III)	Bone fragility, variable skeletal deformities, severe growth restriction	Variable ocular involvement, may lack blue sclera	Near normal
Type V	Autosomal dominant	IFITM5	mild to moderate	Calcification of the Interosseous Membrane or Hypertrophic Callus	normal sclera	Normal to near normal

OI affects the production, folding, stability, processing, and secretion of type I collagen, as well as osteoblast function and bone matrix mineralization. These abnormalities lead to a broad

spectrum of systemic manifestations, including skeletal abnormalities, bone fragility, ligamentous laxity, abnormal dentition, progressive hearing loss, and cardiovascular involvement. Because collagen is widely distributed throughout ocular tissues, patients with OI may also develop a wide range of ophthalmic manifestations. Large cohort studies have demonstrated an increased risk of multiple eye disorders in individuals with OI, including corneal diseases (such as corneal thinning, keratoconus, small corneal diameter, and congenital absence of Bowman's layer), refractive errors, glaucoma, cataracts, vitreous haemorrhage, retinal tears and detachment, retinopathy, choroidal neovascularization, traumatic eye injuries and optic nerve disorders. Blue sclera is the most characteristic ocular feature; however, all ocular structures may be affected to varying degrees [1, 2, 8]. It was also found that patients with OI experienced ophthalmic problems significantly more often than the healthy control group (13.7% vs. 6.7%) and usually occurred in earlier age than in referenced population[8].

Among the 28 known collagen types, only types I to IX are involved in the composition of the eyeball, with type I collagen accounting for the largest proportion. It is present in most ocular structures, including the sclera, cornea, iris, ciliary body, lens, retina, and choroid, and is primarily responsible for the tensile strength of the globe [2]. Given the crucial role of collagen in maintaining the structural integrity and biomechanical properties of ocular tissues, disorders affecting collagen synthesis may have significant ophthalmic consequences (Table 2.).

Table 2. Distribution of collagen types among eye's tissue.

Collagen Type	Major Ocular Structures
Type I	Cornea, Sclera, Iris, Ciliary body, Retina, Bruch's membrane, Lamina Cribrosa
Type II	Vitreous body
Type III	Cornea, Sclera, Uveal tissues, Bruch's membrane
Type IV	Lens capsule, Bruch's membrane

Type V	Cornea, Vitreous body, Bruch's membrane
Type VI	Cornea, Lamina cribrosa
Type VII	Cornea
Type VIII	Bruch's membrane
Type IX	Vitreous body

Diagnosis of Osteogenesis Imperfecta

OI is a condition primarily diagnosed on the basis of clinical and radiological examinations. Growth deficiency, skeletal deformities, and bone fragility leading to frequent fractures constitute the primary grounds for diagnosis. Patients with this disorder may also present with blue sclerae, hearing impairment, dentinogenesis imperfecta, as well as cardiovascular and respiratory system disorders. Radiographic imaging of the skeletal system reveals, among other findings, generalized osteopenia, bowing of the bones, slender ribs, a narrow thoracic apex, and vertebral compression [4].

In cases of diagnostic uncertainty arising from a mild presentation of symptoms, genetic testing should be performed to determine the underlying cause of such occurrences as incidental bone fractures in children [9]. A blood sample or a skin fragment obtained via biopsy can serve as the source of genetic material for verification [9, 10]. Proper sample processing, which include automated DNA extraction (e.g., QIAcube), fluorometric quantification (e.g., Invitrogen Qubit 3.0), and spectrophotometric quality control (e.g., QIAxpert), facilitates the amplification and sequencing of the genes responsible for the disease. Subsequently, utilizing human gene mutation databases, such as the Online Mendelian Inheritance in Man (OMIM) database (https://www.omim.org), genes associated with OI can be identified and analysed [10]. Confirming OI through genetic testing and identifying the specific mutation in clinically diagnosed patients can significantly influence further therapeutic management. It also provides

crucial information regarding the familial risk of the disease and aids in identifying asymptomatic family members [11].

The diagnosis of OI can also be established prenatally [12]. If skeletal or dental abnormalities are suspected during a second-trimester ultrasound examination, or if there is a family history of the disease, including a known mutation in the expectant mother, genetic testing of the developing fetus is highly recommended. This diagnostic approach relies on cell-free fetal DNA isolated from maternal peripheral blood (non-invasive prenatal testing, NIPT) or on DNA obtained from amniotic fluid or chorionic villi through invasive sampling methods [13].

2. METHODS

Study Design

This article aims to combine a systematic literature review addressing ocular manifestations of OI and important aspects of managing patients with this condition in ophthalmology office with a family-based case series. Particular attention was given to glaucoma and corneal thinning; however, the analysis was not limited to this condition and included a broad spectrum of anterior and posterior segment abnormalities.

Literature Search Strategy

We searched PubMed/MEDLINE, Web of Science, the Cochrane Library, ScienceDirect, and Google Scholar for studies published between 1 January 2015 and 1 July 2026. The date of the final search was 29/SEP/2026. The complete search strategy for each source, including search terms, limits, and the number of records retrieved, is provided in Supplementary Table 1. Two

reviewers [independently AKE and JK] screened records and assessed full texts against predefined eligibility criteria. Disagreements were resolved by discussion. Reasons for full-text exclusion are reported in Figure 1.

The following search terms and Boolean combinations were used:

- *"Osteogenesis Imperfecta AND ocular manifestations"*
- *"Osteogenesis Imperfecta AND eye diseases"*
- *"Osteogenesis Imperfecta AND glaucoma"*
- *"Osteogenesis Imperfecta AND cornea"*
- *"Osteogenesis Imperfecta AND retina"*
- *"Osteogenesis Imperfecta AND optic neuropathy"*
- *"Osteogenesis Imperfecta AND intraocular pressure"*
- *"Osteogenesis Imperfecta AND refractive errors"*
- *"Osteogenesis Imperfecta AND cataract"*
- *"Osteogenesis Imperfecta AND retinal detachment"*
- *"Osteogenesis Imperfecta AND vitreous haemorrhage"*
- *"Osteogenesis Imperfecta AND retinal diseases*

Both Medical Subject Headings (MeSH) and free-text terms were applied.

Eligibility Criteria

Inclusion criteria:

- original research articles, reviews, and case reports,
- studies describing ocular manifestations in osteogenesis imperfecta,
- publications addressing glaucoma, corneal, scleral, retinal, or optic nerve involvement in OI,
- articles published in English,
- full-text availability.

Exclusion criteria:

- studies not related to ocular findings,
- articles without full-text access,
- non-English publications,
- duplicate reports describing the same clinical data.

After removal of duplicates, 48 unique articles were identified. Of these, 34 articles met the inclusion criteria and were included in the qualitative analysis.

Data Extraction and Analysis

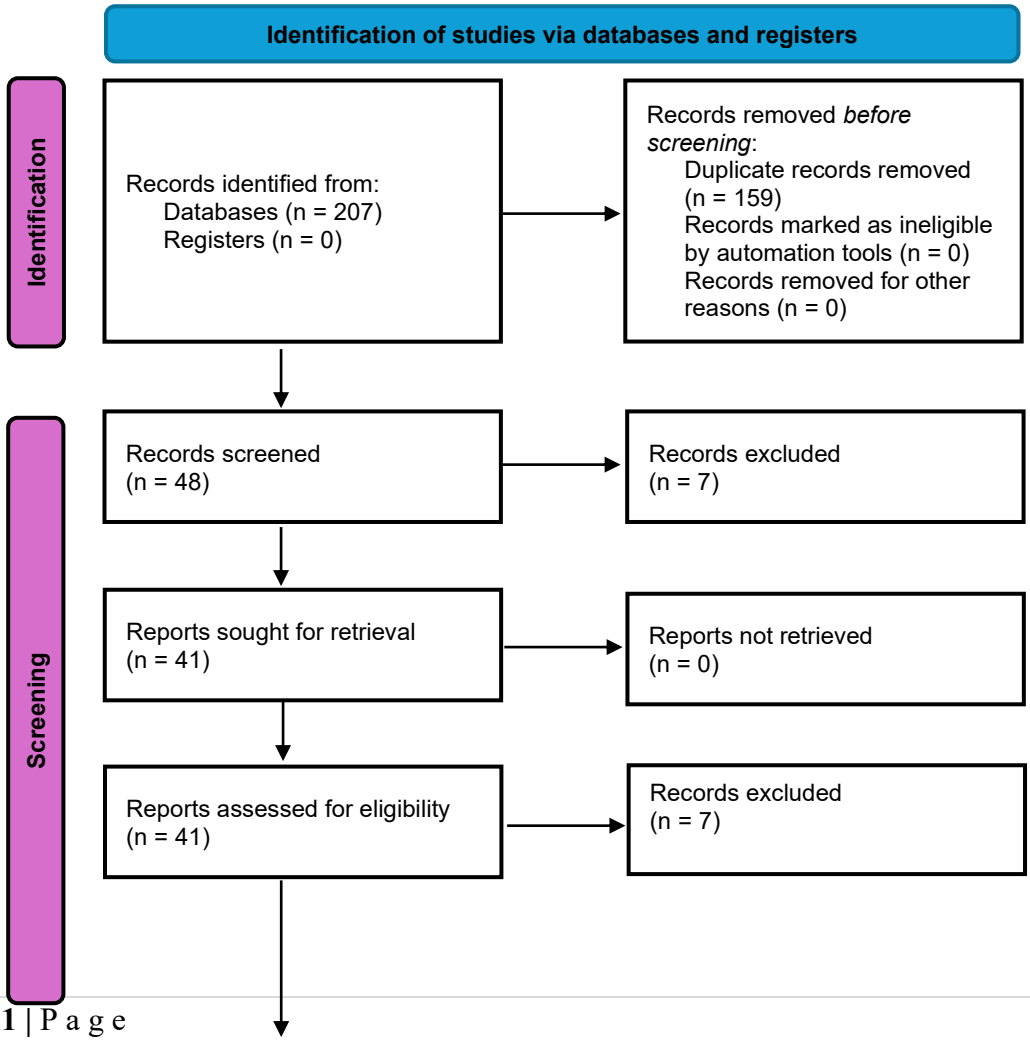
The literature review was descriptive and qualitative in nature. Included studies were categorized according to the primary ocular manifestations described:

- glaucoma and intraocular pressure (IOP) abnormalities,
- corneal structural and biomechanical alterations,
- scleral changes,

- retinal and choroidal pathology,
- optic nerve involvement,
- rare or atypical ophthalmic manifestations.

Findings from the literature were compared with the clinical features observed in the affected family, allowing correlation between reported phenotypes and real-world clinical presentation.

The literature selection process followed a PRISMA-like approach. Records were identified through database searching in PubMed. After removal of duplicates, titles and abstracts were screened for relevance. Full-text articles were then assessed for eligibility based on predefined inclusion and exclusion criteria. The final set of studies included in the qualitative synthesis is presented in a PRISMA-like flow diagram.



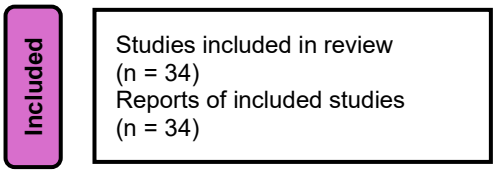


Figure 1. PRISMA flow diagram illustrating the literature search and study selection process for ocular manifestations of osteogenesis imperfecta.

Quality Assessment

Due to heterogeneity of study designs (case reports, case series, cohort studies, and reviews), methodological quality was assessed using the Joanna Briggs Institute critical appraisal tools appropriate for each study type.

The majority of included publications consisted of case reports and small case series, which inherently present a higher risk of bias and limited generalizability.

Most case reports provided clear diagnostic criteria and detailed ophthalmological findings. However, long-term follow-up data were frequently lacking (Table 3.).

Although numerous ocular manifestations of osteogenesis imperfecta have been described, the spectrum remains heterogeneous and based largely on case reports. Further detailed clinical documentation is essential to improve screening and management strategies.

Table 3. Methodological quality assessment of included studies using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist. (table above one A4 page – listed at the end of the article)

Case Description

Members of a single family with a confirmed diagnosis of osteogenesis imperfecta and associated ocular manifestations were included.

Genetic testing was first performed in the proband's first daughter using a targeted next-generation sequencing panel for osteogenesis imperfecta. After identification of a COL1A1 variant, the proband and her second daughter underwent targeted testing for the same familial variant. The analysis included the coding exons of the investigated genes together with 10–20 nucleotide intronic flanking regions. Enriched DNA regions were sequenced on an Illumina NovaSeq X platform using paired-end 2 × 101 bp reads. Sequence alignment and variant identification were performed using the Burrows-Wheeler Aligner (BWA). A control sample was included in each NGS analysis to assess the specificity and sensitivity of the sequencing experiment. The mean sequencing depth was 166.4×, and 98.2% of the analyzed gene regions achieved a minimum coverage of 20×. Identified variants were subsequently assessed using relevant population and clinical databases, including the Warsaw Genomics database, which incorporates genomic data from approximately 100,000 individuals from the Polish population, as well as ClinVar [14, 15] . Variant classification was performed according to established clinical interpretation criteria.

A detailed retrospective review of medical records was performed, including: personal and family medical history, age at onset of ocular manifestations, ophthalmic diagnoses, results of ophthalmologic examinations, including IOP measurements and pachymetry (measured using a non-contact air-puff tonometer Tomey TOP-1000), fundus examination, corneal topography and optical coherence tomography (Heidelberg Spectralis HRA + OCT SPEC-CAM) as well as field od vision test (Zeiss Humprey Field Analyzer 3). Given the potential impact of corneal thickness on measurable intraocular pressure readings, Ehlers formula was used.

$$cIOP = IOP_{measured} + [0.071 \times (545 - CCT)]$$

All patient data were anonymized. Written informed consent to participate in the study as well as publication of clinical data was obtained from all of the participants.

3. RESULTS:

A. SCLERA SIGNS

Blue sclera is the most characteristic and common ocular manifestation of osteogenesis imperfecta. It is usually bilateral, often appears in infancy or early childhood, and may be the first visible clinical sign of the disease [2, 16]. In healthy individuals, thick, irregular type I collagen fibrils are densely packed, forming the opaque and rigid outer shell of the globe. In patients with osteogenesis imperfecta, however, collagen production is reduced, resulting in scleral thinning and increased translucency. This allows the underlying dark choroid to become visible, giving the sclera a bluish-grey appearance [17]. The intensity of scleral discoloration does not correlate well with the degree of visual impairment but reflects the extent of scleral thinning. Associated ocular findings include reduced ocular rigidity and decreased globe dimensions. Consequently, the eyes of patients with osteogenesis imperfecta are more susceptible to injury, and even minor trauma can potentially lead to globe rupture. Furthermore, the management of scleral injuries in OI patients may pose several difficulties as affected tissues are considerably thinned, structurally fragile, and prone to tearing, which increases the risk of intraoperative complications, poor wound healing, and postoperative hypotony [17, 18].

B. CORNEAL SIGNS AND REFRACTING ERRORS

The cornea is responsible for the majority of the eye's refractive power and therefore plays a crucial role in achieving and maintaining good visual acuity. Of five corneal layers only

Bowman's membrane and Descemet membrane do not consist of collagen type I fibrils, although different collagen types can be found in all parts of cornea. In the corneal stroma, narrow, uniformly spaced type I fibrils lie in lamellae arranged orthogonally, giving the cornea its transparency while withstanding IOP [2, 19].

Corneal thinning is a common ocular manifestation of osteogenesis imperfecta. Studies have consistently demonstrated that mean central corneal thickness (CCT) values in patients with OI are significantly lower than those in the healthy population. This thinning is particularly pronounced in individuals exhibiting blue sclerae and those diagnosed with OI type I [16, 19–23]. Due to the compromised biomechanical integrity of the altered collagen matrix, patients with OI are at a substantially elevated risk of corneal laceration or rupture. These severe complications can be precipitated by minor trauma or may even occur spontaneously [24, 25]. Furthermore, isolated case reports have documented instances of Descemet's membrane detachment, further highlighting the profound structural vulnerability of the cornea in this patient cohort [26, 27].

Refractive abnormalities are more prevalent in patients with OI than in the general population [2, 8, 21]. Both high myopia that, may result from corneal structural alterations or axial elongation, and corneal astigmatism are frequently observed, sometimes in association with early keratoconus. In contrast, eyes with microcornea or reduced axial length that are also observed among OI patients, may present with hyperopia. A subset of patients with OI develops keratoconus, leading to progressive irregular astigmatism and high myopia, which may necessitate rigid contact lens correction or, in advanced cases, corneal cross-linking or corneal transplantation [8, 21, 22].

To properly assess corneal deformations in patients with OI the usage of corneal topography is advised [22, 28, 29],

C. INTRAOCULAR PRESSURE (IOP) AND GLAUCOMA

Collagen type I is a major structural component of the trabecular meshwork, playing a crucial role in maintaining the architecture of the aqueous outflow pathway and regulating IOP. In a healthy eye, the extracellular matrix of the trabecular meshwork provides necessary resistance to aqueous humour outflow; however, altered collagen synthesis can disrupt this structural integrity, potentially leading to increased outflow resistance. Furthermore, the optic nerve head (ONH) and the lamina cribrosa are heavily dependent on type I collagen to maintain structural support and safeguard normal axonal function. The lamina cribrosa acts as a vital biomechanical scaffold for retinal ganglion cell axons. Consequently, defects in collagen type I, as observed in osteogenesis imperfecta (OI), compromise both the aqueous outflow mechanisms and the biomechanical stability of the ONH. A structurally weakened lamina cribrosa is more susceptible to deformation, which may mechanically compress axons and disrupt axonal transport, thereby predisposing the optic nerve to glaucomatous damage [23, 29].

Reduced corneal hysteresis (CH)—a metric reflecting the cornea's ability to absorb and dissipate mechanical energy during deformation—is frequently observed in patients with OI due to these underlying collagen defects. This altered biomechanical profile is clinically significant, as reduced CH is strongly associated with a greater susceptibility of the ONH to pressure-related damage. Consequently, patients with OI face an elevated risk of developing glaucomatous optic neuropathy, even at apparently normal IOP levels [23, 28–30].

Consistent with these structural and biomechanical alterations, glaucoma represents one of the more frequently reported ocular complications of osteogenesis imperfecta. Following cataracts, it is the second most commonly diagnosed ocular disorder in this patient population, with an estimated prevalence of up to 3.8% [8]. Although the majority of cases manifest as primary open-

angle glaucoma (POAG), several reports have directly linked *COL1A1* mutations with early-onset and congenital glaucoma, indicating a strong genetic contribution to disease development [29, 31–33].

It is also important to note that the reduced central corneal thickness commonly observed in osteogenesis imperfecta has significant implications for glaucoma diagnosis and management. Thinner corneas may lead to systematic underestimation of IOP when measured using standard applanation tonometry, potentially delaying diagnosis and complicating disease monitoring [34]. Furthermore, altered corneal and scleral biomechanics may contribute to increased susceptibility of the optic nerve to pressure-related damage, thereby elevating the risk of glaucomatous optic neuropathy even at relatively low measured IOP levels [35].

Despite previously mentioned higher risk of potential complications during ophthalmic surgery in OI patients noted higher risk of complication during ophthalmic surgery, successful usage of antiglaucoma invasive treatment in this group has been describe in literature [36].

D. POSTERIOR SEGMENT

Vitreous haemorrhage

Vitreous haemorrhage has been reported more frequently in patients with osteogenesis imperfecta than in the general population. The increased risk likely reflects the underlying defect in type I collagen, which constitutes an essential structural component of retinal vessels and Bruch's membrane. Abnormal collagen architecture may weaken vascular integrity and reduce the mechanical stability of the posterior segment, consequently predisposing to spontaneous or trauma-induced haemorrhage. Vitreous bleeding in OI is often described in association with other forms of ocular haemorrhage, including retinal and subhyaloid haemorrhages, and may occur even after minor trauma due to increased ocular fragility [2, 8, 28].

Retinal detachment

Retinal detachment represents one of the most serious posterior segment complications in osteogenesis imperfecta and has been reported across multiple genetic subtypes [3, 8, 37–40]. The association is multifactorial and likely results from impaired collagen integrity affecting both retinal support structures and the vitreoretinal interface. Type I collagen abnormalities may weaken Bruch's membrane and retinal vessels, whereas reduced ocular rigidity may enhance peripheral vitreoretinal traction.

Furthermore, alterations in collagen post-translational modification may affect the vitreous matrix, potentially predisposing to pathological posterior vitreous detachment and increasing the risk of retinal tears, including giant retinal tears [39]. High myopia, which is common in OI, may further amplify this risk [18].

Surgical repair of retinal detachment in patients with OI is particularly challenging due to phenotypic scleral thinning, often clinically manifesting as blue sclera. The fragile sclera is prone to perforation during surgical manipulation or suture placement, and the risk of intraoperative haemorrhage is increased. Another factor that complicates surgery in patients with osteogenesis imperfecta and increases the rate of complications is an increased tendency for choroidal and vitreous bleeding. For this reason, careful surgical planning and, if necessary, modification of standard techniques are essential to avoid complications [38, 39].

Macular neovascularization and Choroidal neovascularization

Macular neovascularization (MNV) and choroidal neovascularization (CNV) are relatively rare findings in osteogenesis imperfecta with only handful of cases reported worldwide [41–43]. Neovascularization is primarily attributed to structural weakening of Bruch's membrane secondary to type I collagen defects. The inner and outer collagenous layers of this membrane contain type I collagen, and mutations in the *COL1A1* or *COL1A2* genes may lead to the

production of abnormal collagen or reduced collagen synthesis as well as excessive mineralization of Bruch membrane, subsequently compromising its mechanical stability. The resulting fragility predisposes Bruch's membrane to ruptures, including angioid streaks and lacquer cracks, which may develop spontaneously or in association with axial elongation and high myopia due to reduced scleral rigidity. These structural discontinuities create a pathway for choroidal vessels to invade the subretinal space, leading to exudation and subretinal haemorrhage. [18, 40–43].

E. OTHER FINDING

Cataract is among the most frequently reported ocular condition in patients with osteogenesis imperfecta and appears to occur more often than in the general population [8, 28]. Several reports have described early-onset or presenile cataracts in affected individuals, in some cases requiring surgical intervention during childhood or early adulthood [32]. Zonular cataracts have been specifically associated with osteogenesis imperfecta, possibly reflecting underlying abnormalities in collagen structure and lens support [30]. Given that type I collagen contributes to the structural integrity of the lens capsule and zonular apparatus, defects in collagen synthesis may compromise lens stability and transparency, thereby facilitating earlier cataract formation. Importantly, cataracts in OI patients often coexist with other potentially vision-threatening conditions, including high myopia and juvenile open-angle glaucoma [32]. Nevertheless, the increased detection rate should be interpreted with caution, as individuals with osteogenesis imperfecta are more likely to undergo regular ophthalmologic follow-up due to other ocular manifestations, which may contribute to earlier or more frequent diagnosis [8].

In addition to the well-documented ocular manifestations of OI, rare cases of osteogenesis imperfecta coexisting with bilateral retinoblastoma have also been reported in the literature.

This association may be linked to chromosome 17, which hosts both the COL1A1 gene and the SERPINF1 gene, the latter of which is responsible for type VI OI and encodes the pigment epithelium-derived factor (PEDF), which plays a significant role in the neuronal differentiation of retinoblastoma cells [44].

4. CASE PRESENTATION

Members of a single family with clinically diagnosed osteogenesis imperfecta and associated ocular manifestations were included (Figure 2.).

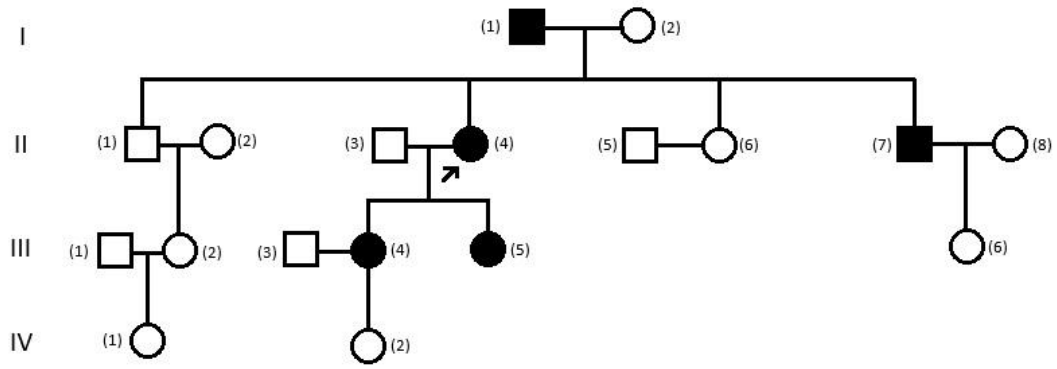


Figure 2. Patient's pedigree; Legend: (II, 4) the proband, our patient, (III, 4) (III, 5) affected daughters, (II, 6) affected patient's brother (we have only information from interview), (I, 1) patient's father (information from interview).

Case I: II, 4 (the proband)

A 68-year-old female patient was admitted to the Department of Ophthalmology, Medical University of Bialystok, Poland, in March 2026. The patient's history includes frequent limb fractures and hearing loss (otosclerosis). The patient has a history of otosclerosis and underwent right ear stapedotomy in 1999 and left ear stapedotomy in 2001. Figure 3 presents the preoperative audiogram, while Figure 4 presents the patient's current audiogram.

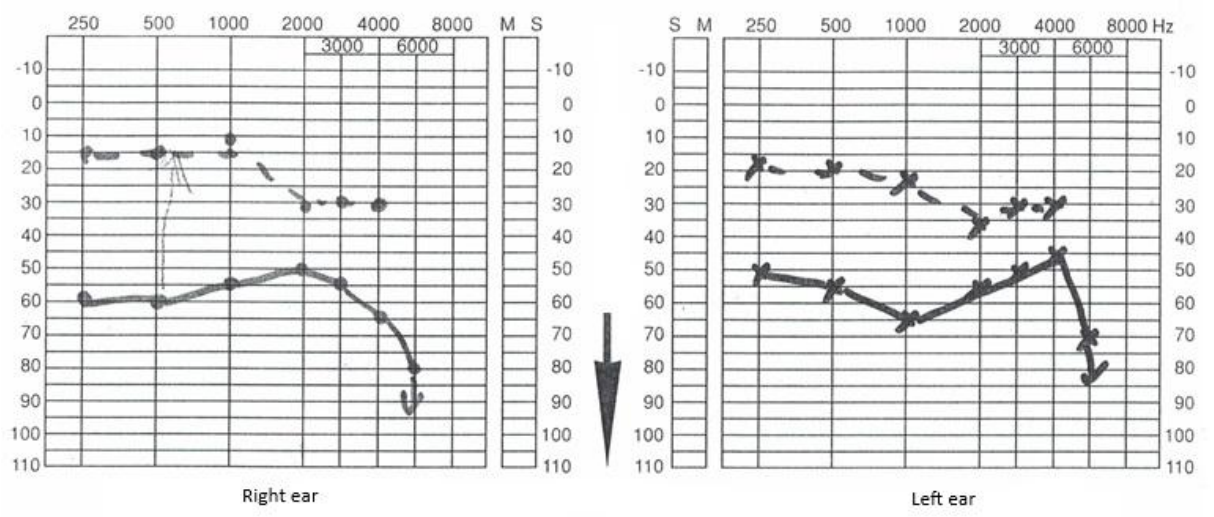


Figure 3. Patient's preoperative audiogram from 1999.

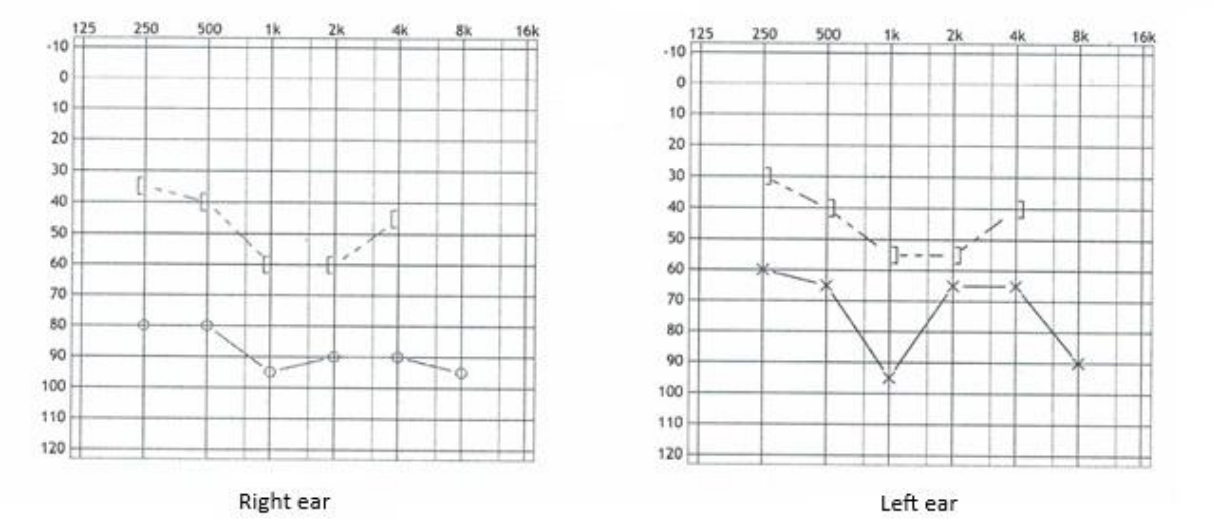


Figure 4. Patient's current audiogram from 2024.

The ophthalmological examination revealed the following findings:

Visual Acuity and Refraction

Uncorrected distance visual acuity (UDVA) was 0.1 in the right eye (OD) and 0.2 in the left eye (OS). Best-corrected visual acuity (BCVA) improved to 0.9 OD with a myopic astigmatic correction of -3.75 DS / -2.00 DC x 168°, and 1.0 OS with a correction of -2.25 DS / -1.00 DC x 178°.

Intraocular Pressure and Pachymetry

Measured IOP was 24.1 mmHg in the right eye (OD) and 22.9 mmHg in the left eye (OS). Central corneal thickness was 457 µm and 447 µm, respectively. Because corneal thickness and biomechanics may affect topometric readings, these measurements were interpreted together with the optic nerve examination, retinal nerve fiber layer OCT, and visual field results. The tonometry method and instrument are specified in the Methods section. Adjusting for the reduced CCT, the corrected IOP (cIOP) was significantly higher, reaching 30.348 mmHg OD and 28.58 mmHg OS.

Anterior Segment Examination

Slit-lamp biomicroscopy of the anterior segment was generally unremarkable, with the exception of the blue sclera, bilateral corneal thinning and the presence of early corticonuclear lens opacities (cataracts) in both eyes. Specular microscopy revealed a corneal endothelial cell density of 2166 cells/mm² OD and 2113 cells/mm² OS.

Posterior Segment and Ancillary Testing

Dilated fundus examination showed a normal posterior pole with a cup-to-disc (C/D) ratio of 0.4 OD and 0.5 OS. OCT of the macula and the optic nerve head (ONH) demonstrated no

structural abnormalities in either eye with a global thickness (G) of 94 µm OD and 91 µm OS (Figure 5.). Conducted computerized visual field testing and corneal topography were within normal limits for both eyes (Figure 6.). Further diagnostic imaging and functional testing yielded normal results; standard automated perimetry (visual fields) was within normal limits bilaterally (Figure 7.).

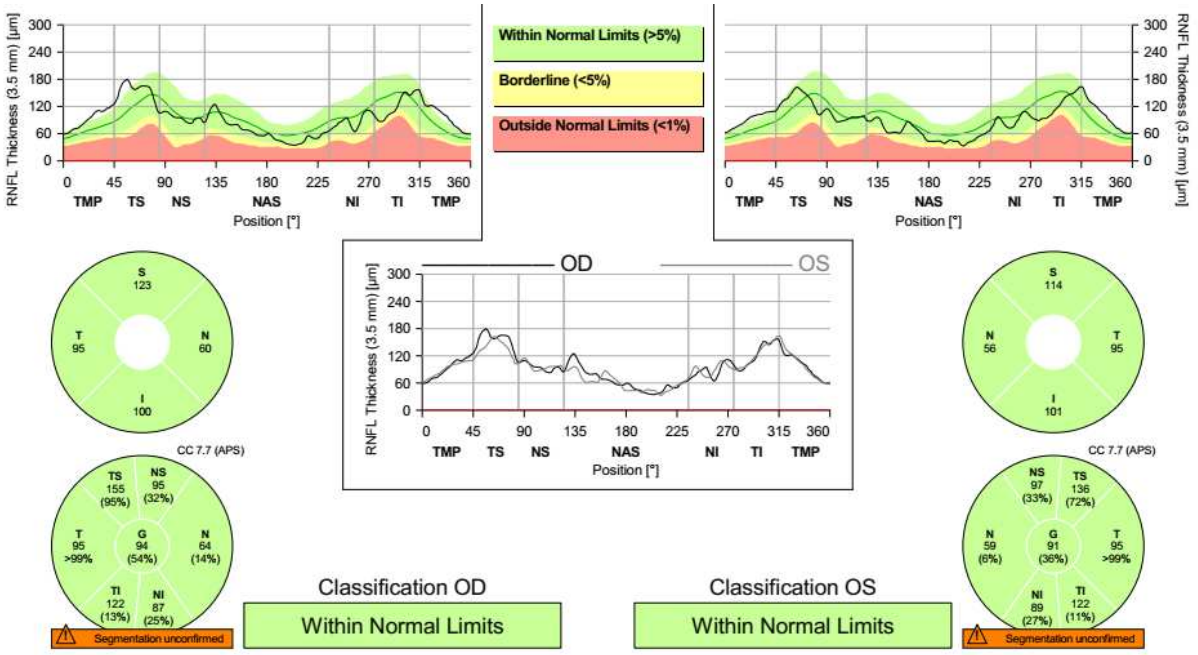
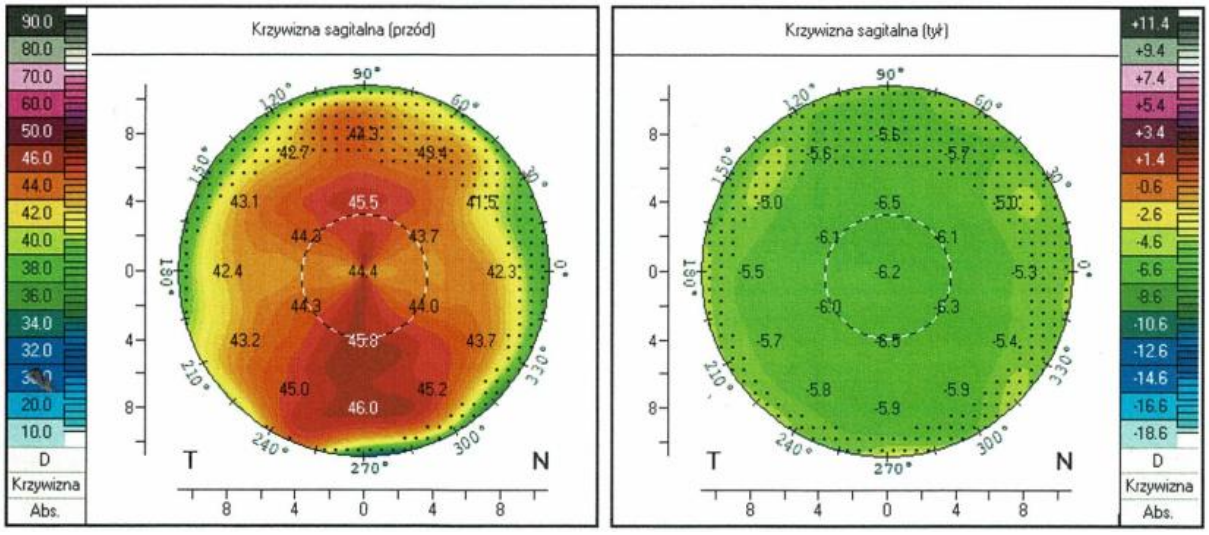


Figure 5. RNFL thickness – the Proband.



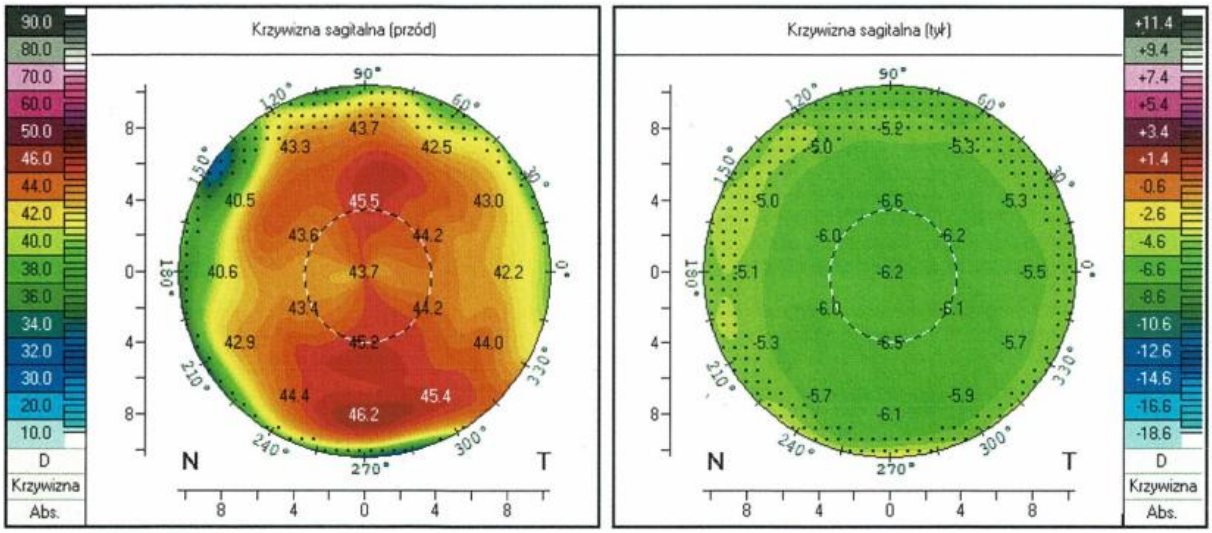


Figure 6. Corneal topography – the Proband. Right eye (top) and left eye (bottom).

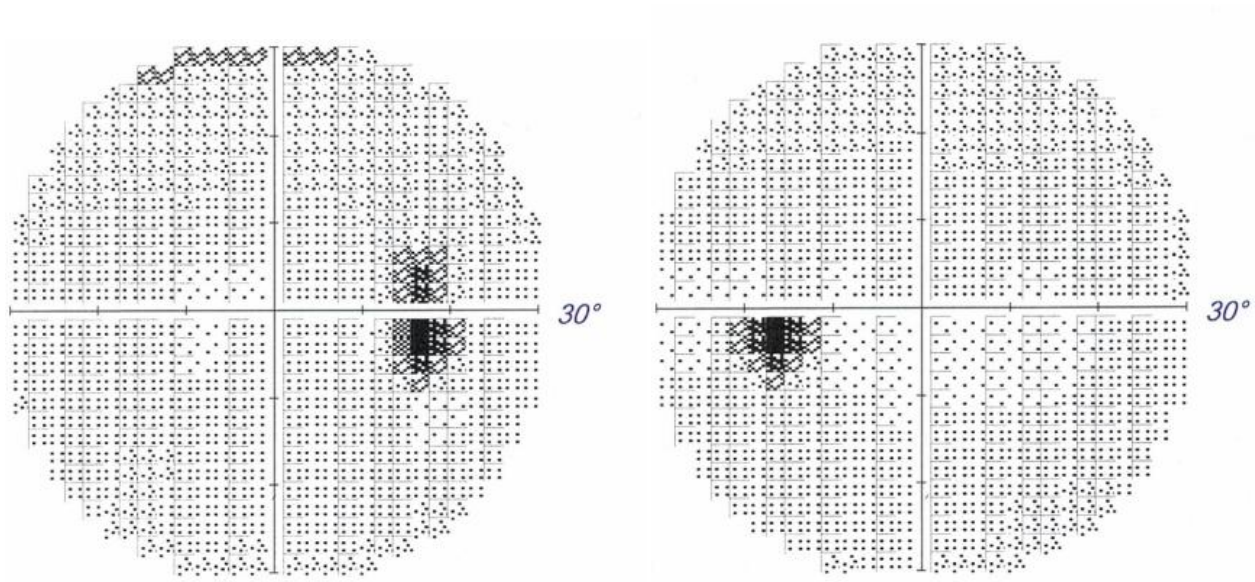


Figure 7. Visual field testing – the Proband. Right eye (left) and left eye (right).

On the follow-up visit, 6 month later best-corrected visual acuity remained unchanged. There was no progression in OCT scans and standard automated perimetry (visual fields) was within normal limits bilaterally (Figure 8., Figure 9. And Figure 10.). The measured IOP was near the

upper limit of the norm with 20,8 mmHg OD and 20,6 mmHg OS, central corneal thickness (CCT) measured 449 µm OD and 453 µm OS, while the corrected IOP (cIOP) reached 27,616 mmHg OD and 27,132 mmHg OS.

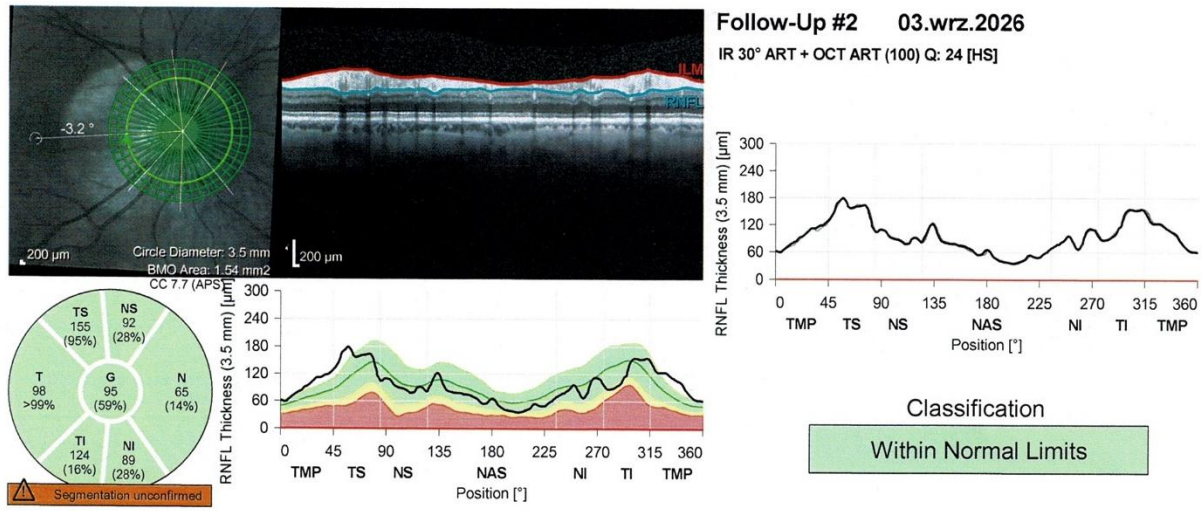


Figure 8. The follow-up RNFL thickness – the Proband – right eye.

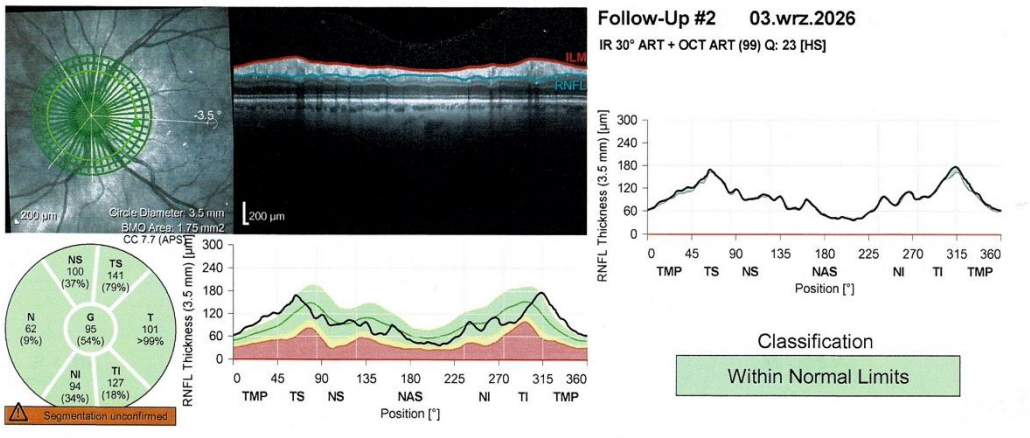


Figure 9. The follow-up RNFL thickness – the Proband – left eye.

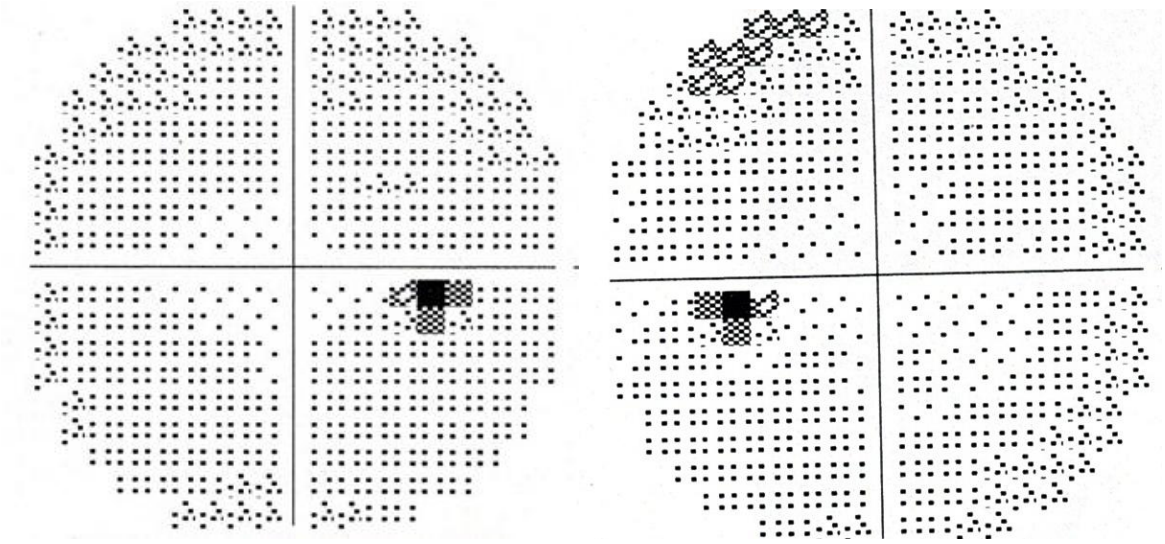


Figure 10. Follow-up visual field testing – the Proband. Right eye (left) and left eye (right).

Given the family history of osteogenesis imperfecta in the patient's family, the woman's daughters were invited for an ophthalmological examination.

Case II: III, 4 (the proband's first daughter)

A 42- year-old female diagnosed with osteogenesis imperfecta in 1999 on the basis of a history of hearing loss and multiple limb fractures. Blue sclera were observed, as in her mother. She underwent two stapedotomies, the first in 2013 and the second in 2014. Figure 11 presents the preoperative audiogram, while Figure 12 presents the patient's current audiogram.

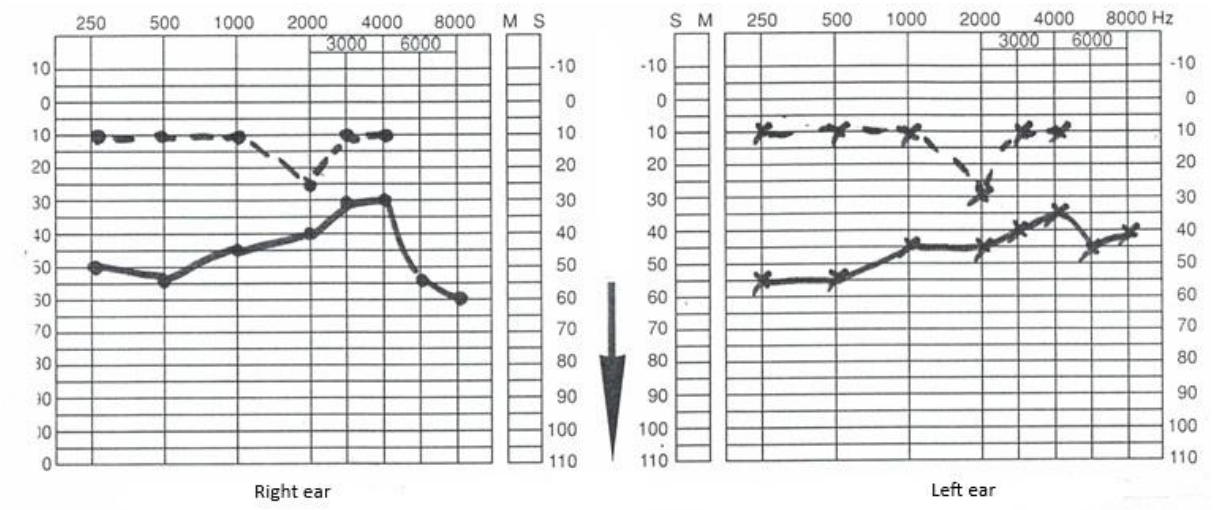


Figure 11. Patient's preoperative audiogram from 1999.

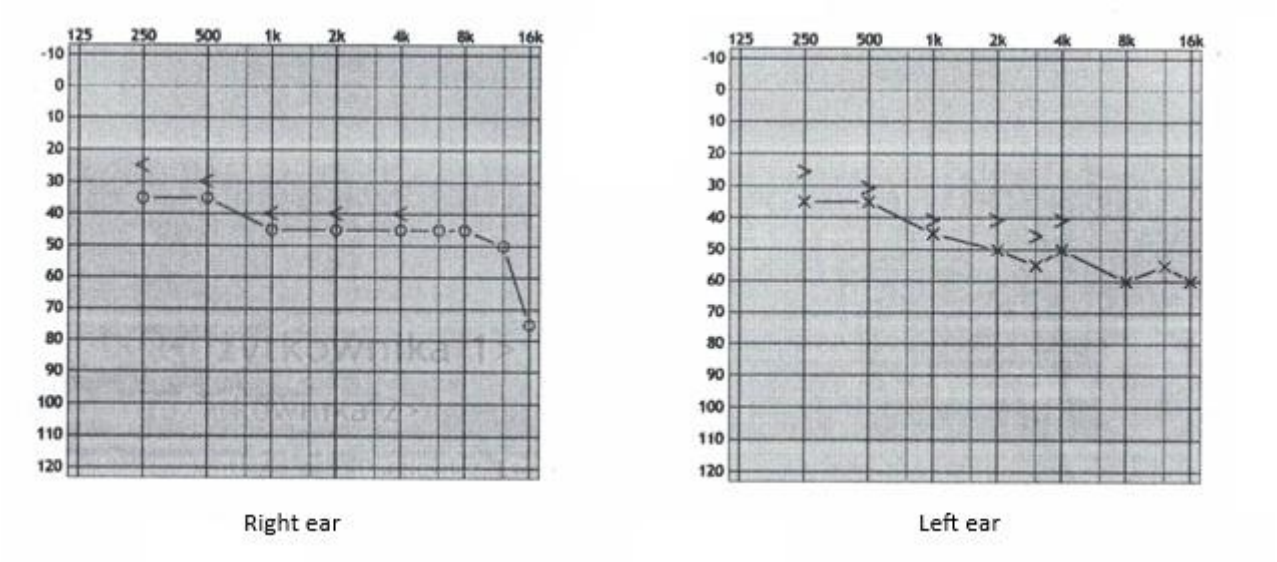


Figure 12. Patient's current audiogram from 2021.

An eye examination conducted in March 2026 revealed the following changes:

Visual Acuity and Refraction

Uncorrected visual acuity was 0.08 in the right eye (OD) and 0.1 in the left eye (OS). Best-corrected visual acuity (BCVA) was 1.0 (20/20) in both eyes, achieved with a myopic correction of -3.50 Dsph OD and a sphero-cylindrical correction of -3.00 Dsph / -0.50 Dcyl x 180 OS.

Slit-Lamp Examination and Pachymetry Anterior segment examination was notable for a pronounced blue-tinted sclera bilaterally, a classic ophthalmic manifestation of the patient's underlying type I collagen deficiency. Ultrasonic pachymetry revealed significant bilateral corneal thinning, with a central corneal thickness (CCT) of 463 µm OD and 465 µm OS.

Tonometry Measured IOP demonstrated marked asymmetry, recording at 21.6 mmHg OD and 8.9 mmHg OS.

The relatively thin corneas complicate interpretation of the measured IOP. Pachymetry-adjusted intraocular pressure (C.IOP) reached 27.422 OD and 14.58 mmHg OS.No glaucomatous structural or functional damage was identified at this examination.

Posterior Segment and Ancillary Testing Despite the elevated corrected IOP in the right eye, structural and functional evaluations showed no evidence of glaucomatous damage at the time of examination. OCT demonstrated that the retinal nerve fiber layer (RNFL) was within normal limits bilaterally, with a global thickness (G) of 99 µm OD and 104 µm OS (Figure 13.). Furthermore, computerized visual field testing and corneal topography were unremarkable and within normal limits for both eyes (Figure 14., Figure 15.).

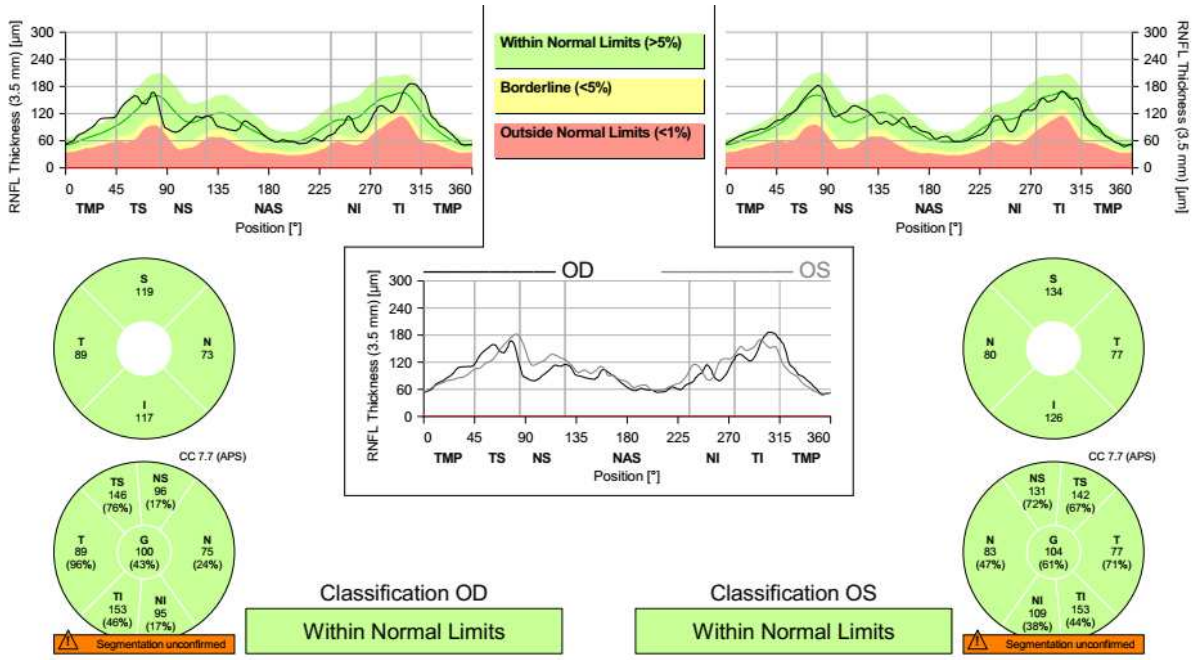
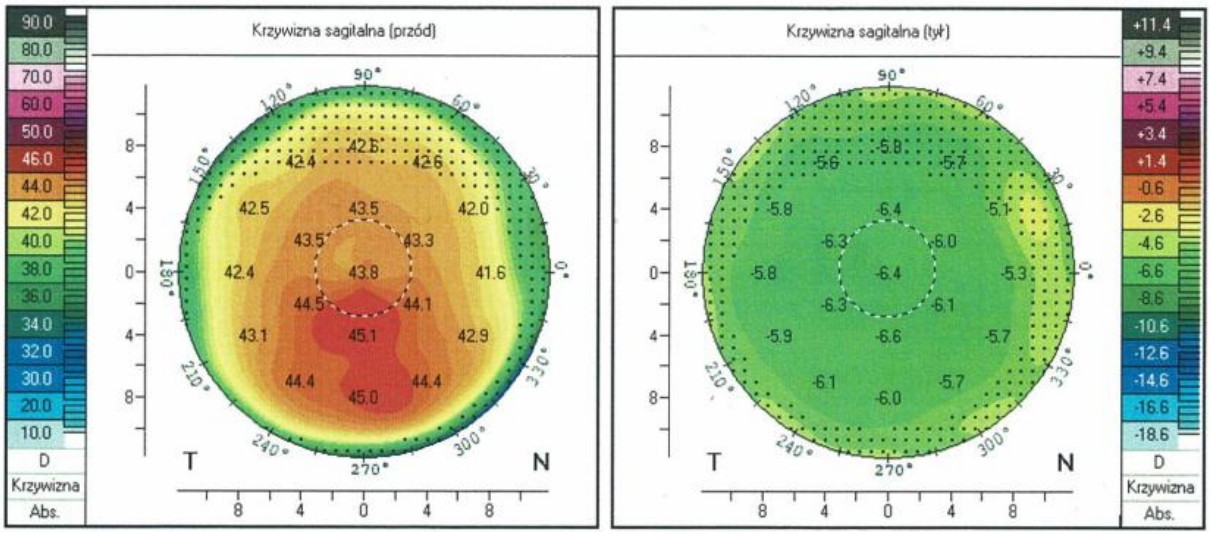


Figure 13. RNFL thickness – the First Daughter.



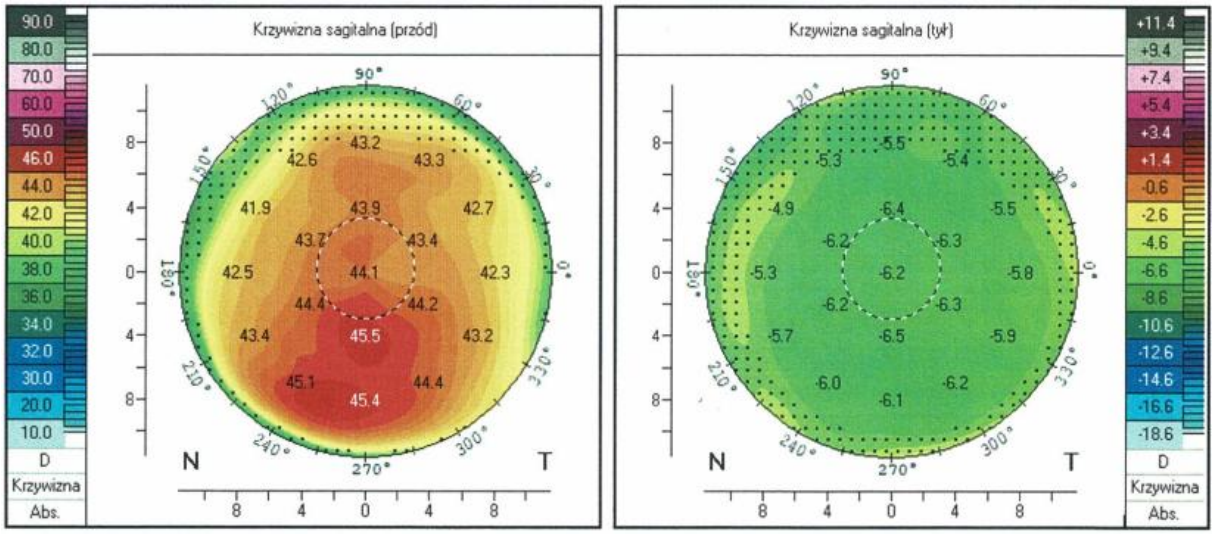


Figure 14. Corneal topography – the First Daughter. Right eye (top) and left eye (bottom).

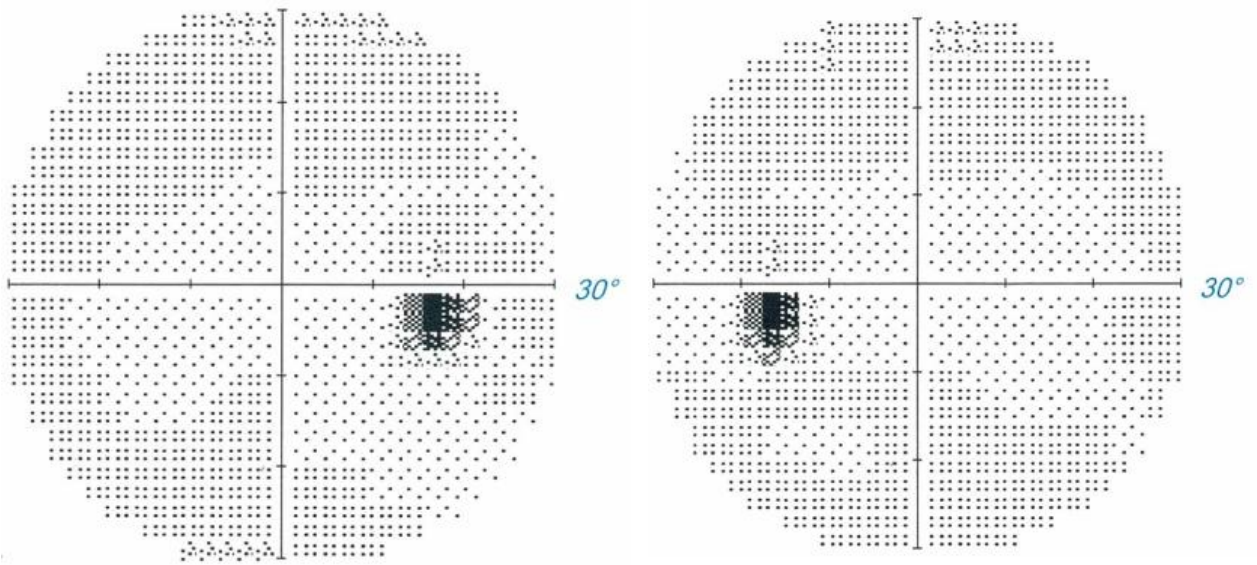


Figure 15. Visual field testing – the First Daughter. Right eye (left) and left eye (right).

A follow-up appointment after 6 months showed no changes in best-corrected visual acuity and similar IOP readings in the right eye (IOP = 21.9 mmHg, CCT = 445 um, cIOP = 29.0 mmHg), whilst the IOP in the left eye was higher than at the previous appointment, though still within the normal range (IOP = 18.0 mmHg, CCT = 458 um, cIOP = 24.177 mmHg). No progression

was observed on OCT and standard automated perimetry (Visual Fields) (Figure 16. and Figure 17.).

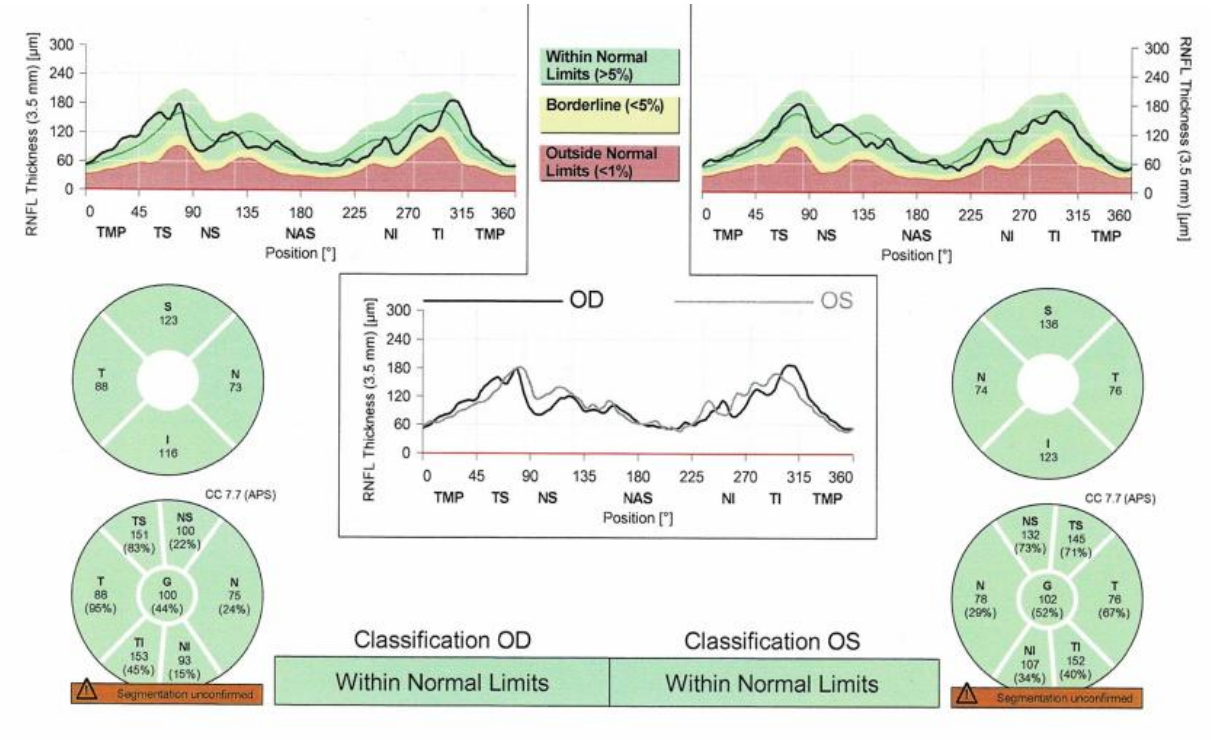


Figure 16. RNFL thickness on follow-up visit – the First Daughter.

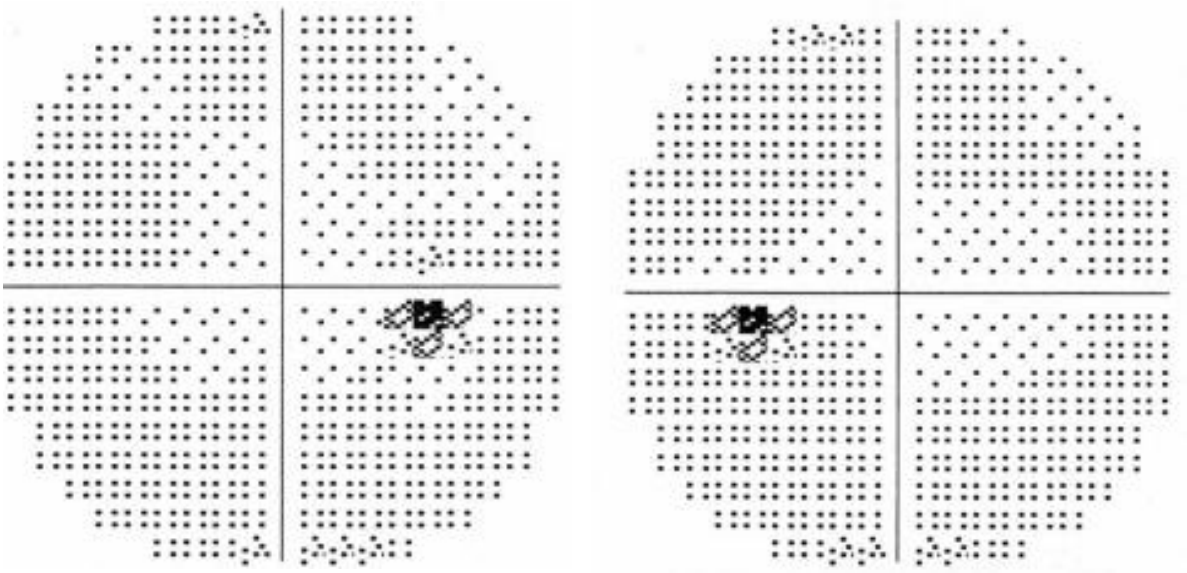


Figure 17. Visual field testing on follow-up visit – the First Daughter. Right eye (left) and left eye (right).

Case III: III, 5 (the proband's second daughter)

A 37-year-old female with congenital hearing loss, diagnosed at approximately 3 years of age. Her medical history is notable for multiple fractures and similarly to her mother and sister, blue sclera. The patient has never undergone surgery for otosclerosis. Figure 18 presents one of the earliest audiograms, while Figure 19 presents the patient's current audiogram.

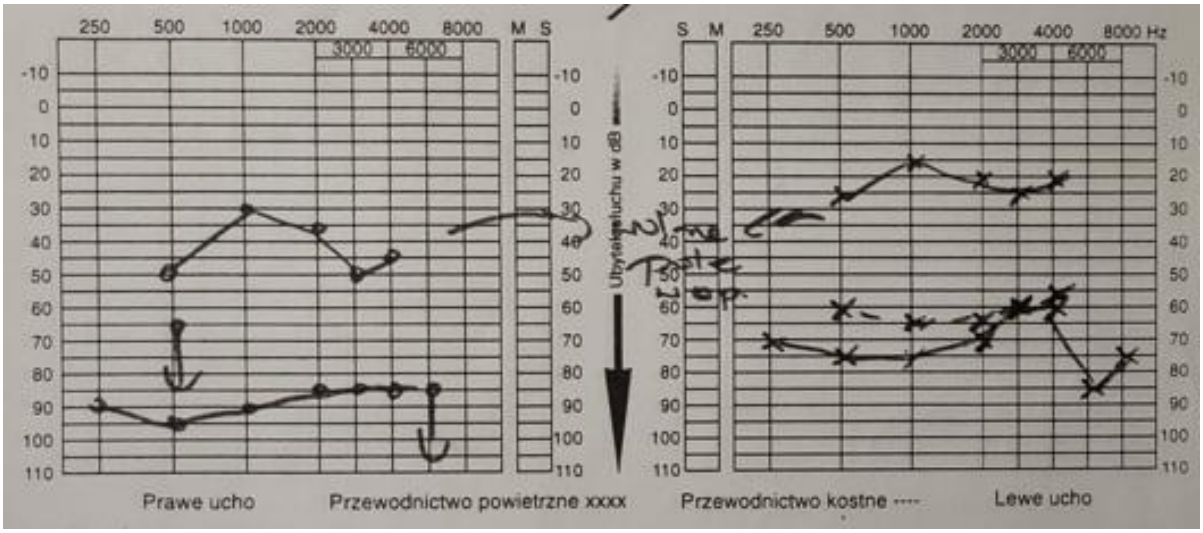


Figure 18. Patient's audiogram from 2001.

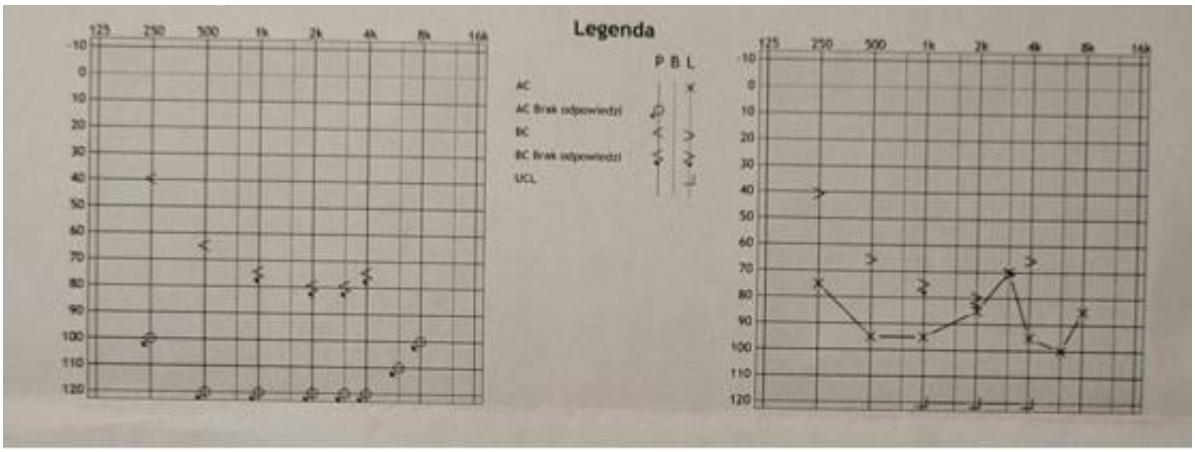


Figure 19. Patient’s current audiogram from 2025.

The patient reported to the Ophthalmology Clinic in April 2026 for an eye examination.

Visual Acuity and Refraction

Uncorrected visual acuity (UCVA) was excellent, measuring 1.0 (20/20) in both the right (OD) and left (OS) eyes, requiring no refractive correction.

Slit-Lamp Examination and Pachymetry

Consistent with the systemic diagnosis of a type I collagen synthesis defect, anterior segment evaluation revealed a prominent blue-tinted sclera bilaterally. Ultrasonic pachymetry demonstrated severe bilateral corneal thinning, with a central corneal thickness (CCT) measuring 451 µm OD and 455 µm OS.

Tonometry

Standard tonometry yielded IOP readings within the statistically normal range: 18.1 mmHg OD and 16.6 mmHg OS. However, upon adjusting these values for the patient's significantly thin

corneas, pachymetry-corrected C.IOP revealed bilateral elevated IOP. The corrected values were calculated at 24.774 mmHg OD and 22.99 mmHg OS.

Posterior Segment and Ancillary Testing

Dilated fundus examination of the right eye showed a healthy optic nerve with a cup-to-disc (C/D) ratio of 0.3, characterized by a dense vascular network on the optic disc. Despite the bilateral elevation in corrected IOP, structural and functional testing showed no indications of glaucomatous neuropathy. OCT confirmed that the retinal nerve fiber layer (RNFL) thickness was well within normal limits bilaterally, with global (G) thickness values of 110 µm OD and 106 µm OS (Figure 20.). Furthermore, visual field testing and corneal topography were completely normal for both eyes (Figure 21, Figure 22.).

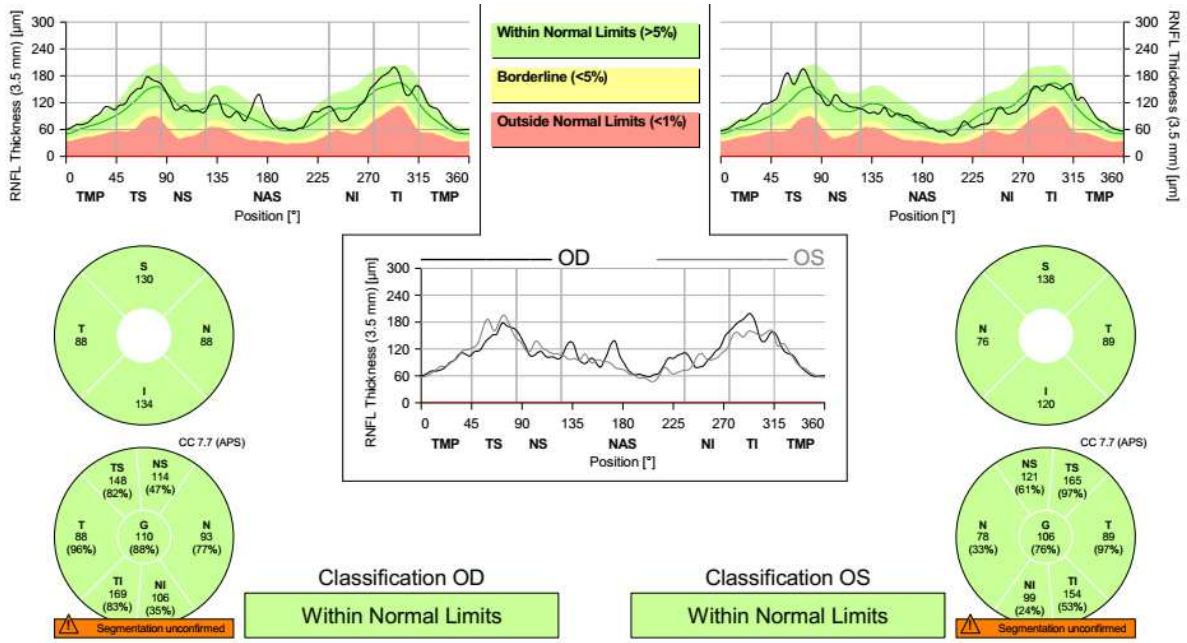


Figure 20. RNFL thickness – the Second Daughter.

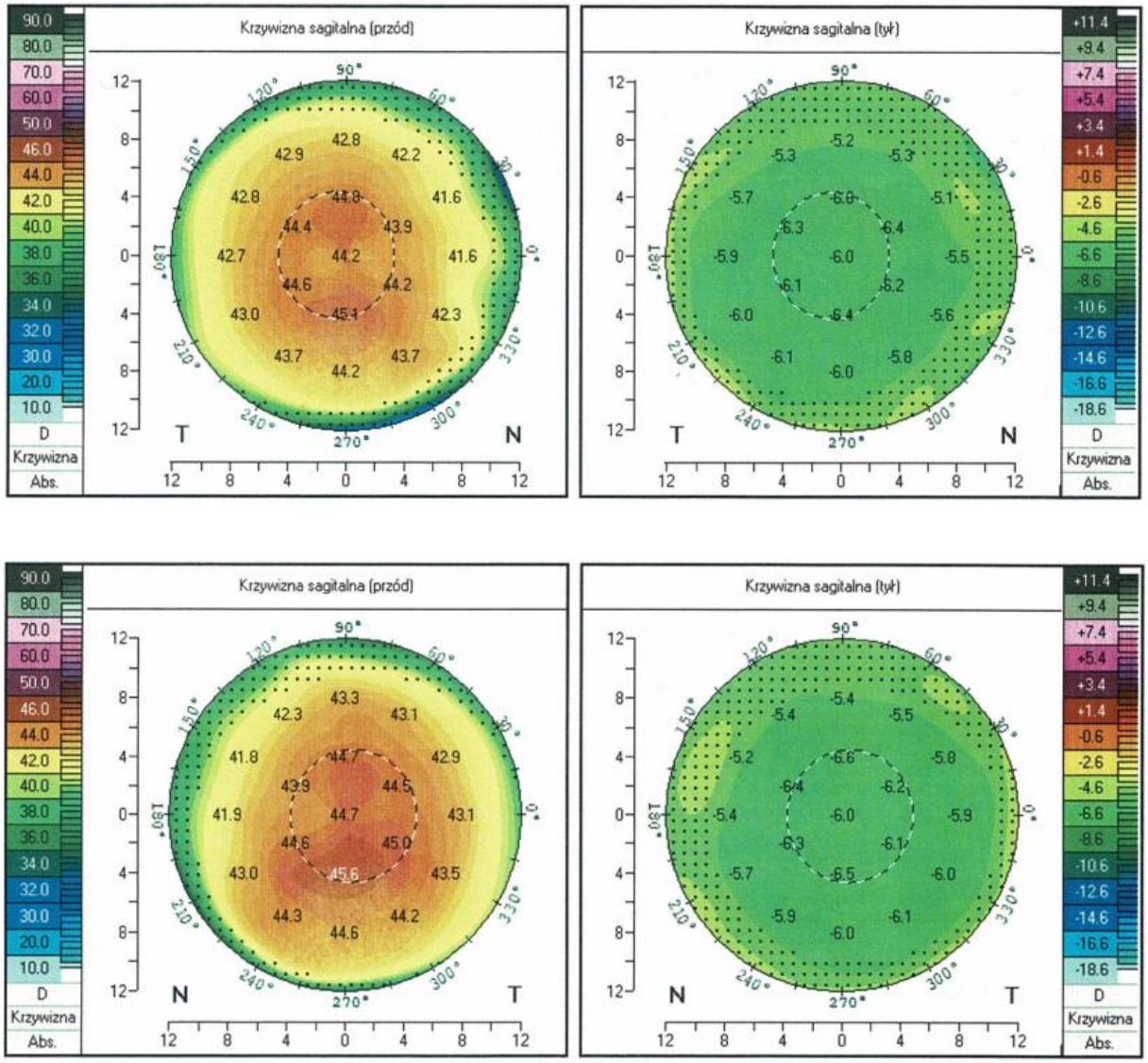


Figure 21. Corneal topography – the Second Daughter. Right eye (top) and left eye (bottom).

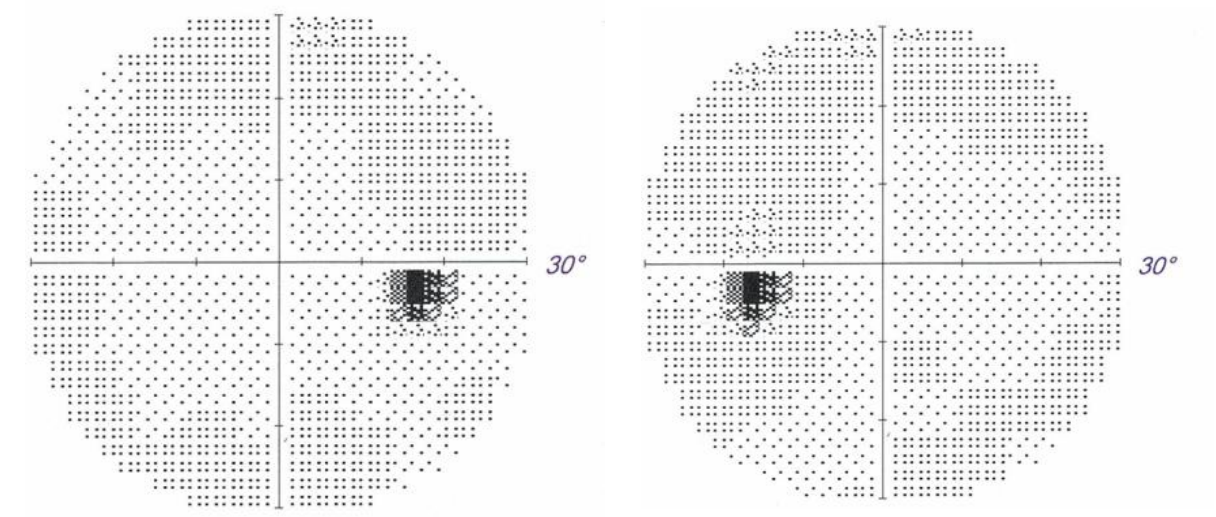


Figure 22. Visual field testing – the Second Daughter. Right eye (left) and left eye (right).

Table 3. Collected measurements of IOP, CCT and cIOP of all included patients.

	The Proband		First Daughter		Second Daughter	
Eye	Right	Left	Right	Left	Right	Left
IOP [mmHg]	24.1	22.9	21.6	8.9	18.1	16.6
CCT [µm]	457	447	463	465	451	455
C.IOP [mmHg]	30.348	28.58	27.422	14.58	24.774	22.99
IOP [mmHg] - II visit	20.8	20.6	21.9	18.0	-	-
CCT [µm] - II visit	449	453	445	458	-	-
C.IOP [mmHg]- II visit	27.616	27.132	29.0	24.177	-	-

CCT – central cornea thickness, IOP – intraocular pressure, C.IOP – corrected intraocular pressure calculated using Ehlers formula

GENETIC TESTING

Given the characteristic skeletal and ocular phenotype and the familial occurrence of osteogenesis imperfecta, genetic testing was initiated in the first daughter of the proband. A pathogenic variant in the *COL1A1* gene *COL1A1* c.1127delC (p.Pro376fs) was identified. Following this finding, targeted genetic testing was subsequently performed in the proband and her second daughter, confirming the presence of the same pathogenic variant in both individuals.

The identification of the same pathogenic variant in three affected family members confirmed the molecular basis of the familial phenotype and was consistent with autosomal dominant inheritance.

5. DISCUSSION

Osteogenesis imperfecta (OI) is a systemic connective tissue disorder characterized by abnormalities in type I collagen that affect multiple organ systems, including the eye. Given that collagen is a fundamental component of most eye tissues, abnormalities in its synthesis, structure, or post-translational processing can lead to a wide range of ophthalmic symptoms. The present study combines a systematic review of the recent literature with a series of case reports involving members of a single family affected by osteogenesis imperfecta.

The results of our observations support previous reports that this disease affects various parts of the eye and its functions. Each of our patients demonstrated characteristic systemic manifestations of osteogenesis imperfecta, including recurrent fractures, hearing impairment, and blue sclera. Ophthalmologic examination revealed corneal thinning and myopic refractive errors, both commonly reported ocular features of the disease. In the proband, significantly elevated corrected IOP values were identified after adjustment for reduced central corneal thickness, highlighting the diagnostic challenge posed by altered corneal biomechanics in OI patients.

The identified variant affects the *COL1A1* gene, which encodes the pro-alpha1 chain of type I collagen, the most abundant fibrillar collagen in the human body and a major structural

component of bone, tendon, skin, cornea, and blood vessels. Heterozygous pathogenic variants in *COL1A1* are a well-established cause of autosomal dominant osteogenesis imperfecta. In the present family, the identified c.1127delC (p.Pro376fs) variant is predicted to result in haploinsufficiency through premature termination of translation and nonsense-mediated mRNA decay. The molecular finding was consistent with the clinical phenotype and familial occurrence of the disease.

From a clinical perspective, early recognition of ocular manifestations in osteogenesis imperfecta is essential. Routine ophthalmic screening should include measurement of central corneal thickness, corneal topography when indicated, careful assessment of IOP with consideration of corneal biomechanics, and periodic examination of the posterior segment. Early detection of glaucoma, retinal complications, or corneal pathology may allow timely intervention and prevent irreversible visual impairment. Importantly, some ophthalmic abnormalities may remain asymptomatic for long periods, emphasizing the importance of routine eye exam in affected individuals.

In the proband, elevated measured IOP coexisted with thin corneas, while OCT and visual field testing did not show glaucomatous damage during the reported follow-up. This finding supports careful longitudinal assessment but does not establish glaucoma or quantify the degree to which standard tonometry underestimated IOP.

Several limitations of the present study should be acknowledged. First, the literature review included studies of heterogeneous design, many of which were case reports or small case series, limiting the strength of available evidence. Second, the series of cases from this family involved a limited number of patients, which reduces the significance of the results when viewed in the context of the broader population. Genetic confirmation was available for all three examined family members; however, the findings from a single family cannot establish the frequency of ocular manifestations or genotype–phenotype associations in osteogenesis imperfecta.

Despite these limitations, this study provides a comprehensive overview of ocular manifestations associated with osteogenesis imperfecta and highlights the importance of interdisciplinary care involving both genetic and ophthalmologic evaluation. Further prospective studies with larger cohorts and genetic characterization are needed to better define the prevalence, pathophysiology, and optimal management of ocular complications in this rare connective tissue disorder.

6. CONCLUSION

Osteogenesis imperfecta is associated with a broad spectrum of ocular manifestations, including an increased risk of glaucoma related to structural and biomechanical abnormalities of the eye. Reduced corneal thickness, decreased corneal hysteresis, and altered collagen architecture may contribute to both underestimation of IOP and increased susceptibility of the optic nerve to damage. Therefore, patients with osteogenesis imperfecta should undergo regular ophthalmologic evaluation, including careful assessment for glaucoma, even in the presence of normal IOP measurements. As glaucoma may remain asymptomatic until substantial optic nerve damage has occurred, regular functional assessment, including visual field testing, together with structural evaluation of the optic nerve, should be considered even in the absence of subjective visual symptoms. Early detection and appropriate monitoring may help prevent irreversible visual impairment in this population.

7. ABBREVATION LIST

Abbreviation	Full term
BWA	Burrows-Wheeler Aligner
BCVA	Best-corrected visual acuity
CCT	Central corneal thickness
CH	Corneal hysteresis
cIOP	Corrected intraocular pressure
CNV	Choroidal neovascularization
CRF	Corneal resistance factor
DNA	Deoxyribonucleic acid
IOP	Intraocular pressure
JBI	Joanna Briggs Institute
MNV	Macular neovascularization
NGS	Next-generation sequencing
NIPT	Non-invasive prenatal testing
OCT	Optical coherence tomography
OD	Right eye (*oculus dexter*)
OI	Osteogenesis imperfecta
OMIM	Online Mendelian Inheritance in Man

Abbreviation	Full term
ONH	Optic nerve head
OS	Left eye (*oculus sinister*)
PEDF	Pigment epithelium-derived factor
POAG	Primary open-angle glaucoma
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RNFL	Retinal nerve fiber layer
UCVA	Uncorrected visual acuity
UDVA	Uncorrected distance visual acuity

8. DECLARATIONS

Ethics approval and consent to participate

Not applicable. According to Polish legislation specified in "Ustawa z dnia 5 grudnia 1996 r. o zawodach lekarza i lekarza dentysty", ethics committee approval was not required for this study. Written informed consent to participate in the study was obtained from all the participants.

Consent for publication

All patient data were anonymized. Written informed consent for publication of clinical data was obtained from all the participants. The participant has consented to the submission of the case report to the journal.

Data availability

All materials and information are available upon an e-mail request on corresponding author.

The datasets analysed during the current study are available in the dbSNP and ClinVar repository (www.ncbi.nlm.nih.gov/clinvar/variation/859292/) and https://www.ncbi.nlm.nih.gov/snp/rs72645369). Additional clinical data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to applicable ethical and data protection restrictions.

Competing interests

The authors declare that they have no competing interests

Financial Disclosure

No author has a financial or proprietary interest in any material or method mentioned.

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Authors contributions

AKE worked on the main text. ED, AZ worked on figures and tables. JK reviewed whole article. All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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9. REFERENCE

1. Deguchi M, Tsuji S, Katsura D, Kasahara K, Kimura F, Murakami T (2021) Current Overview of Osteogenesis Imperfecta. Medicina 2021, Vol 57, Page 464 57:464
2. Treurniet S, Burger P, Ghyczy EAE, et al Ocular characteristics and complications in patients with osteogenesis imperfecta: a systematic review. https://doi.org/10.1111/aos.14882
3. Travessa AM, Romeu JC, Mirco T, et al (2025) CRTAP-Related Osteogenesis Imperfecta: Clinical Variability and a Potential Founder Variant in CRTAP. Mol Syndromol 1–8
4. Forlino A, Marini JC, Branch EM, Shriver EK (2015) Osteogenesis imperfecta. Lancet 387:1657
5. Subramanian S, Anastasopoulou C, Viswanathan VK (2023) Osteogenesis Imperfecta. StatPearls
6. Deguchi M, Tsuji S, Katsura D, Kasahara K, Kimura F, Murakami T (2021) Current Overview of Osteogenesis Imperfecta. Medicina (B Aires) 57:464
7. Jovanovic M, Guterman-Ram G, Marini JC (2021) Osteogenesis Imperfecta: Mechanisms and Signaling Pathways Connecting Classical and Rare OI Types. Endocr Rev 43:61
8. Lyster ML, Hald JD, Rasmussen ML, Grauslund J, Folkestad L (2022) Risk of eye diseases in osteogenesis imperfecta – A nationwide, register-based cohort study. Bone 154:116249
9. Marlowe A, Pepin MG, Byers PH (2002) Testing for osteogenesis imperfecta in cases of suspected non-accidental injury. J Med Genet 39:382–386
10. Körkkö J, Ala-Kokko L, De Paepe A, Nuytinck L, Earley J, Prockop DJ (1998) Analysis of the COL1A1 and COL1A2 genes by PCR amplification and scanning by conformation-sensitive gel electrophoresis identifies only COL1A1 mutations in 15 patients with osteogenesis imperfecta type I: identification of common sequences of null-allele mutations. Am J Hum Genet 62:98–110

11. Aliyeva L, Ongen YD, Eren E, Sarisozen MB, Alemdar A, Temel SG, Sag SO (2024) Genotype and Phenotype Correlation of Patients with Osteogenesis Imperfecta. J Mol Diagn 26:754–769

12. Tauer JT, Robinson ME, Rauch F (2019) Osteogenesis Imperfecta: New Perspectives From Clinical and Translational Research. JBMR Plus. https://doi.org/10.1002/JBM4.10174

13. Byers PH, Krakow D, Nunes ME, Pepin M (2006) Genetic evaluation of suspected osteogenesis imperfecta (OI). Genet Med 8:383–388

14. https://www.ncbi.nlm.nih.gov/snp/rs72645369

15. https://www.ncbi.nlm.nih.gov/clinvar/variation/859292/

16. Hald JD, Folkestad L, Swan CZ, et al (2018) Osteogenesis imperfecta and the teeth, eyes, and ears-a study of non-skeletal phenotypes in adults. Osteoporos Int 29:2781–2789

17. Verdonk SJE, Willemse J, Zoutenbier VS, et al (2024) Polarization-sensitive optical coherence tomography and scleral collagen fiber orientation in osteogenesis imperfecta. Exp Eye Res 247:110048

18. Jen M, Nallasamy S (2016) Ocular manifestations of genetic skin disorders. Clin Dermatol 34:242–275

19. Magalhaes OA, Rohenkohl HC, De Souza LT, Schuler-Faccini L, Félix TM (2018) Collagen I Defect Corneal Profiles in Osteogenesis Imperfecta. Cornea 37:1561–1565

20. Swierkowska J, Gajecka M (2017) Genetic factors influencing the reduction of central corneal thickness in disorders affecting the eye. Ophthalmic Genet 38:501–510

21. Keleş A, Doğuizi S, Şahin NM, Koç M, Aycan Z (2020) Anterior Segment Findings in Patients With Osteogenesis Imperfecta: A Case-Control Study. Cornea 39:935–939

22. Correia Barão R, Santos M, Marques RE, Quintas AM, Guerra P (2023) Keratoconus tomographic indices in osteogenesis imperfecta. Clin Exp Ophthalmol 261:2585–2592

23. Lagrou LM, Gilbert J, Hannibal M, Caird MS, Thomas I, Moroi SE, Bohnsack BL (2018) Altered corneal biomechanical properties in children with osteogenesis imperfecta. J AAPOS 22:183-187.e1

24. Campagna G, Al-Mohtaseb Z, Khandelwal S, Chang E (2018) Sequential traumatic corneal open globe rupture in a patient with osteogenesis imperfecta type I. Am J Ophthalmol Case Rep 11:35

25. Oh EK, Choi HJ, Oh JY, Kim MK, Wee WR (2016) Sequential traumatic and spontaneous corneal rupture in patient with osteogenesis imperfecta. Canadian Journal of Ophthalmology 51:e81–e84

26. Eberly HW, Rosen DB, Pantanelli SM (2024) Spontaneous Corneal Clearing after Descemet Membrane Rupture and Near-Total Detachment in Keratoglobus: A Case Report. Case Rep Ophthalmol 15:189

27. Polat N, Ulucan PB (2015) Nontraumatic Descemet Membrane Detachment with Tear in Osteogenesis Imperfecta. Ophthalmol Ther 4:59

28. Moussa S, Rocci J, Hamdy R, Grauslund J, Lyster ML, Tsimicalis A (2024) Ophthalmological screening guidelines for individuals with Osteogenesis Imperfecta: a scoping review. Orphanet J Rare Dis 19:316

29. Doolan E, O'Brien C (2021) Abnormal corneal properties in osteogenesis imperfecta and glaucoma: a case series. BMJ Open Ophthalmol 6:e000684

30. Moshirfar M, Barke MR, Huynh R, Waite AJ, Ply B, Ronquillo YC, Hoopes PC (2021) Controversy and Consideration of Refractive Surgery in Patients with Heritable Disorders of Connective Tissue. J Clin Med 10:3769

31. Wallace DJ, Chau FY, Santiago-Turla C, Hauser M, Challa P, Lee PP, Herndon LW, Rand Allingham R (2014) Osteogenesis imperfecta and primary open angle glaucoma: Genotypic analysis of a new phenotypic association. Mol Vis 20:1174

32. Mauri L, Uebe S, Sticht H, et al (2016) Expanding the clinical spectrum of COL1A1 mutations in different forms of glaucoma. Orphanet J Rare Dis 11:108

33. Bohnsack BL (2016) Infantile-onset glaucoma and anterior megalophthalmos in osteogenesis imperfecta. J AAPOS 20:170–172

34. Singh P, Karmacharya S, Rizyal A (2025) Central Corneal Thickness and Intraocular Pressure Measured with Goldmann Applanation Tonometer among Patients with Normal Intraocular Pressure. J Nepal Health Res Counc 23:94–100

35. Chou CC, Shih PJ, Jou TS, Hsu MY, Chen JP, Hsu RH, Lee NC, Chien YH, Hwu WL, Wang IJ (2023) Corneal Biomechanical Characteristics in Osteogenesis Imperfecta With Collagen Defect. Transl Vis Sci Technol 12:14

36. Laroche D, Nkrumah G (2020) Combined microinvasive glaucoma surgery in osteogenesis imperfecta patient with refractory open angle glaucoma. Am J Ophthalmol Case Rep 18:100617

37. de Souza LT, Nunes RR, de Azevedo Magalhães O, Maria Félix T (2021) A new case of osteogenesis imperfecta type VIII and retinal detachment. Am J Med Genet A 185:238–241

38. Fleissig E, Barak A (2019) SURGICAL MANAGEMENT OF RETINAL DETACHMENT IN OSTEOGENESIS IMPERFECTA: CASE REPORT AND REVIEW OF THE LITERATURE. Retin Cases Brief Rep 13:43–46

39. Scollo P, Snead MP, Richards AJ, Pollitt R, DeVile C (2018) Bilateral giant retinal tears in Osteogenesis Imperfecta. BMC Med Genet 19:8

40. Banerjee M, Venkatesh P, Azad SV, Verma S (2023) Retinal manifestations in osteogenesis imperfecta. BMJ Case Rep 16:e256366

41. Sato Y, Kimoto K, Takaki Y, Kubota T (2022) Macular neovascularisation in a patient with osteogenesis imperfecta exhibiting a novel COL1A1 mutation. BMJ Case Rep 15:e251763

42. Bellanca RF, Scarinci F, Parravano M (2020) Multimodal imaging in a young male with osteogenesis imperfecta complicated with choroidal neovascularization. Eur J Ophthalmol 30:NP21–NP24

43. Klug SE, Bek T (2017) Subretinal neovascularization as the only ocular sign of osteogenesis imperfecta: a case report. Acta Ophthalmol 95:e159–e160

44. De Francesco S, Sgheri A, Di Maggio A, Rana F, Anna Maria P, Alessandra R, Hadjistilianou T (2021) Bilateral retinoblastoma and osteogenesis imperfecta, a very rare association: Two cases. Eur J Ophthalmol 31:NP81–NP84

45. Chougui K, Addab S, Palomo T, Morin SN, Veilleux LN, Bernstein M, Thorstad K, Hamdy R, Tsimicalis A (2020) Clinical manifestations of osteogenesis imperfecta in adulthood: An integrative review of quantitative studies and case reports. Am J Med Genet A 182:842–865

Table 3. Methodological quality assessment of included studies using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist.

First author	Year	Study design	Ocular focus	Risk of bias	Strengths	Main limitation
M. L. Lyster [8]	2022	Nationwide retrospective cohort	Risk of ophthalmic diseases in patients with OI including: cataract, glaucoma, retinal detachment, vitreous, haemorrhage, other retinal disorders.	Low risk of bias (high methodological quality)	Large nationwide cohort Population-based design Long-term follow-up Use of standardized national registries Statistical control for confounders	Registry-based diagnoses may introduce misclassification bias Limited clinical detail (e.g., severity of ocular disease, genetic subtype of OI)

S. Treurniet [2]	2022	Systematic review	Reported ocular manifestations: blue sclera, reduced central corneal thickness, myopia, glaucoma, retinal complications, surgical risks and other ophthalmic abnormalities.	Low risk of bias (high methodological quality)	Structured systematic search Transparent study selection Critical appraisal of included studies Comprehensive overview of ocular manifestations in OI	Evidence quality dependent on included studies (many small observational studies) Heterogeneity prevented meta-analysis
S. Moussa [28]	2024	Scoping review	Ophthalmological screening in individuals with osteogenesis imperfecta	Low to moderate	Structured search strategy Transparent study selection process Focus on clinical screening recommendations in a rare disease population	Limited formal quality appraisal of included studies Narrative synthesis without quantitative evaluation Potential publication bias not assessed
O. Megalhaes [19]	2018	Cross-sectional case–control	Corneal structural parameters in patients with osteogenesis imperfecta	Moderate	Clearly defined OI and control groups Objective ophthalmologic measurements Direct assessment of corneal structural parameters	Small sample size Limited control of confounders Cross-sectional design prevents causal inference
C. C. Chou [35]	2023	Cross-sectional case–control	corneal hysteresis (CH) corneal resistance factor (CRF) central corneal thickness (CCT), IOP measurements influenced by corneal biomechanics.	Moderate	Objective biomechanical measurements Clear comparison between OI and control groups Modern corneal biomechanics assessment methods	Observational cross-sectional design Small sample size Limited adjustment for confounding variables
L. Lagrou [23]	2018	Prospective case–control	Corneal biomechanical parameters in children with osteogenesis	Moderate	Prospective data collection Objective and validated	Small sample size, minimal adjustment for potential

			imperfecta and healthy controls		measurement tools Presence of a control group	confounding factors
J. D. Hald [16]	2018	observational cross-sectional cohort study	ocular findings (blue sclera, myopia, other ophthalmic abnormalities)	Moderate	Well-described national adult OI sample Comprehensive evaluation of non-skeletal manifestations Standardized clinical examinations	Cross-sectional design limits causal inference Limited adjustment for potential confounders Focus on adults only, which may limit generalizability to pediatric populations
K. Chougui [45]	2020	Integrative review		Low–moderate	Comprehensive overview of adult manifestations of OI Inclusion of multiple study types (quantitative studies and case reports) Transparent search and synthesis strategy	Heterogeneity of included studies Limited formal assessment of publication bias Narrative rather than quantitative synthesis
M. Jen [18]	2016	Literature review	Ocular manifestations associated with genetic dermatologic disorders	Moderate	Comprehensive overview of ocular findings in genetic skin disorders Extensive citation of clinical studies and case reports	No systematic literature search methodology Potential for selection bias in included literature