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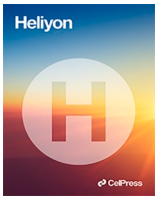

Research article

Characterization of the anterior segment in Trisomy 21-associated cataract using ultrasound biomicroscopy

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ABSTRACT

Backgroundobjectives: To compare the structural anatomy of the anterior segment in pediatric Trisomy 21 (T21) subjects with and without cataracts to age-matched controls.
Design: Prospective case-control study.
Participants: 40 subjects (57 eyes) age 0–25 years old (9.1 ± 10.6 years).
Methods: This prospective case-control study evaluated anterior segment measurements from ultrasound biomicroscopy (UBM) imaging on 342 images.
Results: Among persons with T21 cataract, the iris was significantly thinner than T21 individuals without cataract (0.28 vs 0.32 mm, p = 0.0181). T21/cataract subjects also had significantly thinner lenses than subjects without cataract, regardless of whether they have T21 or are controls (3.1 mm vs 3.5 mm, p = 0.0074).
Thinner lens (<3.5 mm) was insignificantly associated with increased odds of cataract (OR = 9.5 [0.872,104], p = 0.065). Thinner iris (<0.32 mm) was associated with increased odds of cataract (OR = 8.4 [1.188, 59.273], p = 0.033).
Conclusions: These findings support the hypothesis that subtle quantitative anatomic variants are present in the anterior eye of individuals with T21. Specific anatomic variants are unique to the presence of cataract among subjects with T21.

1. Introduction

Trisomy 21 (T21), or Down syndrome, is caused by a full or partial duplication of chromosome 21. The incidence (1 in 700 live births in the United States) has steadily increased due to advancing maternal age, improved disability services, and decreased abortion rates [1]. T21 can cause neurodevelopmental, cardiovascular, respiratory, musculoskeletal, and craniofacial manifestations [2,3]. Ophthalmic disorders are present in 60 % of individuals with T21 [2]. Even children without ocular anomalies tend to have reduced visual acuity and accommodation compared to controls, and incidence of ocular disorders increases with age [4]. The most common sight-threatening ocular association of T21 is early-onset cataract, with an incidence of 15 % [5,6].

Despite the relatively high incidence of cataracts, few studies detail structural variations in the anterior segment of pediatric T21

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subjects with and without cataracts, demonstrating a need for improved understanding of anterior segment anatomy in this unique population. Ultrasound biomicroscopy (UBM), a high-resolution imaging technique, allows quantitative assessment of the anterior segment and can be successfully performed in non-cooperative and young subjects [7,8]. This prospective case-control study compares structural features in UBM images among T21 subjects with cataract, T21 subjects with no cataract, and age-matched controls.

2. Materials and methods

2.1. Setting and subjects

Subjects between age 0 and 25 years old were recruited for the study during outpatient examination. Pediatric T21 subjects with cataracts were recruited at time of cataract diagnosis. Pediatric T21 subjects without cataracts were recruited in the cardiology and ophthalmology outpatient setting. Pediatric control subjects were recruited in the ophthalmology outpatient setting. Exclusion criteria included existing non-cataract ocular disease or eye trauma. Verbal and written informed consent were obtained from the parent or guardian of each participant. Institutional Review Board (IRB) Ethics Committee approval was obtained prior to initiating this study. This research adhered to the tenets of the Declaration of Helsinki.

2.2. UBM imaging

Pediatric T21 subjects with cataracts, without cataracts, and age-matched controls were enrolled, consented, and imaged with bilateral UBM prior to an ophthalmic exam or surgery. Subjects with cataracts were imaged prior to lensectomy, while subjects without cataracts were imaged during an outpatient appointment or prior to an extra-ocular surgical intervention. The Aviso Ultrasound Platform A/B UBM (Quantel Medical, Bozeman, MT, USA) or UBM Plus (Accutome, Malvern, PA, USA) equipment were used. Aviso imaging included optional use of Afonso eyelid speculum, Hypromellose ophthalmic solution (2.5 %) coupling gel, and ClearScan probe cover. Standardized lighting conditions were ensured using the same rooms with constant lights-on conditions (approximately 6000–9000 lux) to maintain ambient light and constant pupillary response. Subjects were not pharmacologically dilated. Accommodative effort was held constant by ensuring each image was acquired under general anesthesia immediately prior to surgery, or by contralateral distance fixation on a movie or cartoon for awake subjects. Imaging was performed without speculum in awake subjects. Subjects selected to image with eye open or closed, depending on comfort and preference.

A standard imaging protocol included the anterior segment cross section (horizontal and vertical angle to angle images axially), and dedicated images of the angle (at 12, 3, 6, and 9 o' clock longitudinally) [9]. The probe was placed at the center of the eye, marker facing towards the brow for the vertical image and towards the nose for the horizontal image. Angle images were taken with the probe centered on the trabecular-iris angle (TIA) marker in the respective clock positions (12, 3, 6, and 9 o'clock). Examples of UBM images are displayed in Fig. 1.

2.3. Image analysis

Each image was measured by an observer twice using ImageJ software, to manually measure 8 anterior segment parameters in each image. Repeatability and reliability of current image analysis protocol has been previously tested [10].

2.4. Statistical analysis

Following image analysis, the measurements were compared between the three groups: T21 with cataracts (T21/cataract), T21 without cataracts (T21), and controls. Univariate analysis was performed for each parameter stratified by group and by age. Student's t-test was used to compare each pair of groups to identify significant differences between T21/cataract, T21, and controls. Generalized estimating equations were used to account for inclusion of more than one eye per subject. Multivariate analysis was used to model which anterior segment measurements are associated with T21 and cataract.

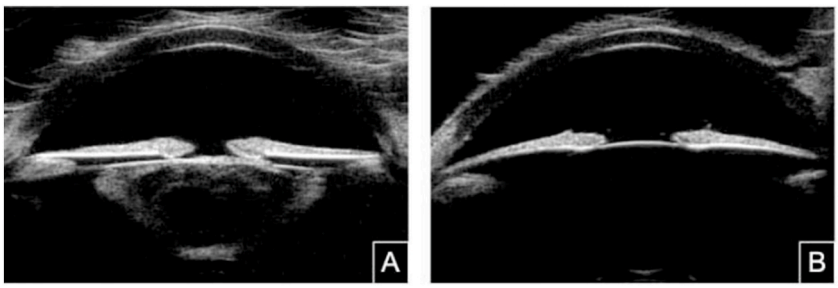

Fig. 1. Representative UBM images from a subject with T21 (A) cataract and an age-matched control (B).

3. Results

Anterior segment measurements were performed on 342 UBM images from 40 subjects (57 eyes) age 0–25 years old (9.1 ± 10.6 years). We examined 5 subjects (9 eyes) for each of the T21 groups with 2:1 age matching for each eye with T21 for a total of 36 control subjects. Both T21 groups consisted of 2 subjects (4 eyes) that were 1 month old, 1 subject (1 eye) that was 2 years old, and 2 subjects (4 eyes) that were 20–25 years old, and control subjects were recruited in these age ranges. Subject demographics are displayed in Table 1.

3.1. Univariate analysis

Subjects were stratified into four age groups: 0–1 years, 1–3 years, 4–5 years, and 20–25 years. Our cohort was 54 % female, 12.5 % Hispanic ethnicity, and 46 % White, 33 % Black, 8 % Asian, and 12.5 % Other.

3.2. Overall findings

Among all subjects of all ages, T21 eyes had thicker, less dense sclera and thinner maximal iris thickness compared to controls. Subjects with T21/cataract had thinner lens and thinner iris compared to controls. T21/cataract eyes had thicker, denser sclera and thinner lens compared to T21 without cataract.

3.3. Trends by age group

Significant differences between T21 groups and controls were predominantly in the youngest (<1 year) and oldest (>20 years) age groups. The differences were dissimilar between the two age groups. Other age groups showed few differences between T21 and controls.

3.4. Infants

Among infants (0–1 year age group), the central corneal thickness was thinner in T21 subjects compared to controls (0.516 mm vs. 0.555 mm, $p = 0.045$). Sclera was also significantly thinner in T21 subjects compared to controls (0.656 mm vs. 0.832 mm, $p = 2.56 \times 10^{-5}$). T21/cataract subjects had deeper anterior chamber depth (2.929 mm vs. 1.923 mm, $p = 0.007$), thicker central cornea (0.638 mm vs. 0.555 mm, $p = 0.002$), and thinner lens (3.02 mm vs 3.669 mm, $p = 8.61 \times 10^{-5}$) than healthy controls. Among subjects with T21, T21/cataract subjects had deeper chamber (2.979 mm vs 1.941, $p = 3.89 \times 10$^-5), thinner cornea (0.638 vs 0.516, $p = 0.007$), and thinner lens (3.02 mm vs 3.535 mm, $p = 0.027$) compared to T21 subjects without cataract. The iris was significantly thinner in T21/cataract compared to T21 (peripheral iris was 0.243 mm vs 0.341 mm, $p = 0.005$ and mid-iris was 0.334 mm vs 0.407 mm, $p = 0.020$). All other findings in this age group were found to be non-significant between conditions.

3.5. Young adults

For subjects in the young adult age group (20–25 years old) with T21, the chamber depth was shallower compared to controls (2.141 mm vs. 2.952 mm, $p = 0.003$). Maximal iris thickness was thinner in T21 compared to controls (0.539 mm vs. 0.796 mm, $p = 0.0002$). Lens was thicker in T21 subjects compared to controls (3.3941 mm vs. 3.33 mm, $p = 0.011$). T21/cataract subjects had thinner measurements for all 3 measures of iris thickness compared to control subjects (peripheral iris thickness: 0.347 mm vs. 0.526 mm, $p = 0.0007$; mid-iris thickness: 0.395 mm vs. 0.702 mm, $p = 3.16 \times 10^{-5}$); maximal iris thickness: 0.616 mm vs. 0.796 mm, $p = 0.002$). T21/cataract subjects had thinner lens than T21 subjects without cataract (3.01 mm vs 3.941 mm, $p = 0.003$). A detailed table of significant parameters can be found in Table 2, 3 and 4.

Table 1
Trisomy 21 and cataract groups, with mean age by group.

	Age group	Mean age (years)
Control	0–1 years (n = 14)	0.3 ± 0.2
	1–5 years (n = 11)	3.0 ± 1.5
	20–25 years (n = 12)	23.8 ± 0.8
T21	0–1 years (n = 4)	0.8 ± 0.02
	1–5 years (n = 3)	3.9 ± 1.3
	20–25 years (n = 4)	20.3 ± 5.5
T21/Cataract	0–1 years (n = 4)	0.1 ± 0.001
	1–5 years (n = 1)	2.2
	20–25 years (n = 4)	23.8 ± 0.3

Table 2
Paired comparisons between T21 subjects with and without cataract.

Parameter	Age group	T21/cataract	T21	p-value[a]
Angle to angle distance (mm)	0–1 years	10.55 ± 0.415		
	1–3 years	12.4		
	4–5 years		8.429 ± 0.002	
	20–25 years		11.54 ± 1.116	
Anterior chamber depth (mm)	**0–1 years**	**2.979 ± 0.133**	**1.941 ± 0.141**	***p*<0.0001**
	1–3 years	2.679	2.085	
	4–5 years		2.483 ± 0.435	
	20–25 years	2.414 ± 1.060	2.412 ± 0.329	$p = 0.4$
Trabecular Iris Angle (TIA) (∘)	0–1 years	46.82 ± 2.898	39.56 ± 5.724	p=0.06
	1–3 years	41.23		
	4–5 years		47.00 ± 3.993	
	20–25 years	32.41 ± 18.18		
Central corneal thickness (mm)	**0–1 years**	**0.638 ± 0.059**	**0.516 ± 0.016**	***p*=0.007**
	1–3 years	0.585	0.524	
	4–5 years		0.562 ± 0.017	
	20–25 years	0.528 ± 0.039	0.600 ± 0.024	p=0.02
Scleral thickness (mm)	0–1 years	0.819 ± 0.101	0.656 ± 0.038	$p = 0.02$
	1–3 years	0.811		
	4–5 years		0.736 ± 0.071	
	20–25 years	0.910 ± 0.045	0.74	
Lens thickness (mm)	0–1 years	3.02 ± 0.036	3.535 0.076	$p = 0.02$
	1–3 years	3.846	3.651	
	4–5 years		3.104 ± 0.233	
	20–25 years	**3.01 ± 0.036**	**3.941 ± 0.057**	***p*=0.003**
Maximal iris thickness (mm)	0–1 years	0.435 ± 0.080	0.487 ± 0.039	$p = 0.3$
	1–3 years	0.561	0.541	
	4–5 years		0.532 ± 0.012	
	20–25 years	0.616 ± 0.111	0.562 ± 0.049	$p = 0.4$
Mid-iris thickness (mm)	0–1 years	0.344 ± 0.017	0.407 ± 0.036	$p = 0.02$
	1–3 years	0.277		
	4–5 years		0.528 ± 0.043	
	20–25 years	0.395 ± 0.076	0.578 ± 0.031	$p = 0.04$
Minimal (peripheral) iris thickness (mm)	**0–1 years**	**0.243 ± 0.009**	**0.341 ± 0.044**	***p*=0.005**
	1–3 years	0.16		
	4–5 years		0.426 ± 0.058	
	20–25 years	0.347 ± 0.07	0.397	$p = 0.04$

[a] $p < 0.01$ denoted in bold was considered significant, given multiple comparisons.

3.6. Multivariable analysis

A multivariable parsimonious model controlling for age, with criteria for inclusion in the model of $p < 0.2$, was performed to understand which anterior segment variables were associated with T21 and T21/Cataract. Sex was omitted from the model because by chance there were no females in some groups and no males in other groups. The analysis revealed that young subjects with T21, regardless of cataract status, have thinner irises than controls, but the difference is not significant (0.32 vs 0.37 mm, $p = 0.0826$). Furthermore, subjects with T21/cataract have significantly thinner iris than T21 individuals without cataract (0.28 vs 0.32 mm, $p = 0.0181$). Therefore, thin iris was associated with the presence of cataract in subjects with T21. T21 subjects had similar lens thickness to controls (3.5 mm vs 3.5 mm, $p = 0.4785$) while T21/cataract subjects had significantly thinner lenses (3.1 mm) than subjects without cataract (3.5 mm), regardless of whether they have T21 or are controls ($p = 0.0074$).

We evaluated the odds of cataract in subjects with T21, with iris and lens thickness as predictive features, controlling for age of subject and inclusion of 2 eyes per subject. Thinner lens (less than 3.5 mm) was associated with increased odds of cataract (OR = 9.5 [0.872,104]), but the difference was not significant ($p = 0.065$). Thinner iris (less than 0.32 mm) was associated with increased odds of cataract (OR = 8.4 [1.188, 59.273], $p = 0.033$).

4. Discussion/conclusion

The purpose of this study was to characterize structural differences in the anterior segment of T21 eyes with and without cataract to better understand which features were specifically associated with cataract, a sight-threatening condition. Previous research on the anterior segment features in Trisomy 21 evaluated corneal features, but very few studies have been done on the iris, lens, and sclera. We hypothesized that features of the lens, cornea, iris, and sclera would be different in T21 subjects with cataracts compared to T21 subjects without cataracts due to alterations of redox homeostasis and oxidative stress in Trisomy 21, with differences in the iris, sclera, and cornea primarily associated with Trisomy 21 and differences in the lens primarily associated with cataracts.

Table 3
Paired comparisons between T21 subjects without cataract and controls.

Parameter	Age group	Control	T21	p-value[a]
Angle to angle distance (mm)	0–1 years	9.735 ± 0.808		
	1–3 years	11.042 ± 0.338		
	4–5 years	**10.257 ± 0.153**	**8.429 ± 0.002**	***p*=0.004**
	20–25 years	10.836 ± 1.01	11.54 ± 1.116	$p = 0.4$
Anterior chamber depth (mm)	0–1 years	1.923 ± 0.669	1.941 ± 0.141	$p = 0.9$
	1–3 years	2.728 ± 0.238	2.085	
	4–5 years	2.729 ± 0.139	2.483 ± 0.435	$p = 0.3$
	20–25 years	2.897 ± 0.328	2.412 ± 0.329	$p = 0.02$
Trabecular Iris Angle (TIA) (∘)	0–1 years	43.95 ± 5.921	39.56 ± 5.724	p=0.2
	1–3 years	42.75 ± 4.088		
	4–5 years	46.21 ± 1.586	47.00 ± 3.993	p=0.8
	20–25 years	43.63 ± 6.162		
Central corneal thickness (mm)	0–1 years	0.555 ± 0.034	0.516 ± 0.016	$p = 0.04$
	1–3 years	0.579 ± 0.021	0.524	
	4–5 years	0.565 ± 0.029	0.562 ± 0.017	$p = 0.9$
	20–25 years	0.595 ± 0.045	0.600 ± 0.024	$p = 0.8$
Scleral thickness (mm)	**0–1 years**	**0.832 ± 0.044**	**0.656 ± 0.038**	***p*<0.0001**
	1–3 years	0.841 ± 0.085		
	4–5 years	0.840 ± 0.081	0.736 ± 0.071	$p = 0.2$
	20–25 years	0.829 ± 0.109	0.74	
Lens thickness (mm)	0–1 years	3.669 ± 0.151	3.535 ± 0.076	$p = 0.2$
	1–3 years	3.467 ± 0.238	3.651	
	4–5 years	3.466 ± 0.208	3.104 ± 0.233	$p = 0.1$
	20–25 years	**3.262 ± 0.229**	**3.941 ± 0.057**	***p*=0.002**
Maximal iris thickness (mm)	0–1 years	0.510 ± 0.08	0.487 ± 0.039	$p = 0.6$
	1–3 years	0.657 ± 0.055	0.541	
	4–5 years	0.583 ± 0.057	0.532 ± 0.012	$p = 0.3$
	20–25 years	**0.771 ± 0.074**	**0.562 ± 0.049**	***p*=0.0001**
Mid-iris thickness (mm)	0–1 years	0.413 ± 0.119	0.407 ± 0.036	$p = 0.9$
	1–3 years	0.419 ± 0.029		
	4–5 years	0.461 ± 0.057	0.528 ± 0.043	$p = 0.2$
	20–25 years	0.677 ± 0.073	0.578 ± 0.031	$p = 0.09$
Minimal (peripheral) iris thickness (mm)	0–1 years	0.287 ± 0.050	0.341 ± 0.044	$p = 0.08$
	1–3 years	0.299 ± 0.02		
	4–5 years	0.339 ± 0.022	0.426 ± 0.058	$p = 0.05$
	20–25 years	0.509 ± 0.068	0.397	

[a] $p < 0.01$ denoted in bold was considered significant, given multiple comparisons.

4.1. Anterior chamber

A few studies have noted the anterior chamber to be significantly smaller in subjects with T21, while others have found minimal differences between T21 and age-matched controls [11]. We found minimal difference, with one T21 group demonstrating slightly smaller chamber. No significant findings were found regarding anterior chamber angle measurements.

4.2. Cornea and sclera

Previous studies found thinner corneas and lower corneal volume in T21 subjects, which predisposes them to corneal diseases like keratoconus [11,12]. Corneal radius of curvature and pupil diameter were also found to be smaller in the T21 group, with these differences leading to more visual impairment [11]. We found thinner cornea in T21 and thicker cornea in T21/cataract, suggesting that both age and cataract status may influence corneal features in T21.

4.3. Iris and lens

Brushfield spots and Wölfin nodules are known iris features in T21 individuals. These iris features are of variable size and lighter color in the midperipheral and peripheral iris, respectively, with the adjacent iris to these structures noted to be hypoplastic [13]. In prior studies, biometric analysis using a Scheimpflug camera showed thinner lens thickness and weaker calculated lens power in T21 subjects compared to healthy controls, suggesting reduced lens plasticity and reduced accommodation [11]. Prior studies looking at lens curvature and lens density found very minimal differences between T21 and control subjects [11,12].

Our study provides better understanding of the iris and lens in T21 individuals. Our analysis revealed that young subjects with T21, regardless of cataract status, have thinner irises than controls, but the difference is not significant. However, specifically among persons with T21 who have cataract, the iris was significantly thinner than T21 individuals without cataract such that iris thickness independently predicted the presence of cataract in subjects with T21. Furthermore, we identified lens thickness as a quantitative marker for the presence of cataract in subjects with T21. One possible mechanism for this finding is global hypoplasia, in which the

Table 4
Paired comparisons between T21 subjects with cataract and controls.

Parameter	Age group	Control	T21/cataract	p-value[a]
Angle to angle distance (mm)	0–1 years	9.735 ± 0.808	10.55 ± 0.415	p = 0.08
	1–3 years	11.042 ± 0.338	12.4	
	4–5 years	10.257 ± 0.153		
	20–25 years	10.836 ± 1.01	11.37 ± 0.215	p = 0.3
Anterior chamber depth (mm)	**0–1 years**	**1.923 ± 0.669**	**2.979 ± 0.133**	***p*** = 0.007
	1–3 years	2.728 ± 0.238	2.678	
	4–5 years	2.729 ± 0.139		
	20–25 years	2.897 ± 0.328	2.414 ± 1.060	p = 0.2
Trabecular Iris Angle (TIA) (∘)	0–1 years	43.95 ± 5.921	46.82 ± 2.898	*p*=0.4
	1–3 years	42.75 ± 4.088	41.23	
	4–5 years	46.21 ± 1.586		
	20–25 years	43.63 ± 6.162	32.41 ± 18.18	*p*=0.07
Central corneal thickness (mm)	**0–1 years**	**0.555 ± 0.034**	**0.638 ± 0.059**	***p*** = 0.002
	1–3 years	0.579 ± 0.021	0.585	
	4–5 years	0.565 ± 0.029		
	20–25 years	0.595 ± 0.045	0.528 ± 0.039	p = 0.02
Scleral thickness (mm)	0–1 years	0.832 ± 0.044	0.819 ± 0.101	p = 0.7
	1–3 years	0.841 ± 0.085	0.811	
	4–5 years	0.840 ± 0.081		
	20–25 years	0.829 ± 0.109	0.910 ± 0.045	p = 0.07
Lens thickness (mm)	**0–1 years**	**3.669 ± 0.151**	**3.02 ± 0.273**	***p*** < 0.0001
	1–3 years	3.467 ± 0.238	3.846	
	4–5 years	3.466 ± 0.208		
	20–25 years	3.262 ± 0.229	3.01 ± 0.036	p = 0.2
Maximal iris thickness (mm)	0–1 years	0.510 ± 0.08	0.435 ± 0.080	p = 0.1
	1–3 years	0.657 ± 0.055	0.561	
	4–5 years	0.583 ± 0.057		
	20–25 years	**0.771 ± 0.074**	**0.616 ± 0.111**	***p*** = 0.006
Mid-iris thickness (mm)	0–1 years	0.413 ± 0.119	0.344 ± 0.017	p = 0.30
	1–3 years	0.419 ± 0.029	0.277	
	4–5 years	0.461 ± 0.057		
	20–25 years	**0.677 ± 0.073**	**0.395 ± 0.076**	***p*** < 0.0001
Minimal (peripheral) iris thickness (mm)	0–1 years	0.287 ± 0.050	0.243 ± 0.009	p = 0.1
	1–3 years	0.299 ± 0.02	0.16	
	4–5 years	0.339 ± 0.022		
	20–25 years	**0.509 ± 0.068**	**0.37 ± 0.070**	***p*** = 0.001

[a] $p < 0.01$ denoted in bold was considered significant, given multiple comparisons.

anomalous iris and lens structure arise simultaneously. Another possible mechanism is the known interplay between iris and lens, where abnormality of the iris or lens directly causes the other one to become abnormal, a "causation hypothesis" rather than two abnormal features in parallel [14,15]. The lens does not grow independently, and its growth influences the development of adjacent structures. This has been seen in prior experiments where reduced lens growth was associated with a proportionate decrease in the size of the globe. Similarly, extralenticular factors from adjacent structures such as the iris, cornea, and retina have been shown to impact lens shape and size [14]. Given our significant findings of thinner irises being associated with increased odds of cataract, it is plausible that flawed development of the iris in turn influences dysfunctional lens growth and function, and vice versa.

4.4. Potential mechanisms and biological plausibility of findings

The overexpression of genes on chromosome 21 has been linked to multisystem anomalies. Dysregulation of *COLA6A1* and *COLA6A2* genes, located on chromosome 21, leads to an increase in collagen type VI expression, which disrupts endocardial cushion differentiation during cardiac development [16]. Overexpression of type IV collagen increases the activity of extracellular matrix proteins and metalloproteinases, leading to increased adhesiveness of cells and a failure of embryonal endocardial cushion to septum fusion [17]. This results in the most common T21-associated cardiac anomaly, atrioventricular septal defect [18]. Abnormalities in extracellular matrix genes are known to be associated with cataract production and lens capsular rupture, suggesting a link between the development of congenital heart disease and early onset cataracts among T21 patients [19]. Overexpression of other genes on chromosome 21 also impairs mitochondrial function in fibroblasts of T21 cells, leading to an accumulation of reactive oxygen species, affecting cardiomyocyte differentiation, autophagy, and apoptosis [17]. In the anterior segment of the eye, oxidative stress and reactive oxygen species (ROS) are associated with cataract formation in the aging eye. Through aging, the mitochondria in epithelial cells of the lens are damaged, resulting in production of ROS. Increased ROS levels alter the phospholipid composition of human lens membranes through lipid peroxidation, exacerbating the development of cataracts. Since ROS production is increased inherently in T21 cells, patients with this disease might be susceptible to earlier onset cataracts compared to the general population.

4.5. Strengths and limitations

Strengths of this study were a broad range of ages recruited from various pediatric populations, inclusion of pediatric subjects, and analysis of multiple image types from each eye. Limitations of this study include small sample size and limited number of observations. Additionally, some T21 subjects that were recruited might have subclinical ophthalmic conditions affecting anterior segment structures. Our cohort's age distribution was driven by the T21/cataract cohort as subjects with T21 and controls were matched to the available cohort. This resulted in no data on the 5–20-year-old age range. Conclusions cannot be drawn regarding sex-based differences due to sex differences occurring by chance among the three groups. However, no sex-based patterns in T21 have been previously described related to ocular, cardiac, neurologic, or other system involvement, so this is unlikely an important contributor. Finally, measurements among the three groups also used two different imaging platforms. Two subjects were imaged with both platforms and results were nearly identical; however, formal comparison of platforms was beyond the scope of this study.

In summary, we found differences in the cornea, iris, and lens among subjects with T21 compared to controls. Furthermore, some anterior segment features were more specific to eyes with T21 and cataract, namely the lens thickness and mid-iris thickness, suggesting a need for further study to determine if young T21 individuals with clear lens and thinner iris and lens are at higher risk for early onset of cataract, or if lens and iris thickness can predict the presence of cataract among individuals with T21. Subjects with thin iris and lens may benefit from closer monitoring, particularly in the context of developmental delay which may impede a patient's ability to communicate or articulate vision compromise.

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Ethics and consent

This study was reviewed and approved by Institutional Review Board (IRB) Ethics Committee of the Human Research Protections Office (HRPO), with the approval number: HP-00057992. All participants/patients and their legal guardians provided written informed consent to participate in the study. All participants/patients and their legal guardians provided written informed consent for the publication of their anonymized case details and images.

This study is an observational case control study, and the study followed STROBE guidelines.

Data availability

Sharing research data helps other researchers evaluate your findings, build on your work and to increase trust in your article. We encourage all our authors to make as much of their data publicly available as reasonably possible. Please note that your response to the following questions regarding the public data availability and the reasons for potentially not making data available will be available alongside your article upon publication.

Has data associated with your study been deposited into a publicly available repository?

No, the data that has been used is confidential.

CRediT authorship contribution statement

Dhruv M. Shah: Writing – review & editing, Writing – original draft, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Esther Xu:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation. **Radhika Gholap:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation. **Zahur F. Sallman:** Investigation, Data curation, Conceptualization. **Taylor Kolosky:** Methodology, Investigation. **Moran R. Levin:** Methodology, Investigation. **Sudhir Vashist:** Investigation, Data curation. **Janet L. Alexander:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e34118.

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