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RESEARCH ARTICLE

Identifying Eye Changes in Children and Adolescents with Congenital Heart Disease with the Aid of a Smartphone: An Observational Study

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ABSTRACT

Background: Among congenital diseases, congenital heart disease is one of the most frequent defects, accounting for high morbidity and mortality rates. Coexistence of ocular sequelae, especially in retinal microvascularization, is frequent, and may be a marker of vascular damage and severity of underlying disease.

Aims: To identify ocular anatomical repercussions in children with congenital heart diseases; to describe the prevalence of potential markers associated with retinal vessels using a smartphone.

Methods: This was a cross-sectional observational study with children diagnosed with congenital heart disease treated at the Instituto de Cardiologia in Porto Alegre-RS from 4 up to (but not over) 18 years old.

Results: Of a total of 218 patients assessed, 206 were included in the study. Mean age was 10.19 years +- 3.88. Uncorrected visual acuity poorer than 0.6 in at least one eye was found in 11.65% (24) of all patients. Regarding retinal findings, estimated mean arterial tortuosity was 437.79 μ m, and estimated mean venous tortuosity was 336.41 μ m. Taking only the cyanotic group, the arterial mean reached 557.29 μ m, and the venous mean reached 401.86 (p=.001 and p=.004, respectively). In the multivariate analysis, estimated mean arterial tortuosity of cyanotic patients undergoing clinical treatment was 699.13 μ m versus 489.74 μ m for those without clinical treatment (p<0.001).

Conclusion: Presence of retinal vascular tortuosity, especially in the arterial bed, is associated with cyanotic CHD. Identification of ocular changes, especially through an easily accessible and universal method such as the smartphone, may have diagnostic and prognostic significance.

1. INTRODUCTION

Among congenital diseases, congenital heart disease (CHD) is one of the most frequent, occurring in up to 1% of live births and accounting for high morbidity and mortality rates.1 Progress with clinical and surgical treatments have brought about a significant increase in the survival of these patients. Coexistence of ocular sequelae, especially in retinal microvascularization, is frequent, and can be a marker of vascular damage and severity of underlying disease.1,2

Association of low oxygen saturation of retinal vessels with chronic systemic hypoxemia secondary to CHD has been described in considerable detail.3,4 Among patients with congenital heart disease, cyanotic disease accounts for an important share of mortality and loss of quality of life. These patients develop chronic hypoxemia with consequent increased risk of systemic damage: cardiovascular, renal and retinal.3

In view of the unique possibility of noninvasive visualization of its microcirculation, the retina shows a close relationship with morphological changes of coronary vessels.3,5-7 This probable relationship is addressed in several studies, commonly with small case series or case reports. The low frequency of more robust studies with relevant samples, in addition to the high cost of equipment for retinal photodocumentation, continue to be considered the main factors responsible for the lack of information.2,8 In view of this, evidence is growing that smartphone fundoscopy can play a relevant role, given the good sensitivity and specificity of the method. Obtaining images of the fundus of the eye using this technique has improved and democratized the teaching of fundoscopy and, in particular, has contributed to the screening of diseases with high rates of blindness.9

Observation of retinal vessels is considered, by many authors, as a unique non-invasive window, which allows systemic circulatory consequences to be related with heart diseases.3,6 The objective of this study is to describe ocular anatomical repercussions in children with congenital heart diseases. We also expect to describe the prevalence of potential markers associated with retinal vessels (caliber and pathway) with the aid of a smartphone.

2. METHODS

This is a cross-sectional observational study with children and adolescents diagnosed with congenital heart disease treated at the Instituto de Cardiologia/Fundação Universitária de Cardiologia in Porto Alegre, Rio Grande do Sul, Brazil. Children and adolescents cared for at the institution's outpatient clinic and infirmary were analyzed from July 2021 to March 2022.

Patients aged 4 to 18 years old were included in the study. Patients with Still's murmur, first appointments without definite diagnosis of heart disease, clinical conditions that prevent ophthalmological assessment and associated syndromes were excluded.

Demographic data were collected during the review of the medical records. Type of heart disease, clinical heart treatment (drugs commonly used for heart failure and/or hypertension) and/or heart surgery were analyzed. In line with previous studies, patients were subdivided into five groups according to the mechanism of the underlying heart disease, based on clinical and echocardiographic examination: (1) minimal lesion (patent forame ovale, arrhythmias and mitral valve prolapse); (2) acyanotic with left-right shunts (atrial and/or ventricular septal defects, patent ductus arteriosus); (3) acyanotic obstructive (coarctation, valve stenosis); (4) cyanotic (Tetralogy of Fallot, transposition of the great arteries, pulmonary atresia); (5) non-structural (cardiomyopathy). Patients who had more than one underlying heart disease mechanism were allocated to the group considered to have the greatest cardiac impairment.

ophthalmological The examination consisted of measuring visual acuity (logarithmic chart) with and without optical correction in each eye separately. Patients who did not reach 20/20visual acuity in either eye were assessed using the pinhole principle. Presence of extrinsic ocular motor imbalance and accommodative function was assessed using the cover-uncover tests. Direct and consensual pupillary light reflexes were assessed. using mydriatic Fundoscopy eye drops (Tropicamide 1%, 3 drops every 5 minutes) was performed with the aid of a Smartphone (iPhone 11, Apple [®]) and indirect 20 diopter lens (Ocular ® MaxField 20D).

Fundus photographs were obtained and reviewed by one of the authors. (CSM). The smartphone camera application was used in video mode (2x digital zoom) with a lamp aligned with the condenser lens and the patient's central visual axis. Images were taken from the video, and those considered to be of low quality were excluded from the study. The "ImageJ" application,10 a public domain Java image processing platform, was used to analyze retinal vessel calibers and tortuosity. The distance in pixels from the diameter of an optical disc, equivalent to the known standard distance of 1850 micrometers (μ m), as established by the "Early Treatment Diabetic Retinopathy Study" as a known unit of measurement, was used for scale. Two

retinal arterial calibers and two retinal vein calibers of the major arcades were assessed, with subsequent calculation of their mean value in each bed. The calibers were measured between the distance of one and two disc diameters from the external limit of the optic disc. The degree of tortuosity was calculated by how much the vessel deviated from a straight line at a known equivalent peridiscal distance of two disc diameters (subtracting the vascular pathway from the straight line). Marked presence of peridiscal vascularization was also assessed.

The demographic data and clinical ophthalmology data were analyzed using "SPSS Statistics" software. Prevalence rates were described as proportions along with their respective 95% confidence intervals (CI). Continuous variables were described using means and standard deviations, or medians and interquartile ranges. For variables with normal univariate or multivariate distribution, generalized estimating equation analysis with identity link function was used. For those that did not show normal distribution, such as tortuosity, the analysis of generalized estimating equations with gamma distribution and log link function was used. Significance values >0.05 were used.

Patients identified as having low visual acuity or ophthalmological risks, were referred to reference ophthalmology services. The study was approved by the institution's Research Ethics Committee and informed consent was obtained from parents/guardians in all cases analyzed. In addition, the study complied with the requirements of the Declaration of Helsinki.

3. RESULTS

Of a total of 218 patients assessed, 206 were included in the study. Losses included images considered to be of poor quality and drop-out before fundus examination (Figure 1).



Figure 1. Participant flowchart.

The minimal lesions group (G1) included 12.1% (25) of the patients; acyanotic patients with left-right shunts (G2) accounted for 40.8% (84); acyanotic obstructive (G3) 26.7% (55); cyanotic (G4) 15.0% (31); and non-structural (G5) 5.3% (11). Of the total sample, females accounted for 52.4% (108), while patients of White race accounted for 87.4% (180). Mean age analyzed was 10.19 years +- 3.89 (4-17 year), with no

statistical difference between the groups. Prematurity was found in 11.2% (23), and positive prior medical history was found in 13.6% (28), neither of which showed statistical significance between the groups. Clinical heart treatment was present in 16.5% (34) of the sample, while surgical heart treatment was present in 51.0% (105) (Table 1).

Table 1.	Demographic and	l cardiovascular	characteristics	of the po	pulation b	y subgroup.
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Variable	G1	G2	G3	G4	G5	p-value
	n (%)	n (%)	n (%)	n (%)	n (%)	
Sex						
Male	15 (60.0)	22 (26.2)	36 (65.5)	19 (61.3)	6 (54.5)	.000
Female	10 (40.0)	62 (73.8)	19 (34.5)	12 (38.7)	5 (45.5)	
Race						
White	22 (88.0)	69 (82.1)	52 (94.5)	29 (93.5)	8 (72.7)	
Black	3 (12.0)	15 (17.9)	3 (5.5)	2 (6.5)	3 (27.3)	.096
Gestational Age Term						
Drometure	22 (88.0)	76 (90.5)	46 (83.6)	30 (96.8)	9 (81.8)	270
Frematore	3 (12.0)	8 (9.5)	9 (16.4)	1 (3.2)	2 (18.2)	.372
Prior Medical History						
Absence	21 (84.0)	74 (88.1)	46 (83.6)	29 (93.5)	8 (72.7)	
Presence	4 (16.0)	10 (11.9)	9 (16.4)	2 (6.5)	3 (27.3)	.436
Clinical Heart Treatment						
Absence	24 (96.0)	77 (91.7)	47 (85.5)	21 (67.7)	3 (27.3)	
Presence	1 (4.0)	7 (8.3)	8 (14.5)	10 (32.3)	8 (72.7)	.000
Surgical Heart Treatment						
	25 (100)	49 (58.3)	19 (34.5)	1 (3.2)	7 (63.6)	000
Presence	0 (0.0)	35 (41.7)	36 (65.5)	30 (96.8)	4 (36.4)	.000

Uncorrected visual acuity poorer than 0.6 in at least one eye was found in 11.7% (24) of total patients. When analyzing the groups individually, 19.4% (6) of the patients in the cyanotic group, followed by 11.9% (10) in the left-right shunts group had visual acuity poorer than 0.6 in at least one eye. Of the 24 patients, 14 showed visual acuity improving to at least 0.6 using the pinhole principle. The assessment of the visual acuity of the eyes individually is shown in Table 2. Ocular motor defects were found in 11.7% (24) of the patients, with horizontal defects being the most frequent (72.7%), with no difference between groups. Duane syndrome was found in a female patient in Group 2 with a membranous ventricular septal defect. Congenital ptosis was found in two patients, both diagnosed with Tetralogy of Fallot. Physiological anisocoria was found in one patient from the cyanotic group diagnosed with truncus arteriosus type 1. Nevus of Ota was found in 5 patients, 4 of them from Group 2 Medical Research Archives

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Variable	G1	G2	G3	G4	G5	p-value
	n (%)	n (%)	n (%)	n (%)	n (%)	
Visual acuity right eye						
= > 0.6	23 (92.0)	77 (91.7)	53 (96.4)	28 (90.3)	10 (90.9)	
< 0.4	2 (8.0)	7 (8.3)	2 (3.6)	3 (9.7)	1 (9.1)	.817
Visual acuity left eye						
= > 0.6	23 (92.0)	75 (89.3)	50 (90.9)	26 (83.9)	10 (90.9)	.857
< 0.4	2 (8.0)	9 (10.7)	5 (9.1)	5 (16.1)	1 (9.1)	
Strabismus						
Absence	24 (96.0)	72 (85.7)	48 (87.3)	27 (87.1)	11 (100)	.471
Presence	1 (4.0)	12 (14.3)	7 (12.7)	4 (12.9)	0 (0.0)	
Accentuated peridiscal vascularization (both eves)						
Absence	48 (96.0)	155 (92.3)	105 (95.5)	60 (96.8)	15 (68.2)	.020
Presence	2 (4.0)	13 (7.7)	5 (4.5)	2 (3.2)	7 (31.8)	

Table 2. Ophthalmic findings for the population by subgrou

Regarding retinal findings, the estimated mean arterial diameter of the entire sample was 115.52 μ m (micrometers) (95% Cl: 113.6-117.4). Estimated mean vein diameter was 182.61 μ m (95% Cl: 180.3- 184.9). Estimated mean arterial tortuosity was 437.79 μ m (95% Cl: 414.4- 461.1), and estimated mean vein tortuosity was 336.41 μ m (95% Cl: 321.9- 350.9). The diameter and tortuosity values for the different groups are

provided in Table 3, showing a statistical difference in relation to the tortuosity values of both vascular beds (p=.001 in the arterial bed and p=.004 in the venous bed). Marked peridiscal vascularization was found in 31.8% of patients in G5 (p=.020) (Figure 2 and Table 2). Figure 3 illustrates the technique used in the present study to measure vascular calibers and tortuosity using the ImageJ application.



Figure 2: Smartphone fundoscopy images of an eye with no changes (A), an eye with increased peridiscal vascularization (B) and eyes with different degrees of retinal vascular tortuosity (C-H).

Variable	Arterial Diameter	Vein Diameter	Arterial Tortuosity	Vein Tortuosity
G1	113.86	181.74	415.65	320.58
	(95% Cl:	(95% Cl:	(95% Cl:	(95% Cl:
	106.3-121.4)	173.4- 190.0)	353.4- 488.9)	293.2- 350.5)
G2	115.95	181.28	443.24	323.07
	(95% Cl:	(95% Cl:	(95% Cl:	(95% Cl:
	112.4- 119.5)	177.1- 185.4)	400.3- 490.8)	302.7- 344.8)
G3	116.52	182.54	393.13	308.69
	(95% Cl:	(95% Cl:	(95% Cl:	(95% Cl:
	112.0- 121.0)	177.4- 187.6)	348.5- 443.5)	288.0- 330.8)
G4	113.63	184.79	557.29	401.86
	(95% Cl:	(95% Cl:	(95% Cl:	(95% Cl:
	107.7- 119.6)	177.7- 191.9)	469.96- 660.8)	361.2- 447.0)
G5	116.32	188.93	333.05	428.47
	(95% Cl:	(95% Cl:	(95% Cl:	(95% Cl:
	105.4- 127.2)	177.9- 199.9)	278.0- 398.9)	258.4- 710.5)
p-value	.933	.723	.001	.004

 Table 3. Retinal findings for the population with means estimated in micrometers and respective confidence intervals.

In the multivariate analysis, the interaction of arterial vascular tortuosity with clinical heart treatment and the groups was significant. Taking all patients undergoing clinical heart treatment, estimated mean arterial tortuosity was 457.26 μ m (95% CI: 421.0-496.6). Among those not undergoing this treatment, the estimated mean was 416.96 µm (95% Cl: 381.1-456.2). When filtering the groups, estimated mean arterial tortuosity of the cyanotic patients in clinical treatment was 699.13 μm (95% CI: 588.3- 830.8) versus 489.74 μm (95% Cl: 385.4- 622.3) for those not undergoing clinical treatment (p<0.001). Regarding vein tortuosity, the estimated mean among patients undergoing clinical treatment was $370.31 \ \mu m$ (95%) Cl: 318.8-430.1) versus 351.21 µm (95% Cl: 315.4-391.1) not undergoing clinical treatment. Similar values were found between the study's different groups.

Presence of probable papilledema was found in both eyes of two patients, one in G2 (interatrial septal defect) and the other in G4 (Tetralogy of Fallot). Presence of microhemorrhages/hemorrhages in the fundus of the eye was seen in 4 patients, 2 from G3 (both with coarctation of the aorta) and 2 from G4 (one with Tetralogy of Fallot and the other with pulmonary atresia + ventricular septal defect + patent ductus arteriosus). Lesions suggestive of retinocytoma were found in one of the eyes of a patient in G5 (dilated cardiomyopathy with moderate systolic dysfunction + mild mitral regurgitation). Presence of nevus in the fundus of the eye was found in one patient from G2. Optic nerve suspicious for glaucoma (enlarged excavation and/or overpass vessel) was found in 5 patients (2 from G2, 1 from G3 and 2 from G4)

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Figure 3: ImageJ application for measuring venous vascular caliber (A), arterial vascular caliber (B) and arterial vascular tortuosity (C and D).

4. **DISCUSSION**

In the present study, children and adolescents with congenital heart disease had high prevalence of ocular repercussions, especially among cases with cyanotic disease. In the literature variability regarding its prevalence is extensive, with studies demonstrating 6.3% to 65% ocular involvement.2 Data from our study indicate 73 patients (35.44%) with some degree of ocular involvement, similar to the average of 32.5% found in a systematic review with meta-analysis.2

Among patients with congenital heart disease, cyanotic disease accounts for an important share of mortality and loss of quality of life. About 25% of live births with heart disease have cyanosis and require some form of intervention in the first year of life.11,12 These patients develop chronic hypoxemia with consequent increased risk of systemic damage: cardiovascular, renal and retinal.3

Studies ophthalmological related to changes in patients with CHD are scarce, many of them restricted to just one cardiac anomaly, syndromes with cardiac anomalies, case reports/series or literature reviews.13-16 ln 2016, a systematic review and meta-analysis covered 8 articles with 1061 patients with CHD.2 Mean prevalence of ocular abnormalities was 32.5% (95% Cl: 19.3-49.3%), with strabismus, cataracts and retinopathy being the most commonly encountered abnormalities. Although we did not identify patients with cataracts, both strabismus and retinopathy were prevalent in our study. Exclusion of patients with syndromes may be related to this finding.

4.1 RETINAL VASCULAR CHANGES AND CHD

Finding tortuosity can signal the underlying disease, but it is suggested that measuring these changes can be used to quantify the degree of impairment imposed on retinal microcirculation.17-18 In studies with CHD, tortuosity rates reach up to 35% of cases.2 In the present study, the significant levels of vascular tortuosity, especially arterial, found in cyanotic patients may infer that this variable represents a marker of severity of heart disease and systemic impairment. Concomitantly, treatment with antihypertensive drugs proved to be significant. In patients with heart disease, this may mean an associated diagnosis of heart failure or hypertension, among others.

The exact mechanism of vascular tortuosity remains unestablished, with exhaustion of selfregulatory capacity being proposed.4,19 There is association with age, transmural pressure, release of vascular endothelial growth factor (VEGF), increased vascular viscosity and endothelial injury.12,20-22 Officially discovered in 1983, VEGF ends up contributing strongly to retinal vascular pathological changes.4,23-25 Abnormal levels of VEGF, together with other cytokines such as interleukin-6 and interleukin-8, induce changes in the basement membrane of the endothelium and neovascularization. Tip cells are formed, which determine longitudinal growth of vessels.26-28

Kohner EM et al.13 described the electroencephalogram and retinal vessels in 12 patients with cyanotic congenital heart disease before and after surgical intervention. Retinal photographs were obtained with a Zeiss fundus camera and Kodachrome film. There have been reports of reversal of retinal abnormalities after correction of cardiac lesion, such as decreased tortuosity and dilation of vessels and lighter color of the fundus. Gardiner PA *et al.*14 reported higher incidence of ocular lesions in patients with Tetralogy of Fallot and transposition of the great vessels compared to other congenital defects, reinforcing the findings regarding cyanotic CHD in the present study.

Fettah N et al.12 describe their retinovascular findings in a case series of 43 newborns with CHD. They separated two groups according to type of congenital heart disease (left obstructive and right obstructive). Retinovascular changes were found in 48% of the patients, being more frequent in the left obstructive group (p=0.04). Vascular tortuosity was the most common finding, reinforcing our findings as to the significance of retinal vascular tortuosity.

When investigating ophthalmologic changes in 13 patients with cyanotic CHD, Cordina N et al.20 found an increase in the prevalence of vessel dilation, increased branching and vascular tortuosity when compared to healthy individuals. The arteriovenous relationship was not significant between the cyanotic groups and controls. Spectral domain optical coherence tomography images were used in data analysis. The arteriovenous relationship, considering the measurements of vascular calibers with the fundoscopy technique on a smartphone, was preserved in the current study, also with no difference between the groups.

Mansour AM et al.1 describe ocular findings in 240 patients with CHD (105 with syndromes), subdivided into 3 groups: volume overload, cyanotic and obstructive. In 132 of the cases studied, there were pathological ocular findings. There was a strong correlation between vascular tortuosity and low hematocrit levels (p=0.000) and low arterial oxygen saturation (p=0.002). They suggested that high prevalence of ocular findings in this population is associated with the high number of cardiovascular syndromes and complexities.

In addition to the abnormal vascular tortuosity found in up to 35% of CHD cases,2 other prevalent retinal repercussions include changes in diameters and increased vascular branching.8 In addition to the significant correlations reported between decreased arterial caliber and increased vein caliber with cardiovascular disease, there are reports of retinal vessel capillary disease (ischemia, hemorrhage), thromboembolic events.29-38,40 According to the literature, these changes also occur more frequently in individuals with cyanotic CHD.20

Prematurity and low birth weight also play an important role in increasing vascular tortuosity, regardless of retinopathy of prematurity.19,39 In addition to the presence of retinopathy, strabismus was highly prevalent in patients with congenital heart disease (11.7%) in the present study. Strabismus is reported in 2.1% to 3.5% of the general population. If we filter for patients with heart disease, these values can reach 14%,8,41-43 similar to the data we obtained.

4.2 MEASURING RETINAL VASCULAR TORTUOSITY

Even though retinal vascular tortuosity is being studied as a potential biomarker of cardiovascular diseases, there are no criteria for universally standardizing the results. In the clinical routine, assessments become qualitative and subjective according to the experience of each examiner, so that there exist high levels of bias.4,33,44 Semi-automated or automated measurement ensures greater reliability and reproducibility.45,46

Different attempts to estimate vascular quantitatively have tortuosity been described.47,48 Roque WL & Costa RRA 49 describe a plugin for estimating tortuosity measurement using the "ImageJ" application based on pixels for two-dimensional images and on voxels for three-dimensional images. The technique follows the principle of geodesic reconstruction. Another criterion proposed to define tortuosity is to consider the integral curvature along the pathway of the vessel normalized by the length of the pathway.4,44,45,50 In order to use a low-cost public domain method, this latter proposal served as the basis for the present study in addition to the ImageJ application and smartphone fundoscopy.

The limitations of measuring vascular tortuosity remain present in view of the scarcity of studies with adequate samples associated with relevant demographic data (gender, race, age, refraction) with ocular and/or systemic diseases. The high cost of equipment for retinal photodocumentation also continues to be considered an important cause of lack of information.2,8 In addition to adequate reproducibility and reliability, a system that is easy to format, universal and compatible with different tools is expected. In this scenario, the smartphone gains strength to become a possible tool for this purpose.4,9

4.3 THE SMARTPHONE AS A TOOL FOR DIAGNOSIS

In view of the emerging scenario of retinal photodocumentation, evidence is growing that smartphone fundoscopy has good sensitivity and specificity.9 This tool has been incorporated, in the last two decades, as a source of accessibility, connectivity and portability.51 Obtaining images of the fundus of the eye using this technique has improved and democratized the teaching of fundoscopy and, in particular, has contributed to the screening of diseases with high rates of blindness.9,52

Smartphone ophthalmoscopy is essentially a cheap and safe method, facilitating public policies for population screening.53-56 Different health professionals can access and use this tool with adequate reproducibility.57 A systematic review meta-analysis investigated and agreement between images obtained using smartphones and conventional methods (fundoscopic examination and retinal cameras) in 4219 eyes.58 Regardless of the smartphone brand, lens used (20 or 28 diopters) or adapter, agreement between methods was substantial, with a Kappa coefficient of 77.77% (95% CI: 70.34% - 83.70%). The area under the receiver operating characteristic curve (ROC) was 0.86%, and cutoff point sensitivity and specificity was 80%. Murtaza et al.59 reported similar data, with detection of ophthalmological changes in 74.3% of cases assessed using a smartphone versus 77.1% using traditional retinal cameras.

The images obtained can be remotely assessed either synchronously or asynchronously. Primary health care environments with limited resources, both due to lack of specialized doctors and lack of equipment, can strongly benefit from smartphone ophthalmoscopy with undeniable costbenefit, cost-effectiveness and reduction of disparities.58,60-63 This technique has high agreement with traditional methods, being a powerful arsenal for early screening and diagnosis of various systemic diseases, such as cardiovascular diseases. In addition to streamlining the medical workflow and bringing gains to public health policies, this technology can enable safe and quality assessment for the population.64-68

Using an accessible and low-cost method, the present study becomes relevant in view of obtaining data similar to those found in the literature with high-end equipment and, often, limited to large urban centers. Because it is a crosssectional study, it has limitations that are inherent to its design, such as information on the possible constancy of vascular tortuosity. The measurement of vascular caliber was performed using a software in a subjective and operator-dependent manner. To minimize these factors, the same researcher (CSM) was responsible for measuring all retinal vessels, blindly in relation to the base heart disease groups. Many studies address the mere existence of retinal changes in patients with congenital heart diseases, addressing only qualitative data. In this sense, our study gains strength with the presentation of quantitative information on retinal vessel caliber and tortuosity in patients with congenital heart disease based on an accessible and low-cost method like the smartphone.

5. CONCLUSION

Children and adolescents with congenital heart disease have high prevalence of retinal changes. Presence of vascular tortuosity, especially in the arterial bed, is greater in those with CHD and presence of clinical heart treatment. Identification of ocular changes, especially through an easily accessible and universal method such as the smartphone, may have diagnostic and prognostic significance. We therefore emphasize the importance of ophthalmic assessments for all patients with heart disease, especially cyanotic patients, in order to monitor them clinically and minimize complications.

REFERENCES

1. Mansour AM, Bitar FF, Traboulsi El, Kassak KM, Obeid MY, Megarbane A, et al. Ocular pathology in congenital heart disease. Eye. 2005;19(1):29–34.

2. Vilela MAP, Sbruzzi G, Pellanda LC. Prevalence of ophthalmological abnormalities in children and adolescents with CHD: Systematic review and meta-analysis of observational studies. Vol. 26, Cardiology in the Young. 2016.

3. Li C, Zhong P, Yuan H, Dong X, Peng Q, Huang M, et al. Retinal microvasculature impairment in patients with congenital heart disease investigated by optical coherence tomography angiography. Clin Exp Ophthalmol. 2020;48(9).

4. Vilela MAP, Amaral CEV, Ferreira MAT. Retinal vascular tortuosity: Mechanisms and measurements. Eur J Ophthalmol.

2021;31(3):1497-506.

5. Tai ELM, Kueh YC, Hitam WHW, Wong TY, Shatriah I. Comparison of retinal vascular geometry in obese and non-obese children. PLoS One. 2018;13(2).

6. Malek J, Azar AT, Tourki R. Impact of retinal vascular tortuosity on retinal circulation. Neural Comput Appl. 2015;26(1):25–40.

7. Le Gloan L, Chakor H, Mercier LA, Harasymowycz P, Dore A, Lachapelle P, et al. Aortic coarctation and the retinal microvasculature. Int J Cardiol [Internet]. 2014;174(1):25–30. Available from:

http://dx.doi.org/10.1016/j.ijcard.2014.03.129

8. Vilela MAP, Colossi C, Freitas H, Valle G, Pellanda LC. Ocular alterations associated with primary congenital heart disease - A cross-sectional study. Middle East Afr J Ophthalmol. 2020;27(1).

9. Rajalakshmi R, Arulmalar S, Usha M, Prathiba V, Kareemuddin KS, Anjana RM, et al. Validation of smartphone based retinal photography for diabetic retinopathy screening. PLoS One. 2015 Sep 24;10(9).

10. Abràmoff MD, Magalhães PJ, Ram SJ. Image processing with imageJ. Biophotonics Int. 2004;11(7):36–41.

11. Gilboa SM, Salemi JL, Nembhard WN, Fixler DE, Correa A. Mortality Resulting From Congenital Heart Disease Among Children and Adults in the United States, 1999 to 2006. Circulation. 2010;122(22):22-54–2263.

12. Fettah N, Kabatas EU, Dogan V, Zenciroglu A, Dilli D, Ozyazici E, et al. Retinovascular findings in newborns with critical congenital heart disease: A case series. Arch Argent Pediatr. 2017;115(3):e175–8.

13. Kohner EM, Allen EM, Saunders KB, Emery VM, Pallis C. Electroencephalogram and Retinal

Vessels in Congenital Cyanotic Heart Disease Before and After Surgery. Br Med J. 1967;4(5573):207–10.

14. Gardiner PA, Joseph M. Eye Defects in Children with Congenital Heart Lesions: A Preliminary Study. Dev Med Child Neurol. 1968;10(1):42–8.

15. Johns KJ, Johns JA, Feman SS. Retinal Vascular Abnormalities in Patients with Coarctation of the Aorta. Arch Ophthalmol. 1991;109(9):1266–8.

16. Eisalo A, Raitta C, Kala R, Halonen Pl. Fluorescence angiography of the fundus vessels in aortic coarctation. Br Heart J. 1970;32(1):71–5.

17. Maccormick IJC, Somner J, Morris DS, Macgillivray TJ, Bourne RRA, Huang SS, et al. Retinal Vessel Tortuosity in Response to Hypobaric Hypoxia. Higt Alt Med Biol. 2012;13(4):263–8.

18. Wagener HP, Clay GE, Gipner JF. Classification of retinal lesions in the presence of vascular hypertension. Trans Am Ophthalmol Soc. 1947;45:57–73.

19. Taarnhøj NCBB, Munch IC, Sander B, Kessel L, Hougaard JL, Kyvik K, et al. Straight versus tortuous retinal arteries in relation to blood pressure and genetics. Br J Ophthalmol. 2008;92(8):1055– 60.

20. Cordina R, Leaney J, Golzan M, Grieve S, Celermajer DS, Graham SL. Ophthalmological consequences of cyanotic congenital heart disease: Vascular parameters and nerve fibre layer. Clin Exp Ophthalmol. 2015;43(2):115–23.

21. De Aguiar Remigio MC, Brandt CT, Santos CCL, Arantes TE, De Aguiar MIR. Macular and peripapillary retinal nerve fibre layer thickness in patients with cyanotic congenital heart disease. Eye [Internet]. 2015;29(4):465–8. Available from: http://dx.doi.org/10.1038/eye.2014.330

22. Patrick S. McQuillena, Donna A. Goffb and DJL. Effects of congenital heart disease on brain development Patrick. Prog Pediatr Cardiol [Internet]. 2010;29(2):79–85. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3 624763/pdf/nihms412728.pdf

23. Gariano RF, Gardner TW. Retinal angiogenesis in development and disease. Nature. 2005;438(7070):960–6.

24. Sun Y, Smith LEH. Retinal Vasculature in Development and Diseases. Annu Rev Vis Sci. 2018;4(1):101–22.

25. Selvam S, Kumar T, Fruttiger M. Retinal vasculature development in health and disease. Prog Retin Eye Res [Internet]. 2017;63:1–19. Available from: https://doi.org/10.1016/j.preteyeres.2017.11.0 01

26. Yasuda S, Kachi S, Kondo M, Ueno S, Kaneko H. Significant Correlation between Retinal Venous Tortuosity and Aqueous Vascular Endothelial Growth Factor Concentration in Eyes with Central Retinal Vein Occlusion. PLoS One. 2015;10(7):1–11.

27. Gerhardt H, Golding M, Fruttiger M, Ruhrberg C, Lundkvist A, Abramsson A, et al. Article VEGF guides angiogenic sprouting utilizing endothelial tip cell filopodia. J Cell Biol. 2003;161(6):1163–78.

28. Zeng G, Taylor SM, Mccolm JR, Kappas NC, Kearney JB, Williams LH, et al. Plenary paper Orientation of endothelial cell division is regulated by VEGF signaling during blood vessel formation. Blood. 2007;109(4):1345–53.

29. Wieder MS, Blace N, Szlechter MM, Shulman E, Thankenchen J, Mbekeani JN. Central retinal artery occlusion associated with patent foramen ovale: a case report and literature review. Arq Bras Oftalmol. 2021;84(5):494–8.

30. Tsui I, Shamsa K, Perloff JK, Lee E, Wirthlin RS, Schwartz SD. Retinal vascular patterns in adults with cyanotic congenital heart disease. Semin Ophthalmol. 2009;24(6):262–5.

31. Goel N, Kumar V, Seth A, Ghosh B. Proliferative retinopathy in a child with congenital cyanotic heart disease. J AAPOS [Internet]. 2010;14(5):455–6. Available from:

http://dx.doi.org/10.1016/j.jaapos.2010.08.005 32. HO I-V, Spaide R. Central Retinal Artery Occlusion Associated With A Patent Foramen Ovale. Retina. 2005;27(2):259–60.

33. Cheung CYL, Zheng Y, Hsu W, Lee ML, Lau QP, Mitchell P, et al. Retinal vascular tortuosity, blood pressure, and cardiovascular risk factors. Ophthalmology [Internet]. 2011;118(5):812–8. Available from:

http://dx.doi.org/10.1016/j.ophtha.2010.08.045 34. Dascalu J, Liu M, Lycett K, Grobler AC, He M, Burgner DP, et al. Retinal microvasculature: Population epidemiology and concordance in Australian children aged 11-12 years and their parents. Vol. 9, BMJ Open. 2019.

35. Boillot A, Zoungas S, Mitchell P, Klein R, Klein B, Ikram MK, et al. Obesity and the Microvasculature: A Systematic Review and Meta-Analysis. PLoS One. 2013;8(2).

36. Ding J, Wai KL, McGeechan K, Ikram MK, Kawasaki R, Xie J, et al. Review: Retinal vascular caliber and the development of hypertension: A meta-analysis of individual participant data. J Hypertens. 2014;32(2):207–15.

37. McGeechan K, Liew G, MacAskill P, Irwig L, Klein R, Klein BEK, et al. Prediction of incident stroke events based on retinal vessel caliber: A systematic review and individual-participant meta-analysis. Am J Epidemiol. 2009;170(11):1323–32.

38. MBoistat KM, Liew G, Macashill P, Irwig L, Klein R, K. KBE, et al. Retinal Vessel Caliber and Risk for Coronary Heart Disease: A Systematic Review and Meta-Analysis. Ann Intern Med. 2007;151(June 2009):404–13.

39. Gishti O, Jaddoe VWV, Duijts L, Steegers E, Reiss I, Hofman A, et al. Impact of birth parameters and early life growth patterns on retinalmicrovascular structure in children: The Generation RStudy. J Hypertens. 2015;33(7):1429–37.

40. Li LJ, Liao J, Fan Q, Cheung YCL, Kamran Ikram M, Cheng CY, et al. Familial correlation of retinal vascular caliber in Singapore Chinese. Investig Ophthalmol Vis Sci. 2013;54(8):5638–42.

41. David S. Friedman, Michael X. Repka, Joanne Katz, Lydia Giordano, Josephine Ibironke, Patricia Hawse and JMT. Prevalence of Amblyopia and Strabismus in White and African- American Children Aged 6 through 71 Months: The Baltimore Pediatric Eye Disease Study. Ophthalmology. 2009;116(11):1128-34.el – 2.

42. Repka MX, Lum F, Burugapalli B. Strabismus, Strabismus Surgery, and Reoperation Rate in the United States: Analysis from the IRIS Registry. Ophthalmology [Internet].

2018;125(10):1646–53. Available from: https://doi.org/10.1016/j.ophtha.2018.04.024

43. Won Yeol Ryu SRL. Incidence of strabismus and amblyopia among children initially diagnosed with pseudostrabismus using the Optum® dataset. Physiol Behav. 2020;211:98–104.

44. Hart WE, Goldbaum M, Côté B, Kube P, Nelson MR. Measurement and classification of retinal vascular tortuosity. Int J Med Inform. 1999;53(2-3):239-52.

45. Soares JVB, Leandro JJG, Cesar RM, Jelinek HF, Cree MJ. Retinal vessel segmentation using the 2-D Gabor wavelet and supervised classification. IEEE Trans Med Imaging. 2006;25(9):1214–22.

46. Wenstedt EFE, Beugelink L, Schrooten EM, Rademaker E, Rorije NMG, Wouda RD, et al. Highsalt intake affects retinal vascular tortuosity in healthy males: an exploratory randomized crossover trial. Sci Rep [Internet]. 2021;11(1):1–9. Available from: https://doi.org/10.1038/s41598-020-79753-6

47. Lotmar W, Freiburghaus A, Bracher D. Measurement of vessel tortuosity on fundus photographs. Albr von Graefes Arch für Klin und Exp Ophthalmol. 1979;211(1):49–57.

48. Capowski JJ, Kylstra JA, Freedman SF. A numeric index based on spatial frequency for the

tortuosity of retinal vessels and its application to plus disease in retinopathy of prematurity. Retina. 1995;15(6):490–500.

49. Roque WL, Costa RRA. A plugin for computing the pore/grain network tortuosity of a porous medium from 2D/3D MicroCT image. Appl Comput Geosci [Internet]. 2020;5(January):100019. Available from: https://doi.org/10.1016/j.acags.2020.100019

50. Imran A, Li J, Pei Y, Yang JJ, Wang Q. Comparative Analysis of Vessel Segmentation Techniques in Retinal Images. IEEE Access. 2019;7:114862–87.

51. Shahbaz R, Salducci M. Law and order of modern ophthalmology: Teleophthalmology, smartphones legal and ethics. Eur J Ophthalmol. 2021;31(1):13–21.

52. Sharafeldin N, Kawaguchi A, Sundaram A, Campbell S, Rudnisky C, Weis E, et al. Review of economic evaluations of teleophthalmology as a screening strategy for chronic eye disease in adults. Br J Ophthalmol. 2018;102(11):1485–91.

53. Hong SC. 3D printable retinal imaging adapter for smartphones could go global. Graefe's Arch Clin Exp Ophthalmol. 2015;253(10):1831–3.

54. Kohler J, Tran TM, Sun S, Montezuma SR. Teaching smartphone funduscopy with 20 diopter lens in undergraduate medical education. Clin Ophthalmol. 2021;15:2013–23.

55. Wintergerst MWM, Jansen LG, Holz FG, Finger RP. Smartphone-based fundus imaging -Where are we now? Asia-Pacific J Ophthalmol. 2020;9(4):308–14.

56. Omari A, Samad M, Bakhsh SR, Tajran J, Williams GA. Accuracy of Remote Diagnosis of Acute Posterior Segment Pathology by Residents and Attendings Captured with a Smartphone and Standard 20/28D Lens. Clin Ophthalmol. 2022;16(June):2751–7.

57. Kim Y. Comparison of smartphone ophthalmoscopy vs conventional direct ophthalmoscopy as a teaching tool for medical students : the COSMOS study. 2019;13:391–401.

58. Vilela MAP, Valença FM, Barreto PKM, Amaral CEV, Pellanda LC. Agreement between retinal images obtained via smartphones and images obtained with retinal cameras or fundoscopic exams – Systematic review and metaanalysis. Clin Ophthalmol. 2018;12:2581–9.

59. Murtaza K. Adam, Christopher J. Brady, Alexis M. Flowers, Alexander T. Juhn, Jason Hsu, Sunir J. Garg et al. Quality and Diagnostic Utility of Mydriatic Smartphone Photography: The Smartphone Ophthalmoscopy Reliability Trial. Ophthalmic Surg Lasers Imaging Retin. 2015;46:631–7.

60. Jones S, Edwards RT. Diabetic retinopathy screening: A systematic review of the economic evidence. Diabet Med. 2010;27(3):249–56.

61. Law MX, Pimentel MF, Oldenburg CE, de Alba Campomanes AG. Positive predictive value and screening performance of GoCheck Kids in a primary care university clinic. J AAPOS [Internet]. 2020;24(1):17.e1-17.e5. Available from: https://doi.org/10.1016/j.jaapos.2019.11.006

62. Ting DSW, Pasquale LR, Peng L, Campbell JP, Lee AY, Raman R, et al. Artificial intelligence and deep learning in ophthalmology. Br J Ophthalmol. 2019;103(2):167–75.

63. Wintergerst MWM, Petrak M, Li JQ, Larsen PP, Berger M, Holz FG, et al. Non-contact smartphone-based fundus imaging compared to conventional fundus imaging: a low-cost alternative for retinopathy of prematurity screening and documentation. Sci Rep. 2019;9(1):1–8.

64. Chalam K V., Brar VS, Keshavamurthy R. Evaluation of modified portable digital camera for screening of diabetic retinopathy. Ophthalmic Res. 2009;42(1):60–2.

65. Fleming AD, Philip S, Goatman KA, Olson JA, Sharp PF. Automated assessment of diabetic retinal image quality based on clarity and field definition. Investig Ophthalmol Vis Sci. 2006;47(3):1120–5.

66. Tran K, Mendel TA, Holbrook KL, Yates PA. Construction of an inexpensive, hand-held fundus camera through modification of a consumer "pointand-shoot" camera. Investig Ophthalmol Vis Sci. 2012;53(12):7600–7.

67. Bifolck E, Fink A, Pedersen D, Gregory T. Smartphone imaging for the ophthalmic examination in primary care. J Am Acad Physician Assist. 2018;31(8):34–8.

68. Pujari A, Saluja G, Agarwal D, Sinha A, P R A, Kumar A, et al. Clinical Role of Smartphone Fundus Imaging in Diabetic Retinopathy and Other Neuro-retinal Diseases. Curr Eye Res [Internet]. 2021;46(11):1605–13. Available from:

https://doi.org/10.1080/02713683.2021.1958 347