Investigation of Optic Disc and Retinal Microvasculature by Optical Coherence Tomography Angiography in Children with Asthma

Abdulkerim Karaaslan

Mustafa Kemal University Tayfur Ata Sokmen Faculty of Medicine: Mustafa Kemal Universitesi Tayfur Ata Sokmen Tip Fakultesi

Bengi Ece Kurtul (✉ becekurtul@yahoo.com)

Mustafa Kemal University Tayfur Ata Sokmen Faculty of Medicine, Hatay-Turkey

Ayşe Idil Cakmak

Mustafa Kemal University Tayfur Ata Sokmen Faculty of Medicine: Mustafa Kemal Universitesi Tayfur Ata Sokmen Tip Fakultesi

Cigdem El

Mustafa Kemal University Tayfur Ata Sokmen Faculty of Medicine: Mustafa Kemal Universitesi Tayfur Ata Sokmen Tip Fakultesi

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Abstract

Purpose

To investigate the optic disc and retinal microvasculature by optical coherence tomography angiography (OCTA) in children with asthma and compare them with healthy ones.

Methods

Sixty eyes of 30 asthmatic children (asthma group), 60 eyes of 30 control age- and sex- matched healthy subjects (control group) were included to this study, prospectively. Demographic features and ophthalmological examination including OCTA measurements were evaluated. The OCTA was performed with 6x6 mm sections for macula and 4.5x4.5 mm sections for optic disc in all eyes. Retinal nerve fiber layer (RNFL) thickness, vessel density in different sections of retina, and optic nerve head were analyzed.

Results

RNFL thickness for temporal quadrants and flow area for outer retina levels were significantly lower in asthma group. However, inside disc densities were significantly higher in asthma group when compared to controls ($72.58 \pm 10.99 \mu\text{m}$ vs $77.73 \pm 9.73 \mu\text{m}$, $p = 0.015$, $0.60 \pm 0.31 \text{ mm}^2$ vs $0.72 \pm 0.31 \text{ mm}^2$, $p = 0.047$, and $55.16 \pm 3.71\%$ vs $52.08 \pm 3.79\%$, $p < 0.001$, respectively).

Conclusions

Asthmatic children seem to have lower values of temporal quadrant RNFL, and flow area for outer retina, but higher levels of inside disc density. These results may have significant implications for understanding of how asthma could affect retinal microvasculature.

Introduction

Asthma is a common and chronic disease in children, involving airway inflammation, obstruction, hypoxia and hypercapnia, hyper responsiveness, and also requires long-term follow-up [1–3]. Allergen-specific type 2 CD4 + T-helper cells and related cytokines mediate the inflammatory process, and several cells, including eosinophils, mast cells, macrophages, and epithelial cells, play essential roles in the pathogenesis of asthma [1].

Optical coherence tomography angiography (OCTA) is a noninvasive tool that provides visualization of the microvascular structure of the retina, allowing the identification of the superficial retinal capillary plexus, the deep retinal capillary plexus, the choroid and the optic nerve head [4, 5]. Associated inflammatory cytokines and hypoxia initiate many pathways resulting in systemic effects of asthma. The

effects of obstructive sleep apnea syndrome and chronic obstructive pulmonary disease, chronic respiratory insufficiency on retina and choroidal microvasculature are already defined in the literature including chronic hypoxemia, systemic inflammation, vascular dysregulation, and increased sympathetic activity [6–10].

Given the role of inflammation and hypoxia in pathogenesis of asthma, we hypothesized that detection of dysfunction in retinal microvasculature by OCTA may be an useful marker in the follow up of these before the patients become symptomatic and moreover may be helpful for identification of early signs of decompensation stage in asthmatic children population. In addition, early detection, monitoring and selection of these patients for active treatment has a major importance before the severe retinal vascular changes regarding visual impairment occur. In this context, to the best of our knowledge, there is no study evaluating the association of asthma with retinal microvasculature. Therefore, we aimed to assess the retinal and optic disc microvasculature by OCTA in children with asthma, and compare with age- and sex-matched healthy children.

Subjects And Methods

This prospective cross-sectional study was performed at the ophthalmology department of our tertiary care facility, from February 2020 to December 2020. Thirty asthmatic children aged 6 to 17 years diagnosed according to GINA 2006 guidelines¹¹ (asthma group) and 30 age- and sex- matched healthy children (control group) who referred by our department of pediatrics to our ophthalmology outpatient clinic were enrolled, consecutively. The cohort was divided into two groups, with 60 eyes in the asthma group and 60 eyes in the control group. The asthma group was then divided into 2 subgroups according to presence of inhaled steroid use (flucitasone propionate 250 µg per day for at least one year). Exclusion criteria were refractive error of $\geq \pm 2.00$ diopters, amblyopia, history of intraocular surgery or trauma, conjunctivitis, corneal opacity or dystrophy, glaucoma, uveitis, contact lens use, and topical eye drops use. Children with acute exacerbations of asthma, diabetes mellitus, hypertension, dyslipidemia, any cardiovascular, renal, neurological, thyroid, mental or metabolic disorders, genetic syndromes and other inflammatory diseases except asthma, systemic steroid use were also excluded. Both eyes of all subjects underwent full ophthalmologic examination including best-corrected visual acuity, biomicroscopic anterior segment and fundus examination. Intraocular pressure (IOP) and central corneal thickness (CCT) measurements were assessed by noncontact tonometer.

The OCTA images were obtained by a single technician using a spectral-domain OCT system with the AngioVue OCTA software (Avanti RTVue-XR 100, OptovueInc, Fremont, CA). This device uses an increased A scan rate of 70 kHz, which allows the generation of high axial resolution of 5 µm in tissue. Volumetric angiograms were semi-automatically segmented into three layers allowing for separate angiograms of the inner retina, outer retina and choroid. The OCTA provides vascular information of retinal layers as an enface angiogram, a vessel density map and a vessel density percentage (%) calculated as the area covered by flowing blood vessels in the selected region. The OCTA image protocol involved two raster scans covering a 6x6 mm area centered on macula and 4.5x4.5 mm area centered in optic nerve head.

Foveal retinal thickness (FRT), retinal nerve fiber layer thickness (RNFL), vessel density in fovea of superficial and deep capillary plexus, 300 μm width around the foveal avascular zone (FAZ) were measured. FAZ was defined as the area without vessels that covers the center of the fovea. Fovea was defined as an annulus centered on the foveal avascular zone with inner and outer ring diameters of 1 mm. Flow areas of outer retina and choriocapillaris were also recorded. Radial peripapillary capillary densities were noted, too. Peripapillary border was described as a 700- μm wide elliptical annulus expanding from the optic disc region. OCTA scans with a quality level less than 8, artifacts or decentered were not used in the study.

For biochemical analysis, venous blood samples were obtained from the antecubital vein after fasting at least 8 h. The serum hemoglobin, serum total immunoglobulin E (IgE), total eosinophil counts, and C-reactive protein (CRP) levels were analyzed in asthma subgroups.

This study was carried out with the local Ethics Committee approval (2020/23). The research adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from all parents after explaining the nature and purpose of the study.

Statistical Analysis

All analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows (version 21.0, SPSS, Chicago, IL). All measurements taken from the both eyes of each subject were selected for the analysis. The normality of distribution of the continuous variables was determined using the Kolmogorov–Smirnov test, and non-normally distributed data were presented as median (inter quartile range, IQR). The distribution of all variables was found to be normal. Continuous variables were compared by Student's t-test and expressed as means $\pm$ standard deviation. Categorical variables were expressed as number and percentage, with differences between groups determined using the chi-squared test. A one-way ANOVA was used to compare the levels of the OCTA findings among the control group and asthma subgroups according to presence of steroid use. Subgroup analysis was interpreted with Bonferroni test. A two-tailed p value < 0.05 was considered as statistically significant.

Results

Baseline demographic characteristics and clinical data of the study population are summarized in Table 1. The mean ages were 12.57 ± 2.78 years for asthma group and 12.33 ± 2.98 years for control group ($p = 0.756$). BMI was $20.37 \pm 4.49 \text{ kg/m}^2$ in asthma group, and $19.70 \pm 3.26 \text{ kg/m}^2$ in control group ($p = 0.674$). Best corrected visual acuities were 20/20 in all study patients. Number of eyes with refractive errors ($\leq \pm 1.75$ Diopter) in asthma group were significantly higher than control group [20 (33.33%) vs 4 (6.66%), respectively, $p < 0.001$]. Gender rates, CCT values, and intraocular pressures were similar between the groups. RNFL thickness for temporal quadrants and flow area for outer retina levels were significantly lower in asthma group. However, optic disc radial peripapillary capillary inside disc densities were significantly higher in asthma group when compared to controls ($72.58 \pm 10.99 \mu\text{m}$ vs $77.73 \pm 9.73 \mu\text{m}$, $p =$

0.015, $0.60 \pm 0.31 \text{ mm}^2$ vs $0.72 \pm 0.31 \text{ mm}^2$, $p = 0.047$, and $55.16 \pm 3.71\%$ vs $52.08 \pm 3.79\%$, $p < 0.001$, respectively). (Fig. 1–4). The outcomes of retina and optic disc parameters by OCTA between groups are shown in Table 2, and Table 3, respectively.

Table 1
Comparison of demographic and clinical characteristics between the groups

Characteristics	Asthma Group n = 60 eyes	Control Group n = 60 eyes	P value
Number of subjects, n	30	30	
Age, years (Mean $\pm$ SD)	12.57 ± 2.78	12.33 ± 2.98	0.756
Gender, n (%)			
Female	11 (36.70)	15 (50.00)	0.297
Male	19 (63.30)	15 (50.00)	
Body mass index (kg/m^2) (Mean $\pm$ SD)	20.37 ± 4.49	19.70 ± 3.26	0.674
Central corneal thickness (μm) (Mean $\pm$ SD)	563.81 ± 25.14	559.84 ± 25.39	0.391
Intraocular pressure (mmHg) (Mean $\pm$ SD)	16.83 ± 2.34	17.78 ± 3.22	0.067
Number of eyes with refractive errors ($\leq \pm 1.75$ Diopter), n (%)	20 (33.33)	4 (6.66)	< 0.001
Duration of asthma (year) (Mean $\pm$ SD)	4.11 ± 3.00	-	
Foveal thickness (μm) (Mean $\pm$ SD)	240.74 ± 14.90	242.91 ± 16.67	0.457
SD: Standard deviation.			

Table 2
The outcomes of retina parameters by OCTA

	Asthma group (n = 60 eyes)	Control group (n = 60 eyes)	p
Superficial Vessel Density (%)			
Whole image	51.30 ± 2.42	51.74 ± 2.33	0.321
Fovea	22.06 ± 6.25	22.81 ± 6.96	0.540
Parafovea	54.60 ± 3.18	54.97 ± 2.37	0.471
Perifovea	51.81 ± 2.44	52.21 ± 2.28	0.364
Deep Vessel Density (%)			
Whole image	56.75 ± 5.04	55.80 ± 4.59	0.288
Fovea	39.15 ± 6.65	39.33 ± 8.60	0.902
Parafovea	59.84 ± 3.45	59.28 ± 3.19	0.363
Perifovea	58.24 ± 5.51	57.36 ± 4.83	0.358
FAZ area (mm ²)	0.28 ± 0.09	0.27 ± 0.142	0.795
FAZ, FD (%)	56.42 ± 3.81	56.68 ± 3.36	0.689
Flow area for outer retina (mm ²)	0.60 ± 0.31	0.72 ± 0.31	0.047
Flow area for choriocapillaris (mm ²)	2.24 ± 0.88	2.22 ± 0.10	0.133
OCTA: optical coherence tomography angiography, FRT: foveal retinal thickness, FAZ: area of 300 µm width around the foveal avascular zone, SD:standard deviation			

Table 3
The outcomes of optic disc parameters by OCTA

	Asthma Group n = 60 eyes	Control Group n = 60 eyes	p
RNFL thickness (μm) (Mean ± SD)	110.96 ± 25.81	117.80 ± 26.59	0.192
Inferior quadrant (μm)	146.85 ± 21.77	145.52 ± 35.78	0.817
Superior quadrant (μm)	137.01 ± 22.17	146.15 ± 32.23	0.094
Temporal quadrant (μm)	72.58 ± 10.99	77.73 ± 9.73	0.015
Nasal quadrant (μm)	104.82 ± 21.95	105.95 ± 33.71	0.838
RPC density (%) (Mean ± SD)			
Whole image	49.76 ± 1.91	49.03 ± 2.72	0.111
Inside disc	55.16 ± 3.71	52.08 ± 3.79	<0.001
Peripapillary	50.90 ± 2.70	50.37 ± 3.10	0.359
OCTA: optical coherence tomography angiography, RNFL: retinal nerve fiber layer, RPC: radial peripapillary capillary, SD:standard deviation			

There was no statistically significant difference regarding Ig E, eosinophil, and CRP values between asthma subgroups according to presence of steroid use. The outcomes and comparison of clinical and laboratory parameters between asthma subgroups according to presence of steroid use are shown in Table 4, and Table 5, respectively. CCT values were significantly decreased in asthma without steroid use subgroup when compare to with steroid use subgroup and control group ($p = 0.006$). The mean RNFL thickness for temporal quadrants was significantly lower, flow area for outer retina and peripapillary capillary inside disc densities were significantly higher in patients without steroid use group when compared to others ($p = 0.012$, $p = 0.036$, $p < 0.001$, respectively). The outcomes clinical parameters and macular and optic disc parameters by OCTA among groups are shown in **Table 6**, and Table 7, respectively.

Table 4

The outcomes clinical and laboratory parameters between asthma subgroups according to presence of steroid use

	Asthma subgroup Steroid (+) (n = 34 eyes)	Asthma subgroup Steroid (–) (n = 26 eyes)	p
Duration of asthma (years)	2.00 (1.50–6.00)	4.00 (2.00–6.00)	0.371
Central corneal thickness (μm) (Mean ± SD)	555.08 ± 25.06	575.23 ± 20.58	0.002
Intraocular pressure (mmHg) (Mean ± SD)	16.46 ± 1.94	17.30 ± 2.75	0.171
Foveal thickness (μm) (Mean ± SD)	240.11 ± 12.47	241.62 ± 18.04	0.708
RNFL thickness (μm) (Mean ± SD)	109.67 ± 31.06	112.95 ± 14.92	0.647
Inferior quadrant (μm)	149.91 ± 23.98	142.13 ± 17.30	0.195
Superior quadrant (μm)	136.67 ± 24.59	137.54 ± 18.35	0.888
Temporal quadrant (μm)	74.50 ± 12.66	69.63 ± 7.02	0.106
Nasal quadrant (μm)	104.64 ± 19.45	105.09 ± 25.84	0.942
C-reactive protein (mg/L) Meadian (interquartile range)	3.11 (3.02–3.30)	3.30 (3.14–11.60)	0.070
Immunoglobulin E Meadian (interquartile range)	207.00 (32.40–1050.00)	258.00 (113.00–611.00)	0.806
Hemoglobin (g/dL)	13.24± 0.95	13.90± 1.40	0.165
Eosinophil count (%) Meadian (interquartile range)	3.20 (1.10–7.90)	3.20 (2.50–5.80)	0.979
RNFL: retinal nerve fiber layer, SD:standard deviation			

Table 5

The outcomes of macular and optic disc parameters between asthma subgroups by OCTA according to presence of steroid use

	Asthma subgroup Steroid (+) (n = 34 eyes)	Asthma subgroup Steroid (-) (n = 26 eyes)	p
Superficial Vessel Density (%)			
Whole image	51.62 ± 2.54	50.85 ± 2.22	0.238
Fovea	22.47 ± 6.07	21.49 ± 6.59	0.559
Parafovea	54.63 ± 3.64	54.54 ± 2.46	0.914
Perifovea	52.12 ± 2.55	51.38 ± 2.27	0.263
Deep Vessel Density (%)			
Whole image	56.67 ± 5.58	56.85 ± 4.28	0.898
Fovea	38.88 ± 5.93	39.53 ± 7.67	0.718
Parafovea	59.83 ± 3.81	59.85 ± 2.94	0.986
Perifovea	58.06 ± 6.16	58.50 ± 4.56	0.772
FAZ area (mm ²)	0.27 ± 0.07	0.28 ± 0.11	0.863
FAZ, FD (%)	56.22 ± 3.93	56.70 ± 3.70	0.643
Flow area for outer retina (mm ²)	0.63 ± 0.37	0.56 ± 0.20	0.439
Flow area for choriocapillaris (mm ²)	2.23 ± 0.12	2.28 ± 0.07	0.061
RPC density (%) (Mean ± SD)			
Whole image	50.02 ± 1.73	49.38 ± 2.13	0.255
Inside disc	54.94 ± 4.19	55.51 ± 2.87	0.580
Peripapillary	51.31 ± 2.23	50.28 ± 3.27	0.167
OCTA: optical coherence tomography angiography, FRT: foveal retinal thickness, FAZ: area of 300 µm width around the foveal avascular zone, RNFL: retinal nerve fiber layer, RPC: radial peripapillary capillary, SD: standard deviation			

Table 6. The outcomes clinical parameters among subgroups

	Asthma subgroup Steroid (+) (n = 34 eyes)	Asthma subgroup Steroid (–) (n = 26 eyes)	Control Group (n = 60 eyes)	p
Central corneal thickness (μm) (Mean ± SD)	555.08 ± 25.06*	575.23 ± 20.58* ^Δ	559.84 ± 25.39 ^Δ	0.006
Intraocular pressure (mmHg) (Mean ± SD)	16.46 ± 1.94	17.30 ± 2.75	17.78 ± 3.22	0.098
Foveal thickness (μm) (Mean ± SD)	240.11 ± 12.47	241.62 ± 18.04	242.91 ± 16.67	0.713
RNFL thickness (μm) (Mean ± SD)	109.67 ± 31.06	112.95 ± 14.92	117.80 ± 26.59	0.387
Inferior quadrant (μm)	149.91 ± 23.98	142.13 ± 17.30	145.52 ± 35.78	0.603
Superior quadrant (μm)	136.67 ± 24.59	137.54 ± 18.35	146.15 ± 32.23	0.247
Temporal quadrant (μm)	74.50 ± 12.66	69.63 ± 7.02 [▲]	77.73 ± 9.73 [▲]	0.012
Nasal quadrant (μm)	104.64 ± 19.45	105.09 ± 25.84	105.95 ± 33.71	0.973
RNFL: retinal nerve fiber layer, SD: standard deviation				
*p = 0.006, ^Δ p = 0.024				

[▲] p = 0.01

Table 7
The outcomes of macular and optic disc parameters among groups by OCTA

	Asthma subgroup Steroid (+) (n = 34 eyes)	Asthma subgroup Steroid (-) (n = 26 eyes)	Control Group (n = 60 eyes)	p
Superficial Vessel Density (%)				
Whole image	51.62 ± 2.54	50.85 ± 2.22	51.74 ± 2.33	0.294
Fovea	22.47 ± 6.07	21.49 ± 6.59	22.81 ± 6.96	0.711
Parafovea	54.63 ± 3.64	54.54 ± 2.46	54.97 ± 2.37	0.766
Perifovea	52.12 ± 2.55	51.38 ± 2.27	52.21 ± 2.28	0.337
Deep Vessel Density (%)				
Whole image	56.67 ± 5.58	56.85 ± 4.28	55.80 ± 4.59	0.565
Fovea	38.88 ± 5.93	39.53 ± 7.67	39.33 ± 8.60	0.945
Parafovea	59.83 ± 3.81	59.85 ± 2.94	59.28 ± 3.19	0.662
Perifovea	58.06 ± 6.16	58.50 ± 4.56	57.36 ± 4.83	0.626
FAZ area (mm ²)	0.27 ± 0.07	0.28 ± 0.11	0.27 ± 0.142	0.957
FAZ, FD (%)	56.22 ± 3.93	56.70 ± 3.70	56.68 ± 3.36	0.816
Flow area for outer retina (mm ²)	0.63 ± 0.37	0.56 ± 0.20	0.72 ± 0.31	0.104
Flow area for choriocapillaris (mm ²)	2.23 ± 0.12	2.28 ± 0.07*	2.22 ± 0.10*	0.036
RPC density (%) (Mean ± SD)				
Whole image	50.02 ± 1.73	49.38 ± 2.13	49.03 ± 2.72	0.171
Inside disc	54.94 ± 4.19▲	55.51 ± 2.87 ^Δ	52.08 ± 3.79 ^Δ ▲	< 0.001
* p = 0.037				
^Δ p = 0.002 ▲ p = 0.003				

	Asthma subgroup Steroid (+) (n = 34 eyes)	Asthma subgroup Steroid (-) (n = 26 eyes)	Control Group (n = 60 eyes)	p
Peripapillary	51.31 ± 2.23	50.28 ± 3.27	50.37 ± 3.10	0.283
OCTA: optical coherence tomography angiography, FRT: foveal retinal thickness, FAZ: area of 300 µm width around the foveal avascular zone, RNFL: retinal nerve fiber layer, RPC: radial peripapillary capillary, SD: standard deviation				
* p = 0.037				
Δ p = 0.002 ▲ p = 0.003				

Discussion

To the best of our knowledge, this is the first study evaluating the association of asthma with retinal and optic disc microvasculature by OCTA in children population. We have found lower values of temporal quadrant RNFL, and flow area for outer retina, but higher levels of inside disc density in asthmatic children when compared with controls.

Abnormalities in ocular blood flow (e.g., increased resistance), systemic inflammation, increase in endothelin-like systemic vasoconstrictor levels, and nocturnal hypoxia resulting in neuronal damage over the axons are proposed mechanisms of the progressive RNFL loss. This may be a possible result of chronic hypoxia and systemic inflammation triggered by the disease, cytokine release, and disturbed oxidant/antioxidant balance. In our study, significant lower values of temporal quadrant RNFL, and flow area for outer retina variables were found in asthma group when compared to controls. Nevertheless, significant elevated values of inside disc density were seen in asthmatic children than controls in our study. When the inflammation and inadequate delivery of oxygen occur, blood vessels dilate themselves [9]. Therefore, retinal-vascular changes may be the result of these conditions.

Macular microvascular measurements in healthy pediatric individuals using OCTA analysis was reported previously [12]. Studies demonstrated that several variables such as age, sex, and amblyopia could influence the density of retinal and choroidal capillary plexuses [12, 13]. In diabetic children without diabetic retinopathy, enlargement of the FAZ area detected by OCTA was reported [14]. In another study, when compared to healthy ones, no significant change regarding OCTA findings was found in children with type 1 diabetes [14, 15]. Veronese et al. [16] mentioned that OCTA was capable of evaluating and characterizing pediatric choroidal neovascularization and their associated vascular patterns. The OCTA enables clear visualization of progressive impairment of the retinal vascular perfusion in children also with acute events such as retinal artery occlusion and may be an alternative to the standard fluorescein angiography [17].

It is known that there may be changes in the retinal and optic disc vascular structure in many ocular and systemic diseases such as choroidal neovascularization, diabetes, and retinopathy of prematurity in which inflammation plays a role in the etiology [14, 16, 18]. Decreased retinal microvascular patterns in children with diabetes [14], and retinopathy of prematurity [19] was reported. Despite recent advances in pharmacological treatment and standardized management guidelines, asthma continues to cause significant morbidity in children. There are several clinical studies regarding ocular findings in patients with asthma [20–26]. Most of them were about intranasal or inhaled corticosteroid use in asthmatic children, and the results were controversial. In a study, lower RNFL levels were found under steroid use. In contrast to this study Dereci et al. [20] reported that asthmatic children with inhaled fluticasone propionate have similar peripapillary RNFL measurements compared to controls. Jhonson et al. [23] did not find a significant effect on CCT and IOP by using inhaled fluticasone at the regular dose used over a short period (6–24 months) in asthmatic children. In our study, significant lower values of temporal quadrant RNFL, and elevated CCT levels were found in asthmatic children without inhaled steroid use when compared with asthmatic children with steroid use and controls. However, IOP were not significant among the groups. This means that the reduction in RNFL and higher levels of CCT are not due to inhaled steroids but to hypoxia and inflammation in the pathogenesis of asthma. Arjamaa et al. [27] reported that hypoxia in human retinal pigment epithelial cells leads to release of vascular endothelial growth factor followed by a strong inflammatory reaction by the secretions of IL-6 and IL-8. Vascular remodeling in asthma results from increased angiogenesis, which is mainly mediated by vascular endothelial growth factor [28–30]. Flow areas for choriocapillaris in asthma patients with steroid use and controls were similarly low. It may be due to the anti-inflammatory properties of steroids such as reducing mediator release, and inhibiting angiogenesis effect of them [30–31].

There are some study limitations. Firstly, the study has relatively small number of patients. Secondly, we could not measure the axial lengths of patients which could affect the results, but in children population it is hard to apply such ocular examinations by various ophthalmic devices. Finally, numbers of eyes with refractive errors in asthma group were significantly higher than control group, but these refraction errors were $\leq \pm 1.75$ Diopter. Therefore, we thought that it would not affect the outcomes.

Air way inflammation, obstruction and hypoxia are thought to be the underlying mechanism in asthma, which may influence retinal OCTA parameters. Decrease in vascular densities in macula and optic nerve head may affect the visual ability in these children, which should be kept in mind during their follow-up. It is necessary to provide monitoring these patients and to prescribe proper therapeutic treatment in order to preserve visual functions. Therefore, children who are defined as asthmatic children in pediatric clinics should have eye examinations before severe retinal alterations develop. In the light of our study, it is evident that children with asthma should be evaluated in more details in terms of accompanying retinal microvascular pathologies that appear as a result of systemic inflammation and hypoxemia.

In conclusion, lower values of temporal quadrant RNFL, and flow area for outer retina, but higher levels of inside disc density by OCTA can be seen in children with asthma. These results may shed light on understanding of how asthma could affect retinal microvasculature. Therefore, we suggest that

pediatricians and ophthalmologists should keep in mind the impact of asthma on retinal microvasculature while examination of these children. To confirm our results, new randomized- and larger-sized controlled further trials on the correlation of asthma and OCTA measurements; and the effects of the chronic inflammation and hypoxic status of asthmatic patients on ocular tissues should be carried on in the future.

Declarations

Conflict of Interest

No conflict of interest was declared by the authors.

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The authors declared that this study received no funding.

Contributions

AK, BEK, AIC, CE—conception or design of the work; the acquisition, analysis, interpretation of data, AK, BEK, AIC, CE —drafted the work or revised it critically for important intellectual content. AK, BEK, AIC, CE — Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data availability

All data are included in this paper.

Compliance with Ethical Standards:

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

This article does not contain any studies with animals performed by any of the authors.

All authors approved the version to be published.

Informed consent: Informed consent was obtained from all individual participants included into the study.

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Figures

Figure 1

Optical coherence tomography angiography retinal image of a 14 year-old-female patient with asthma.

Figure 2

Optical coherence tomography angiography retinal image of a 14 years old female healthy control subject.

Figure 3

Optical coherence tomography angiography optic disc image of a 14 year-old-female patient with asthma.

Figure 4

Optical coherence tomography angiography optic disc image of a 14 years old female healthy control subject.