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Choroidal thickness in juvenile open angle glaucoma: insights from a south asian case–control study

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Abstract

Purpose The purpose of this study is to compare choroidal thickness in juvenile open angle glaucoma (JOAG) and healthy controls using spectral domain optical coherence tomography (SD-OCT) and study its correlations.

Methods In this case–control study, 56 eyes of 28 JOAG patients and an equal number of controls were recruited. SD-OCT was used to measure the *choroidal thickness* (ChT), in the *macular region* at 5 locations: subfoveal, 1500 µm and 3000 µm nasal and temporal to the foveal center, and in the *peripapillary region* at 6 locations: up to 1500 µm, nasal and temporal to the disc, respectively. The ChT and its correlations with age, intraocular pressure, cup-to-disc ratio, central corneal thickness, mean deviation, and axial length were studied.

Results The average macular ChT in JOAG was 306.30 ± 56.49 µm vs. 277.12 ± 64.68 µm in controls. The average peripapillary ChT in JOAG was 197.79 ± 44.05 µm vs. 187.24 ± 38.89 µm in controls. The average total ChT ($p = 0.042$), the average macular ChT ($p = 0.022$), the subfoveal ChT ($p = 0.022$), the ChT 1500 µm ($p < 0.001$), and 3000 µm temporal to the fovea ($p = 0.002$) were significantly thicker in the JOAG group. In the JOAG group, the average macular ChT had a significant negative correlation with age, whereas axial length was positively correlated with the average peripapillary ChT.

Conclusions In this South Asian cohort of JOAG, the average total ChT, average macular ChT, subfoveal ChT, and ChT at 1500 µm, and 3000 µm temporal to the fovea were significantly thicker when compared to healthy controls.

Key messages

What is known:

- Research indicates that the choroid, which has a high blood flow rate, may play a role in glaucoma development and progression. Understanding the relationship between macular and peripapillary choroidal circulation and glaucomatous optic neuropathy is crucial but debated.
- There is a scarcity of studies examining the relationship between juvenile open angle glaucoma (JOAG) and the choroid.

What is new:

- This novel study focused on a South Asian JOAG cohort, highlighting that choroidal thickness in the subfoveal region, temporal macula, average macular, and overall, was significantly elevated in the JOAG group when contrasted with healthy controls.

Keywords Choroid · Choroidal thickness · Imaging · Juvenile open-angle glaucoma · JOAG · Optical coherence tomography

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Introduction

Juvenile open angle glaucoma (JOAG) is a rare disorder diagnosed between the ages of 3 and 40 years [1–3]. It is believed to occur as a result of the immaturity of outflow pathways (angle dysgenesis) and is usually inherited as an autosomal dominant trait with mutations in the myocilin protein [4–6]. Intraocular pressure (IOP) is usually high, with medical therapy frequently insufficient and requiring surgery[7–9].

The maximum blood flow per mass of tissue in the human body is found in the choroid [10–12]. The vulnerability of the peripapillary choroidal circulation to IOP rise has been studied with conflicting findings; however, fluorescein angiography studies in normal tension, ocular hypertension, and open angle glaucoma has revealed perfusion abnormalities of the optic nerve head, choroid, and retina, impaired ocular blood flow, filling defects, and delays in peripapillary choroidal filling, which may contribute to glaucomatous optic neuropathy [10–15]. Ocular blood flow is an elaborate and complicated network involving the retinal, choroidal, and retrobulbar vasculature [10]. There is evidence that choroidal thickness (ChT) and circulation are involved in glaucoma pathogenesis and may be compromised in chronic open angle glaucomas [11, 12]. In angle closure subjects, the choroid is thicker, and in primary open angle glaucomas, it is not significantly thinner or thicker when compared with healthy controls [11, 12] It is questionable whether the process of open angle glaucoma largely affects or involves blood perfusion in the choriocapillaris and if ChT is a reliable additional diagnostic biomarker in glaucoma pathogenesis. Optical coherence tomography (OCT) allows for a quantitative assessment of the choroid, which may be combined with a qualitative and functional assessment to provide assistance in glaucoma management. Choroidal thickness has not been studied in JOAG. Since there are conflicting results and the relationship is unclear, further studies on glaucoma pathomechanisms are warranted.

The rationale of this study is to compare ChT between JOAG and age-, gender-, central corneal thickness (CCT)-, and axial-length (AL)-matched controls and to observe any differences and correlations with other parameters.

Methods

Study design: A cross-sectional case–control study.

Recruitment

Inclusion criteria were patients younger than 40 years of age diagnosed with JOAG [56 eyes of 28 patients] who were recruited from 1st August, 2021 to 31st July, 2022, with convenience sampling after a comprehensive eye exam including visual acuity, refraction, Goldmann tonometry, gonioscopy, slit lamp exam, fundus evaluation, pachymetry, optical coherence tomography of the optic disc, nerve fiber layer assessment and ganglion cell complex thickness evaluation and SITA-standard central 24–2 perimetry (Humphrey visual field analyser Model 720, Carl Zeiss® Meditex Dublin, CA, USA). JOAG was diagnosed on the basis of an open angle on gonioscopy, glaucomatous optic disc changes, raised intraocular pressure or visual field defects on Humphrey perimetry central 24–2 with reliable indices. Other causes of possible glaucoma like secondary glaucoma, previous glaucomatous damage, steroid usage, uveitis, trauma, angle closure was excluded out on the basis of history and examination. These JOAG subjects were included at first presentation to the clinic at the stage of diagnosis, before topical medication was started; which was done after perimetry and OCT imaging. Inclusion criteria for healthy controls (56 eyes of 28 subjects) (age, gender, CCT, and axial length-matched ($p > 0.05$)) was best-corrected Snellen visual acuity of 6/6 (LogMAR 0.0), normal anterior segments, intraocular pressure (IOP) ≤ 21 mm Hg, healthy, perfused optic discs and no retinal pathology. Controls were recruited from the OPD after a thorough eye exam, and then pachymetry, axial length measurement, and OCT scans were performed. Systemic diseases were excluded as well on the basis of history. Informed consent was taken from the participants as well as controls. The study was approved by the Ethical Review Committee of Fauji Foundation Hospital, Rawalpindi, Pakistan [492/RC/FFH/RWP], which is according to the Declaration of Helsinki.

Ophthalmic examination

The examination protocol followed for every case included slit lamp biomicroscopy (Takagi Slit lamp microscope SM-10N®) with fundus assessment (Volk Superfield® lens), Goldmann applanation tonometry (Haag-Streit®), and Posner 4-mirror gonioscopy (Ocular®). Quantel Medical® Axis- II PR France A-scan was used to calculate axial length (AL) via the contact method [11 MHz], optical pachymetry, and then optical coherence tomography of the optic nerve head and macula were done with SOCT Copernicus REVO80® SD-OCT (Optopol Technology, Software Version 10.0.1, Poland) (840 nm superluminescent diode source, transverse resolution of 12 µm, axial resolution of 5 µm, and 80 000 A-scan/sec scanning speed).

Choroidal thickness measurement

The subjects were explained the OCT examination procedure that it was a chin and forehead mounted, non-contact

device and that they need to look into the lens and focus on the internal fixation target and blink freely. They were asked to hold still while the images were captured manually, taking care to prevent motion, blink, or other errors in examination. The *chorioretinal setting* of the OCT was used for clear visualization of the choroid. For peripapillary choroid assessment, a horizontal *7 X 7 mm 3D macular scan* was taken centred at the fovea with a scan angle set to 0°, and a *horizontal 6 X 6 mm 3D optic disc scan* was taken using an internal fixation target. For the macular choroid evaluation, a 7 × 7 mm macular 3D scan was taken separately. All images were manually captured ensuring a *quality index (QI)* ≥ 7 without any errors or artefacts. To reduce diurnal variability, all measurements were made between 9:00 am and 12:00 noon. A single skilled observer performed the ChT analysis twice in the macular region. For *macular choroidal thickness*, the vertical distance between the hyper-reflective lines corresponding to the retinal pigment epithelium and the sclera-choroidal junction were measured *manually* with a '*line measuring tool'* to determine the ChT. Each eye underwent a total of five measurements at the foveal centre, nasally and temporally, 1500 µm, and 3000 µm from the foveal center, also measured manually with the *line measuring tool*. (Fig. 1) The *peripapillary choroidal thickness* was measured twice with the line measurement tool, nasally & temporally, 500 µm, 1000 µm, and 1500 µm from the Bruch's membrane opening (BMO), identified manually in every case. (Fig. 2) The choroidal thickness measurement has been detailed in a previous study [16].

Statistical analysis

The data was analysed using *IBM SPSS statistics version 20*. For the variables, frequencies, means, and standard deviations were computed for the descriptive data. Both eyes were included in the data which was entered as within subjects' fashion. The average macular ChT, the average peripapillary ChT, the average total ChT, retinal nerve fiber layer (RNFL) thickness in four quadrants and on average, the average and sectoral ganglion cell complex (GCC) thickness were computed via SPSS. The paired t-tests were used to compare means between the JOAG group and controls. The means of the variables were compared across genders and between the two eyes using the independent t-tests. The correlation between the variables was evaluated using Pearson's correlation coefficient and linear regression analysis. A p-value of 0.05 or lower was regarded as significant. The missing data analysis was done for the

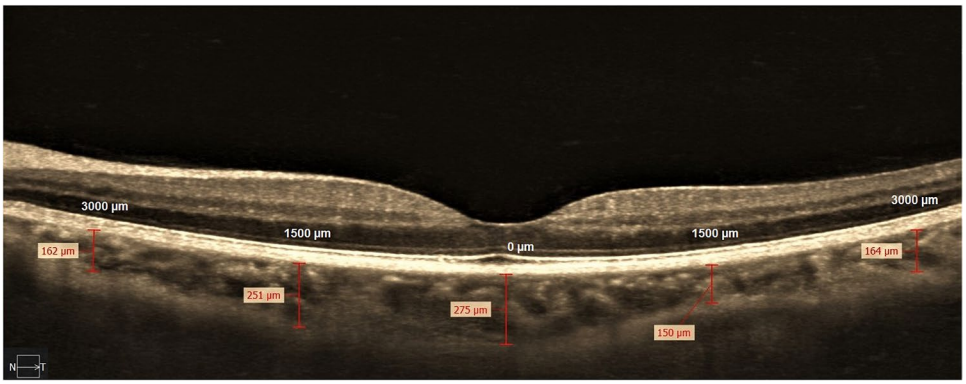

Fig. 1 Shows the choroidal thickness measurement at the macula up to 3000 µm from the fovea

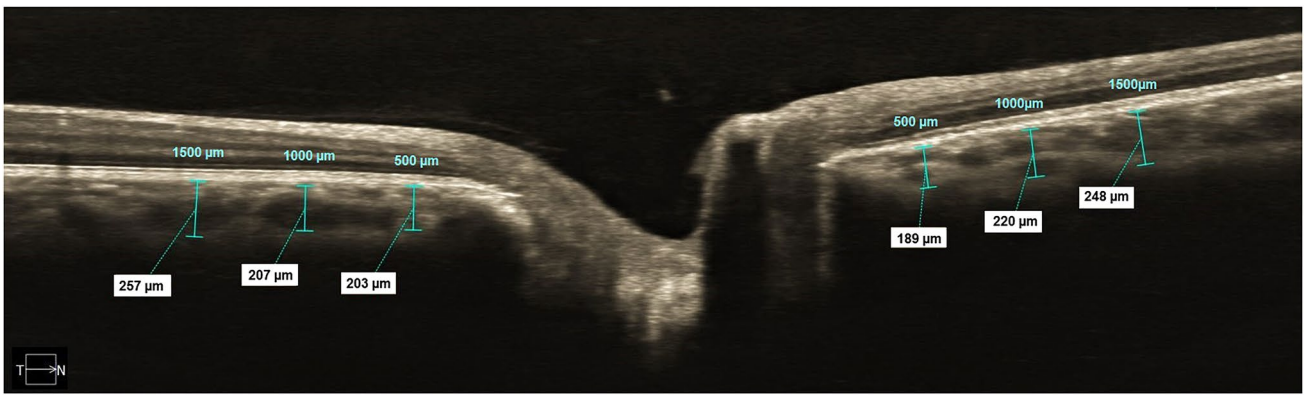

Fig. 2 Shows the peripapillary choroidal thickness measurements up to 1500 µm from the BMO. BMO: Bruch's membrane opening

JOAG group. Regression based imputation was used for the missing data.

Results

Mean age of the participants in the JOAG group was 20.79 ± 8.68 years [Range 8–38 years]. The majority were female in 20 cases (71.4%) and the rest were males; 8 (28.6%). The mean subfoveal ChT in the JOAG group was 380.09 ± 71.64 µm vs. 344.71 ± 82.72 µm in the control group ($p = 0.022$). The average macular ChT in the JOAG group was 306.30 ± 56.49 µm vs. 277.12 ± 64.68 µm in the control group ($p = 0.022$). The average peripapillary ChT in the JOAG group was 197.79 ± 44.05 µm vs. 187.24 ± 38.89 µm in the control group ($p = 0.232$). The average total ChT in the JOAG group was 247.11 ± 40.02 µm vs. 228.09 ± 45.55 µm in the control group ($p = 0.042$). The choroid was observed to be thicker in the JOAG group in all locations except 3000 µm nasal to the fovea. ChT was significantly more in the JOAG group at the subfoveal location, 1500 µm & 3000 µm temporal to the fovea, at an average at the macula, and at an average total ($p < 0.05$). Figure 3 displays total choroidal thickness, average macular choroidal thickness, and peripapillary choroidal thickness between JOAG and healthy controls.

Table 1 depicts the baseline characteristics, macular and peripapillary ChT and paired differences between the two groups.

The average and inferior RNFL thickness were significantly less in the JOAG group ($p < 0.05$). The sectoral and average RNFL thickness in the two groups are displayed in Table 2.

The sectoral GCC was compared between the two groups in 6 locations; superior, superonasal, superotemporal, inferior, inferonasal, inferotemporal, and on average and was found to be significantly less in the JOAG group in all locations ($p < 0.001$), shown in Table 3. Figure 4 displays the average RNFL and GCC thicknesses of the two groups.

All the variables were analysed for correlation with the Pearson's correlation coefficient and linear regression analysis. The subfoveal ChT (r = -0.367 $p = 0.005$) and average macular ChT were significantly negatively correlated with age (r = -0.364 $p = 0.006$). The average peripapillary ChT was positively correlated with axial length (r = 0.268 $p = 0.046$).

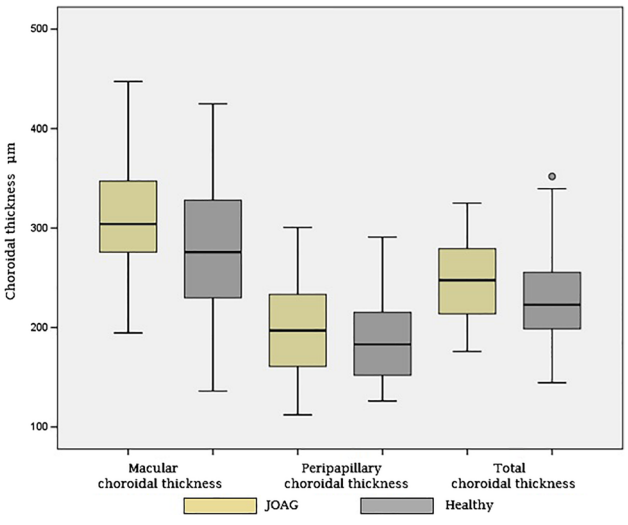

Fig. 3 Depicting box plots of total choroidal thickness, average macular choroidal thickness, and peripapillary choroidal thickness between JOAG and healthy controls JOAG: juvenile open angle glaucoma

Discussion

Glaucoma is a multifaceted optic neuropathy, characterized by neurodegeneration of retinal ganglion cells, retinal nerve fiber layer thinning, optic nerve head changes, and a controversial mechanism of damage. Its genesis, progression, and visual field loss have also been linked to the *choroid*, in addition to other known factors like IOP, age, family history, genetics, myopia, vascular dysregulation, blood pressure, and CSF pressure, according to research conducted previously. [12, 17–21]

Role of choroid in glaucoma pathogenesis

Amongst all the vascular beds in the human body, the choroid has the highest perfusion rate with a blood flow rate of 1400 mL/min per 100 g tissue [17–21]. The choroidal vasculature is responsible for about 70–80% of the ocular blood flow (OBF) [17–21]. Neurohumoral and local processes are used to autoregulate the choroidal blood flow (ChBF). Although, ChBF remains stable over a high range of ocular perfusion pressure (OPP), it is thought to have impaired autoregulation in glaucomatous eyes. Vascular factors may be responsible for glaucoma pathogenesis. Hence, the choroid merits being thought of as a prospective participant. The peripapillary region appears to be impacted by the choroidal vasculature, and the choroid may affect IOP modulation in open angle glaucoma [14, 22–24]. The uveoscleral outflow occurs into the supraciliary and suprachoroidal space and may also be affected by the choroid. Aqueous has direct access from the anterior chamber to the ciliary muscle's interstitial spaces, and from there to the supraciliary and suprachoroidal regions, as there is no continuous cellular layer on the anterior iris face. There is ongoing debate on the method by which fluid from the supraciliary and suprachoroidal areas leaves the eye: either by diffusion or by osmotic

Table 1 Characteristics of JOAG and controls

JOAG group (56 eyes)				Characteristics	Control group (56 eyes)				*P* value
Mean	Std Deviation	Minimum	Maximum		Mean	Std Deviation	Minimum	Maximum	
20.79	8.68	8	38	Age in years	20.07	8.54	8.00	37.00	0.504
20.18	6.526	11	37	IOP (mm Hg)	14.50	2.68	10.00	21.00	0.000
533.53	40.49	422	640	CCT (µm)	529.04	26.23	478.00	589.00	0.483
0.56	0.20	0.20	0.90	CDR	0.36	0.16	0.10	0.70	0.000
-8.66	10.46	-35.39	2.63	Mean deviation (dB)	-	-	-	-	-
23.31	0.95	21.13	25.20	Axial Length (mm)	23.08	0.69	21.58	24.22	0.083
				Macular choroidal thickness					
380.09	71.64	205.00	528.00	*Sub-foveal choroidal thickness (µm)*	344.71	82.72	142.00	519.00	0.022*
308.73	62.87	157.00	413.00	*1500 µm nasal to fovea (µm)*	291.86	76.08	147.00	483.00	0.265
216.21	61.70	104.00	355.00	*3000 µm nasal to fovea (µm)*	242.28	85.18	97.00	386.00	0.105
336.34	75.08	150.00	546.00	*1500 µm temporal to fovea (µm)*	257.12	80.98	118.00	442.00	0.000*
290.12	69.78	147.00	487.00	*3000 µm temporal to fovea (µm)*	251.41	66.04	106.00	379.00	0.002*
				Peripapillary choroidal thickness					
161.95	55.86	54.00	265.00	*500 µm nasal to disc (µm)*	146.00	42.46	77.00	251.00	0.108
192.32	55.69	69.00	295.00	*1000 µm nasal to disc (µm)*	184.66	51.54	81.00	335.00	0.510
208.84	54.45	84.00	326.00	*1500 µm nasal to disc (µm)*	206.52	64.24	85.00	369.00	0.859
170.64	54.54	85.00	285.00	*500 µm temporal to disc (µm)*	155.37	43.76	77.00	263.00	0.119
212.73	49.47	117.00	329.00	*1000 µm temporal to disc (µm)*	203.77	46.02	115.00	297.00	0.330
240.53	49.29	150.00	354.00	*1500 µm temporal to disc (µm)*	227.12	54.79	134.00	362.00	0.175
306.30	56.49	194.60	447.40	*Average Macular ChT*	277.12	64.68	136.00	425.00	0.022*
197.79	44.05	112.17	300.67	*Average PP ChT*	187.24	38.89	126.17	291.00	0.232
247.11	40.02	175.91	325.00	*Average total ChT*	228.09	45.55	144.55	351.91	0.042*

* Significant p value

Table 2 RNFL characteristics of JOAG and controls RNFL: retinal nerve fiber layer thickness

JOAG group (56 eyes)				RNFL thickness	Control group (56 eyes)				*P* value
Mean	Std Deviation	Minimum	Maximum		Mean	Std Deviation	Minimum	Maximum	
131.43	20.28	93.00	176.00	*RNFL Inferior (µm)*	139.84	20.78	91.00	176.00	0.049*
128.73	16.43	90.00	158.00	*RNFL Superior (µm)*	135.8	19.44	81.00	173.00	0.052
97.32	13.93	67.00	129.00	*RNFL Nasal (µm)*	95.71	14.49	69.00	133.00	0.505
74.03	11.75	56.00	106.00	*RNFL Temporal (µm)*	75.53	11.74	55.00	115.00	0.462
108.28	12.19	85.00	131.00	*RNFL Average (µm)*	116.69	13.10	88.00	142.00	0.001*

* Significant p value

absorption by the choroid and then into the vortex veins [14, 22–24]. Being a dynamic tissue, the ChBF can be directly impacted by a number of variables, including OPP, blood pressure, IOP, and even emotional and stress levels. While measuring choroidal characteristics, the circadian cycle and other relevant physiologic elements should be taken into account. It is crucial to understand how the macular and peripapillary choroidal circulation and glaucomatous optic neuropathy (GON) are related [25–29].

Conflicting reports on choroid status in open angle glaucoma

There have been conflicting reports on the status of the choroid in primary open angle glaucoma (POAG) with laser doppler flowmetry suggesting reduced choroidal perfusion [30]. In the Leuven Eye Study, which is the largest clinical trial on blood flow in glaucoma utilizing retinal oximetry, dynamic contour tonometry, enhanced-depth

Table 3 GCC characteristics of JOAG and controls GCC: ganglion cell complex

JOAG group (56 eyes)				GCC thickness	Control group (56 eyes)				*P* value
Mean	Std Deviation	Minimum	Maximum		Mean	Std Deviation	Minimum	Maximum	
110.12	7.74	93.00	127.00	*GCC Superior (µm)*	117.46	9.24	99.00	137.00	0.000*
115.03	7.78	100.00	130.00	*GCC Superonasal (µm)*	121.23	8.57	107.00	142.00	0.001*
98.23	6.23	85.00	108.00	*GCC Superotemporal (µm)*	104.28	7.86	87.00	124.00	0.000*
109.68	8.39	84.00	121.00	*GCC Inferonasal (µm)*	117.09	9.17	96.00	136.00	0.000*
114.02	7.64	99.00	127.00	*GCC Inferior (µm)*	121.03	9.09	102.00	143.00	0.000*
99.96	6.47	84.00	112.00	*GCC Inferotemporal (µm)*	106.38	7.91	88.00	125.00	0.000*
107.62	6.80	93.00	118.00	*GCC Average (µm)*	114.32	8.28	97.00	134.00	0.000*

* Significant p value

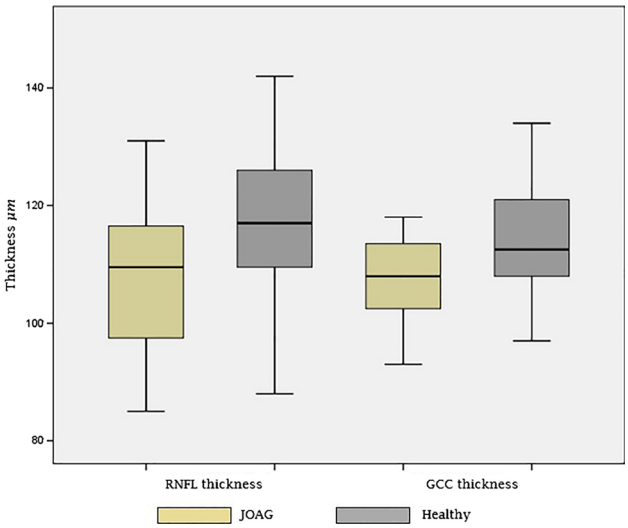

Fig. 4 Is a boxplot of average RNFL and GCC thickness between the two groups RNFL: retinal nerve fiber layer GCC: ganglion cell complex

OCT, and colour Doppler imaging of the retrobulbar vessels, [31]; comparison of POAG, normal-tension glaucoma (NTG), ocular hypertension (OHT), glaucoma suspects and healthy controls, it was observed that the glaucoma groups had a greater mean ocular perfusion pressure than the control group, with lower retrobulbar velocities, greater retinal venous saturation, and asymmetry in choroidal thickness seen in glaucoma groups. Laser interferometry too has revealed reduced optic disc perfusion in OAG [32]. Color Doppler imaging has shown ocular blood flow (OBF) decrease and choroidal thinning in a recent study on OHT [33]. An OCT angiography study on juvenile OHT subjects has revealed that nasal-inferior and temporal peripapillary vessel density (VD) were slightly lower and the peripapillary temporal VD showed a weakly negative correlation with IOP, while VD of five locations of the radial peripapillary capillaries showed a strong positive correlation with high CDR. There was a slight positive correlation of certain macular regions with high IOP [34].

Histological evidence of loss of choroidal vasculature, choriocapillaris thinning and loss of larger choroidal blood vessels in GON, and choroidal thinning have also been reported [24–29]. The depth of the choroid tissue is primarily regarded as a biomarker of sound functional tissue margins, similar to the RNFL thickness. With the rise of OCT investigations, it is strongly advised to synthesize the data available to address ongoing issues with obtaining reliable, repeatable results. [12–35]

Choroid characteristics in JOAG

Studies depicting a relationship between JOAG and the choroid are scarce, with only Abou Shousha and Nabil [35] reporting their results mixed with POAG; suggesting a thinner choroid in both juvenile and POAG, compared to healthy controls. This is a novel study reporting the results of JOAG and ChT in a South Asian cohort with spectral-domain OCT. In this study, with the exception of the macular area 3000 µm nasal to the fovea, the choroid was found to be thicker in the JOAG group in every location. In the subfoveal region, 1500 µm and 3000 µm temporal to the fovea, at an average at the macula, and at an average total, the ChT was substantially higher in the JOAG group ($p < 0.05$) when compared with healthy controls. These findings suggest that choroidal vasculature may not be significantly affected in JOAG eyes or that choroidal thinning may not be a feature of this glaucoma sub-type.

Contrasting studies on choroidal thickness and POAG

Numerous researchers have presented conflicting reports on the relationship between either peripapillary or macular or total choroidal thickness and open angle glaucoma, with

Table 4 Table illustrating studies on choroidal thickness in open angle glaucoma vs healthy controls

Investigator	Glaucoma Type	Choroid Region	OCT	ChT (μm) Mean ± SD/SE	*p*-value
Maul et al. *2011* [38]	Glaucoma (37) vs. glaucoma suspects (37)	Macular & peripapillary ChT	Spectral-domain OCT (Heidelberg Spectralis)	Macular: Glaucoma: 221 ± 17 vs. Glaucoma suspects: 276 ± 15 Peripapillary: Glaucoma: 175 ± 11 vs. Glaucoma suspects: 196 ± 13	> 0.05
Ehrlich et al. *2011* [44]	POAG (31) vs. glaucoma suspects (39)	Peripapillary ChT	Spectral-domain OCT	OAG:135.0 Glaucoma suspects: 135.9	0.92
Mwanza et al. *2011* [46]	OAG (56) vs. NTG patients (20) vs. healthy controls (38)	Macular ChT	Enhanced depth OCT (Spectralis OCT)	OAG & NTG: 216.16 Healthy controls: 214.68	0.92
Cennamo et al. *2012* [45]	POAG (16) vs. healthy controls (21)	Macular ChT	Spectral-domain OCT (Spectralis HRA-OCT)	OAG patients: 411.56 ± 33.6 Healthy controls: 343.8 ± 29.06	< 0.001
Roberts et al. *2012* [47]	OAG (89) vs. healthy controls (76)	Peripapillary ChT	Spectral-domain OCT	Focal (126 ± 44), diffuse (135 ± 57) & sclerotic (92 ± 30) optic disc damage Healthy controls: 154 ± 40	< 0.001
Wang et al. *2014* [12]	POAG (52) vs. healthy controls (76)	Macular ChT	Enhanced depth OCT (Spectralis HRA-OCT)	POAG: 221.5 ± 44.1 Healthy controls: 224.1 ± 43.7	0.747
Hosseini et al. *2014* [40]	OAG (58) vs. healthy controls (33)	Macular & peripapillary ChT	Spectral-domain OCT (Cirrus HD-OCT)	Subfoveal: OAG: 242 ± 14.6 vs. Healthy controls: 264.3 ± 27.8 Peripapillary: OAG: 154.1 ± 12.3 vs. Healthy controls: 116.6 ± 13.1	0.546 0.083
Nakakura et al. *2014* [48]	POAG (40) vs. healthy controls (48)	Macular ChT	Swept-source OCT (Topcon 3-D)	POAG: 219.1 ± 11.2 Healthy controls: 216.6 ± 10.2	0.869
Jonas et al. *2015* [29]	OAG (39) vs. healthy controls (189)	Macular ChT	Enhanced depth OCT	OAG: 241 ± 91 Healthy controls: 258 ± 83	0.18
Abou Shousha et al. *2017* [35]	JOAG & POAG (100) vs. healthy controls (100)	Macular ChT	Spectral-domain OCT (Cirrus HD-OCT)	The foveal centre plus 5 temporal points at 500 µm & 5 nasal points at 500 µm	< 0.05
Sacconi et al. *2017* [43]	Advanced POAG (35) vs. healthy controls (35)	Macular ChT	Enhanced depth spectral-domain OCT	OAG: 209.9 ± 8.37 Healthy: 234.78 ± 8.37	0.042
Kutluksaman et al. *2019* [42]	POAG (49) vs. healthy controls (47)	Macular ChT	Spectral-domain OCT (Cirrus HD-OCT)	POAG: 254.92 ± 37.65 Healthy controls: 287.78 ± 26.77	< 0.01
Li et al. *2021* [39]	PXG (50) vs. POAG (56) vs. healthy controls (54)	Macular ChT	Enhanced depth OCT (Spectralis HRA-OCT)	PXG: 171.81 ± 50.46 POAG: 193.56 ± 68.26 Healthy controls: 197.74 ± 46.82	PXF vs controls < 0.05 POAG vs controls > 0.05

ChT: choroidal thickness POAG: primary open angle glaucoma JOAG: juvenile open angle glaucoma NTG: normal tension glaucoma PXG: pseudoexfoliative glaucoma OCT: optical coherence tomography SD: standard deviation SE: standard error

most reports refuting an association and reporting no significant differences [12, 29, 36–43]. Some have reported a thinner ChT [44, 45] in POAG, while other studies reported a thickened choroid in POAG with increased vessel diameter vertically and luminal area [46]. Sclerotic glaucomatous optic neuropathy [14, 47] has been associated with a thinner ChT and since juvenile patients are less likely to have atherosclerosis, it is possible that decreased ChT may not be a found in JOAG. The relationship between POAG and choroidal thickness is still debatable despite significant attempts at understanding it. Table 4 summarizes the various studies on ChT in various types of open angle glaucomas done previously.

Correlations and associations of choroidal thickness

Significant negative correlations of the subfoveal ChT (r = -0.367 $p = 0.005$) and average macular ChT (r = -0.364 $p = 0.006$) were observed with age in our study. The average peripapillary ChT was positively correlated with axial length (r = 0.268 $p = 0.046$). IOP, CCT, CDR, and MD were not significantly correlated with ChT. Nakakura et al. [48] in their study of ChT and variables in POAG found significant negative correlations with age and axial length and comparisons, but no correlation with CCT or MD. Maul et al.[38] found significant correlations of a thin choroid with older age, greater AL and thicker CCT. Sacconi et al. [43] found a correlation of ChT with age and axial length, but not with IOP. Lin et al. [49] also reported no association of peripapillary ChT with white-on-white MD, but a significant correlation with blue-on-yellow MD in open angle glaucoma. Kutluksaman et al. [42] failed to find correlation of ChT with CDR in their research. Li et al. [50] reported no correlation with MD. So, currently there are conflicting results and more good quality studies are needed to establish a definitive correlation.

Strengths and limitations of the study

Strengths of this study are that it is the first cross-sectional study to report choroidal thickness in exclusively JOAG patients, both at the macula and peripapillary area.

Limitations of this study include small sample size, a single-center study, and manual ChT measurements with SD-OCT. Also, a South Asian ethnicity may be a limitation towards the generalization of findings.

It is absolutely essential to try to understand the exact relationship between ChT, choroidal circulation and GON. The advent of OCT has provided us a direct view of this vascular structure with great importance. Substantial prospective and perhaps longitudinal studies are the need of the hour to delineate the precise connection between glaucoma and the choroid.

Conclusions and future perspectives

When compared to healthy controls, this South Asian JOAG cohort showed significant differences in the average total ChT, average macular ChT, subfoveal ChT, and at 1500 µm and 3000 µm temporal to the fovea; the choroid also on average being thicker in the macula and peripapillary regions. Further OCT studies are warranted to reach conclusive evidence.

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Data availability Data sharing statement: The data for this study is available from Open Science framework with the DOI: https://doi.org/10.17605/OSF.IO/Z564W and link https://osf.io/z564w/?view_only=5d4d064cf9a844acbd38e641cdb0e85d

Declarations

Ethics approval and consent to participate The Ethical Review Committee of Fauji Foundation Hospital, Rawalpindi, Pakistan granted approval for this study which is according to the Declaration of Helsinki [492/RC/FFH/RWP].

Consent for publication Informed consent was obtained from the patients.

Competing interests The author has no conflict of interest.

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