• Clinical Research •

Retinal capillary density among healthy Egyptian and South Asian students: an optical coherence tomography angiography study

Abdussalam M Abdullatif, Alimulhaq Mohammad Moamnlhaq, Tamer A. Macky, Noha Ahmed Edris

Department of Ophthalmology, Kasr ElAini Hospital, Cairo University, Cairo 1141, Egypt

Correspondence to: Tamer A Macky. 29th, 1th Street, Apt.11 Maadi Cairo 1141, Egypt. tamermacky@gmail.com; tamermacky@kasralainy.edu.eg

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Abstract

● **AIM:** To compare the macular and optic nerve perfusion and vascular architecture using optical coherence tomography angiography (OCTA) in normal eyes of Egyptian (Caucasians) and South Asian (Asians) volunteers.

● **METHODS:** Cross-sectional analytical OCTA study performed on 90 eyes of South Asian (*n*=45) and Egyptians (*n*=45) were analyzed. All participants underwent best-corrected visual acuity test, slit lamp, and fundus examination. OCTA images; macular 6×6 mm^2 grid and optic nerve 4.5×4.5 mm^2 grid were used to examine the parafoveal and peripapillary regions, respectively.

● **RESULTS:** The mean capillary vessel density (CVD) in macular sectors among South Asians and Egyptians participants were (50.31%±2.53%, 51.2%±5.93%) and (49.71%±3.6%, 51.94%±4.79%) in superficial (SCP) and deep capillary plexuses (DCP), respectively (*P*>0.05). Mean CVD in both groups was higher in DCP compared to SCP in all sectors but was not significant (*P*>0.05). Mean foveal CVD increases with an increase in central retinal thickness in both SCP and DCP (*P*<0.001), among both groups. Mean area of the foveal avascular zone (FAZ) was 0.28±0.09 and 0.27±0.08 mm^2 in South Asian and Egyptians, respectively. FAZ area decreases with an increase in the thickness and foveal CVD (*P*<0.001). Mean CVD in the peripapillary area was 48.23%±5.78% in South Asian and 49.52%±2.38% in Egyptian volunteers. The mean retinal nerve fiber layer thickness was found to be higher in the nasal quadrant among South Asian females than the Egyptian females (*P*<0.05).

● **CONCLUSION:** No significant racial disparity is found in this study. The findings are helpful for assessing and improving the normative data on the differences in South Asian and Egyptian populations.

● **KEYWORDS:** South Asian; Egyptian; optical coherence tomography angiography; macular perfusion; peripapillary vessel flow density

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INTRODUCTION

Optical coherence tomography angiography (OCTA) is a noninvasive high resolution imaging method to assess retinal and choroidal blood vessels in terms of vascular density and blood flow[1-2]. Racial and ethnic differences in retinal and choroidal blood vessels structure and flow have been in few reports[3-4]. Thus any potential variation may be important in interpreting the test results and therefore the treatment of patients. These racial difference should be considered when comparing OCTA results between different populations.

Medical students from South Asian countries, Nepal and Bangaldish, study regularly at Kasr Alainy Medical School Cairo University. Racially, they belong to the "Asian" race, while Egyptian medical students are racially considered "Caucasians". This study aimed to investigate and compare OCTA macular and optic nerve perfusion and vascular architecture structure between normal eyes in age-matched Egyptian and South Asian population and to investigate any sex and age relations with the OCTA parameters in both races.

PARTICIPANTS AND METHODS

Ethical Approval This is a cross-sectional analytical study conducted in the Department of Ophthalmology, Kasr Al Ainy Hospital, Cairo University, Cairo, Egypt. All selected volunteers received a thorough explanation of the study design and aims, and informed consent was obtained. The study protocol was revised thoroughly and approved by the Department Ethics Committee and followed tenets of the Declaration of Helsinki.

Participants

Inclusion criteria Medical students from South Asian countries; Nepal and Bangladesh; studying at Kasr Alainy Medical School Cairo University were recruited together with Egyptian Medical Students. Forty-five South Asian medical student volunteers and 45 age-matched and refraction-matched Egyptian medical student volunteers were enrolled in this study.

Exclusion criteria Participants with any ocular or systemic medical conditions, dense opacity hindering OCTA imaging, refractive error of ≥6 D, history of previous intraocular surgery or ocular trauma, any medications that may affect ocular vasculature were excluded from the study.

Clinical Evaluation All participants were subjected to a comprehensive ophthalmologic examination, including a review of their medical history, refraction, best corrected visual acuity (BCVA; converted to decimals), slit lamp examination, intraocular pressure (IOP) measurement using Goldmann applanation tonometer, and fundus examination. OCTA of the macula and optic nerve was done using AngioVue (Optovue Inc., Fremont, CA, USA).

Retina and Optic Nerve Imaging Using OCTA Angio-OCT was performed for all volunteers using the RTVue XR Avanti (AngioVue; optovueInc, Fremont, California, USA).

Macula Split-spectrum amplitude-decorrelation angiography (SSADA) was obtained as described by Nakamichi *et al*[5]. Scanning 6×6-mm^2 area centered on the fovea and automatically segmented into 4 slabs: superficial (SCP) and deep retinal capillary vascular plexuses (DCP), outer retina, and choriocapillaris: SCP: 5.6 μm beneath the inner limiting membrane (ILM) and 12.6 μm beneath the inner plexiform layer (IPL), DCP at 15.6 and 70.2 μm beneath the IPL[5].

Optic Nerve A 4.5×4.5 mm^2 peripapillary vessels were analyzed in the most superficial OCTA slab; the radial peripapillary capillary (RPC) layer from the ILM to the retinal nerve fiber layer (RNFL). The peripapillary region is 700 μm-wide elliptical annulus to optic disc boundary[5].

Quantitative Analysis The foveal avascular zone (FAZ) area, capillary vessel density (CVD), and the adjusted flow index (AFI) measurements assessed by Image J software[6]. The analysis was follows:

1) The FAZ area is delineated as a preset area of absolute no flow, measured in square millimeters automatically and calculated accordingly.

2) The CVD was defined as the percentage of the sample area occupied by vessel lumens following binary reconstruction of images. Using the ETDRS grid overlay centered on the FAZ area, both the SCP and DCP levels were obtained, then the CVD in the SCP and DCP is automatically measured. CVD is displayed as a percentage numerically in tables and qualitatively in color coded vessel density maps.

3) OCTA en face image was used to show the percentage of pixels of vessels in the defined sectors or in the entire. The percentage of vessels was defined in the following zones: a) whole image; b) para-fovea (within 3 mm of the fovea); c) peri-fovea (within 6 mm of the para-fovea).

4) Adjusted flow index calculation: adjusted flow index is an indirect measure of blood flow based on pixel intensity that correlates well with flow velocity in OCTA. It was calculated from full retinal thickness and choriocapillaris angiograms exported into Image J[7].

5) The following parameters were measured: a) CVD of SCP and DCP in the foveal and parafoveal areas of the macula; b) CVD of peripapillary plexus, RPC whole, RPC disc and superior, inferior, nasal, temporal quadrants in the peripapillary area; c) FAZ area; d) central foveal thickness (CFT); e) optic nerve fiber thickness.

Outcome Measures Comparing the 2 groups in primary outcomes: 1) capillary vascular density of superficial capillary plexus and deep capillary plexus in foveal and parafoveal areas of the macula; 2) capillary vascular density of peripapillary plexus, whole radial peripapillary capillaries, disc radial peripapillary capillaries, superior, inferior, nasal, and temporal quadrants in peripapillary area; 3) FAZ area. Secondary outcomes: 1) CFT; 2) optic nerve fiber thickness.

Statistical Analysis We used Statistical Package for Social Sciences (SPSS) in our analysis. The median/range for non-parametric data and ordinal (scores) data, numerical data were shown in means±standard deviation (SD), and categorical data were shown as numbers and percentages. Student's *t*-test, the Mann-Whitney test, a nonparametric test equivalent to the *t*-test, was used for non-normally distributed variables. The Chi-square test or the Fisher's exact test was used to compare between the groups with respect to categorical data. All *P*-values were two-sided and *P*-values < 0.05 were considered significant[8].

Sample Size Assuming α=0.05 (two-tailed), β=0.05, a total sample size of 90 volunteers, that will be allocated equally into 2 equal groups (45 eyes per group), is required to detect an effect size (*d*) of 0.25 in the change between the study groups at the three test points with a power of 95.79%. Estimation of sample size was performed for the repeated measures ANOVA using computer program G*Power 3.1.9 (Franz Faul, Universität Kiel, Germany).

RESULTS

Thirty South Asian medical student volunteers and 30 age-matched Egyptian medical student volunteers were enrolled in this study. There was no statistical significant difference (*P*=0.39) between the mean age of South Asian volunteers

(27.8±3.8y) and Egyptian volunteers (28.7±6.2y). The proportion of male/female was 23/7 in South Asian and 20/10 in Egyptian volunteers (P=0.39). The mean refraction was -2.78±0.82 and -2.5±0.75 D for the South Asian and Egyptian students respectively, which was not significant (P=0.234).

OCTA images of the superficial and deep capillary plexus of the macula were taken and their CVD was measured in both the South Asian and Egyptian volunteers. CVD of the superficial and deep layer of the macular regions is shown in Table 1. No significant statistical finding was observed between the South Asian and Egyptian groups (P>0.05).

The mean foveal CVD of SCP was higher in the Egyptian volunteers group, while the SCP superior hemi, SCP inferior hemi was higher among South Asian volunteers. For South Asian volunteers, mean superficial CVD was higher in the superior quadrant, followed by the temporal, inferior, and nasal quadrants, respectively. While for Egyptian volunteers, the mean superficial CVD was higher in the inferior quadrant, followed by the superior, temporal, and nasal quadrants, respectively.

For both groups, the CVD was higher in the deep retinal layer than in the superficial layer. Regarding the deep retinal layer, it also was higher in the nasal quadrant, followed by the temporal, superior, and inferior quadrants, respectively. There is no statistically significant difference between groups in macular CVD in the superficial and deep retinal plexuses when male or female volunteers are analyzed separately.

OCTA images of the RPC CVD, whole image, inside the disc, and the peripapillary area divided into four quadrants were taken from the volunteers. Mean RNFL thickness was 113.93±16.57 μm in South Asian and 114.53±12.05 μm in Egyptian volunteers. The mean RNFL thickness was highest in South Asian volunteers in the inferior quadrant, followed by superior, nasal, and temporal quadrants. While in the Egyptian volunteers it was seen that the highest RNFL thickness was in superior quadrant, followed by inferior, nasal, and temporal quadrant respectively (Table 2). The mean peripapillary CVD was highest in South Asian volunteers in the inferior quadrant, followed by superior, nasal, and temporal quadrants. While in the Egyptian volunteers it was also seen that the highest retinal nerve fiber thickness was in the inferior quadrant, followed by superior, temporal, and nasal quadrant respectively (Table 2).

RNFL peripapillary thickness and RPC peripapillary CVD were positively correlated which was (P=0.001, R=0.53) in South Asian volunteers, no such correlation was seen in Egyptian volunteers. There is no statistically significant difference between groups in optic disc and peripapillary capillary CVD when male or female volunteers are analyzed separately.

Table 1 OCTA of macular CVD in the central foveal and parafoveal subfields, measured in different retinal plexuses among South Asian and Egyptian volunteers mean±SD

Vessel density	South Asian, %	Egyptian, %	*P*
Superficial capillary plexus			
Fovea			
SCP whole	50.31±2.53	49.71±3.60	0.46
SCP superior hemi	50.27±2.48	49.65±3.76	0.45
SCP inferior hemi	47.14±12.46	49.84±3.55	0.25
SCP fovea	21.38±6.84	21.91±7.88	0.78
Parafovea			
SCP parafoveal	53.15±2.9	51.68±5.51	0.20
SCPF superior hemi	53.81±3.05	51.88±5.39	0.09
SCPF inferior hemi	52.56±3.34	51.83±4.93	0.50
SCP temporal	53.22±3.2	51.22±6.10	0.11
SCP superior	78.22±99.7	52.22±7.44	0.27
SCP nasal	52.41±3.24	50.18±6.74	0.10
SCP inferior	52.92±3.80	52.32±5.82	0.64
Deep capillary plexus			
Fovea			
DCP whole	51.2±5.93	51.94±4.79	0.59
DCP superior hemi	50.8±6.25	51.86±4.84	0.47
DCP inferior hemi	24.61±5.77	51.94±5.02	0.81
DCP fovea	38.08±7.01	39.25±8.71	0.57
Parafovea			
DCP parafovea	55.09±3.87	55.28±4.14	0.85
DCPF superior hemi	71.71±87.67	55.81±4.49	0.32
DCPF Inferior hemi	71.89±95.63	54.79±4.14	0.33
DCP temporal	55.88±4.03	56.26±4.98	0.74
DCP superior	55.04±4.64	54.76±6.08	0.84
DCP nasal	73.37±96.51	56.96±3.23	0.35
DCP inferior	53.54±4.09	53.69±5.09	0.90

OCTA: Optical coherence tomography angiography; CVD: Capillary vessel density; SCP: Superficial capillary plexuses; DCP: Deep capillary plexuses.

Table 2 OCTA of RNFL showing the measured RNFL thickness and peripapillary CVD mean±SD

Parameters	South Asian	Egyptian	*P*
RNFL thickness (μm)			
RNFL PP thickness	113.93±16.57	114.53±12.05	0.87
Superior	136.60±22.09	146.63±54.91	0.35
Nasal	95.60±26.21	93.90±18.43	0.77
Inferior	144.43±20.78	142.56±21.87	0.73
Temporal	82.06±17.22	82.40±13	0.93
RPC vessel density (%)			
RPC whole	48.23±5.78	49.52±2.38	0.26
RPC disc	51.81±3.64	48.98±9.52	0.13
Peripapillary	50.84±3.22	51.87±2.39	0.16
Superior	50.96±3.89	52.40±3.46	0.13
Nasal	50.80±4.55	51.43±4.46	0.58
Inferior	52.20±4.23	53.30±3.65	0.28
Temporal	50.16±4.72	51.70±4.90	0.22

OCTA: Optical coherence tomography angiography; CVD: Capillary vessel density; RNFL: Retinal nerve fiber layer; PP: Peripapillary; RPC: Radial peripapillary capillary.

Table 3 Correlation of CRT with superficial retinal plexus CVD or deep retinal plexus CVD in the macular sectors among Egyptian volunteers mean±SD

Parameters	CRT (μm)	Egyptian (%)	Correlation (*R*)	*P*
Superficial retinal plexus				
Fovea	240.4±21.1	21.91±7.88	0.35	0.05
Parafovea	311.3±21.1	51.68±5.51	-0.03	0.85
Temporal	301.3±20.6	51.22±6.10	-0.18	0.35
Superior	315.1±22.2	52.22±7.44	-0.16	0.41
Nasal	315.8±20.5	50.18±6.74	0.00	0.99
Inferior	312.1±23.1	52.32±5.82	-0.08	0.69
Deep retinal plexus				
Fovea	240.4±21.1	39.25±8.71	0.32	0.07
Parafovea	311.3±21.1	55.28±4.14	0.006	0.97
Temporal	301.3±20.6	56.26±4.98	-0.02	0.90
Superior	315.1±22.2	54.76±6.08	0.006	0.97
Nasal	315.8±20.5	56.96±3.23	0.39	0.04
Inferior	312.1±23.1	53.69±5.09	0.38	0.05

CRT: Central retinal thickness; CVD: Capillary vessel density.

Table 4 Correlation of CRT with superficial retinal plexus CVD or deep retinal plexus CVD in the macular sectors among South Asian volunteers mean±SD

Parameters	South Asian (%)	Central retinal thickness (μm)	Correlation (*R*)	*P*
Superficial retinal plexus				
Fovea	21.38±6.84	241.4±19.0	0.79	0.05
Parafovea	53.15±2.9	319.6±16.1	-0.05	0.76
Temporal	53.22±3.2	310.7±14.2	0.09	0.63
Superior	78.22±99.7	323.3±14.8	0.04	0.80
Nasal	52.41±3.24	323.3±18.6	-0.21	0.26
Inferior	52.92±3.80	320.8±16.4	-0.02	0.91
Deep retinal plexus				
Fovea	38.08±7.01	241.4±19.0	0.85	0.001
Parafovea	55.09±3.87	319.6±16.1	-0.02	0.89
Temporal	55.88±4.03	310.7±14.2	-0.009	0.96
Superior	55.04±4.64	323.3±14.8	-0.04	0.81
Nasal	73.37±96.51	323.3±18.6	0.27	0.15
Inferior	53.54±4.09	320.8±16.4	0.12	0.50

CRT: Central retinal thickness; CVD: Capillary vessel density.

Correlations Between Macular CVD and RNFL Radial Peripapillary Capillary CVD RNFL peripapillary thickness is negatively correlated with SCP parafovea CVD (*P*=0.03, *R*=-0.37) in Egyptian volunteers, which was not seen in the South Asian group. RPC disc CVD was negatively correlated with SCP fovea CVD (*P*=0.001, *R*=-0.63) in Egyptian volunteers. In the south Asian group, RPC disc CVD was positively correlated with SCP parafovea CVD (*P*=0.01, *R*=0.42). RPC whole CVD was negatively correlated with DCP fovea CVD (*P*=0.04, *R*=-0.73) in South Asian volunteers only and not in the Egyptian group.

Correlation of Central Foveal Thickness and Foveal Avascular Zone The CFT was 241.4±19.01 μm and 240.4±21.1 μm among South Asian and Egyptian volunteers respectively, while the FAZ area was 0.28±0.09 mm^2 and 0.27±0.08 mm^2 among South Asian and Egyptian volunteers respectively with no significant difference (*P*=0.68). There was no significant difference in CFT and FAZ between male and female volunteers among the Egyptian volunteers [CFT: 240.6 and 240.1 (*P*=0.9), and FAZ: 0.25 and 0.3 (*P*=0.1) for male and female respectively], while there was a significant difference in CFT and FAZ between male and female volunteers among the Asian volunteers [CFT: 246.4 and 224.9 (*P*=0.002), and FAZ: 0.25 and 0.36 (*P*=0.03) for male and female respectively].

When we examined ocular variables, correlations emerged between CFT and foveal SCP CVD and foveal DCP CVD and were negatively correlated to RPC disc CVD in South Asian volunteers, and no such correlation was observed among Egyptian volunteers (Tables 3 and 4).

The area of FAZ was negatively correlated with foveal CVD in SCP (*R*=-0.74, -0.47, both *P*<0.05) among South Asian volunteers and Egyptian volunteers respectively. Similarly, a

negative correlation was also detected between DCP, foveal CVD, and FAZ (R=-0.74, P<0.05) in Egyptian volunteers only but not in the South Asian volunteers group. The area of FAZ and CFT was negatively correlated in both South Asian and Egyptian volunteers which were (P=0.001, R=-0.79) and (P=0.04, R=-0.37) respectively.

DISCUSSION

OCTA enable visualization retinal and choroidal microvasculature[9]. enabling us to qualitatively and quantitatively study and compare OCTA scans of healthy eyes in the macular and peripapillary regions in South Asian and Egyptian volunteers. To our knowledge, this is the first study to show any racial disparities in OCTA and any possible baseline differences of retinal vasculature between South Asian and Egyptian subjects. Our findings showed no significant differences in blood flow in the DCP and SCP of our South Asian compared to our Egyptian subjects. Parafovea superior-hemi was found higher in South Asian males than the Egyptian males and also the mean RNFL thickness was found higher in the nasal quadrant among south Asian females than the Egyptian females. These results could be significant in the context of the high prevalence of open-angle glaucoma in South Asian populations.

A study done on Japanese subjects found a correlation between SCP and DCP CVD[10]. Similar to Egyptian volunteers, FAZ area was negatively correlated with SCP CVD, DCP CVD, and CMT, however, in Asian volunteers, FAZ area was negatively correlated with SCP CVD, and CMT but not the DCP CVD. In the same Japanese study, the FAZ was larger and CMT was lower in Japanese women than men as what we found in Asian volunteers but not the Egyptians[10]. In one study, the fovea was found to be statistically significant thinner in African Americans and females than in Caucasians and males[4].

In another study, Africa Americans were found to have decreased macular capillary vasculature, even in the absence of any ocular or systemic pathologies[11]. A study was done in Hong Kong showed males to have lower SCP vascular density, and eyes with longer axial length and higher level of creatinine had a lower DCP vascular density[12].

The inconsistency of CVDs between studies including with our values could be due to the use of a slightly different OCTA algorithm[13], or the different machines[14-18] and versions of the software may also generate different values[19-22]. Samara *et al*[19] studied the morphology of FAZ using OCTA and found that it is slightly irregular in all eyes, similar to what was described in our study. The mean area of FAZ in the superficial plexus measured in their study (0.26 mm^2) was slightly smaller compared to our results (0.28 mm^2 & 0.27 mm^2) among both groups. This may be attributed to using Image J software to manually delineate and measure the area of FAZ. However, there were no significant FAZ area difference was found between both groups in our study.

Peripapillary CVD is of important significant and was studied in glaucomatous eyes[23-24], myopic ones[25], pediatric[26], and different diseases[27-31]. In our study, we did not see any significant difference in the mean CVD in the peripapillary region between South Asian and Egyptian groups. No significant correlation was found between the CVD and RNFL thickness in the normal population, which may be secondary to our small sample size. The mean RNFL thickness was found higher in the nasal quadrant among South Asian females than the Egyptian females.

Our study is limited by a relatively small sample size, and a homogenously young healthy adults which hinders the wide applicability of the results. Thus, the retinal vasculature of older subjects with systemic diseases could be different[11].

Our findings suggest that people's racial or ethnic identity should be considered in comparative studies and the development of normative databases. Considering potential differences in people's microvasculature, we can improve management guidelines of glaucoma and retinal diseases. Further studies with a larger number of subjects and more diverse study population are needed for better understanding of the retinal microvasculature and for elucidating any clinical associations with racial and ethnic identity, social and environmental factors.

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