

Interocular symmetry of retinal nerve fiber layer and optic nerve head parameters measured by Cirrus high-definition optical coherence tomography in a normal pediatric population

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Purpose: To determine interocular differences in the retinal nerve fiber layer (RNFL) and optic nerve head (ONH) parameters in a pediatric population using Cirrus high-definition optical coherence tomography (HD-OCT). **Methods:** Seventy normal Indian children aged 5–17 years presenting to the Pediatric Clinic were included in this observational cross-sectional study. All subjects underwent a comprehensive ophthalmologic examination and an evaluation of the RNFL and ONH by Cirrus HD-OCT. Differences between the right and left eyes were calculated and values were compared by means of a paired *t*-test. Subjects were also divided into two groups based on age (under or over 10 years of age). Interocular differences in RNFL and ONH parameters together with sex and age variations for these differences were determined. **Results:** The mean age of studied pediatric population was 11.83 ± 3.3 years (range 5–17). Average RNFL thickness was $94.46 \pm 8.7 \mu\text{m}$ (\pm SD) (range 77–111). Differences in the average RNFL between right and left eyes were not statistically significant ($P = 0.060$). Superior quadrant RNFL was thicker in the left eye and temporal quadrant was thicker in the right eye. Among ONH parameters, there were no statistically significant differences in any parameters, except vertical cup-disc (CD) ratio which was significant ($P = 0.007$). The 2.5%–97.5% limits of asymmetry were $9 \mu\text{m}$ for average RNFL, 0.14 for average CD ratio, and 0.22 for vertical CD ratio. Mean interocular RNFL thickness differences in superior, superior nasal, and temporal superior quadrants were 10.61 ($P < 0.001$), 12.57 ($P < 0.001$), and 4.46 ($P = 0.002$) μm , respectively. Interocular nerve fiber layer thickness differences were not significantly correlated with sex, while only significant differences with age were observed in 12 clock hour sector analysis, mainly in nasal inferior and inferior quadrant. **Conclusions:** We report the degree of interocular symmetry of RNFL and ONH parameters measured by Cirrus HD-OCT in a healthy pediatric population. The normal interocular RNFL asymmetry should not exceed $9 \mu\text{m}$ and vertical CD ratio beyond 0.22 should be considered for further investigations. The physiologic asymmetry provided by this study may assist in identifying changes in RNFL thickness and ONH parameters in pediatric glaucoma and ONH disorders.

Key words: Interocular asymmetry, optical coherence tomography, retinal nerve fiber layer thickness, spectral-domain

Although the human body looks symmetrical on the outside, most of our vital organs are not exactly symmetrical and there exists some physiologic asymmetry. The same applies to retinal parameters of both eyes where some amount of physiological variations can occur. Few studies have been published in limited ethnic populations on interocular asymmetry of retinal nerve fiber layer (RNFL) in adult and pediatric healthy eyes.^[1–8]

Optical coherence tomography (OCT) has a well-established structural imaging role in ophthalmic disease diagnosis and management and has proven its importance in visualization and quantification of ocular structures. The most common clinical implication of this noncontact high-resolution technology is in glaucoma, retinal diseases, neuro-ophthalmology, and anterior segment applications.^[1]

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Spectral-domain OCT (SD-OCT) images faster with a high axial image resolution than earlier domain-based generations of this technology. The quantification of structural and ultrastructural changes with SD-OCT expands the utility of OCT in pediatric ophthalmology in evaluating pediatric and juvenile glaucoma, pediatric neuro-ophthalmology, and pediatric retinal disorders.^[2,3] To enhance the information provided by structural diagnostic tool of OCT for pediatric optic and retinal disorders, a comparison with population-derived normative data is needed to identify deviations from the normal range. The studies on variations in normal morphology in RNFL also emphasizes the need for normative data and interocular symmetry in the pediatric population.^[2–8]

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Methods

This was a cross-sectional study of healthy Indian children 5–17 years of age visiting the pediatric ophthalmology clinic at a tertiary eye care center. Ethical review board permission was taken. Informed consent was obtained from parents or guardians. Included in the study were subjects with no ocular abnormality, except refractive error with spherical equivalent (SE) less than ± 3.5 diopters (D) or astigmatism less than 1.5D and normal fundus examination.

Patients with strabismus, amblyopia, retinal pathology, optic nerve cup-to-disc (CD) ratio >0.7 or asymmetry of >0.2 between fellow eyes, and history of previous intraocular surgery were excluded. Patients with history of prematurity, developmental delay, neurological, metabolic or other systemic diseases were also excluded. All subjects received a comprehensive ophthalmologic examination from a pediatric ophthalmologist. The visual acuity of each eye was recorded using the Snellen chart, and intraocular pressure (IOP) was recorded by applanation or noncontact tonometer (where possible). Slit-lamp biomicroscopy, cycloplegic refraction, and dilated funduscopy were performed. Pupils were dilated using tropicamide 1% and phenylephrine 2.5% and cyclopentolate 1% eyedrops. The manual retinoscopy was also confirmed by automated refraction (Topcon KR 8900).

The Cirrus high-definition OCT (HD-OCT) (Model 4000 software version 5.1.1.4; Carl Zeiss Meditec, Dublin, CA, USA) was used to obtain high-definition images. The OCT measurement of all children was performed by the same experienced technician with the pupil dilated. The macula and peripapillary RNFL examinations were performed using an internal fixator. The scans with a signal strength of at least 6 were included in the study.

Optic disc cubes of 200×200 protocol were utilized to assess peripapillary RNFL thickness. RNFL thickness (all four quadrants: superior, nasal, inferior, and temporal; average, and 12 clock hours), RNFL symmetry, rim area, disc area, average CD ratio, vertical CD ratio, and cup volume were recorded. The clock hour RNFL thicknesses and 12 30° sectors were defined in clockwise order for the right eye and counterclockwise for the left eye.

Statistical analysis

The differences between right and left eyes were calculated and values were compared by means of a paired *t*-test. Descriptive statistics were reported as means and SDs and 2.5th, 5th, 95th, and 97.5th percentiles for continuous variables and frequency and percentage for categorical variables. Mean differences for all parameters were calculated by subtracting left eye parameters from right eye parameters, and their *P* values reported using the paired sample *t*-test. *P* value lesser than 0.05 was considered as statistically significant. The Spearman correlation coefficient was computed to measure the interocular agreement/correlation. All statistical analysis was performed by STATA 11.1 (Texas, USA).

Results

Ninety subjects consented to participate in this study. Twenty cases were excluded because scan quality was not good. Thus, 70 subjects were eligible for statistical analysis. For interocular

symmetry evaluation, all eyes were studied. The mean age of the studied pediatric population was 11.83 ± 3.3 years (range 5–17). There was no statistically significant difference between male and female subjects for refraction ($P = 0.26$) and age ($P = 0.959$). The mean SE was 0.61 ± 0.9 diopters (D) in the right eyes and 0.69 ± 0.9 D in the left eyes ($P = 0.133$).

Mean global RNFL thickness was 94.46 ± 8.7 μm , (range, 77–111). The RNFL thickness was 93.60 ± 9.5 μm (range 69–119) in right eye and 94.71 ± 8 μm (range 72–117) in left eye; the difference was statistically insignificant ($P = 0.06$). Fig. 1 scatter plot shows that there was no significant difference in average RNFL thickness of the right and left eyes. The mean RNFL thickness in four quadrants and for all clock hours and gender-wise distribution is provided in Table 1. The mean RNFL thickness was highest in the inferior quadrant followed by superior, nasal, and temporal quadrants [Table 1]. The RNFL was thickest inferiorly (122.99 ± 17.9 μm) and superiorly (118.26 ± 14.50 μm), thinner nasally (72.91 ± 17.1 μm), and thinnest temporally (60.41 ± 9.7 μm). RNFL quadrant thicknesses in the right and left eyes followed a pattern similar to adults, with the thickest quadrant being the inferior, then the superior, followed by the nasal and finally the temporal segments (ISNT rule). The average RNFL thickness, quadrants, and 12 clock hour thickness were not statistically different between the males and females.

Table 2 shows the mean differences of OCT RNFL and optic nerve head (ONH) parameters between right and left eyes. The RNFL of superior quadrant was thicker in the left eye and temporal quadrant was thicker in the right eye. We found statistically significant interocular differences in superior and temporal RNFL quadrants but not in average RNFL thickness. There were statistically significant differences between superior, superior nasal, and temporal superior quadrants in both eyes.

Among ONH parameters, the right eye had a greater vertical CD ratio in our study, and the other ONH parameters did not have statistically significant differences between eyes.

Table 3 lists the data for interocular differences in RNFL parameters and ONH parameters, including mean interocular differences with respective *P* values, in addition to the 2.5th, 5th,

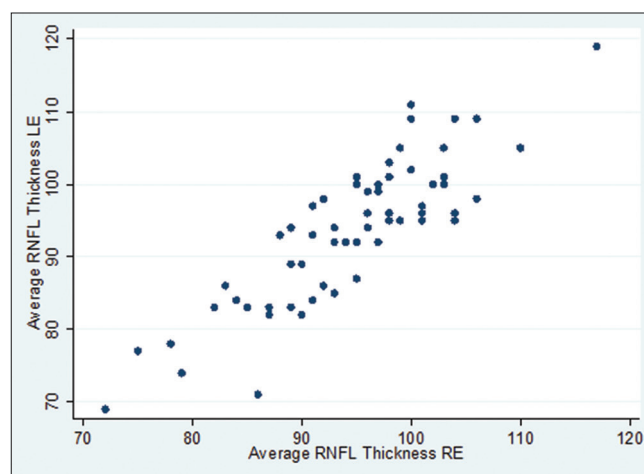


Figure 1: Scatter plot for average retinal nerve fiber layer thickness between right eye and left eye

Table 1: Retinal nerve fiber layer thickness in four quadrants and for all clock hours and gender wise distribution

RNFL thickness parameter, μm (range)	Female (n=27)	Male (n=43)	Total (SD)	P*
Average RNFL	96.07 (93.29-98.85)	93.44 (90.50-96.39)	94.46 (8.7)	0.221
Temporal	59.85 (55.59-64.11)	60.77 (57.97-63.57)	60.41 (9.7)	0.704
Superior	120.52 (115.85-125.18)	116.83 (111.92-121.76)	118.26 (14.5)	0.306
Nasal	76.48 (70.42-82.55)	70.67 (65.16-76.19)	72.91 (17.1)	0.168
Inferior	126.19 (119.62-132.75)	120.98 (115.25-126.70)	122.99 (17.9)	0.239
Quadrants				
Superior	127.37 (119.56-135.18)	127.07 (119.31-134.83)	127.19 (23.1)	0.958
Superior-nasal	116.19 (109.65-122.72)	108.44 (101.86-115.03)	111.43 (19.9)	0.114
Nasal-superior	88.85 (82.57-95.13)	83.21 (76.89-89.52)	85.39 (18.9)	0.228
Nasal	56.78 (52.94-60.61)	56.33 (52.64-60.01)	56.50 (11.1)	0.869
Nasal-inferior	71.37 (66.094-76.65)	65.05 (59.76-70.33)	67.49 (16.0)	0.108
Inferior-nasal	110.85 (102.89-118.81)	108.21 (99.39-117.03)	109.23 (25.6)	0.677
Inferior	147.67 (139.25-156.08)	136.77 (128.48-145.05)	140.97 (25.3)	0.079
Inferior-temporal	123.63 (112.45-134.81)	127.35 (118.80-135.90)	125.91 (27.8)	0.589
Temporal-inferior	62.30 (56.12-68.47)	66.63 (62.83-70.43)	64.96 (13.8)	0.202
Temporal	48.30 (45.05-51.54)	50.14 (47.66-52.62)	49.43 (8.1)	0.358
Temporal-superior	73.85 (68.61-79.09)	70.67 (66.73-74.62)	71.90 (13.0)	0.322
Superior-temporal	126.54 (118.11-134.97)	118.14 (111.45-124.83)	121.30 (21.7)	0.119

SD: Standard deviation, RNFL: Retinal nerve fiber layer, *Mann Whitney test

Table 2: Interocular differences in retinal nerve fiber layer parameters and optic nerve head parameters between right and left eyes (n=140 eyes)

Variables	Right eye	Left eye	P*
Rim area	1.31 (0.27)	1.34 (0.26)	0.264
Disc area	2.45 (0.48)	2.46 (0.52)	0.718
Average C/D ratio	0.64 (0.13)	0.63 (0.14)	0.071
Vertical C/D ratio	0.61 (0.11)	0.59 (0.13)	0.007
Cup volume	0.45 (0.28)	0.42 (0.27)	0.200
RNFL	93.60 (9.5)	94.71 (8.0)	0.060
Superior	114.57 (16.5)	121.31 (13.9)	<0.001
Temporal	62.59 (8.4)	59.54 (10.1)	0.002
Inferior	122.36 (16.8)	122.69 (17.3)	0.885
Nasal	72.71 (15.3)	73.80 (18.2)	0.622
Superior	122.52 (26.1)	133.14 (24.3)	<0.001
Superior-nasal	105.33 (22.5)	117.90 (19.8)	<0.001
Nasal-superior	87.49 (17.4)	85.33 (17.9)	0.315
Nasal	58.27 (11.5)	56.0 (10.7)	0.064
Nasal-inferior	68.44 (16.3)	67.23 (16.5)	0.542
Inferior-nasal	105.34 (24.3)	108.03 (23.6)	0.272
Inferior	139.23 (26.3)	139.69 (24.6)	0.857
Inferior-temporal	127.41 (23.6)	126.43 (27.9)	0.704
Temporal-inferior	66.34 (11.8)	65.66 (15.8)	0.695
Temporal	50.17 (8.5)	49.00 (8.9)	0.073
Temporal-superior	74.14 (13.9)	69.69 (13.5)	0.002
Superior-temporal	119.51 (22.4)	118.19 (23.4)	0.514

RNFL: Retinal nerve fiber layer, C/D: Cup-disc, *Paired t test

95th, and 97.5th percentile distribution of the mean differences. The 2.5%–97.5% limits of asymmetry were 9 μm for average RNFL, 0.14 for average CD ratio, and 0.22 for vertical CD ratio. Mean interocular RNFL thickness differences in

superior, superior nasal, and temporal superior quadrants were 10.61 ($P < 0.001$), 12.57 ($P < 0.001$), 4.46 ($P < 0.002$) μm , respectively.

Table 4 shows that there was no correlation with gender in either group in RNFL and ONH parameters, while Table 5 shows interocular symmetry in subjects <10 years and >10 years. It depicts significant differences with respect to age in 12 clock hour sector analysis mainly in nasal inferior and inferior quadrant.

The Spearman correlation coefficient was 0.8169, 0.6590, 0.6590, 0.8020, 0.8431, 0.8489, 0.8054 for average RNFL, rim area, disc area, average CD ratio, vertical CD ratio, cup volume, respectively ($P < 0.001$), showing good correlation in these parameters.

Discussion

The structural functional assessment by OCT is currently included in most clinical protocols for diagnosis and follow-up of pediatric glaucoma and optic nerve diseases (glioma, compressive optic neuropathies, idiopathic intracranial hypertension, hereditary neuropathies, and macular and retinal diseases). It is important to determine what the normative data are with spectral OCT for pediatric eyes and which values of asymmetry should be considered an early sign of pathology. The consideration of deviation from normal physiologic values could aid in diagnostic accuracies and modifying treatment modalities in the field of pediatric ophthalmology.^[2]

Various studies have agreed on intravisit and intervisit reproducibility of measurements of peripapillary RNFL thickness and ONH parameters in the pediatric population.

This study aimed to examine symmetry of the average RNFL thickness and ONH parameters in a normal pediatric population. The RNFL measurements obtained may vary

Table 3: Percentile distribution of interocular differences in retinal nerve fiber layer thickness and optic nerve head parameters

Variables	Mean±SD	All ages (percentiles)			
		2.5 th	5 th	95 th	97.5 th
RNFL (μm)					
Superior	-6.74±12.4	-28.0	-26.0	10.0	25.0
Nasal	-1.09±18.4	-51.0	-49.0	17.0	33.0
Temporal	3.04±7.9	-17.0	-9.0	14.0	19.0
Inferior	-0.33±18.8	-33.0	-30.0	32.0	64.0
Average	-1.11±4.9	-9.0	-8.0	6.0	9.0
Optic nerve					
Rim area	-0.03±0.2	-0.56	-0.44	0.26	0.28
Disc area	-0.01±0.3	-0.63	-0.59	0.40	0.54
Average C/D ratio	0.01±0.1	-0.11	-0.08	0.13	0.14
Vertical C/D ratio	0.02±0.1	-0.10	-0.07	0.15	0.22
Cup volume (mm³)	0.02±0.2	-0.22	-0.20	0.32	0.42
RNFL					
Superior	-10.61±18.9	-45	-42	20	36
Superior-nasal	-12.57±20.7	-58	-46	21	32
Nasal-superior	2.19±17.8	-37	-29	30	34
Nasal	2.31±10.3	-19	-16	22	23
Nasal-inferior	1.21±16.6	-42	-24	25	34
Inferior-nasal	-2.69±20.3	-40	-32	29	36
Inferior	-0.46±21.1	-40	-32	38	44
Inferior-temporal	0.99±21.6	-34	-29	38	49
Temporal-inferior	0.69±14.6	-45	-26	17	21
Temporal	1.17±5.4	-11	-8	8	16
Temporal-superior	4.46±11.7	-17	-15	25	26
Superior-temporal	3.01±23.7	-34	-30	34	40

SD: Standard deviation, RNFL: Retinal nerve fiber layer, C/D: Cup-disc

according to the OCT model used, depending on software algorithms, different models, and display scans.^[5-17] Published literature has evidence-based proof that SD-OCT technology can determine the changes in RNFL thickness much earlier than the time-domain OCT.^[18-24]

The average RNFL thickness in our study was determined $94.46 \pm 8.70 \mu\text{m}$ which is consistent with findings reported in the literature.^[2-10] Table 6 shows OCT values of the previous studies of pediatric population with Cirrus HD-OCT, interocular symmetry and our present study as well.^[21-29]

The distribution of RNFL thickness (thickest inferiorly and superiorly, thinner nasally, and thinnest temporally) in our study is in agreement with the normal distribution of RNFL in accordance with ISNT rule.^[6] Chen *et al.* reported the thickest RNFL to be the superior quadrant, followed by the inferior quadrant, temporal quadrant, and nasal quadrant.^[27] Zhu *et al.* found ISTN pattern in their study.^[23] Dave *et al.* found that ISNT rule on the RNFL in an Indian population was followed only by 30 eyes (23.8%), while the IST (inferior thickest followed by superior and temporal) rule was followed by 66 eyes (52.4%) ($P < 0.001$).^[4] Rao *et al.* found the RNFL to be thickest in the superior, inferior, nasal, and temporal quadrants in an Indian pediatric population.^[26] The deviation from ISNT

has been reported in other pediatric and adult studies in various ethnic populations.^[4,26-23]

The published data obtained with earlier versions of stratus time-domain OCT show slightly higher values for RNFL thickness compared to our present results, with differences ranging from $19.52 \mu\text{m}$ to $3.94 \mu\text{m}$. The different versions of the software algorithm could be accountable for differences between values.^[8-19]

Average RNFL thickness values for our study were comparable with those of Noemi *et al.*, Barrio *et al.*, Al-Haddad *et al.*, Altemir *et al.*, Dalgilesh *et al.*, Rao *et al.* but lower than those of the younger subjects reported by Zhu *et al.* (population mostly Asian Indian), Chen *et al.*, Turk *et al.*, Tsai *et al.*, Yanni *et al.*, and Dave *et al.*^[4,22-27,30]

The few studies carried out with the Cirrus OCT in pediatric population have reported that the mean average RNFL thickness ranged from 92 to 99.44, which would include our result of $94.46 \mu\text{m}$.^[4,21-27,30]

In accordance with other studies, gender in the present study did not influence RNFL thickness and ONH parameters.^[2,7] The mean RNFL thicknesses were similar between boys and girls. Huynh *et al.* reported significantly thicker average RNFL ($P = 0.007$) and inferior quadrant RNFL ($P = 0.02$) in boys than in girls after adjusting for age, height, axial length, ethnicity, and cluster sampling.^[7,9] Zhu *et al.* found that the average RNFL thickness and temporal and inferior quadrants were significantly greater in girls.^[23] A study done by Turk *et al.* showed there was no significant correlation between age, refractive error, axial length values, and RNFL thickness.^[24]

The effects of refraction on RNFL thickness have varied results. Huynh *et al.*, Salchow *et al.*, and Qian *et al.* reported a positive correlation of the average RNFL thickness with refractive error in children.^[8-10,19] Budenz *et al.* and Cheung *et al.* reported thinning RNFL with increasing myopia in White and Asian adults. In a study by Zhu *et al.*, a significant positive correlation of the average RNFL thickness was seen with refractive error in even in low myopia population.^[23]

Most studies reported that the RNFL thickness was greater in the right than in the left eye for the temporal quadrant and thicker in the left eye than the right eye for the inferior nasal sector. Studies done with previous versions of OCT showed similar results, and RNFL in the right eyes were thicker than in the left eyes.

In our study, there were no interocular differences between right and left average RNFL. Superior quadrant RNFL was thicker in the left eye and temporal quadrant was thicker in right eye. We found statistically significant interocular differences in RNFL quadrants but not in average RNFL thickness. The average RNFL thickness in the right and left eyes of children differed from those in previous studies. Qian *et al.* found thicker RNFL in the left eye.^[19] Al-Haddad *et al.* also found thicker nasal and temporal quadrant in the right eyes and a thicker superior quadrant in the left eyes with Cirrus HD-OCT. They found no differences in average RNFL thickness but statistically significant interocular differences in RNFL quadrants. These differences were significant in the older age group (>10 years) while some of the RNFL clock hours depicted significant differences.^[29] Similarly,

Table 4: Gender-wise interocular differences in retinal nerve fiber layer and optic nerve head parameters

	Female		Male		P
	Mean±SD	Range	Mean±SD	Range	
RNFL (μm)					
Superior	-6.07±11.3	-27-25	-7.16±13.1	-44-40	0.570*
Nasal	-3.41±17.5	-56-25	0.37±19.0	-51-70	0.422*
Temporal	4.74±9.2	-17-37	1.98±6.8	-19-19	0.204*
Inferior	1.19±22.1	-33-64	-1.28±16.7	-32-68	0.726*
Average	-1.26±5.6	-15-9	-1.02±4.4	-8-11	0.933*
Optic nerve					
Rim area	-0.06±0.2	-0.6-0.26	-0.006±0.2	-0.47-0.63	0.458*
Disc area	-0.04±0.3	-0.63-0.57	0.004±0.3	-0.83-0.54	0.368*
Average C/D ratio	0.02±0.1	-0.08-0.14	0.008±0.1	-0.16-0.22	0.616*
Vertical C/D ratio	0.04±0.1	-0.1-0.22	0.013±0.1	-0.1-0.25	0.113*
Cup volume (mm ³)	0.02±0.2	-0.325-0.45	0.025±0.2	-0.219-0.419	0.914*
RNFL					
Superior	-6.41±21.6	-45-38	-13.26±16.7	-46-36	0.136*
Superior-nasal	-10.78±21.8	-50-51	-13.70±20.1	-63-29	0.995*
Nasal-superior	-2.04±17.9	-42-29	4.84±17.5	-37-47	0.138*
Nasal	2.67±9.4	-12-26	2.09±10.9	-24-23	0.823*
Nasal-inferior	2.93±21.1	-42-45	0.14±13.2	-42-25	0.488*
Inferior-nasal	-3.26±21.5	-50-36	-2.33±19.8	-40-71	0.962*
Inferior	-0.81±23.2	-54-44	-0.23±20.0	-40-81	0.952*
Inferior-temporal	3.11±26.6	-65-83	-0.35±18.1	-34-49	0.514*
Temporal-inferior	0.37±16.6	-54-29	0.88±13.4	-45-20	0.947*
Temporal	1.93±4.9	-9-16	0.70±5.6	-13-20	0.217*
Temporal-superior	6.33±8.3	-17-25	3.28±13.3	-48-31	0.184*
Superior-temporal	-0.07±30.9	-86-97	4.95±17.9	-34-40	0.259*

SD: Standard deviation, RNFL: Retinal nerve fiber layer, C/D: Cup-disc, *Mann Whitney test

Altamir *et al.* found RNFL in the right eyes to be thicker in the temporal and nasal quadrants, whereas the left eye showed thicker RNFL in the superior quadrant, while there were no statistically significant differences in the average RNFL between right and left eyes.^[2]

Dave *et al.* reported RNFL and the posterior pole asymmetry analysis (PPAA) macular thickness values were statistically significantly different between the right and the left eyes, except for the average RNFL ($P=0.4$) and the superior RNFL ($P=0.09$) thickness values in Indian pediatric population by Spectralis OCT. Dalglish *et al.* in their study found that only the inferior quadrant and the corresponding clock hours of 5 o'clock in the right eye and 7 o'clock in the left eye did not have a significant interocular difference.^[30]

Al-Haddad *et al.*, Qian *et al.*, and Dalglish *et al.* found no significant differences in any ONH parameters.^[19,29,30] Similarly, Huynh *et al.* and Altamir *et al.* reported CD area ratio to be most symmetrical parameter of the optic disc.^[2,7] Only, Huynh *et al.* (6 years age group) reported neural rim area, disc area less in the right eye.^[7,9] In the present study, among ONH parameters, right eye was having more vertical CD ratio; rest ONH parameters did not have significant differences though the 97.5th outlier value in our study for vertical CD ratio was 0.22, suggesting that asymmetry beyond this should be considered pathologic. Similarly, Altamir *et al.*

also suggested that any asymmetry greater than 0.25 between both eyes represent outlier and should be subjected to further examinations.^[2]

In our study, cutoff limit for interocular RNFL normalcy was 9 μm. Dave *et al.* reported the normal interocular RNFL and PPAA macular thickness asymmetry should not exceed 12.5 μ and 21 μ, respectively, in Indian children by Spectralis OCT.^[8] Altamir *et al.* in their study reported a cutoff limit of 13 μm for average RNFL thickness, similar to 11.7 μm reported by Budenz *et al.*, and 8.8 μm reported by Mwanza *et al.* in their study of adult patients.^[1,31] Budenz *et al.* and Mwanza *et al.* included adult patients in their study, suggesting that normal physiological asymmetry is also demonstrated even in adult patients as well though there is some element of ongoing age-related decaying process.^[1,31] The Sydney Childhood Eye Study reported RNFL thickness range of 16–17 μm in large population-based series study of school-going children.^[7,9] However, Dalglish *et al.* in their study of young adults found cutoff limit of asymmetry to be 9.3 μm in average RNFL (with 2.5% to 97.5% limits).^[30]

The data from previous published studies on normal physiologic asymmetry concluded that although ethnic differences in the thickness of RNFL and ONH parameters may exist, the average degree of interocular symmetry is well preserved.^[8,30]

Table 5: Interocular difference in retinal nerve fiber layer and optic nerve parameters in below 10 and above 10 years of pediatric age group

	10 and below		Above 10		P
	Mean±SD	Range	Mean±SD	Range	
RNFL (μm)					
Superior	-3.16±15.0	-28-40	-8.60±10.4	-44-10	0.213
Nasal	-1.13±15.2	-49-33	-1.07±20.0	-56-70	0.710
Temporal	2.21±8.0	-19-16	3.48±7.8	-17-37	0.733
Inferior	-3.83±18.1	-30-64	1.50±19.2	-33-68	0.089
Average	-2.17±5.5	-15-9	-0.56±4.5	-9-11	0.236
Optic nerve					
Rim area	-0.018±0.16	-0.37-0.26	-0.033±0.23	-0.6-0.63	0.931
Disc area	0.036±0.28	-0.47-0.40	-0.039±0.32	-0.83-0.57	0.400
Average C/D ratio	0.009±0.05	-0.08-0.09	0.017±0.07	-0.16-0.22	0.848
Vertical C/D ratio	0.018±0.05	-0.10-0.14	0.024±0.07	-0.10-0.25	0.624
Cup volume (mm ³)	0.049±0.16	-0.175-0.419	0.010±0.15	-0.325-0.45	0.338
RNFL					
Superior	-5.25±21.8	-46-38	-13.41±16.8	-45-20	0.166
Superior-nasal	-10.00±26.3	-63-51	-13.91±17.3	-58-29	0.573
Nasal-superior	2.38±19.3	-37-47	2.09±17.2	-42-34	0.848
Nasal	3.13±8.3	-19-22	1.89±11.2	-24-26	0.528
Nasal-inferior	-5.08±13.4	-24-22	4.50±17.3	-42-45	0.007
Inferior-nasal	-3.33±25.6	-50-71	-2.35±17.2	-40-36	0.603
Inferior	-8.75±20.2	-54-44	3.87±20.5	-40-81	0.007
Inferior-temporal	0.38±29.0	-65-83	1.30±16.9	-33-49	0.647
Temporal-inferior	2.75±12.9	-24-29	-0.39±15.5	-54-21	0.560
Temporal	1.38±5.6	-7-20	1.07±5.3	-13-16	0.682
Temporal-superior	3.17±10.8	-15-26	5.13±12.2	-48-31	0.389
Superior-temporal	-2.17±17.6	-34-26	5.72±26.1	-86-97	0.149

SD: Standard deviation, RNFL: Retinal nerve fiber layer, C/D: Cup-disc

Within the 2.5th and 97.5th percentiles lie 95% of the values, and this range is called the 95% central range. Therefore, the values below the 2.5th and above the 97.5th percentiles represent outliers, and pathology should be considered. Most of the studies in the literature of normative age-matched data had RNFL analysis by including randomly selected eyes or including only right eye or left eye, considering the fact that either eye could be assessed while calculating normative data by OCTs.^[9-16] The present study illustrates that normal asymmetry should always be taken consideration while assessing average RNFL, quadrant and 12 sector analysis which could be decisive in diagnosing and management, whenever unilateral optic nerve pathology such as unilateral disc edema, optic neuritis, compressive optic neuropathy, and amblyopia is suspected. Diagnosing pediatric glaucoma suspect, periodical follow-up of suspect cases, and established cases of pediatric glaucoma could be monitored if the ophthalmologist is well aware of this asymmetry in RNFL and ONH parameters.

The clinical judgment of CD ratio can differ from OCT machine values, so clinicians should be cautious while interpreting asymmetry.

The limitations of our study include the relatively small number of subjects. Furthermore, we used only Indian

pediatric subjects, so the results may not be applicable to other ethnic populations. However, we have not taken axial length measurement into consideration in our study since we have limited our subjects to only mild and moderate refractive errors, thus excluding high refractive errors. Inclusion of high refractive errors could have an impact on measurements of the RNFL. Hence, our conclusions may not be extrapolated to otherwise normal children with higher refractive errors.

In published literature, various studies evaluated normative data <18 years of age for various commercially available OCTs.^[3-20] All these studies concluded that measurements provided by each of the existing commercial imaging devices differ, and measurements taken with one device cannot be used interchangeably with measurements from another device. Even the same device with upgraded software could also depict some variations, and moreover, ethnic variations do exist. In the same manner, physiological variation can also occur when different OCT imaging devices are used.

As the number of applications of OCT in pediatric ophthalmology is increasing, it is essential that a normative database of physiologic variations is developed for the Cirrus OCT and ophthalmologist should be extremely cautious when diagnosing disorders and management based on the same.

Table 6: Optical coherence tomography values of previous studies of children with spectral domain optical coherence tomography and interocular symmetry

Author	Ethnicity	Number of children	Age (mean±SD)	Average global RNFL thickness (μm) (mean±SD)	OCT version	ISNT/ISTN/SITN rule	Interocular symmetry
Our study	Indian	70	5-17 (11.83±3.3)	94.46±8.7	Cirrus HD OCT	ISNT	Studied Significant differences in superior and temporal quadrant ONH parameters-vertical C/D ratio difference significant
Elía <i>et al.</i> , 2012 ^[22]	Spanish	344	6-13 (9.16±1.7)	98.46±10.79	Cirrus HD OCT	ISNT	Not studied
Yanni <i>et al.</i> , 2013 ^[25]	North American	83	5-15	107.6±1.2	Spectralis SD OCT	ISNT	Not studied
Tsai <i>et al.</i> , 2012 ^[21]	Taiwan	400	7-12	109.4±10.0	RTVue-100	ISNT	Not done
Zhu <i>et al.</i> , 2013 ^[23]	Chinese	1955	12	103.08±9.01	Ivue-100 SD OCT	ISTN	Not done
Barrio-Barrio <i>et al.</i> , 2013 ^[3]	Spanish	283	4-17 (9.6±3.1)	97.40±9.0	Cirrus	ISNT	Not done
Chen <i>et al.</i> , 2013 ^[27]	Chinese	2324	6-17	106.89±12.84	OCT-iVue 100	SITN	Not done
Dalgliesh <i>et al.</i> , 2015 ^[30]	White, East Asian, South Asian, Middle East	1500	16-19 (17.3)	Right eye: 99.3 Left eye: 99	Cirrus HD OCT	ISNT	9.3 μm in average RNFL (with 2.5%-97.5% limits)
Turk <i>et al.</i> , 2012 ^[24]	Turkish	107	6-16 (10.46±2.94)	106.45±9.41	Spectralis SD OCT	ISNT	Not done
Dave <i>et al.</i> , 2015 ^[4]	Indian	126	5-18 (11.42±3.59)	100.3±8.3	Spectralis SD OCT	ISNT 30 eyes IST 66 eyes	Not done
Rao <i>et al.</i> , 2013 ^[26]	Indian	74	4-17 (10±3.4)	94±10.9 right eye 93±10.6 left eye	Cirrus HD OCT	SINT	Not done
Al Haddad <i>et al.</i> , 2014 ^[29]	Lebanese	108	6-17 (10.7±3.1)	95.6±8.7	Cirrus HD OCT	ISNT	Interocular symmetry studied, significant differences in superior, nasal, temporal quadrant. ONH parameters no differences
Dave <i>et al.</i> , 2017 ^[8]	Indian	126	5-15	Right eye: 100.12±7.71 Left eye: 100.49±8.84	Spectralis SD OCT	Not mentioned	Difference in the average and superior RNFL between the right and the left eye was not statistically significant

RNFL: Retinal nerve fiber layer, C/D: Cup-disc, SD OCT: Spectral domain optical coherence tomography, SD: Standard deviation, HD: High definition, ONH: Optic nerve head, ISNT: Inferior superior nasal temporal, ISTN: Inferior superior temporal nasal, SITN: Superior inferior temporal nasal, IST: Inferior superior temporal

Conclusions

We have provided here a reference to normative data for Cirrus OCT measurements of RNFL in a normal pediatric population. These measurements were not found to be influenced by the gender of the children. Normal variation in interocular symmetry does exist, which should be taken into consideration when diagnosing any pathology of pediatric retinal disorder, glaucoma, or ONH disorder by OCT.

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Conflicts of interest

There are no conflicts of interest.

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