



# Retinal Nerve Fiber Layer Thickness in Normal Indian Pediatric Population of North India Measured with Optical Coherence Tomography

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## Authors' contributions

*This work was carried out in collaboration between all authors. All authors read, designed and approved the study.*

## Article Information

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## ABSTRACT

**Purpose:** To measure the peripapillary retinal nerve fiber layer thickness in normal paediatric population of rural India

**Materials and Methods:** 59 normal Indian children (117 eyes) of age range 5-17 years presenting to the Pediatric Clinic were included in this Observational cross sectional study. RNFL thickness was measured with cirrus high definition optical coherence tomography (OCT).

**Inclusion Criteria:** Any child of age 5 years to 17 years but cooperative for OCT.

**Exclusion Criteria:** Children with refractive errors strabismus or amblyopia, with neurological, metabolic, vascular, or other disorders and those with abnormal optic discs were excluded. Both eyes of each subject were scanned and selected for statistical analysis. The effect of age and gender on RNFL thickness was investigated statistically.

**Results:** The mean global RNFL thickness in males was  $92.75 \pm 15.107 \mu\text{m}$  (range 48-144  $\mu\text{m}$ ) and that in females was  $89.98 \pm 11.080 \mu\text{m}$  (range 68-101  $\mu\text{m}$ ) and the difference was not statistically significant ( $p=0.193$ ). RNFL was thickest inferiorly ( $123.5 \pm 19.56 \mu\text{m}$ ) and superiorly

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( $112.7 \pm 25.16 \mu\text{m}$ ), thinner nasally ( $68.95 \pm 13.24 \mu\text{m}$ ), and thinnest temporally ( $66.36 \pm 12.97 \mu\text{m}$ ). In correlation analysis, age had no statistically significant ( $P = 0.702$ ) effect on RNFL thickness.

**Conclusion:** Although in normal children, variation in RNFL thickness is large OCT can be used to measure and analyse RNFL thickness in children. The normative data provided by this study may assist in identifying changes in RNFL thickness in children of rural Indian population.

*Keywords: Optical coherence tomography; pediatric normative database; retinal nerve fiber layer in children.*

## 1. INTRODUCTION

Optical coherence tomography (OCT) is a non-invasive, non-contact imaging technology giving a cross sectional image of the retina and its substructures in a real time mode and *in vivo* [1,2] display of all the 10 layers of retina and nerve fiber layer thickness assessment around the disc. OCT can measure the thickness of the retinal nerve fiber layer (RNFL) with micrometer-scale sensitivity. Optical coherence tomography can be used for the diagnosis and follow up of different types of retinal disorders and glaucoma [2,3,4]. The reproducibility and good diagnostic ability of OCT for both adults and children have been proven in various studies [5,6].

Several reference data exist regarding normative values of retinal thickness across different age distributions, ethnicities, and ocular disease states [7,8,9,10,11]. Preliminary studies have shown that retinal thickness changes with age and ethnicities [9,10,11]. The normal range of RNFL thickness in adults has been measured by several investigators using OCT [7,8] but normative RNFL thickness values in children has not been thoroughly investigated. The published reports of OCT values in the healthy eyes of children are limited due to consideration of either a single age group or a single race. The population distribution of RNFL thickness as measured by cirrus OCT has not yet been established for young children in India. This study may allow the development of reference standards for better investigation and detection of various ocular disease in children.

All subjects were recruited from patients' ages 5 years to 17 years presenting to the Pediatric Clinic. Permission from the Institutional ethical committee was taken. Informed consent from parents was taken.

### 1.1 Inclusion Criteria

Any child of age 5 years to 17 years but cooperative for OCT.

The selection criteria for further evaluation were a cup-disc ratio of less than 0.7 or cup-disc ratio asymmetry of less than 0.2 on careful examination of the optic nerve head.

### 1.2 Exclusion Criteria

Children with strabismus or amblyopia any abnormalities of the disc or the retinal nerve fiber layer family history of glaucoma any other hereditary eye disease history of intraocular surgery or any kind of laser therapy, mentally challenged children with neurological, metabolic, vascular disorders, other systemic disease possibly affecting the eye, presence of a media opacity, best-corrected visual acuity of less than 20/30, hypermetropia more than + 3D, myopia more than -5D, or astigmatism more than 2D were also excluded.

The subjects enrolled had no ocular visual problems. The children came for routine eye hospital in Ophthalmology or paediatrics OPD were enrolled when they met the inclusion and exclusion criteria.

The complete Ophthalmological examination was done in all children. The complete ophthalmic examination included BCVA, IOP, slit lamp anterior segment examination, assessment of ocular motility and dilated posterior segment examination with slit lamp using 90D or Indirect ophthalmoscopy.

Pupils were dilated with tropicamide 1% and cyclopentolate 1% or 2% drops (for cycloplegic refraction where required), depending on age of the subject for cycloplegic refraction and fundus examination. RNFL measurements were obtained through dilated pupils using a 3-generation optical coherence tomographer (stratus OCT, software version 4.0.4, Carl Zeiss, Dublin, CA). This OCT uses partial coherence interferometry technology (wavelength, 840 nm) to obtain cross-sectional images (equivalent to B-scan ultrasound) and achieves an axial resolution of approximately 5  $\mu\text{m}$  with scanning rate of 27 kHz. OCT also has been shown to

have good intra-observer and inter-observer reproducibility, [5,6] and generally is not affected by optical aberrations or pupil diameter [12]. Peripapillary measurements were performed using the fast scan protocol (fast RNFL thickness scan [3.4 protocol]; this consists of a circular scan pattern in which the diameter is 3.46 mm for eyes with standard axial length [24.46 mm] and refraction 0 diopters [D]). Each scan consists of 256 individual Ascans along a circular scan path. Three such circular scans were performed successively. The average of the 3 scans was used in the analysis. All scans were performed by the same investigator. An internal fixation target was used in all scans, and the location of each scan on the retina was monitored on the built-in infrared-sensitive video camera. Scans were accepted only if they were free of artifacts and had signal strengths of at least 7. Mean RNFL thickness in micrometers along the whole circle circumference, four quadrants, 12'o clock hours, and at 256 A-scan lengths were obtained. 12 30° sectors were also defined in clockwise order for the right eye and in counterclockwise order for the left eye: 1-superior-nasal, 2-nasal-superior, 3-nasal, 4-nasal-inferior, 5-inferior-nasal, 6-inferior, 7-inferior-temporal, 8-temporal-inferior, 9-temporal, 10-temporal-superior, 11-superior temporal, and 12-superior). Maximum RNFL thickness in superior and inferior quadrants was also analyzed.

Mean age of the children included in this study have been shown in Table 1.

**1.2.1 Statistics**

Both eyes of every subject were selected for statistical analysis. Univariate and multivariate progression analyses were used to analyze the effect of age and gender on RNFL thickness. Statistical comparisons of variables between right and left eyes were performed using the paired student's t test. For comparisons of variables between genders, the unpaired Student's t test was used. All statistics were done using the Stata: Data analysis and statistical software.

**Table 1. Showing mean age of the subjects**

	Sex	N	Mean	Std. deviation	Std. error mean
Age	M	71	11.21	2.762	.328
	F	46	9.48	2.795	.412

**2. RESULTS**

**2.1 Demographics**

70 subjects consented for the study. Out of these 5 (7.1%) were uncooperative and scan could not be done in them. One (1) subject had leucomatous corneal opacity in the left eye. 12 (9.3%) scans out of 129 were excluded because quality was not good. So a total of 117 eyes scans were included in statistical analysis. There was no statistically significant difference between male and female subjects for age (P =0.833).

**2.2 RNFL Thickness**

The mean global RNFL thickness in was 91.66±13.682 µm (range was from 48 µm-144 µm). The mean global RNFL thickness in males was 92.75±15.107 µm (range 48-144 µm) and that in females was 89.98±11.080 µm (range 68-101 µm) and the difference was not statistically significant (p=0.193). This data has been shown with the help of histogram in Fig. 1. On average, the RNFL was thickest inferiorly, thin superiorly and thinner nasally and thinnest temporally. RNFL was thickest inferiorly (123.5±19.56 µm) and superiorly (112.7±25.16 µm), thinner nasally (68.95±13.24 µm), and thinnest temporally (66.36±12.97 µm). In correlation analysis, age had no statistically significant (P =0.0702) effect on RNFL thickness.

**3. DISCUSSION**

OCT is an imaging modality that relies on low-coherence interferometry to measure the echo time delay and intensity of backscattered and back reflected light from internal microstructures in biologic tissues. It allows real-time, high-resolution imaging and cross sectional analysis of the optic disc and retina. With the advent of this investigative procedure, a major goal is to validate it's usefulness in allowing early diagnosis of various ocular pathologies involving changes in retina and optic nerve head. To allow such utilization, it is necessary to have reliable comparative data establishing the normal ranges of healthy RNFL thickness and optic disc topography. Reproducibility of optic disc and RNFL analysis using OCT has been established in previous studies [13,14]. Normative reference values for RNFL thickness have previously been established [15]. But there is very limited data available for paediatric age group. The published reports of OCT values in the healthy eyes of children are limited by consideration of either a

single age group or a single race. Appropriate OCT signal strength is necessary for reliable RNFL measurements [16]. OCT signal strength may be influenced by optical media opacification such as cataract, corneal pathology, vitreous opacities, etc; however, in our study significant ophthalmic comorbidities were absent. During establishment of the RNFL normative database only 12 of 129 (9.3%) scans were excluded due to poor OCT signal strength. Our finding of a large number of disqualified scans due to poor OCT signal strength and suggests that even under "ideal" examination conditions, appropriate scan quality may be difficult to obtain and expertise in image acquisition is required to optimize OCT image quality and analysis.

Normative data are provided automatically by OCT, but the database only includes individuals 18 years and older, which limits its use in children.

The average RNFL thickness in our study was in males was  $91.66 \pm 13.682 \mu\text{m}$  (range 48-144  $\mu\text{m}$ ) and that in females was  $89.98 \pm 11.080 \mu\text{m}$  (range 68-101  $\mu\text{m}$ ) which is lesser than that reported in other studies done for assessment of paediatric RNFL (Table 2). This difference might be due to the higher prevalence of malnutrition in our subjects which is expected in rural Indian population and also the difference in the versions

of devices used and the different algorithms used for analysis.

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 around the optic nerve as has been previously reported for OCT data from the normal children [17] and adults [3,5].

Measurements of RNFL thickness were not dependent on age in our population of children. The mean RNFL for males was slightly greater than that for females. Age had no statistically significant ( $P = 0.702$ ) effect on RNFL thickness.

The measurements obtained from the different OCT models can vary [18]. Furthermore, this difference may also occur among different models of certain SDOCT devices [18,19]. Taken together, these findings suggest that differences in OCT technology may be responsible for the differences between our results and previously published data on RNFL thickness. The reason why different versions of OCT yield different values for RNFL thickness is not clear. It is possible that different software algorithms used to delineate the RNFL may be among the factors responsible for this observation.

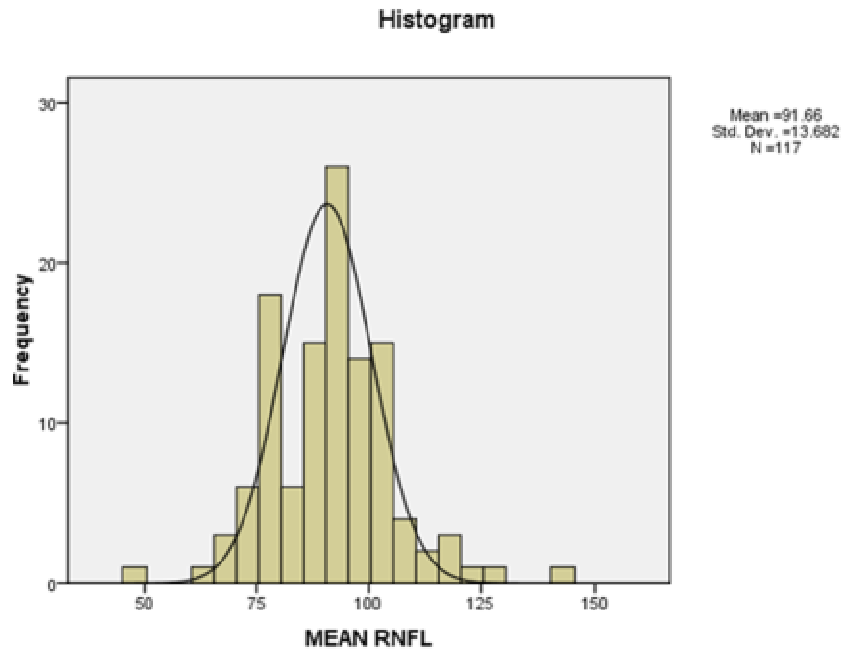


Fig. 1. Histogram showing distribution of RNFL thickness in normal pediatric population in our study

**Table 2. Showing comparison of our study with various studies done for RNFL with OCT on normal subjects**

Author	Ethnicity	Number of subjects	Age (years) (Mean±SD)	Global RNFL thickness $\mu\text{m}$ (Mean±SD)	OCT version
Our study	Rural Indian	59	5-15 10.55±2.9	91.66±13.682 $\mu\text{m}$	Cirrus HD OCT
Gupta et al. [20]		18	6-13	100±2.64	Not mentioned
Parikh et al. [11]	Asian Indian	59	5-20	100.15±10.8	Stratus OCT
Ahn et al. [17]	Korean	72	9-18	105.53±0.33	Stratus OCT
Turk et al. [19]	Turkish	107	6-16 10.46±0.94	106.45±9.41	Spectralis OCT
Neelam Pawar et al. [21]	Indian	120	5-17 10.8±3.24	106.11±9.5	Stratus OCT
Huynh et al. [6]	White and east Asian	1765	6	103.7±11.4	Stratus OCT
Leung et al. [22]	Hong Kong	97	9.75	113±9.8 RE 113.1 LE	Stratus OCT

RNFL thickness is significantly correlated with age and axial length. However, in this study we did not consider potential influential factors for RNFL measurements, including refraction, axial length, optic disc size. Limited numbers and the exclusion of eyes with refractive errors may have limited our ability to identify additional relationships with RNFL thickness.

#### 4. CONCLUSION

In conclusion this study demonstrates normative values of retinal thickness and RNFL thickness in the pediatric age group of north India. This information would facilitate evaluation of OCT scans performed in children with diagnosed or suspected glaucoma as well as those with other optic nerve pathologies and will be helpful in labelling a scan to be pathological or belong to normative database.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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