

Original Research Article

Retinal nerve fiber layer thickness in normal Indian pediatric population of north India measured with optical coherence tomography

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(117eyes)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 μm) and that in females was $89.98 \pm 11.080 \mu\text{m}$ (range 68-101 μm) and the difference was not statistically significant($p=0.193$). RNFL was thickest inferiorly ($123.5 \pm 19.56 \mu\text{m}$) and superiorly ($112.7 \pm 25.16 \mu\text{m}$), 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.

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

33 **Keywords:** optical coherence tomography, pediatric normative database,
 34 retinal nerve fiber layer in children

35 INTRODUCTION

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

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

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

60 Inclusion criteria

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

62 The selection criteria for further evaluation were a cup-disc ratio of less than
63 0.7 or cup-disc ratio asymmetry of less than 0.2 on careful examination of the
64 optic nerve head

65

66 Exclusion criteria

67 Children with strabismus or amblyopia

68 any abnormalities of the disc or the retinal nerve fiber layer

69 family history of glaucoma

70 any other hereditary eye disease

71 history of intraocular surgery or any kind of laser therapy,

72 mentally challenged children with neurological, metabolic, vascular disorders,

73 other systemic disease possibly affecting the eye, presence of a media opacity,

74 best-corrected visual acuity of less than 20/30,

75 hypermetropia more than + 3D, myopia more than -5D, or astigmatism more
76 than 2D were also excluded.

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

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

84 Pupils were dilated with tropicamide 1% and cyclopentolate 1% or 2% drops (
85 for cycloplegic refraction where required), depending on age of the subject for
86 cycloplegic refraction and fundus examination. RNFL measurements were
87 obtained through dilated pupils using a 3 -generation optical coherence
88 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 μ 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 A-scans 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, 10temporal-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

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

RESULTS:

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 ($P = 0.833$).

RNFL thickness:

The mean global RNFL thickness in males was $92.75 \pm 15.107 \mu\text{m}$ (range 48-144 μm) and that in females was $89.98 \pm 11.080 \mu\text{m}$ (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 ($123.5 \pm 19.56 \mu\text{m}$) and superiorly ($112.7 \pm 25.16 \mu\text{m}$), 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 ($P = 0.0702$) effect on RNFL thickness.

DISCUSISION:

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 $92.75 \pm 15.107 \mu\text{m}$ (range 48-144 μm) and that in females was $89.98 \pm 11.080 \mu\text{m}$ (range 68-101 μm) 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.

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.

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.

BIBLIOGRAPHY:

1. Huang D, Swanson EA, Lin CP, Schuman JS, Stinson WG, Chang W, et al. Optical coherence tomography. *Science*. 1991;254:1178–81.
- 2 Jaffe GJ, Caprioli J. Optical coherence tomography to detect and manage retinal disease and glaucoma. *Am J Ophthalmol*. 2004;137:156–69.
- 3 Wollstein G, Schuman JS, Price LL, Aydin A, Stark PC, Hertzmark E, et al. Optical coherence tomography longitudinal evaluation of retinal nerve fiber layer thickness in glaucoma. *Arch Ophthalmol*. 2005;123:464–70.
- 4 Liu X, Ling Y, Luo R, Ge J, Zheng X. Optical coherence tomography in measuring retinal nerve fiber layer thickness in normal subjects and patients with openangle glaucoma. *Chin Med J (Engl)* 2001;114:524–9.
- 5 Blumenthal EZ, Williams JM, Weinreb RN, Girkin CA, Berry CC, Zangwill LM. Reproducibility of nerve fiber layer thickness measurements by use of optical coherence tomography. *Ophthalmology*. 2000;107:2278–82.

- 216 6 Wang XY, Huynh SC, Burlutsky G, Ip J, Stapleton F, Mitchell P.
217 Reproducibility of and effect of
218 magnification on optical coherence tomography measurements in children. Am
219 J Ophthalmol. 2007;143:484–8.
- 220 7 Varma R, Bazzaz S, Lai M. Optical tomography measured retinal nerve
221 fiber layer thickness in normal latinos. Invest Ophthalmol Vis Sci.
222 2003;44:3369–73.
- 223 8 Ramakrishnan R, Mittal S, Ambatkar S, Kader MA. Retinal nerve fibre
224 layer thickness measurements in normal Indian population by optical
225 coherence tomography. Indian J Ophthalmol. 2006;54:11–5.
- 226 9 Bowd C, Zangwill LM, Blumenthal EZ, Vasile C, Boehm AG, Gokhale PA, et
227 al. Imaging of the optic disc and retinal nerve fiber layer: The effects of age,
228 optic disc area, refractive error, and gender. J Opt Soc Am A Opt Image Sci Vis.
229 2002;19:197–207.
- 230 10 Alamouti B, Funk J. Retinal thickness decreases with age: An OCT study.
231 Br J Ophthalmol. 2003;87:899–901.
- 232 11 Parikh RS, Parikh SR, Sekhar GC, Prabakaran S, Babu JG, Thomas R.
233 Normal age related decay of retinal nerve fiber layer thickness.
234 Ophthalmology. 2007;114:921–6.
- 235 12 Savini G, Zanini M, Barboni P. Influence of pupil size and cataract on
236 retinal nerve fiber layer thickness measurements by Stratus OCT. J Glaucoma.
237 2006;15:336–40.
- 238 13 Olmedo M, Cadarso-Suarez C, Gomez-Ulla F, et al. Reproducibility of
239 optic nerve head measurements obtained by optical coherence tomography.
240 Eur J Ophthalmol. 2005; 15:486–492.[PubMed: 16001383]
- 241 14 Paunescu LA, Schuman JS, Price LL, et al. Reproducibility of nerve fiber
242 layer thickness, macular thickness, and optic nerve head measurements using
243 Stratus OCT. Invest Ophthalmol Vis Sci. 2004;45:1716–1724. [PubMed:
244 15161831]

- 245 15 Budenz DL, Anderson DR, Varma R, et al. Determinants of normal retinal
246 nerve fiber layer thickness measured by Stratus OCT. *Ophthalmology*. 2007;
247 114:1046–1052. [PubMed: 17210181]
- 248 16 Cheung CY, Leung CK, Lin D, et al. Relationship between retinal nerve
249 fiber layer measurement and signal strength in optical coherence tomography.
250 *Ophthalmology*. 2008; 115:1347–1351.[PubMed: 18294689]
- 251 17 Ahn HC, Son HW, Kim JS, Lee JH. Quantitative analysis of retinal nerve
252 fiber layer thickness of normal
253 children and adolescents. *Korean J Ophthalmol*. 2005;19:195–200.
- 254 18 Seibold LK, Mandava N, Kahook MY. Comparison of retinal nerve fiber
255 layer thickness in normal eyes using time domain and spectral domain optical
256 coherence tomography. *Am J Ophthalmol*. 2010;150:807–14.
- 257 19 Turk A, Ceylan OM, Arici C, Keskin S, Erdurman C, Durukan AH, et al.
258 Evaluation of the nerve fiber layer and macula in the eyes of healthy children
259 using spectral domain optical coherence tomography. *Am J*
260 *Ophthalmol*. 2012;153:552–559.e1.
- 261 20 Gupta G, Donahue JP, You T. Profile of the retina by optical coherence
262 tomography in the pediatric age group. *Am J Ophthalmol*. 2007;144:309–10
- 263 21 Neelam Pawar, Devendra Maheshwari, Meenakshi Ravindran, and
264 Renagappa Ramakrishnan. Retinal nerve fiber layer thickness in normal Indian
265 pediatric population measured with optical coherence tomography. *Indian J*
266 *Ophthalmol*. 2014 Apr; 62(4): 412–418
- 267 22 Leung MM, Huang RY, Lam AK. Retinal nerve fiber layer thickness in
268 normal Hong Kong chinese children measured with optical coherence
269 tomography. *J Glaucoma*. 2010;19:95–9

270

271 **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

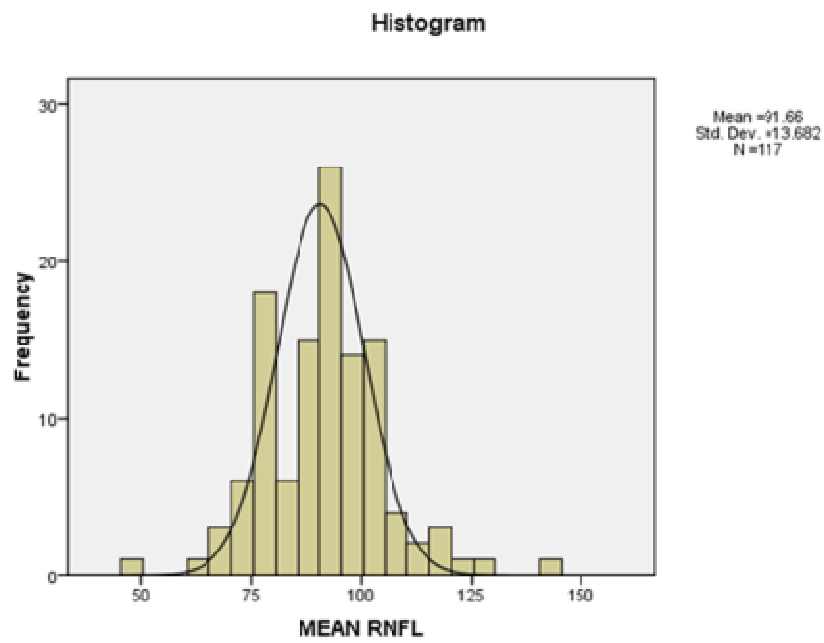
272

273 **Table :2** showing various studies done for RNFL with OCT on normal subjects

Author	Ethnicity	Number of subjects	Age (years) (mean±SD)	Global RNFL Thickness μm (mean±SD)	OCT Version
Our study	Rural indian	59	5-15 10.55±2.9	92.75 ± 15.107 μm	Cirrus hd OCT
Gupta <i>et al</i> [20]		18	6-13	100±2.64	Not mentioned
Parikh <i>et al</i> [11]	Asian indian	59	5-20	100.15±10.8	Stratus oct
Ahn <i>et al</i> [17]	Korean	72	9-18	105.53±0.33	Stratus oct
Turk <i>et al</i> [19]	Turkish	107	6-16 10.46±0.94	106.45±9.41	Spectralis oct
Neelam pawar <i>et al</i> [21]	Indian	120	5-17 10.8±3.24	106.11±9.5	Stratus oct
Huynh <i>et al</i> [6]	White and east asian	1765	6	103.7±11.4	Stratus oct
Leung <i>et al</i> [23]	Hong kong	97	9.75	113±9.8 RE 113.1 LE	Stratus oct

274

275 **Fig:1**



276

277