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Ophthalomology

NORMATIVE DATA FOR RNFL THICKNESS IN NORTH INDIAN PAEDIATRIC POPULATION

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KEYWORDS :

INTRODUCTION

Optical coherence tomography (OCT) is an established medical imaging technique that uses light to capture micrometre resolution, three-dimensional images from optical scattering media (e.g, biological tissue). Optical coherence tomography is based on low-coherence interferometry, typically employing near infrared light. The use of relatively long wavelength light allows it to penetrate into the scattering medium.

At present, OCT imaging is used extensively for imaging the macula, optic nerve and RNFL, and aids in analysing the morphology and quantifying changes in various disease states [1,2].

The **retinal nerve fibre layer** (**RNFL**) is formed by the expansion of the fibres of the optic nerve; it is thickest near the optic disc, gradually diminishing toward the ora serrata. As the nerve fibres pass through the lamina cribrosa sclerae they lose their medullary sheaths and are continued onward through the choroid and retina as simple axis-cylinders.

Most of the fibres are centripetal, and are the direct continuations of the axis-cylinder processes of the cells of the ganglionic layer, but a few of them are centrifugal and ramify in the inner plexiform and inner nuclear layers, where they end in enlarged extremities [3].

RNFL thickness can vary physiologically in refractive errors for instances like in myopia where the thickness of macula and ganglion cells decreases, it can also vary with sex and in different age groups. It has been found that RNFL thickness varies significantly among different ethnic groups [4].

Conditions in which RNFL thickness varies in adults includes Severe retinal ischemia [5], Refractive errors [6], Glaucoma [7], Post intra ocular surgeries [8], Demylinative diseases [9], Optic neuropathy[10], Ocular hypertension [11], Amyotrophic lateral sclerosis (ALS) [12], Optic neuritis [13], Retro bulbar neuritis [14], Alzheimer's disease [15], Parkinson's disease [16], Multiple sclerosis [17], Neuro degenerative diseases [18], Optic atrophy [19], Cerebral venous thrombosis [20]

Paediatric diseases in which RNFL thickness varies includes X-linked adrenoleukodystrophy [21], To rule out treatment induced RNFL loss [22](Anti Tuberculosis, Vigabatrin for tuberous sclerosis), Friedreich ataxia [23], Foveal hypoplasia [24], Retinal dystrophies [25], Retinal findings associated with paediatric storage disorders [26], Infantile neuronal ceroid lipofuscinosis [27], Cognitive deficits [15], Tumors of the Visual Pathway (gliomas)[28], Optic neuritis [13], Optic atrophy [19], Papilledema [29]

There are many ophthalmological pathologies where measurement of RNFL thickness is helpful in the diagnosis and management. However, no normative data base is provided in the current OCT soft wares for the paediatric population. In our study, we derive a normative data base for the RNFL thickness in the North Indian paediatric population.

Review Of Literature

The first in vivo retinal images were obtained in 1993 by Swanson et al. Retinal imaging was also demonstrated independently by the Medical University of Vienna, Fercher et al. By 1996, Zeiss released its first regulatory cleared commercial OCT unit. The first OCT instruments became commercially available in 1996. In 2006 the first Food and Drug Administration (FDA)-approved spectral-domain (SD)-OCT system was introduced. It was introduced by Optovue [30].

Normative data is data from a reference population that establishes a baseline distribution for a measurement, and against which the measurement can be compared. Normative data is typically obtained from a large, randomly selected representative sample from the wider population[31]. Coming on to different studies which attempted to find out the normal RNFL thickness, O Rese J Knight et al (2012) [33] who studied the effect of race, age, and axial length on optic nerve head parameters and retinal nerve fiber layer thickness measured by Cirrus HD-OCT in 284 normal adult subjects of different ethnicity showed that the average RNFL thickness was 94 µm, the inferior RNFL thickness was 123.2 µm superior RNFL thickness was 119 µm, nasal RNFL thickness was 69.8 µm and the temporal RNFL thickness was 64 µm.

Linda Yi-Chieh Poon et al (2018) [4] conducted study to evaluate the effects of age, race, and ethnicity on the optic nerve and peripapillary retina using spectral-domain optical coherence tomography (SD-OCT), showed a significant difference in the RNFL thickness among different ethnic groups.

The study of Salchow et al (2006) [34] showed that average RNFL thickness was107 µm, inferiorly RNFL thickness was 136.9, superiorly RNFL thickness was 135.4 µm, nasally it was 83 µm thick , and temporally 72.5 µm thick.

Coming on to the studies conducted in the Indian paediatric population, Neelam Pawar et al (2014)[35] conducted a study showed that age and gender had no effect on the RNFL thickness while refractive error and axial length showed significant correlation with the RNFL thickness.

Ramakrishnan et al (2006)[36] who conducted study in 70 children in South Indian paediatric population showed that the mean average peripapillary RNFL thickness was 105 µm. RNFL thickness for superior, inferior, nasal, and temporal quadrants were 138.2 µm, 129.1 µm, 85.71 µm and 66.38 µm respectively.

Leung CK et al (2006) [37] conducted a study in Chinese adult myopic population showed that there was a linear correlation between RNFL thickness and axial length/spherical equivalent, they did not find any association between age and RNFL thickness.

Frederick M. Rauscher et al (2009) [38] conducted a "study to assess the effect of myopia on RNFL thickness by OCT" showed no correlation between the RNFL thickness and the age.

Shin hee et al (2010) [39] studied the "Effect of Myopia on the Thickness of the Retinal Nerve Fibre Layer Measured by Cirrus HD Optical Coherence Tomography" among 269 south Korean young adults, they also found the same correlation between the average RNFL thickness and SE and axial length as the previously discussed studies that is, decrease in the RNFL thickness with increase in the axial length and increase in the myopia.

Similar result was observed in the study of Iqra Nehal et al (2019)[40] also who studied the RNFL thickness and correlation with refractive error in Pakistani adult population.

AIM

Measure the retinal nerve fibre layer thickness in paediatric population using OCT.

MATERIALS AND METHODS

The study was conducted in Shroff Eye Centre, Kailash colony, New

Delhi.The total duration of the study was 24 months. The study was conducted in 221 children presented in our outpatient department. All the children fulfilling the inclusion criteria and exclusion criteria underwent the sequence of data collection. An informed consent was obtained from each one of the subject followed by a history and brief general examination was done. Vision was evaluated by Snellens chart. IOP was measured using NIDEK 530 p non-contact tonometer. A cycloplegic refraction was done by cyclopentolate 1% eye drops in all the subjects, followed by that a detailed slit lamp examination was done for assessing the anterior segment. Retina evaluation was done by both 90 D and indirect ophthalmoscopy. Followed by that RNFL thickness was assessed by OCT done in Optovue(RTVue -100), and axial length was measured by TOMEY-OA-2000 optical biometer.

Inclusion Criteria: All children in the age group of 6 to 16.

Exclusion Criteria:

1. Patients with strabismus, amblyopia, or any abnormalities of optic disc.
2. Patients with glaucoma or any hereditary eye disease.
3. Kids with h/o intra ocular surgeries, laser therapy, mentally challenged.
4. Children with metabolic vascular, neurological or any systemic disease that has a probability of affecting eye, presence of media opacity.
5. Inability to co-operate for the examination.

STATISTICALANALYSIS

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected, then non parametric test was used.

Statistical tests were applied as follows-

1. Quantitative variables were compared using Independent t test/Mann-Whitney Test (when the data sets were not normally distributed) between the two groups and ANOVA/Kruskal Wallis test (when the data sets were not normally distributed) between more than two groups.
2. Spearman rank correlation coefficient was used to assess the association of various parameters with axial length.
3. Univariate linear regression was used to find out effect of I unit change in axial length on RNFL thickness.

A p value of <0.05 was considered statistically significant.

The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

OBSERVATION & RESULTS

The total number of subject's in the study was 221 children aged 6 to 16 years. So a total of 442 eyes were examined.

Table 1

	Frequency	Percentage
N	442	100.00%
Total	442	100.00%

Age Distribution (Table 2)

	Frequency	Percentage
1) 6-10	119	53.85%
2)11-16	102	46.15%
Total	221	100.00%

The total number of children aged 6 to 10 years was 119 (53.85%) 11 to 16 years was 102 in number (46.15 %).

Gender Distribution (Table 3)

	Frequency	Percentage
F	130	58.82%
M	91	41.18%
Total	221	100.00%

Total females in the study were 130 (58.82%) and males were 91 (41.18 %).

Classification Of Population Based On Spherical Equivalent (Table 4)

	Percentage
Emmetropia	49.77%
High hyperopia	1.81%
high myopia	8.82%
low hyperopia	8.82%
low myopia	30.77%
Total	100.00%

The study population was classified according to refractive error in to five groups. Emmetropia was classified as spherical error (SE) ranging from +0.50 to -0.50 D, myopia less than -0.75 D(low myopia -0.75- -3D & high myopia less than -3.5D), hypermetropia more than 0.75 D (low hypermetropia 0.75-3D & high hypermetropia more than 3D).

Classification Of Population Based On Axial Length (Table 5)

AXIAL LENGTH	Frequency	Percentage
1)19-20	4	0.90%
2)20.1-22	74	16.74%
3)22.1-24	248	56.11%
4)24.1-26	102	23.08%
5)>=26	14	3.17%
Total	442	100.00%

The total eyes were also classified based on the axial length into five groups. Group one axial length from 19 to 20 mm. group two 21 to 22 mm, group three 23 to 24 mm, group four 25 to 26 mm, group five more than 27mm.

The mean axial length in the group one was 19.8 ±0.2 mm, the median was 19.8 mm. In group two the mean axial length was 21.34±0.57 mm, median as 21.45 mm. In group three the mean axial length was 22.94 ± 0.57 mm, median was 22.95 mm. In group four the mean axial length was 24.74±0.52 mm, median was 24.6 mm. In group five the mean axial length was 26.44 ± 0.48 mm and 26.6 mm was the median.

Mean RNFL thickness

The mean average RNFL thickness of all the 442 eyes was 109±14.21 µm. The mean RNFL thickness of the inferior and superior half was 106.25 ± 13.91 µm, 109.2 ± 15 µm respectively. The mean RNFL thickness in the superior quadrant was 140.09 ± 21.12 µm. The mean RNFL thickness of inferior quadrant was 134.67 ± 19.65 µm. The mean RNFL thickness of nasal and temporal quadrant was 80.49 ± 18.13 µm and 78.24 ± 12.91 µm respectively.

DISCUSSION

The total number of children who participated in our study was 221, a total of 442 eyes were examined for the study. The age group we examined varied from 6 to 16 years. The mean age of the population was 10.36 ± 2.16 years. A total of 130 girls and 91 boys were examined. In our study, percentage of population with emmetropia, myopia and hypermetropia was 49.77%, 39.59%, 10.63% respectively, which is not matching with the study of Rakhi Dandona et al, who did a population based study of percentage of children with refractive error in the rural population of Andhra Pradesh, in which the prevalence of hypermetropia was 0.68% and myopia was 5.6% [41]. The percentage of children with refractive error in the urban population of New Delhi was 15.1% with 7.7% hypermetropia and 7.4% myopia (Murthy et al) [42]. The probable reason of disparity in the percentage of children with refractive errors in our study is mainly because our study is a hospital based study whereas other prevalence studies are population based study.

The mean RNFL thickness of our study was 109±14.21 µm, which is comparable to the study of Marcelo Ayela et al (Swedish paediatric population)[43] (105 ± 10.3 µm) and Ramakrishnan et al (south Indian paediatric population)[36] (106.11 ± 9.50 µm), but considerably higher compared to the study of Neelam Pawar et al [35] (94.46 ± 8.7 µm) who studied the peripapillary RNFL thickness in 70 normal south Indian children of 5-17 years of age.

Study name	Number of eyes	Race	Type of OCT	Mean age	Mean RNFL thickness
Marcelo Ayela et al (2016) [43]	138	Swedish	Topcon 3D OCT 2000	9.1	105± 10.3 µm
Kang MT et al (2016) [44]	2179	Chinese	SD OCT	7	102.01± 8.02µm

Neelam Pawar et al (2017) [35]	70	Indian	Cirrus HD OCT	11.83	94.46 ± 8.7 µm
Bharti Nigam et al (2017) [45]	340	Indian	Cirrus HD OCT	10.4	110.81 ± 13.74 µm
Yadollah Eslami et al (2017) 46	115	Iran	SD OCT	12.44	101.01± 7.74 µm
Salchow et al (2005) [34]	92	Hispanic	Stratus OCT (Carl Zeiss, Dublin, CA)	9.7	108.0± 11.4 µm
Ramakrishnan et al (2012) [36]	120	Indian	Stratus OCT (Carl Zeiss, Dublin, CA)	10.8	106.11 ± 9.50 µm
Asmaa N Ali et al (2018) [47]	100	Egypt	SS OCT 3D DRI OCT	10.96	111.26±20.46 µm
Jody goh et al (2017) [48]	243	Chinese	Cirrus SD OCT	9.47	99.00±11.45 µm
Our study	442	Indian	Optovue OCT	10.36	109±14.21 µm

In our study, the RNFL was thickest in the superior (140.09 ± 21.12 µm) quadrant followed by inferior (134.67 ± 19.65 µm) then nasal (80.49 ± 18.13 µm) and least at the temporal quadrant (78.24 ± 12.91 µm). So ISNT rule was not followed in our study. Our study showed a SINT distribution of RNFL thickness. But ISNT rule was followed in the study of Neelam Pawar et al [35] and Ramakrishnan et al [36] who studied RNFL thickness in South Indian paediatric population. Dave P et al (western Indian paediatric population)[57] showed that The ISNT rule on the RNFL was followed only by 23.8 % of the cases, while the IST rule was followed by 52.4 %($p<0.001$). In his study, the superior RNFL was thicker than the inferior in 45.2 %while the temporal RNFL was thicker than the nasal in 50 %. Pradhan ZS et al (south Indian adult population)[58] also showed that mean RNFL thickness in normal eyes showed that 25.9% obeyed the ISNT rule and 70.4% conformed to the "IST" rule. Qiu K et al (Chinese adult population)[59], who studied RNFL thickness in healthy myopic subjects, showed that 88.4% of eyes did not comply with the ISNT rule on RNFL thickness.

SUMMARY AND CONCLUSION

This is a cross sectional study conducted to find out the normative data base for the RNFL thickness in Indian paediatric population.

In our study the average, superior, inferior, nasal, temporal RNFL thickness was 109±14.21 µm, 140.09 ± 21.12 µm, 134.67 ± 19.65 µm, 80.49 ± 18.13 µm, 78.24 ± 12.91 µm respectively, which can be used as a reference for RNFL thickness in North Indian paediatric population. Ours is the first study in North Indian Paediatric Population for giving a normative data base for RNFL thickness.

Limitation Of Our Study

Since ours is a hospital based study; it has over estimated prevalence of refractive error in the population, which has an influence in the mean values of the RNFL thickness also.

For a normative data base, a bigger study sample will yield a better and more reliable result.

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