OCT Based Macular Thickness in a Normal Indian Pediatric Population

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Abstract

Purpose: Cirrus optical coherence tomography (OCT) provides high resolution cross-sectional images of the retina, vitreous humor, and optic nerve head with an axial resolution of 5 µm and a reproducibility of 1.6 µm. An integrated normative database is available only for adult subjects ≥18 years of age; the normal reference ranges of the macular thicknesses of pediatric subjects are not available. The purpose of this study was to determine the normal reference range of macular thickness of pediatric.

Methods: A total of 340 eyes of 170 children 5-17 years of age were recruited for this study. Participants received a full ophthalmic examination including a vision assessment, cycloplegic refraction, fundus examination, intraocular pressure measurement, assessment of ocular motility, and alignment. Macular thickness measurements were obtained through dilated pupils using Cirrus HD-OCT.

Results: The mean macular thickness was 114.88 ± 14.74 in the right eye and 113.99 ± 15.62 in the left eye (P = 0.589). On further evaluation, macular thickness was highest in the inner macula, followed by the outer macula and central fovea (P < 0.001).

Conclusion: The normative data of macular thickness in pediatric subjects 5-17 years of age will help diagnose macular disorders.

Keywords: Macular Thickness; Optical Coherence Tomography; Pediatric Age

INTRODUCTION

Optical coherence tomography (OCT) is a non-invasive, non-contact, transpupillary imaging method for objective, high-resolution imaging of retinal tissue. OCT enables observation, measurement, and identification of structures that are otherwise not easily visible, such as the external limiting membrane and the junction between the internal and external segments of the photoreceptors. Cirrus HD-OCT is spectral domain OCT with a speed of 27,000 A scans/s and a resolution of 5 µm,[1] allowing faster scanning and higher resolution images than time domain OCT technology.

The OCT devices have an integrated normative database for adult subjects >18 years of age. Spectral domain OCT (SD-OCT) is a non-invasive technique and is becoming more popular for the identification,
monitoring, and classification of children with genetic retinal diseases. SD-OCT, the most recent generation of the technology, provides higher resolution and decreased acquisition time; thus it is very useful for pediatric patients. However, normal reference values of pediatric macular thickness on HD-OCT are needed, as the software of Cirrus HD-OCT scanners has no pediatric normogram for comparison.

The purpose of this study was to provide a normative database for the macular thickness of healthy children of an Indian population using Cirrus HD-OCT. The effects of age and gender on macular thickness were also analyzed. These reference standards for pediatric subjects will be useful for the early detection of various ocular diseases in children.

**METHODS**

A total of 192 children aged 5-17 years presented at the pediatric outdoor patient department (OPD) and their guardians were counseled by our resident doctors for inclusion in this study. Of the 192 children, 22 were uncooperative; most showed difficulty while measuring the intraocular pressure (IOP) and conducting OCT, and were excluded. The eyes of 170 children were finally analyzed (Figure 1 gives a detailed algorithm into the selection process).

The research followed the tenets of Declaration of Helsinki; IRB approval and informed consents were obtained after explanation of the study. The institutional review board of Era’s Lucknow Medical College and Hospital, approved the study.

All patients between the ages of 5-17 years were referred from the pediatric OPD to the ophthalmic OPD for enrolment in the study over duration of 18 months (March 2015 to August 2016). The children were selected after ensuring they were healthy and did not have any serious systemic illnesses. All subjects had been full-term infants (≥37 weeks gestational age) of normal birth weight (≥2500 g). The children were divided in three groups according to their ages.

Patients were excluded if they had any type of refractive error; any ocular pathology such as retinitis pigmentosa, posterior staphyloma, strabismus, or amblyopia; any abnormality of the optic disc or maculopathy; a family history of glaucoma or other hereditary eye disease; a history of any ocular injury or intraocular surgery; or any kind of laser therapy; and a history of any systemic disease that was likely to affect the eye.

Each subject underwent a full ophthalmic examination, including a vision assessment by Snellen’s drum both with and without pinhole, cycloplegic refraction, slit lamp biomicroscopy of the anterior segment, fundus examination by direct and indirect ophthalmoscope, IOP measurement, and assessment of ocular motility and alignment.

After thorough ophthalmic and systemic histories and examinations, macular measurements were obtained through dilated pupils using Cirrus OCT. The Cirrus HD-OCT 4000 (Version: 6.5.0.772, Carl Zeiss Meditec. Inc., Jena, Germany) scans optic disc and macular thicknesses in an area 6 mm² area consisting of macular cube 512 × 128.

The macula was divided into 3 concentric circles centered on the fovea. This division was a superimposition of the Early Treatment Diabetic Retinopathy Study (ETDRS) map over the OCT map of the macula. It consists of 3 zones: the fovea (<1 mm in diameter), the inner macula (1-3 mm), and the outer macula (3-6 mm). The zones were further divided into superior, inferior, nasal, and temporal regions of the inner and outer macula and the central foveal zone. Figure 2 depicts an example of macular thickness measurements obtained using an SD-OCT system.

Three OCT volume scans (200 × 200 axial scans) were taken; the scan used for analysis was the scan with the best signal strength, which was centered on the fovea centralis. The macular thicknesses of all scans were determined. All scans were evaluated automatically by the Cirrus OCT system software (version 6.5.0.772; Carl Zeiss Meditec. Inc., Dublin, CA, USA).

**Statistical Analysis**

The macular thicknesses of the central foveal area and all four quadrants (superior, inferior, nasal, and temporal) of the outer and inner maculae were evaluated. Scans with a signal strength ≥6 were included in the analysis. The P value was calculated by Gaussian Z Test.
RESULTS

A total of 170 children 5-17 years of age were included in this study. The mean age was 10.4 ± 2.7 years. There were 100 (59%) males and 70 (41%) females; the M: F ratio was 1.42:1.

The mean macular thickness was found to be 114.88 ± 14.74 µm in the right eye (RE) and 113.99 ± 15.62 in the left eye (LE); the difference was not significant (P = 0.562) [Table 1]. The mean normal macular thickness was 114.77 ± 15.52 in males and 113.81 ± 15.95 in females (P = 0.562). No sex-based differences in normal macular thickness were observed [Table 1]. The mean central macular volume was 9.85 ± 0.57 mm³ in the RE and 9.79 ± 0.55 mm³ in the LE; the difference was not significant (P = 0.323) [Table 2].

The mean macular thicknesses of the different quadrants were assessed in children of different ages. The groups were divided as follows: 62 children were 5-9 years of age, 57 children were 10-13 years of age, and 51 children were 14-17 years of age. In all age groups, the maximum thickness was observed in the inner macula, followed by the outer macula. The nasal quadrant of the macula was the thickest, followed by the superior, inferior, and temporal quadrants in both the inner and outer maculae. The differences were significant (P < 0.001). The difference between the inner and outer macular thicknesses in all quadrants was significant (P < 0.001) [Table 3]. The central foveal thickness was 235.51 µm in children 5-9 years of age, 237.11 µm in children 10-13 years of age, and 240.10 µm in children 14-17 years of age [Table 4].

DISCUSSION

OCT is increasingly used as a diagnostic and monitoring tool of vision loss in children. In the present study, we examined 340 eyes of 170 randomly selected full-term children 5-17 years of age. The primary objective of the study was to provide a normative database of macular thicknesses for healthy children of an Indian population using Cirrus SD-OCT. Effect of age and gender on macular thickness were also analyzed in this study.

The inner macula was the thickest, followed by the outer macula; the central macular area was the thinnest. This finding was consistent with reports by Eriksson et al[2] and Katiyar et al[3]. In the present study, the mean macular thicknesses of the different areas were slightly higher than those reported by Huynh et al,[4] who observed similar results.

The nasal macula was thickest in all age groups, with mean values of 311.32 µm in the 5-9-year age group, 314.56 µm in the 10-13-year age group, and 316.24 µm in the 14-17-year age group. This finding was consistent with the results of Katiyar et al,[3] who reported that the nasal macula was the thickest in both the inner (312.60 µm) and the outer (292.67 µm) macula.

In our study, the nasal quadrant was the thickest in both the inner and outer macula, followed by the superior, inferior, and temporal quadrants. We also found that the macular thickness increased with age, though the difference was not significant. We found no studies that compared the normal distribution of macular thickness in pediatric patients of different ages.

Table 1. The mean macular thickness in the right and left eyes as well as different genders

| Eyes    | RE   | LE   | P   |
|---------|------|------|-----|
| Mean    | 114.88 | 113.99 | 0.562 |
| SD      | 14.74 | 15.62 |     |

Table 2. Comparison of the central macular volume between the two eyes

| Central Macular | Volume (mm³) | Mean | Median | SD | P |
|-----------------|--------------|------|--------|----|---|
| RE              | 9.85         | 9.8  | 0.57   | 0.323 | |
| LE              | 9.79         | 9.0  | 0.55   |     |   |

RE, right eye; LE, left eye; SD, standard deviation Based on Gaussian Z Test.
Table 3. Quadrantic ranges of macular thickness (n=170) children aged 5-17 years.

| Parameters | 5-9 Years | 10-13 Years | 14-17 Years |
|------------|-----------|-------------|-------------|
|            | Range     | Sd          | Range       | Sd          | Range       | Sd          |
| Cft        | 163.0-298.0 | 18.78       | 163.0-298.0 | 18.24       | 163.0-298.0 | 18.69       |
| Inner macula |           |             |             |             |             |
| Superior (sim) | 240-343   | 17.47       | 244-345     | 18.07       | 245-345     | 18.47       |
| Nasal (nim) | 264-360   | 17.02       | 266-362     | 17.15       | 267-361     | 17.72       |
| Inferior (iim) | 262-354   | 17.10       | 265-350     | 17.84       | 263-351     | 17.81       |
| Temporal (tim) | 250-347   | 16.97       | 252-340     | 16.07       | 253-343     | 16.07       |
| Outer macula |           |             |             |             |             |
| Superior (som) | 235-319   | 17.94       | 230-324     | 18.54       | 230-326     | 18.54       |
| Nasal (nom) | 225-340   | 18.60       | 229-345     | 19.28       | 228-345     | 19.30       |
| Inferior (iom) | 208-304   | 29.72       | 210-302     | 29.68       | 208-307     | 30.72       |
| Temporal (tom) | 201-289   | 25.60       | 199-291     | 26.64       | 199-288     | 26.60       |

Based on Gaussian Z Test.

Table 4. Quadrantic values of macular thickness (n=170) children aged 5-17 years.

| Parameters | 5-9 Years | 10-13 Years | 14-17 Years |
|------------|-----------|-------------|-------------|
|            | Mean      | Median      | P           | Mean      | Median      | P           | Mean      | Median      | P           |
| Cft        | 235.51    | 235         | <0.001      | 237.11    | 236         | <0.001      | 240.10    | 241         | <0.001      |
| Macula     |           |             |             |             |             |             |             |             |             |
| Superior (sim) | 306.62   | 306         | <0.001      | 309.11    | 309         | <0.001      | 312.05    | 310         | <0.001      |
| Superior (som) | 270.30   | 274         |             | 274.19    | 273         |             | 275.09    | 276         |             |
| Nasal (nim) | 311.32    | 310         | <0.001      | 314.56    | 312         | <0.001      | 316.24    | 316         | <0.001      |
| Nasal (nom) | 295.10    | 293         |             | 298.12    | 296         |             | 300.09    | 300         |             |
| Inferior (iim) | 306.78   | 306         | <0.001      | 308.12    | 308         | <0.001      | 308.67    | 307         | <0.001      |
| Inferior (iom) | 267.12   | 260         | <0.001      | 265.11    | 265         | <0.001      | 267.19    | 264         |             |
| Temporal (tim) | 293.45   | 294         | <0.001      | 299.10    | 298         | <0.001      | 301.06    | 301         | <0.001      |
| Temporal (tom) | 257.11   | 253         |             | 260.12    | 261         |             | 261.06    | 263         |             |

The mean central volume of the macula was 9.85 mm³ ± 0.57) in the present study, which was higher than the results reported by Eriksson et al. The central foveal thickness was consistently thinnest in all age groups. This finding was consistent with reports by Huynh et al., Eriksson et al., and Katiyar et al.; who found the central fovea to be thinner than both the inner and outer macula.

The normal macular thickness of adults included in the Handan eye study was reported by Duan et al. The mean foveal minimum, central, inner, and outer macular thicknesses were 150.3 µm, 176.4 µm, 255.3 µm, and 237.7 µm, respectively (P < 0.001). The mean total macular volume was 6.761 mm³, which is lower than the findings of our study. In the inner region, the nasal quadrant was thinner than the superior and inferior quadrants; in the outer region, the nasal quadrant was the thickest (P < 0.001).

In a study of normal healthy Indian eyes by Natung et al., the mean macular thickness was 287.87 ± 18.07 µm, which was higher than the mean macular thickness observed in our study. We also tried to assess the variation in macular thickness between the two eyes; the difference was not significant. The difference in the mean macular thicknesses between boys and girls was also not significant, and was in accordance with the results of Katiyar et al. Previous reports by Barrio-Barrio et al., Huynh et al., and Al-Haddad et al. reported that gender differences applied only to central macular thickness measurements, which were significantly increased in males; we did not observe a significant difference.

The limitations of our study included the ethnic uniformity of the subjects (north Indian population); hence the effects of race and ethnicity were not observed. Patients with refractive errors were also excluded, so the normative data for these groups were not established.

In conclusion, the normative data provided for the paediatric population of 5-17 years will be very helpful in the diagnosis of macular disorders. Currently, the results on the SD-OCT do not give the corresponding color coding of the macular thickness with the age matched...
data. We hope, the results provided by our study will help in establishing the coding in the future.

Financial Support and Sponsorship
Nil.

Conflicts of Interest
There are no conflicts of interest.

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