

Assessment of choroid thickness by swept-source optical coherence tomography (SS-OCT) in patients with posterior uveitis

Abhishek Agarwal, Shishir Narain, Charu Gupta, Priyanka Gupta, Daraius Shroff, Cyrus M Shroff

Shroff Eye Centre, Kailash Colony, New Delhi, India

ABSTRACT

BACKGROUND: This study aimed to measure the changes in choroid thickness using Swept-Source Optical Coherence Tomography (SS-OCT) after treatment of posterior uveitis along with changes in fundus auto-fluorescence pattern.

MATERIAL AND METHODS: This prospective observational cohort study was conducted from December 2018 to May 2020, in which 32 eyes of 20 patients presenting in the out-patient department with a clinical diagnosis of posterior uveitis were enrolled. Best-corrected visual acuity (BCVA) by Snellen chart, intraocular pressure (IOP) Measurement using a non-contact tonometer, choroidal thickness by SS-OCT, and fundus imaging by Fundus Autofluorescence was done. All tests were done at baseline, first follow-up of 2 ± 1 weeks and the second follow-up of 6 ± 2 weeks. Data was compiled and analyzed.

RESULTS: The mean age of patients was 31 ± 6.9 years with M:F of 3:1. During the second follow-up, with the healing of the lesions, there was a significant reduction in the choroidal thickness at all levels by SS-OCT ($p < 0.05$), with significant improvement in BCVA (0.05 vs. 0.14 vs. 0.31, $p < 0.05$). IOP increased significantly at the first follow-up to 17.31 from baseline (16.25) ($p = 0.032$). However, the rise at the second follow-up was not significant (17.03 vs. 16.25 at baseline, $p = 0.15$). On fundus autofluorescence, normal autofluorescence and hypofluorescence increased at the second follow-up of 6 weeks ($p < 0.0001$).

CONCLUSION: SS-OCT showed a significant decrease in the choroidal thickness at all levels during the follow-ups. The healing of the posterior uveitis lesions and fundus autofluorescence became normal simultaneously.

KEY WORDS: choroidal thickness; fundus autofluorescence; swept-source optical coherence tomography

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INTRODUCTION

Swept-source optical coherence tomography (SS-OCT) is the latest milestone in retinal and choroidal imaging. Because of its wavelength of 1050 nm, which is superior to the 840 nm of spectral-domain optical coherence tomography (SD-OCT),

it can overcome ocular opacities such as cataracts and vitritis, allowing the retinal and choroidal visualization of eyes whose fundus is not clearly visible. For the same reason, SS-OCT allows visualization of the retinal and choroidal vascular networks, even in eyes with medium opacity [1].

CORRESPONDING AUTHOR:

Dr Abhishek Agarwal, Shroff Eye Centre, Kailash Colony, 110048 New Delhi, India; e-mail: abhishek100393@gmail.com

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Choroidal thickness is measured on the SS-OCT by calculating the distance from the hyperreflective line representing the outer border of the retinal pigment epithelium (RPE) to the inner edge of the suprachoroidal space, which is represented by a hyporeflexive line on the OCT [2]. SS-OCT gives us an objective value of the choroidal thickness. Since posterior uveitis describes the inflammation of the choroid, the disease activity and the healing of the condition are proposed to be associated with the decreasing thickness of the choroid and decreasing cell infiltration of the choroid, thus, minimizing the inflammation. Thus with SS-OCT, one may detect early signs of relapse and treat it earlier, even before the visual symptoms develop [3].

Thus we conducted this study intending to assess choroidal thickness using SS-OCT in active and healed posterior uveitis in the follow-up period of 2–6 weeks. During the study, we also tried to correlate the sub-foveal choroidal thickness measured on SS-OCT with the changes in fundus auto-fluorescence pattern. This was done because RPE, which is assessed by fundus autofluorescence (FAF), may be involved in most of the posterior segment inflammations [4, 5].

MATERIAL AND METHODS

This prospective observational cohort study was conducted at Shroff Eye Centre, New Delhi, from December 2018 to May 2020. 32 eyes of 20 patients presenting in the out-patient department with a diagnosis of posterior uveitis were enrolled after applying inclusion/exclusion criteria and taking duly informed written consent.

Inclusion criteria were as follows:

- patients with a clinical diagnosis of posterior uveitis;
- age — 18 to 60 years.

Exclusion criteria were as follows:

- patients who had undergone any intra-ocular surgery in the affected eye in the past 6 months;
- post-traumatic cases and sympathetic ophthalmitis;
- predominant anterior segment involvement without active chorioretinal lesion;
- any disease which may be associated with or masquerade as uveitis;
- eyes that were poorly imaged due to significant media opacities (vitreous hemorrhage, cataract) or unstable fixation;

- poor patient co-operation;
- patients who were lost to follow-up.

Sample size

The sample size for the study was based on the results of the previously published study by Maruko et al. [6], where observed mean choroidal thickness in 16 eyes decreased from $805 \pm 173 \mu\text{m}$ at the first visit to $524 \pm 151 \mu\text{m}$ at 3 days and $341 \pm 70 \mu\text{m}$ by 2 weeks. Taking these values as a reference, “the minimum required sample size with 99% power of study and 1% level of significance” is 9 patients. To reduce the margin of error, the total sample size taken for this study was 20.

The formula used is:

$$N \geq \frac{(\text{standard deviation})^2 * (Z_{\alpha} + Z_{\beta})^2}{(\text{mean difference})^2}$$

For comparing pre with post

Where Z_{α} is the value of Z at a two-sided alpha error of 1% and Z_{β} is the value Z at the power of 99% and mean difference is the difference in mean values of pre and post.

Brief ocular and systemic history were taken. Best-corrected visual acuity (BCVA) examination was done using the Snellen chart, and intraocular pressure (IOP) measurement was performed using a non-contact tonometer (Nidek NT-530P, Nidek Co. Ltd., Gamagori, Aichi, Japan). Anterior segment examination was done with slit lamp (Haag Streit BQ 900, Haag Streit USA, Inc., Mason, OH, USA). Evaluation of the fundus was done with indirect ophthalmoscopy using 20 D (Volk Double Aspheric Lens) with indentation. For imaging the choroid, SS-OCT was used (Zeiss PLEX Elite 9000, Carl Zeiss Meditec, Inc., Dublin, CA, USA). The choroidal thickness on SS-OCT was measured as the perpendicular distance from the outer portion of the hyperreflective line corresponding to the retinal pigment epithelium (RPE) to the posterior edge of the choroid as demarcated by the hyporeflexive line corresponding to the sclerochoroidal interface using inbuilt software calipers at five points: the sub-foveal area, and at the temporal and nasal points at a distance of 1500 and 3000 μm to the fovea.

All the scans in the study were taken between 10 am and 2 pm to avoid diurnal variation of choroidal thickness. The patients were made to sit comfortably for at least 20 minutes before the scan was performed. The quality of the scan was ensured by the in-built scoring system in the SS-OCT ma-

chine. A score out of 10 is rewarded by the machine for every scan. Scans with a score ≥ 6 (highlighted as green) were accepted for analysis. A single good quality scan was obtained per eye by a single observer.

Fundus imaging was performed with fundus autofluorescence (Heidelberg Spectralis HRA, Heidelberg Engineering Inc., Franklin, MA, USA) and Color Fundus Camera (Topcon TRC-NW400, Topcon Medical Systems Inc., Oakland, NJ, USA).

Treatment

After assessing all the parameters at the baseline, the patients were treated with methylprednisolone 1 g intravenous for 3 days followed by prednisolone 60 mg oral for 1 week, which was then tapered by 10–20 mg weekly depending on clinical response. If the medication was required for the long term, 25 mg of prednisolone (along with 5 mg folic acid after a day's gap) was started with continuous monitoring of side effects under the rheumatologist's opinion and care. The blood tests, which included complete blood count, liver function tests, and kidney function tests, were performed every 3 months.

Follow-ups

The above examination, imaging, and measurements were done at baseline and repeated at 2 ± 1 weeks and 6 ± 2 weeks, after which data was compiled and analysis was performed.

Statistical analysis

The data was entered in the MS Excel file. Then it was analyzed and presented in the tables and figures. The data normality was checked by using Kolmogorov-Smirnov test. Quantitative variables were analyzed using the paired t-test/Wilcoxon signed-rank test across follow-up. Qualitative variables were analyzed using the χ^2 test/Fisher's Exact test.

Analysis was done with the use of Statistical Package for Social Sciences (SPSS) software version 21.0. The p-value of less than 0.05 was considered statistically significant.

RESULTS

In our study on 20 patients (32 eyes), the mean age (\pm SD) of patients was 31 (\pm 6.9) years, with 15 males and 5 females (M:F = 3:1). Out of 32 eyes, the right eye was affected in 18 (56.25%) cases and the left eye in 14 (43.75%) cases. The causes of posterior uveitis included: multifocal choroiditis

in 6 patients, tuberculosis in 5 patients, multiple evanescent white dot syndrome in 3 patients, Vogt-Koyanagi-Harada in 2 patients, neuroretinitis in 2 patients, and CMV retinitis in one patient and Systemic lupus erythematosus in one patient.

The mean (SD) BCVA at baseline was 0.31 (0.36), and mean (SD) IOP was 16.25 (2.77) mm Hg. Inflammatory cells were present in 10 cases of varying severity. Flair was observed in 4 cases. No eyes had posterior synechiae. Vitreous haze was present in five eyes. Optic disc showed edema in 4 cases and hyperemia in 3 cases. Retinal vasculitis was present in one eye. The lesions were creamy white in 27 cases and mixed in five cases. The location of the lesions varied from diffuse, central, focal, juxtapapillary, and multifocal. Sub-retinal fluid was present in nine eyes (Tab. 1).

During the follow-up, with the healing of the lesions, BCVA showed a significant improvement from a mean value of 0.31 at baseline to 0.14 at the first follow-up ($p = 0.001$) and 0.05 at the second follow-up ($p = 0.0003$).

Table 1. Demographic and clinical characteristics of the study patients

Demographic and clinical characteristics	Frequency	Percentage
Age [years]		
≤ 30	11	55.00%
31–40	7	35.00%
> 40	2	10.00%
Mean \pm SD	31 \pm 6.9	
Median (IQR)	29.5 (25.5–36.25)	
Range	21–44	
Gender		
Female	5	25.00%
Male	15	75.00%
Eye		
Left	14	43.75%
Right	18	56.25%
BCVA (logMAR)		
Mean \pm SD	0.31 \pm 0.36	
Median (IQR)	0.2 (0–0.5)	
Range	0–1.3	
IOP [mm Hg]		
Mean \pm SD	16.25 \pm 2.77	
Median (IQR)	16 (15–18)	
Range	11–24	

Table 1. Demographic and clinical characteristics of the study patients		
Demographic and clinical characteristics	Frequency	Percentage
Cells (SUN working group grading)		
No cells	22	68.75%
Trace	2	6.25%
1 + cells	5	15.63%
2 + cells	2	6.25%
3 + cells	1	3.13%
Flare (SUN)		
No flare	28	87.50%
Faint	3	9.38%
Moderate	1	3.13%
Baseline fundus	Frequency	Percentage
Vitreous haze (NIH grading)		
Absent	27	84.38%
Minimal	4	12.50%
Marked	1	3.13%
Optic disc		
Edema	4	12.50%
Hyperemia	3	9.38%
Normal	25	78.13%
Vessels		
No retinal vasculitis	31	96.88%
Retinal vasculitis	1	3.13%
Lesion		
Creamy white	27	84.38%
Mixed	5	15.63%
Distribution		
Central	9	28.13%
Diffuse	2	6.25%
Focal	1	3.13%
Juxtapapillary	2	6.25%
Multifocal	18	56.25%
Subretinal fluid		
Absent	23	71.88%
Present	9	28.13%

SD — standard deviation; IQR — interquartile range; BCVA — best-corrected visual acuity; IOP — intraocular pressure; SUN — Standardisation of Uveitis Nomenclature; NIH — National Institutes of Health

IOP showed various changes as it was increased significantly at the first follow-up to 17.31 from baseline (16.25) ($p = 0.032$). However, the rise at the second follow-up was not significant (17.03 *vs.* 16.25 at baseline, $p = 0.15$).

The eye examination (anterior segment and optic disc) showed that there was a reduction

in the inflammation, flare, vitreous haze, optic disc edema, hyperemia, sub-retinal fluid, and retinal vasculitis until the second follow-up, but the values reached statistical significance only for inflammation, sub-retinal fluid, and retinal vasculitis ($p < 0.05$) (Tab. 2).

We measured the choroidal thickness at various levels (sub-foveal, 411.09 ± 104.23 ; 1500 μm nasal to the fovea, 333.44 ± 94.01 ; 1500 μm temporal to the fovea, 349.72 ± 89.69 ; 3000 μm nasal to the fovea, 250.06 ± 87.22 ; and 3000 μm temporal to the fovea, 334.94 ± 99.92).

Overall during the follow up, we found a significant reduction in the choroidal thickness at all levels (sub-foveal: first follow-up 352.94 ± 87.25 , p value ≤ 0.0001 , second follow-up 315.28 ± 79.47 , p -value ≤ 0.0001 *vs.* baseline 411.09 ± 104.23 , 1500 μm nasal to fovea: first follow-up 283.78 ± 77.04 , p value = 0.0003, second follow-up 258.06 ± 70.66 , p -value ≤ 0.0001 *vs.* baseline 333.44 ± 94.01 , 1500 μm temporal to fovea: first follow-up 308.81 ± 82.09 , p -value = 0.0001, second follow-up 285.34 ± 86.2 , p -value .0001 *vs.* baseline 349.72 ± 89.69 , 3000 μm nasal to fovea: first follow-up 217.94 ± 72.98 , p -value = 0.005, second follow-up 190.88 ± 55.06 , p -value = 0.0001 *vs.* baseline 250.06 ± 87.22 and 3000 μm temporal to fovea:- first follow-up 294.84 ± 81.17 , p -value = 0.013, second follow-up 272.66 ± 78.93 , p -value = 0.0003 *vs.* baseline 334.94 ± 99.92 respectively) (Tab. 3).

On fundus autofluorescence, hyperfluorescent edges were dimmed to hyperfluorescent significantly from 34.38% at baseline to 6.25% at the second follow-up. Overall, normal autofluorescence and hypofluorescence increased at the final second follow-up of 6 weeks ($p < 0.0001$) (Tab. 4).

A representative case image of the patient (SS-OCT and fundus autofluorescence images) is shown in Figure 1–4.

DISCUSSION

The present study holds strength in being one of the few Indian studies that evaluated SS-OCT as an essential imaging modality in measuring the choroidal thickness in patients with active posterior uveitis and thereby assessing the disease activity in association with fundus autofluorescence. The study results showed a significant decrease in the choroidal thickness at all levels during the first and second follow-up of healed lesions (compared to the baseline of active disease).

Table 2. Comparison of variables between baseline and first and second follow-up				
Variables	Baseline (n = 32)	First follow-up (n = 32)	Second follow-up (n = 32)	p-value
Cells (SUN working group grading)				
No cells	22 (68.75%)	27 (84.38%)	29 (90.63%)	Baseline vs. first follow-up: 0.300 [†]
Trace	2 (6.25%)	3 (9.38%)	3 (9.38%)	Baseline vs. second follow-up: 0.034 [†]
1 + cells	5 (15.63%)	2 (6.25%)	0 (0%)	
2 + cells	2 (6.25%)	0 (0%)	0 (0%)	
3 + cells	1 (3.13%)	0 (0%)	0 (0%)	
Flare (SUN)				
No flare	28 (87.50%)	31 (96.88%)	32 (100%)	Baseline vs. first follow-up: 0.355 [†]
Faint	3 (9.38%)	1 (3.13%)	0 (0%)	Baseline vs. second follow-up: 0.113 [†]
Moderate	1 (3.13%)	0 (0%)	0 (0%)	
Vitreous haze (NIH grading)				
Absent	27 (84.38%)	32 (100%)	32 (100%)	Baseline vs. first follow-up: 0.053 [†]
Minimal	4 (12.50%)	0 (0%)	0 (0%)	Baseline vs. second follow-up: 0.053 [†]
Marked	1 (3.13%)	0 (0%)	0 (0%)	
Optic disc				
Normal	25 (78.13%)	27 (84.38%)	26 (81.25%)	Baseline vs. first follow-up: 0.892 [†]
Edema	4 (12.50%)	2 (6.25%)	0 (0%)	Baseline vs. second follow-up: 0.078 [†]
Hyperemia	3 (9.38%)	3 (9.38%)	6 (18.75%)	
Vessels				
No retinal vasculitis	31 (96.88%)	31 (96.88%)	32 (100%)	Baseline vs. first follow-up: 1 [†]
Retinal vasculitis	1 (3.13%)	1 (3.13%)	0 (0%)	Baseline vs. second follow-up: 1 [†]
Subretinal fluid				
Absent	23 (71.88%)	30 (93.75%)	32 (100%)	Baseline vs. first follow-up: 0.043 [†]
Present	9 (28.13%)	2 (6.25%)	0 (0%)	Baseline vs. second follow-up: 0.002 [†]

[†]Fisher exact test; [‡] χ^2 test. SUN — Standardisation of Uveitis Nomenclature; NIH — National Institutes of Health

Table 3. Comparison of choroidal thickness [μm] between baseline and follow-up			
Choroidal thickness [μm]	Baseline (n = 32)	First follow-up (n = 32)	Second follow-up (n = 32)
Sub-foveal	411.09 \pm 104.23	352.94 \pm 87.25	315.28 \pm 79.47
p-value	–	< 0.0001 [†]	< 0.0001 [†]
1500 μm nasal to fovea	333.44 \pm 94.01	283.78 \pm 77.04	258.06 \pm 70.66
p-value	–	0.0003 [†]	< 0.0001 [†]
1500 μm temporal to fovea	349.72 \pm 89.69	308.81 \pm 82.09	285.34 \pm 86.2
p-value	–	0.0001 [†]	< 0.0001 [†]
3000 μm nasal to fovea	250.06 \pm 87.22	217.94 \pm 72.98	190.88 \pm 55.06
p-value	–	0.005 [†]	0.0001 [†]
3000 μm temporal to fovea	334.94 \pm 99.92	294.84 \pm 81.17	272.66 \pm 78.93
p-value	–	0.013 [†]	0.0003 [†]

[†]paired t-test

As reported by one such Indian study, Copete et al. [7] compared the choroidal thickness measured by SD-OCT with SS-OCT in normal eyes.

They found that SS-OCT provided accurate identification of the choroido-scleral border in all eyes, which indicated SS-OCT as a superior modality for

Table 4. Comparison of fundus autofluorescence between baseline and follow-up				
Fundus autofluorescence	Baseline (n = 32)	First follow-up (n = 32)	Second follow-up (n = 32)	p-value
Normal fluorescence	0 (0%)	0 (0%)	4 (12.50%)	
Hypofluorescence	5 (15.63%)	11 (34.38%)	18 (56.25%)	Baseline vs. first follow-up: 0.121*
Hyperfluorescence	11 (34.38%)	8 (25%)	5 (15.63%)	Baseline vs. second follow-up: < 0.0001*
Mixed	4 (12.50%)	2 (6.25%)	0 (0%)	
Hypofluorescent with hyperfluorescent edge	11 (34.38%)	6 (18.75%)	2 (6.25%)	
Hyperfluorescent with hypofluorescent edge	1 (3.13%)	5 (15.63%)	3 (9.38%)	
Total	32 (100%)	32 (100%)	32 (100%)	

*Fisher exact test

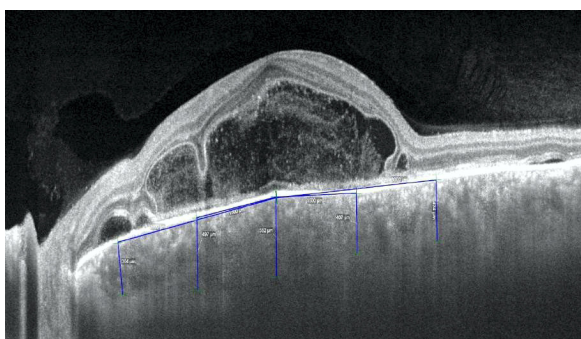


FIGURE 1. Swept-source optical coherence tomography (SS-OCT) of the left eye measuring the choroidal thickness in a patient of Vogt-Koyanagi-Harada syndrome (at presentation). Choroidal thickness (sub-foveal) — 552 μm; choroidal thickness (1500 μm nasal to fovea) — 497 μm; choroidal thickness (1500 μm temporal to fovea) — 407 μm; choroidal thickness (3000 μm nasal to fovea) — 364 μm; choroidal thickness (3000 μm temporal to fovea) — 424 μm

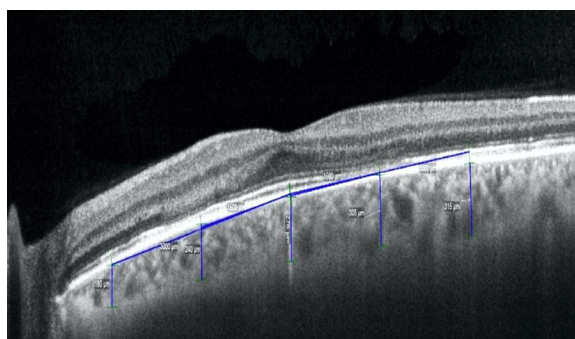


FIGURE 3: Swept-source optical coherence tomography (SS-OCT) of the left eye measuring the choroidal thickness of the same patient (after treatment). Choroidal thickness (sub-foveal) — 276 μm; choroidal thickness (1500 μm nasal to fovea) — 240 μm; choroidal thickness (1500 μm temporal to fovea) — 305 μm; choroidal thickness (3000 μm nasal to fovea) — 180 μm; choroidal thickness (3000 μm temporal to fovea) — 315 μm

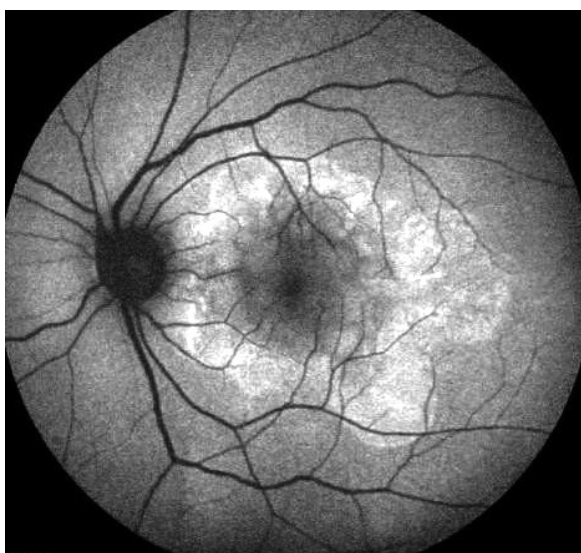


FIGURE 2. Fundus autofluorescence of the same eye showing mixed hypofluorescence and hyperfluorescence (at presentation)

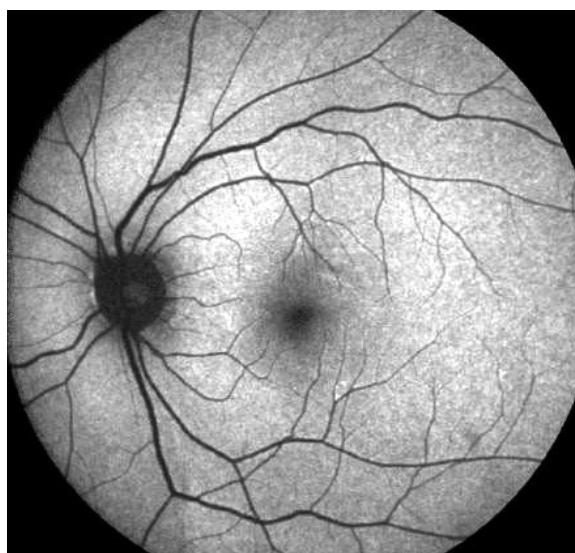


FIGURE 4. Fundus autofluorescence of the left eye showing normal autofluorescence (after treatment)

measuring choroidal thickness. Similarly, Adhi et al. [8] compared SS-OCT and SD-OCT in 19 healthy eyes. The choroido-scleral interface was clearly visualized in all eyes imaged with SS-OCT, compared to 73.6% and 68.4% of eyes imaged with SD-OCT.

Bhayana et al. [9] used SS-OCT to measure choroidal thickness in 238 healthy eyes and reported that the choroidal thickness measured with SSOCT was slightly higher than that reported with the spectral-domain platforms because of better delineation of the sclerochoroidal junction (particularly in eyes with thicker choroid).

Akhtar et al. [10] also used SS-OCT and found the mean subfoveal and macular choroidal thickness were $307 \pm 79 \mu\text{m}$ and $285 \pm 75 \mu\text{m}$, respectively. Mean choroidal thickness was found to decrease with age, but no difference in choroidal thickness between genders was noted. Our findings are similar to those shown in the study by Jaisankar et al. [11]. Using SS-OCT, they measured the sub-foveal choroidal thickness before and after systemic corticosteroid therapy. They found that the mean SFCT of patients before treatment was $503.81 \mu\text{m}$ and significantly reduced to $301.19 \mu\text{m}$ after treatment.

Moreover, we also assessed fundus autofluorescence since it may be altered in posterior uveitis. Typically the fundus is dark or hypofluorescence, which may show hyperfluorescence when inflamed. The mechanism behind this is a transition to inactive inflammatory disease. Finally, the lesions become hypoautofluorescence (inactive) in the final FAF images. An increase in FAF (hyperautofluorescence) is expected in the presence of increased metabolic activity of the RPE, a predictor of dysfunction, and a decrease in FAF (hypoautofluorescence) with the loss of photoreceptors or the RPE [4].

The study analysis showed that fundus autofluorescence became normal until the second follow-up period, which was previously confirmed in a few studies [12–20]. Bansal R et al. [21] found that fundus autofluorescence and enhanced depth imaging-OCT imaging through active lesion showed diffuse choroidal thickening at presentation, which decreased at 17 days, and 28 days after starting therapy, and localized choroidal atrophy at 12 weeks in the region of hypoautofluorescence lesion.

Since posterior uveitis may affect the vision, BCVA was monitored and showed corresponding changes. BCVA showed significant improvement after treatment of posterior uveitis, which was an objective parameter without any considerable

effect on the IOP. Our findings were in line with the study by Maruko et al. [6]. They reported that the mean decimal BCVA levels improved from 0.71 (20/28) (0.15 logMAR) at baseline to 1.04 (20/19) (20.02 logMAR) after resolution of serous retinal detachment (which occurred in 12 eyes by day 14 and in all eyes by 1 month). In the case study by Vezzola et al. [1], BCVA was 20/20 in her right eye and 20/200 in the woman's left eye, and at a 2-months follow-up, the BCVA was improved to 20/25 in her left eye. In their study, Ishikawa et al. [22] also showed that LogMAR decreased gradually after the initiation of infliximab treatment, but there was no significant difference.

LIMITATIONS

The study had limitations of small sample size and short-term follow-up. A large sample size would have helped to derive better statistical associations.

Since our study is a single-center hospital-based study, its results cannot be generalized to all types of the population.

SSOCT was not compared with any other modality such as SDOCT or EDI-OCT. So, its superiority over other modalities cannot be evaluated in the case of Indian patients.

This study included patients of Indian ethnicity only, therefore the geographical variability of posterior uveitis needs to be further characterized.

Point-to-point measurements provide only limited information about changes in the entire choroid.

The number of prior recurrences of uveitis was not considered in the present study.

CONCLUSION

SS-OCT showed a significant decrease in the choroidal thickness at all levels during the follow-ups. The healing of the posterior uveitis lesions and fundus autofluorescence became normal simultaneously.

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Conflicts of interest

None declared.

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