Original Article

Role of choroidal thickness assessment in unilateral acute anterior uveitis

Sunil Thapa, Ranju Kharel (Sitaula), Jyoti Baba Shrestha

Purpose: The aim of our study was to investigate the change in the subfoveal choroidal thickness in unilateral acute anterior uveitis with treatment. Choroidal inflammation is uncommon but can occur in the acute stage of anterior uveitis. **Methods:** All diagnosed patients with the first episode of unilateral acute anterior uveitis were included in the study conducted for a period of July 2017–July 2018. Choroidal thickness at subfoveal region was measured with spectralis spectral domain optical coherence tomography using enhanced depth-imaging scans. Standardized, masked manual measurement of the choroidal thickness was performed in the center of the ETDRS fields. The unaffected fellow eye of the same patient was taken as a control group and their subfoveal choroidal thickness was measured. Follow up of the patients was done at 2 weeks posttreatment to reevaluate the choroidal thickness. **Results:** A total of 61 eyes of 61 patients with unilateral acute anterior uveitis were included in the study. The mean central subfoveal choroidal thickness was significantly higher (304.82 ± 73.17 μm) as compared to that of controls (251.28 ± 66.38 μm) at presentation ($P < 0.001$). Following treatment and at two weeks follow up, the subfoveal choroidal thickness significantly reduced from 304.82 ± 73.17 to 274.46 ± 63.82 μm ($P < 0.001$). Also the subfoveal choroidal thickness was positively correlated with visual acuity ($r = 0.22$, $P < 0.251$) before treatment. **Conclusion:** Acute anterior uveitis is associated with an increase in the subfoveal choroidal thickness followed by the significant decrease in choroidal thickness with treatment, suggesting that choroid is also inflamed along with anterior segment inflammation.

Key words: Anterior uveitis, choroidal thickness, HLA B 27+, macular edema, unilateral, uveitis

Acute anterior uveitis (AAU) is the most common type of intraocular inflammation, with the varying incidence of 50–90% of all uveitis diagnosed worldwide.[1,2] In Nepal, it contributes to 61.8% of the total uveitis cases.[3]

Currently, enhanced depth imaging (EDI) with spectral-domain OCT provides details of the choroidal anatomy and permits qualitative and quantitative analyses of this layer.[4] Though choroidal involvements are found only in posterior uveitis, there have been numerous studies where they showed that central choroidal thickness in acute anterior uveitis does differ from that of normal controls[4,5] but there has been no study conducted yet among Nepalese uveitic eyes.

Therefore, we aim to determine the difference in subfoveal choroidal thickness (SFCT) between eyes with acute AAU at the first onset and unaffected fellow eyes (FE) in Nepalese population. Changes in SFCT were also compared at baseline and after the treatment of uveitis in eyes with AAU. To our knowledge, this is the first report analyzing SFCT in AAU from Nepal.

Methods

The study was planned as a prospective, quantitative, and observational analytical at the uveitis clinic of a tertiary eye care center of Nepal. Adults with a newly diagnosed (within a week), unilateral, first episode of AAU between July 2017 to July 2018 were recruited for the study and the unaffected fellow eye of the same patient was considered as the control group.

The exclusion criteria were include high myopia >6D, another additional ocular disease (Vogt Koyanagi Harada disease, central serous chorioretinopathy, diabetic macular edema), history of use of ocular drugs or ocular surgery in the past 3 months, and patients with media opacities.

All patients underwent careful history taking and laboratory investigations for specific ocular entities or systemic disease association. The array of laboratory investigations undertaken include complete blood count, erythrocyte sedimentation rate, random blood sugar, urine routine examination, anti-HIV antibody testing, hepatitis serological profiles, antinuclear antibody (ANA), rheumatoid factor, serum calcium, serum uric acid, Treponema pallidum hemagglutination test, chest radiography and Mantoux test. Other augmented tests were carried out in selected cases based on clinical suspicion. These tests included human leukocyte antigen (HLA)-B27 for ankylosing spondylitis, serum ACE for sarcoidosis, serum

Department of Ophthalmology, Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University, B. P. Koirala Lions Centre for Ophthalmic Studies, Maharajgunj, Kathmandu, Nepal

Correspondence to: Dr. Ranju Kharel (Sitaula), Department of Ophthalmology, Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University, B. P. Koirala Lions Centre for Ophthalmic Studies, Maharajgunj, Kathmandu, Nepal. E-mail: helloranju50@gmail.com

and vitreous toxoplasma antibodies for toxoplasmosis, quantiFERON TB gold test for suspected intraocular tuberculosis. Based on the laboratory findings and ocular examinations, AU was diagnosed according to the International Uveitis Study Group criteria.[1] Acute inflammation was defined: sudden onset and limited duration (3 months), as defined by the established criteria of the Standardization of Uveitis Nomenclature (SUN) Working Group.[2]

Data on age, sex, and possible etiology were collected. Visual acuity (VA) was measured using a Snellen letter chart, and transformed to Log MAR (Logarithm of the minimum angle of resolution) for statistical analyses.

The Spectral Domain EDI-OCT images of the macular region were obtained (Heidelberg Engineering, Heidelberg, Germany version 6.0 with built-in EDI-OCT software, 870 nm wavelength) and used for evaluation of the choroid in all subjects at the same time of the day to avoid the diurnal variations. All measurements were performed by one technician who was blinded to which eye was affected. SFCT was measured at the central foveal subfield of 1 mm diameter of ETDRS macular map by calculating the distance from a hyperreflective line representing the outer border of the retinal pigment epithelium to the inner edge of the suprachoroidal space, which was represented by a hyporeflective line on EDI-OCT images. The choroidal thickness of both the eyes was measured by two authors where the unaffected eye served as the control group and the average mean reading was considered.

A repeat EDI-OCT scanning was done at follow up to measure SFCT after the second week of treatment. A descriptive statistical analysis was reported as mean, medians, and standard deviation for continuous variables, and numbers (n) and percentages (%) were used for categorical variables. Data were analyzed using SPSS 21.0 (SPSS Inc., Chicago, IL, USA).

The comparison of the mean subfoveal choroidal thickness of the eyes with unilateral acute anterior uveitis and fellow eyes before and after treatment was done by Paired t-test. Linear regression analysis was done to predict the change in visual acuity in relation to change in choroidal thickness. *P* value <0.05 was considered statistically significant.

The study adhered to the tenets of the Declaration of Helsinki and obtained permission from the Institutional Review Board (IRB) of the Institute of Medicine. Written consent was obtained from the participating patients.

Results

Thus out of 75 enrolled cases (150 eyes), a total of 122 eyes of 61 patients meeting the inclusion criteria were included of which, 61 affected eyes were cases and 61 fellow eyes served as control. Rest 14 cases were excluded as they had other associated ocular pathology like diabetic macular edema, CSR, and old uveitis.

The mean age of the patients was 39.02 ± 13.76 years with the range of 15–69 years; 38 (62.3%) were males and 23 (37.7%) were females (Male to Female ratio = 1.65:1) [Table 1]. Among these 61 cases, the etiological diagnosis could be established in the 39 cases (63.9%). HLA-B27 associated AAU was the most common underlying cause ($n = 21$, 34.4%), followed by Herpes Zoster virus infection ($n = 5$, 8.2%), traumatic uveitis ($n = 4$, 6.5%), sarcoidosis ($n = 3$, 4.9%), gout ($n = 3$, 4.9%), Fuch's uveitis ($n = 2$, 3.2%), and tuberculosis ($n = 1$, 1.6%). The right eye (56%) was affected more than the left eye (44%) and 18.04% cases were of granulomatous uveitis. The posterior segment findings were within normal limits.

The mean intraocular pressure using Goldmann applanation tonometry (IOP) of the case eyes before treatment was 12.45 ± 6.89 mmHg (range 8–42 mmHg) and the mean IOP of the control eyes was 14.02 ± 2.36 mmHg (range 10–20 mmHg. All cases were treated with topical steroids and cycloplegics; five patients (8.2%) were supplemented with oral steroid. Oral acyclovir 800 mg/thrice/day was given to the HZO patients, oral methrotexate 15 mg/week for the HLA B27 cases, and ATT was added to the tuberculosis case.

During the first visit, the mean SFCT in uveitic eye was 304.82 μm (range 479 μm–146 μm), whereas the mean SFCT in fellow eyes was 251 μm (range 391 μm–128 μm). The mean difference between the uveitic and fellow eyes was 53.54 μm which was statistically significant (*P* value <0.001). After 2 weeks of treatment, the mean SFCT in the uveitic eyes reduced to 274.46 μm (range 401 μm–144 μm) [Fig. 1]. The mean difference of SFCT before and after the treatment in the uveitic eyes was 30.36 μm which was statistically significant using Paired t- test with a *P* value of <0.001 [Table 2].

The mean visual acuity, in these 61 uveitic eyes before and after treatment was 0.36 + 0.24 log MAR and 0.20 + 0.21 log
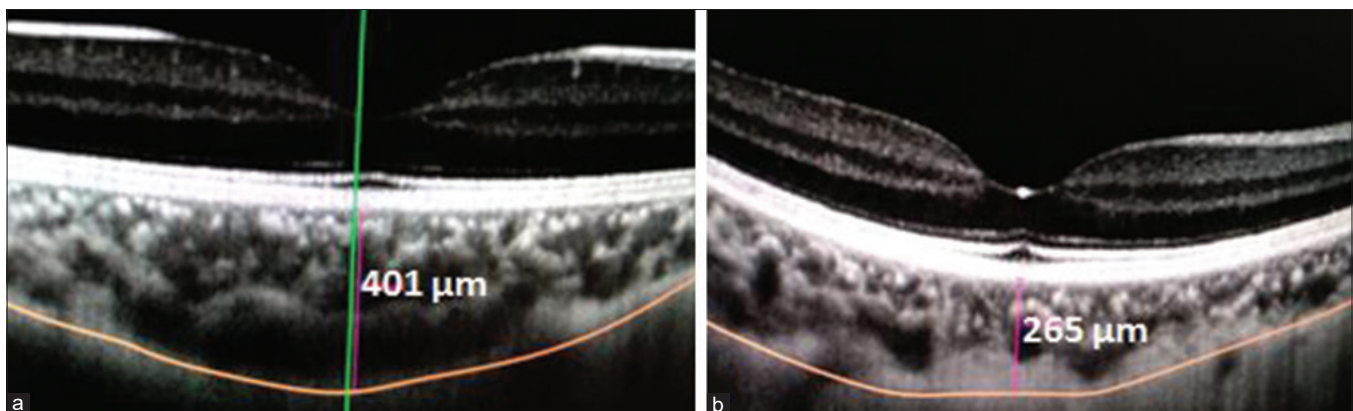

Figure 1: Representative EDI-OCT images of the choroid of a HLA B27+ patient with uveitis showing change in the SFCT before (a) and after treatment (b)

MAR, respectively. Thus the mean difference of VA with the treatment in the diseased eye was 0.16 log MAR which was statistically significant using Paired t- test (*P* value of <0.001).

Correlation of the SFCT was done with the VA of the both eyes. Linear regression estimator demonstrated that better visual acuity in the fellow eye was significantly correlated with the near normal choroidal thickness [Table 3]. However, in the uveitic eyes, SFCT was positively correlated with the visual acuity (*r* = 0.22, *P* value <0.251) before treatment. However, the regression analysis showed that upon decreasing the choroidal thickness towards the normal range of 200–300 μm, the visual acuity did not show any improvement. Hence, a correlation could not be established. But after the treatment, the reduced SFCT was correlated with a better visual acuity (*r* = 0.206, *P* value <0.01) [Fig. 2].

We evaluated the association between choroidal thickening and the degree of intraocular inflammation in a dose–response relationship [Fig. 3]. The linear regression scatter plot clearly demonstrated that as the disease severity increases based on AC reaction, the SFCT clearly begins to increase from normal range of 200–300 μm with a r-value of 0.27 which according to Pearson's coefficient relation signifies a moderate association. Hence, the subfoveal choroidal thickness was significantly greater during the acute and severity of the disease.

After two weeks of treatment, the most severe form of the disease began to improve towards normal. As supported by the scatter plot graph, most clusters of the cases began to normalize from 5+ cells to 1+ cells. In addition, their SFCT decreased when the severity of the disease began to improve [Fig. 4]. It is also supported statistically by Pearson correlation with a *P* value of <0.001.

Discussion

The report aimed to provide the baseline data of choroidal thickness of unilateral AAU cases in Nepal to monitor its change with the treatment and finally to compare with the unaffected fellow eye. To the best of our knowledge, there are only limited number of reports across the world on choroidal thickness in acute anterior uveitis using optical coherence.[1-4]

Among our 61 participants, 62.3% were males and 37.7% were females with a (M:F ratio of 1.6:1) as shown in Table 1. Male predominance has been documented in earlier reports of unilateral acute anterior uveitis from our part of the world.[5] This predominance could be due to the strong relation of male gender toward the HLA-B27 antigen. The mean age of presentation of our study population was 39.20 ± 13.76 years (Range 15 to 69 years) which indicates that anterior uveitis are more common among the most economically productive age group.

Modern tools, such as EDI-OCT, have improved the patients' diagnostics and treatment by monitoring the choroidal parameters. Studies from various parts of world have evaluated different normal SFCT values for different ethnic groups like 249.6 (SD ± 36) μm in Indians[6] and 252.80 (SD ± 46.95) μm in Chinese.[7] We here observed the mean SFCT in the unaffected fellow eye to be 251 ± 66.38 μm which can be considered as the SFCT of healthy Nepalese population.

The development of EDI version in the SD-OCT has been a boon to demonstrate the subclinical involvement of the posterior retina and choroid in AAU cases.[1,8] The involvement of the choroid may cause changes in the choroidal thickness (CT) or correlate with lower visual acuity in these patients.[1,8]
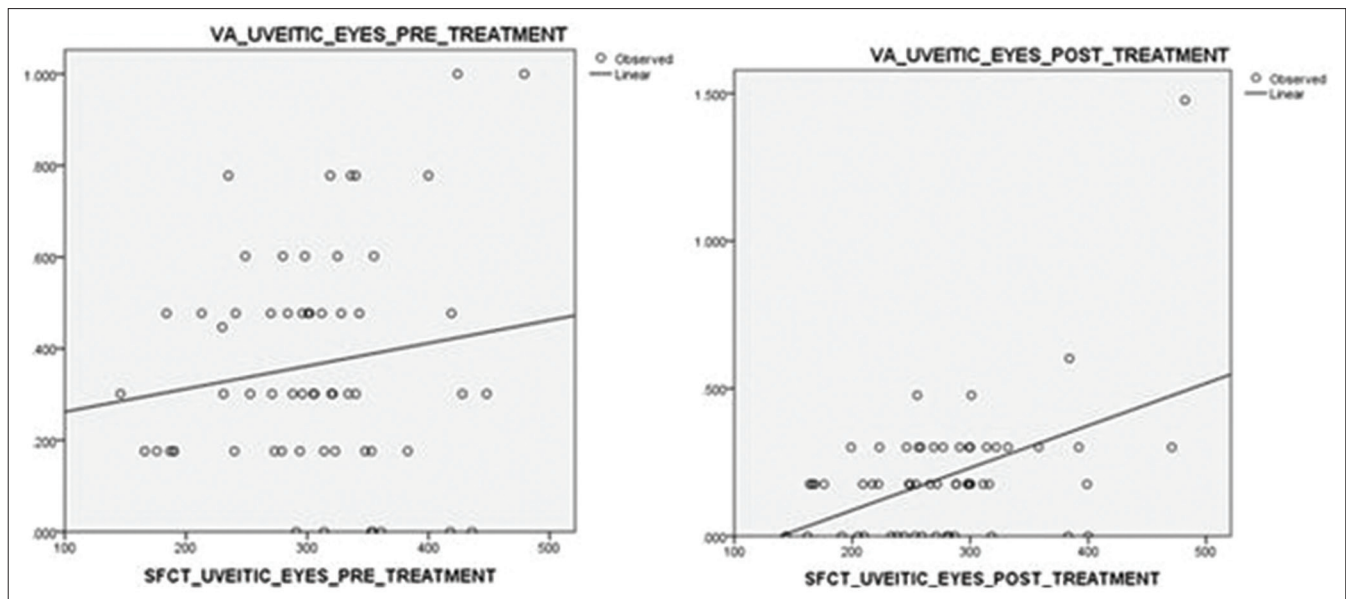
Table 1: Age and gender distribution of unilateral acute anterior uveitis cases

Age Group in years	Number (*n*=patients)	Percentage (%)
15-25	9	14.8
26-35	17	27.9
36-45	17	27.9
46-55	8	13.8
56-65	9	14.8
>65	1	1.6
Total	61	100

Table 2: Comparison between SFCT of fellow eye and uveitic eye before and after treatment

Sub-foveal choroidal Thickness	Uveitic Eye		Fellow Eye		95% Confidence interval of the difference		P
	Mean	Standard Deviation	Mean	Standard Deviation	Lower	Upper	
	304.82	73.17	251.28	66.38	-42.46	-64.62	<0.001

Sub-foveal choroidal Thickness	Uveitic Eye before Treatment		Uveitic Eye after Treatment		95% Confidence interval of the difference		P
	Mean	Standard Deviation	Mean	Standard Deviation	Lower	Upper	
	304.82	73.17	274.46	63.82	-19.96	-40.76	0.001

Table 3: Correlation of VA before and after treatment in Uveitic eyes and with the fellow eye

Linear Regression	R square	F	df 1	df 2	Sig.	Constant	b 1
Uveitic Eye before Treatment	0.22	1.342	1	59	0.251	0.212	0.00
Uveitic Eye after Treatment	0.206	15.068	1	58	0.000	248.962	146.217
Fellow Eye	0.94	6.132	1	59	.016	-2.10	0.02

Figure 2: Scatter plot showing the correlation between SFCT and visual acuity in uveitic eyes before and after treatment
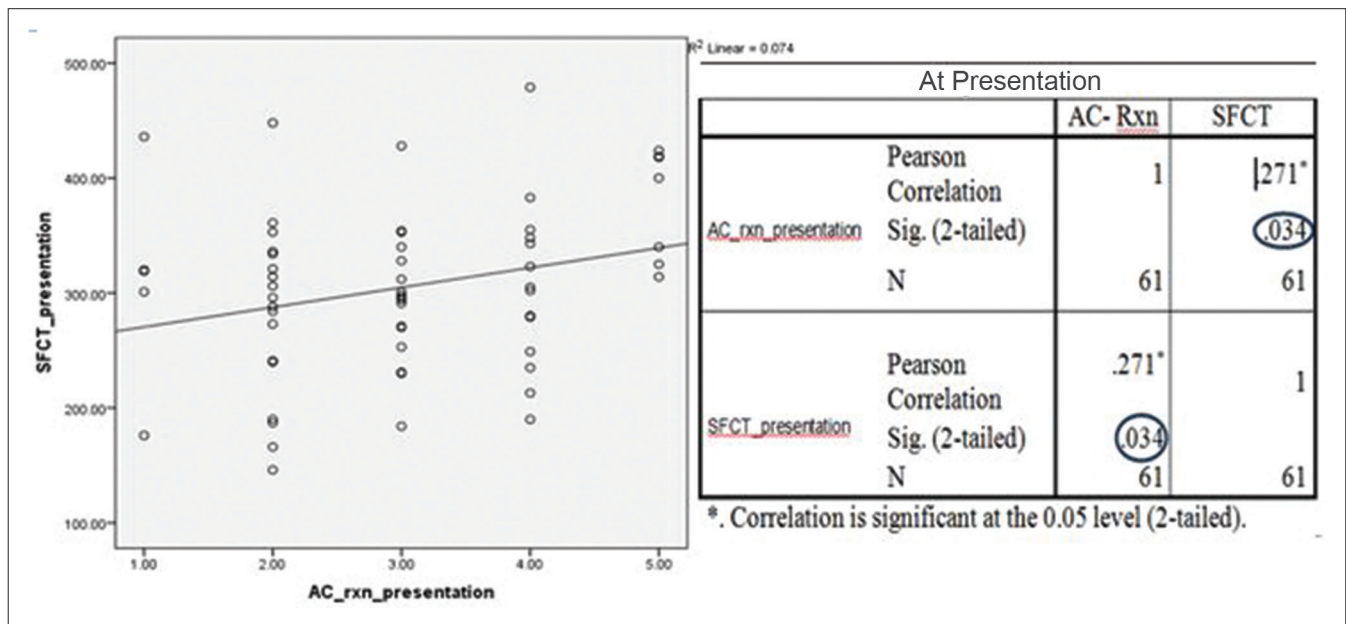

Figure 3: Correlation of SFCT and anterior chamber reaction in the uveitic eyes before treatment

Using EDI-OCT, our study also proved that the SFCT is increased in uveitic eye compared with the unaffected fellow eye and decreases with the treatment. The linear regression estimator identified significant correlation demonstrating better visual acuity among eyes with near normal choroidal thickness.

Although the range of tissues involved in the inflammatory processes in AAU is anatomically supposed to be limited only upto the anterior segment, we could verify with EDI-OCT that there can be a subclinical involvement of the posterior retina and choroid in AAU cases. One of the reasons for the change in the posterior segment in the anterior segment inflammation could be the blood supply of the iris and ciliary body which has associations with the choroid. Thus, the breakdown of the blood–aqueous barriers in AAU could insult the blood–retinal

barriers too and thereby the increased hydrostatic pressure levels could result in vascular permeability[9] and the retinal–choroidal congestion with enlarged Haller's and Sattler's leading to the increased SFCT.[4,10]

The next evidence to explain the increased SFCT in AAU is the release of the inflammatory mediators during the active stage of AU which too alter the vascular permeability of choriocapillaris resulting in the choroidal effusion and thickened choroid. But with the appropriate treatment of AAU, the breach in the blood ocular barriers and release of inflammatory mediators decrease leading to the decrease in the SFCT.

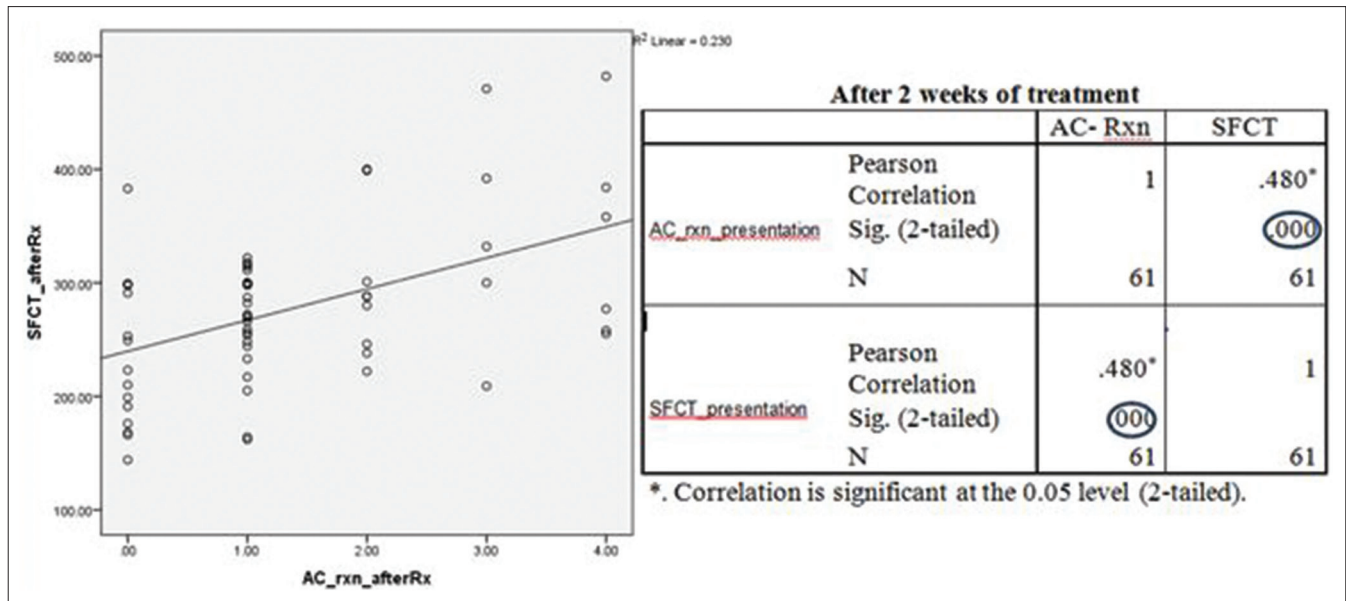Though there is no universal agreement among researchers on the influence of AAU on CT, few authors[1] have shown

Figure 4: Correlation of SFCT and anterior chamber reaction in the uveitic eyes after treatment

significant changes but some have not been found to be significant.[2] We aim to support evidence in the literature which signifies that there is a significant increase in the choroidal thickness in the uveitic eye when compared to normal fellow eyes and the thickness returns back after treatment of AAU.

Our study also advocates the need for bilateral OCT evaluation even in patients with unilateral anterior uveitis. Despite, the AAU group had significant choroidal thickening, it could be considered as being within the normal range if not for the consideration of the unaffected eye, and hence, we should perform bilateral OCT to confirm.In addition to above, EDI-OCT proves to be a valuable guide to monitor the specific disease processes as the choroid is a frequent target for any intraocular inflammation.

As with all previous studies, our study has few limitations. First, the study has a small number of the patients with a short duration of follow-up. Longer follow-ups even after stoppage of treatment would have helped us to assess whether the reduction in SFCT was due to treatment or due to resolution of inflammation. Second is the use of inbuilt manual calipers for the measurement of the choroidal thickness which may cause different results for different examiners. To reduce such discrepancies, our OCT measurements were performed by a single experienced technician and each SFCT was measured by two of the authors, and the average values were considered. There may be a doubt about the reliability and repeatability of manual measurement of choroidal thickness using EDI-OCT images. But Rahman *et al.*[11] had reported intra- and interobserver coefficients of repeatability of 23 and 32 µm, respectively. Thirdly, the choroidal thickness could be influenced by many variables such as age, sex, and axial length. We did not measure the axial length; however, as the controls were the unaffected eyes of the same person, we presume there was no statistically significant refractive difference between the affected eyes and healthy fellow eyes. We had also excluded the high myopic eyes to reduce the influence of the eye axis, but this may not be sufficient. Fourth limitation could be the lack of comparison between the macular thickness and the subfoveal

choroidal thickness. Next limitation could be the lack of follow up measurements after the complete resolution phase of the inflammation. Further detailed investigation of the AAU cases of Nepal with particular emphasis on inflammatory etiology, human leukocyte antigen-B27 status, and disease activity in the anterior chamber would be better.

Conclusion

Taken together, we conclude that the change in the subfoveal choroidal thickness appears to be significant in cases of unilateral acute anterior uveitis compared to the unaffected fellow eye. The increased choroidal thickness is positively correlated with the decreased visual acuity and the thickness normalizes with the treatment.

Ethics approval

Ethical approval for the study was obtained from the Institutional Review Board of Institute of Medicine and consent to participate was obtained from all the cases and controls.

Conflicts of interest

There are no conflicts of interest.

References

1. Ahn SJ, Kim JH and Lee BR. Choroidal change in acute anterior uveitis associated with human leukocyte antigen-B27. PloS One 2017;12: e0180109.

2. Géhl Z, Kulcsár K, Kiss HJ, Németh J, Maneschg OA, Resch MD. Retinal and choroidal thickness measurements using spectral domain optical coherence tomography in anterior and intermediate uveitis. BMC Ophthalmol 2014;14:103.

3. Basarir B, Celik U, Altan C, Celik NB. Choroidal thickness changes determined by EDI-OCT on acute anterior uveitis in patients with HLA-B27-positive ankylosing spondylitis. Int Ophthalmol 2018;38:307-12.

4. Gabriel M, Kruger R, Shams-Mafi F, Hermann B, Zabihian B, Schmetterer L, *et al.* Mapping retinal and choroidal thickness in unilateral nongranulomatous acute anterior uveitis using three-dimensional 1060-nm optical coherence tomography. Invest Ophthalmol Vis Sci 2017;58:4778-83.

5. Majumdar AK, Kumar A, Roy R, Dutta Majumder P. Clinical profile of HLA B-27-associated uveitis patients in a Tertiary Care Eye Hospital in Eastern India. Ocul Immunol Inflamm 2019;27:718-21.

6. Chhablani J, Rao PS, Venkata A, Rao HL, Rao BSK, Kumar U, *et al.* Choroidal thickness profile in healthy Indian subjects. Indian J Ophthalmol 2014;62:1060-3.

7. Qi Y, Li L, Zhang F. Choroidal thickness in Chinese children aged 8 to 11 years with mild and moderate myopia. J Ophthalmol 2018;2018:7270127.

8. Yan H, Li J, Zhang J, Yang L. Retinal and choroidal thickness in patients with uveitis. Ocular Immunol Inflamm 2017;25:202-9.

9. Balci O, Tanriverdi C, Aydin A, Ozsutcu M, Gulkilik G, Kocabora MS. Evaluation of changes in retinal and choroidal thickness using spectral domain optical coherence tomography in unilateral non granulomatous acute anterior uveitis. J Fr Ophtalmol 2019;42:138-45.

10. Onal S, Tugal-Tutkun I, Neri P, Herbort CP. Optical coherence tomography imaging in uveitis. Int Ophthalmol 2014;34:401-35.

11. Rahman W, Chen FK, Yeoh J, Patel P, Tufail A, Da Cruz L. Repeatability of manual subfoveal choroidal thickness measurements in healthy subjects using the technique of enhanced depth imaging optical coherence tomography. Invest Ophthalmol Vis Sci 2011;52:2267-71.