

Assessment of Choroidal Thickness in Acute Central Serous Chorioretinopathy Using Swept Source Optical Coherence Tomography: A Case-control study

ARJUN BAMEL¹, PARAG K SHAH², RAHUL BHARADWAJ³, AESHVARYA DHAWAN⁴, ANUPAM SINGH⁵

ABSTRACT

Introduction: Central Serous Chorioretinopathy (CSCR) is a disease characterised by localised Neurosensory Detachment (NSD) with or without focal Pigment Epithelial Detachments (PED) and altered Retinal Pigment Epithelium (RPE). Since, CSCR being a pachychoroid entity the visualisation and evaluation of choroidal vessels have shown that vascular layers are altered in the disease process.

Aim: To assess Subfoveal Choroidal Thickness (SFCT), in acute CSCR patients in both affected and fellow unaffected eyes using Swept Source Optical Coherence Tomography (SS-OCT), and to compare these with age-matched control group.

Materials and Methods: This was a hospital-based case-control study, conducted between July 2018 to May 2019 at Outpatient Department (OPD) of Aravind Eye Hospital, Coimbatore, India. Total of 41 patients and 41 controls from OPD were included. Uncorrected Visual Acuity (UCVA) and Best Corrected Visual Acuity (BCVA) were measured on Snellen's chart. After pupil dilatation, posterior segment evaluation with slit lamp bio

microscopy using a 90D lens and documentation with fundus photograph were done. All subjects were examined using SS-OCT which was done for both the eyes. Descriptive analysis such as mean, standard deviation and percentage were used to exhibit the clinical parameters. Independent t-test analysis was more suitable for this data. All the statistical tests were examined with 5% ($p\text{-value}\leq 0.05$) level of significance.

Results: The age (mean \pm SD) of cases and controls were 38.44 \pm 6.14 years and 37.21 \pm 2.72 years, respectively. The mean SFCT of affected and unaffected fellow eye of cases were 465.39 \pm 60.02 μm and 407.12 \pm 57.29 μm respectively, ($p\text{-value}<0.001$). The mean SFCT of affected eyes of cases and control group eyes were 465.39 \pm 60.02 μm and 267.5 \pm 34.40 μm respectively, ($p\text{-value}<0.001$).

Conclusion: The choroid was significantly thicker in affected as well as unaffected eye of CSCR patient. This implies that the CSCR affect the choroidal thickness in both affected as well as unaffected eye of patient as compared to control group.

Keywords: Bullous retinal detachment, Pachychoroid, Pigment epithelial detachment

INTRODUCTION

The CSCR is a disease characterised by localised NSD with or without focal PED and altered Retinal Pigment Epithelium (RPE) [1]. CSCR is an idiopathic disease commonly affecting the young and middle-aged individuals [2]. Prevalence is more in males as compared to females [1]. Idiopathic CSCR has been associated with type-A personality and elevated endogenous cortisol level. It is also associated with the administration of inhalational, intranasal, topical and periocular steroids. Other risk factors included antibiotic use, alcohol use, untreated hypertension and allergic respiratory disorders [3].

The type of CSCR as described in the literature includes Classic Acute Chorioretinopathy, Chronic Diffuse Retinal Pigment Epitheliopathy (DRPE) and Bullous Retinal Detachment. Classic or acute CSCR is the most common form, consisting of a solitary, localised NSD in the posterior pole. Serous retinal PED are also commonly seen in association with CSCR [4].

Excessive tissue hydrostatic pressure within the choroid from the vascular hyperpermeability may leads to mechanical disruption of the RPE barrier, damage of RPE cells, and abnormal egress of fluid under the retina [3]. It has been shown that leaks at the levels of the RPE seen on the fluorescein angiography were contiguous with the areas of vascular hyperpermeability in Indocyanine Green Angiography (ICGA) [5].

However, all the areas of choroidal hyperpermeability are not associated with actual fluorescein leaks. These areas may be

clinically silent and could affect the ability of overlying RPE to pump fluid from retina to the choroid [6].

In pathophysiology of CSCR, a new concept of role of vortex vein anastomosis is being evolved. The congestion of vortex veins in CSCR might contribute to development of anastomosis between superior and inferior vortex vein. Hence, venous overload theory may explain pathophysiology behind pachychoroid spectrum [7,8].

Recent advances in OCT offers new horizons in understanding the pathology of CSCR and highlights morphologic anomalies in the choroid and retina of CSCR patient. There are a few studies that were performed to assess choroidal thickness in patient with CSCR to determine if there is a relation between choroidal thickness and CSCR [9].

The aim of this study was to assess SFCT, in acute CSCR patients in both affected and fellow unaffected eye using SS-OCT and to compare them with age matched control group.

MATERIALS AND METHODS

This was a hospital-based prospective case-control study, conducted between July 2018 to May 2019 at OPD of Aravind Eye Hospital, Coimbatore, Tamil Nadu, India. The study was approved by the Institutional Review Board of the parent institution Ref No.: PSG/IIHEC/2018/Appr/Exp/195 and adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients.

Inclusion criteria: Patients with treatment naïve unilateral idiopathic CSCR only, clear ocular media, with adequate pupil dilatation and not having history of CSCR were included in this study. Individuals aged 18-50 years with no evidence of any ocular pathology and willing to undergo investigation by SS-OCT were controls in this study.

Exclusion criteria: Patients with associated any other ocular disease, on treatment for CSCR, with previous history of CSCR in either eye and with history of more than three months of CSCR were excluded from this study.

Sample size calculation: The sample size was estimated based on the power analysis with the following parameters- power (80%), α (5%), $\mu_D=446.6$, $\mu_F=378.3$, $\sigma=108.8$ and the sampling ratio of 1. The following formula was used to compute the sample size:

$$n_A = k n_B \text{ and } n_B = (1 + 1/k) [\sigma(z_{1-\alpha/2} + z_{1-\beta}) / (\mu_A - \mu_B)]^2$$

$$1 - \beta = \Phi(z - z_{1-\alpha/2}) + \Phi(-z - z_{1-\alpha/2}), z = (\mu_A - \mu_B) / \sigma(1/n_A + 1/n_B)^{1/2}$$

Where, $K=n_A/n_B$ is the matching ratio, σ =standard deviation, α =Type I error, $1-\beta$ =Type II error. The estimated sample was 41 for each arm.

Study Procedure

Total 41 patients and 41 controls from OPD were included. A detailed medical and ocular history of the participant was taken. All patients underwent comprehensive ophthalmic and systemic examination. UCVA and BCVA were measured on Snellen's chart. After pupil dilatation, posterior segment evaluation with slit lamp biomicroscopy using a +90D lens and documentation with fundus photograph were done. Indirect ophthalmoscopy was done using +20D lens for peripheral retinal examination.

All subjects were examined using SS-OCT, Topcon for both the eyes. The technology uses a laser sweeping through different wavelengths up to 1050 nm, which is much higher than the conventional 850 nm used in SD-OCT. This enables a scanning speed of 100,000 A-scans/sec, which leads to single B scans with a 1 μ m axial resolution and 12 mm width. Serial horizontal and vertical macular scans were taken (5x5 mm). 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. Choroidal thickness was measured under the fovea using the scale supplied with the OCT software. The mean SFCT horizontal and vertical scan was taken manually by single observer.

STATISTICAL ANALYSIS

The analysis was done in Statistical Package for the Social Sciences version 20.0 for windows. Descriptive analysis such as mean, standard deviation and percentage were used to exhibit the clinical parameters. Independent t-test, Chi-square test, Mann Whitney test was also applied for this data. All the statistical tests were examined with 5% (p -value \leq 0.05) level of significance.

RESULTS

Total 41 patients attending the OPD and with treatment-naïve unilateral CSCR were identified. Similarly, 41 age and gender matched controls were enrolled.

The age/gender were similar in cases and controls ($p < 0.244$) [Table/Fig-1]. Among cases, 24 (58.53%) patients had right eye and 17 (41.46%) had left eye involvement, the [Table/Fig-2] which shows no significant difference (p -value=0.092).

The mean SFCT in affected eye of cases was more than in the fellow eye. In control group, the mean SFCT was 267.50 \pm 34.40 μ m [Table/Fig-3]. The mean \pm SD Central Macular Thickness (CMT) in affected eye of cases was 428 \pm 171.26 μ m and mean \pm SD Sub Retinal Detachment Height (SRDH) in affected eye cases was 285 \pm 177.72 μ m [Table/Fig-3]. A majority were emmetropes in both cases 26 (63.4%) and controls 31 (75.6%) [Table/Fig-4].

Variables	Cases	Controls	p-value (Chi-square test)
Age (years)			
(Mean \pm SD)	38.44 \pm 6.14	37.21 \pm 2.72	<0.244
Gender (n, %)			
Male	38 (92.68%)	34 (82.93%)	0.177
Female	3 (7.32%)	7 (17.07%)	

[Table/Fig-1]: Age and gender distribution among cases and controls.

Category	Right eye n (%)	Left eye n (%)	Total n (%)	p-value (Chi-square test)
CSCR (affected eye)	24 (58.53%)	17 (41.46%)	41 (100%)	0.092
Normal (unaffected eye)	17 (41.46%)	24 (58.53%)	41 (100%)	
Total	41 (50%)	41 (50%)	82 (100%)	

[Table/Fig-2]: Distribution of eyes in CSCR patients. CSCR- central serous chorioretinopathy

Variables	Cases (mean \pm SD)		Controls (Both eyes)
	Affected eye	Fellow eye	
Number of eyes	41	41	82
SFCT (μ m)	465.39 \pm 60.02	407.12 \pm 57.29	267.50 \pm 34.40
CMT (μ m)	428.00 \pm 171.26	-	-
SRDH (μ m)	285.17 \pm 177.72	-	-

[Table/Fig-3]: CMT, SRDH and SFCT among cases and SFCT in controls. CMT-Central macular thickness, SRDH-Sub retinal detachment height, SFCT-Sub-foveal choroidal thickness

Refractive status	Cases n (%)	Controls n (%)	p-value (Chi-square test)
Emmetropia	26 (63.41%)	31 (75.61%)	0.2
Hypermetropia	9 (21.95%)	1 (2.44%)	
Myopia	6 (14.63%)	9 (21.95%)	
Total	41 (100%)	41 (100%)	

[Table/Fig-4]: Refractive status among cases and controls.

The PED was more in affected eye among cases as compared to fellow eye of cases (p -value<0.001). Hyper Reflective Dots (HRD) in SRDH were present in 22 (53.65%) of affected eye among cases [Table/Fig-5].

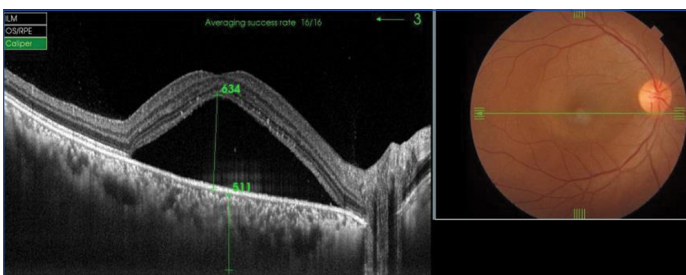
Variables	Present n (%)	Absent n (%)	Total n (%)	p-value (Chi-square test)
PED				
Affected eye	29 (70.7%)	12 (29.3%)	41(100%)	<0.001
Fellow unaffected eye	10 (24.39%)	31 (75.61%)	41 (100%)	
Total	39 (47.56%)	43 (52.44%)	82 (100%)	
HRD in SRD				
CSCR (affected eyes)	22 (53.7%)	19 (46.3%)	41 (100%)	<0.001
Normal (unaffected eyes)	-	41 (100%)	41 (100%)	
Total	22 (26.82%)	60 (73.18%)	82 (100%)	

[Table/Fig-5]: Showing association of CSCR with PED and HRD in SRD among cases. PED-pigment epithelial detachment, CSCR-central serous chorioretinopathy, SRD-sub retinal detachment

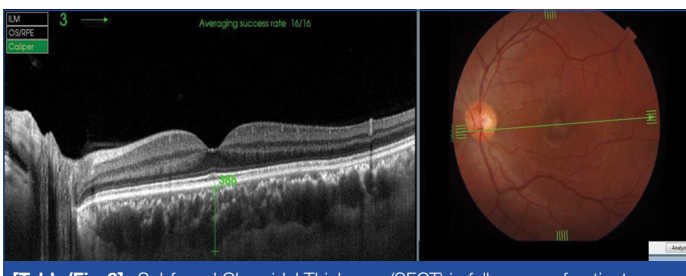
The [Table/Fig-6,7] shows the increased mean SFCT of affected eyes as compared to that of unaffected fellow eye of cases with (p -value<0.001). The [Table/Fig-6,8] shows the mean SFCT of affected eyes of cases was more than control group eyes (p -value<0.001). The mean SFCT of unaffected fellow eye of cases was also more than control group eyes, (p -value<0.001). The mean CMT and SFCT of affected eyes of cases were 428.00 \pm 171.26 μ m and 465.39 \pm 60.02 μ m respectively, (p -value=0.192).

Category		N	Thickness (in μm) (Mean \pm SD)	p-value
SFCT (cases)	CSCR (affected eye)	41	465.39 \pm 60.02	<0.001
	Unaffected fellow eye	41	407.12 \pm 57.29	
SFCT	CSCR (affected eye)	41	465.39 \pm 60.02	<0.001
	Control group	82	267.5 \pm 34.40	
SFCT	Unaffected fellow eye of cases	41	407.12 \pm 57.29	<0.001
	Controls	82	267.5 \pm 34.40	
CSCR	CMT (affected eye)	41	428.00 \pm 171.26	0.192
	SFCT (affected eye)	41	465.39 \pm 60.02	

[Table/Fig-6]: Independent t-test analysis of mean SFCT and CMT.



[Table/Fig-7]: Subfoveal Choroidal Thickness (SFCT) in involved eye of patient.



[Table/Fig-8]: Subfoveal Choroidal Thickness (SFCT) in fellow eye of patient.

DISCUSSION

This study aimed to assess SFCT, in acute CSCR patients in both affected and fellow unaffected eye using SS-OCT and to compare them with age matched control group. This study found that the choroidal thickness was increased in affected eyes and also in fellow unaffected eyes.

The CSCR international group has introduced diagnostic criteria for CSCR. It includes major and minor criteria. The major criteria includes-

- Presence or evidence of prior SRD documented on OCT involving the posterior pole unrelated to another disease process.
- Minimum one area of RPE alteration on Fundus Autofluorescence (FAF), spectral-domain OCT, or infrared imaging. The minor criteria include one or more focal leaks on Fundus Fluorescein Angiography (FFA), mid-phase hyperfluorescent placoid areas on ICGA, or SFCT of 400 μm or greater [10].

Among, 41 affected eyes of cases, the involvement of right (24) and left (17) eye was not statistically significant (p-value=0.092).

In this study, PED was present in 29 (70.73%) of affected eye and 10 (24.39%) of the fellow eye among cases. Lehmann M et al., included 29 eyes and they observed that 13 eyes with active acute and active recurrent CSCs had PED, whereas only five eyes with active chronic CSCs showed PED [11]. Carrai P et al., detected serous PED in 11 eyes [12].

Development of HRD is associated with remodeling of chorioretinal structures. In the present study, HRD in SRDH was present in 22 (53.70%) cases. In a study by Lehmann M et al., out of 29 eyes, 19 (65.51%) showed HRD in SRDH [11].

Thus, in this study, choroidal thickness was greater in both the eye of affected patient with CSCR than the choroidal thickness

in normal control group. Kim YT et al., found mean choroidal thicknesses of the affected eyes were significantly greater than those of the unaffected fellow eyes (p-value<0.001) and normal eyes (p-value<0.001) [9]. Maruko I et al., found that SFCT in symptomatic eyes was significantly thicker than that in the fellow eyes and age-matched normal eyes [13]. Chung YR et al., found that the SFCT in active state was 446.8 \pm 101.0 which was quite similar to findings of our study [14]. Lehmann M et al., observed the thickest choroids in the active recurrent (521 μm) and quiescent (530 μm) CSCR [11].

In this study, the mean SFCT, in normal population was 267.50 \pm 34.40 μm which was similar to study done by Chhablani J et al., and Margolis R and Spaide RF [15,16]. This study emphasises the fact that in CSCR, pachychoroid thickness is increased in unaffected eye indicating that in unilateral presentation of the CSCR patients, fellow eye may also have significant changes. Hence, ophthalmologist must not be ignorant and should examine the fellow eye with equal importance to look for any ongoing dormant pathologic process in CSCR patients.

Limitation(s)

The main limitation of the study is its observational and cross-sectional nature. No further follow-up of the patient was done to see the behaviour of choroidal vasculature, and effect of treatment on choroidal thickness.

CONCLUSION(S)

This study demonstrated that the choroid was significantly thicker in affected as well as unaffected eye of CSCR patient. This implies that the CSCR affect the choroidal thickness in both affected as well as unaffected eye of patient as compared to control group. Similarly, there was significant difference in SFCT of affected eye and fellow eye of cases. Further studies with larger cohort are needed to establish fact that unaffected eye in CSCR patient also have increase choroidal thickness. Studies combining IGCA, OCT and OCT angiography can be done to study and understand about natural course of CSCR.

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PARTICULARS OF CONTRIBUTORS:

1. Postgraduate Resident (3rd year), Department of Ophthalmology, Aravind Eye Hospital, Coimbatore, Tamil Nadu, India.
2. Consultant (Vitreo-Retina), Department of Vitreo-Retina, Aravind Eye Hospital Coimbatore, Tamil Nadu, India.
3. Associate Professor, Department of Glaucoma, Regional Institute of Ophthalmology, Sitapur, Uttar Pradesh, India.
4. Fellow, Department of Comprehensive Ophthalmology, Sitapur Eye Hospital, Sitapur, Uttar Pradesh, India.
5. Postgraduate Student, Department of Ophthalmology, Regional Institute of Ophthalmology, Sitapur, Uttar Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Aeshvarya Dhawan,
Doctors Hostel, Sitapur Eye Hospital, Prem Nagar, Sitapur, Uttar Pradesh, India.
E-mail: aeshvarya.dhawan@gmail.com

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