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Choroidal Thickness Measurement in Systemic Lupus Erythematosus Patients with or Without Ocular Manifestation

Prajita Khadka,[1] Ranju Kharel (Sitaula),[1] Sanjeeb Kumar Mishra,[1] Saket Jha,[2] Srijana Lamichhane,[1] Parash Gyawali,[1] Aayush Chandan[1]

[1]B. P. Koirala Lions Centre for Ophthalmic Studies, Tribhuvan University, Institute of Medicine, Kathmandu, Nepal, [2]Department of Internal Medicine, Tribhuvan University Teaching Hospital, Kathmandu, Nepal,

ABSTRACT

Background: Systemic Lupus Erythematosus is a multi-systemic disease that has a high morbidity rate. Choroids usually have a distinct structural makeup in different systemic disorders which makes it easier to be used as a potential tool for the study of disease activity.

Methods: This study was an observational cross-sectional prospective study with a total of 51 Systemic Lupus Erythematosus patients and 51 normal controls were included. The choroidal thickness values were determined using the Spectralis Spectral Domain Optical Coherence Tomography instrument (Heidelberg Engineering).

Results: The results showed that the mean subfoveal, nasal, and temporal choroidal thickness in Systemic Lupus Erythematosus patients with ocular manifestations had thinner choroidal thickness compared to normal controls with $p<0.001$, $p=0.008$, and $p<0.001$, respectively. On the other hand, Systemic Lupus Erythematosus patients without ocular manifestations had relatively thicker subfoveal choroidal thickness compared to normal controls ($p<0.001$) but nasal and temporal choroidal thickness were not statistically significant ($p=0.264$ and $p=0.347$ respectively).

Conclusions: The findings suggested that choroidal thickness measurement may serve as an indicator of disease activity and prognosis in Systemic Lupus Erythematosus patients, as well as a potential tool to predict the occurrence of ocular manifestations. Thinning of the choroid may be associated with factors such as decreased blood flow leading to atrophy or chronic inflammation, while thickening of the choroid may indicate active stage of the disease and the possibility of severe ocular manifestations in the future.

Keywords: Choroidal thickness; SLE; spectral-domain optical coherence tomography; ocular manifestation.

INTRODUCTION

SLE is a systemic autoimmune disorder that is more common in women, triggered by contact with an environmental stimulus and includes a genetic predisposition.[1] Diagnosis is made based on the Systemic Lupus International Collaborating Clinics (SLICC) criteria.[2] Ocular signs may serve as a sign of systemic disease activity.[3] Keratoconjunctivitis sicca is the most common ocular manifestation.[1] Lupus choroidopathy and retinopathy with microangiopathy, which is frequently accompanied by vision loss, are the most severe ocular symptoms.[4]

As the most vascular part of the eye, the choroid is probably more prone to ocular inflammation in multi-systemic diseases.[5] Few studies had been done on the association of choroidal thickness in SLE patients, however, some studies showed thickened choroids,[6] while other studies reported thinner choroids in the SLE population.[7,8] This inconsistency regarding the results of choroidal thickness in SLE patients provides the importance of conducting this study.

METHODS

This study is a hospital-based, cross-sectional study that was carried out at B.P. Koirala Lions Centre for Ophthalmic Studies (BPKLCOS), a tertiary eye care center in Nepal. The Ethical approval for this study (IRC 118(6-11) E[2] 078/079) was provided by the Institutional

Correspondence: Dr Ranju Kharel (Sitaula), B.P. Koirala Lions Centre for Ophthalmic Studies, Tribhuvan University, Institute of Medicine, Kathmandu, Nepal, Email: helloranju50@gmail.com.

Review Committee (IRC) of the Institute of Medicine, Tribhuvan University, Nepal on 15 September 2021 over 12 months from September 2021 to September 2022. Each patient who participated in this study, provided written informed consent, and the Tenets of Helsinki statement were followed. The study aimed to investigate the ocular manifestations in patients diagnosed with SLE based on the criteria set by the Systemic Lupus International Collaborating Clinics (SLICC).[2] The study included SLE patients attending the B.P. Koirala Lions Centre for Ophthalmic Studies or referred from various departments such as Rheumatology, General medicine, Dermatology, Nephrology, and others at the Tribhuvan University Teaching Hospital (TUTH). This research had been documented by the STROCSS (Strengthening the Reporting of Cohort, Cross-Sectional, and Case-Control Studies in Surgery) guidelines.[9]

The participants were divided into three groups: SLE patients with ocular manifestations, SLE patients without ocular manifestations, and a control group consisting of age-matched and gender-matched healthy individuals. SLE patients with ocular manifestions comprised of SLE patients who had recent onset of any ocular abnormalities like scleritis, episcleritis, lupus retinopathy, uveitis, choroidopathy etc whereas SLE patients without ocular manifestation included patient with no any recent ocular abnormalities. The study included 51 SLE patients and the control group also comprised 51 individuals. Certain exclusion criteria were applied, and patients with pre-existing glaucoma, corneal disease, retinal diseases, history of refractive surgery, high spherical refractive errors exceeding ±3.00 diopters, contact lens wearers, diabetes mellitus, pregnancy, hypertension, and other systemic diseases were excluded from the study.

As per proforma, detailed history was obtained. All the patients underwent the Schirmer II test and grading was done as 10-15mm for mild dry eyes, 5-10mm for moderate dry eyes, and <5 mm for severe dry eyes. (1) Examination of the anterior chamber was done with Haag-Streit 900 slit-lamp biomicroscopy. Pupillary dilatation was done with 1% tropicamide for fundus examination. Dilated fundus examination was examined with 90 D volk lenses with a slit lamp biomicroscopy. Sub-foveal choroidal thickness (SFCT) was measured by Spectral-Domain Optical Coherence Tomography (SD-OCT) (Spectralis Heidelberg Engineering Germany, version 6.0) using built-in Enhanced Depth Imaging (EDI)-OCT software. All images were taken between 9 AM and 4 PM in our routine OPD, to avoid possible diurnal variation in choroidal thickness.[10]

Data was analyzed in IBM SPSS version 26 and analysis was done using standard statistical tests. A normality test was done by Kolmogorov-Smirnov for each variable. Measures of central tendency were used to describe demographic profiles. To compare the normally distributed data, an Independent Sample t-test was performed. With a confidence interval (CI) of 95%, P values under 0.05 were deemed statistically significant.

RESULTS

A total of 51 SLE subjects (102 eyes) and 51 age and sex-matched controls (102 eyes) were recruited for this study. The case and control groups were selected in a

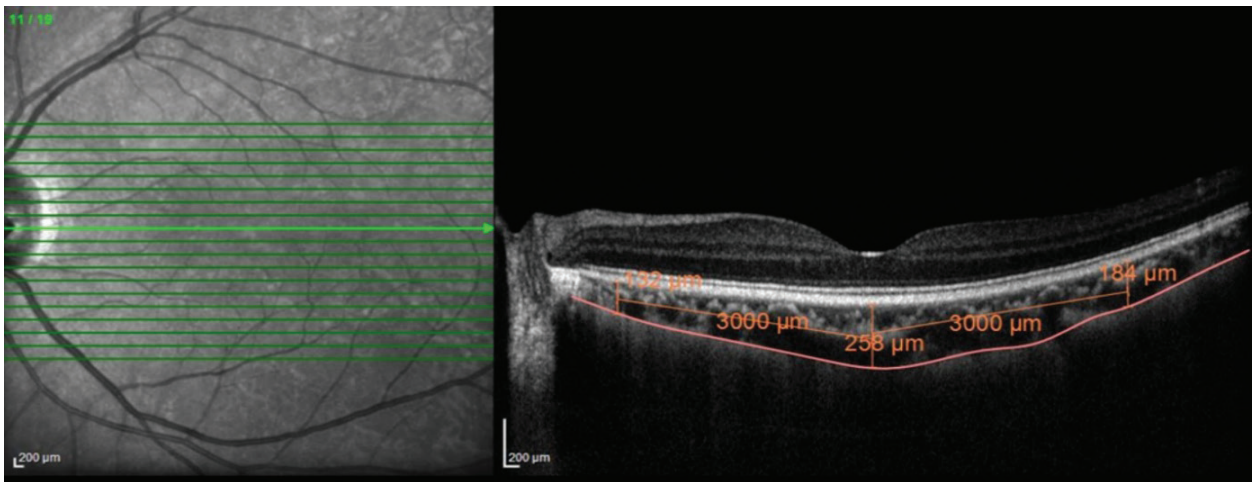

Figure 1. EDI-OCT scan of SLE patient showing choroidal thickness at subfoveal, nasal (3mm from SFCT), and temporal (3mm from SFCT) areas with labeled RPE-Bruch's membrane junction (hyper-reflective layer) and choroido-scleral junction (hypo-reflective layer).

1:1 ratio. Among 51 SLE patients, 88.2% (n= 45) were females and 11.8% (n=6) were males. There were 15:2 more women than men. The mean age of both the subjects was (31.78 ± 10.37 years), with minimum and maximum ages being 20 and 57 years respectively. Dry eye was the most common in SLE patients seen among 58.8% (n= 31) of the cases. Among the patients who presented with dry eyes, 29.4% (n= 15) cases were severe, 27.5% (n=14) were moderate and 1% (n=2) were mild dry eyes.

There were 13 cases of SLE patients with ocular manifestions. Anterior segment ocular manifestations were in the form of non-necrotizing scleritis 3.92% (n=2) and episcleritis 1.96% (n=1). As for the involvement of the posterior segment, lupus retinopathy was the most common ocular manifestation that occurred in 21.56% (n=11) out of 51 SLE patients.

Table 1. Comparison of choroidal thickness in SLE patients with ocular manifestation and control.

Choroidal thickness values	SLE Patients with ocular manifestation	Controls	P-value
Sub-foveal choroidal thickness	275.05 ± 51.48 µm	328.96 ± 52.34 µm	**p <0.001**
Nasal choroidal thickness (3mm from SFCT)	163.86 ± 58.55 µm	195.70 ± 48.10 µm	**p= 0.008**
Temporal choroidal thickness (3mm from SFCT)	230.32 ± 52.51µm	270.89 ± 42.12 µm	**p<0.001**

*(Independent t-test)

Table 1 illustrated the comparison of choroidal thickness in SLE patients with ocular manifestation and normal controls. The mean sub-foveal, nasal, and temporal CT values of SLE patients with ocular manifestation (275.05 ± 51.48 µm, 163.86 ± 58.55 µm, and 230.32 ± 52.51 µm respectively) were found thinner than normal controls which were 328.96 ± 52.34 µm, 195.70 ± 48.10 µm and 270.89 ± 42.12 µm respectively.

Table 2. Comparison of choroidal thickness in SLE without ocular manifestation and control.

Choroidal thickness values	SLE Patients without ocular manifestation	Controls	P-value
Sub-foveal choroidal thickness	353.47 ± 65.21	325.69± 25.43 µm	**p <0.001**
Nasal Choroidal thickness (3mm from SFCT)	204.80 ± 61.40 µm	196.60 ± 46.10 µm	**p= 0.264**
Temporal choroidal thickness (3mm from SFCT)	277.50 ± 52.48µm	271.98 ± 32.02 µm	**p=0.347**

*(Independent t-test)

Similarly, Table 2 summarized the comparison of choroidal thickness in SLE patients without ocular manifestation and normal controls. The CT values of the SLE patients without ocular manifestation, when compared with the normal controls using Independent t-tests, the sub-foveal choroidal thickness (353.47 ± 65.21µm) of the SLE patients without ocular manifestation was only thicker than normal controls (p<0.001). The nasal and temporal choroidal thickness, (204.80 ± 61.40 µm and 277.50 ± 52.48 µm respectively) of SLE patients without ocular manifestation also showed thicker choroid than controls but it was not statistically significant.

DISCUSSION

SLE is a multi-systemic disease that has significant impact on numerous organs and systems in the body.[1] Ocular manifestations of SLE are also important to be aware of since they can indicate the disease's activity.[1] In this study, we included 102 eyes of 51 SLE patients. SLE was found to be predominant in females. Among 51 SLE patients, 45 (88.2%) of them were females and 6 (11.8%) were males.

Around 58.8% (30) of the SLE patients were found to have dry eyes (Schirmer's II tests), out of which 29.4% (15) had severe, 27.5% (14) had moderate and 2% (1) had mild dry eyes. Ocular manifestations in the anterior segment were in the form of non-necrotizing scleritis 3.92% (2) and episcleritis 1.96% (1). As for the involvement of the posterior segment, lupus retinopathy was most common 21.56% (11) out of 51 SLE patients. Similar ocular manifestations were reported in a study done by Kharel et al.[1] Ocular manifestations differ from patient to patient and can be utilized to link systemic disease activity.[3,11]

In this study, the CT scans of SLE patients—whether they had ocular manifestations or not—were compared to those of healthy controls. The mean choroidal thickness of sub-foveal, 3mm nasal from SFCT, and 3mm temporal choroidal thickness from SFCT of the SLE patients with ocular manifestations and controls was significantly thinner than healthy controls. ($p < 0.001$, $p = 0.008$, and $p < 0.001$ of sub-foveal, nasal, and temporal choroidal thickness respectively). Altinkaynak et al also reported that the mean subfoveal, nasal, and temporal CT readings were considerably lower in SLE patients in comparison to healthy controls, with $p < 0.001$. This study included only the 'inactive' state in SLE patients and measured the choroid in 3 locations: sub-foveal and only at 1500 microns nasally and temporally.[7] Vasculitis, immunological, and complement deposits lead to a constriction of the choroidal vascular structures; as a result, the choroidal blood supply is decreased due to the loss of choriocapillaris, and choroidal thinning may result.[7] Atrophy in the choroidal tissue as a result of vascular diseases causing prolonged ischemia is another cause of choroidal thinning.[8] Thus, thinning might be associated with factors such as decreased blood flow, atrophy, repeated flares or chronic inflammation. These findings might also indicate that ocular manifestations like scleritis, episcleritis, and mild to moderate lupus retinopathy [12] are more likely to appear at the inactive or chronic stage since thinning of choroidal thickness occurred in SLE patients having ocular manifestations.

Conversely, SLE patients without ocular manifestation were found thicker than controls, but only sub-foveal choroidal thickness had statistical significance at $p < 0.001$. ($p = 0.264$ and $p = 0.347$ of nasal and temporal choroidal thickness respectively). A different study was conducted by Ferreira et al. in which measurements were made at sub-foveal and at 500 µm intervals from fovea to 1500 µm temporal, 1500 µm nasal, 1500 µm superior and 1500 µm inferior (13 locations). They found similar findings, which concluded that the CT value was thicker than in healthy controls and the CT value was only assessed in the horizontal foveal meridian.[6] It is believed that immune complex deposition, inflammatory cell infiltration in the choroidal vessel basement membrane, vascular leakage, and subsequent choroidal thickening are the causes of clinical choroidopathy.[6] Thus, in SLE patients without ocular manifestations, increased choroidal thickness may be a sign of sub-clinical lupus choroidopathy, which may manifest later. Choroid is highly vascular so multi-sytemic diseases, which mostly affect vascular system, also has impact on choroid. So, increased sub-foveal choroidal thickness in SLE patients without ocular manifestation may suggest that the SLE is in active phase as a result may also cause inflammation of ocular tissues. Furthermore, there was an elevation of sub-foveal choroidal thickness which suggests choroidal or retinal abnormalities might affect the fovea at first, resulting in significant vision loss. In addition to changes in choroidal thickness, SLE could also affect the retina, leading to various ocular complications such as retinal vasculitis, retinopathy, and macular edema.[12] These retinal changes might further influence choroidal thickness measurements.[13]

Likewise, treatment with medications such as corticosteroids and immunosuppressants could also influence choroidal thickness.[3,11] The course of treatment for SLE is based on the organs involved and severity of disease. Systemic medication is necessary to treat the underlying disease, but additional local therapy may be essential for the ocular manifestations of SLE. Keratoconjunctivitis Sicca can be treated with artificial tears, while scleral, orbital, retinal, and choroidal manifestations frequently require systemic therapy. For five years, hydroxychloroquine >6.5 mg/kg is linked to a high risk of toxicity that may even lead to bull's eye maculopathy.[1] As it affects multiple organs, customized therapy frequently necessitates cooperation with specialists (rheumatologists, nephrologists, dermatologists, and ophthalmologists).

The prospective nature of the study is the strength of this study but the limited small size, and lack of follow-

up are the limitations of study. Thus, future researches are required to better understand the relationship between SLE choroidopathy and systemic vasculopathy and to evaluate the relationship between disease state and changes in choroidal thickness.

CONCLUSIONS

Increased thickness of the choroid may suggest active disease and the potential indicator for severe ocular manifestation like lupus choroidopathy in future whereas thinning of the choroid may be linked to chronic inflammation, subsequently leading to atrophy. Early screening and diagnosis are key to effective therapy and a better prognosis.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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