Type of the Paper (Research article)

Central macular thickness Changes in Systemic Lupus erythematosus Patients on Hydroxychloroquine using Optical Coherence Tomography Angiography

Helana S. Raafat[1]*, Mahrous H. Shaheen[1], Mohamed A. Ibrahim[1], Mohamed M. Said[1]

[1]Department of Ophthalmology, Faculty of Medicine, Fayoum University, Fayoum 63511, Egypt.

*Correspondence: Helana S. Raafat, hs1261@fayoum.edu.eg, Tel: (002) 01026929089

Received: 15 July, 2024 Reviewed: 12 August, 2024
Accepted: 3 September, 2024 Published online: 2 November, 2024

Abstract:

Introduction: Hydroxychloroquine (HCQ) is widely used to treat Systemic lupus erythematosus (SLE). HCQ retinopathy is a recognized and extensively documented negative consequence of HCQ. Optical coherence tomography angiography (OCTA) can be used to evaluate this condition.

Aim of the study: To evaluate central macular thickness on OCTA in SLE patients who are receiving HCQ.

Subjects and Methods: This study is a cross-sectional observational study that focused on the right eyes of 90 persons diagnosed with SLE. The participants were divided into three groups. Group 1 comprises 30 patients who are not receiving HCQ. Group 2 comprises 30 patients who received HCQ for less than 2 years. Group 3 comprises 30 patients who were given HCQ for more than 2 years. The OCTA procedure was performed on all patients using the Optovue, Inc. equipment located in Fremont, CA, USA.

Results: There was no statistically significant difference, with a p-value more than 0.05, seen between the study groups in terms of central macular thickness. There was no statistically significant connection, with a p-value greater than 0.05, between the duration of HCQ administration and macular thickness.

Conclusion: The central macular thickness in SLE patients on HCQ therapy utilizing OCTA did not show any notable alterations.

Keywords: Hydroxychloroquine; Systemic lupus erythematosus; optical coherence tomography angiography.

1. Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that impacts the entire body. This condition is marked by the creation of abnormal autoantibodies that form immune complexes and accumulate in tissues, resulting in harm to vital organs. SLE can be present in every organ system [1].

Approximately one-third of people with SLE experience ocular problems. The ocular observations can result in vision loss due to the underlying illness or the adverse effects of treatment [2].

Hydroxychloroquine (HCQ) is the main therapeutic option for SLE. All individuals with SLE are advised to follow this recommendation unless there are medical contraindications or potential negative outcomes. HCQ has had a favorable impact on outcomes associated with SLE, such as decreased organ damage, reduced disease activity, and increased survival rates [3].

Prolonged use of HCQ is linked to negative effects, including vortex keratopathy and irreversible maculopathy that can lead to vision loss. The risk factors for HCQ-induced retinopathy are prolonged administration for over 5 years, cumulative consumption of more than 1000 g of HCQ, daily dosage over 6.5 mg/kg, presence of renal sickness, and preexisting maculopathy [4].

Retinopathy is a condition that cannot be reversed. Early detection is crucial in order to prevent significant loss of central vision. Nevertheless, when test findings are uncertain, it is advisable to do additional tests in order to prevent the premature discontinuation of important medication [5].

Optical coherence tomography angiography (OCT-A) is a noninvasive method that allows for the imaging of the micro-perfusion of blood vessels in the retina and choroid. Additionally, it has the capability to identify any alterations in these blood vessels resulting from different diseases and throughout the therapy process. Additionally, conducting a quantitative assessment of the central macular thickness would be advantageous [6].

2. Subjects & Methods

1.1. Subjects

This study is a type of research that involves observing and analyzing data from a specific group of individuals at a certain point in time. The investigation was conducted on the right eyes of 90 individuals with SLE, who were divided into three groups according to precise inclusion criteria. The study involved patients who visited the outpatient clinic of the Ophthalmology department at Fayoum University hospitals. These patients were referred by the Rheumatology department. The study was conducted between January 2023 and October 2023.

Inclusion criteria

The patients were categorized into three distinct groups:

- **Group 1:** Right eye of 30 recently diagnosed SLE patients who aren't receiving HCQ.
- **Group 2:** Right eye of 30 patients with SLE who were treated with HCQ for less than 2 years.
- **Group 3**: Right eye of 30 patients with SLE who were treated with HCQ for over 2 years.

Exclusion criteria

- Systemic vascular disease DM, HTN.
- History of ocular vascular disease.
- Any ocular opacity. e.g. (Cataract).
- Low signal strength intensity below 7/10.
- Refractive error e.g. (Myopia > -5).

1.2. Study design

A cross-sectional observational comparison study was conducted.

1.3. Methods

History Data collection

- Demographic data (age & gender).
- Exclusion of systemic diseases other than SLE as diabetes, hypertension and cardiovascular disorders.
- How long it has been since diagnosis with SLE.
- Medications received for SLE.
- Duration and dose of HCQ intake

Examination

Patients were examined for:

- Visual acuity was assessed using a Landolt chart and the findings were transformed into log minimum angle of resolution (LogMAR) for statistical evaluation.

- The Goldmann applanation tonometry is a method used to measure the pressure inside the eye.
- The anterior region of the eye is examined with a slit lamp.
- Fundus examination with an indirect ophthalmoscope with dilation of the pupil.

Diagnostic Procedure

The optical coherence tomography angiography (OCTA) equipment from Optovue, Inc. in Fremont, CA, USA was used to perform optical coherence tomography angiography (OCT-A). This approach uses a commercially accessible spectral domain optical coherence tomography (SD-OCT) to accurately evaluate the thickness of the central macula.

- The entire image, the upper half, the lower half, and the central part of the retina called the fovea.
- The parafovea is divided into different regions: superior hemisphere, inferior hemisphere, temporal region, superior region, nasal region, and inferior region.
- The perifovea is divided into different regions: superior hemisphere, inferior hemisphere, temporal region, superior region, nasal region, and inferior region.

3. Results

Regarding demographic characteristics of enrolled patients, the mean age was (31.02±11.1) years old ranging from 11 to 56 years. 16 patients were males (17.8%) while 74 patients were females (82.2%) (**Table 1 and Figure 1**).

Table 1: Demographic characters of enrolled patients.

Variables	**Mean ±SD**	**Range**
Age (years)	31.02 ±11.1	11-56
Sex	**No.**	**%**
Male	16	17.8%
Female	74	82.2%

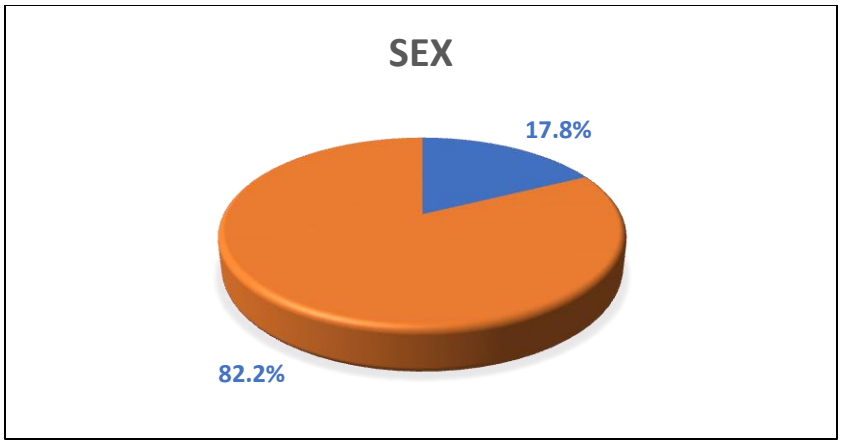

Figure 1: Pie chart for sex distribution among patients.

On comparing the central macular Thickness(µm) in different quadrants, there was no statistically significant difference between the study groups, as shown by a *p* >0.05 (**Table 2**).

There was no statistically significant link (*p* >0.05) found between the duration of HCQ therapy and thickness measures in all areas of the picture, including the total image, parafovea, and perifovea (**Table 3**).

Table (2): Comparisons of macular thickness measures in different study groups.

Thickness	Group I (N=30)	Group II (N=30)	Group III (N=30)	*P*-value
Whole image	281.1 ±13.9	282.7 ±12.2	280.5 ±10.9	0.78
Superior hemi	283.9 ±14.5	283.9 ±12.7	282.9 ±10.7	0.93
Inferior hemi	278.2 ±13.8	281.7 ±12.2	278.3 ±11.5	0.47
Fovea	237.9 ±18.3	236.3 ±19.5	240.2 ±18.1	0.33
Parafovea	315.1 ±17.1	317.1 ±13.5	318.6 ±11.1	0.61
Superior hemi	316.5 ±16.8	317.8 ±13.1	3 19.8 ±11.6	0.66
Inferior hemi	313.8 ±17.9	316.4 ±14.5	317.5 ±11.01	0.60
Temporal	305.7 ±15.8	306.8 ±2.4	311.1 ±11.4	0.27

Superior	321.2 ±17.2	322.9 ±13.6	323.9 ±11.9	0.76
Nasal	317.4 ±17.9	319.9 ±15.3	319.6 ±11.9	0.77
Inferior	316.3 ±19.5	318.9 ±15.6	320.1 ±11.4	0.64
Perifovea	279.3 ±14.9	281.4 ±12.9	277.9 ±11.9	0.59
Superior hemi	282.6 ±15.2	283.2 ±13.1	280.7 ±11.6	0.76
Inferior hemi	276.1 ±15.3	279.5 ±13.1	275.1 ±12.9	0.43
Temporal	266.1 ±14.4	266.7 ±11.1	265.7 ±11.7	0.95
Superior	283 ±14.9	283.2 ±13.9	281.3 ±11.9	0.83
Nasal	296.9 ±17.7	299.5 ±16.6	294.1 ±13.3	0.42
Inferior	271.2 ±15.3	275.7 ±13.6	270.6 ±14.4	0.33

Table 3: Correlation between HCQ treatment duration and macular thickness measures among treated groups.

Thickness	HCQ treatment duration (yrs)	
	r	***P*-value**
Whole image	-0.005	0.97
Superior hemi	0.05	0.69
Inferior hemi	-0.06	0.62
Fovea	0.08	0.54
Parafovea		
Parafovea	0.08	0.51
Superior hemi	0.13	0.34
Inferior hemi	0.05	0.7
Temporal	0.16	0.21
Superior	0.11	0.42
Nasal	-0.002	0.98
Inferior	0.07	0.60
Perifovea		
Perifovea	-0.05	0.69
Superior hemi	0.006	0.96
Inferior hemi	-0.09	0.45
Temporal	0.02	0.88
Superior	0.03	0.84
Nasal	-0.10	0.44
Inferior	-0.09	0.45

4. Discussion

HCQ-induced retinopathy is the most severe and permanent complication of HCQ that poses a threat to vision. Therefore, timely identification is crucial to avert severe harm to the retina. The occurrence of this condition significantly rises as the treatment continues and surpasses 1% after 5-7 years [7]. HCQ exhibits substantial accumulation in the pigmented ocular tissues, specifically in the retinal pigment epithelium (RPE). HCQ binds to melanin, impairs the function of RPE lysosomes, and reduces the process of swallowing discarded outer segments of photoreceptor cells. Consequently, there are negative changes to the RPE, resulting in RPE atrophy and the deterioration of the photoreceptors [8].

SD-OCT enables an impartial and thorough evaluation of the macula in patients who are susceptible to HCQ retinopathy. Early HCQ retinopathy is distinguished by the disruption of the linkage between the inner and outer segments of photoreceptors, as shown by SD-OCT. The central fovea exhibits weakening of the outer nuclear layer, whereas the outer retinal structures around the fovea remain unaffected, resulting in a noticeable "flying saucer" indication [9].

OCTA is a non-invasive imaging technology that allows for the three-dimensional visualization of the microvasculature in the retina. Additionally, conducting a quantitative assessment of the central macular thickness would be advantageous [10].

This study compared the macular thickness (µm) in several parts of the eye, such as the entire image, upper half, lower half, fovea, parafovea, and perifovea. The findings indicated that there was no statistically significant difference in macular thickness among the study groups. No statistically significant correlation was observed between the length of HCQ therapy and the thickness in the total image, parafovea, and perifovea.

In a similar vein, Mihailovic et al. (2020) discovered that there was no notable disparity in the thickness of the central retina among patients with SLE who had been using HCQ for over 5 years, those who had been using it for less than 5 years, and individuals in good health [11].

In contrast to our study, Tarakcioglu et al. discovered that the superficial entire, parafoveal, and perifoveal thickness, as well

as the deep whole, parafoveal, and perifoveal thickness, were reduced in the group treated with HCQ compared to the control group, which consisted of newly diagnosed individuals not receiving HCQ treatment. The results also showed that patients who had been using HCQ for 5 years or less had consistently higher thickness measurements [12].

The research undertaken by Esser et al. investigated persons diagnosed with rheumatoid arthritis who had been prescribed HCQ for a duration exceeding 5 years, individuals with rheumatoid arthritis who had been using HCQ for less than 5 years, and a control group of healthy individuals. The study findings revealed a decrease in the thickness of the retina after long-term use of HCQ [13].

In a study conducted by Hamed et al, patients with RA who were taking HCQ did not show any notable differences in the characteristics of superficial and deep retinal thickness compared to the tested groups. This encompasses measurements obtained for the entire picture, upper hemisphere, lower hemisphere, fovea, parafovea, and perifovea [14].

5. Conclusion

OCTA is a non-invasive method that can be valuable for quantitatively assessing the thickness of the central macula in patients with SLE who are undergoing HCQ treatment.

Ethical approval and consent to participate: Prior to its commencement, the research received permission from the ethics committee of Fayoum University Hospital in December 2022, under the reference number M632. The participants were provided with information regarding the study's aims, examinations, investigations, confidentiality of their information, and their freedom to choose not to participate.

Funding: The authors do not have any financial sources to disclose for this manuscript.

Conflicts of Interest: All authors declare they have no conflicts of interest.

References

1. Read RW. Clinical mini-review: systemic lupus erythematosus and the eye. Ocul Immunol Inflamm. 2004;12(2):87-99. doi: 10.1080/09273940490895308.
2. Shoughy SS, Tabbara KF. Ocular findings in systemic lupus erythematosus. Saudi J Ophthalmol. 2016;30(2):117-121. doi: 10.1016/j.sjopt.2016.02.001.

3. Dima A, Jurcut C, Chasset F, Felten R, Arnaud L. Hydroxychloroquine in systemic lupus erythematosus: overview of current knowledge. Ther Adv Musculoskelet Dis. 2022;14:1759720X211073001. doi: 10.1177/1759720X211073001.
4. Dammacco R. Systemic lupus erythematosus and ocular involvement: an overview. Clin Exp Med. 2018;18(2):135-149. doi: 10.1007/s10238-017-0479-9.
5. Marmor MF, Kellner U, Lai TY, Melles RB, Mieler WF; American Academy of Ophthalmology. Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy (2016 Revision). Ophthalmology. 2016;123(6):1386-1394. doi:10.1016/j.ophtha.2016.01.058
6. Fang PP, Lindner M, Steinberg JS, Müller PL, Gliem M, Charbel Issa P, Krohne TU, Holz FG. Klinische Anwendungen der OCT-Angiographie [Clinical applications of OCT angiography]. Ophthalmologe. 2016;113(1):14-22. German. doi: 10.1007/s00347-015-0192-6.
7. Wolfe F, Marmor MF. Rates and predictors of hydroxychloroquine retinal toxicity in patients with rheumatoid arthritis and systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2010;62(6):775-784. doi: 10.1002/acr.20133.
8. Stokkermans TJ, Falkowitz DM, Trichonas G. Toxicity of Chloroquine and Hydroxychloroquine. January 11, 2024. Source: StatPearls [Internet]. Treasure Island, Florida: StatPearls Publishing; January 2024 forward.
9. Chen E, Brown DM, Benz MS, Fish RH, Wong TP, Kim RY, Major JC. Spectral domain optical coherence tomography as an effective screening test for hydroxychloroquine retinopathy (the "flying saucer" sign). Clin Ophthalmol. 2010;4:1151-1158. doi: 10.2147/OPTH.S14257.
10. Coscas F, Sellam A, Glacet-Bernard A, Jung C, Goudot M, Miere A, Souied EH. Normative Data for Vascular Density in Superficial and Deep Capillary Plexuses of Healthy Adults Assessed by Optical Coherence Tomography Angiography. Invest Ophthalmol Vis Sci. 2016;57(9):OCT211-23. doi: 10.1167/iovs.15-18793.
11. Mihailovic N, Leclaire MD, Eter N, Brücher VC. Altered microvascular density in patients with systemic lupus erythematosus treated with hydroxychloroquine-an optical coherence tomography angiography study. Graefes Arch Clin Exp Ophthalmol. 2020;258(10):2263-2269. doi: 10.1007/s00417-020-04788-4.
12. Tarakcioglu HN, Ozkaya A, Yigit U. Is optical coherence tomography angiography a useful tool in the screening of hydroxychloroquine retinopathy? Int Ophthalmol. 2021;41(1):27-33. doi: 10.1007/s10792-020-01549-4.
13. Esser EL, Zimmermann JA, Storp JJ, Eter N, Mihailovic N. Retinal microvascular density analysis in patients with rheumatoid arthritis treated with hydroxychloroquine. Graefes Arch Clin Exp Ophthalmol. 2023;261(5):1433-1442. doi: 10.1007/s00417-022-05946-6.
14. Hamed A, Ganeb S, Abdel Azim E, elsayed M, Elbeshry H. Optical coherence tomography angiography (OCTA) is used to identify changes in the retina of individuals who are using hydroxychloroquine (HCQ). Benha Medical Journal. 2023;40:39-47. Doi: 10.21608/bmfj.2023.198370.1776.