http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v10i12.12

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Article

Retinal nerve fibre layer and macular thickness in patients of migraine –an optical coherence tomography based study

Authors
Dr Luxmi Singh[1], Dr Aashna Agarwal[2], Dr Deeksha Tyagi[3]
[1]Professor and Head of Department, Department of Ophthalmology, Era's Lucknow Medical College and Hospital, Era University, Lucknow, Uttar Pradesh.
[2]Junior Resident, Department of Ophthalmology, Era's Lucknow Medical College and Hospital, Era University, Lucknow, Uttar Pradesh.
[3]Junior Resident, Department of Ophthalmology, Era's Lucknow Medical College and Hospital, Era University, Lucknow, Uttar Pradesh
*Corresponding Author
Dr Aashna Agarwal
Junior Resident, Department of Ophthalmology, Era's Lucknow Medical College and Hospital, Era University, Lucknow, Uttar Pradesh, India

Abstract
Introduction: *To study the correlation of Macular and RNFL thickness in relation to duration, type and severity of migraine.*
Methods: *The study included migraine patients with and without aura. All the study participants underwent a thorough clinical evaluation, fundus examination, visual field assessment after due consent and ethical clearance. RNFL thickness was measured using optical coherence tomography (OCT). RNFL and macular thickness was correlated with MIDAS score grading system.*
Result: *There is a significant association of RNFL thickness in nasal segments in association with MIDAS score grading. (p=0.05)*
Macular thickness at VC was significantly thinner in those with <1 year disease as compared to patients having disease for 2-5 years and >5 years.
Conclusion: *Significant association of RNFL thickness in nasal segments in association with MIDAS score grading. (p=0.05)*
Further studies are required to further investigate the relationship between migraine and macular/RNFL thickness.
Keywords: *Retinal nerve fiber layer; macular layer; migraine; OCT; MIDAS score grading.*

Introduction

Migraine is one of the most common devitalizing diseases in the world.[1] It is divided into two major groups: classic migraine or migraine with aura (MA) and common migraine or migraine without aura.[1]

Migraine is often associated with visual aura symptoms (VASs) which occur in 98–99% of MAs, whereas disturbances of sensation and

language occur in 36% and 10% of auras, respectively.[2]The most frequently reported symptoms are flashes of bright light, "foggy" vision, zigzag lines, and scotoma.[2]

The underlying pathophysiology of migraine is not fully established and many theories have been suggested[3], the neurovascular theory remains one of the most significant mechanisms involved in the pathogenesis of migraine.

The blood supply of the optic nerve and retina are derived from the intracranial vasculature. Migraine-related vasospasm of the arterial vasculature supplying the retina and optic nerve head could cause ischemia and retinal nerve fiber loss which may lead to ganglion cell death in migraine patients.[4]

Although the vasoconstriction of cerebral and retinal blood vessels is a transient phenomenon, the chronic nature of migraines might cause permanent structural abnormalities in the brain as well as in the retina and choroid.[5]

Retinal nerve fiber layer (RNFL) thickness measurements can be used as an index to assess ganglion cell and retinal nerve fiber damages. With the introduction of optic coherence tomography (OCT), the RNFL thickness measurements with 8-10 micrometers scale sensitivity have been possible.[6]

OCT is a reliable and reproducible technique in RNFL thickness measurement. It is a noninvasive imaging procedure that gives high-resolution, cross-sectional images of the RNFL, ganglion cell layer (GCL), and the optic nerve head.[7]

Although some studies have investigated the RNFL thickness in patients who have migraine with and without aura by using OCT but the results are inconclusive and more studies are required.

We aim to analyse the macular and RNFL thickness changes in relation to duration, type and severity of migraine.

Material and Methods

This was a cross sectional study done on a total of 84 eyes of 42 patients which were enrolled in the study after obtaining written and informed consent at department of ophthalmology of a tertiary care centre in Uttar Pradesh.

After their enrolment demographic details, i.e. age and gender were noted. Cases completed the Migraine Disability Assessment (MIDAS) questionnaire, which asks a series of lifestyle questions to assess level of pain and disability due to migraine and then assigned a score of I-mild to IV-severe.

A general and systemic examination of the patients was carried out and medical history regarding systemic and chronic illnesses such as hypertension, ischemic heart disease, nephropathy and neuropathy were enquired for. All the patients were also enquired about current medications, if any.

After preliminary medical evaluation and history taking, the patients were subjected to hemodynamic evaluation. Blood pressure (both systolic and diastolic) were also measured. Random blood sugar levels were also measured.

Subsequent to this, ophthalmological assessment of the patients were done. Best corrected visual acuity was measured using Snellen's chart for both the eyes which was followed by Torch light examination, distant direct ophthalmoscopy, slit lamp examination, fundus evaluation by direct ophthalmoscope and fundus photography by Zeiss. Intraocular pressure (IOP) was measured using Goldmann's Applanation Tonometer.

Measurement of Retinal Nerve Fiber Layer/Optic Disc Imaging was done using Cirrus HD Spectral Domain Optical Coherence Tomography (SD-OCT), Carl Zeiss Meditec, Inc. SW Ver: 6.0.0.599. The average Retinal Nerve Fiber Layer (RNFL) thickness (µm) was calculated by taking an average of all the four quadrants.

Exclusion Criteria: Eyes with retinal and optic disc pathology, glaucoma, dens cataract or corneal opacity and eyes previously subjected to intraocular surgery or ocular laser treatment were excluded.

Patients with diabetes mellitus, hypertension, cardiovascular and renal disease, history of central nervous system disorders including brain tumors, infarction, encephalitis, epilepsy, Alzheimer's disease, head or eye trauma and any type of headache except for migraine were excluded from the study.

Statistical Analysis: Data was analysed using SPSS 21.0 package. ANOVA and independent samples 't'-test were employed.

Results

The present study included a total of 42 migraine patients. A total of 84 eyes of these 42 patients were examined.

Majority of these patients were aged ≤30 years (57.1%), were females (88.1%) and had migraine with aura (66.7%). Maximum number of cases had migraine for ≤1 year (45.2%) followed by those having migraine for 2-5 years (42.9%) and only 5 (11.9%) had migraine for >5 years. The proportion of patients with Midas Score Grade 1, 2, 3 and 4 was 35.7%, 38.1%, 14.3% and 11.9% respectively (Table 1).

A total of 84 eyes of these 42 patients were examined. Mean macular thickness at CCT, ACT,VC, IS, IT, II, IN, OS, OT, OI and ON was 520.80±31.71, 270.43±13.84, 9.70±0.60, 312.70±18.39, 300.63±19.22, 305.73±36.07, 312.73±17.55, 268.43±31.25, 255.27±15.04, 257.93±18.15 and 286.75±21.21 µm respectively. Mean RNFL thickness at superior, temporal, inferior and nasal quadrants was 113.19±17.77, 59.18±9.44, 110.99±23.54 and 67.96±12.71 µm respectively. Average RNFL thickness was 87.00±12.35 µm (Table 2).

No significant association of macular and RNFL thickness was observed with duration of disease except macular thickness at VC which was found to be significantly thinner in those with ≤1 year disease (9.48±0.70 µm) as compared to those having disease for 2-5 years (9.91±0.47 µm) and >5 years (9.77±0.30 µm) respectively (p=0.007) (Table 3).

No significant difference in macular and RNFL thickness was observed between patients having migraine with or without aura (p>0.05) (Table 4).

No significant association of macular or RNFL thickness was observed with Midas Score Grade except for RNFL thickness at nasal segment where it was found to be borderline significantly higher in lower grades as compared to that in higher grade (p=0.050) (Table 5).

Table 1: Demographic and Clinical Profile of Patients (n=42)

SN	Characteristic	Statistic
1.	Age	
	≤30 Years	24 (57.1%)
	>30 Years	18 (42.9%)
2.	Gender	
	Male	5 (11.9%)
	Female	37 (88.1%)
3.	Duration of illness	
	≤1 Year	19 (45.2%)
	2-5 Years	18 (42.9%)
	>5 Years	5 (11.9%)
4.	Type of migraine	
	With aura	28 (66.7%)
	Without aura	14 (33.3%)
5.	Midas Score	
	1	15 (35.7%)
	2	16 (38.1%)
	3	6 (14.3%)
	4	5 (11.9%)

Table 2: Macular and RNFL thickness (n=84)

SN	Variable	Mean	SD
1.	Macular		
	CCT	520.80	31.71
	ACT	270.43	13.84
	VC	9.70	0.60
	IS	312.70	18.39
	IT	300.63	19.22
	II	305.73	36.07
	IN	312.63	17.55
	OS	268.43	31.25
	OT	255.27	15.04
	OI	257.93	18.15
	ON	286.75	21.21
2.	RNFL		
	Average	87.00	12.35
	Superior	113.19	17.77
	Temporal	59.18	9.44
	Inferior	110.99	23.54
	Nasal	67.96	12.71

Table 3: Association of Macular and RNFL thickness with duration of disease

SN	Variable	Duration of disease						Statistical significance (ANOVA)	
		≤1 Year (n=38)		2-5 Years (n=36)		>5 Years (n=10)			
		Mean	SD	Mean	SD	Mean	SD	F	'p'
1.	Macular								
	CCT	519.08	30.64	518.64	35.20	535.10	18.46	1.161	0.318
	ACT	267.97	15.44	273.31	12.53	269.40	10.72	1.418	0.248
	VC	9.48	0.70	9.91	0.47	9.77	0.30	5.329	0.007
	IS	310.29	21.12	316.03	16.43	309.90	12.48	1.033	0.361
	IT	299.89	20.72	301.92	18.16	298.80	18.59	0.151	0.860
	II	307.03	22.21	303.22	50.39	309.80	6.91	0.172	0.843
	IN	311.76	18.64	314.42	18.28	309.50	9.34	0.386	0.681
	OS	270.37	16.45	266.08	44.48	269.50	12.60	0.177	0.838
	OT	254.11	15.44	257.03	15.89	253.40	10.19	0.431	0.651
	OI	253.92	17.73	262.25	19.43	257.60	11.58	1.996	0.143
	ON	284.37	23.74	291.72	19.18	277.90	13.93	2.157	0.122
2.	RNFL								
	Average	83.66	14.33	88.94	9.58	92.70	10.32	3.046	0.053
	Superior	110.37	20.46	114.42	15.42	119.50	13.49	1.201	0.306
	Temporal	59.05	10.91	58.47	7.30	62.20	10.59	0.611	0.545
	Inferior	107.55	23.86	111.03	23.96	123.90	17.39	1.952	0.149
	Nasal	66.79	11.09	68.64	13.38	70.00	16.59	0.336	0.716

Table 4: Association of Macular and RNFL thickness with AURA

SN	Variable	Migraine With Aura				Statistical significance (Independent samples 't'-test)	
		Yes (n=56)		No (n=28)			
		Mean	SD	Mean	SD	F	'p'
1.	Macular						
	CCT	525.09	30.82	512.21	32.28	1.78	0.079
	ACT	270.23	15.01	270.82	11.37	-0.18	0.855
	VC	9.71	0.62	9.67	0.57	0.29	0.769
	IS	311.93	20.39	314.25	13.73	-0.54	0.589
	IT	299.30	19.57	303.29	18.55	-0.89	0.374
	II	304.55	41.52	308.07	21.91	-0.42	0.676
	IN	311.91	18.92	314.07	14.65	-0.53	0.598
	OS	266.16	36.80	272.96	14.52	-0.94	0.350
	OT	254.48	14.93	256.86	15.43	-0.68	0.499
	OI	259.75	18.78	254.29	16.54	1.31	0.195
	ON	286.80	22.14	286.64	19.62	0.03	0.974
2.	RNFL						
	Average	88.09	13.17	84.82	10.39	1.15	0.255
	Superior	112.75	20.22	114.07	11.68	-0.32	0.750
	Temporal	58.34	9.38	60.86	9.49	-1.16	0.251
	Inferior	111.09	26.75	110.79	15.68	0.06	0.956
	Nasal	69.45	13.87	65.00	9.52	1.52	0.131

Table 5: Association of Macular and RNFL thickness with MIDAS Score

SN	Variable	MIDAS Score Grade								Statistical significance (ANOVA)	
		I (n=30)		II (n=32)		III (n=12)		IV (n=10)			
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	F	'p'
1.	Macular										
	CCT	521.97	26.44	524.44	30.56	499.08	40.67	531.70	31.18	2.560	0.061
	ACT	273.17	16.64	268.44	14.33	271.58	8.38	267.20	5.31	0.816	0.489
	VC	9.76	0.69	9.57	0.64	9.93	0.41	9.62	0.19	1.218	0.309
	IS	314.70	21.18	312.81	17.98	317.25	13.79	300.90	11.45	1.786	0.157
	IT	304.87	20.94	297.06	18.36	306.83	20.36	291.90	9.12	2.032	0.116
	II	310.57	21.20	307.78	21.56	292.58	82.35	300.40	17.51	0.813	0.490
	IN	315.60	21.82	311.34	13.54	315.67	18.66	304.20	11.08	1.243	0.300
	OS	274.87	16.77	259.94	45.14	274.00	21.16	269.60	9.75	1.361	0.261
	OT	255.93	15.97	255.16	15.64	256.42	16.27	252.30	9.32	0.168	0.918
	OI	261.27	21.67	253.38	14.15	260.67	21.96	259.20	11.06	1.122	0.345
	ON	287.37	29.82	286.78	17.60	288.17	11.38	283.10	6.35	0.121	0.947
2.	RNFL										
	Average	88.53	16.43	89.41	6.71	83.25	8.97	79.20	12.98	2.370	0.077
	Superior	112.67	23.87	114.66	12.72	112.92	17.90	110.40	10.47	0.159	0.923
	Temporal	59.53	10.63	59.00	8.24	59.33	10.28	58.50	9.63	0.035	0.991
	Inferior	111.83	28.21	116.19	16.80	94.58	24.27	111.50	19.96	2.622	0.056
	Nasal	71.57	14.60	68.03	11.54	59.58	7.89	67.00	11.40	2.723	0.050

Discussion

In this study that was dominated by a relatively younger population of migraine patients (57.1% aged ≤30 years), having only 5 (11.9%) patients with migraine for >5 years and a dominance of lower grades of migraine (73.8% Midas Grade 1 and 2) we failed to find a distinct association of RNFL and macular thickness with duration of disease, presence or absence of aura and Midas Grade respectively. These findings rule out an association of migraine with RNFL or macular thickness at least in younger patients not having a prolonged history of disease. These findings are in agreement with the observation made by Gunes *et al.* (2018)[4] who also carried out their study in a relatively younger population with migraine (Mean age 37 years) and duration of migraine ranging from 11 to 240 months and failed to find

out any difference from age, sex matched controls. In their study, similar to present study, no significant association of migraine duration, presence of aura and frequency and length of migraine attacks could be seen with RNFL, GCL and choroidal thickness. However, in a recent study Labib *et al.* (2020)[8] despite including a relatively younger migraine population (mean age 30.6 years) not only found the RNFL in migraine patients to be significantly thinner as compared to that of controls but also found it to be significantly thinner in migraine patients with aura as compared to those without aura but failed to find a significant association with duration of disease, headache frequency, and headache intensity. In present study we did not find either a significant association of presence of aura with macular or RNFL thickness in general but also failed to derive distinct significant differences with respect to duration of disease and MIDAS scores. One of the differences between the present study and that of Labib *et al.* (2020)[8] could be the fact that they included only chronic migraine patients as compared to present study where no such inclusion criteria was used.

The relationship between RNFL/macular thickness and migraine remains to be controversial with lack of consistent evidence supporting any such relationship. Acer *et al.* (2016)[9] in a recent study that included migraine patients without aura (mean age 30.17 years; mean duration of disease 3.72 months) did not find a significant difference in macular thickness as compared to controls. For RNFL thickness too, they found only significant difference between cases and controls for measurements at temporal and nasal superior sextants. Two previous studies[10,11] reported a reduction inRNFL thickness in migraine patients with and without aura. However, Yurtoğulları*et al.* (2021)[12] in a recent study despite finding the RNFL to be significantly thinner in central and inner inferior quadrant in both with and without aura migraine patients as compared to controls and significantly thinner RNFL in inner nasal quadrant of with aura migraine patients as compared to that in controls failed to find out a significant difference in RNFL thickness between migraine patients with and without aura. The present study also failed to find out any significant difference in macular thickness as well as RNFL thickness between with and without aura migraine patients. Another recent study[13] found that migraine was associated with retinal changes as measured by RNFL thinning in the superior macula. They also highlighted the association of longer duration of migraine with thinner temporal peripapillary RNFL. In present study, we had only few patients with migraine duration >5 years and probably this could be one of the reasons for absence of any significant association of disease severity, duration and with and without aura with RNFL thickness. In a recent systematic review too[14], inconsistencies in pattern of RNFL thinning and other OCT measured structural changes in migraine patients were reported both favouring such relationship as well as not favouring this relationship. Moreover, different studies showed difference in retinal thickness at different segments of peripapillary RNFL layer.

The underlying mechanism guiding the relationship of RNFL/macular thinning in migraine is considered to be guided by the explanation that attacks of migraine may be related to decreased blood flow in the retina and optic nerve. This in turn may lead to unstable ocular perfusion and thereby to ischemia and reperfusion damage in duration of migraine history[7]. However, it must be understood that the anatomical effect of these ischemic and reperfusion damages in terms of RNFL and macular thinning occurs after frequent repetitions of these attacks over a prolonged period and hence migraine patients with relatively shorter duration of disease and less severe migraine attack frequencies might not come up with structural changes in RNFL and macular thickness.

The findings of the present study thus support further research in exploring the relationship of macular and RNFL thickness in migraine patients with various factors affecting the disease. Further

studies on a larger sample size with inclusion of patients with wide demographic and clinical profile along with a control population are recommended to provide further evidence regarding existence of a relationship between migraine and macular/RNFL thickness.

Conclusion

There is a significant association of RNFL thickness in nasal segments in association with MIDAS score grading.(p=0.05)

Macular thickness at VC was significantly thinner in those with <1 year disease as compared to patients having disease for 2-5 years and >5 years.

Further studies on a larger sample size and a longer history of migraine are recommended to further investigate the relationship between migraine and macular/RNFL thickness.

Financial Disclosure: This study received no financial support

Reference

1. Sorkhabi R, Mostafaei S, Ahoor M, et al. Evaluation of retinal nerve fiber layer thickness in migraine. Iran J Neurol. 2013;12(2):51–5.
2. Viana M, Tronvik EA, Do TP, et al. Clinical features of visual migraine aura: a systematic review. *J Headache Pain*. 2019;20(1):64
3. Sacco S, Ricci S, Carolei A. Migraine and vascular diseases: a review of the evidence and potential implications for management. Cephalalgia. 2012;32:785–95.
4. Gunes A, Karadag AS, Yazgan S, et al. Evaluation of retinal nerve fiber layer, ganglion cell layer and choroidal thickness with optical coherence tomography in migraine patients: a case-control study. Clin Exp Optom. 2018;101(1):109–15.
5. Michael NDB, Hussein A, Abd Halim S, et al. Evaluation of optic nerve head parameters, retinal nerve fiber layer thickness, and ocular perfusion pressure in migraine patients. Cureus. 2019;11(5):e4599.
6. Pagliara MM, Lepore D, Balestrazzi E. The role of OCT in glaucoma management. *Prog Brain Res.* 2008;173:139–48
7. Demircan S, Ataş M, ArıkYüksel S, et al. The impact of migraine on posterior ocular structures. *J Ophthalmol*. 2015;2015:868967.
8. Labib DM, Hegazy M, Esmat SM, et al. Retinal nerve fiber layer and ganglion cell layer changes using optical coherence tomography in patients with chronic migraine: a case-control study. Egypt J Neurol Psychiatry Neurosurg 2020; 56: 86.
9. Acer S, Oğuzhanoğlu A, Çetin EN, Ongun N, et al. Ocular pulse amplitude and retina nerve fiber layer thickness in migraine patients without aura. BMC Ophthalmol. 2016;16:1.
10. Gipponi S, Scaroni N, Venturelli E, et al. Reduction in retinal nerve fiber layer thickness in migraine patients. NeurolSci. 2013;34(6):841–5.
11. Martinez A, Proupim N, Sanchez M. Retinal nerve fibre layer thickness measurements using optical coherence tomography in migraine patients.Br J Ophthalmol. 2008;92:1069–75.
12. Yurtoğulları Ş, Timur İEE, Eyidoğan D. Retinal Thickness Alterations in Patients with Migraine. Turk J Neurol. 2021; 27(1): 69-74.
13. Barrett DA, Hashemi N, Adesina OOO. Retinal Nerve Fiber Layer Thickness in Migraine and its Correlation to Duration and Severity of Disease. Investigative Ophthalmology & Visual Science 2018; 59: 617.
14. Ascaso FJ, Marco S, Mateo J, Martínez M, et al. Optical Coherence Tomography in Patients with Chronic Migraine: Literature Review and Update. Front Neurol. 2017;8:684.