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Ocular Association of Dyslipidemia and Migraine: a Comparative study

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Abstract:

Migraine is one of the most frequently encountered neurological disorders and has varying presentations. It can be predisposed due to multiple factors and Dyslipidemia may be one of them. It is easy to diagnose deranged lipid profile and this may be helpful in preventing long term consequences if treated in time. Migraine headache often begins with pain around the eye and temple region, so ocular co-morbidity may not be denied. This was a prospective, randomized, case control study done between September 2021 to September 2022 in the Ophthalmology department of our medical college to see the associations between the lipid profile and migraine headache. We also intended to find out whether any physiological change occurs in the eyes during the attack phase**.** Two groups A and B of 200 patients in each were made. Group A was the control group, having no significant complaint and B included cases having hemicranial headache due to migraine. It was observed that mean serum total cholesterol, LDL and triglyceride was 136.14 ± 6.08, 86.68 ± 5.92 and 107.82 ± 5.64 mg/dl in group A (controls), while 201.5 ± 5. 21, 147.28 ± 5.69 and 138.32 ± 5.86 mg/dl in group B (cases) respectively. Mean HDL

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was lower in group B as compared to group A and the difference was statistically significant. Eye pain, raised intraocular pressure and tortuous retinal vessels were observed during the migraine headache on the ipsilateral side. This study found a significant correlation between deranged lipid profile, migraine and ocular morbidity.

Key words: Headache, Vascular tortuosity, Lipid profile

Introduction

Migraine is a highly complex and commonly prevalent neurovascular disorder distributed throughout the world. The pathophysiology of this disease is still an enigma and not completely understood. Causes related to vascular, neuronal and some genetic predispositions have been studied in past. Cerebral and meningeal arterial vasodilatation has been thought to initiate migraine headache.[1,2] Ocular association of migraine in the form of aura, transient vision loss, pain or photopsia has been documented.There might be some physiological or pathological changes in the eyes due to acute or chronic migraine as this type of headache is often associated with eye pain too.[3,4]

Some studies have proved association of deranged lipid profile with migraine[5,6] and with vascular disorders.[7,8] Dyslipidemia is a silent disease and may behave as a chronic destructor, leading to vascular occlusive disorders and may affect the vital systems of the body. Some studies suggest that the severity and frequency of migraine attack varies according to the serum lipid profile.[9,10]As we see that migraine is a multidisciplinary disease, this topic should be studied more. Seeing the high prevalence rate of migraine and dyslipidemia in India, we conducted this study to explore the associations of this disease with other pathologies.

The aim of this study was to evaluate the association of migraine with ipsilateral pain in the eye, intraocular pressure and its impact on retinal blood vessels during acute migraine attacks. The lipid profile of these patients was studied and analyzed to observe the frequency distribution of Dyslipidemia in migraine and also to determine the correlation between Dyslipidemia and ocular association in these patients.

Materials and Methods:

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This was a prospective case control study, conducted in the Department of Ophthalmology at our medical college and hospital from September 2021 to September 2022. A total of 400 patients of both the genders were included in this study, out of which 200 patients were taken as control having no significant complaint under group A and 200 patients having hemi-cranial pain between the age group of 20-50 years, were taken as cases under group B. Permission from the ethical committee (Ref. No.; MMC/IEC/2019/10) and signed informed consent from all the patients were taken prior to the study commencement. Patients having glaucoma, vascular disorders, hypertension, deranged body mass index, alcoholic or smoker, taking any medication were excluded from the study. The patients who lost to follow-up were also excluded.

Detailed history regarding patients' demographic data, presenting symptoms, duration, progression and associated conditions were recorded. Detailed history regarding migraine such as its type, symptoms related to aura, duration, type of treatment taken in the past. Differentiation between migraine and non-migraine headache was diagnosed on the basis of second International Classification of Headache Disorders (ICHD II).[11]

These patients either visited to eye department directly or were referred to our OPD from the medicine department of our medical college. Eye examination was done including intraocular pressure, gonioscopy, central corneal thickness measurement, fundus examination and field analysis using slit lamp, applanation tonometer, indirect ophthalmoscope, gonioscope, fundus camera and visual field analysis in each and every case to rule out prior vascular disorders and any type of glaucoma. Blood sample of all the patients was taken under aseptic condition and serum cholesterol, HDL, LDL and triglyceride were measured using biochemistry auto-analyzer.

Result and Discussion:

Table-1: Comparison of Lipid profile among study groups

Variable	Group A (n=200) Controls		Group B (n=200) Cases			
	Mean(mg/dl)	SD	Mean(mg/dl)	SD	*Z* test	p value

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S Cholesterol	136.14	6.08	201.5	5.21	115.4	<0.01
LDL	86.68	5.92	147.28	5.69	104.37	<0.01
HDL	44.08	5.18	41.06	6.02	5.38	<0.01
Triglyceride	107.82	5.64	138.32	5.86	53.03	<0.01

Table-2: Comparison of Ocular findings among study groups

	Group A (n=200) Controls	Group B (n=200) Cases	X^2 -Test	p value
Ocular pain	9	126	8.15	<0.05
Raised IOP(>21 mm Hg)	23	106		
Retinal vascular tortuosity	4	38		

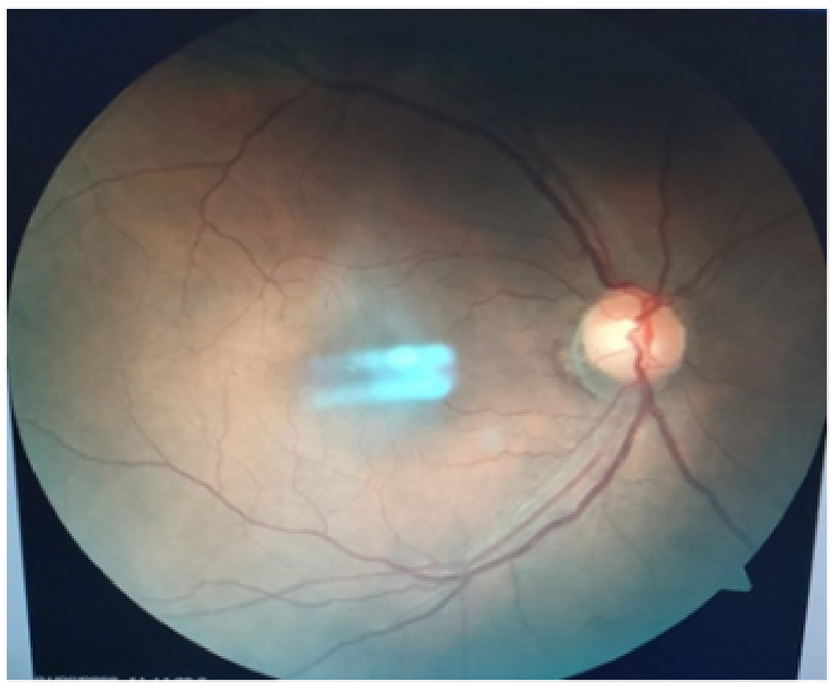

Fig-1: Right fundus normal

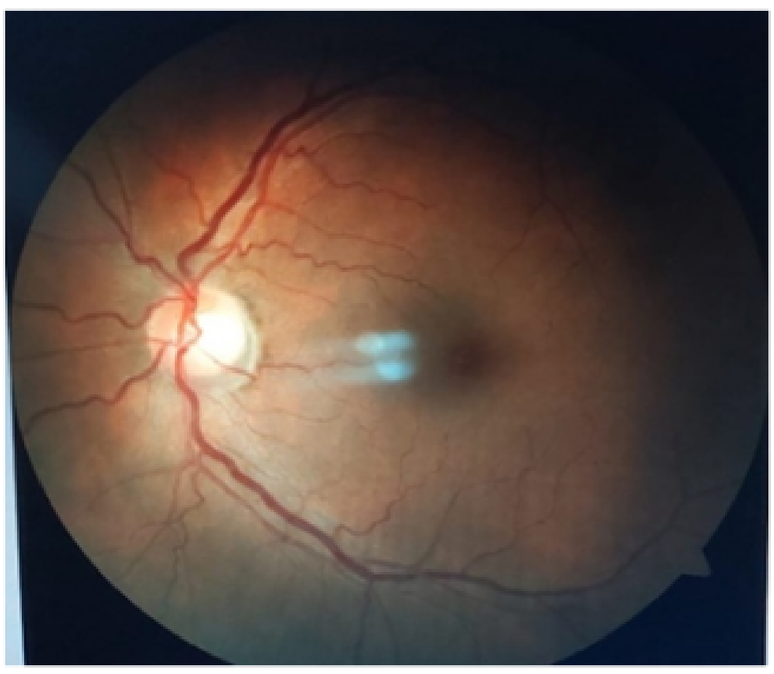

Fig-2: Left fundus with vascular tortuosity

It has been documented that, 1-year prevalence of migraine was 14.12% - 25% in Indian population.[12,13] DALY (Disabity Adjusted Life Year) showed maximum burden of this disease was found among women in the age range of between 30 and 34 years.[12]

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In our study, mean serum total cholesterol and Mean LDL was reported about 136.14 ± 6.08 and 86.68 ± 5.92 mg/dl in group A (controls) i.e. patients not having migraine, while the same was found to be 201.5 ± 5.21 and 147.28 ± 5.69 mg/dl in group B (cases) i.e. patients having migraine respectively. Mean HDL was lower in group B as compared to group A and the difference was statistically significant. The mean value of triglyceride was 107.82 ± 5.64 and 138.32 ± 5.86 mg/dl in group A and B respectively. When mean total serum cholesterol, LDL, HDL and triglyceride level was compared among group A and B using the z test, the difference was found to be statistically significant as p value was <0.01 (Table-1).

In a study Farhad et al[14] found that out of 50 migraine patients, 21 patients (42%) revealed high levels of cholesterol and 22 revealed high levels of LDL (44%). Gruber HJ et al[8] and Pamel et al[15] in their studies documented that migraineurs had increased levels of total cholesterol, LDL-C and oxidized LDL-C compared to non-migraineurs.

In another study by Scher et al[16] indicated that migraine patients with aura were more likely to show an unsatisfactory level of cholesterol profile i.e. the mean total cholesterol was higher in migraineurs with aura when compared with normal population. Alia et al[17] reported that hyper-triglyceridemia and hypercholesterolemia were more frequent in patient with migraine.

Our second objective was to find if there was any ocular association with migraine and we found that there was a significant association between these two. On ipsilateral fundus examination during migraine attack it was observed that out of 200 patients of group B, 126 (63%), 106 (53%) and 38 (19%) patients had ocular pain, raised IOP and retinal vascular tortuosity respectively (Fig 1 & 2) whereas in group A, the percentage of the above ocular findings was quite less i.e. 9 (4.5%), 23 (11.5%) and 4 (2%). The IOP that we recorded on the follow-up visits in the pain free period was considered as baseline IOP and the mean difference in IOP during attack was 5+/-2 mm of Hg in group B. The statistical analysis was done using *chi square* test and the difference between the cases and controls was found to be statistically significant i.e. p value <0.05% (Table-2). The above mentioned findings were absent in the contra-lateral eye during or after the attack.

While vasodilatation itself may not contribute to migraine, it remains possible that vessels play an important role in migraine pathophysiology. Blood vessels consist of a variety of cell types that both release and respond to numerous mediators including growth factors;

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cytokines, adenosine triphosphate (ATP) and nitric oxide (NO). Many of these mediators have actions on neurons that can contribute to migraine. Conversely, neurons release factors such as norepinephrine and calcitonin gene-related peptide (CGRP) that act on cells of blood vessels.[18]

Both normal and pathological events occurring within the vascular cells could thus mediate bi-directionally to communicate between vessels and the nervous system, which may or may not change the vascular tone.[19] It has been proven in older studies that lipid disorders may lead to vascular endothelial dysfunction and this dysfunction may lead to endothelium-dependent vasodilatation.[19,20]

As we all know that the retina is the only place, where we can see the vessels directly, this study was conducted to analyze whether there is any correlation between deranged lipid profile and ocular abnormality in migraine patients or not. Formal definition of 'vessel tortuosity' and migraine specific variation in retinal vessels' are lacking, retinal arteries and veins were identified by visual inspection of the appearance of blood vessels using indirect ophthalmoscope and also compared on fundus photography. We suggest the need to conduct advanced researches to prove the role of vascular and neuronal mechanisms in the eye that either instigates the attack of migraine or is a consequence of migraine.

We found a potential positive correlation in abnormal lipid profile and the retinal vascular tortuosity along with ocular pain and raised IOP during migraine attacks. None of the previous study reported any association between retinal vessels tortuosity and Dyslipidemia in migraine. The relationship between migraine and retinal vessels tortuosity has not been established yet.

We have not studied on all the parameters of lipid profile, like VLDL and oxidized LDL cholesterol and total cholesterol to HDL ratio, hence it is recommended that longitudinal studies in future with a larger sample size including all the parameters should be conducted to get a more conclusive result and also to understand the pathophysiology of the associations.

This was an observational study and quantitative assessment of retinal vessel's diameter was not done. All the parameters of lipid profile were not taken into consideration and due to the lack of *in vivo* 'real time retinal vessel analyzer' the exact change in retinal

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vessel diameter could not be measured, neither quantified during migraine attack. The comparison was solely done using indirect ophthalmoscope and fundus photographs, so the chances of subjective variation cannot be denied.

Conclusion: This study proved a significant correlation between deranged lipid profile, migraine and ocular morbidity and further longitudinal studies are required to be more conclusive.

Conflict of Interest: Nil

Source of support: Nil

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