

**Original Article**

## **Study of Association of Serum Lipid Levels with Migraine**

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### **Abstract**

**Background:** Migraine is associated with increased prevalence of cardiovascular risk factors and vascular biomarkers and migraine with aura is associated with increased risk of ischemic stroke. Lipid abnormality is a risk factor for both cardiovascular and cerebrovascular disease. The vast majority of previous studies evaluated the association between lipid levels and migraine among young and middle aged persons abroad. So far we know, no study has been conducted in Bangladesh regarding association of lipid levels with migraine. **Objectives:** The present study is aimed to evaluate the association between serum lipid levels in patients with migraine. **Materials and Methods:** This observational, cross-sectional study was carried out on 100 patients in outpatient departments of Enam Medical College and Hospital, Dhaka and Mymensingh Medical College Hospital, Mymensingh over a period of one year (December 2017 to November 2018). Patients were selected by purposive sampling. Fifty migraine and 50 non-migraine patients were recruited in the study. **Results:** The serum total cholesterol and LDL-C were significantly higher in migraine than in non-migraine group. HDL-C was below normal and triglyceride was within normal range in both groups. Serum total cholesterol and LDL-C were significantly higher in migraine with aura than migraine without aura. HDL-C level was lower in migraine without aura and was of normal level in migraine with aura, which was statistically significant. **Conclusion:** Elevated levels of serum total cholesterol and LDL cholesterol were associated with migraine than non-migraine group. Serum total cholesterol and LDL cholesterol were significantly higher in late age of migraine group and migraine with aura.

**Key words:** Migraine with aura; Migraine without aura; Serum lipid profile

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### **Introduction**

Headache is one of the most common presenting complaints in neurology. The lifetime prevalence for any type of headache as estimated from population-based studies is more than 90% for men and 95% for women.<sup>1</sup> Migraine, the second most common cause of headache, affects approximately 15% of women and 6% of men. Migraine is a chronic and common disease

that presents with mild to severe recurrent headaches, accompanied by autonomic and neurologic symptoms. It is a ubiquitous familial disorder characterized by periodic, commonly unilateral, often pulsatile headaches that begins in childhood, adolescence, or early adult life and recur with diminishing frequency during advancing years. Migraine is more common

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among females with a ratio of male to female 1:3.<sup>2</sup> Migraine is associated with certain features such as sensitivity to light, sound or movement, nausea and vomiting which often accompany the headache. A useful description of migraine is a benign and recurring syndrome of headache associated with other symptoms of neurologic dysfunction in varying admixtures. Migraine can often be recognized by its activators, referred to as triggers.<sup>3</sup>

Migraine occurs at all ages and may even begin in infancy.<sup>4</sup> The disorder begins before age 20 years in 50% of cases.<sup>5</sup> The prevalence of migraine may be as high as 2.5% of children less than seven years of age. By the age of 17 years as many as 8% of male and 23% of female have experienced migraine.<sup>6-8</sup> There are also many active migraine patients aged  $\geq 60$  years.<sup>9</sup>

Severe disabling headache is reported to occur at least annually by 40% of individuals worldwide.<sup>10</sup> The morbidity associated with the millions of migraine sufferers is staggering. Approximately 64 million workdays each year are estimated to be lost in the United States due to migraine.<sup>11</sup>

Migraine is a common recurrent primary headache disorder that has close links to the neuronal and vascular system and in some patients is accompanied by transient neurological symptoms, mostly of the visual field that are known as migraine aura.<sup>12,13</sup> There is increasing evidence that migraine with aura is associated with increased risk of ischemic stroke<sup>14-17</sup> and other vascular disease events.<sup>18,19</sup> Furthermore, migraine has been associated with increased prevalence of specific cardiovascular risk factors<sup>20,21</sup> including some vascular biomarkers.<sup>22,23</sup> Association of migraine with other vascular risk factors, such as hypercholesterolemia has been proposed.<sup>20</sup>

There are several explanations for the pathophysiology of migraine headache attacks. Sicuteri explained the pathogenesis of migraine headache with the dopamine hypothesis in 1977. In his hypothesis, prodromal clinical and postdromal sign-symptoms of

migraine headache are attributed to increased activity of the dopaminergic system. Postsynaptic receptor hypersensitivity of the dopamine in areas of central nervous system is involved in pain, vomiting and arterial blood pressure.<sup>24</sup>

Prolactin secretion is one measure of dopaminergic function. Dopamine decreases prolactin secretion. An abnormal pattern of hypothalamic secretion specially decreased nocturnal prolactin peak, was found in chronic migraine.<sup>25</sup> Administrations of dopaminergic drugs can trigger and maintain a migraine attack.<sup>11</sup> Dopamine antagonist may help the migraine patients.

Migraine is associated with increased prevalence of cardiovascular risk factors and vascular biomarkers and migraine with aura is associated with increased risk of ischemic stroke and other vascular disease events. Lipid abnormality is a risk factor for both cardiovascular and cerebrovascular disease. So the purpose of this study is to find out the association between lipid levels and migraine.

The vast majority of previous studies evaluated the association between lipid levels and migraine among young and middle aged persons abroad. So far we know, no study has been conducted in Bangladesh regarding association of lipid levels with migraine. The present study is aimed at to evaluate the association between lipid levels and migraine.

## Material and Methods

This cross-sectional observational study was carried out in outpatient departments of Enam Medical College & Hospital, Savar, Dhaka and Mymensingh Medical College Hospital, Mymensingh from December 2017 to November 2018. A total of 100 patients (50 migraine and 50 non-migraine) were recruited in the study. Ethical clearance and permission were taken from the concerned authorities. Patients were categorized as migraineur according to International Headache Society criteria and as non-migraineur if other primary headaches, particularly tension type headache. Patients were selected by purposive sampling.

Blood samples were obtained after 12-hour fasting for lipid analysis. Plasma total cholesterol (TC), triglycerides (TG) and high density lipoprotein cholesterol (HDL-C) were measured after phosphotungstic acid precipitation, using standard enzymatic methods. Low density lipoprotein cholesterol (LDL-C) was calculated using Friedewald's formula ( $LDL=TC-HDLc-TG/5$ ) (mg/dL). In case of migrainous headache males and females >18 years of age to 60 years of age, patients who satisfied the diagnosis of migraine headaches with or without aura (according to International Headache Society) and in case of non-migrainous headache, patients who did not satisfy the diagnostic criteria of migraine headache with or without aura (according to International Headache Society) and who presented with headache were included in our study. Age ≤18 years and >60 years, known structural brain disease, and patient taking lipid lowering drugs were excluded. All the relevant information were recorded in a pre-designed data collection sheet. Collected data were compiled and appropriate analyses were done by using computer based software, Statistical Package for Social Sciences (SPSS) version 20.0. For statistical analysis Chi-square test, t test, ANOVA test were

done. Level of significance was 5% and confidence limit was 95%.

**Results**

Most of the patients (40%) with migraine were in 19–30 years age group. Mean age of migraine patients was 34.20±11.35 years and non-migraine patients was 29.20±8.80 years (Table I). Female predominance was found in both groups. In migraine group, 80% were female and in non-migraine group 76% were female. Male-female ratio was 1:4 in migraine and 1:3.16 in non-migraine group (Table II). Serum total cholesterol and LDL were significantly higher in migraine group than in non-migraine group. HDL was below normal and triglyceride was within normal range in both groups. Their difference was not significant (p>0.05) (Table III).

Serum total cholesterol and LDL-C were significantly higher in patients with migraine with aura than patients with migraine without aura. HDL-C level was lower in patients with migraine without aura and was normal level in patients with migraine with aura, which was statistically significant. Triglyceride was normal in both groups and the difference was statistically not significant (Table IV).

Table I: Distribution of study subjects by age (n=100)

Age (years)	Migraine patients		Non-migraine patients	
	No	%	No	%
19–30	20	40	19	38
31–40	15	30	19	38
41–50	5	10	3	6
51–60	10	20	9	18
Total	50	100	50	100
Mean± SD	34.20±11.35		29.20±8.80	

Table II: Distribution of study subjects by sex (n=100)

Sex	Migraine patients		Non-migraine patients		p value
	No	%	No	%	
Male	10	20	12	24	0.629
Female	40	80	38	76	
Total	50	100	50	100	

Table III: Distribution of study subjects by lipid parameters (N=100)

Lipid parameters	Migraine	Non-migraine	p values
	Mean± SD	Mean± SD	
S. total cholesterol	209.38±46.70	139.04±21.63	0.0001
LDL-C	146.29±39.66	83.82±12.97	0.0001
HDL-C	36.72±8.05	35.24±8.22	0.517
Triglyceride	119.66±55.18	110.50±54.48	0.153

Table IV: Distribution of migraine patients with aura and without aura by lipid parameters (N=50)

Lipid parameter	Migraine		p values
	(with aura)	(without aura)	
S. total cholesterol	228.12±33.90	205.80±48.25	0.0001
LDL-C	163.30±35.10	143.05±40.03	0.0001
HDL-C	41.25±7.68	35.85±7.91	0.0001
Triglyceride	105.62±28.71	122.33±58.76	0.256

## Discussion

In this study majority (80%) of the subjects were of 19–50 years of age which was similar to the findings observed by Lipton et al<sup>26</sup>. Mean age of migraine group was 34.20±11.35 years while non-migraine was 29.20±8.80 years. Lichten et al<sup>27</sup> studied a group with mean age of 37.85±1.53 years, which was higher in relation to this study. Kelman et al<sup>28</sup> found mean age of migraine patient 37±11.7 years which was again higher than present study. The difference may be due to geographical status and race of the patient.

In this study in migraine group 10 (20%) were male and 40 (80%) were female whereas in non-migraine group, 12 (24%) were male and 38 (76%) were female. The male female ratio was more or less same in both groups (1:4 in migraine group and 1:3.16 in non-migraine group). Number of female in both migraine and non-migraine groups were not significantly higher than male. The male female ratio observed by Lipton et al<sup>26</sup> and Russel et al<sup>29</sup> was 1:3 and 1:2 respectively. The present study is consistent with these findings.

Regarding co-morbidity IHD, depression and stroke were found significantly higher in migraine group. But hypertension and epilepsy occurred equally in

both groups ( $p>0.05$ ). Kurth et al<sup>14</sup> found association of ischemic stroke in migraine patients. Tietjen et al<sup>30</sup> found association of depression with headache. The present study is consistent with these findings.

In this study group, the mean serum total cholesterol and LDL cholesterol levels were significantly higher in migraine group than in non-migraine group. Monastero et al<sup>31</sup> also reported total cholesterol and LDL cholesterol significantly higher in migraine group. Pamela et al<sup>32</sup> found strong association of total cholesterol and triglyceride in patients with migraine. Alia et al<sup>33</sup> reported that hypertriglyceridemia and hypercholesterolemia were more frequent in patient with migraine. But in the present study triglyceride was found within normal range in migraine group.

Regarding migraine patient with or without aura serum cholesterol and LDL cholesterol were significantly raised in aura group. Pamela et al<sup>32</sup> found elevated total cholesterol in migraine with aura. The present study is almost consistent with the findings of this study.

In this study in respect of age, the mean total cholesterol was significantly higher in migraine group than in non-migraine group and more in 51–60 years

age group. Pamela et al<sup>32</sup> revealed elevated total cholesterol and triglyceride in migraine with aura in late age. The present study is consistent with the findings of this study.

Regarding LDL cholesterol level in respect of age, LDL was significantly higher in migraine group than in non-migraine group and more in 51–60 years age group. Monastero et al<sup>31</sup> reported that total cholesterol and LDL cholesterol were significantly higher in migraine group. Our study is consistent with the previous study.

In this study, there was no significant difference of HDL-C levels between migraine and non-migraine group in respect of age. Alia et al<sup>33</sup> found less incidence of low HDL cholesterol in migraine patients compared to non-migraine patients.

In this study there was no significant difference of triglyceride between two groups in respect of age. Russel et al<sup>29</sup> found elevated total cholesterol and triglyceride in migraine. The present study is not consistent with the findings of this study which may be due to small sample size and different food habit of the patients of two studies.

Elevated level of serum total cholesterol and LDL cholesterol were associated with migraine. Serum total cholesterol and LDL cholesterol were significantly higher in late age of migraine group and migraine with aura.

## References

1. Boes CJ, Capobianco DJ, Cutrer FM, Dodick DW, Garza I, Swanson JW et al. Headache and other craniofacial pain. In: Daroff RB, Fonichol GM, Jankovic J, Mazziotta J (eds). *Bradley's neurology in clinical practice*. 5<sup>th</sup> edn. Philadelphia, Butterworth-Heinemann Elsevier, 2008; 2: 2011–2062.
2. Rasmussen BK, Jensen R, Schroll M. Epidemiology of headache in a general population: a prevalence study. *J Clin Epidemiol* 1991; 94: 1147–1157.
3. Goadsby PJ, Raskin NH. Headache. In: Hauser SL, Josephson SA (eds). *Harrison's neurology in clinical medicine*. 2<sup>nd</sup> edn. USA, McGraw-Hill, 2013: 50–69.
4. Mortimer MJ, Kay J, Jaron A. Epidemiology of headache and childhood migraine in an urban general practice using Ad Hoc, Vahlquist and HIS criteria. *Dev Med Child Neurol* 1992; 34: 1095–1101.
5. Elser JM, Woody RC. Migraine headache in the infant and young child. *Headache* 1990; 30: 366–368.
6. Dalsgaard-Nielsen T. Some aspects of the epidemiology of migraine in Denmark. *Headache* 1970; 10: 14–23.
7. Deubner DC. An epidemiologic study of migraine and headache in 10–20 years old. *Headache* 1977; 17: 173–180.
8. Congdon PJ, Forsythe WI. Migraine in childhood: a study of 300 children. *Dev Med Child Neurol* 1979; 21: 209–216.
9. Hasan J, Hollander J, Ferrari MD. Migraine in the elderly: a review. *Cephalgia* 2007; 27: 97–106.
10. Raskin NH. Migraine and the cluster headache syndrome. In: *Harrison's principles of internal medicine*. Fauci AS (ed). 16<sup>th</sup> edn. New York, Mc Graw-Hill Companies, 2005; 1: 85–94.
11. Peroutka SJ. Drugs effective in therapy of migraine, in *Goodman and Gillman's: the pharmacological basis of therapeutics*. Hardman JG (ed). 9<sup>th</sup> edn. New York, McGraw-Hill Books Inc., 1996: 487–502.
12. Lipton RB, Bigal ME. The epidemiology of migraine. *Am J Med* 2005; 118(suppl 1): 3–10.
13. Goadsby PJ, Lipton RB, Ferrari MD. Migraine—current understanding and treatment. *N Engl J Med* 2002; 346: 257–270.
14. Kurth T, Slomke MA, Kase CS, Cook NR, Lee IM, Gaziano JM et al. Migraine headache and the risk of stroke in women: a prospective study. *Neurology* 2005; 64: 1020–1026.
15. MacClellan LR, Giles WH, Cole J, Wozniak MA, Stern B, Mtichell B et al. Probable migraine with visual aura and risk of ischemic stroke: The Stroke Prevention in Young Women Study. *Stroke* 2007; 38: 2438–2845.
16. Schurks M, Rist PM, Bigal ME, Buring JE, Lipton RB, Kurth T. Migraine and cardiovascular disease: systematic review and meta-analysis. *BMJ* 2009; 339: b3914.
17. Kurth T, Mohamed S, Maillard P, Zhu YC, Chabriat H, Mazoyer B et al. Headache, migraine, and structural brain lesions and function: population based epidemiology of vascular ageing-MRI study. *BMJ*

- 2011; 342: c7357.
18. Kurth T, Gaziano JM, Cook NR, Logroscino G, Diener HC, Buring JE. Migraine and risk of cardiovascular disease in women. *JAMA* 2006; 296: 283–291.
  19. Bigal ME, Kurth T, Santanello N, Buse D, Golden W, Robbins M et al. Migraine and cardiovascular disease: a population-based study. *Neurology* 2010; 74: 628–635.
  20. Scher AI, Terwindt GM, Picavet HS, Verschuren WM, Ferrari MD, Launer LJ. Cardiovascular risk factors and migraine: the GEM population-based study. *Neurology* 2005; 64: 614–620.
  21. Hamed SA, Hamed EA, Ezz Eldin AM, Mahmoud NM. Vascular risk factors, endothelial function, and carotid thickness in patients with migraine: relationship to atherosclerosis. *J Stroke Cerebrovasc Dis* 2011; 19: 92–103.
  22. Kurth T, Ridker PM, Buring JE. Migraine and biomarkers of cardiovascular disease in women. *Cephalalgia* 2008; 28: 49–56.
  23. Tietjen GE, Herial NA, White L, Utley C, Kosmyna JM, Khuder SA. Migraine and biomarkers of endothelial activation in young women. *Stroke* 2009; 40: 2977–2982.
  24. Gladstone JP. Dopamine and migraine: trigeminovascular nociception, genetics and therapeutics. *Cephalgia* 2007; 27(11): 1315–1320.
  25. Peres MF, del Rio MS, Seabra ML, Tufik S, Abucham J, Cipolla-Neto J et al. Hypothalamic involvement in chronic migraine. *J Neurol Neurosurg Psychiatry* 2001; 71: 747–751.
  26. Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevalence and burden of migraine in the USA: data from the American Migraine Study-II. *Headache* 2001; 41: 646.
  27. Lichten EM, Lichten JB, WhittyAJ, Pieper D. The Use of leuprolide acetate in the diagnosis and treatment of menstrual migraine: the role of artificially induced menopause headache quarterly. *Current Treatment and Research* 1995; 6: 313–317.
  28. Kelman, L. Migraine changes with age: IMPACT on migraine classification. *Headache* 2006; 46: 1161–1171.
  29. Russel MB, Rasmussen BK, Thomverdesen P, Olesen J. Prevalence and sex ratio of the subtypes of migraine. *Int J Epidemiol* 1995; 24: 1612–1618.
  30. Tietjen GE, Brandes JL, Digre KB, Baggaley S, Martin V, Recober A et al. High prevalence of somatic symptoms and depression in women with disabling chronic headache. *Neurology* 2007; 68: 134–140.
  31. Monastero R, Pipia C, Cefalu AB, Liveri ET, Rosano R, Camarda R et al. Association between plasma lipid levels and migraine in subjects aged  $\geq 50$  years, preliminary data from the Zabut Aging Project. *Neurol Sci* 2008; 29 (Suppl 1): S 179–181.
  32. Pamela MR, Tzourio C, Kurth T. Associations between lipid levels and migraine: cross-sectional analysis in the EVA study. *Cephalgia* 2011; 31(14): 1459–1465.
  33. Saberi A, Hatamian HR, Kazemnezad E, Ghorbannejad N. Hyperlipidaemia in migraine: is it more frequent in migraineurs? *Iranian Journal of Neurology* 2011; 10(3–4): 46–50.