

Association between serum total cholesterol and migraine

Shill SK¹, Uddin A², Imam SD³, Hasina A⁴

Abstract

Background: There is increasing evidence that migraine with aura is associated with increased risk of ischemic stroke and other vascular disease events. Furthermore migraine has been associated with increased prevalence of specific cardiovascular risk factors, such as hypercholesterolemia has been proposed. **Aims and objectives:** The present study is aimed at to evaluate the association between serum total cholesterol and migraine. **Material and methods:** This observational cross sectional study was carried out in Neurology Department in Mymensingh Medical College from December 2016 to November 2018 for a period of 2 years. Patients were selected by purposive sampling. Among 100 patients, 50 grouped as migraineur and 50 grouped as non-migraineur for the study. **Results:** Serum total cholesterol was significantly higher in migraine than non-migraine. Serum total cholesterol was significantly higher in late age of migraine group and migraine with aura. **Conclusion:** Elevated level of serum total cholesterol was associated with migraine than non-migraine. Serum total cholesterol was significantly higher in late age of migraine group and migraine with aura.

Key words: Migraine with aura; Migraine without aura; Serum total cholesterol

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.¹

Migraine, the second most common cause of headache, afflicts approximately 15% of women and 6% of men. It is usually an episodic headache that is associated with certain features such as sensitivity to light, sound, or movement; nausea and vomiting 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.²

Migraine occurs at all ages and may even begin in infancy. The disorder begins before age 20 years in 50% of cases.^{3,4}

The prevalence of migraine may be as high as 2.5% of children less than seven years of age. By the age 17

years as many as 8% of male and 23% of female have experienced migraine.⁵⁻⁷ Family history is positive in the majority of patient. There are also many active migraine patient aged ≥ 60 years.⁸

Severe disabling headache is reported to occur at least annually by 40% of individuals worldwide.⁹ A large percentage of headache patients will be diagnosed as having migraine, a specific subtype of headache affecting approximately 10-20% of the general population. 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.¹⁰ Migraine is a chronic, 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.

1. Dr. Sajal Kumar Shill, Assistant Professor of Neurology, Kumudini Women's Medical College & Hospital, Mirzapur, Tangail.
2. Dr. Md. Abbas Uddin, Assistant Professor of Surgery, Kumudini Women's Medical College & Hospital, Mirzapur, Tangail.
3. Dr. Shah Didar Imam, Assistant Professor of Neurology, Monno Medical College & Hospital, Manikgonj.
4. Dr. Ayesha Hasina, Consultant, Sheikh Fazilatunnessa Mujib Memorial KPJ Specialized Hospital & Nursing College, Gazipur.

Correspondence: Dr. Md. Abbas Uddin, Mob: 01710945613, E-mail: abbas_uddin78@yahoo.com.

Migraine is more common among females with a ratio of male to female 1:3.¹¹ In the USA, 18% of women and 6% of men had had at least one migraine attack in the previous year. More than two-thirds of patients either have never consulted a physician for their migraine or have stopped doing so. This is mainly due to fatalistic expectations, lack of physician's empathy or misdiagnosis. Recent progress on scientific basis of diagnosis, epidemiology, pathology and pharmacology of migraine has significantly improved diagnostic and therapeutic options.¹²

Migraine is a common recurrent primary headache disorder that has close links to the neuronal and vascular system and is, in some patients accompanied by transient neurological symptoms mostly of the visual field that are known as migraine aura.^{13,14} There is increasing evidence that migraine with aura is associated with increased risk of ischemic stroke¹⁵⁻¹⁸ and other vascular disease events.^{19,20} Furthermore migraine has been associated with increased prevalence of specific cardiovascular risk factors.^{21,22} including some vascular biomarkers.^{23,24} Association of migraine with other vascular risk factors, such as hypercholesterolemia has been proposed.²¹

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. So the purpose of this study is to find out the association between serum total cholesterol level and migraine.

METHODOLOGY

This was an observational cross-sectional study. This study was carried out in the Neurology outpatient department of Mymensingh Medical College Hospital, Mymensingh. For limitation of time, logistic support, availability of patient and lack of sufficient fund, sample size was reduced to 100. This sampling was purposive. To conduct the study, ethical clearance and permission were taken from the concerned authorities with due procedures. Patients were categorized as migraineur according to international headache society criteria and as

non-migraineur of other primary headaches particularly tension type headache. Data collection tools were written questionnaire. Blood samples were obtained after 12h fasting for analysis. Plasma total cholesterol (TC) was measured after phosphotungstic acid precipitation, using standard enzymatic methods. Selection criteria Inclusion criteria for case (migraine).

1. Enrollment of population included males and females >18 years of age to 60 years of age
2. Patients who satisfy the diagnosis of migraine headaches with or without aura (according to International Headache Society).

INCLUSION CRITERIA FOR CONTROL (NON-MIGRAINE)

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 with age and sex matched.

EXCLUSION CRITERIA FOR MIGRAINE AND NON-MIGRAINE

1. Age: ≤ 18 years and >60 years.
2. Known structural brain disease.
3. Patient taking lipid lowering drugs.

All the relevant information was 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. Results were expressed as frequency, percentage, mean \pm SD. For statistical analysis Chi-square test, t test, ANOVA test were done. Level of significance was 5% and confidence limit was 95%.

RESULTS

Association between total cholesterol level and Migraine This observational cross-sectional study was performed in the department of Neurology, Mymensingh Medical College Hospital from December 2016 to November 2018. The main objective of the study was to assess the association between serum total cholesterol level and Migraine. The Patients presented with clinical features of migraine grouped as migraineur and those not clinical features of migraine grouped as non-migraineur.

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

Age(yrs)	Migraine		Non- migraine		p value
	No	%	No	%	
19-30	20	40.0%	19	38.0%	0.789
31-40	15	30.0%	19	38.0%	
41-50	5	10.0%	3	6.0%	
51-60	10	20.0%	9	18.0%	
Total	50	100.0%	50	100.0%	
Mean ±SD	34.20±11.35		29.20±8.80		

p value obtained from Chi square test
Above table demonstrates distribution of study subjects by age. The mean age difference between migraine and non migraine was found statistically not significant (p=0.789). Most of migraine patients were 19-30age (40%) group. Mean age of migraine was 34.20±11. 35 years and non-migraine was 29.20±8.80 years.

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

Sex	Migraine		Non-migraine		p value
	No	%	No	%	
Male	10	20.0%	12	24.0%	0.629
Female	40	80.0%	38	76.0%	
Total	50	100.0%	50	100.0%	

p value obtained from Chi square test
Regarding distribution of study subjects by sex, between migraine and non- migraine, a female dominance was found in both groups. However the difference was statistically not significant (p=0.629). In migraine, 80% were female and in non-migraine 76% were female. Male-female ratio was 1:4 in migraine and 1:3.16 in non-migraine group.

Table – III: - Distribution of study subjects by family history of headache (n=100).

Family History	Migraine		Non-migraine		p value
	No	%	No	%	
Present	39	78.0%	14	28.0%	0.0001
Absent	11	22.0%	36	72.0%	
Total	50	100.0%	50	100.0%	

Significant at 1% level (p<0.01)
p value obtained from Chi square test

Above table demonstrates distribution of study subjects by family history of headache. The difference was statistically significant (p=0.0001). 78% of migraine patient had positive family history.

Table –IV: - Distribution of migraine patient with aura and without aura (n=50).

Aura	Migraine	
	No	%
With Aura	8	16.0
Without Aura	42	84.0
Total	50	100

The above table shows aura status of the migraine patient.16% patient presented with aura and 84% patient presented without aura.

Table–V: Distribution of study subjects by serum cholesterol (n=100).

Lipid parameter	Migraine	Non- migraine	p value
	Mean ±SD	Mean ±SD	
S. total cholesterol	209.38 ±46.70	139.04 ±21.63	0.0001

Significant at 1% level (p<0.01)
p value obtained from t test
Above table demonstrates distribution of study subjects by lipid parameter. The S. total cholesterol was significantly (p=0.0001) higher in migraine than non-migraine group.

Table - VI: Distribution of migraine patient with aura and without aura by serum cholesterol (n=50).

Lipid parameter.	Aura		p value
	(With Aura)	(Without Aura)	
S. total cholesterol	228.12±33.90	205.80±48.25	0.0001

Significant at 1% level (p<0.01)
p value obtained from t test
Above table demonstrates distribution migraine patient with aura and without aura by serum total cholesterol .S. total cholesterol was significantly (p=0.0001) higher in migraine with aura than migraine without aura.

Table – VII: - Distribution of study subjects in respect of age with S. total cholesterol (n=100).

Age(yrs)	S. total cholesterol		p value
	Migraine	Non-migraine	
	Mean± SD	Mean± SD	
19-30	198.05±49.79	133.47±25.49	
31-40	212.67±43.87	144.68±18.05	0.0001
41-50	186.00±54.24	149.67±24.11	
51-60	238.80±27.77	135.33±17.85	

Significant at 1% level ($p < 0.01$)

p value obtained from ANOVA test.

Above table demonstrates distribution of study subjects in respect of age with S. total cholesterol. The mean S. total cholesterol was significantly higher in 51-60 years age in migraine than non-migraine group ($p = 0.0001$).

DISCUSSION

In the study, majority (80%) of the study subjects were between age 19-50 years of age which was similar to the findings observed by Lipton et al²⁷. Mean age of migraine group was 34.20 ± 11.35 years while non-migraine was 29.20 ± 8.80 years. Lichten et al²⁸ studied a group with mean age of 37.85 ± 1.53 years, which was a bit higher in relation to this study. Kelman et al²⁹ found mean age of migraine patient 37 ± 11.7 years which was again a bit 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 higher than male but not significantly higher. The ratio observed by Lipton et al²⁷ was 1:3 (approximately). In Russel et al³⁰ study, the subtype of migraine had male female ratio of approximately 1:2. The present study is more or less consistent with these findings.

In this study, in migraine group, family history was present in 39 (78%) cases and was absent in 11 (22%) cases. But it may be present up to 90% cases in migraine group by Boes et al¹. Boru et al³¹ reported positive family history in 33.1% cases in migraine group. In non-migraine group, family history was

present in 14 (28%) cases and was absent in 36 (72%) cases. The difference may be due to small number of sample size.

In this study, migraine with aura was 8 (16%) and migraine without aura was 42 (84%) and ratio was 1:5.2. In previous cross sectional population study the ratio was 1:5 by Ropper et al³². These findings are almost similar.

In this study group, the mean S. total cholesterol was significantly higher in migraine group than non-migraine group. Monastero et al³³ also reported total cholesterol was significantly higher in migraine group. Pamela et al³⁴ found strong association of total cholesterol and triglyceride in patient with migraine. Alia Saberi et al³⁵ reported, hypertriglyceridaemia and hypercholesterolaemia were more frequent in patient with migraine.

Regarding migraine patient with or without aura, the S. cholesterol was significantly raised in aura group. Pamela et al³⁴ found elevated total cholesterol in migraine with aura. The present study is almost consistent with this study.

In this study in respect of age, the mean S. total cholesterol was significantly higher in migraine group than non-migraine group and more in 51-60 years age group. Pamela et al³⁴ revealed elevated total cholesterol and triglyceride in migraine with aura in late age. The present study is consistent with Pamela et al.

CONFLICT OF INTEREST-

There is no conflict of interest with other person or any other articles that published previously.

ACKNOWLEDGEMENT-

We are very much grateful to the patients those who are agreed to examine them and treatment accordingly. We are also grateful to the department of Biochemistry, who helped us sincerely by giving the investigation reports timely.

CONCLUSION

Elevated level of S. total cholesterol was associated with migraine than non-migraine group. S. total cholesterol was 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, et al. Headache and other craniofacial pain. In: Robert B, Daroff, Gerald M, Fonichol, Jankovic J, Mazziotta J. 5th edn. *Bradley's Neurology in clinical Practice*, Philadelphia, Butterworth-Heinemann Elsevier, 2008; 2: 2011-62.
2. Peter J. Goadsby, Neil H. Raskin. Headache, In: Hauser SL, Josephson SA, 3rd edition, *Harrison's Neurology in Clinical Medicine*, USA, McGraw-Hill, 2013:53.
3. 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* 2009;34:1095.
4. Elser JM, Woody RC. Migraine headache in the infant and young child. *Headache* 2007; 30:366.
5. Dalsgaard-Nielsen T. Some aspects of the epidemiology of migraine in Denmark. *Headache* 2008;10:14
6. Deubner DC. An epidemiologic study of migraine and headache in 10-20 years old. *Headache* 2010; 17:173.
7. Congdon PJ, Forsythe, WI. Migraine in childhood: a study of 300 children. *Dev Med Child Neurol* 2005;21:209.
8. Hasan J, Hollander J. Ferrari MD. Migraine in the elderly; a review. *cephalgia* 2007; 27:97-106.
9. Raskin NH. Migraine and the cluster headache syndrome, in *Harrison's Principles of Internal Medicine*, Fauci, AS (ed.), 16th edn, New York, Mc Graw-Hill Companies, 2005; 1: 85-94.
10. Peroutka SJ. Drugs effective in therapy of migraine, in *Goodman and Gillman's: The Pharmacological Basis of Therapeutics*, Hardman, JG (ed.), 9th edn, New York, McGraw-Hill Books Inc.,2008: 487-502.
11. Rasmussen BK, Jensen R, Schroll M . Epidemiology of headache in a general population: A prevalence study. *J Clin Epidemiol* 1991; 94: 1147-57.
12. Ferrari MD . Migraine. *Lancet*2009; 351: 1043-51.
13. Lipton RB, Bigal ME. The epidemiology of Migraine. *Am J Med.*2005;118(suppl-1):03-10
14. Goadsby PJ, Lipton RB, Ferrari MD. Migraine current understanding and treatment. *N Engl J Med*2002;346:257-70.
15. 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; 64:1020–6.
16. 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; 38:2438–45.
17. 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.
18. Kurth T, Mohamed S, Maillard P, Zhu YC, Chabriat H, Mazoyer B, et al. Headache, migraine structural brain lesions and function: population based Epidemiology of Vascular Ageing-MRI study. *BMJ* 2011; 342:c7357.
19. Kurth T, Gaziano JM, Cook NR, Logroscino G, Diener HC, Buring JE. Migraine and risk of cardiovascular disease in women. *JAMA* 2010;296:283–91
20. Bigal ME, Kurth T, Santanello N, Buse D, Golden W, Robbins M, et al. Migraine and cardiovascular disease: a population-based study. *Neurology* 2010; 74:628–35.
21. Scher AI, Terwindt GM, Picavet HS, Verschuren WM, Ferrari MD, Launer LJ. Cardiovascular risk factors and migraine: the GEM population-based study. *Neurology* 2005; 64:614–20.
22. Hamed SA, Hamed EA, Ezz Eldin AM, Mahmoud NM. Vascular risk factors, endothelial function, and carotid thickness in patients with

23. Kurth T, Ridker PM, Buring JE. Migraine and biomarkers of cardiovascular disease in women. *Cephalalgia* 2008;28:49–56
24. Tietjen GE, Herial NA, White L, Utley C, Kosmyrna JM, Khuder SA. Migraine and biomarkers of endothelial activation in young women. *Stroke* 2009; 40:2977–82.
25. Gladstone JP. Dopamine and migraine: trigeminovascular nociception, genetics and therapeutics, 2007.
26. Peres MFP, Rio MSD, Seabra MLV, Tufik S, Abuchman J. Hypothalamic involvement in chronic migraine. *J Neurol Neurosurg Psychiatry* 2001: 747-751.
27. 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.
28. Lichten EM, Lichten JB, Whitty AJ, 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* 2011; 6: 313-317.
29. Kelman, L. Migraine Changes with Age: IMPACT on Migraine Classification. *Headache* 2006; 46: 1161-1171.
30. Russel MB, Rasmussen BK, Thomverdesen P, Olesen J. Prevalence and sex ratio of the subtypes of migraine. *Int J Epidemiol* 2009; 24:1612-8.
31. Boru. UT, Kocer A, Luleci A, Sur H, Tutkan H, et al . Prevalence and Characteristics of Migraine in Women of Reproductive Age in Istanbul, Turkey: A Population Based Survey, *Tohkou J. Exp. Med.* 2005; 206: 51-59.
32. Ropper AH, Brown RH. Headache and other craniofacial pains, in Adams and Victor's Principles Of Neurology, 8th ed.,New York, McGraw-Hill Book Inc.,2005:144-67.
33. Monastero R, Pipia C, Cefalu AB, Liveri ET, Rosano R, Camarda R, et al. Association between plasma lipid levels and migraine in subjects aged > or = 50 years, preliminary data from the Zabut Aging project. *Neurol Sci* 2008; suppl:s 179-81.doi:10.1007/s10072-008-0919-0.
34. 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.
35. Saberi A, Hatamian HR, Kazemnejad E, Ghorbannejad N. Hyperlipidaemia in migraine: is it more found in migraine? *Iran Neurol* 2011; 10(34):46-50.