ORIGINAL ARTICLE

Associations between Lipid Levels and Intracerebral Hemorrhage

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Background: Intracerebral hemorrhage (ICH) is a complex medical condition found to be associated with various factors, including advanced age, male gender, Asian ethnicity, tobacco use, hypertension, and chronic renal insufficiency. Despite the aforementioned associations, the relationship between lipid fractions and ICH remains ambiguous and has received limited attention in the literature, particularly with respect to Thai populations.

Objective: To investigate the potential association between lipid levels and primary ICH.

Materials and Methods: The present study employed a retrospective case-control design and enrolled 314 primary ICH cases presented at Rajavithi Hospital between 2012 and 2022. A control group of 366 subjects was established using an age-matching procedure and computer-generated randomization. Participants with coagulopathies or those receiving anticoagulant therapy were excluded. Statistical analysis was performed using binomial and multivariate logistic regression to evaluate the relationship between ICH and the various factors.

Results: The present study identified six factors that were independently associated with ICH through bivariate analysis, including male gender (odd ratio [OR] 2.497, 95% confidence interval [CI] 1.829 to 3.407; p<0.001), systolic blood pressure (SBP) (OR 1.023, 95% CI 1.016 to 1.029; p<0.001), diastolic blood pressure (DBP) (OR 1.050, 95% CI 1.037 to 1.062; p<0.001), total cholesterol (OR 0.994, 95% CI 0.991 to 0.998; p=0.001), high-density lipoprotein cholesterol (HDL) (OR 0.985, 95% CI 0.975 to 0.995; p=0.003), and low-density lipoprotein cholesterol (LDL) (OR 0.994, 95% CI 0.991 to 0.998; p=0.002). Multivariate logistic regression revealed five factors to be associated with ICH, including male gender (adjusted OR 1.904, 95% CI 1.293 to 2.803; p=0.001), elevated SBP (adj. OR 1.024, 95% CI 1.017 to 1.032; p<0.001), elevated DBP (adj. OR 1.051, 95% CI 1.037 to 1.064; p<0.001), decreased total cholesterol levels (adj. OR 0.993, 95% CI 0.988 to 0.997; p=0.001), and decreased LDL (adj. OR 0.994, 95% CI 0.990 to 0.999; p=0.010). HDL was found to not be significantly associated with ICH (adj. OR 1.003, 95% CI 0.990 to 1.016; p=0.643).

Conclusion: The results of the present study suggest that male gender and elevated levels of SBP and DBP were independently associated with ICH, as were decreased levels of total cholesterol and LDL.

Keywords: Lipid; Cholesterol; LDL; HDL; Intracerebral hemorrhage

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Stroke is a leading cause of death and disability globally, with intracerebral hemorrhage (ICH) accounting for 10% to 15% of all stroke cases[1,2]. The incidence of ICH is particularly high in Asian populations, with an estimated 20% of all stroke cases being attributed to ICH[2]. This type of stroke is associated with high mortality and morbidity rates, with a mortality rate of 25% to 50% within the first month and only 12% to 39% of survivors being able to perform normal daily activities without assistance[3-5].

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Additionally, ICH is often followed by secondary ischemic strokes and other blood vessel abnormalities in the brain[6]. The location of ICH within the brain can be classified as ganglionic, lobar, cerebellar, or pontine[7]. Similarly, lipids can be classified into many types, such as total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL), and low-density lipoprotein cholesterol (LDL), which have different functions. Moreover, diagnostic criteria for hyperlipidemia vary in definition based on the lipid type.

Several risk factors have been identified as being associated with ICH including advanced age, male gender, Asian ethnicity, genetics, smoking, hypertension, alcohol consumption, chronic renal failure, high uric levels, and coagulopathy[2,3,5-9]. Interestingly, high cholesterol levels have been documented to be a protective factor against ICH[2,3,5,7-9]. The relationship between ICH risk and various factors such as lipid levels, diabetes

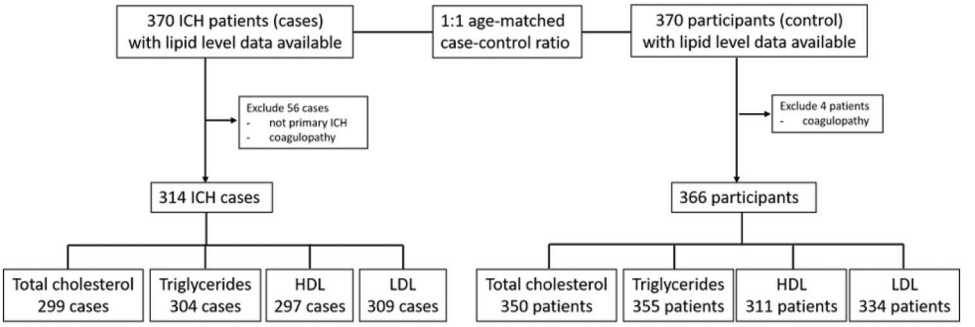

Figure 1. Flowchart of patient selection.

ICH=intracerebral hemorrhage; HDL=high-density lipoprotein cholesterol; LDL=low-density lipoprotein cholesterol

mellitus, body mass index (BMI), exercise, smoking, and alcohol consumption remains uncertain, with numerous studies yielding inconsistent results[2]. Currently, there is no empirical evidence to support the use of statins for the prevention of recurrent ICH[10-12].

Given the severe health consequences and the urgency of treatment required for ICH, it is important to explore associated factors to develop preventive measures that may reduce its incidence. Research on the association between lipid levels and ICH is still limited, particularly in the Thai population. Furthermore, some investigations have been carried out in patients receiving recombinant tissue-type plasminogen activators, anti-coagulants, and anti-platelet aggregation medications. There is still a need for further research in this area.

Materials and Methods

The present study was designed as a retrospective case-control investigation, wherein the data were collected through a review of medical records from both inpatients and outpatient departments between 2012 and 2022. The study population consisted of 370 Thai individuals diagnosed with ICH at Rajavithi Hospital, and had at least one recorded lipid level result, served as the case group. An additional 370 Thai individuals free of ICH, having recorded lipid level results, were enrolled through 1:1 age-matching by means of computer randomization constituted as the control group. The exclusion criteria were the presence of health conditions that could lead to ICH, such as atrioventricular aneurysm, head injury, and coagulopathy, as evidenced by factors such as low platelet count or prolonged international normalized ratio (INR). Consequently, 56 participants from the case group and four participants from the control group were excluded from the analysis.

Rajavithi Hospital's laboratory system had obtained certification from the International Organization for Standardization (ISO) for both 15189 and ISO 15190. The certification of Rajavithi Hospital's laboratory system for both standards demonstrate the hospital's commitment to maintaining a high level of quality and competency in its medical laboratory services, as well as its effective use of technology to support laboratory processes.

Three hundred seventy patients diagnosed with ICH were enrolled in the present study, of which 314 were eligible for analysis after exclusion of 56 cases due to non-primary ICH diagnosis or presence of coagulopathy. The control group consisted of 366 age-matched participants, randomized by computer, with four cases excluded due to coagulopathy. Ultimately, both the study group with 314 cases, and the control group with 366 participants, were included in the analysis, as demonstrated in Figure 1.

The present study utilized statistical methods to analyze the associations between ICH and the various factors. Continuous variables were compared using either the t-test or the Mann-Whitney U test, depending on the distribution of the data. Categorical variables were compared using the chi-square test or Fisher's exact test. Bivariate and multivariate logistic regression analyses were performed using Stata Statistical Software, version 16 (StataCorp LLC, College Station, TX, USA) to explore the association between ICH and the different factors. The level of statistical significance was set at p-value less than 0.05, indicating that a p-value less than 0.05 was considered statistically significant.

Additionally, collinearity was assessed for the data and found to be not significant. Effect modification (interaction effect) was also evaluated and found to be not significant.

Table 1. Characteristics of both ICH and non-ICH patients

Factors	Cases (n=314)	Controls (n=366)	p-value
Age (years); mean±SD	60.03±13.84	59.61±13.66	0.687
Sex; n (%)			<0.001*
Female	110 (35.03)	210 (57.38)	
Male	204 (64.97)	156 (42.62)	
BMI (kg/m^2); mean±SD	25.01±5.04	24.68±4.69	0.429
Underlying health conditions; n (%)	140 (44.59)	182 (49.73)	0.181
Diabetes mellitus; n (%)	46 (14.65)	70(19.13)	0.123
Hypertension; n (%)	114 (36.31)	155 (42.35)	0.108
Chronic kidney disease; n (%)	27 (8.60)	19 (5.19)	0.081
Atrial fibrillation; n (%)	5 (1.59)	2 (0.55)	0.199
Antiplatelet; n (%)	16 (5.10)	30 (8.2)	0.112
SBP (mmHg); mean±SD	148.14±32.82	133.17±19.23	<0.001*
DBP (mmHg); mean±SD	86.52±20.92	74.11±11.83	<0.001*
TC (mg/dL); mean±SD	187.05±48.31	199.48±44.56	0.001*
Triglycerides (mg/dL); mean±SD	137.13±93.76	140.67±90.10	0.621
HDL (mg/dL); mean±SD	50.67±16.71	54.62±15.39	0.003*
LDL (mg/dL); mean±SD	117.70±44.34	128.19±42.20	0.002*
GFR (mL/minute/1.73 m^2); mean±SD	83.48±26.28	81.13±21.95	0.219
Platelet (×10^3/mL); mean±SD	259.47±84.78	270.23±75.63	0.095

SD=standard deviation; BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure; TC=total cholesterol; HDL=high-density lipoprotein cholesterol; LDL=low-density lipoprotein cholesterol; GFR=glomerular filtration rate

Ethical considerations

The present study was granted ethical approval by the Ethics Committee of Rajavithi Hospital in May 2022 (approval number 083/2022).

Results

The present study comprised a sample of 680 participants, with a mean age of 59.80 (±13.73) years and a mean BMI of 24.83 (±4.85) kg/m². A significant proportion or 47.35% of the participants had preexisting health conditions, including 17.06% with diabetes mellitus, 39.56% with hypertension, 6.76% with chronic kidney disease, and 1.03% with atrial fibrillation. Additionally, 46 participants (6.76%) were taking antiplatelet medication. The patient characteristics are presented in Table 1.

The majority of participants diagnosed with ICH were male at 204 participants (64.97%), whereas the majority of participants in the control group were female at 210 participants (57.38%). Significant differences were observed between the two groups with regards to gender, systolic blood pressure (SBP) (148.14±32.82 mmHg versus 133.17±19.23 mmHg), diastolic blood pressure (DBP) (86.52±20.92 mmHg versus 74.11±11.83 mmHg), total cholesterol levels (TC) (74.11±11.83 mg/dL versus 199.48±44.56 mg/dL), HDL (50.67±16.71 mg/dL versus 54.62±15.39 mg/dL), and LDL (117.70±44.34 mg/dL versus 128.19±42.20 mg/dL). These findings are presented in Table 1.

The results of the logistic regression analyses revealed that six factors were independently associated with ICH, male gender (odds ratio [OR] 2.497, 95% confidence interval [CI] 1.829 to 3.407); p<0.001), SBP (OR 1.023, 95% CI 1.016 to 1.029; p<0.001), DBP (OR 1.050, 95% CI 1.037 to 1.062; p<0.001), TC (OR 0.994, 95% CI 0.991 to 0.998; p=0.001), HDL (OR 0.985, 95% CI 0.975 to 0.995; p=0.003), and LDL (OR 0.994, 95% CI 0.991 to 0.998; p=0.002), as demonstrated in Table 2.

The results of the multivariate logistic regression analyses revealed that five factors were associated with ICH, male gender (adjusted OR 1.904, 95% CI 1.293 to 2.803; p=0.001), SBP (adj. OR 1.024, 95% CI 1.017 to 1.032; p<0.001), DBP (adj. OR 1.051, 95% CI 1.037 to 1.064; p<0.001), TC (adj. OR 0.993, 95% CI 0.988 to 0.997; p=0.001), and LDL (adj. OR 0.994, 95% CI 0.990 to 0.999; p=0.010), as demonstrated in Table 2.

Discussion

The results of the current study revealed that six factors were found to be independently associated with increased risk of ICH, including male gender,

Table 2. Multivariate logistic regression analysis of factors associated with ICH

Factor	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Sex				
Female	Ref.		Ref.	
Male	2.497 (1.829 to 3.407)	<0.001*	1.904 (1.293 to 2.803)	0.001*
SBP	1.023 (1.016 to 1.029)	<0.001*	1.024 (1.017 to 1.032)	<0.001*
DBP	1.050 (1.037 to 1.062)	<0.001*	1.051 (1.037 to 1.064)	<0.001*
TC	0.994 (0.991 to 0.998)	0.001*	0.993 (0.988 to 0.997)	0.001*
HDL	0.985 (0.975 to 0.995)	0.003*	1.003 (0.990 to 1.016)	0.643
LDL	0.994 (0.991 to 0.998)	0.002*	0.994 (0.990 to 0.999)	0.010*

OR=odds ratio; CI=confidence interval; SBP=systolic blood pressure; DBP=diastolic blood pressure; TC=total cholesterol; HDL=high-density lipoprotein cholesterol; LDL=low-density lipoprotein cholesterol

elevated SBP and DBP, and decreased levels of TC, HDL, and LDL levels. After conducting multivariate logistic regression analysis, it was found that only five factors remained to be significantly related to elevated risk of ICH, which are male gender, elevated SBP and DBP, reduced levels of TC and LDL.

The finding of a relationship between gender and ICH is similar to the conclusions of previous studies, which stated that male gender was associated with an increased risk of ICH[2,5,8,13]. However, Lofissa et al.[11], in their research in Indonesia, reported a greater prevalence of ICH in females than in males. They found a higher rate of ICH among young males of 21 to 78 years old. However, among older aged participants, of more than 70 years old, they reported a higher prevalence in females. This could be attributable to the fact that females usually have a longer life expectancy than males.

Hypertension, as an underlying health condition, has been found to be a major risk factor for ICH, together with high SBP and DBP[2,3,5,7-9,13,14]. This disease has been reported in many studies to be the strongest factor associated with ICH[5,9], and Carlsson et al.[2] found that 84% of ICH cases had this underlying disease. Interestingly, hypertensive patients whose blood pressures were well controlled did not have an increased risk of ICH, and this is compatible with the findings of other large multinational studies[2,15]. Rasool et al.[14] found that blood pressure was also related to health outcomes after the incidence of ICH, potentially increasing the number of complications, such as rebleeding and expansion of hematoma. Despite this, in several countries, blood pressure has been observed to decrease over time, which might reflect an improvement in the availability of treatment for hypertension, but the overall incidence of ICH has remained stable[2,15]. In contrast, blood pressure levels among female populations have been found to have decreased, and this has been accompanied by a lower incidence of ICH[16-18]. This could be because of the longer female life expectancy of the global population or the ageing demographic transition, together with the fact that the effect of blood pressure on the vessels in the brain could be different in the two genders.

The results found that low TC and LDL in combination were associated with ICH, while low HDL was independently related, and no association was found between triglycerides and the disease. These results were quite similar to the findings of various previous studies. TC has been reported to be inversely related to ICH[5,8,9,11,12,19-22], and some researchers have claimed that intensively controlled lipid levels increase the risk of ICH[12]. Not only does lower TC increase the chance of an ICH event, but it is also independently related to the severity of the neurological symptoms on presentation[22]. Furthermore, it entails poorer prognosis and recovery outcomes than those of low BMI patients[22], and it is related to a high mortality rate in ICH patients especially in the elderly[23].

With regard to LDL, other studies have reported results compatible with the results. Low LDL has been found to be related to the incidence of ICH[5,11], along with poorer prognosis and increased mortality[24]. It has also been reported to promote hematoma expansion, which can be fatal[24].

Low HDL was independently associated with ICH, but when combined with other factors, there was no association, and this is similar to the results of the Framingham Heart Study[3]. Some researchers have found that high HDL increases the risk of ICH[9] in females, and high HDL has also been reported to be related to poor prognosis of ICH[24]. Therefore, gender could affect the pathophysiology of ICH.

The results found no association between triglycerides and ICH, and this is in keeping with the

findings of other published research[22,24,25]. Although it has been reported that low levels of triglycerides increase the risk of ICH in females, as well as having poorer prognosis[24], some researchers have found that high triglycerides are especially associated with lobar ICH[26].

Giroud et al.[27] found no association between total cholesterol and ICH, while others have reported that high total cholesterol levels increase the risk of developing the disease[9,28], and these apparent anomalies may well be a result of different definitions employed in the studies. On the whole, most meta-analyses have found an inverse correlation.

Hypolipidemia has been identified as one of the risk factors of small vessel abnormalities such as ICH, lacunar infarction, white matter hyperintensity and cerebral microbleed[21]. Analysis of the results from participants in the Framingham Heart Study showed that low total cholesterol levels were related to an increased risk of cerebral microbleed in patients with previous ICH[3]. However, lipid-lowering medications were found to be beneficial for small vessel disease and intracranial atherosclerosis[11], and statins can stabilize vulnerable plaques[21].

The association between lipid-lowering agents and ICH is still uncertain[29]. Several studies have found no association between risk of ICH and the use of statins with ezetimibe[30], while some researchers have reported that statins increase the risk of ICH[31].

As yet, there is no consensus on the best strategy for controlling lipid levels in primary and secondary preventative treatment of ICH. Recurrent ICH is considered to be one of the adverse effects of strictly controlled lipid levels[32], while Yu et al.[26] concluded that statins increased the risk of ICH independently of their lipid-lowering effect. Ma et al.[3] explained that statins did not increase the risk of ICH because they have a pleiotropic effect that inhibits inflammation of blood vessels and improves the prognosis of ICH. However, high-dose statins in older adults might increase the risk of the disease. Judge et al.[33] asserted that the advantages of using of lipid-lowering treatment in the prevention of ischemic stroke and ischemic heart disease greatly outweighed the drawback of increased risk of ICH.

The present study has limitations that should be acknowledged. As a retrospective case-control study, it did not take into consideration the potential confounding factors such as smoking, alcohol consumption, and psychological factors. Conducting future gender-specific analyses could help to mitigate the impact of gender on the results. The connection between lipids and cerebrovascular disease appears to be complex, with the underlying pathogenesis of blood vessels in the brain potentially differing between genders and locations in the brain. Further investigation into the pathophysiology of lipids and ICH is essential, as well as a comprehensive meta-analysis of gender-specific risk factors.

Conclusion

The aim of the present study was to determine the association between lipid levels and ICH. The results revealed that five factors were significantly related to increased risk of ICH, male gender, high SBP and DBP, and low levels of TC and LDL. Additionally, low HDL levels were independently related to increased risk of ICH. However, when combined with other factors, there was no significant association between HDL levels and ICH.

These findings provide insights into the potential risk factors for ICH and may inform the development of preventive strategies. Further research is needed to fully understand the complex interplay between these factors and the development of ICH.

What is already known on this topic?

Studies found an association between lower cholesterol and the incidence of ICH. However, there are many types of cholesterol, which might provide different results about the association. Thus, the results might bring about a better understanding and improvement in controlling the lipid levels of patients.

What this study adds?

The relationship between lipid levels and the incidence of ICH is an area of ongoing investigation. Some studies have reported an association between lower levels of cholesterol and increased incidence of ICH. However, it is important to note that cholesterol is a complex molecule exists in several distinct forms, including TC, LDL, HDL and triglycerides. These different types of cholesterol may exhibit different associations with ICH. This examination can provide a deeper understanding of the relationship and may inform the development of strategies for controlling lipid levels in patients. This, in turn, may help to mitigate the risk of ICH and improve patient outcomes.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Siriyutwattana C, Srisuwannanukorn S, Winitprichagul S. Incidence and associated factors of intracranial hemorrhage after intravenous thrombolysis for acute ischemic stroke in Vajira Hospital. Thai J Neurol 2020;36:51-6.
2. Carlsson M, Wilsgaard T, Johnsen SH, Johnsen LH, Løchen ML, Njølstad I, et al. The impact of risk factor trends on intracerebral hemorrhage incidence over the last two decades-The Tromsø Study. Int J Stroke 2019;14:61-8.
3. Ma Y, Li Z, Chen L, Li X. Blood lipid levels, statin therapy and the risk of intracerebral hemorrhage. Lipids Health Dis [Internet] 2016 [cited 2022 Sep 30];15:43. Available from: https://doi.org/10.1186/s12944-016-0213-8.
4. Shoamanesh A, Selim M. Use of lipid-lowering drugs after intracerebral hemorrhage. Stroke 2022;53:2161-70.
5. Lioutas VA, Beiser AS, Aparicio HJ, Himali JJ, Selim MH, Romero JR, et al. Assessment of incidence and risk factors of intracerebral hemorrhage among participants in the framingham heart study between 1948 and 2016. JAMA Neurol 2020;77:1252-60.
6. Chaturbedi A, Thakur J. Functional outcome, survival and independent risk factors in patients with spontaneous intracerebral hemorrhage from chronic arterial hypertendion. J Neurol Neurophysiol 2020;11:1-5.
7. An SJ, Kim TJ, Yoon BW. Epidemiology, risk factors, and clinical features of intracerebral hemorrhage: an update. J Stroke 2017;19:3-10.
8. Li L, Poon MTC, Samarasekera NE, Perry LA, Moullaali TJ, Rodrigues MA, et al. Risks of recurrent stroke and all serious vascular events after spontaneous intracerebral haemorrhage: pooled analyses of two population-based studies. Lancet Neurol 2021;20:437-47.
9. Arnao V, Fedele M, Altavilla R, Caso V. Conventional vascular and specific risk factors for intracerebral hemorrhage in females. Ital J Gender-Specific Med 2017;3:98-103.
10. Ariesen MJ, Claus SP, Rinkel GJ, Algra A. Risk factors for intracerebral hemorrhage in the general population: a systematic review. Stroke 2003;34:2060-5.
11. Lofissa SP, Ong PA, Atik N. Demographic and risk factors of intracerebral hemorrhage stroke patients in Dr. Hasan Sadikin General Hospital Bandung in 2007-2016. Althea Med J 2018;5:32-7.
12. Hemphill JC 3rd, Greenberg SM, Anderson CS, Becker K, Bendok BR, Cushman M, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2015;46:2032-60.
13. Chen CY, Lin PT, Wang YH, Syu RW, Hsu SL, Chang LH, et al. Etiology and risk factors of intracranial hemorrhage and ischemic stroke in young adults. J Chin Med Assoc 2021;84:930-6.
14. Rasool AH, Rahman AR, Choudhury SR, Singh RB. Blood pressure in acute intracerebral haemorrhage. J Hum Hypertens 2004;18:187-92.
15. Iso H, Jacobs DR Jr, Wentworth D, Neaton JD, Cohen JD. Serum cholesterol levels and six-year mortality from stroke in 350,977 men screened for the multiple risk factor intervention trial. N Engl J Med 1989;320:904-10.
16. Ramírez-Moreno JM, Casado-Naranjo I, Portilla JC, Calle ML, Tena D, Falcón A, et al. Serum cholesterol LDL and 90-day mortality in patients with intracerebral hemorrhage. Stroke 2009;40:1917-20.
17. Liu Q, Zhao W, Xing Y, Hong Y, Zhou G. Low triglyceride levels are associated with unfavorable outcomes in patients with spontaneous intracerebral hemorrhage. Neurocrit Care 2021;34:218-26.
18. Chow CK, Teo KK, Rangarajan S, Islam S, Gupta R, Avezum A, et al. Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. JAMA 2013;310:959-68.
19. Sacco S, Ornello R, Degan D, Tiseo C, Pistoia F, Carolei A. Declining incidence of intracerebral hemorrhage over two decades in a population-based study. Eur J Neurol 2016;23:1627-34.
20. Khan NA, McAlister FA, Pilote L, Palepu A, Quan H, Hill MD, et al. Temporal trends in stroke incidence in South Asian, Chinese and white patients: A population based analysis. PLoS One [Internet]. 2017 [cited 2022 Sep 30];12:e0175556. Available from: https://doi.org/10.1371/journal.pone.0175556.
21. Hopstock LA, Bønaa KH, Eggen AE, Grimsgaard S, Jacobsen BK, Løchen ML, et al. Longitudinal and secular trends in blood pressure among women and men in birth cohorts born between 1905 and 1977: The tromsø study 1979 to 2008. Hypertension 2015;66:496-501.
22. Champawong K, Jetjumnong C. Association of low serum cholesterol levels with increased risk of primary intracerebral hemorrhage. Chiang Mai Med J 2020;57:165-71.
23. Feng H, Wang X, Wang W, Zhao X. Lipid levels and 3-month prognosis after spontaneous intracerebral hemorrhage in women. Front Neurol 2021;12:690194.
24. Kim JS. Role of blood lipid levels and lipid-lowering therapy in stroke patients with different levels of cerebral artery diseases: Reconsidering recent stroke guidelines. J Stroke 2021;23:149-61.
25. Chen YW, Li CH, Yang CD, Liu CH, Chen CH, Sheu JJ, et al. Low cholesterol level associated with severity and outcome of spontaneous intracerebral hemorrhage:Results from Taiwan Stroke Registry. PLoS One [Internet]. 2017 [cited 2022 Sep 30];12:e0171379. Available from: https://doi.org/10.1371/journal.pone.0174293.

26. Yu Z, Zhang L, Zhang G, Xia K, Yang Q, Huang T, et al. Lipids, apolipoproteins, statins, and intracerebral Hemorrhage: A Mendelian Randomization Study. Ann Neurol 2022;92:390-9.
27. Giroud M, Creisson E, Fayolle H, André N, Becker F, Martin D, et al. Risk factors for primary cerebral hemorrhage: a population-based study--the Stroke Registry of Dijon. Neuroepidemiology 1995;14:20-6.
28. Paciaroni M, Agnelli G, Giustozzi M, Caso V, Toso E, Angelini F, et al. Risk factors for intracerebral hemorrhage in patients with atrial fibrillation on non-vitamin K antagonist oral anticoagulants for stroke prevention. Stroke 2021;52:1450-4.
29. Hackam DG, Woodward M, Newby LK, Bhatt DL, Shao M, Smith EE, et al. Statins and intracerebral hemorrhage: collaborative systematic review and meta-analysis. Circulation 2011;124:2233-42.
30. Mihaylova B, Emberson J, Blackwell L, Keech A, Simes J, Barnes EH, et al. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. Lancet 2012;380:581-90.
31. Vergouwen MDI, de Haan RJ, Vermeulen M, Roos YB. Statin treatment and the occurrence of hemorrhagic stroke in patients with a history of cerebrovascular disease. Stroke 2008;39:497-502.
32. Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:2889-934.
33. Judge C, Ruttledge S, Costello M, Murphy R, Loughlin E, Alvarez-Iglesias A, et al. Lipid lowering therapy, low-density lipoprotein level and risk of intracerebral hemorrhage - A meta-analysis. J Stroke Cerebrovasc Dis 2019;28:1703-9.