Original Article

Prevalence and Major Cardiac Causes of Cardio-embolic Stroke and In-Hospital Mortality in Eastern Nepal

Rajesh Nepal1, MD, DM; Manoj Kumar Choudhary4, MD; Sahadev Dhungana1, MD, DM; Sushant Katwal1, MD; Sunil Babu Khanal1, MBBS; Madhav Bista1, MD; Abdul Khaliq Monib1, MD; Dilli Ram Kafle2, MD, DM

1Department of Internal Medicine, Cardiology Unit, Nobel Medical College Teaching Hospital, 2Department of Internal Medicine, Neurology Unit, Nobel Medical College Teaching Hospital, Biratnagar, Nepal

INTRODUCTION

Stroke is the leading cause of disability and the second most common cause of death worldwide.1 About 15%–30% of all ischemic strokes are cardio-embolic.2,3 Atrial fibrillation (AF), ischemic cardiomyopathy, rheumatic mitral valve disease, and left ventricular failure are the most common causes of cardio-embolism. Major sources of embolism have an established causal relationship with stroke, and their identification is usually clinically pertinent.1,4 In some reports, two-thirds of ischemic strokes were considered as cardio-embolic.4,5 AF was the most common source of cardio-embolic stroke,5,7 while hypertension was the major associated risk factors.8 AF-related strokes constitute about 60% of all cardio-embolic strokes.9 As there are no gold standard diagnostic criteria for cardio-embolic stroke, the presence of a potential major cardiac source of embolism in the absence of significant arterial disease remains the mainstay of clinical diagnosis. There are no population-based surveys on stroke mortality found in Nepal. According to the WHO estimates, cerebrovascular diseases accounted for 107.5/100,000 deaths (age-standardized death rate) from cerebrovascular diseases in 2002 with a total DALY rate of 543/100,000.10 A study conducted in Kathmandu reported 88% of ischemic stroke among 281 young patients.11 Some studies reported that cardio-embolic stroke is less prevalent in South Asia than in Western countries.12,13 Nevertheless, some other studies from South Asia reported a high prevalence and incidence of mortality among cardio-embolic stroke patients.14,15

To the best of our knowledge, there is a paucity of data related to the prevalence of cardio-embolic stroke among ischemic stroke patients, cardiac disorder-related cardio-embolic stroke, and hospital mortality in Nepal. Our study aims to assess the prevalence of cardio-embolic stroke among ischemic stroke patients, conventional risk factors, and major cardiac causes of cardio-embolic stroke and in-hospital mortality in Eastern Nepal.

Abstract

Background: Cardioembolism accounts for 15%–30% of all ischemic strokes. The study aims to assess conventional and major cardiac causes of cardio-embolic stroke, its prevalence, lesions associated with the side of weakness, and in-hospital mortality. Materials and Methods: Patients with cardio-embolic stroke over 18 months were included in the study. Groups were compared using Chi-square test and Student’s t-test. Results: In 384 patients with ischemic stroke, 168 (44%) had a cardio-embolic stroke. Among these 168 cardio-embolic patients, 56% were male and 44% female with a mean age of 69 ± 1 year. Dyslipidemia (72%), hypertension (69%), smoking (34%), and diabetes (33%) were the most prevalent conventional cardiovascular risk factors in these patients. Atrial fibrillation (AF) (71%) was the most common specific cardiac cause for cardio-embolic stroke. Hypertension was present in more than 76%, while dyslipidemia in 66% of patients with AF. Seventeen patients (10%) had in-hospital mortality, while nine (5%) left the hospital against medical advice. The in-hospital mortality rates were not different in AF patients as compared to those with sinus rhythm (59% vs. 41%, P = 0.225). However, patients with left ventricular ejection fraction ≤50% had a higher rate of mortality when compared to patients with normal ejection fraction (P < 0.001). Patients with AF had a higher incidence of left-sided weakness when compared to sinus rhythm (P = 0.049). Conclusion: Hypertension and dyslipidemia were the most prevalent conventional risk factors, while AF was the most common cardiac cause of cardio-embolic stroke. Reduced left ventricular ejection fraction less than 50% was significant predictor of in-hospital mortality in cardio-embolic stroke patients.

Keywords: Atrial fibrillation, cardio-embolic stroke, ischemic stroke, prevalence

Received: 26-12-2019. Revised: 15-01-2019. Accepted: 31-01-2020. Published: 16-03-2020.

Address for correspondence: Dr. Rajesh Nepal, MD, DM, Department of Internal Medicine, Cardiology Unit, Nobel Medical College Teaching Hospital, Biratnagar, Nepal. E-mail: rajesh328@hotmail.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.
for cardio-embolic stroke and outcome in patients admitted in Nobel Medical College.

**Materials and Methods**

Between January 2017 and June 2018, data of 384 ischemic stroke patients admitted to the Department of Internal Medicine of Nobel Medical College Teaching Hospital were prospectively entered in a stroke registry. Performa was designed to collect patient information, which included demographic variables, cerebrovascular risk factors, and data on clinical and neurological findings, topography, diagnostic studies, and outcome of stroke patients. To be included in the study, patients had to be admitted to the hospital within 48 h of the onset of symptoms. For this study, data from patients with cardio-embolic stroke (n = 168) were included. Patients with hemorrhagic stroke, stoke with major organ failure such as chronic kidney or liver diseases, proven malignancy, recurrent stroke, and age <18 years were excluded from the study.

To diagnose a patient having cardio-embolic stroke requires, the presence of a medium-sized (maximal diameter of the lesion 1.5–3 cm) or large (>3 cm) cerebral infarction, cerebral cortex involvement on the brain computed tomography (CT) and/or magnetic resonance imaging (MRI) scans, sudden (minutes) or acute (hours) onset, stroke onset during ordinary daily activities, peak of deficit at onset, duration of focal neurological deficit >24 h, absence of lacunar clinical syndrome, and identification of a commonly accepted cardiac source of embolus in the absence of confirmatory clinical (ipsilateral carotid bruit) or investigative results (echocardiography, direct imaging plus Doppler ultrasonography, carotid angiography, or angio-MRI) of lesions (stenosis ≥50% and/or ulcerated atherosclerotic plaques) in the ipsilateral supra-aortic trunks.

The institutional review committee of Nobel Medical College approved the study protocol. On admission, demographic characteristics, salient features of clinical and neurological examination, results of routine laboratory tests (blood cell count, biochemical profile, serum electrolytes, and urinalysis), chest radiography, and 12-lead electrocardiography were recorded. A brain CT scan was obtained from all patients. In addition to electrocardiography recorded on admission, cardiac investigations included one or various electrocardiographic, Holter monitoring when dysrhythmia was suggested by the patient’s medical history, as well as color Doppler echocardiography in all cases.

All cardio-embolic stroke patients were assessed by a cardiologist for the etiological diagnosis of a cardiac source of emboli. The following subgroups were established: atrial arrhythmias (AF and atrial flutter), rheumatic heart disease, prosthetic cardiac valve, nonrheumatic degenerative mitral or aortic valve calcification; ischemic cardiomyopathy (clinical or coronary angiographically proven), dilated cardiomyopathy, cardiac tumors, and endocarditis.

**Cardiovascular risk factors were defined as follows**

**Smoking**

It included a history of cigarette smoking (regularly smokes one or more cigarettes per day).

**Dyslipidemia**

Any of the following values in fasting sample taken within 24 h of the event were as follows: total cholesterol (TC) ≥200 mg/dL, low-density lipoprotein cholesterol (LDL-C) ≥130 mg/dL, triglycerides ≥150 mg/dL, and high-density lipoprotein cholesterol ≤40 mg/dL or patients already on medication for dyslipidemia.

**Hypertension**

Hypertension included systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg and/or concomitant use of antihypertensive medications.

**Diabetes mellitus**

It included fasting plasma glucose ≥126 mg/dL or postprandial glucose ≥200 mg/dL or the patients being treated for diabetes.

**Alcohol intake**

It included weekly consumption of more than 14 units for males and 7 units for female or daily intake of alcohol was taken as significant alcohol consumption.

**Statistical analysis**

The demographic and laboratory data were analyzed using analysis of variance, and the Bonferroni correction was applied in the post hoc analyses. Categorical variables were reported as a percentage (%) and continuous variables were reported as the mean ± standard error of the mean. Groups were compared using the Chi-square test (cross-tabulation method) for categorical variables and Student’s t-test was used for the comparison of continuous variables. P < 0.05 was considered statistically significant with a 95% confidence interval. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 17.0 for Windows (SPSS, Inc., Chicago, Illinois, and the USA).

**Results**

**Demographic and study characteristics**

Among 384 patients with ischemic stroke, we identified 168 (44%) patients with cardio-embolic stroke [Figure 1a]. The data presented in this study are for 168 patients with cardio-embolic stroke. The mean age of the study population was 69 ± 1 years (32–93 years), while the mean age of males was 67 ± 1 years and female 71 ± 1 years. The mean age of improved patients was 69 ± 1 years, while the mean age of patients with mortality was 67 ± 3 years. Among 168 patients, 95 (56%) were male and 73 (44%) were female. Hypertension was present in 116 (69%). Diabetes was present in 55 (33%). Among 168 cardio-embolic stroke patients, dyslipidemia was reported in 121 (72%) patients. History of alcohol intake was present in 25 (15%), while 57 (34%) were smokers [Table 1]. In the subgroup analysis of patients according to their age, there was no significant difference between patients younger than 65 years or older (data not shown).

**Specific cardiac disorder**

Several cardiac conditions have been proposed as potential sources of embolism. Among 168 cardio-embolic strokes,
120 (71%) patients had AF, within which 17 (14%) had lone AF, while 103 (86%) were associated with structural cardiac disease. Sinus rhythm (48, 29%) and left ventricular ejection fraction ≤50% were reported in 66 (40%) patients; among them, dilated cardiomyopathy was found in 45 (27%) patients, ischemic cardiomyopathy in 21 (13%), and rheumatic mitral valve disease in 22 (13%) patients [Table 2].

Among 120 patients with AF, 91 (76%) patients had hypertension and 79 (66%) had dyslipidemia when compared with patients without the above risk factors (P < 0.05). While dyslipidemia was significantly higher among patients diagnosed with ischemic cardiomyopathy, dilated cardiomyopathy and left ventricular ejection fraction ≤50% than patients without the above risk factors. (P < 0.05). Among the potential sources of embolism, sex was not a determinate factor [Table 3].

**Cardiac disorder related to in-hospital mortality and side of weakness**

The in-hospital mortality rates were not different in AF patients as compared to those with sinus rhythm (59% vs. 41%, P = 0.225). Patients with dilated cardiomyopathy and left ventricular ejection fraction ≤50% had higher mortality versus patients without the above corresponding diseases (P < 0.001 for all) [Table 4]. Patients with AF had a higher incidence of left-sided weakness when compared to sinus rhythm (P = 0.049). Similarly, patients with ischemic cardiomyopathy had a higher number of left-sided hemiparesis when compared to cardio-embolic stroke patients without ischemic cardiomyopathy [Table 5].

**DISCUSSION**

There is a paucity of studies on the prevalence of cardio-embolic stroke among ischemic stroke patients, major cardiac causes, and lesion associated with in-hospital mortality of cardio-embolic stroke patients in Nepal. Although some studies had reported the incidence of ischemic stroke and outcome in Nepal,[15,17-19] a study reported 36% cardio-embolic stroke prevalence among ischemic stroke based on the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification.[13] The present results showed 44% cardio-embolic stroke prevalence among ischemic stroke based on the TOAST calcification which was higher compared to a study previously done in Nepal, which reported 36% cardio-embolic stroke prevalence among 56 ischemic stroke patients.[20] While there were similar reports from Pakistan (40%),[16] among ischemic stroke patients, all these reports validate that cardiac disorder might be the most common cause of ischemic stroke. The previous study reported a low incidence of cardio-embolic stroke in patients younger than 65 years while the higher rate in older patients. [20] we are trying to state that women are increasingly at risk of stroke, with higher number of (women) suffer from ischemic stroke.[17] In contrast, our result did not found any difference when subgroup analysis was performed according to the age and gender for cardio-embolic stroke, which may be due to a small sample size. Further large studies are required to find an association between age, gender, and cardio-embolic stroke.

Hypertension is a major risk factor for ischemic stroke.[18,19,21-23] Hypertensive patients are at risk for the development of conduction arrhythmia especially. Muscular hypertrophy can interrupt conduction pathways predisposing to AF, which can lead to ischemic stroke.[24] The previous study has reported that hypertension was present in 80% of patients with AF,[25] while hypertension with a risk ratio of 2.8 was a significant independent risk factor for thromboembolic stroke. AF patients with hypertension increases the incidence of stroke by
In the present study, among 168 patients, 114 (68) had AF (P < 0.001); the biggest difference was in male versus female (41 versus 27, 65% versus 30%, 71% versus 41%, and 40% versus 29%). The MATCH study[26,27] showed a higher risk of AF in women but not in men[28]. Smoking, alcohol intake, and dyslipidemia were associated with a higher risk of AF in women but not in men[29,30]. In the present study too, hypertension and dyslipidemia were the most common risk factors associated with AF, whereas dyslipidemia was associated with dilated cardiomyopathy, Left ventricular ejection fraction ≤50%, and ischemic cardiomyopathy. Thus, optimum control of blood pressure and lipids with drug treatment is also very crucial.

AF is the most important cause of cardio-embolic stroke.[1,3,5,6] AF causes cardio-embolic stroke because it leads to inadequate contraction, and hence, the formation of thrombus within the left atrial appendage. In our current study too, 71% of the patients had an incidence of AF authorizing that AF is the most common cause of cardio-embolic stroke also in Nepal. Arboix et al. too reported a similar finding that patients with cardio-embolic infarction and AF accounted for 76.6% of their total cases.[31] Stroke patients with AF are at high risk of death both at the acute phase of stroke and during the subsequent years after the first acute stroke event. Mortality from cardiac diseases prevailed in the AF group during the acute phase of the stroke.[32] In agreement with the study, even in our study, patients with AF with associated cardiac diseases numerically had a higher rate of in-hospital mortality.

In the present study, among 28 patients treated with clopidogrel, 16 patients were treated in a combination of aspirin for ischemic cardiomyopathy. In the previous study, about 2.5% of patients with acute myocardial infarction experienced a stroke within 2–4 weeks of the infarction.[33] Whereas in the CURE trial, the combination of aspirin and clopidogrel was associated with an RR of 0.89 (P < 0.001); the biggest difference was in the rate of myocardial infarction. This combination therapy has beneficial effects in patients with acute coronary syndromes[34] but carried an increased risk of major bleeding; however, there were no difference in life-threatening or fatal bleeding and no increase in hemorrhagic strokes.[35] The MATCH study reported that patients treated with clopidogrel (75 mg) alone who had an ischemic stroke were at high risk of another event compared to combination therapy with clopidogrel (75 mg) plus aspirin (75 mg).[36] In the present study, patients with cardio-embolic stroke who were not treated with clopidogrel in a combination of warfarin/aspirin had high numerical inhospital mortality though statically nonsignificant. Further studies are required to clarify the combination therapy effect on cardio-embolic stroke patients.

Salem et al. reported an annual incidence of cardio-embolism of 8% in patients with mitral stenosis and sinus rhythm and 32% in patients with mitral stenosis and AF.[37] while a prospective hospital-based stroke registry with 402 cardio-embolism patients showed an incidence of cardio-embolism of 12.4% in patients with rheumatic mitral valve disease.[38] In the present study, among 168 cardio-embolic stroke patients, 22 (13%) patients source of embolism was rheumatic mitral valve disease; among them, 60% of the patients had AF. Although the overall prevalence of rheumatic heart disease is higher in Nepal, long-term anticoagulation therapy decreases the risk of cardio-embolic stroke, as also seen in the previous studies,[38,39] which might

| Table 3: Cardio-embolic sources and risk factors |
|-----------------------------------------------|
| AF (120)                                      |
| Hypertension (%)                              |
| Diabetes (%)                                  |
| Smoking (%)                                   |
| Alcohol intake (%)                            |
| Dyslipidemia (%)                              |
| Male (%)                                      |
| AF (120)                                      |
| 91 (76)*                                      |
| 36 (30)                                       |
| 40 (33)                                       |
| 16 (13)                                       |
| 79 (66)*                                      |
| 67 (56)                                       |
| Left ventricular ejection fraction ≤50% (66) |
| 43 (65)                                       |
| 27 (41)                                       |
| 18 (27)                                       |
| 11 (17)                                       |
| 60 (91)*                                      |
| 40 (61)                                       |
| Ischemic cardiomyopathy (21)                  |
| 13 (62)                                       |
| 9 (43)                                        |
| 5 (24)                                        |
| 4 (19)                                        |
| 21 (100)*                                     |
| 12 (57)                                       |
| Dilated cardiomyopathy (45)                   |
| 30 (67)                                       |
| 18 (40)                                       |
| 13 (29)                                       |
| 7 (16)                                        |
| 39 (87)*                                      |
| 28 (62)                                       |
| Rheumatic mitral valve disease (22)           |
| 11 (50)                                       |
| 6 (27)                                        |
| 7 (32)                                        |
| 2 (9)                                         |
| 14 (64)                                       |
| 13 (59)                                       |

*P<0.05 versus no risk factor and for male versus female

| Table 4: Cardiac disorder and its prognosis |
|--------------------------------------------|
| In-hospital death (%)                      |
| χ² (df)                                    |
| P                                          |
| Left ventricular ejection fraction ≤50%    |
| No                                         |
| 3 (18)                                     |
| 19.79 (1) <0.001                           |
| Yes                                        |
| 14 (82)                                    |
| Dilated cardiomyopathy                     |
| No                                         |
| 5 (29)                                     |
| 18.50 (1) <0.001                           |
| Yes                                        |
| 12 (71)                                    |
| P values were calculated by the Chi-squared test for trends in proportions

| Table 5: Correlation between lesion and side of weakness |
|---------------------------------------------------------|
| Lesions                                                |
| Left-sided weakness (%)                                |
| Right-sided weakness (%)                               |
| χ² (df)                                                |
| P                                                       |
| Ischemic cardiomyopathy                                |
| No                                                      |
| 114 (68)                                                |
| 33 (20)                                                 |
| 4.082                                                   |
| 0.043                                                   |
| Yes                                                     |
| 12 (7)                                                  |
| 9 (5)                                                   |
| 1 (1)                                                   |
| ECG                                                     |
| Sinus rhythm                                            |
| 41 (24)                                                 |
| 7 (4)                                                   |
| 3.889                                                   |
| 0.049                                                   |
| AF                                                      |
| 85 (51)                                                 |
| 35 (21)                                                 |
| 1 (1)                                                   |
| P values were calculated by the Chi-squared test for trends in proportions. AF=Atrial fibrillation, ECG=Electrocardiogram

an additional 2–3 times.[26,27] Our result also correlates with the above finding, as we found that 76% of the patients with AF were hypertensive. The relationship between lipids and stroke is complex. Yaghi and Elkind reported that there is a direct association between cholesterol levels and ischemic stroke and the relationship is most strong for TC and LDL-C.[28] In patients with metabolic syndrome, elevated blood pressure and dyslipidemia were associated with a higher risk of AF in both African-American and native American population.[29] In another study, dyslipidemia was associated with an increased risk of new onset of AF in women but not in men.[30] whereas multiple studies have reported dyslipidemia associated with an increased incidence of heart failure and ischemic cardiomyopathy.[31,32] In the present study too, hypertension and dyslipidemia were the most common risk factors associated with AF, whereas dyslipidemia associated with dilated cardiomyopathy, Left ventricular ejection fraction ≤50%, and ischemic cardiomyopathy. Thus, optimum control of blood pressure and lipids with drug treatment is also very crucial.

AF is the most important cause of cardio-embolic stroke.[1,3,5,6] AF causes cardio-embolic stroke because it leads to inadequate contraction, and hence, the formation of thrombus within the left atrial appendage. In our current study too, 71% of the patients had an incidence of AF authorizing that AF is the most common cause of cardio-embolic stroke also in Nepal. Arboix et al. too reported a similar finding that patients with cardio-embolic infarction and AF accounted for 76.6% of their total cases.[31] Stroke patients with AF are at high risk of death both at the acute phase of stroke and during the subsequent years after the first acute stroke event. Mortality from cardiac diseases prevailed in the AF group during the acute phase of the stroke.[32] In agreement with the study, even in our study, patients with AF with associated cardiac diseases numerically had a higher rate of in-hospital mortality.

In the present study, among 28 patients treated with clopidogrel, 16 patients were treated in a combination of aspirin for ischemic cardiomyopathy. In the previous study, about 2.5% of patients with acute myocardial infarction experienced a stroke within 2–4 weeks of the infarction.[33] Whereas in the CURE trial, the combination of aspirin and clopidogrel was associated with an RR of 0.89 (P < 0.001); the biggest difference was in the rate of myocardial infarction. This combination therapy has beneficial effects in patients with acute coronary syndromes[34] but carried an increased risk of major bleeding; however, there were no difference in life-threatening or fatal bleeding and no increase in hemorrhagic strokes.[35] The MATCH study reported that patients treated with clopidogrel (75 mg) alone who had an ischemic stroke were at high risk of another event compared to combination therapy with clopidogrel (75 mg) plus aspirin (75 mg).[36] In the present study, patients with cardio-embolic stroke who were not treated with clopidogrel in a combination of warfarin/aspirin had high numerical in-hospital mortality though statically nonsignificant. Further studies are required to clarify the combination therapy effect on cardio-embolic stroke patients.

Salem et al. reported an annual incidence of cardio-embolism of 8% in patients with mitral stenosis and sinus rhythm and 32% in patients with mitral stenosis and AF.[37] while a prospective hospital-based stroke registry with 402 cardio-embolism patients showed an incidence of cardio-embolism of 12.4% in patients with rheumatic mitral valve disease.[38] In the present study, among 168 cardio-embolic stroke patients, 22 (13%) patients source of embolism was rheumatic mitral valve disease; among them, 60% of the patients had AF. Although the overall prevalence of rheumatic heart disease is higher in Nepal, long-term anticoagulation therapy decreases the risk of cardio-embolic stroke, as also seen in the previous studies,[38,39] which might
be the reason for the relatively small number of patients with rheumatic mitral valve disease in our study.

Among patients with dilated cardiomyopathy, stroke is a common sequel, whereas left ventricular dysfunction and older age are both independent predictors of an increased risk of stroke.\cite{De Jong et al.} In agreement with the above report, in our current study, patients with dilated cardiomyopathy and left ventricular ejection fraction ≤50% had the highest rate of-hospital mortality.

Approximately 80% of emboli primarily lodge into the anterior circulation of the brain (middle cerebral artery) and 20% into the posterior circulation.\cite{In the present study} In the present study for the first time, we have reported that patients with AF have more incidences of left-sided hemiparesis compared to sinus rhythm, whereas patients with AF associated with ischemic cardiomyopathy too have a higher rate of left-sided weakness compared to the patient not suffering from ischemic cardiomyopathy. This may be due to easy access for thrombus to travel straighter path in the right carotid artery than the long and double bent path of the left carotid artery.

In the previous study, a higher incidence of mortality was reported from Nepal, and among 20 cardio-embolic patients, 3-month mortality was recorded in 12 (60%) patients.\cite{In the present study} While in our current study, in-hospital mortality was 10%, and leave against medical advice (LAMA) were nine (5%) patients (Figure 1b). Among nine LAMA patients, eight were above 65-year-old, with very poor prognosis, in which case death can be assumed at home. Thus, even in our study, high in-hospital mortality was recorded among cardio-embolic patients.

There are a few limitations to the present study. First, the study was performed at the tertiary care center in Eastern Nepal, and the results cannot be generalized to the public and could just represent the patients with the referral bias. Second, the study shows the presence of admission bias, as only sick patients requiring urgent admission and medical attention were admitted. Third, the actual outcome of LAMA patients could not be ascertained.

**CONCLUSION**

Hypertension and dyslipidemia were the most prevalent conventional cardiovascular risk factors, while AF was the most common cardiac cause of cardio-embolic stroke. Patients associated with cardiac diseases such as dilated cardiomyopathy and ejection fraction ≤ 50% were significant predictors of in-hospital mortality in cardio-embolic stroke patients. These data may help the clinician to establish an early prognosis of this stroke subtype more accurately.

**Acknowledgments**

The authors express gratitude to the staff of the Coronary Care Unit, Nobel Medical College, for their valuable cooperation in the preparation of this manuscript.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES**

1. Weir NU. An update on cardioembolic stroke. Postgrad Med J 2008;84:133-42.
2. Murtagh B, Smalling RW. Cardioembolic stroke. Curr Atheroscler Rep 2006;8:310-6.
3. Khoo CW, Lip GY. Clinical outcomes of acute stroke patients with atrial fibrillation. Expert Rev Cardiovasc Ther 2009;7:371-4.
4. Kim Y, Kim TJ, Park JB, Lee S, Kim YJ, Lee JS, et al. Novel echocardiographic indicator for potential cardioembolic stroke. Eur J Neurol 2016;23:613-20.
5. Miller VT, Rothrock JF, Pearce LA, Feinberg WM, Hart RG, Anderson DC. Ischemic stroke in patients with atrial fibrillation: Effect of aspirin according to stroke mechanism. Stroke prevention in atrial fibrillation investigators. Neurology 1993;43:32-6.
6. Miller VT, Pearce LA, Feinberg WM, Rothrock JF, Anderson DC, Hart RG. Differential effect of aspirin versus warfarin on clinical stroke types in patients with atrial fibrillation. Stroke prevention in atrial fibrillation investigators. Neurology 1996;46:238-40.
7. Kim YD, Park B, Cha MJ, Nam CM, Nam HS, Ha JW, et al. Stroke severity in concomitant cardiac sources of embolism in patients with atrial fibrillation. J Neurol Sci 2010;298:23-7.
8. Aronow WS, Fleg JL, Pepine CJ, Artinian NT, Bakris G, Brown AS, et al. ACCF/AHA 2011 expert consensus document on hypertension in the elderly: A report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus documents developed in collaboration with the American Academy of Neurology, American Geriatrics Society, American Society for Preventive Cardiology, American Society of Hypertension, American Society of Nephrology, Association of Black Cardiologists, and European Society of Hypertension. J Am Coll Cardiol 2011;57:2037-114.
9. Han SW, Nam HS, Kim SH, Lee JY, Lee KY, Heo JH. Frequency and significance of cardiac sources of embolism in the TOAST classification. Cerebrovasc Dis 2007;24:463-8.
10. World Health Organization. Global Health Observatory (GHO) Data. World Health Organization. Available from: http://www.who.int/gho/en/. [Last accessed on 2019 Sep 30].
11. Pokharel B, Kharel G, Thapa L, Rana P. Stroke in young patients – A new trend in nepalese perspective? J Nutr Disord Ther. 2015;S1:001. doi:10.4172/2161-0509.S1-001.
12. Syed NA, Khealani BA, Ali S, Hasan A, Akhtar N, Brohi H, et al. Ischemic stroke subtypes in Pakistan: The Aga Khan University stroke data bank. J Pak Med Assoc 2003;53:584-8.
13. Aquil N, Begum I, Ahmed A, Vohra EA, Soomro BA. Risk factors in various subtypes of ischemic stroke according to TOAST criteria. J Coll Physicians Surg Pak 2011;21:280-3.
14. Pathak A, Kumar P, Pandit AK, Chakravarty K, Misra S, Yadav AK, et al. Is Prevalence of hypertension increasing in first-ever stroke patients? A hospital-based cross-sectional study. Ann Neurosci 2018;25:219-22.
15. Shrestha S, Poudel RS, Khatiwada D, Thapa L. Stroke subtype, age, and baseline NIHSS score predict ischemic stroke outcomes at 3 months: A preliminary study from Central Nepal.
16. Zafar F, Tarig W, Shoab RF, Shah A, Siddique M, Zaki A, et al. Frequency of Ischemic stroke subtypes based on toast classification at a tertiary care center in Pakistan. Asian J Neurosurg 2018;13:984-9.

17. Thapa A, Ke B, Shakya B, Yadav DK, Lama K, Shrestha R. Changing epidemiology of stroke in nepalese population. Nepal J Neurosci 2018;15:10-8.

18. Pathak V, Kanth R, Pant H. Stroke: A case series study in Nepal Medical College Teaching Hospital. Nepal Med Coll J 2006;8:180-1.

19. Devkota KC, Thapamagar SB, Malla S. Retrospective analysis of stroke and its risk factors at Nepal medical college teaching hospital. Nepal Med Coll J 2006;8:269-75.

20. Arboix A, Alió J. Cardioembolic stroke: Clinical features, specific cardiac disorders and prognosis. Curr Cardiol Rev 2010;6:150-61.

21. Stroke and Hypertension. World Heart Federation. Available from: https://www.world-heart-federation.org/resources/stroke-and-hypertension/. [Last accessed on 2019 Sep 30].

22. Boehme AK, Esenwa C, Elkind MS. Stroke risk factors, genetics, and prevention. Circ Res 2017;120:472-95.

23. Putaala J. Ischemic stroke in the young: Current perspectives on incidence, risk factors, and cardiovascular prognosis. Eur Stroke J 2016;1:28-40.

24. Tackling G, Borhade MB. Hypertensive heart disease. In: StatPears Treasure. Island (FL): StatPears Publishing; 2019.

25. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014;64:e1-76.

26. Toghi H, Tajima T, Konno T, Towada S, Kamata A, Yamazaki M. The risk of cerebral infarction in non-valvular atrial fibrillation: Effects of age, hypertension and antihypertensive treatment. Eur Neurol 1991;31:126-30.

27. Predictors of thromboembolism in atrial fibrillation: II. Echocardiographic features of patients at risk. The Stroke Prevention in Atrial Fibrillation Investigators. Ann Intern Med 1992;116:6-12.

28. Yaghhi S, Elkind MS. Clinical reasoning: An 87-year-old woman with left-sided numbness. Neurology 2015;85:e110-5.

29. Chamberlain AM, Agarwal SK, Ambrose M, Folsom AR, Solomon EZ, Alonso A. Metabolic syndrome and incidence of atrial fibrillation among blacks and whites in the Atherosclerosis Risk in Communities (ARIC) Study. Am Heart J 2010;159:850-6.

30. Watanabe H, Tanabe N, Yagihara N, Watanabe T, Aizawa Y, Kodama M. Association between lipid profile and risk of atrial fibrillation. Circ J 2011;75:2767-74.

31. Velagaleti R, Sims C, Gazzano J. Dyslipidemia Treatment and Heart Failure Risk. Am Coll Cardiol 2019;61 Suppl 10:E435.

32. Nepal R, Bista M, Monib AK, Choudhary MK, Bhattachar A. Prevalence of conventional risk factors in acute coronary syndrome patients in Eastern part of Nepal. J Nobel Med Coll 2017;6:48.

33. Arboix A, Garcia-Eroles L, Massons JB, Oliveres M, Pujades R, Targa C. Atrial fibrillation and stroke: Clinical presentation of cardioembolic versus atherothrombotic infarction. Int J Cardiol 2000;73:33-42.

34. Kaarisalo MM, Immonen-Räihä P, Marttila RJ, Salomaa V, Kaarsoalo E, Salmi K, et al. Atrial fibrillation and stroke. Mortality and causes of death after the first acute ischemic stroke. Stroke 1997;28:311-5.

35. Cardiogenic brain embolism. The second report of the Cerebral Embolism Task Force. Arch Neurol 1989;46:727-43.

36. Yusuf S, Zhao F, Mehta SR, Chrolavicus S, Tognoni G, Fox KK, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med 2001;345:494-502.

37. Diener HC, Bogousslavsky J, Brass LM, Cimminiello C, Csiba L, Kaste M, et al. Aspirin and clopidogrel compared with clopidogrel alone after recent ischemic stroke or transient ischaemic attack in high-risk patients (MATCH): Randomised, double-blind, placebo-controlled trial. Lancet 2004;364:331-7.

38. Salem DN, Levine HJ, Pauker SG, Eckman MH, Daudelin DH. Antithrombotic therapy in valvular heart disease. Chest 1998;114:590S-601S.

39. Pujadas Capmany R, Arboix A, Casasañas-Muñoz R, Angueira-Ferrando N. Specific cardiac disorders in 402 consecutive patients with ischaemic cardioembolic stroke. Int J Cardiol 2004;95:129-34.

40. Loh E, Sutton MS, Wun CC, Rouleau JL, Flaker GC, Gottlieb SS, et al. Ventricular dysfunction and the risk of stroke after myocardial infarction. N Engl J Med 1997;336:251-7.

41. de Jong G, van Raak L, Kessels F, Lodder J. Stroke subtype and mortality. A follow-up study in 998 patients with a first cerebral infarct. J Clin Epidemiol 2003;56:262-8.

42. Crawford TC, Smith WT, Velazquez EJ, Taylor SM, Jollis JG, Kisslo J. Prognostic usefulness of left ventricular thrombus by echocardiography in dilated cardiomyopathy in predicting stroke, transient ischemic attack, and death. Am J Cardiol 2004;93:526-7.

43. Gillum RF. New considerations in analyzing stroke and heart disease mortality trends: The Year 2000 Age standard and the international statistical classification of diseases and related health problems, 10th revision. Stroke 2002;33:1717-21.