

Factors Related to Stroke: A Hospital Based Study

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Abstract

To determine the distribution of common medical conditions related to stroke among Bangladeshi patients. This is an observational study. It involved 336 stroke patients from different medicine wards in Dhaka Medical College Hospital from July 2012 to June 2013. We assessed some common established medical conditions observed among stroke patients e.g. age, sex, family history, hypertension, diabetes, ischemic heart disease, smoking, obesity, dyslipidaemia, alcoholism, use of oral contraceptive pill, etc. A predesigned check list was used for data collection. Among 336 patients, most of the stroke events occurred after the age of forty (82.3%) and the ischemic stroke (72%) being the most common. Other than the non modifiable risk factors (advancing age, sex, Family history of stroke) hypertension was the most common factor found in relation to stroke patients (57.6%) followed by smoking (44.6%), tobacco use (24.3%), OCP use in female (40% of female stroke), diabetes (23%), ischemic heart disease (17.1%), obesity (10.6%) and dyslipidaemia (5.3%). Stroke is common after the age of forty. Ischemic events are the commonest type of stroke. Hypertension, smoking, diabetes, tobacco use, and ischemic heart disease were five most principal conditions associated with stroke.

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Introduction

Stroke is the second leading cause of death worldwide and a major cause of disability among adult in most of the regions^{1,2}. About 16.3 million people suffer from stroke worldwide each year, among which 11.2 million events occur in developing countries including Bangladesh. About 5.8 million people die of stroke each year, the two third of which occurs in developing nations². An estimated 64.5 million stroke patients survived an acute stroke event and living with varying degree of disability². Worldwide, stroke consumes about 2–4% of total health-care costs, and in industrialized countries, stroke accounts for more than 4% of direct health-care costs³. Though the trend of stroke mortality in developing countries is largely unknown, the average age adjusted mortality of stroke differs even among the developed countries⁴. The geographic variation may be due to difference of risk factor prevalence, genetic susceptibility and level of healthcare

facilities. Even though there has been a constant reduction in stroke mortality in developed countries during the past 50 years⁵,

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it is less certain about trends in developing countries. The most acceptable explanation for the reduction in mortality in western countries is improved control of stroke risk factors (especially high blood pressure and cigarette smoking) combined with a parallel improvement in living standards⁶⁻¹³.

Bangladesh is a small country in South Asia with high density of population (an average of 964 inhabitants/ square kilometer)¹⁴.

The prevalence of stroke here is 3 per 1000 above the age of 40 years¹⁵. We could find few such studies involving stroke patients¹⁶⁻¹⁸. In this view point we conducted the study in medicine wards of Dhaka Medical College Hospital (DMCH) involving a considerable factors to the distribution of common determinants related to stroke.

Methods

This cross sectional study was conducted in medicine wards of Dhaka Medical College Hospital involving 336 patients from July 2012 to June 2013. The diagnosis of based on WHO definition of stroke, with the support of convincing history, compatible clinical examination finding and confirmed by CT scan of Head. MRI of brain was done only in required cases eg suspected cerebellar or brain stem stroke. We excluded patients with recurrent stroke, encephalopathy from this study. We collected all the data using a preformed questionnaire. Required information include presence of other factors eg, age, sex, family history, hypertension, diabetes, ischemic heart disease (IHD), smoking, obesity, dyslipidaemia, alcoholism, use of oral contraceptive pill, pregnancy. Patients were evaluated meticulously with history, clinical examination and necessary investigation at the time of hospital visit by specialists in medicine. All findings were noted and recorded.

Result

In this study the majority of strokes were found to occur after the age of 40 years (82.3%), the most common being in 51-60 years age group

(31.1%), followed by 41-50 years age group (27.5%). Ischemic stroke was common in all age groups. Stroke events showed a male preponderance (73.4%). The male to female ratio for ischemic stroke was 3:1, as compared to 2:1 for hemorrhagic stroke. We found that about 6% of the patients had history of stroke within the family (Table-I). Ischemic stroke was the most frequent event (72%), followed by intracerebral hemorrhage (23%) and subarachnoid hemorrhage (5%) (Figure-I). Hypertension was the most common risk factor in stroke patients (56.7%). Smoking was the next common entity (44.6%) in stroke patients after hypertension followed by tobacco use (24.3%) and Diabetes (23%). History of ischemic heart disease, in the form of acute coronary syndrome, was present in 17.1% stroke patients and dyslipidaemia in 5.3%. About 10.6% patients were obese (BMI > 24.9). A good proportion of female stroke patients (40%) took oral contraceptive pills. A very few patients (1.2%) were binge alcohol drinker (Figure-II).

Tables and Figures

Table I: Non modifiable risk factors of stroke (N=336)

Parameter		Percentage		
		Total	ISH	HRG
Age	11-20yr	2.3	0.7	1.6
	21-30yr	3.1	2.4	0.6
	31-40yr	12.3	9.6	2.6
	41-50yr	27.5	22.4	5.1
	51-60yr	31.1	24.1	7.0
	>60 yrs	23.7	18.3	5.4
Sex	Male	73.4	58.1	15.3
	Female	26.6	18.9	7.6

Family History of Stroke

Positive family history of stroke 6

Table-I shows non modifiable risk factors in stroke patients. Most of the patients are older than 40 years and male.

Figure-I:

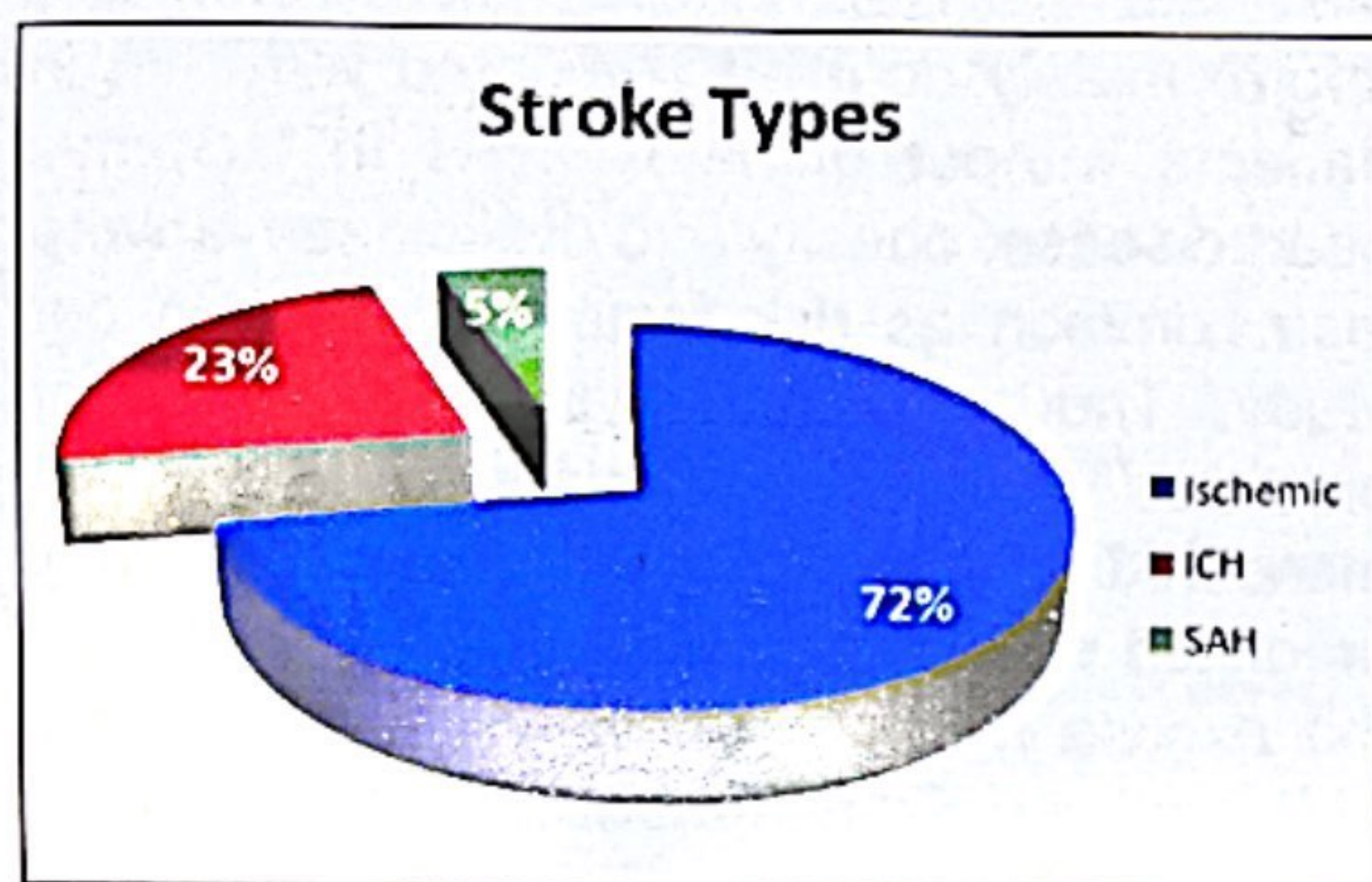


Figure-I: Distribution of stroke subtype, showing that about 3/4th of the patient had ischemic stroke.

Figure-II:

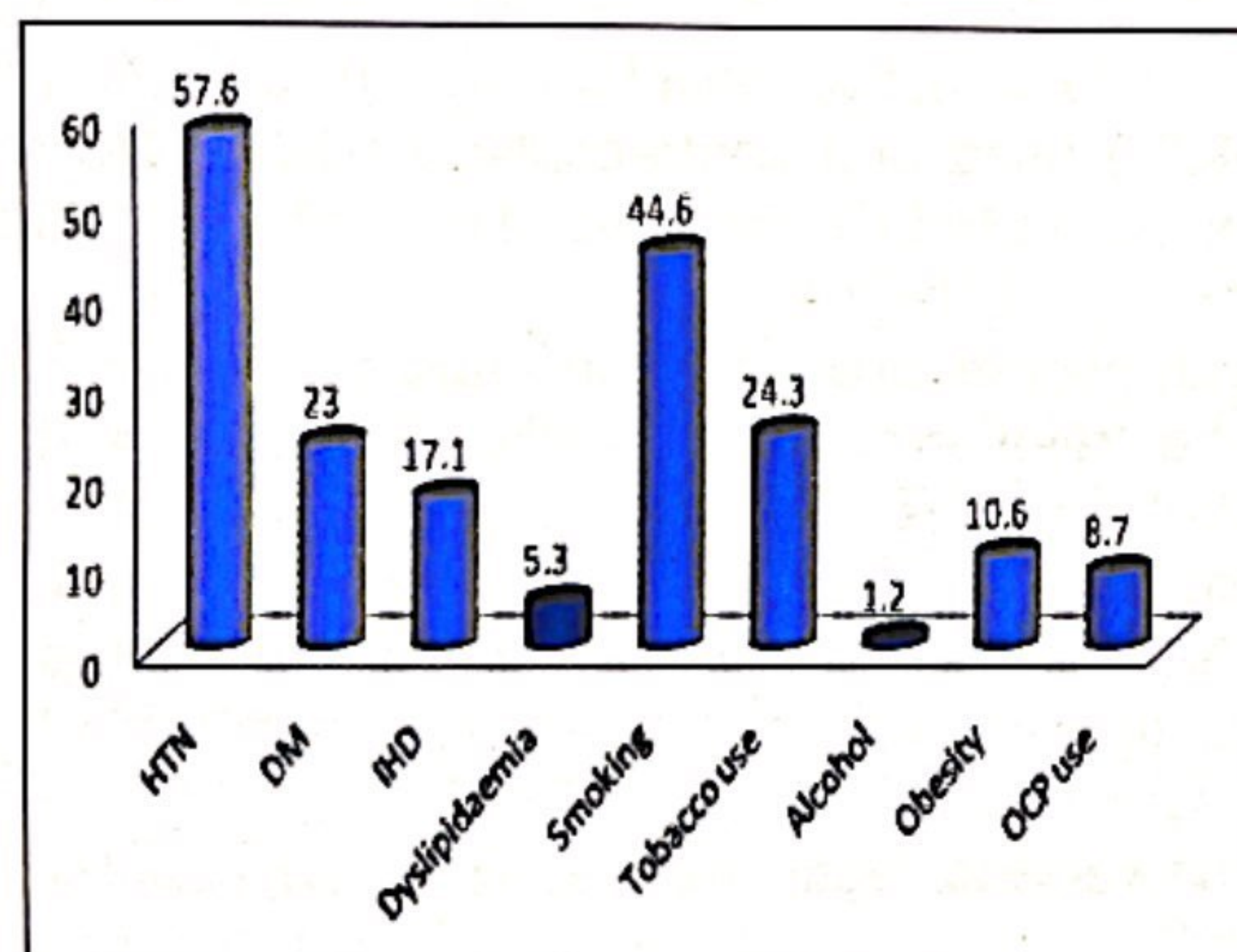


Figure II: shows modifiable risk factors of stroke. The most common are HTN, DM, Smoking, IHD, Obesity and Dyslipidaemia.

Discussion

Hospital-based stroke registries help to study the interrelationship between stroke, risk factors and prognosis. The present report provides the detail information regarding stroke subtypes and distribution of common factors and medical conditions related to stroke. Our study provides essential information as in other investigations on common, nonmodifiable and potentially modifiable vascular risk factors, and builds on previous epidemiological studies¹⁹⁻²⁸. It is well

established that the incidence of stroke rises steeply with age²⁹, a finding that is consistent in most of the studies conducted worldwide³⁰⁻³⁴. The highest age specific rates occurred in Japan, Russia, and Ukraine^{31,35,36}. We also have observed age specific increased frequency of stroke after forty and commonly with ischemic events. But in our study stroke events are common at much younger age (40-60 years) than other parts of the world. The overall difference in life expectancy may be a possible explanation for the fact. Though rare, before the age of 20 years, haemorrhagic events were seen frequently. Chen et al³⁷ also reported a relatively higher incidence of haemorrhagic stroke in children below 10 years and 10-19 years, irrespective of sexes. A recent study from Texas also showed higher incidence of haemorrhagic stroke than ischemic (3.2 versus 1.1 per 10000)³⁸. Thus we have confirmed from the observation of previous studies that ischemia is much more common than hemorrhagic events in adulthood stroke³⁹⁻⁴¹. But geographic variation exists for childhood stroke. The estimates of the incidence rates for childhood stroke ranged from 2.1 to 13 per 100,000 children-years in Hong-Kong, the United States and France⁴²⁻⁴⁴. Stroke was three times higher among male in our study, a fact also established by others⁴⁵. The Framingham Heart Study found a higher risk of stroke in men than in women until age 84 years, when risk in women exceeded that in men⁴⁶. Data from a population-based study from Sweden also showed a reversal in the sex difference with advanced age⁴⁷. Others have reported that stroke risk in men remains higher than that in women throughout life, although the magnitude of the sex difference diminishes with age^{48,49}. Still others have reported that the sex differences no longer exist at older ages⁵⁰⁻⁵¹. In the socio economic and cultural context of Bangladesh, female stroke patients are often reluctant to get hospitalized. So not surprisingly we found less number of female stroke patients. Likewise in other developing countries, in our study, ischaemic stroke represents the majority of stroke subtypes, followed by primary intracranial haemorrhage

and subarachnoid haemorrhage^{52,53}. In developed countries, up to 67.3–80.5% of strokes are attributed to ischaemic stroke, whereas 6.5–19.6% are primary intracerebral haemorrhage, about 0.8–7% are subarachnoid haemorrhage, and 2–14.5% are of undefined type⁵⁴. In some developing countries, there is a tendency for a higher proportion of haemorrhagic strokes than in western countries. Most of the East Asian studies have suggested that the proportion of intracerebral haemorrhage is significantly higher (up to 35% of the total) than in people of European descent⁵⁵.

We found the frequencies of the common factors or medical conditions related to stroke in Bangladesh to be similar to those of the other countries^{56,57}. Consistent with previous studies²¹, our findings showed that hypertension was the most common risk factor (57.6%) for all stroke subtypes. Reports from both the developing and developed world are similar in this regard⁵⁸⁻⁶¹. The high frequency of hypertension is probably due to self reporting of patients and the clinic recording of increased blood pressure. Systemic review study also confirms this type of finding⁶²⁻⁶⁵. Consistent with the report of Bak et al⁶⁶ smoking was the next major risk factor of stroke following hypertension in the present study. Daily smoking also doubled the risk of stroke among male in Europe, Honolulu and China^{65,67-69}. Though smoking is uncommon among Bangladeshi women, they are habituated more to tobacco use in the form of betel nut chewing, which is evident by this study (one fourth of the stroke patient chewed betel nut with tobacco). Ischemic heart disease and ischemic stroke shares common modifiable risk factors. So, it is not surprising to find that one in every six stroke patient had associated ischemic heart disease. Our finding is also supported by the report of Jorgensen et al⁷⁰.

We observed an increased frequency of stroke among diabetic population which is also established by several other studies for the last thirty years.⁷¹⁻⁷⁴ This increase has been connected to the pathophysiological changes

seen in the cerebral vessels of patients with diabetes.^{75,76} The relative risk of stroke is approximately doubled compared with that in patients without diabetes⁷⁷. As in ischemic heart disease, obesity and dyslipidaemia were also common as risk factor of stroke in our study. Though truncal fat may be better predictor⁷⁸, most of the epidemiologic studies measured BMI like us. High BMI significantly predicted stroke in several studies⁷⁹⁻⁸¹. Thus, the excess risk was approximately 30% per BMI unit in Framingham men⁶⁷, 10% in Japanese-American men in Honolulu. The role of hyperlipidaemia on stroke has been studied by several researchers. Statins have been shown to reduce stroke incidence by 29% in some trials⁸²⁻⁸⁵. Haque et al⁸⁶ also confirmed a strong association of LDL-cholesterol and triglyceride with ischemic stroke among Bangladeshi patients. A considerable fraction of women in our study (40%) used oral contraceptives (OCP). OCP increases the risk of cerebral infarction up to 9 fold⁸⁷ and the risk cumulates among women with hypertension, migraine and smoking⁸⁶⁻⁹⁰. The relation between alcohol intake and stroke seems complex one. Epidemiological studies confirmed that alcohol intake has a J-shaped relation with ischaemic stroke, but is associated with a graded increased risk of haemorrhagic stroke. Due to social and cultural and legal restrictions in our country, the frequency of drinking alcohol was minimal^{91,92}.

Conclusion

Stroke is common after the age of forty but patients in Bangladesh have stroke at relatively younger age than the west. Similar to other low income countries, our findings suggest that five simple factors or medical conditions are associated with majority of stroke events in Bangladesh. Targeted interventions could substantially reduce the overall burden of stroke.

Nonetheless we had some limitations in this study. Though this hospital based observational study may not reflect the real scenario within the community. Moreover, we

could not measure the odd ratio for individual risk factors due to the nature of the study. This warrants further case control studies to confirm the level of association.

References

1. Feigin VL. Stroke in developing countries: can the epidemic be stopped and outcomes improved? *Lancet Neurol* 2007; 6: 94–97.
2. Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. *Lancet Neurol* 2007; 6: 182–87.
3. American Heart Association. Heart and Stroke Facts Statistics: Dallas: American Heart Association, 1997.
4. Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. *Lancet Neurol*. 2007; 6: 182–87.
5. Bonita R. Epidemiology of stroke. *Lancet* 1992; 339: 342–44.
6. Bonita R, Beaglehole R. Increased treatment of hypertension does not explain the decline in stroke mortality in the United States, 1970–1980. *Hypertension* 1989; 13: 169–73.
7. Thrift AG, Dewey HM, Sturm JW, et al. Greater incidence of both fatal and nonfatal strokes in disadvantaged areas: the Northeast Melbourne Stroke Incidence Study. *Stroke* 2006; 37: 877–82.
8. McQueen MJ, Hawken S, Wang X, et al, for the INTERHEART study investigators. Lipids, lipoproteins, and apolipoproteins as risk markers of myocardial infarction in 52 countries (the INTERHEART study): a case-control study. *Lancet* 2008; 372: 224–33.
9. Yusuf S, Hawken S, Ôunpuu S, et al, on behalf of the INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004; 364: 937–52.
10. Rosengren A, Hawken S, Ôunpuu S, et al, for the INTERHEART investigators. Association of psychosocial risk factors with risk of acute myocardial infarction in 11 119 cases and 13 648 controls from 52 countries (the INTERHEART study): case-control study. *Lancet* 2004; 364: 953–62.
11. Teo KK, Ôunpuu S, Hawken S, et al, on behalf of the INTERHEART Study Investigators. Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. *Lancet* 2006; 368: 647–58.
12. Yusuf S, Hawken S, Ôunpuu S, et al, on behalf of the INTERHEART Study Investigators. Obesity and the risk of myocardial infarction in 27 000 participants from 52 countries: a case-control study. *Lancet* 2005; 366: 1640–49.
13. Donnan GA, Fisher M, Macleod M, Davis SM. Stroke. *Lancet* 2008; 371: 1612–23.
14. Bangladesh Bureau of Statistics. Population and housing census 2011. Preliminary result, July 2011; Page:8.
15. Mohammad QD, Habib M, Hoque A, Alam B et al. Prevalence of stroke above forty years. *Mymensingh Med J* 2011;20(4): 640–4.
16. Hossain MZ, Ahmed SU, Sarder MH et al. Analysis of risk factors associated with stroke in young adults: a prospective study. *J Dhaka Med Coll* 2009;18(2): 95–100.
17. Siddique MAN, Nur Z, Mahbub MS et al. Clinical presentation and epidemiology of stroke: a study of 100 cases. *J medicine* 2009; 10: 86–89.
18. Hossain AM, Ahmed NU, Rahman M et al. Analysis of sociodemographic and clinical factors associated with hospitalized stroke patients of Bangladesh. *Faridpur Med Coll J* 2011; 6(1): 19–23.
19. Philip A Wolf. Prevention of stroke. *Lancet* 1998; 352 (suppl III):15–8.
20. Ezzati M, Hoom SV, Rodgers A, Lopez AD, Mathers CD, Murray CJL, the Comparative Risk Assessment Collaborating Group. Estimates of global and regional potential health gains from reducing multiple major risk factors. *Lancet* 2003; 362: 271–80.
21. Lawes CM, Bennett DA, Feigin VL, Rodgers A. Blood pressure and stroke: an overview of published reviews. *Stroke* 2004; 35: 776–85.
22. Asplund K. What MONICA told us about stroke. *Lancet Neurol* 2005; 4: 64–68.
23. Johnston SC, Mendis S, Mathers CD. Global variation in stroke burden and mortality: estimates from monitoring, surveillance, and modelling. *Lancet Neurol* 2009; 8: 345–54.
24. Hankey GJ. Potential new risk factors for ischemic stroke: what is their potential? *Stroke* 2006; 37: 2181–88.
25. Sacco RL, Khatmi M, Rundek T, et al. Improving global vascular risk prediction with behavioral and anthropometric factors. The multiethnic NOMAS (Northern Manhattan Cohort Study). *J Am Coll Cardiol* 2009; 54: 2303–11.
26. Truelsen T, Mahonen M, Tolonen H, Asplund K, Bonita R, Vanuzzo D. Trends in stroke and coronary heart disease in the WHO MONICA Project. *Stroke* 2003; 34: 1346–52.
27. Feigin V, Lawes C, Bennet D et al. Worldwide stroke incidence and early case fatality in 56 population based studies: a systematic review. *Lancet Neurology* 2009; 8 (4): 355–369.
28. Ezzati M, Lopez A, Rodgers A et al. Comparative quantification of health risks. Global and regional burden of disease attributable to major risk factors. Geneva: WHO 2004.
29. Allen CMC, Lueck CJ, Dennis M. Neurologic disease. In: Colledge NR, Walker BR, Ralston SH, editors. *Davidson's Principles and Practice of Medicine*. 21st edition. Elsevier Limited; 2010: pp-1180.
30. Jamrozik K, Broadhurst RJ, Lai N, Hankey GJ, Burvill PW, Anderson CS. Trends in the incidence, severity, and short-term outcome of stroke in Perth, western Australia. *Stroke* 1999; 30: 2105–11.
31. Morikawa Y, Nakagawa H, Naruse Y, et al. Trends in stroke incidence and acute case fatality in a Japanese rural area: the Oyabe study. *Stroke* 2000; 31: 1583–87.
32. Kolominsky-Rabas PL, Weber M, Gefeller O, Neundorfer B, Heuschmann PU. Epidemiology of ischemic stroke subtypes according to TOAST criteria: incidence, recurrence, and long-term survival in ischemic stroke subtypes, a populationbased study. *Stroke* 2001; 32: 2735–40.
33. Vemmos KN, Bots ML, Tsibouris PK, et al. Stroke incidence and case fatality in southern Greece: the Arcadia stroke registry. *Stroke* 1999; 30: 363–70.
34. Smadja D, Cabre P, May F, et al. ERMANCIA: epidemiology of stroke in Martinique, French West Indies, part I: methodology, incidence, and 30-day case fatality rate. *Stroke* 2001; 32: 2741–47.

35. Feigin VL, Wiebers DO, Nikitin YP, O'Fallon WM, Whisnant JP. Stroke epidemiology in Novosibirsk, Russia: a population-based study. *Mayo Clin Proc* 1995; 70: 847-52.
36. Mihalka L, Smolanka V, Bulecza B, Mulesa S, Bereczki D. A population study of stroke in West Ukraine: incidence, stroke services, and 30-day case fatality. *Stroke* 2001; 32: 2227-31.
37. Chen PC, Chien KL, Chang CW et al. More Hemorrhagic and Severe Events Cause Higher Hospitalization Care Cost for Childhood Stroke in Taiwan. *J Pediatr* 2008;152:388-93.
38. Zahuranec DB, Brown DL, Lisabeth LD, Morgenstern LB. Is it time for a large, collaborative study of pediatric stroke? *Stroke* 2005;36:1825-9.
39. Hu HH, Sheng WY, Chu FL, Lan CF, Chiang BN. Incidence of stroke in Taiwan. *Stroke* 1992;23:1237-41.
40. Jernstorp P, Berglund G. Stroke registry in Malmo, Sweden. *Stroke* 1992; 23:357-61.
41. Zhang LF, Yang J, Hong Z, Yuan GG, Zhou BF, Zhao LC, et al. Collaborative Group of China Multicenter Study of Cardiovascular Epidemiology: Proportion of different subtypes of stroke in China. *Stroke* 2003;34: 2091-6.
42. Chung B, Wong V. Pediatric stroke among Hong Kong Chinese subjects. *Pediatrics* 2004;114:e206-12.
43. Fullerton HJ, Wu YW, Zhao S, Johnston SC. Risk of stroke in children: ethnic and gender disparities. *Neurology* 2003;61:189-94.
44. Giroud M, Lemesle M, Gouyon JB, Nivelon JL, Milan C, Dumas R. Cerebrovascular disease in children under 16 years of age in the city of Dijon, France: a study of incidence and clinical features from 1985 to 1993. *J Clin Epidemiol* 1995;48:1343-8.
45. Kumar P, Clark M, Editors. *Kumar & Clark Clinical Medicine*. 7th edition. Spain: Elsevier limited; 2009: pp-1126.
46. Petrea RE, Beiser AS, Seshadri S, et al. Gender differences in stroke incidence and poststroke disability in the Framingham Heart Study. *Stroke*. 2009;40:1032-1037.
47. Lofmark U, Hammarstrom A. Evidence for age dependent education-related differences in men and women with first-ever stroke: results from a community-based incidence study in northern Sweden. *Neuroepidemiology*. 2007;28:135-141.
48. Lewsey JD, Gillies M, Jhund PS, et al. Sex differences in incidence, mortality, and survival in individuals with stroke in Scotland, 1986 to 2005. *Stroke*. 2009;40:1038-1043.
49. Hollander M, Koudstaal PJ, Bots ML, et al. Incidence, risk, and case fatality of first ever stroke in the elderly population: the Rotterdam Study. *J Neurol Neurosurg Psychiatry*. 2003;74:317-321.
50. Vega T, Zurriaga O, Ramos JM, et al. Stroke in Spain: epidemiologic incidence and patterns; a health sentinel network study. *J Stroke Cerebrovasc Dis*. 2009;18:11-16.
51. Rothwell PM, Coull AJ, Silver LE, et al. Populationbased study of event-rate, incidence, case fatality, and mortality for all acute vascular events in all arterial territories (Oxford Vascular Study). *Lancet*. 2005;366:1773-1783.
52. Oveisgharan S, Sarrafzadegan N, Shirani S, Hosseini S, Hasanzadeh P, Khosravi A. Stroke in Isfahan, Iran: hospital admission and 28-day case fatality rate. *Cerebrovasc Dis*. 2007;24(6):495-499.
53. Ahangar AA, shraf Vaghefi SB, Ramaezani M. Epidemiological evaluation of stroke in Babol, northern Iran (2001-2003) *Eur Neurol*. 2005;54(2):93-97.
54. Feigin VL, Lawes CM, Bennett DA, Anderson CS. Stroke epidemiology: a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. *Lancet Neurol* 2003; 2: 43-53.
55. Sudlow CL, Warlow CP. Comparable studies of the incidence of stroke and its pathological types: results from an international collaboration: International Stroke Incidence Collaboration. *Stroke* 1997; 28: 491-99.
56. Dyken ML, Wolf PA, Barnett HJM, Beran JJ, Hass WK, Kannel WB, Kuller L, Kurtzke YF, Sundt TM. Risk factors in stroke: a statement for physicians by the subcommittee on risk factors and stroke of the stroke council. *Stroke*. 1984;15:1105-1111.
57. Wolf P. An overview of the epidemiology of stroke. *Stroke*. 1990;21(9 Suppl):II-4-II-6.
58. Kumral E, Ozkaya B, Sagduyu A, et al. The Ege Stroke Registry: a hospital-based study in Aegean region, Izmir, Turkey. *Cerebrovasc Dis* 1998; 8:278-88.
59. Moulin T, Tatu L, Chavot D, et al. Besancon Stroke Registry: an acute stroke registry of 2,500 consecutive patients. *Eur Neuro* 1997; 38:10-20.
60. McDonnell R, Fan CW, Johnson Z, Crowe M. Prevalence of risk factors for ischaemic stroke and their treatment among a cohort of stroke patients in Dublin. *Ir J Med Sci Oct-Dec* 2000; 169:253-7.
61. Kaul S, Venkateswamy P, Meena AK, Sahay R, Murthy JM. Frequency, clinical features and risk factors of lacunar infarction (data from a stroke registry in South India). *Neurol India Jun* 2000; 48(2):116-9.
62. Ezzati M, Hoom SV, Rodgers A, Lopez AD, Mathers CD, Murray CJL, the Comparative Risk Assessment Collaborating Group. Estimates of global and regional potential health gains from reducing multiple major risk factors. *Lancet* 2003; 362: 271-80.
63. The Indian Polycap Study (TIPS). Effects of a polypill (Polycap) on risk factors in middle-aged individuals without cardiovascular disease (TIPS): a phase II, double-blind, randomised trial. *Lancet* 2009; 373: 1341-51.
64. Appel LJ, Anderson CA. Compelling evidence for public health action to reduce salt intake. *N Engl J Med* 2010; 362: 650-52.
65. Asplund K, Karvanen J, Giampaoli S et al. Relative Risks for Stroke by Age, Sex, and Population Based on Follow-Up of 18 European Populations in the MORGAM Project. *Stroke*. 2009;40:2319-2326.
66. Bak S, Bak L, Sorensen JS. Prevalence of risk factors in cerebral ischemia. *Ugeskr Laeger* 1995; Jan 23; 157:444-6.
67. Zhang XF, Attia J, D'Este C, Yu XH, Wu XG. A risk score predicted coronary heart disease and stroke in a Chinese cohort. *J Clin Epidemiol*. 2005;58:951-958.
68. Curb JD, Abbott RD, MacLean CJ, Rodriguez BL, Burchfiel CM, Sharp DS, Ross GW, Yano K. Age-related changes in stroke risk in men with hypertension and normal blood pressure. *Stroke*. 1996;27:819-824.
69. Rodriguez BL, D'Agostino R, Abbott RD, Kagan A, Burchfiel CM, Yano K, Ross GW, Silbershatz H, Higgins MW, Popper J, Wolf PA, Curb JD. Risk of hospitalized stroke in men enrolled in the Honolulu Heart Program and the Framingham study: a comparison of incidence and risk factor effects. *Stroke*. 2002;33:230-236.

70. Jorgensen HS, Nakayama H, Raaschou HO, et al. Intracerebral hemorrhage versus infarction: stroke severity, risk factors and prognosis. *Ann Neurol* 1995; 38:45-50.
71. Abbott RD, Donahue RP, MacMahon SW, Reed DM, Yano K. Diabetes and the risk of stroke: the Honolulu Heart Program. *JAMA*. 1987;257:949-952.
72. Davis PH, Dambrosia JM, Schoenberg BS, Shoenberg DG, Pritchard DA, Lilienfeld AM, Whisnant JP. Risk factors for ischemic stroke: a prospective study in Rochester, Minnesota. *Ann Neurol*. 1987;22:319-327.
73. Barrett-Connor E, Khaw KT. Diabetes mellitus: an independent risk factor for stroke? *Am J Epidemiol*. 1988;128:116-123.
74. Boysen G, Nyboe J, Appleyard M, Soelberg S0rensen P, Boas J, Somnier F, Jensen G, Schnohr P. Stroke incidence and risk factors for stroke in Copenhagen. *Stroke*. 1988;19:1345-1353.
75. Alex M, Baron EK, Goldenberg S, Blumenthal HT. An autopsy study of cerebrovascular accident in diabetes mellitus. *Circulation*. 1962;25:663-673.
76. Reske-Nielsen E, Lundback K, Rafaelsen OJ. Pathologic changes in the central and peripheral neurons system of young long term diabetics, I: diabetic encephalopathy. *Diabetologia*. 1965;1:233-241.
77. WHO Study Group on Diabetes Mellitus. World Health Organization Tech Rep Ser 727. Geneva: World Health Organization; 1985.
78. Kragelund C, Omland T. A farewell to body-mass index? *Lancet*. 2005; 366:1589–1591.
79. Li C, Engstrom G, Hedblad B, Berglund G, Janzon L. Risk factors for stroke in subjects with normal blood pressure: a prospective cohort study. *Stroke*. 2005;36:234–238.
80. Jood K, Jern C, Wilhelmsen L, Rosengren A. Body mass index in mid-life is associated with a first stroke in men: a prospective population study over 28 years. *Stroke*. 2004;35:2764–2769.
81. Tanne D, Medalie JH, Goldbourt U. Body fat distribution and long-term risk of stroke mortality. *Stroke*. 2005;36:1021–1025.
82. Hebert PR, Gaziano JM, Chan KS, Hennekens CH. Cholesterol lowering with statin drugs, risk of stroke and total mortality: an overview of randomised trials. *JAMA* 1997; 278:313-21.
83. Shepherd J, Cobble SM, Ford I, et al. Prevention of coronary artery disease with pravastatin in men with hypercholesterolemia. *N Engl J Med* 1995; 333:1301-7.
84. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet* 1994; 344:1383-9.
85. Sack FM, Pfeffer MA, Moye LA, et al, for the Cholesterol and Recurrent Event Trial Investigators. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. *N Engl J Med* 1996; 335:1001-9.
86. Haque AKMF, Islam QT, Rahman KM et al. Serum Lipid as a Risk Factor of Ischaemic Stroke in Bangladeshi People. *J MEDICINE* 2012; 13 : 22-26.
87. Collaborative Group for the Study of Stroke in Young Women: Oral contraception and increased risk of cerebral ischemia or thrombosis. *N Engl J Med* 1973;288:871-78.
88. Collaborative Group for the Study of Stroke in Young Women: Oral contraceptives and stroke in young women, associated risk factors. *JAMA* 1975;231:718-22.
89. Wiebers DO: Ischemic cerebrovascular complications of pregnancy. *Arch Neurol* 1985;42:1106-13.
90. Fung TT, Rexrode KM, Mantzoros CS, Manson JE, Willett WC, Hu FB. Mediterranean diet and incidence of and mortality from coronary heart disease and stroke in women. *Circulation* 2009; 119: 1093–100.
91. Iso H, Baba S, Mannami T, et al. Alcohol consumption and risk of stroke among middle-aged men: the JPHC Study Cohort I. *Stroke* 2004; 35: 1124–29.
92. Reynolds K, Lewis B, Nolen JD, Kinney GL, Sathya B, He J. Alcohol consumption and risk of stroke: a meta-analysis. *JAMA* 2003; 289: 579–88.