ORIGINAL ARTICLE

RISK FACTORS FOR STROKE: A PROSPECTIVE HOSPITAL BASED STUDY

Javed Akhter Rathore, Zulfiqar Ali Kango, Munazza Nazir, Adnan Mehraj*

Department of Medicine, *Surgery, Sheik Khalifa Bin Zyad/Combined Military Hospital Muzaffarabad, Azad Kashmir

Background: The stroke is third leading cause of death in world and most patients die with an acute event in stroke. Various clinical variables have been investigated as risks factors of stroke. The study was aimed to identify these risks factors for stroke. **Methods:** This prospective study included 205 consecutive patients of stroke admitted in Combined Military Hospital/Sheik Khalifa Bin Zyad Hospital Muzaffarabad Azad Kashmir. The risk factors of stroke were investigated. Examination included clinical, neurological evaluation, laboratory tests, and brain CT. The follow-up at 14 days were done for all patients. Patients included were with acute first ever stroke onset of 48 hours of hospital admission. All patients completed a structured questionnaire and a physical examination and most provided blood for relevant investigations. **Results:** Two hundred and five cases stroke sub-types were (n=156, 76%, with ischemic stroke (CI); n=49, 24%, with intra-cerebral hemorrhagic stroke (ICH). The significant risk factors for all stroke were: Hypertension (p=0.003), diabetes (p=<0.001), Hypercholesterolemia (p=0.686); atrial fibrillation (p=0.445), cardiac diseases (p=0.938), smoking (p=0.926) for brain infarction and hypertension (p=0.002), diabetes (p=<0.001), Hypercholesterolemia (p=0.018); atrial fibrillation (p=0.449), cardiac diseases (p=0.749), smoking (p=0.829) for hemorrhagic stroke. Age significance (CI; p=0.247 vs. ICH; p=0.013) and age category significance were (CI; p=<0.001 vs. ICH; p=0.871) for subtype of stroke. High mRS (p<0.001) low GCS score (p<0.001) on admission were associated with worst outcome for both stroke subtype. These risk factors were all significant for CI as well as ICH**. Conclusions:** This study signifies the association of risks factors with acute stroke. Targeted interventions that reduce these risk factors could substantially reduce the burden of stroke

Keywords: Acute stroke; Risk factors, Outcome

J Ayub Med Coll Abbottabad 2013;25(1-2):19–22

INTRODUCTION

The stroke is third leading cause of death worldwide and 10% of patients with an acute ischemic stroke die as acute event.[1–5] Stroke has major impact on mortality, morbidity and economic burden. Various clinical risk factors have been associated with stroke. The identification of these risk factors is of prime importance for specific therapies.[6–8] and underdeveloped countries have largest burden of stroke estimated for more than 85% of stroke mortality worldwide.[4–5] A few studies show data to identify risk factors for stroke specifically for hemorrhagic stroke.[4–8] The international multi-centre case-control study designed to establish the association of risks factors of stroke has been reported previously.[9]

The objective of this study was to identify the risk factors for stroke.

MATERIAL AND METHODS

The patients who presented within 24 hours after symptom onset to our Hospital with a first-ever acute stroke were prospectively included from January 1st 2011 to June 2012. The WHO definition of stroke was used to define stroke.[10] The ethics committee approved this study. The stroke was diagnosed when neurological deficits were confirmed on CT scan brain in every patient. Patients with transient ischemic attack (TIAs) and sub-arachnoid haemorrhage (SAH) were excluded. A 12-lead ECG and echocardiography were done. Stroke severity on admission was assessed with mRS[11] and GCS. The history of pre-existing stroke risk factors was assessed. The hypertension was defined as history of hypertension or antihypertensive treatment or had two measurement of blood pressure BP >160/95 mm Hg or single measurement of BP>180/110 Hg during admission[12,13], diabetes mellitus was defined as by preadmission history of diabetes mellitus and its drugs or venous plasma glucose concentration of 7.0 mmol/l after an overnight fast on at least two separate measurement and or 11.1 mmol/l two hour post prandially[14], current cigarette smoking was defined as who smoked at least one cigarette/tobacco per day for preceding three months or more[7,15], Hypercholesterolemia defined as by preadmission history with cholesterol >5 mmol/l, and LDL-cholesterol >3 mmol/l[14] and history of coronary artery disease. The cause of death due to stroke declared unless another cause of death was found. Our approach to assessment of all key vascular risk factors, history of hypertension and diabetes mellitus, smoking and ischemic heart disease was consistent with international studies.[16–19]

Structured questionnaires were prepared and physical examinations were performed. Patients with stroke measurements were completed in the supine

position wherever appropriate. Blood pressure and heart rate were recorded on admission and after hospitalisation. Hypertension was defined with self-reported history of hypertension with blood pressure of higher than 160/90 mmHg (mean of two measurements). The data entry and analyses were done on SPSS-20. Chi square test both parametric and nonparametric done where appropriate for those in proportion. Quantitative data was expressed as mean and standard deviation. Stroke subtype both CI and ICH were cross tabulated as dependent variable to risk factors of stroke as independent variables to get p value which show association as such to each other. Data was reported in frequency tables. Differences between groups and the effect of patient characteristics on clinical outcome was also assessed

RESULTS

During the January 1st 2011 to June 31st 2012, 205 patients (mean age 63.78±10.03 years, range 45–85 years) were admitted to our hospital with a first-ever acute stroke. There were 111 males and 94 women (54.1% vs. 45.9%). The maximum frequency of stroke was seen between ages 55–74. Mean systolic blood pressure was 162±29.14. Mean diastolic blood pressure 102±19.46. Glasgow coma scale (GCS) and mRS were shown in table. Out of 205 stroke patients 156 (76%) had brain infarctions and 49 (24%) were having haemorrhagic stroke.

Hypertension was the most common risk factor 156 (76%) followed by hypercholesterolemia 145 (70.7 %) smoking 123 (60.0%) coronary artery disease 49 (24%) diabetes mellitus 34 (16.6%)) and atrial fibrillation 23 (11.2%). The mean fasting blood sugar was 6.50±2.42mmol/l and mean random blood sugar was 6.36±3.8 mmol/l. Mean cholesterol was 6.50±1.16 mmol/l.

Out of 205 patients with acute stroke 33 (16%) died. Mortality was common between ages 55–74 years. Significant association of stroke observed between age (p=0.013) and age category (p<0.001) as compared to gender. GCS score <1–8 revealed more mortality as compared to patient having GCS >9. Hemorrhagic stroke showed high mortality 17 (8.2%) as compared to ischemic stroke 16 (7.8%). Both have significant association with mortality. Clustering of risk factors along with comorbidities influenced the hospitals mortality. The mRS score depicting functional disability as well mortality prognosticator was associated with worst outcome with high as compared to lowest score (mRS 6 vs. mRS1-5). In our analysis high mRS score (p<0.001), low GCS score (p<0.001) on admission were associated with high mortality. (Table-1).

Table-1: Characteristics of stroke subtype according to risk factors, gender, GCS and mRS score

	Total	Cerebral infraction	*p*-value	Intra cerebral haemorrhage	**p*-value
N (%)	205	156 (76.0)		49 (24.0)	
Age (year) Mean±SD	63.78±10.03		0.237		0.013
45–54	43 (21.0)		<0.001		0.871
55–64	58 (28.3)				
65–74	67 (32.7)				<0.001
75–84	33 (16.1)				
≥85	1 (2.0)				
Male	111(54.1)	85 (76.6)	0.997	26 (23.4)	0.983
Female	94 (45.9)	71 (75.5)		23 (24.4)	
Risk factors					
Hypertension	156 (76.0)	113 (72.4)	0.003	43 (27.6)	0.002
Hypercholesterolemia	145 (70.7)	109 (75.2)	0.686	36 (24.8)	0.0181
Smoking	123 (60.0)	94 (76.4)	0.926	29 (23.6)	0.829
Cardiac Disease	93 (45.4)	72 (77.4)	0.938	21 (22.6)	0.749
Diabetes	34 (16.6)	25 (73.5)	0.023	9 (26.4)	<0.001**
Atrial Fibrillation	23 (11.2)	20 (87.0)	0.445	3 (13.0)	0.449
Outcome					
GCS 1–8	61 (29.8)		0.001		0.001
9–12	93 (45.4)				
13–15	51 (24.9)				
mRS Score					
Normal=0	4 (2.0)		0.002		0.001
ADL=1	14 (6.8)				
Mod. activity=2–3	37 (18.0)				
Mod. sever activity=4	69 (33.7)				
Sever disability=5	48 (23.4)				
Dead (mRS)=6	16 (7.8)			17 (8.2)	

*p-value for asym. 2-sided, **p-value for univariate analysis

DISCUSSION

Out of 205 patients the stroke subtype were brain infarction 156 (76%) and intra-cerebral haemorrhage 49 (24%) and in this study of risk factors for stroke all cases completed routine neuro-imaging. Our results showed that many risk factors accounted for more than 80% of all stroke, both in ischemic and intra-cerebral haemorrhagic stroke. The significant association of risk factors for stroke subtype were: Hypertension, diabetes, Hypercholesterolemia, atrial fibrillation, cardiac diseases, and smoking.

Age of the patients significantly correlated with ICH (p=0.013) while its correlation with CI was not significant (p=0.237). The high mRS (p<0.001) low GCS score on admission (p<0.001) were associated with worst outcome. Hypertension, IHD, smoking, diabetes mellitus, are common modifiable vascular risk factors for stroke as shown in previous epidemiological studies.[4,5,20–24] For both subtype of stroke we observed significant association with these risk factors which are modifiable save age. Our study help us to guide optimum selection of risk-factor target population to prevent CVA.[21,22.]

Our study showed that hypertension and its level was the most important potential risk factor for both stroke subtype, particularly for intra-cerebral haemorrhagic stroke as observed previously.[23] The hypertension underestimates the association as we used high cut point for blood pressure of 160/90 mm Hg. Estimated actual blood pressure is also problematic as it might be raised in acute stroke phase. Subsequently blood pressure might be lower than usual because of use of antihypertensive drugs and poor food intake. We used two mean reading in order to avoid these biases to minimum levels. The blood pressure is readily reduced by inexpensive drugs and salt reduction.[24]

Studies have shown stronger association of stroke risk with waist to hip ratio than with BMI as well as lack of physical activity.[19]

Smoking in our study was a strong risk factor for all subtype of stroke. Few studies showed smoking has no hazard.[25] The alcohol intake has relation with stroke.[26] Our study showed cholesterol having association with stroke as has been shown in other studies.[27]

An obvious limitation of our studies is apolipoproteins.[27] Waist/hip ratio, body mass index, diet physical activity and abdominal obesity have not been investigated as risk factors and their clustering in stroke as have been observed in previous studies. Diet has association with stroke.[28] However for almost all risk factors that relied on past medical history were substantiated on examination and investigations to establish their relationship to stroke.

In our study 16% patients died of stroke which is consistent with previous studies from Pakistan,[28,29] and developed countries.[30,31]

CONCLUSION

Stroke causes great morbidity and mortality. Hypertension, smoking, diabetes, hyper-cholesterolemia and ischemic heart disease are common risk factors for stroke. Potentially modifiable vascular risk factors needs to be looked for in order to prevent stroke. Larger scale national level case-control studies is required to assess the importance of risk factors for stroke.

REFERENCES

1. Carandang R, Seshadri S, Beiser A, Kelly-Hayes M, Kase CS, Kannel WB, *et al.* Trends in incidence, lifetime risk, severity, and 30-day mortality of stroke over the past 50 years. JAMA 2006;296:2939–46.
2. Rothwell PM, Coull AJ, Giles MF, Howard SC, Silver LE, Bullet LM, *et al*. Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire, UK from 1981 to 2004 (Oxford Vascular Study). Lancet 2004;363:1925–33.
3. Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, *et al*. Harrison's Principles of Internal Medicine. 16th ed. New Delhi: McGraw-Hill, Medical Publishing Division; 2005.p. 2372–93.
4. Feigin VL. Stroke in developing countries: can the epidemic be stopped and outcomes improved? Lancet Neurol 2007;6:94–7.
5. Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. Lancet Neurol 2007;6:182–7.
6. O'Donnell M, Yusuf S. Tackling the global burden of stroke: the need for large-scale international studies. Lancet Neurol 2009;8:306–7.
7. 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.
8. Donnan GA, Hankey GJ, Davis SM. Intracerebral haemorrhage: a need for more data and new research directions. Lancet Neurol 2010;9:133–4.
9. O'Donnell M, Xavier D, Diener C, Sacco R, Lisheng L, Zhang H, *et al*. Rationale and design of INTERSTROKE: a global case-control study of risk factors for stroke. Neuroepidemiology 2010;35:36–44.
10. Hatano S. Control of stroke in the community, methodological consideration and protocol of WHO stroke register. Geneva WHO 1973; 98. Document No. CVD/S/73
11. Sandercock PA, Warlow CP, Jones LN, Starkey IR. Predisposing factors for cerebral infarction: the Oxfordshire community stroke project. Br Med J 1989;298:75–80.
12. Van Rossum CT, van de Mheen H, Breteler MM, Grobbee DE, Mackenbach JP. Socioeconomic difference in stroke among Dutch elderly women. Stroke 1999;30:357–62.
13. Hamidon BB, Raymond AA. The Impact of Diabetes mellitus on in-hospital strokes Stroke mortality. J Postgraduate Med 2003;49:307–10.
14. Togha M, Bakhtavar K. Factors associated with in-hospital mortality following intracerebral hemorrhage: a three-year study in Tehran, Iran. BMC Neurology 2004;4:9.
15. Song YM, Cho HJ. Risk of stroke and myocardial infarction after reduction or cessation of cigarette smoking: a cohort study in Korean men. Stroke 2008;39:2432–8.
16. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F *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(9438):937–52.
17. McQueen MJ, Hawken S, Wang X, Ounpuu S, Sniderman A, Probstfield J, *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.
18. Teo KK, Ounpuu S, Hawken S, Pandey MR, Valentin V, Hunt D, *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.
19. Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commer ford P, *et al*, on behalf of the INTERHEART Study Investigators. Obesity and the risk of myocardial infarction in 27000 participants from 52 countries: a case-control study. Lancet 2005;366:1640–9.
20. Sacco RL, Khatri M, Rundek T, Xu Q, Gardener H, Boden-Albala B, *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.
21. Hankey GJ. Potential new risk factors for ischemic stroke: what is their potential? Stroke 2006;37:2181–8.
22. 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.
23. Ezzati M, Hoorn 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.
24. Appel LJ, Anderson CA. Compelling evidence for public health action to reduce salt intake. N Engl J Med 2010;362:650–2.
25. 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.
26. Prospective Studies Collaboration. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55000 vascular deaths. Lancet 2007;370:1829–39.
27. Di Angelantonio E, Sarwar N, Perry P, Kaptoge S, Ray KK, Thompson A, *et al*. Major lipids, apolipoproteins, and risk of vascular disease. JAMA 2009;302:1993–2000.
28. Razzak AA, Khan BA, Baig SM. Ischemic strokes in young adults of South Asia. J Pak Med Assoc 2002;52:417–22.
29. Fayyaz M, Hassan MA, Atique MH. Risk factors and early prognosis in stroke. Ann King Edward Med Coll 1999;5;12–5.
30. Sarti C, Rastenyte D, Cepaitis Z, Tuomilehto J. International trends in mortality from stroke, 1968 to 1994. Stroke 2000;31:1588–601.
31. Kelly-Hayes M, Wolf PA, Kannel WB, Sytkowski P, D'Agostino RB, Gresham GE. Factors influencing survival and need for institutionalization following stroke: the Framingham Study. Arch Phys Med Rehabil 1988; 69:415–8.

Address for Correspondence:

Dr. Javed Akhtar Rathore, Assistant Professor of Medicine, AJK Medical College, Sheik Khalifa Bin Zyad/Combined Military Hospital Muzaffarabad, Azad Jammu & Kashmir. **Cell:** +92-355-8106847
Email: drjavedrathore111@yahoo.com