Review Article

Stroke in Pakistan

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Abstract

Stroke is the most common cause of disability and a leading cause of mortality world wide. Though the incidence is falling in West but probably is rising in Asia. The burden of stroke risk factors in Pakistan is enormous e.g. by 2020 Pakistan will be 4th most populous country in terms of diabetic patients. Similarly every 3rd person above age of 45 years has hypertension. Ironically a great majority of these patients are unaware of their diagnosis. This is further complicated by the fact that most of diagnosed patients have uncontrolled hypertension, as a result of poor compliance on patients part and poor updated knowledge on physicians part. Data on stroke incidence and prevalence from Pakistan is scarce, however, there are several reported case series in literature highlighting significant differences in terms of stroke epidemiology, risk factors and stroke subtypes/ patterns. Considering a high population, absolute number of stroke in our country would be in millions. Its consequences are myriad ranging form physical disability to death, to psychologic, social and economic consequences. These consequences do not only affect the individual or his/her family but also society as a whole. We reviewed available literature on stroke and its risk factors from Pakistan.

Introduction

Pakistan is sixth most populous country in the world with an estimated population of approximately 167 millions by July 2008.[1] There are no sizeable community based epidemiologic studies on stroke from Pakistan. Stroke is the third most common cause of death and the first leading cause of disability in developed and developing countries.[2] According to World Health Organization estimates, 5.5 million people died of stroke in 2002, and roughly 20% of these deaths occurred in South Asia.[3]

Contrary to decline in the incidence of the disease in the Western population, the burden of the disease in South Asian countries (India, Pakistan, Bangladesh, and Sri Lanka) has inclined and is expected to rise.[4]

Epidemiology

No large scale epidemiological studies are available to determine the true incidence of stroke in Pakistan. Estimated annual incidence is 250/100,000, translating to 350,000 new cases every year.[5] At a major University hospital with a busy Neurology service in Karachi, 519 patients with stroke were admitted over a 22 month period.[6] In a retrospective analysis of patients admitted with stroke in two major hospitals over an 8 years period, 796/12,454 (6.4%) of consecutive cases admitted in medical units had stroke.[7]

A recent community survey in Kolkata, carried out by the Indian Council of Medical Research, showed the average annual incidence of stroke as 145 per 100,000 persons per year.[8] These rates are also much higher than those reported previously from other parts of India. In China, the total average age-adjusted incidence of first-ever stroke ranged from 116 to 219 per 100 000 per year.[9]

There is only one published stroke prevalence study from Pakistan, conducted on adult Pushtoon community residing in Karachi. This study reports a prevalence of 4.8% which was alike in men and women.[10] This is highest ever reported prevalence of stroke in the world. However, the results of this study should be interpreted with caution as a non validated questionnaire was used. A recently reported community survey in Kolkata revealed a stroke prevalence rate of 545 per 100,000 population, which is equal to or higher than that reported from developed countries.[8]

Demographics of stroke in community are lacking but hospital based studies have revealed relatively high proportion of young stroke. Khan JA et al reported that 68/260 (26%) of their patients were of 15-45 years of age.[11] Vohra et al reported that 34% of patients in their series were under age of 50 years7 . Syed et al reported a frequency of 28% of young stroke under age of 55 years.[6]

The mean age of patients with stroke varies from 52-66 years in various studies and the male to female ratio is about 1.5.[6,7,12-14] The relatively younger age of onset in patients with stroke is in keeping with the data of coronary heart disease from the Indian subcontinent which suggest that CHD manifests almost 10 year earlier on average in this region compared with the rest of the world.[15]

Vascular risk factors among Stroke patients

In the only population based study among Pushtoons community in Karachi, Systolic BP, diabetes, and increased dietary salt (extra dietary table salt on top of what has

already been included while cooking) intake were identified as independent risk factors of stroke.[10] This was an epidemiologic survey based on invalidated questionnaire and no imaging study was performed to confirm the diagnosis.

Despite this dearth of population based published literature, a number of hospital-based case series are published on the subject, mainly in local medical journals.

Largest published series on stroke to date, from Pakistan is of 796, published in 2000. Major limitation of this study was that imaging was performed in only 144 (19%) cases and in rest of the patients diagnosis was made on clinical grounds alone.[7] Later from same center prospectively collected data of 281 first ever stroke was published.[16] Second largest study was a prospective stroke data bank at a tertiary care center, which enrolled 596 patients, including subarachanoid haemorrhage, over a period of 22 months.[6]

The profile of major modifiable risk factors is essentially similar to the one seen in stroke patients elsewhere in the world. Most common risk factors in ischaemic stroke were diabetes mellitus and hypertension. Syed et al reported that approximately 77% of their cohort had diabetes mellitus, hypertension or both.[6]

In relatively large case series i.e. series of at least 200 patients, hypertension was the most common modifiable risk factor (43-66%).[6,7,12,14,16,17] Other important modifiable risk factors include diabetes mellitus (27-42%)[6,7,12,14,16,17], dyslipidemia (19-30%)6,12,14,16, smoking (11-43%)[7,12,14,16], ischaemic heart disease (9-46%)[7,12,14,17], previous stroke or TIA (11-26%).[6,7,14,16] These larger series did not report obesity however atrial fibrillation (AF) and oral contraceptive pills (OCP) were reported in 3 and 1% respectively.[12] However, some smaller series have reported a higher frequency for AF and OCP i.e. 12 and 10% respectively.

Interestingly only a few studies reported on extracranial carotid disease. Khan S et al reported that about 19% of patients in their series had 'significant carotid disease', defined by either stenosis of >70% or nonstenotic ulcerated plaque.[16] However they did not report separate figures. Others reported a frequency of significant carotid artery disease, defined by =70% stenosis, 7%.[18]

Hypertension was the commonest risk factor even in young patients (<45 years) with stroke. A series of young stroke report pregnancy (19%), infections (12%) and vaculitis (6%) as important etiologic factors.[11] Other reported risk factors in young stroke patients were dyslipidaemia, smoking and obesity, antiphospholipid antibody syndrome, migraine and secondary thrombocytosis.

Vascular risk factor burden among community

Burden of major vascular risk factors i.e. hypertension, diabetes mellitus, smoking, dyslipidaemia and obesity is enormous in Pakistan. A cross sectional survey at a community health center in a tertiary care hospital revealed that 39% of the people aged 18 years or above have either hypertension, dyslipidaemia and history of active smoking.[19] Same study reported family history of ischaemic heart disease in 42%, obesity in 24%, hypertension in 19%, and diabetes mellitus in15% of the subjects.[19] The participants were healthy adults for routine preventive checkups. Only 40% of hypertensive patients had controlled blood pressure.[19]

Hypertension is the single most important modifiable risk factors for both ischaemic and haemorrhagic stroke. The National Health Survey of Pakistan (1990-4) highlighted the enormous burden of hypertension in the country.[20] The overall prevalence of hypertension in Pakistanis aged 15 years and above was 19.0% (95% CI; 18.9-19.1).[21] Twenty-two percent of the urban Pakistani population over the age of 15 years, and a third of those aged 45 years and above, had hypertension.[20] The age-standardized prevalence varied strikingly, from 17.3 to 25.3% in men and from 9.9 to 41.4% in women, among the various ethnic groups, being highest in Balochi women and lowest in Sindhi women.[24] Higher prevalence of hypertension in the urban dwellers is due to an excess of obesity in this population.[20] They also showed a linear relation between age and systolic blood pressure.[21]

Alarmingly, more than 70% of people with hypertension were unaware of their condition, and less than 3% had adequately controlled blood pressure.[20] Ironically physicians in general practice are using wrong cut offs (higher cut offs) to treat hypertension and this further contributes to under diagnosis, under treatment and poor control of hypertension. This logically can be a major, potentially modifiable, risk factor of stroke. A cross sectional survey among 1000 physician in urban areas of the country, found that approximately 30% of physician were using wrong cut off for diagnosis of blood pressure in persons under age of 60 years and this figure rose to approximately 80% for population aged over 60 years.22 Similarly high proportion of physicians were using inappropriate or suboptimal therapy e.g. 24% using sedatives as first line therapy either alone or in combination with antihypertensive medications.[22]

Diabetes mellitus is another important modifiable risk factor for stroke. Pakistan holds more than 5 millions diabetic patients which is expected to rise to 3.9 millions by 2020, leading Pakistan to 4th most populous country

accommodating patients with diabetes mellitus.[23]

According to the National Health Survey, 25% of peoples over age of 45 years in Pakistan suffer from Diabetes mellitus.[20] Further analysis of this data revealed that prevalence of DM among population aged 15 years and above was 5.4% (95% CI; 4.9-5.9) with significant ethnic differences i.e. highest in Muhajirs and lowest in Balochs.[24]

Ischaemic heart disease (IHD) is an important vascular disorder which not only shares pathophysiology to stroke but also increase risk of ischaemic stroke. In a population-based cross-sectional survey on 320 randomly selected adults aged 40 years or above to determine the prevalence of IHD and its risk factors in Karachi, the overall prevalence of IHD was 26.9% (95% CI; 22.3-32). Thirty percent of the women and 23.7% of men had IHD.[25]

Based on the data of National Health Survey of Pakistan, the overall prevalence of smoking among individuals aged 15 years or older was 15.2%.[26] Gender was the strongest predictor of smoking: the prevalence of smoking was 28.6% in men versus 3.4% in women.[26]

The National Health Survey of Pakistan showed 25.0% of the Pakistani population to be overweight or obese according to the Asian-specific BMI cutoff value of 23 kg/m2 and 10.3% to be obese according to the BMI cutoff value of 27 kg/m^2.[27] Prevalence of obesity among urban residents was 2.5 times greater than among rural residents.[27] Same data revealed ethnic and gender differences with higher waist circumference in Sindhi women and lowest in Sindhi men.[27]

In a study of 370 healthy adult Pakistanis presenting for general medical checkup, 21% patients had fasting cholesterol of 200-239 and 10.3% had greater than 240mg/dl[19] while the National health Survey reported that 12% population above age 15 years is suffering from Hypercholestremia.[20]

Rheumatic heart disease is an important cause of embolic vascular events including strokes in developing countries. In a community based study from rural Pakistan, a prevalence of approximately 6/1000 was observed.[28] High prevalence of these risk factors is further compounded by alarmingly poor awareness in both community and general physicians. Less than 20% of those found to have RHD were aware of their diagnosis before participation in this study and only three affected people (8%) were taking rheumatic prophylaxis.[28] Poor awareness among patients leads to under diagnosis and poor compliance while suboptimal awareness of physicians results in inappropriate and suboptimal treatment.

The incidence of infective endocarditis was found to be 32 per 1000 (3.2%) hospital admissions in a tertiary paediatric cardiology referral center with rheumatic heart disease being the most common underlying heart lesion.[29] Collectively risk of long term vascular outcomes of these chronic diseases would be enormous.

Stroke Subtypes

In hospital-based studies, 22-31% of patients had intracerebral haemorrhage (ICH).[6,7,14,16,30] A higher figure is reported in young stroke patients (32-43%).[11]

Couple of studies has reported about predictors of ischaemic versus haemorrhagic stroke. One study reported that there was significantly high prevalence of diabetes mellitus, heart disease, history of TIA and family history of stroke in patients with ischaemic stroke as compared to haemorrhagic stroke.[16] However they did not look at their independent role in predicting the stroke subtype. Khealani et al reported that in hypertensive patients, diabetes mellitus and ischaemic heart disease are independent predictors of ischaemic stroke.[31]

One study reported ischaemic stroke subtypes in patients prospectively enrolled in the Aga Khan University acute stroke data bank. The ischaemic stroke group was classified according to the TOAST criteria and comprised of lacunar 168/393 (42.7%); large artery atherosclerosis 106/393 (26.9%); cardioembolic 24/393 (6.1%); undetermined 80/393 (20.3%); and other determined types 15/393 (3.8%).[6] The high proportion of lacunar strokes in our population was attributed to high burden of inadequately treated hypertension and diabetes. Cardioembolic stroke were relatively infrequent. Similar results have been noted in other studies.

Outcome of stroke

Stroke-related mortality in the acute stage has been reported in the range of 11-30%.[7,13,14,32] One study found hyperglycaemia in acute ischaemic stroke in non-diabetic patients to be a predictor of both mortality and poor functional outcome at one month. Forty four percent of patients in the hyperglycaemic group and 20% in the normoglycaemic group died within 4 weeks of stroke.[33] Age>60 years, unconsciousness at the time of presentation, severe hypertension, and diabetes mellitus have been identified as poor prognostic factors.[7,32] Ahmed et al in their retrospective series of 221 patients with ICH reported that intraventricular extension, low GCS and systolic BP >180mmHg predict inpatient mortality.[32] Half of the patients, who died, expired during first 2 days of admission.

In one study, investigators followed up the patients at one month with modified Rankin Scale and Glasgow Coma Scale. Mortality was noted in 2%, poor outcome in 76% and excellent outcome in 22% of patients.[34]

A study by Hassan et al reported that 23% of patients with stroke developed stroke associated pneumonia, of which 34% died during hospital stay. Same study reported median hospital stay of 9 days inpatients with pneumonia compare to 4 days in patients who did not develop pneumonia.[35]

Conclusions

Despite the lack of high quality epidemiological data, the burden of stroke seems to be high in Pakistan as in other south Asian countries. Not only the mean age of patients with stroke is less compared to patients in the developed world, approximately 20% of patients are under the age of 45 years. Hypertension is by far the most common risk factor also in young stroke patients. Hypertension and other conventional risk factors are highly prevalent in the country. Although Ischaemic strokes are more common than haemorrhagic strokes, the relative proportion of intracerebral haemorrhage is higher compared to the Western population. Lacunar infarct is the most common stroke subtype while cardioembolic strokes are less common. High quality stroke services are not widely available and there is an urgent need of improvement in infrastructure to conduct well-designed epidemiological studies, create awareness in general public regarding stroke and improve capacity building in order to meet the future challenges.

References

1. Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet 1997; 349: 1269-76.
2. Feigin VL. Stroke epidemiology in the developing world. Lancet 2005; 365: 2160-61.
3. World Health Organization (WHO). The Atlas of Heart Disease and Stroke. http://www.who.int/cardiovascular_diseases/resources/atlas/en/
4. Bulatao RA, Stephens PW. Global estimates and projections of mortality by cause. Washington, DC: Population, Health and Nutrition Department; World Bank, preworking paper 1992;1007.
5. www.pakstroke.com. An official website of Pakistan stroke society. Last accessed on April 5, 2008.
6. 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: 584-88.
7. Vohra EA, Ahmed WU, Ali M. Aetiology and prognostic factors of patients admitted for stroke. J Pak Med Assoc. 2000; 50: 234-36.
8. Das SK, Banerjee TK, Biswas A, Roy T, Raut DK, Mukharjee CS et al A prospective community based study of stroke in Kolkata , India. Stroke 2007;38: 906-10. Epub 2007.
9. Liu M, Wu B, Wang WZ, Lee LM, Zhang SH, Kong LZ. Stroke in China: Epidemiology, prevention and management strategies. Lancet Neurol 2007;6:456-64
10. Jafar TH. Blood pressure, diabetes and increased dietary salt associated with stroke- results from a community-based study in Pakistan. J Hum Hypertens 2006;20:83-85
11. Khan JA, Shah MA. Young stroke : Clinical aspects. J Coll Physicians Surg Pak 2000;10:461-66
12. Khan H, Afridi AK, Ashraf S. A hospital based study on stratification of risk factors of stroke in Peshawar. Pak J Med Sci 2006;22:304-07
13. Alam I, Haider I, Wahab F, Khan W, Taqweem MA, Nowsherwan. Risk factors stratification in 100 patients of acute Stroke. J Postgrad Med Inst 2004;18:583-91.
14. Qureshi M A , Jamshaid T D , Siddiqui A M . Stroke - A study of clinical patterns and risk factors. Ann King Edward Med Coll Jun 2003;9:98-100.
15. Yusuf S, Hawken S, Ounpuu S, Dans T, Avesum A, Lanas F. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004; 364 : 937-52.
16. Khan SN, Vohra EA. Risk factors of stroke: A hospital based study. Pak J Med Sci 2007;23:17-22.
17. Razzaq AA, Khan BA, Baig SM. Ischemic stroke in young adults of South Asia. J Pak Med Assoc 2002; 52:417-22.
18. Razzaq AA, Khan BA, Jadoon CK, Baig SM. Carotid Doppler ultrasonography in young stroke patients. J Pak Med Assoc 1999; 49:97-99.
19. Iqbal SP, Dodani S, Qureshi R. Risk factors and behaviors for coronary artery disease (CAD) among ambulatory Pakistanis. J Pak Med Assoc 2004;54:261-66.
20. Jafar TH, Levey AS, Jafary FH, White F, Gul A, Rahbar MH, et al. Ethnic subgroup differences in hypertension in Pakistan. J Hypertens 2003;21:905-12.
21. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of Diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004; 27: 1047-53.
22. Jafar TH, Levey AS, White FM, Gul A, Jessani S, Khan AQ, et al. Ethnic differences and determinants of diabetes and central obesity among South Asians of Pakistan. Diabet Med 2004;21:716-23.
23. Jafar TH, Jafary FH, Jessani S, Chaturvedi N. Heart disease epidemic in Pakistan: women and men at equal risk. Am Heart J. 2005;150:221-26.
24. Ahmad K, Jafary F, Jehan I, Hatcher J, Khan AQ, Chaturvedi N, et al. Prevalence and predictors of smoking in Pakistan: results of the National Health Survey of Pakistan. Eur J Cardiovasc Prev Rehabil. 2005;12:203-08.
25. Jafar TH, Chaturvedi N, Pappas G. Prevalence of overweight and obesity and their association with hypertension and diabetes mellitus in an Indo-Asian Population. CMAJ 2006;24:1071-77.
26. Rizvi SF, Khan MA, Kundi A, Marsh DR, Samad A, Pasha O. Status of rheumatic heart disease in rural Pakistan. Heart 2004;90:394-99.
27. Sadiq M, Nazir M, Sheikh SA. Infective endocarditis in children-incidence, pattern, diagnosis and management in a developing country. Int J Cardiol. 2001;78:175-82.
28. Li C, Engstrom G, Hedblad B, Berglund G, Janzon L. Blood pressure control and risk of stroke. A population based prospective cohort study. Stroke 2005;36:725-30 Epub 2005.
29. Jafar TH, Jessani S, Jafary FH, Ishaq M, Orakzai R, Orakzai S, Levey AS, Chaturvedi N. General practioners' approach to hypertension in urban Pakistan. disturbing trends in practice. Circulation 2005;111:1278-83.
30. Iqbal F. Patient profile of 200 cases of stroke: A hospital based study. Proceeding Shaikh Zayed Postgrad Med Inst. 2001; 15:11-22.
31. Khealani BA, Syed NA, Maken S, Mapari UU, Hameed B, Ali S, et al. Predictors of ischemic versus hemorrhagic strokes in hypertensive patients. J Coll Physicians Surg P 2005;15:22-25.
32. Ahmed R, Shakir AH, Moizuddin SS, Haleem A, Ali S, Durani K, et al. Predictors of in hospital mortality for intracerebral hemorrhage: A hospital based study in Pakistani adults. J Stroke Cerebrovasc Dis. 2001; 10:122-27.
33. Saif M Saif I, Khan MN, Jehanzeb, Anwar W. Stress hyperglycemia and mortality in patients with acute ischemic stroke. Pak Armed Forces Med J 2006;56:120-4
34. Khan SN, Vohra EA. Evaluating the outcome of stroke: a prospective hospital based study. J Postgrad Med Inst 2006;20:30-35.
35. Hassan A, Khealani BA, Shafqat S, Aslam M, Salahuddin N, Syed NA, et al. Stroke associated pneumonia: microbiologic data and outcome. Singapore Med J 2006;47:204-07.