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Ischemic Stroke Subtypes in Pakistan: The Aga Khan University Stroke Data Bank

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Abstract

Objective: Frequency of ischemic stroke subtypes is influenced by ethnic and geographic variables. Our objective was to identify various stroke subtypes and its determinants at a tertiary care hospital.

Methods: We prospectively collected data on ischemic stroke subtypes admitted to The Aga Khan University Hospital in Karachi.

Results: A total of 596 patients were enrolled in 22 months in the Aga Khan Universtiy Stroke Registry. These included 393 patients with Ischemic stroke, 126 patients with intracerebral hemorrhage, 50 patients with subarachnoid hemorrhage and others. The ischemic stroke group was classified according to the TOAST criteria and comprised of lacunar 168/393 (42.7%); large artery atherosclerosis 106/393 (26.9°/x); cardioembolic 24/393 (6.1%); undetermined 80/393 (20.3°!0); and other determined types 15/393 (3.8%). The high proportion of lacunar strokes in our population may be due to high burden of inadequately treated hypertension and diabetes. Clear cut cardioembolic stroke was relatively infrequent in our population.

Conclusion: Lacunar stroke is the most common subtype of stroke in our patient population. This is most likely secondary to uncontrolled hypertension (JPMA 53:584;2003).

Introduction

The various stroke subtypes have demonstrated significant variability between different geographical regions as well as different ethnic groups within the same geographic region.[1-10] These differences in stroke characteristics have significant impact on strategies of stroke prevention, diagnosis and treatment.

Stroke data banks are helpful in elucidating the risk factors and stroke subtypes in target populations. Although population based studies are superior in answering questions such as incidence and prevalence, hospital based stroke data banks have the advantage of more uniformly evaluating patients with ancillary investigations such as magnetic resonance imaging (MRI), carotid doppler ultrasonography etc. This may result in a more reliable determination of stroke subtype and underlying risk factors.

This paper presents the results of the hospital based Aga Khan University Stroke Data Bank evaluating stroke patients admitted to a large tertiary care medical center between August 1999 and May 2001.

In the present study we analyzed the data to study the distribution of different stroke types, and to determine the relative frequency of some well established vascular risk factors in our stroke population. To our knowledge, such a prospective study has not been undertaken in Pakistan.

Methods

The Aga Khan University Hospital is a major tertiary care health facility with a busy Neurology service. Acute stroke patients presenting to the hospital were admitted to the Neurology Service. All acute stroke patients over the age of 14 yrs are eligible to be enrolled in the Aga Khan University Stroke Data Bank. Patients with subarachnoid, subdural or epidural hemorrhage are excluded from the Data bank. The data Bank has been prospectively enrolling acute stroke patients since August 1999.

Acute stroke was defined as rapidly evolving focal or global loss of cerebral function with symptoms leading to death or lasting more than 24 hours due to a vascular etiology.

The definition of the strokes subtypes was adapted from the TOAST trial 12 (Trial of Org 10 172 in Acute Stroke Treatment):

1) Large artery atherosclerosis; clinical and radiological findings of either occlusion or stenosis (>50 %) of major brain artery or branch cortical artery and absence of features suggestive of other stroke subtypes,

2) Small artery occlusion (lacunar strokes); clinical lacunar syndrome, with no evidence of cortical dysfunction, and either a normal brain CT/MRI or a relevant subcortical hemispheric / brain stem infarction of less than 1.5 cin. No evidence of other stroke subtype.

3) Cardioembolism; at least one major cardiac risk factor for embolism and absence of features to suggest other stroke subtype,

4) Stroke of other determined etiology; absence of features suggestive of aforementioned stroke subtypes and evidence of other risk factors of stroke e.g. a hypercoagulable state, nonatherosclerotic vasculopathy etc, and

5) Stroke of undetermined etiology; presence of two or more potential causes of stroke or no etiology found despite extensive workup or no etiology found because of cursory evaluation.

Table. 1. Distribution of ischemic stroke subtypes in **our study.**

Stroke Type	Lacunar	Large vessel	Other determined	Cardioembolic	Undetermined
No. of patients	168	106	15	24	80
Percentage	42.7%	26.9%	3.8%	6.1%	20.3%

Table 2. Age **and sex distribution across different stroke subtypes (adapted from** Yip et a127).

Characteristics	Large-artery atherosclerosis (n=106)	Lacunae (n=168)	CEI (n=24)	Stroke of other determined etiology (n=15)	All ischemic strokes	Stroke of undetermined etiology 01=80)
Men	79(74.5%)	99(58.9%)	14(58.3%)	8 (53.3%)	246(62.6%)	46 (57.5%)
Mean (SD)	60.6+ 14.3	60.7+ 11.8	58.8+ 14.6	57+ 14.5	60.5+ 13.1	59.8+14.4

Hypertension was defined as a past medical history of hypertension (whether treated or not) or electrocardiographic or echocardiographic evidence of hypertension

Diabetes Mellitus was defined as a past medical history of diabetes mellitus or sustained blood sugar elevation requiring treatment with hypoglycemic agents or insulin throughout hospitalization.

Abnormal cholesterol elevation was defined as history of high cholesterol in the past or documentation of elevated cholesterol during hospital stay.

Cardiac disease was defined as cardiac arrhythmia, valvular heart disease, ischemic heart disease, or congestive cardiac failure present on past medical history or documented during hospitalization.

Patients were worked up according to established clinical pathway, and investigations included Neuroimaging (CT or MRI), electrocardiogram, transthoracic echocardiogram, complete blood count, coagulation profile, serum electrolytes, blood urea nitrogen, creatinine, Urine detailed report, and carotid doppler ultrasonography (ischemic stroke). Selected patients underwent transesophageal echocardiogram with bubble contrast, 24 hours hotter monitoring and work up for hypercoagulable state.

All patients were evaluated by a consultant neurologist, and the data was encoded by neurology housestaff on a standardized data entry form. The data was collected during the patient's hospital stay and the patient's discharge was the end point for the purpose of this study.

The data was analyzed using SPSS 10.0 for Windows. The data is presented in means, median and percentages.

Results

During the 22 month period, there were 596 patients enrolled in the AKU acute stroke data bank. Three hundred and ninety three of these patients suffered from ischemic stroke and 126 were diagnosed with a primary intracerebral hemorrhage. Twenty seven patients were considered not to have suffered a stroke (22 TIA, two psychogenic symptoms and one metabolic encephalopathy presenting as a stroke). An additional 50 patients with subarachnoid hemorrhage were enrolled, but excluded from analysis.

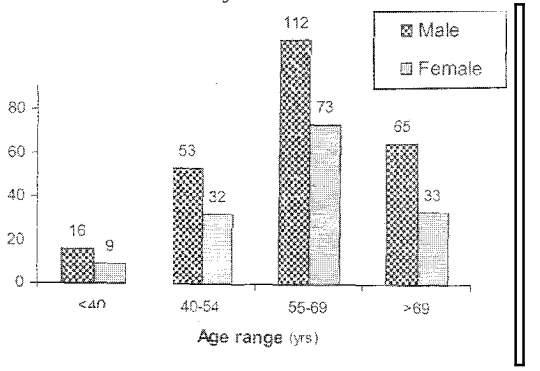

Figure. Age and sex distribution for all ischemic stroke patients

Our study focuses on the ischemic stroke group. 1i,. this group, there were 246 (62.6%) men and 147(37.4%) women, male to female ration of 1.67. The mean age was 60.5 years (sd 13.1), with median of 61 years and range 15-100 years (Figure). The frequency of various stroke subtypes is summarized in Table 1.

Hypertension was the most common risk factor (260 patients, 66.2%), followed by Diabetes (163 patients, 41.5%).

'fable 3. Relative Incidences of Cerebral Infarction Subtypes Reported From Selected Stroke Registry Studies.

Study	Author	No. of patients	Large-vessel atherosclerotic	Lacunar	Embolic	Cardioembol is	Undetermined Cause
Harvard	Mohr[28]	579	233(40)	131 (23)	215 (37)	112(19)	---
Austin Hospital	Chambers[29]	580	263(45)	140(24)	---	51 (9)	126(21)
Pilot SDB	Kunitz[30]	708	172(24)	100(14)	200(28)	---	236(33)
CHSPs	Yatsu[31]	3727	1 880 (50)	---	636(17)	---	1240 (33)
Lausanne	Bogousslavsky[32]	891	427(48)	147(16)	---	204 (23)	74(8)
Lehigh Valley	Friday[33]	2386	1590 (67)	246(10)	516(22)	---	34(l)
NINCDS SDB	Sacco et a[34]	1273	182 (14)2	337(27)	---	246(19)	508(40)
UCSD SDB	Rothrock et a[1 35]	500	88 (18)	133 (27)	---	110(22)	117(23)
SCAN IV	Yip et al, 1997	676	113 (17)	195(29)	---	133 (20) -	196(29)
AKU	Syed et al, present study	---	106(26.9%)	168(42.7%)	---	24(6.1%)	80(20.3%)

Of all patients admitted with an ischemic stroke, 301 (76.6%) had either diabetes mellitus or hypertension or both. A history of previous stroke or TIA was found in 103 ischemic stroke patients (26.2%). Dylipidemia was present in 87 patients (22.1 %).

The age and sex distribution across different stroke subtypes is shown in Table 2. There was little variability in age across the different stroke subtypes. Interestingly, patients suffering large vessel atherosclerotic strokes revealed a higher probability of being male.

Discussion

Stroke is the second most common cause of death world wide [13] and the third most common cause of death in the developed world. Strokes cause over 5.5 million deaths annually [14] and two thirds of these occur in the developing world.[15]

The burden *of* stroke on the society is immense with emotional, financial and functional loss that is difficult to estimate. There is no cost effective curative therapy for stroke and the bulk of public health initiatives are focused on prevention. Prevention of strokes (and indeed diagnosis and therapy) requires an in-depth understanding of the stroke subtypes and etiologic factors which differ by geographic region, and even by ethnicity within the same region. The variation in stroke subtypes is of global relevance in view of the world wide migration of populations.

Large Community based stroke registries are likely to provide more accurate analysis of incidence while hospital based studies are likely to underestimate very mild and immediately fatal strokes. However, hospital based studies would be able to provide a more uniform work-up of stroke, allowing for a more accurate analysis of stroke subtypes and etiologic factors.

Our hospital based prospective study aims to elucidate the various stroke subtypes among ischemic stroke in Pakistan. Toast criteria were chosen for determining stroke subtypes for this prospective study due to well established interphysician agreement.[16] To our knowledge, this is the only prospective study *of* stroke subtypes in Pakistan.

Hypertension is the most powerful and important modifiable risk factor for stroke.[17-19] An increase of the diastolic blood pressure of as little as 6 mm hg results in 36% higher risk of stroke.'-[0]

The prevalence of hypertension in our study is high (66.2%), and is similar to other published studies such as OXVASC (55.9%,), OCSP (65.5%). [21,22]

Our data contrast with lower rates reported from Sweden (32%)[23] and Switzerland (44%)."[4] This variability in prevalence of hypertension is well established in the multinational MONICA project.'-[5]

Our high prevalence of hypertension is comparable to stroke patients in other south-east Asian countries.=[6] it underscores the need to target under treatment of major public health problems and indicates the need to incorporate treatment of hypertension into health care policy measures to reduce the morbidity and mortality of stroke.

A limitation of our study is although the study spanned over a long period of time, but due to logistical reasons, there were intervals during the study period when the patients were not recruited into the stroke data bank. However, the patients that were recruited into the data bank are representative of the stroke population admitted to our

hospital. So although our numbers may be relatively small compared to the larger stroke registries, but we are still able to derive useful information and inferences from our data.

Table 3 compares the finding of ischemic stroke subtypes in our study with other selected stroke registries.[27]

The lower incidence of cardioembolic stroke in our population (6.1 %) is in contrast to the rates generally noted in stroke registries, which are often above 20%. This may be due to ethnic differences such as the relatively higher incidence of lacunar strokes in our population. Additionally, higher incidence of co-morbid conditions such as hypertension, diabetes and dyslipidemias may lead to a greater proportion of cardioembolic strokes being classified into the undetermined etiology category due to the concomitant presence of 2 or more etiologic processes. Additionally, the under recognition and under treatment of hypertension and diabetes in the population could hypothetically lead to over representation of strokes etiologically related to hypertension and diabetes in our population. Our criteria for diagnosing cardioembolic stroke were strict. Over fifty percent of electrocardiograms (198/371) were abnormal, but all these patients were not considered cardioembolic strokes. Categorization as a cardioembolic required a clear abnormality such as atrial fibrillation, and the absence of features suggestive of other stroke subtypes (for example large artery atherosclerosis, and small vessel occlusion).

The most common stroke subtype was lacunar infarction. Our study reveals a much higher frequency of lacunar infarction compared to the western literature (as low as 10% (Table 3). The higher frequency of lacunar infarctions in our study is more comparable to other South East Asian countries. Other comparative studies have noted a higher frequency of lacunar infarctions in South East Asian populations compared to Caucasian populations.[36]

Our finding of a higher incidence of lacunar stroke confirm ethnic variation in susceptibility to different stroke subtypes in different population suggested by several studies. This propensity towards cerebrovascular disease may be partly accounted for by the risk factor profile of South Asian profile. Hyperinsulinemia may be associated with a higher risk of ischemic stroke.[37-39] South Asian populations (relative to Caucasians populations) have been reported to suffer from higher plasma insulin levels and insulin resistance[40,41] and the associated risk factors such as adverse lipid profile, and hypertension[40,42,43] Elevated tissue plasminogen activator has also been associated with the pathogenesis of atherothrombotic risk in South Asian stroke patients.[44]

There is a paucity of data on ischemic stroke in Pakistan. A medline search revealed only two references to studies examining epidemiology of stroke in urban Pakistan.[45,46]

One retrospective analysis from Pakistan revealed a prevalence of hypertension of 50.2% (304/606) patients with stroke (both ischemic and hemorrhagic), but prevalence in ischemic stroke is not reported.[46] The other study looked at young stroke, and in this selected population found a prevalence of hypertension of 43% (51/118). These studies support a strong role for hypertension in ischemic stroke in our population. We further hypothesize that our population may be susceptible to lacunar infarction, compared to other ischemic stroke subtypes, in part due to the high burden of hypertension.

Interestingly, patients with large artery atherosclerosis are significantly more likely to be male (74.5%) than female (25.5%) (Table 2). This finding may be attributable to difference in risk factors such as smoking and diet across the genders in our population.

In conclusion, the stroke subtypes in our Population differ from those typically reported in the Western literature. This finding confirms for our local population, the influence of ethnic and geographic variables suggested by othes studies.[47-49]

Diabetes and hypertension are the strongest risk factors for lacunar infarction, and they are common amongst patients with ischemic stroke in our population. The high frequency of lacunar infarction arnongst ischemic stroke most likely represents susceptibility to the cumulative effect of the frequency and the severity of hypertension, diabetes and other risk factors in our population. We recommend that any national stroke prevention program should take into account the differences in ischemic stroke Subtypes in our local. population.

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