

# STROKE IN PAKISTAN: REALITY, CHALLENGES AND A CALL FOR ACTION

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## ABSTRACT

Stroke is the leading cause of sustained neurological disability. Several studies from Pakistan have shown an increased prevalence of stroke. There are no population-based prevalence and incidence studies on stroke from Pakistan. In Pakistan, the mean age of stroke is about 60 years. The major risk factors are hypertension and diabetes mellitus. In this article we have attempted to focus our attention on the situation in Pakistan and take an objective look at where we stand, trying to stimulate some ideas that may lead to a coherent plan to tackle this situation.

According to recently released statistics for the United States, age-adjusted death from stroke has dropped by 24.4% between 1994 and 2004. However, the situation in developing countries is quite the opposite and stroke-related death and disability is reaching epidemic proportions.<sup>1,2</sup> If these trends continue, projected figures indicate that stroke will be the number one killer by the year 2020, while it is already the number one cause of disability in adults.<sup>2</sup> In this article, we focus our attention on the situation in Pakistan and take an objective look at where we stand, trying to stimulate some ideas that may lead to a coherent plan to tackle this situation.

## STROKE STATISTICS FROM PAKISTAN

A search for stroke-related statistics published from Pakistan leads to very few articles from indexed journals. We expanded our search to include articles (mostly retrospective audits and registries) posted on PakMediNet (pakmedinet.com), a Pakistani medical search engine. We have used statistics on hypertension, diabetes mellitus, age, gender, smoking and dyslipidemia from these articles. The following points are noteworthy:

- Age.** In most studies, mean age at stroke onset was between 57 to 62 years. In our own hospital's database, 57.2% patients with stroke were below 60 years, mean age in males was 58.2 years and in females it was 60 years.<sup>3-8,13,14</sup>
- Gender.** Except for one report showing female preponderance of 52% (Mayo Hospital, Lahore), there is a clear male preponderance with percentages ranging from 59.2 % to 71.42%. The true number seems to be nearer to 60% males and 40% females for patients admitted with stroke.<sup>7-12</sup>
- Hypertension** was found in 50 to 82% of patients with stroke. In 8 studies it was found in 60% or more patients, and in 3 studies it ranged from 50-58% of patients.<sup>5-14</sup>
- Diabetes mellitus** was found in 18-41.5% of patients with stroke.<sup>5-14</sup>
- Dyslipidemia.** This was studied in 7 reports and its prevalence ranged among stroke patients from as low as 9.9% to as high as 32%.<sup>5,7-9,11,13,14</sup>
- Smoking** was found in 22-53% of patients. A high prevalence of 53% was seen in a study conducted on indigent patients. These numbers are significant in a society where the rate of smoking is often negligible in women. Although tobacco chewing is commonly seen in women, it was not reported in any of the studies reviewed.<sup>5-7,9,11-13</sup>
- Body mass index and sedentary lifestyle** were only reported by the study on indigent patients in Lahore; a sedentary life style was seen in 38%. Body mass index (BMI) was reported in only 3 studies; obesity was seen in 11%, 32% and 31.3% of patients with stroke.<sup>5,12,13</sup>
- Ischemic versus hemorrhagic stroke.** The frequency of ischemic stroke was found to be 61% to

88.8%. Most studies ranged between 60 to 73%. This discrepancy might be due to the selection bias for imaging done on patients with more severe symptoms in some hospitals.<sup>3-7,9,11,13,15</sup> However, there is an increased incidence of hemorrhagic strokes, as has been reported in other studies from Asian countries as well.

9. **Ischemic subtypes.** This was reported in one study, conducted at Aga Khan University. Large-vessel stroke was found in 26.9% and small-vessel lacunar stroke in 42.7%.<sup>8</sup>
10. **Extra/intracranial stenosis.** Extracranial carotid disease was reported in young patients in the Aga Khan University study. According to the stroke database at our own hospital, 14.42% patients with ischemic stroke had > 50% stenosis of the ipsilateral internal carotid artery, and 8.65% had >70% stenosis.<sup>8,16</sup>

Salient points related to stroke demographics and risk factors are summarized in Table 1.

### STROKE IN SOUTH ASIANS SETTLED IN UK AND CANADA

A few studies from the United Kingdom and Canada have looked at risk factors for stroke and coronary artery disease (CAD) in the local South Asian population (immigrants from

India, Pakistan and Bangladesh). Most of these are comparison between South Asians (SA) and Caucasians.<sup>17-21</sup> In a study from UK, the prevalence of CAD risk factors were compared among subgroups within the SA (Indians, Pakistanis and Bangladeshis) as well as collectively with Europeans.<sup>17</sup> Pakistanis were less likely than Indians or Europeans to perform aerobic activity and had significantly higher impaired glucose tolerance and diabetes than Indians or Europeans. Compared with Indians, Pakistanis had higher total cholesterol and LDL levels, higher LDL/HDL ratios, and lower HDL levels. Body mass index (BMI) was also higher in Pakistani men as compared to Indian or European men. This difference in BMI was less marked in women. Hypertension was less common in Pakistanis as compared to Indians or Europeans in this study. High levels of lipoprotein (a) were most commonly seen in Pakistani women, while high levels of fibrinogen were most common in Pakistani men.

This study demonstrated that the risk factor profile varies within the SA population. There were other differences affecting CAD risk factors seen between the Pakistani, Indian and Bangladeshi populations, such as socioeconomic factors. Indians were the better placed as compared to Pakistanis, and Bangladeshis were worse when compared with Pakistanis.<sup>18</sup> In a study from UK, Patel et al compared SA with Caucasian patients having hypertension and followed them for 5 years; they found that the incidence of myocardial infarction was double in SA as

**TABLE 1.** Stroke statistics from the Pakistani literature

Study	HTN	DM	Age
Basharat et al. (Reference no. 3)	No data		Mean 57 years
Usman et al. (Reference no. 4)	No data		Mean 63.3 years
Basharat et al. (Reference no. 5)	61%	33%	No data
Fayyaz et al. (Reference no. 6)	58%	18%	Most patients aged 60-70 years
Alam et al. (Reference no. 7)	60%	28%	Mean 59 years
Syed et al. (Reference no. 8)	66.20%	41.50%	Mean 61 years
Khan et al. (Reference no. 9)	56.04%	33%	Peak 7th decade in men, 6th decade in women
Iqbal et al. (Reference no. 10)	82%	No data	Mean 60.8 years
Naseem et al. (Reference no. 11)	23.07% 31.73%	No data	No data
Javed et al. (Reference no. 12)	62%	32%	No data
Khan et al. (Reference no. 13)	64%	49.20%	Mean 62 years
Vohra et al. (Reference no. 14)	50%	18%	Mean 60 years in men, 58.8 years in women

**TABLE 2.** Stroke sub-types from Pakistani studies

Study	Ischemic (%)	Hemorrhage (%)	SAH* (%)
Vohra et al. (Reference no. 14)	69	31	-
Basharat et al. (Reference no. 3)	25	21	-
Usman et al. (Reference no. 4)	88.8	11.2	-
Basharat et al. (Reference no. 5)	79	21	-
Fayyaz et al. (Reference no. 6)	61	34	5
Alam et al. (Reference no. 7)	68	31	1
Khan et al. (Reference no. 9)	71.4	28.6	-
Iqbal et al. (Reference no. 15)	70	27	3
Naseem et al. (Reference no. 11)	66.4	27.9	5.7
Khan et al. (Reference no. 13)	70.1	29.9	-

\*Subarachnoid hemorrhage

compared to Caucasians. The main risk factor responsible appeared to be diabetes mellitus, the prevalence of which appears to be 22.9% higher in SA, while mean serum cholesterol and triglyceride levels were higher amongst Caucasians.<sup>19</sup> Bhopal et al have shown that SA are acquiring European patterns of social inequalities and with it the risk factor profile is also changing; the rate at which it is changing is different in different SA subgroups (Indians, Pakistanis and Bangladeshis).<sup>18</sup> Lower socioeconomic status was associated with a worse CAD risk factor profile. This also demonstrates the changing pattern of risk factor profile in a given population and hence the need to have population-based longitudinal studies.

The SHARE study from Canada showed that SA patients had the highest prevalence of association between increasing carotid intima-media thickness (CIMT) and the increased incidence of myocardial infarction.<sup>21</sup> This association was only partly explained by conventional risk factors, although there were differences observed in the prevalence of risk factors between the groups studied. South Asians had 2 to 3 times the prevalence of diabetes as compared to Caucasians and Chinese. The presence of hypertension was actually higher in the Chinese population. Anand et al argued that perhaps the SA population had a more “unstable” plaque, more prone to rupture due to an

interaction of prothrombotic risk factors and atherosclerosis, as well as perhaps one or more unexplained or undiscovered factors.

## EPIDEMIOLOGICAL STUDIES FROM PAKISTAN

There are no population-based prevalence and incidence studies on stroke from Pakistan. There are, however, some WHO multi-center cross-sectional studies that have looked at the prevalence of stroke and CAD risk factors at participating centers.<sup>22</sup> Two population-based studies from Pakistan on leading cardiac and stroke risk factors have outlined some important differences in the prevalence of risk factors in different socio-economic and ethnic groups.<sup>23,34</sup> Diabetes mellitus was found to be present in 4.5% of the affluent population and 1.8% in low-income segments. In the affluent population, 25% of the people between the ages of 55 and 64 years had diabetes. However, the prevalence of hypertension was similar in both groups.<sup>34</sup> Similarly, in a study looking at the prevalence of stroke and CAD risk factors in different ethnic groups within Pakistan, some interesting differences were identified. The age-standardized prevalence of hypertension was highest among Baluchis (25.3% in men and 41.4% in women), followed by Pashtuns (23.7% in men and 28.4% in women) and Muhajirs (24.1% in men and 24.6% in women), and was lowest among Punjabis (17.3% in men and 16.4% in women) and Sindhis (19.0% in men and 9.9% in women) ( $P = 0.001$ ). There was a higher prevalence of hypertension in the urban population which when adjusted for waist measurement and BMI was insignificant.<sup>23</sup>

## STROKE CHARACTERISTICS IN PAKISTAN

### Hemorrhagic stroke

Several studies from Pakistan have shown an increased prevalence and incidence of hemorrhagic strokes.<sup>6,7,9,11,13-15</sup> Uncontrolled hypertension is felt to be the main culprit. A large proportion of these patients are relatively young, placing an increased financial burden on society as a whole, and affected families in particular.

### Stroke subtypes

According to the study from Aga Khan University Hospital, there is a preponderance of small-vessel disease in our stroke population, and this pattern has been observed in other non-Caucasian racial groups in studies that have compared the pattern of ischemic stroke sub-types seen in Caucasians, African-American, and Hispanic patients.<sup>8,25,26</sup> A similar pattern is also observed in Chinese patients. We need more studies and larger sample sizes to draw reliable

conclusions since there is ethnic diversity in Pakistan, making comparisons across ethnic sub-groups important. Classification of stroke subtypes is explained in Table 2.

### **Extracranial (EC) versus intracranial (IC) vascular involvement**

Several studies have looked at the pattern of vascular involvement in different races, and there seems to be a clear pattern of Caucasians having an increased burden of EC carotid stenosis. This pattern has not been explained by conventional risk factors.<sup>27-32</sup> Among non-Caucasians, there is an increased burden of IC middle/large vessel involvement of varying degree in different studies in Chinese, Hispanic and African races.<sup>27-32</sup> We found no published study that has looked at this issue either from India or Pakistan. Preliminary data from our own institution shows that there was an increased amount of IC carotid involvement even in the presence of EC carotid disease.<sup>16</sup> This dual existence of EC and IC disease is also seen in other racial groups. Wang et al, in patients from Southern California, found a similar pattern of EC carotid disease being more common in whites. In this study, important differences between whites, Hispanics, and blacks were observed in the prevalence of various stroke risk factors. Hispanics were found to be twice as likely as blacks and Asians to have > 79% stenosis of the carotid artery, but 50% less likely than whites.<sup>33</sup>

### **Stroke Risk Factors**

The mean age of a patient presenting with stroke in most studies from Pakistan, as well as in the MONICA study, is about 60 + 10 years.<sup>2-8,13,14,22</sup> Stroke is therefore presenting at least 10 years earlier in the Pakistani population. In fact it appears that almost 60% stroke patients in Pakistan present before the age of 60 years, making it a particular health hazard at a productive time in life, causing tremendous economic damage to the individual, the family, and society in general. The prevalence of hypertension in Pakistan has been reported to be about 33% in the population over 45 years of age. Greater than 70% of the rural population are unaware that they have hypertension, and do not come to medical notice until end-organ damage has taken place.

Diabetes mellitus has reached epidemic proportions in the Pakistani population, both in Pakistanis living in Pakistan, as well as in expatriates; the numbers of patients with Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT) is also very high.<sup>5-14,19</sup> This is felt by some to be one of the major factors responsible for the increased incidence of stroke in Pakistan. Studies comparing Pakistanis, Indians, Bangladeshis and Caucasians show that Pakistanis have a higher BMI and a more sedentary lifestyle; this is felt to be

directly related to glucose metabolism. Pakistanis were twice as likely to have high HDL levels, while total cholesterol levels were comparable in the three groups.<sup>17</sup>

### **PROPOSAL FOR ACTION**

Our work as neurologists in Pakistan is cut out. The need of the hour is to:

1. Organize larger multicenter studies looking at stroke risk factors in racial/ethnic subgroups as well as any regional differences that might exist. Also needed are population-based prevalence and incidence studies.
2. Conduct multicenter clinical studies to look at the efficacy of drugs used in the treatment and prevention of stroke.
3. Raise the level of awareness in the population in general and physicians in particular regarding the importance of recognizing the presence and appropriate management of risk factors for stroke. Also required is the need to mass educate regarding lifestyle choices in order to avoid future atherosclerotic diseases.
4. Develop guidelines for the treatment and prevention of stroke that are specific for our region.
5. Set measurable goals with specific timelines.

### **CONCLUSION**

In summary, there is strong evidence that Pakistanis have a tendency for cerebrovascular atherosclerotic disease affecting vessels and causing stroke sub-types that are similar to other non-Caucasians. The age at which it presents is 10 years younger - this is again similar to most non-Caucasian populations. As elsewhere in the world, in Pakistan too hypertension appears to be the major risk factor, compounded by lack of awareness and poor compliance with anti-hypertensive medication. The number of stroke patients with hypertension is not very different in Pakistanis, when compared with Caucasians. Of particular interest are the low levels of physical activity and high BMI, as well as the prevalence of diabetes, IFG and IGT seen in the Pakistani population. Population-based research, mass health education, and comprehensive and feasible treatment guidelines are necessary to tackle the burden of stroke in Pakistan.

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