

## ORIGINAL ARTICLES

# Etiology and risk factors of ischemic stroke in Indian-American patients from a hospital-based registry in New Jersey, USA

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### Abstract

**Background and Objective:** The stroke center at the New Jersey Neuroscience Institute is located in Edison township in New Jersey which has one of the largest fractions of Asian immigrants in USA. This study aims to compare risk factors and etiology of ischemic stroke in patients of Indian origin with those of the White-Americans. **Methods:** Information pertaining to stroke risk factors was prospectively collected between July 2005 to June 2008. The patients underwent a stroke work-up, which included computerized tomograms, magnetic resonance imaging and magnetic resonance angiography of brain, carotid duplex, Holter monitoring and two dimensional echocardiogram. Etiology of ischemic stroke was ascertained using the classification developed for the Trial of Org 10172 in Acute Stroke Treatment (TOAST). **Results:** The data of 378 patients (mean age = 71±12 years, 54% females, White-Americans=347) with ischemic stroke were collected over 3 years. The 31 Indian patients (mean age = 64±10 years) had a higher proportion of diabetics mellitus (p=0.001) and were significantly younger than the White-Americans. There were significantly lower proportion of persons who smoked (p=0.03) or used alcohol (p=0.03). The commonest cause of ischemic stroke was small vessel occlusive disease, rather than large artery atherosclerosis among the White-Americans (p=0.009).

**Conclusions:** when compared to White-Americans, The Indian-American developed stroke at a younger age, despite a lower rate of alcohol and tobacco use. They have a higher prevalence of diabetes and physical inactivity. The commonest cause of ischemic stroke was small vessel occlusive disease.

### INTRODUCTION

Stroke is defined as a sudden onset focal neurological deficit of vascular etiology and is a major cause of mortality and morbidity around the world. Ranked as the second leading cause of death worldwide, stroke is more often disabling than fatal. The estimated cost of stroke-related health care is a staggering 68.9 billion dollars measured in both health care dollars and lost productivity.<sup>1</sup>

Studies of Indian immigrants to industrialized countries have shown that they are more susceptible than Caucasians to coronary artery disease and stroke.<sup>2</sup> The United States data on prevalence and risk factors for stroke in Indian-Americans is scarce, as Indian immigrants are not classified separately in any United States national health surveys or hospital data banks. It has been shown in various studies conducted in India that hypertension was a major risk factor for stroke in

Indians.<sup>3</sup> The study by Baweja *et al*<sup>2</sup> is the only study that has look at risk factors of stroke among Indian-Americans but there has been no study that look at the etiology and clinical subtypes of ischemic stroke among Indian-Americans.

The stroke centre at the New Jersey Neuroscience Institute is located in Edison township in New Jersey, which has one of the largest fractions of Asians (14%) in the USA. The White-Americans (68%) constitute the major ethnic subgroup in the area. The aims of this study was firstly to compare the risk factors of ischemic stroke of the Indian-American patients with the other major ethnic group (White-Americans), i.e., age, gender, hypertension, diabetes, hypercholesterolemia, smoking, alcohol use, physical inactivity, atrial fibrillation (AF), coronary artery disease (CAD), peripheral vascular disease (PVD) and carotid stenosis (CS) ≥ 70%. Secondly, to determine the etiology of

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ischemic stroke according to the classification developed for the Trial of Org 10172 in Acute Stroke Treatment (TOAST)<sup>4</sup>; thirdly, to identify clinical subtypes of ischemic stroke of Indian-American stroke patients according to Oxfordshire classification.<sup>5</sup>

## METHODS

The data of 378 ischemic stroke patients admitted from 1<sup>st</sup> of July 2005 to 30<sup>th</sup> June 2008 in the New Jersey Neuroscience Institute were collected prospectively and were worked up to ascertain the etiology of ischemic stroke using the TOAST criteria; namely cardioembolic, large artery disease, small vessel occlusion, other known but rare causes like hyperviscosity, coagulopathy, vasculitis like anti-phospholipid antibody syndrome and other unknown causes.<sup>4</sup> The risk factors of ischemic stroke, i.e., age, race, gender, physical activity, hypertension, diabetes, hypercholesterolemia, smoking and alcohol use or history suggestive of PVD and CAD was also noted.

The following definitions of risk factors were adopted for this study:-

*Hypertension:* History of antihypertensive intake or clinically documented history of hypertension (blood pressure of more than 140/90 on at least 3 occasions) as provided by previous medical records.

*Diabetes mellitus:* History of intake of oral hypoglycemic or history of insulin requirement or history of clinically documented diabetes mellitus (as per American Diabetes Association criteria i.e. fasting plasma glucose  $\geq$  126mg/dl or random blood glucose  $\geq$  200mg/dl with symptoms of diabetes) as provided by previous medical records.

*Hypercholesterolemia:* Fasting LDL cholesterol (low density lipoprotein cholesterol) of  $\geq$  130mg/dl.

*Physical activity:* Leisure time physical activity like jogging, walking, swimming, aerobic or muscle building exercise at least 5 times a week.

*Significant alcohol use:* More than one drink a day in females and more than two drinks a day in males.

*CAD:* History of chronic stable angina, myocardial infarction, percutaneous coronary interventions or coronary artery bypass surgery or echocardiographic evidence of hypokinesia.

*PVD:* History of limb claudication, ulcer or gangrene, peripheral vascular interventions or Doppler ultrasound evidence of PVD.

Clinical examination was carried out in each patient, data on peripheral pulses, carotid bruit and blood pressure were recorded. Apart from standard blood tests for glucose, lipids and coagulation profile, CT scans, MRI, MRA, carotid duplex, Holter monitoring and 2D transthoracic echocardiogram were conducted in all the patients. Doppler ultrasound studies of peripheral blood vessels were done in patients with symptoms suggestive of PVD. 2D transesophageal echocardiogram was carried out in patients with AF to rule out right atrial clots or any interatrial shunts. Vasculitis work-up was performed in clinically suspected cases. Approval was taken from institutional ethics committee and informed consent was obtained from all participating patients (or their close relations) for the study.

The data obtained from Indian patients were compared with Whites Americans. The continuous variables were analyzed using student's t-test and categorical variables were analyzed using Fisher's exact test for statistical significance. The SPSS version 10.0 (Chicago, IL) was used for statistical analysis.

## RESULTS

A total of 378 patients (mean age  $\pm$  standard deviation = 71 $\pm$ 12 years) were admitted during these 3 years in the Institute. Fifty four percent of the patients were females (Male = 172, female= 206)

The 31 Indian patients were significantly younger than (mean age  $\pm$  standard deviation = 64 $\pm$ 10) the White-Americans (mean age  $\pm$  standard deviation = 71 $\pm$ 13,  $p=0.001$ ). The Indian patients had a significantly higher proportion of diabetics mellitus ( $p=0.001$ ), but a significantly lower proportion who smoked ( $p=0.03$ ) or used alcohol ( $p=0.03$ ). There was a significantly large number of Indian patients who had little or no physical activity (only 2 Indian-American patient undertook some form of physical exercise at least 5 days a week as opposed to 135 White-American stroke patients,  $p=0.0001$ ).

Although there were fewer Indian-American

patients with AF, the association was not significant ( $p = 0.1$ ). There were no difference in the proportion of patients with hypertension, hypercholesterolemia, coronary artery disease, peripheral vascular disease and carotid stenosis in the two groups (Table 1)

The work-up plan to characterize the etiology of ischemic stroke according to TOAST classification revealed that small vessel occlusive disease was the commonest cause of ischemic stroke in Indian-Americans. It was significantly different ( $p = 0.009$ ) from the White-Americans, where large artery atherosclerosis was the most common (Table 2).

The subtype of stroke according to the Oxfordshire classification of ischemic strokes<sup>5</sup> showed that Indian-American stroke patients had a higher percentage of lacunar (LACI) and partial anterior circulation infarctions (PACI) as compared to the White-American. But the differences were not statistically significant (Table 3)

## DISCUSSION

In summary, the present study conducted over a period of 3 years showed that Indian-American ischemic stroke patients developed stroke at a younger age when compared to White-Americans. This was despite lower rate of alcohol and tobacco use, but a higher prevalence of diabetes and physical inactivity when compared to White-Americans. The most common cause of ischemic stroke was small vessel occlusion as compared to large artery disease among White-Americans. The Indian-American stroke patients had a higher percentage of lacunar and partial anterior circulation infarctions as compared to White-American stroke patients.

Cerebral ischemia is caused by a reduction in blood flow that lasts longer than several seconds. Ischemic strokes constitute 85% of the strokes and the rest is hemorrhagic. Our study showed that small vessel occlusive disease was the most common cause of ischemic stroke in the Indian-

**Table 1: The prevalence of risk factors of stroke among Indian-American and White-American patients.**

Risk factors	Indian-American stroke patients (percent)	White-American stroke patients (percent)	P value
Age in years (mean± standard deviation)	64±10	71±13	0.001
Male : female	18 : 13	154 : 193	NS
Smoking	9.7	28.2	0.03
Alcohol intake	0	11.8	0.03
Physical inactivity	93.6	61.1	0.0001
Diabetes mellitus	64.5	35.2	0.001
Atrial fibrillation	9.7	22.5	NS
Hypertension	87.1	79.3	NS
LDL cholesterol $\geq$ 130mg/dl	38.7	30.6	NS
CAD	35.5	37.5	NS
PVD	3.2	6.6	NS
Carotid stenosis > 70%	25.8	20.5	NS

CAD: coronary artery disease; LDL-low density lipoprotein; PVD-peripheral vascular disease; NS: not significant

**Table 2: Etiology of ischemic stroke in Indian-American and White-American stroke patients**

Etiology of ischemic stroke*	Indian-American patients (percent)	White-American stroke patients (percent)	P value
Cardio embolic	9.7	23.6	NS
Large artery disease	22.6	34.9	NS
Small vessel occlusion	45.2	22.8	0.009
Others-unknown	22.6	15.6	NS
Other-known	0	3.2	NS
Total	100	100	

\*According to Trial of org 10172 in acute stroke treatment (TOAST) criteria<sup>4</sup>; NS: not significant

American population as compared to large vessel atherosclerotic disease in the White-American stroke patients. The available limited data indicate that stroke occurring in developing countries is more often small vessel atherothrombotic in origin<sup>6,7</sup>, in contrast with developed countries where large artery disease predominate.<sup>8-11</sup> The relative proportion of large artery disease in different western stroke registries vary from 14 to 66%<sup>8-11</sup> and 34.9% of White-American patients had large artery disease in our study. Variations in study designs, methods of patient selection and definitions of stroke subtypes may partially account for the wide variations in the reported frequency of large artery disease.

There is very limited literature on stroke among Asian Indian patients in USA. In a community based study in Atlanta, Georgia, Baweja *et al*<sup>2</sup>

reported that Indian-Americans stroke subjects had increased odds of having several risk factors for atherosclerosis, including systemic hypertension, diabetes mellitus, myocardial infarction, end stage renal disease, coronary artery disease, family history of stroke and myocardial infarction.

More than two-thirds of the global burden of stroke is borne by developing countries, where the average age of patients with stroke is 15 years younger than in developed countries.<sup>12</sup> The current study also showed that Indian-Americans developed stroke at a younger age when compared to the White-Americans, with mean age difference of 7 years ( $p=0.001$ ). It has been shown by various studies conducted in India that there is a higher prevalence of diabetes, impaired fasting glucose, alcohol intake, hypertension, obesity

**Table 3: Vascular territory (clinical subtypes of ischemic stroke) involved in Indian-American stroke patients and White-American stroke patients**

Vascular territory involved	Indian-American stroke patients (percent)	White-American stroke patients (percent)	P value
PACI	32.3	31.9	NS
TACI	19.4	17	NS
LACI	41.9	31.1	NS
POCI	6.5	19.9	NS
Total	100	100	

LACI: lacunar infarcts; PACI: partial anterior circulation infarcts; POCI: posterior circulation infarcts; TACI: total anterior circulation infarcts; NS: not significant

and metabolic syndrome in Indian population, and it has strong inverse correlation with the socioeconomic status of the family.<sup>12-15</sup> Lipska *et al* showed that key components of metabolic syndrome and smoking are associated with ischemic stroke in south Indians.<sup>16</sup> Our study however shows lower rate of alcohol and tobacco use among the ischemic stroke patients and a higher prevalence of diabetes compared with the White-Americans and probably the better socioeconomic status of the Indian-Americans are moving towards adaptation of healthy lifestyle practices. However, physical inactivity was significantly associated with ischemic stroke in Indian-American stroke patients. The increased risk of small vessel stroke correlates with known association with diabetes mellitus.<sup>17</sup>

The frequency of concomitant CAD and PVD is less among Indian-American stroke patients as compared to the White-American stroke patients in this study. It has been previously been documented that Indian Asian men have less PVD than European men for equivalent levels of coronary artery disease.<sup>18</sup> Further studies on PVD among Indian-American with larger sample size need to be conducted to confirm this finding.

Non-rheumatic AF confers a five-fold increase in the risk of stroke. In our study, the proportion of patients with AF among the Indian-Americans was lower than that of the White-Americans. A previous comparative study between Asian and Caucasian stroke registries also reported lower incidence of AF among Asians and attributed the difference to younger age among the Asians.<sup>6</sup> Younger age may also be the reason for lower rate of AF among the Indian-American in this study. A previous study has shown that the predominant associated medical condition among Indians living in Birmingham, England with AF was ischemic heart disease.<sup>19</sup>

Our study had several practical limitations. The major weakness was the lack of a 'gold standard' such as pathologic confirmation of exact mechanisms of stroke. The etiologic classification based on the TOAST criteria may not be totally reliable. Another limitation was the inclusion bias attributable to the single center, hospital-based design of the study with a small number of Indian-American stroke patients. Risk factors such as CAD and PVD were not documented by angiography in subclinical and asymptomatic cases. Multivariate analysis was not a part of the statistical data analysis. It is also likely that patients with paroxysmal AF were missed. Most of the Indian-American stroke patients were first

and second generation Indians and studies need to be conducted with second and third generation Indian-Americans to find out whether these trends are sustained. A large scale, multi-centric and community based prospective study needs to be conducted to look into the epidemiology of ischemic stroke in greater details since the genetic makeup, dietary habits and lifestyle practices are different among Indians living in United States.

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