Frequency and Determinants of Intracranial Atherosclerotic Stroke in Urban Pakistan

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Background: Intracranial atherosclerosis (ICAD) is a frequent underlying mechanism of ischemic stroke. There is little direct evidence on its frequency and determinants from regions of high prevalence. This study explores the conventional and socioeconomic risk factors of ICAD in a South Asian population. *Methods:* The Karachi Intracranial Stenosis Study is a case–control study of 313 cases of ischemic stroke secondary to ICAD and 331 controls enrolled from 4 major hospitals in Karachi, Pakistan. Stroke subtype was verified by a vascular neurologist using the Trial of Org 10172 in Acute Stroke Treatment classification. Relationships of conventional and socioeconomic risk factors with ICAD-related strokes are reported by calculating odds ratios (ORs) and their 95% confidence intervals (CIs). *Results:* ICAD was the cause of stroke in 81.1% cases with large-artery atherosclerosis and 19.5% of all stroke events. Along with risk factors like history of hypertension (OR, 3.33; CI, 2.31-4.78), history of diabetes (OR, 2.29; CI, 1.56-3.35), use of tobacco (OR, 1.49; CI, 1.03-2.16), waist-to-hip ratio (OR, 1.58; CI, 1.04-2.41), and family history of stroke (OR, 1.89; CI, 1.21-2.95), other significant social determinants of ICAD strokes were

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monthly income (OR, 1.59; CI, 1.01-2.51), unemployment (OR, 2.15; CI, 1.21-3.83), and chronic stress (OR, 3.67; CI, 2.13-6.34). These social determinants were independent predictors of the risk of ICAD, in addition to those described in other world populations. *Conclusions:* ICAD accounted for one fifth of all strokes making it the most common ischemic stroke mechanism. In addition to aggressive risk factor control, data also indicated broader holistic efforts on ameliorating inequity, unemployment, and stress reduction to reduce stroke because of ICAD. **Key Words:** Intracranial stenosis—risk factors—international—ischemic stroke.

Background

The burden of stroke has increased by 100% during the last decade in developing countries.[1] The sharpest increase in the risk has taken place among the 1.5 billion people living in South Asia. Intracranial atherosclerotic disease (ICAD), which is an important proximate mechanism of ischemic stroke, is thought to be prevalent in Asians, African Americans, Hispanics, and South East Asians, in contrast to Caucasians in whom ICAD is an infrequent underlying mechanism for atherothrombotic large-vessel stroke.[2-12] Compared with Western countries, Asians also show a relatively higher proportion of hypertensive intracranial hemorrhage and small-vessel disease, thus illustrating the need to describe stroke subtypes regionally. For optimum utilization of limited health-care resources in comparable low–middle-income regions, studies that can identify the underlying risk factors for each stroke subtype are required for effective primary and secondary prevention strategies.

Similar to other regions in South Asia, the increase in burden of stroke is disconcerting in Pakistan—a country with a population of more than 180 million. Despite widespread appreciation of the importance of noncommunicable diseases as a public health problem, there is little actionable evidence on the distribution and determinants of cerebrovascular diseases in Pakistan.[13,14] The Karachi Intracranial Stenosis Study is an ongoing case–control investigation aimed to identify lifestyle, biomarker, and socioeconomic risk factors of ICAD in this region.[15] This article reports the main findings of this study. Before Karachi Intracranial Stenosis Study, studies with information on ischemic stroke subtypes did not exist in Pakistan. The objective of this article is to describe the relative proportions of ICAD in patients presenting with acute stroke in different tertiary care hospitals in Karachi, Pakistan, and identify determinants of ICAD-related strokes in these populations.[14]

Methods

Study Setting

The Karachi Intracranial Stenosis Study, as described previously, was a hospital-based, case–control study of patients with intracranial atherosclerosis and healthy stroke-free controls. Briefly, between 2007 and 2010, cases and controls were enrolled from 4 tertiary care hospitals in Karachi, a southern metropolis of Pakistan with a socioeconomically diverse multiethnic population. Of the contributing hospitals, 2 are academic referral centers (with specialized stroke care teams) that follow fee-for-service models and the rest are heavily subsidized publicly funded hospitals.[15] These centers together cater to the bulk of patients for stroke and cover the diverse ethnicities, socioeconomic backgrounds of Karachi, a microcosm of Pakistan.

Selection of Study Participants

Cases

Inclusion criteria for cases

Men and women aged 18 years or older, who present to the emergency rooms of participating hospitals and are subsequently admitted with a diagnosis of stroke because of atherosclerosis, were enrolled in this study by trained medical research officers (physicians). The qualifying event for enrollment in this group is sudden neurologic deficit consistent with the World Health Organization criteria for stroke. The definition by World Health Organization is that "a clinical syndrome characterized by rapidly developing symptoms and/or signs of focal or global loss of cerebral function, with symptoms lasting more than 24 hours, with no apparent cause other than a vascular one." Furthermore, the diagnosis of stroke had to be supported by evidence of stroke on magnetic resonance imaging (MRI) or noncontrast computed tomography (CT) of the brain. Finally, to determine that the stroke was because of intracranial stenosis, magnetic resonance angiography (MRA) was used.

Exclusion criteria for cases

Patients with both intracranial and extracranial diseases were excluded. Patients with cardioembolism, ongoing atrial fibrillation, iatrogenic stroke, and suspected alternate mechanisms like dissection, moyamoya syndrome, and nonatherosclerotic vasculopathy were excluded. Patients presenting after 72 hours since they