Risk Factors in Various Subtypes of Ischemic Stroke According to TOAST Criteria

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ABSTRACT

Objective: To identify the frequency of risk factors in various subtypes of acute ischemic stroke according to TOAST criteria.

Study Design: Cross-sectional, observational study.

Place and Duration of Study: Ziauddin Hospital, Karachi, from January to December 2007.

Methodology: Patients with acute ischemic stroke were enrolled. Studied variables included demographic profile, history of risk factors, physical and neurological examination, and investigations relevant with the objectives of the study. Findings were described as frequency percentages. Proportions of risk factors against subtypes was compared using chi-square test with significance at $p < 0.05$.

Results: Out of the 100 patients with acute ischemic stroke, mean age at presentation was 63.5 years. Risk factor distribution was hypertension in 85%, Diabetes mellitus in 49%, ischemic heart disease in 30%, dyslipedemia in 22%, smoking in 9%, atrial fibrillation in 5%, and previous history of stroke in 29%. The various subtypes of acute ischemic stroke were lacunar infarct in 43%, large artery atherosclerosis in 31%, cardioembolic type in 8%, stroke of other determined etiology in 1% and stroke of undetermined etiology in 18%. Hypertension and Diabetes were the most important risk factors in both large and small artery atherosclerosis. In patients with cardio-embolic stroke significant association was found with ischemic heart disease (p=0.01).

Conclusion: Importance and relevance of risk factors evaluated for subtypes rather than ischemic stroke as a whole should be reflected in preventive efforts against the burden of ischemic stroke.

Key words: Risk factors. Ischemic stroke. TOAST criteria. Subtypes. Hypertension.

INTRODUCTION

Worldwide, stroke is the number one cause of major disability.[1]

The incidence of stroke varies among various countries. In United States it is about 200 patients per 100,000 population.[1] During the last decade, the age-adjusted prevalence rate of stroke in India was between 250-350/100,000.[2] In Pakistan the estimated incidence of stroke is close to 250 per 100,000 population projecting to 350,000 new cases of stroke patients per year. Due to sub-optimal medical care about 40% die within 6 months while the remaining 60% are added to the pool of disabled people.[3]

Stroke is a preventable disease. Hypertension is the most powerful and important modifiable risk factor for stroke. According to National Health Survey of Pakistan, it affects one out of every 3 persons over the age of 45 years in the country.[4] Approximately 30-40% stroke risk reduction can be achieved with lowering of blood pressure only.

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Diabetes is a clear cut risk factor for stroke. The prevalence of Diabetes in Pakistan is high. According to Diabetes Association of Pakistan, 12% of people above 25 years of age suffer from this condition and 10% have impaired glucose tolerance.[5] Some 12% population above the age of 15 years is suffering from high cholesterol.[4] Smoking prevalence among Pakistani adults is 23%.[6] The other risk factors of ischemic stroke include atrial fibrillation, history of coronary artery disease, obesity and use of oral contraceptive pills.

Different local studies have identified risk factors for stroke in Pakistan.[7-10] However, variability has been shown between different geographical regions as well as different ethnic groups within the same geographical regions in various studies. Ischemic stroke is comprised of subtypes with variable underlying pathogenesis and studies on ischemic stroke as a whole may inadequately evaluate risk factors being influenced by subtypes distribution among the studied population. These differences in stroke characteristics have significant impact on strategies of stroke prevention, diagnosis and treatment.

The TOAST system has been shown to have a modest reliability even when applied retrospectively to medical records from study participants who received their care for stroke in diverse clinical settings.[11] Subtyping stroke is one way of reducing the heterogeneity of the ischemic

stroke phenotype.[12] The prevention of stroke requires in depth understanding of stroke subtypes and etiological factors in individual subtypes. In a country with limited resources the need for preventive strategies should be emphasized to reduce the economic burden of this major public health problem.

The aim of this study was to identify risk factors in various subtypes of ischemic stroke according to TOAST criteria.

METHODOLOGY

This study was conducted at medical wards of Ziauddin University Hospital, North campus, Karachi, for one year, from January to December 2007 in 100 patients with acute ischemic stroke. All patients above 18 years of age admitted with acute ischemic stroke, confirmed by CT / MRI scan, were included in the study. The patients with haemorrhagic stroke or focal neurological deficit secondary to meningitis, encephalitis, brain abscess, space occupying lesion and multiple sclerosis were excluded from the study.

A complete history was taken regarding hypertension, diabetes, dyslipidemia, ischemic heart disease, atrial fibrillation, smoking, use of oral contraceptive pills, previous history of stroke, family history of stroke and history of other known medical problems such as valvular heart disease, hyperlipidemia, connective tissue disease, bleeding disorders and hyper viscosity was noted in the questionnaire.

Acute ischemic stroke was defined as, neurological syndrome characterized by acute disruption in blood flow to an area of brain and corresponding onset of neurological deficits related to concerned area lasting for more than 24 hours. Hypertension was defined as systolic blood pressure (SBP) > 140 mmHg, diastolic blood pressure > 90 mmHg or both on two separate occasions, or the use of anti hypertensive medication at any time before the onset of stroke. Diabetes was defined if fasting plasma glucose levels are 126 mg/dl or higher after an overnight fast on more than one occasion or as random blood glucose level 200 mg/dl or higher on more than one occasion. Patients were also labelled as Diabetic on the history of diabetes confirmed in patients' medical records, or insulin or an oral hypoglycemic agent use. Dyslipidemia was defined as total serum cholesterol levels of 240 mg/dl or higher, low density lipoprotein cholesterol (LDL-C) levels of 130 mg/dl or higher and high density lipoprotein (HDL-C) levels of 35 mg/dl or lower. Patients were also labelled as hyperlipidemic if the patient was already on lipid lowering medication for more than 4-6 weeks.

The definition of stroke sub types is adapted from TOAST CRITERIA (trial of org 10172 in acute stroke treatment).[16]

Large artery atherosclerosis was defined as clinical and radiological findings of either occlusion or stenosis > 50% of major brain artery or branch cortical artery and absence of features suggestive other stroke subtypes. Small artery atherosclerosis was defined as small artery occlusion (lacunar stroke) clinical lacunar syndrome with no evidence of cortical dysfunction and either a normal brain CT/MRI or relevant sub cortical hemispheric / brainstem infarction of < 1.5 cm with no evidence of other stroke subtypes. Cardio-embolic stroke was defined as at least one major cardiac risk factor for embolism and absence of features to suggest other stroke subtypes. Stroke of other determined etiology was defined as absence of features suggestive of afore mentioned stroke subtypes and evidence of other risk factors of stroke; hypercoagulable states and non atherosclerotic vasculopathy. Stroke of undetermined etiology was defined as presence of two or more risk factors of stroke and no etiology found despite extensive workup or no etiology found because of cursory investigations.

A thorough examination was done including measurement of systolic and diastolic blood pressure of the patient and noted in questionnaire. Fasting blood sugar, random blood sugar and lipid profile was determined, followed by echocardiogram and carotid Doppler scan. MRI brain was done to confirm acute ischemic stroke and to identify vascular territory of stroke in each patient, followed by MRA brain to classify ischemic stroke according to TOAST criteria.

Data was analyzed using SPSS version 12. Mean and standard deviation was calculated for age of the patient, systolic blood pressure (SBP), diastolic blood pressure (DBP) and random blood sugar (RBS). The frequencies and percentages were calculated for risk factors and subtypes. Chi-square test of proportion was applied for significance of patients with risk factors. P-value of < 0.05 was taken as statistically significant.

RESULTS

During the one year period, 100 patients with acute ischemic stroke confirmed by either CT scan or MRI findings were included in the study. The mean age at presentation of patients with acute ischemic stroke was 63.4 years ranging between 35 to 90 years. Median age was 65 years. Mean systolic blood pressure was 154 $\pm$ 29.3 mmHg ranging from 230 to 100. Mean diastolic blood pressure was 85.2 $\pm$ 14.8 mmHg ranging from 60 to 140 mmHg. Mean RBS was 179.9 $\pm$ 98.2 mgdL ranging from 44 to 540.

Risk factor distribution was hypertension in 85%, Diabetes mellitus in 49%, history of ischemic heart disease in 30%, dyslipedemia in 22%, history of smoking in 9%, atrial fibrillation in 5%, and previous history of stroke in 29%. The distribution of various

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Table I: Risk factor distribution in large artery atherosclerosis and small vessel disease.

Risk factors	Large artery atherosclerosis					Small vessel disease				
	Yes	Percentage	No	Percentage	P-value	Yes	Percentage	No	Percentage	p-value
Hypertension	29.00	93.50	2.00	6.40	0.10	37.00	86.00	6.00	13.90	0.79
Diabetes	16.00	51.60	15.00	48.30	0.72	22.00	51.00	21.00	48.80	0.70
Dyslipidemia	9.00	29.00	22.00	70.90	0.33	10.00	23.00	33.00	76.70	0.95
Ischemic heart disease	8.00	25.80	23.00	74.10	0.45	11.00	25.00	32.00	74.40	0.30
Smoking	3.00	9.60	28.00	90.30	0.87	4.00	9.30	39.00	90.60	0.92

Table II: Risk factor distribution in cardio-embolic stroke and stroke of unknown etiology.

Risk factors	Cardi-embolic stroke					Unknown etiology				
	Yes	Percentage	No	Percentage	P-value	Yes	Percentage	No	Percentage	p-value
Hypertension	5.00	62.50	3.00	37.50	0.06	14.00	77.70	4.00	22.20	0.34
Diabetes	3.00	37.50	5.00	62.50	0.49	9.00	50.00	9.00	50.00	0.92
Dysplipidemia	2.00	25.00	6.00	75.00	0.88	3.00	16.60	15.00	83.30	0.48
Ischemic heart disease	6.00	75.00	2.00	25.00	0.01	6.00	33.30	12.00	66.60	0.81
Atrial fibrillation	4.00	50.00	4.00	50.00	-	-	-	-	-	-
Smoking	-	-	-	-	-	1.00	5.50	17.00	94.40	0.57

subtypes of acute ischemic stroke was lacunar in 43%, large artery atherosclerosis in 31%, cardio-embolic in 8%, stroke of other determined etiology in 1% and stroke of undetermined etiology in 18%. Significant associations were found for ischemic heart disease in cardio-embolic stroke (p=0.01). The risk factors in individual stroke subtypes is given in Tables I and II.

DISCUSSION

The risk of stroke has increased by about 100% in developing countries over the last 10 years.[13] The prevalence of stroke in Pakistan has been shown to be twice the highest reported prevalence in the world to date in a community-based prevalence study.[14] This is due to the prevalence of modifiable risk factors for stroke has risen to hypertension in 78%, Diabetes in 43% and dyslipidemia in 31.5%. Only 26% patients with dyslipidemia and 64.5% with hypertension take appropriate medications.[15] This study aimed at evaluating risk factors associated with individual ischemic stroke subtypes as defined by TOAST criteria. The TOAST criterion was chosen because it is easy to use in patients with ischemic stroke and has high inter rater reliability.[16]

Hypertension, the most powerful and modifiable risk factor was found in 85% of these patients. This is higher than 78% shown in recent study of 159 stroke patients, and 65 % in another study.[15,17] According to Pakistan Stroke Society, however, more than 70% patients with stroke are hypertensive. National Health Survey statistics showed that more than 30 % population above 45 years was suffering from hypertension. Up to 63% to 85% were totally unaware of their disease; 17% were aware but had not been treated and 14% were treated but their blood pressure was not controlled. Only 6 were taking medications and blood pressure was controlled. This alarmingly high prevalence of hypertension in patients with ischemic stroke calls for need of major public health initiative regarding treatment of hyper-

tension into health care policy measures in order to reduce morbidity and mortality of stroke.

Diabetes mellitus was recognized as the second most common risk factor for stroke, found in 49% patients. This is comparable to 41.5% by Syed et al.[18] The risk of stroke in diabetic patients is about four times than that found in non-diabetic individuals.

Dyslipidemia was found in 22% of our patients comparable with 21% by Syed et al.[18] but slightly lower (36%) than that reported by Khan et al.[17]

With regard to various subtypes of ischemic stroke in our population, lacunar stroke was the most common type of ischemic stroke seen in 43% of our patients. This is comparable to 42.7% reported previously by Syed et al.,[18] however, lower than 25.8% reported recently in study of 147 ischemic stroke patients.[19] This is higher than that reported from South India (18%),[20] and 21% from China.[21]

Large artery atherosclerosis was found in 31%. This is much lower than that reported from the West but comparable with that reported by Syed et al.[18]

Hypertension and Diabetes were the major risk factors identified in both lacunar and large artery atheroscleorosis as shown in another study.[22] However, lacunar stroke was less likely to be caused by embolism from heart and there was lower frequency of ischemic heart disease in patients with lacunar stroke. This suggests the role of non-atherosclerotic arteriopathy causing lacunar stroke.

The frequency of cardioembolic stroke was 8% in this study. This is much lower than that reported from west but comparable to 6% by Syed et al.[18] and 10% by Kaul.[20] This may be due to ethnic differences such as relatively higher frequency of lacunar stroke in our population. The major risk factors for cardioembolic stroke included ischemic heart disease found in 75% patients followed by atrial fibrillation in 50%.

Strategies should, therefore, be directed towards specific preventive measures. It has been shown that incidence of lacunar stroke has decreased in Japanese patients over last 40 years due to improved hypertension control and decreased prevalence of smoking.[23]

CONCLUSION

The stroke subtypes in our population differ from that reported from the West. The higher frequency of lacunar infarction in our patients suggests the presence of uncontrolled hypertension and Diabetes. This should emphasize the importance of ischemic stroke subtypes and need for collective preventive strategies especially regarding hypertension.

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