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Clinical, radiological and risk factor profiles of acute lacunar stroke in a developing country

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Abstract

Background: Lacunar stroke accounts for a quarter of all acute ischemic infarction. Insufficient information is available with respect to the pattern and risk factor profiles of patients with lacunar stroke from developing countries. We undertook this study to define the clinical features, imaging characteristics, and risk factors in a group of patients with image proven lacunar stroke from southern India, and contrast them with those described from developed countries. *Methods:* We retrospectively reviewed the demographic, risk factor profiles (presence of hypertension, diabetes mellitus, dyslipidemia, smoking) and CT/MRI brain findings (microbleeds, small vessel ischemic changes, old infarcts) and CV Doppler/CT or MR angiography of brain and neck vessels of 132 consecutive patients diagnosed with image proven acute infarct measuring 2-20mm in subcortical white matter, basal ganglia, thalamus or pons, presumed to result from the occlusion of a single small perforating artery(lacunar infarct), in Department of Neurology, Kasturba Medical College, Manipal, Karnataka, India. *Results:* Males comprised 63.6%, with 56% between the ages of 55-75 years. Hypertension was present in 98 (74.2%) and 50 (37.8%) had diabetes mellitus. Pure motor hemiparesis was the most common clinical syndrome 79 (59.8%), followed by ataxic hemiparesis in 32 (24.2%). Chronic lacunar infarct was detected in 68 (51.5%) patients MRI; however, past history of stroke was present only in 10 (7.6%). Small vessel ischemic changes were present in 100 (75.8%), and cerebral micro-bleeds in 10 (7.6%) patients. Angiography showed symptomatic side carotid stenosis of over 50% in 6 (4.5%), intracranial major vessel stenosis in 12.61% of patients.
Conclusion: Lacunar stroke, although less dramatic in its clinical presentation, is frequently associated with modifiable risk factors like hypertension and diabetes. It should be regarded as a warning sign of underlying diffuse small vessel disease; hence, portends recurrent stroke and vascular dementia. Our findings are in accordance with most studies from developed countries.

Keywords: Developing country, lacunar stroke, MRI, risk factors, stroke

INTRODUCTION

Stroke is one of the leading causes of morbidity and mortality worldwide, especially in aging population.[1] Lacunar stroke, accounts for a quarter of all acute ischemic infarction.[2] Lacunar infarcts are caused due to occlusion of the single deep perforating artery, which supplies the deep white matter, where infarct size measures 2-20 mm in diameter.[3] Following a lacunar stroke, one-third of individuals are left dependent for activities of daily living.[4]

The exact mechanism underlying the lacunar stroke is still not clear.[5] One of the possible mechanisms for lacunar stroke is thought to be due to lipohyalinosis of small penetrating cerebral arteries.[6,7] However, there are studies suggesting that lacunar stroke could be caused due to embolism/stenosis of a middle cerebral artery resulting in occlusion of distal perforating arteries like lenticulo-striate artery.[8] Another possible mechanism is thought to be due to intrinsic diffuse small arteriolar diseases.[9] Hypertension and diabetes have been found to be strongly associated with lacunar stroke.[10,11] It is evident that lacunar infarcts are more commonly associated with white matter abnormalities and small vessel ischemic changes, and in long-term are associated with memory impairment.[12,13] Cerebral microbleeds were also more common in patients with lacunar stroke, ranging from 25-50%.[14,15]

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There is limited number of studies on lacunar stroke, which have described the different clinical syndromes, risk factors, angiographic findings, and the brain imaging features from developing countries. This encouraged us to undertake this study from Southern India to delineate the clinical and radiological characteristics, and risk factors of lacunar stroke.

METHODS

This retrospective study was conducted utilizing consecutive patients admitted to the Department of Neurology, Kasturba Medical College, Manipal University, Manipal, Karnataka, India. During the period of June 2016 to June 2018. The objective of the study was to define the risk factor profile, clinical syndromes, imaging characteristics of patients with lacunar stroke and to assess the risk factors predisposing to lacunar stroke.

We included consecutive patients with imaging (MRI/CT) confirmed acute cerebral infarcts (2–20 mm in diameter) in the deep cerebral white matter, basal ganglia, thalamus or pons, presumed to result from the occlusion of a single small perforating artery, who had undergone at least one of the cerebral vascular imaging by Carotid-vertebral artery (CV) Doppler /CT angiography or MRI angiography.

We abstracted the clinical features of the patients from the medical records. In addition to demographic characteristics, the following risk factors were ascertained: History of smoking; Hypertension - either patient was diagnosed previously by a doctor to be hypertensive and on antihypertensive medication or during the hospital stay, found to have consistently elevated blood pressure of >140/90mmHg on multiple occasion after 3days of onset of stroke, with Echo/ECG showing evidence of left ventricular hypertrophy and started on antihypertensive medication. Diabetes - previously diagnosed and on treatment or newly diagnosed with serum glucose level, HbA1c>6.5. Cardiac diseases from history of cardiac disease and ECG/Echo suggestive of cardiac disease, in case of high suspicion 24 hours Holter for ruling out atrial fibrillation, Total cholesterol of >200 mg/dl or LDL >160mg/dl or patients on lipid lowering therapy(statins) were considered to have hyperlipidemia, other comorbidities and drug history was noted.

Depending on the clinical findings, we categorized the patients into following clinical syndromes: pure motor, pure sensory, ataxic hemiparesis, sensory-motor, dysarthria-clumsy hand, hemichorea-hemiballismus and dystonia, eye movement disorders with or without hemiparesis, dysarthria, dysphagia, pseudobulbar signs, cognitive impairment, imbalance, and urinary incontinence.

Brain imaging of each patient was reviewed with the help of Radiology Information System/ Picture Archiving and Communication System (RIS/PACS). Acute infarct was categorized into in anterior (subcortical white matter) or posterior circulation (pontine/thalamus) depending on the arterial supply. Presence of any old infarction (cortical or lacunar) was noted. We also checked whether old infarcts were present in the same arterial territory along with acute infarct. Presence of small vessel ischemic changes and any cerebral micro-bleeds were also noted. Carotid artery stenosis was categorized into significant>50% and non-significant (<50%) occlusions. Occlusion of major intracranial arteries such as middle cerebral, anterior cerebral, vertebral, and basilar artery was examined in patients in whom MR/CT angiogram was done.

We expressed the distribution of patients as number, percentage, mean ± standard deviation and median. We graphically depicted the distribution by bar graphs and pie charts.

RESULTS

Demographic, risk factors and clinical characteristics

We have summarized the demographic features and risk factors in Table 1. There were 84 (63.6%) males and 48 (36.4%) females. Their age ranged from 26 to 89 years, mean age of 60.8 years, and median age of 63 years. Most of our patients belonged to the age group of 55-75 years (Figure 1). Hypertension was present in 98 (74.2%), and Type 2 diabetes mellitus was present in 50 (37.9%) patients. Six (4.5%) patients had cardiac comorbidity, 5 (3.7%) had ischemic heart disease and one patient had ventricular septal defect, all patients had undergone ECG and 2 D ECHO testing, however only four patients, who had high suspicion for Atrial fibrillation underwent Holter monitoring, however no atrial fibrillation detected. Ten (7.6%) had previous history of stroke or TIA. History of smoking was present in 38 (28.8%) patients, hyperlipidemia was present in 23 (17.4%) patients. Other medical comorbidities included, 4 (3.0%) patients had hypothyroidism and 5 (3.8%) had history of carcinoma and undergone chemo or radiotherapy in the past.

Table 1: Distribution of patients according to demographic and clinical characteristics

Characteristics	Distribution
Age (year)	
Mean ± SD	60.8 ± 12.72
Median	63.0
Gender: n (%)	
Male	84 (63.6)
Female	48 (36.4)
Past stroke/TIA: n (%)	10 (7.6)
Hypertension: n (%)	98 (74.2)
Diabetes mellitus: n (%)	50 (37.9)
Smoking: n (%)	38 (28.8)
Hyperlipidemia: n (%)	23 (17.4)
Heart disease: n (%)	6 (4.5)
Cancer: n (%)	5 (3.8)

Abbreviations: SD – standard deviation; TIA – transient ischemic attack; VSD-Ventricular septal defect.

We have depicted acute lacunar stroke subtypes in Figure 2. Pure motor hemiparesis was the most common subtype with 79 (59.8%) patients, followed by ataxic hemiparesis 32 (24.2%). Less common subtypes included sensory-motor 8 (6.1%), pure sensory 4 (3.0%), and dysarthria clumsy hand syndrome 5 (3.8%). Four (3.0%) patients had very rare clinical syndromes such as mild facial weakness, facial weakness with dysarthria, and diplopia.

Imaging characteristics

In Table 2, we have summarized the imaging findings. Eighty-eight (66.7%) patients had acute infarct in the anterior circulation (subcortical

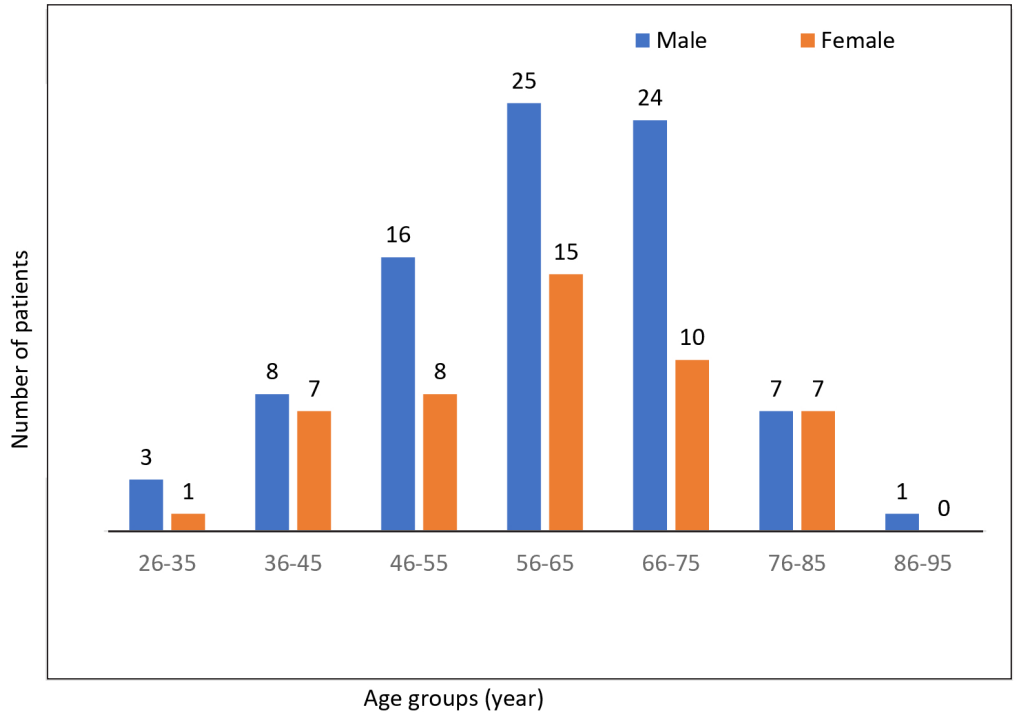

Figure 1. Distribution of patients according to age and gender.

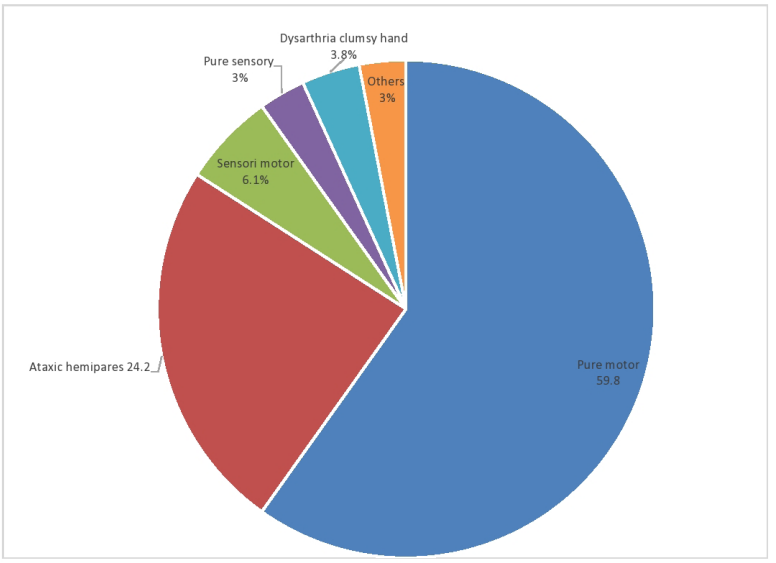

Figure 2. Distribution of patients according to lacunar syndrome subtypes.

white matter, internal capsule or basal ganglia) and remaining 44 (33.3%) in the posterior circulation (thalamus/pons). Chronic lacunar infarct was found in 68 (51.5%) patients, 13 (9.8%) in the same arterial territory, 27 (20.5%) in the different territory, and 28 (21.2%) had multiple chronic lacunar infarcts. Large artery cortical stroke was found in 11 (8.3%) patients. Small vessel ischemic changes were seen in 100 (75.8%) patients. Micro-bleeds were observed in 10 (7.6%) patients.

Extra-cranial carotid and vertebral artery imaging was available for all; however, intracranial imaging was not available for 21 patients since they had undergone only carotid and vertebral artery Doppler. We considered symptomatic carotid stenosis if the stenosis was >50% and stroke happened in the same side of carotid artery

Table 2: Distribution of patients according to brain and vascular imaging findings

Findings	Number (Percentage)
MRI	
Acute infarct in anterior circulation	88 (66.7)
Acute infarct in posterior circulation	44 (33.3)
Chronic lacunar infarct	68 (51.5)
Chronic cortical infarct	11 (8.3)
Small vessel ischemic changes	100 (75.6)
Cerebral microbleeds	10 (7.6)
CV Doppler/CT angiography/MR angiographic findings	
Carotid artery stenosis (symptomatic side)	
>50%	6 (4.5)
<50%	4 (3.0)
Carotid artery stenosis (asymptomatic side)	
>50%	6 (4.5)
<50%	9 (6.8)
Middle cerebral artery stenosis	4 (3.6)
Anterior cerebral artery stenosis	3 (2.7)
Vertebral artery stenosis	4 (3.6)
Basilar artery stenosis	3 (2.7)

territory. Six (4.5%) patients had symptomatic side carotid stenosis, 4 (3.0%) had carotid stenosis of less than <50% diameter in the symptomatic side. In the opposite side of stroke, there were 6 (4.5%) patients having >50% stenosis of carotid artery, 9 (6.8%) cases had <50% stenosis of carotid artery. Patients who had undergone intracranial MR/CT angiography (excluding 21 patients) were studied for intracranial MCA, ACA, vertebral artery and basilar artery occlusion. Four (3.6%) patients had middle cerebral artery stenosis/occlusion and 3 (2.7%) had anterior cerebral artery stenosis. Four (3.6%) patients had vertebral artery and 3 (2.7%) patients had basilar artery stenosis/narrowing on the same side of posterior circulation (pons/ thalamus) (Table 2).

DISCUSSION

In this retrospective study we analyzed the demographic and clinical characteristics, risk factors, and imaging findings of hospitalized patients with lacunar stroke during a 2-year period in a tertiary referral center in southern India. Lacunar stroke affected males predominantly than females in our study population, who belonged to the age of 55-75 years with pure motor hemiparesis being the most common subtype of lacunar stroke. Most common risk factors associated with lacunar stroke was hypertension (three fourth of study population), followed by diabetes mellitus (one third of study population) and smoking. About half of the patients had chronic lacunar infarct, which was silent without any prior neurological deficits. More than three fourth of the patients had small vessel ischemic changes in their MRI imaging. Neck and brain angiography revealed no significant occlusion of either neck vessels or intracranial arteries. We wish to elaborate on our observations and contrast them with those reported from developed countries.

Demographic and clinical features

Out of 132 patients, two-thirds were males. Lacunar stroke occurred in our patients most frequently between the ages of 55 and 75, with mean age of 60.7 years. This is comparable with studies on lacunar stroke from developed countries, where the maximum number of patients were in 55-70 years with male preponderance.[16-18] In a case-control study, the risk of lacunar stroke increased with increasing age for people below 69 years, but after the age of 70 years, the risk of lacunar stroke declined.[19]

Pure motor hemiparesis was the most common clinical syndrome accounting for two-thirds of patients, followed by ataxic hemiparesis in a quarter of patients. This is comparable with other studies in developed countries, in which the prevalence of pure motor hemiparesis was found to be between 40-60%[20,21], and the ataxic hemiparesis ranged between 15-20%.[21,22]

Risk factors

Hypertension was present in three-fourths of our patients, and diabetes was found in one-third of patients. Hypertension and diabetes as the major risk factors for lacunar stroke in developed countries as well. The prevalence of hypertension has been found to be more than 70%[5,23], and diabetes 10-30% in studies on lacunar stroke from developed countries.[24-26] History of past stroke/ TIA was present in 10 (7.5%) our patients. Cardiac abnormalities including ischemic heart disease was present in 6(4.5%), however atrial fibrillation was not confirmed in any cases, which is lower in our series when compared to other studies from developed countries where prevalence of cardiac comorbidity and possible cause for embolism ranged from 17-39%.[6,27] History of smoking was present in 38(28.8%), hyperlipidemia was present in 23 (17.4%) of patients. In a systematic review on risk factors of lacunar infarct there was no clear association between smoking, excess alcohol consumption, or raised cholesterol in lacunar compared with non-lacunar infarction.[28]

Out of our 132 patients, 5 had history of carcinoma and were treated with chemotherapy and radiotherapy. The overall incidence of stroke increases in patients with carcinoma and who have undergone treatment in the form of radio/ chemotherapy. The most common type of stroke is believed to be cardio-embolic, followed by lacunar stroke and large artery atherosclerosis.[29,30] In a study by Rosenberg *et al*. the lacunar stroke was found in 52% of all stroke in carcinoma patients.[31]

Radiological features

In our study, the history of old stroke was present only in 7.5% of the patients, but the brain imaging showed chronic silent lacunar infarction in half of patients. About 10% had chronic infarct was in the same territory. About 20% had chronic lacunar infarcts that were in the different territory or on the opposite side. About 21% patients had multiple lacunar infarcts. In the study by Wessels *et al*. from Germany, in 73 lacunar stroke patients, a single subcortical ischemic area was seen in

only 59% of patients, 22% had large or scattered lesions in one territory and 19% had multiple lesions in multiple territories.[32] Study by Ong *et al*. from Taiwan showed that silent infarct in first ever symptomatic stroke was 20% and mostly were subcortical infarcts with associated small vessel ischemic changes.[33] Small vessel ischemic changes were seen in as high as 76% of our patients. The frequency of cerebral micro bleeds of 7.5% of our study, is less when compared to other studies from developed countries, which showed the higher prevalence of cerebral micro bleed in-patient with lacunar stroke ranging from 23 to 54%.[5,14,34,35]

Few studies suggested the possible mechanism of lacunar stroke could be secondary to dislodging of thrombus from the proximal artery[36,37] or atherosclerosis of proximal arteries like MCA stem blocking the orifices of deeper penetrating arteries and resulting in small subcortical infarcts.[38,39] To test this hypothesis, we examined the angiographic findings of extra and intracranial vessels. There was no significant neck vessel or other intracranial vessel occlusion. Symptomatic Carotid occlusion >50% was seen in only 4.5%, Occlusion of <50% seen in only 3% whereas occlusion of contralateral carotid artery of >50% was also seen in 4.5% of the patients, and <50% seen in 6.8% (Table 2). There are many studies from developed countries, which looked for ipsilateral carotid occlusion, in these studies percentage of stenosis varied from 1-28%.[40-42] Sweeny *et al*. found intracranial arterial stenosis/occlusion by magnetic resonance angiography (MRA) in 21% of patients meeting clinical and radiologic criteria for lacunar infarcts, but only in 10% is the artery disease related to the affected penetrating vessel.[43] Studies from Asian populations have shown that small subcortical infarcts are frequently caused by branch occlusion associated with parental artery atherosclerotic plaque, or by atherosclerotic proximal small-vessel disease.[44-46] However in our study, we found that 12.6% of patients had stenosis of intracranial vessels diagnosed by MRA/CT angiography, which is less in frequency when compared with above mentioned studies.

This study has the following limitations: 1) Small sample size 2) Intracranial vessel imaging was available for only 111 patients in the study 3) MRI imaging of brain was available for 130 patients, two patients had only CT brain, which could have missed cerebral micro-bleeds and small vessel ischemic changes in those two cases. 4) Since it is a retrospective study, history of risk factors, especially history of smoking could have been missed, as this depends entirely on the history sheet, which could not be confirmed by other clinical/hematological or procedural data by the authors.

In conclusion, Lacunar/small vessel ischemic strokes may be less dramatic and less debilitating when compared to cortical stroke at the beginning, but should be considered as the warning sign of an underlying diffuse small vessel disease. It may be the forerunner of vascular Parkinsonism and dementia. Even though mechanism of lacunar stroke is not well understood, from the existing literature and findings from our study, we can presume that diffuse small vessel/arteriolar disease could be the most possible mechanism on the background of hypertension and diabetes, rather than distal embolization from large or medium sized arteries. At present, the treatment of lacunar stroke is similar to that of large artery stroke, with single antiplatelet and statins. Research should be done in this area to gather more information on the pathogenesis and drugs which can target the endothelium and prevent small vessel diseases.

DISCLOSURE

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Conflict of interest: None

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