

## Comparative Study of Risk Factors Between Lacunar and Non-lacunar Ischemic Strokes

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### Abstract:

**Background:** Stroke is a leading cause of mortality and morbidity in both developed as well as developing countries. The risk factors in lacunar stroke differ in comparison to nonlacunar strokes. In this study risk factors of lacunar stroke in comparison to non-lacunar were evaluated. **Objectives:** The aim of the study was to compare the risk factors among lacunar stroke and non-lacunar stroke. **Methodology:** This comparative study conducted in the department of Medicine and Neurology, Dhaka Medical College Hospital, Dhaka from September 2010 to August 2011. MRI of brain was done in 151 patients above 18 years of age with ischemic stroke and Lacunar stroke was found in 31 patients and non-lacunar stroke was detected in 120 patients. Based on the inclusion and exclusion criteria from them 30 patients with lacunar stroke were selected as Group-A patients and equal number of non-lacunar stroke same ages as group B were compared of. The risk factors of stroke were defined as hypertension, diabetes mellitus, hypercholesterolemia, smoking, history of transient ischemic attack, myocardial infarction, atrial fibrillation and carotid artery stenosis. **Results:** Out of 151 patients with ischemic stroke non-lacunar stroke was predominant, which was 79.47% and lacunar stroke was 20.52%. The mean age was found 60.9±10.2 years in Group A and 56.2±11.8 years in Group B, which was almost similar between two groups ( $p>0.05$ ). Male were predominant, which was 63.33% and 76.67% in lacunar and non-lacunar stroke respectively. Male and female ratio was 2.3:1. Regarding the risk factors hypertension was observed most common risk factor among the patients having lacunar and non-lacunar strokes. Hypertension and diabetes mellitus were common in lacunar stroke and myocardial infarction, carotid artery stenosis and hypercholesterolemia were common in non-lacunar stroke which were statistically significant ( $p<0.05$ ) between the both groups. However, the percentage of smoking, previous TIA and atrial fibrillation were not significantly ( $p>0.05$ ) different between lacunar and non-lacunar stroke. **Conclusion:** Hypertension and diabetes mellitus were common in lacunar stroke, and myocardial infarction, whereas carotid artery stenosis and hypercholesterolemia were common in non-lacunar stroke and the both groups were statistically significant ( $p<0.05$ ). So modification of risk factors may reduce the incidence of ischemic stroke.

**Key word:** Lacunar stroke, Non-lacunar Strokes, Ischemic stroke

**Abbreviation:** TIA (transient ischemic stroke)

### Introduction:

Stroke is a neurological disease, which is major cause of death and disability worldwide. Stroke kills about five million people each year making this the

second major cause of death worldwide. At least fifteen million others have non-fatal stroke annually and about a third are disabled as a consequence<sup>1</sup>. The word stroke is used to refer to

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a clinical syndrome of presumed vascular origin, typified by rapidly developing signs of focal or global disturbance of cerebral functions lasting more than 24 hours or leading to death<sup>2</sup>. It is the outward manifestation of a localized sudden interruption of the blood supply to some parts of the brain on etiological basis, of all strokes about 85% are ischemic and 15% are hemorrhagic<sup>3</sup>. In a hospital based study in Bangladesh among stroke patients, it was found that 57.84% were ischemic and 42.16% were haemorrhagic<sup>4</sup>. Ischemic stroke occurs either due to thrombosis or embolism involving the cerebral circulation and categorized as small vessel lesion and large vessel lesion<sup>5</sup>. This distinction can usually be made by means of clinical features and more reliably by CT or MRI scanning<sup>6</sup>. Around 70% of the thrombotic strokes are due to large artery thrombosis and remaining are small infarcts or lacunars infarcts<sup>7</sup>.

Lacunar stroke has been regarded as the least severe subtype of ischemic stroke for many years<sup>8</sup>. Symptomatic lacunar stroke was defined as a stroke presenting one of the 5 classic lacunar syndromes (pure motor stroke, pure sensory stroke, sensorymotor stroke, ataxic hemiparesis, and dysarthria – clumsy hand syndrome) and confirmed by small (<15mm in diameter) subcortical infarct on brain MRI in the absence of any other morphological cause of ischemic stroke found on the neuroimaging examination<sup>9</sup>. These are presumed to result from the occlusion of single, small, perforating arteries supplying the deep subcortical areas of the brain. If the occlusive arterial pathology is distinct from the atherothromboembolic processes that occlude larger arteries, causing most other types of ischemic stroke, the best strategies for the investigation and treatment of patients with lacunar infarction might differ from those for patients with other ischemic stroke subtypes. The arterial pathology of lacunar infarction is based largely on Fisher's meticulous clinicopathological studies, in which he serially dissected the vascular supply of a total of 68 lacunar infarcts in 18 postmortem brains<sup>10</sup>. To be defined as a lacunar stroke by MRI, the following criteria had to be met: (1) be round or oval in shape; (2) measure <1.5 cm in diameter;

(3) be located in the typical territory supplied by deep or superficial small perforating arteries; (4) not be in cortical territories; and (5) not have the morphological and topographical distribution consistent with partial internal border-zone infarcts<sup>11</sup>.

Non-lacunar ischemic stroke was defined as either 2 of the following symptoms: (1) higher cerebral dysfunction (e.g., dysphasia, dyscalculia, visuospatial disorder); (2) homonymous visual field defect; and (3) ipsilateral motor or sensory deficit, or higher cerebral dysfunction alone or a motor or sensory deficit more restricted than those classified as lacunar (e.g., confined to one limb, face, or hand but not the complete arm) and additionally MRI of brain following the event had to show an appropriate cortical, subcortical or combined lesion of > 1.5 cm diameter in the absence of an obvious cardioembolic source<sup>12</sup>.

Pathological studies are rare because autopsy rates are declining, lacunar strokes have a low-case fatality rate<sup>8</sup> and tracing the vascular supply of subcortical lesions is technically difficult and time consuming<sup>10</sup>. Difficulties in imaging the small perforating intracranial arteries has made informative imaging studies scarce. An alternative approach has been to compare the risk factor profiles of patients with lacunar infarcts versus those with non-lacunar infarcts because this may reveal differences suggestive of distinct arterial pathologies.

The cause of lacunar infarction is occlusion of a single small penetrating artery. This occlusion may be due to microatheroma and lipohyalinosis, which are associated with hypertension, smoking, and diabetes, or may result from microembolism from the heart or carotid arteries<sup>7,12</sup>. Atrial fibrillation and ipsilateral carotid stenosis have a stronger association with non-lacunar infarcts<sup>13</sup>.

#### **Materials and Methods:**

This Observational comparative study was conducted in the department of Medicine and Neurology, Dhaka Medical College Hospital, Dhaka from September 2010 to August 2011. MRI of brain was done in 151 patients above 18 of age years with ischemic stroke and lacunar stroke was found in 31 patients and non-lacunar stroke was detected in 120 patients.

Inclusion criteria: were 1) Evidence of lacunar/non-lacunar infarct by MRI of brain 2) History of first ever ischemic stroke. 3) Presenting within two weeks of symptoms. 4) Adult patients Age: 18 years and above Exclusion criteria: 1) MRI of brain not showing a relevant lesion. 2) History of recurrent stroke. 3) Not willing to be included in the study. 4) Age less than 18 years.

MRI of brain was done to every patient to confirm the diagnosis lacunar and non-lacunar stroke by 'AIRIS 2I Hitachi' MRI machine (0.3 Tesla). MRI of brain of all patients was reviewed by the same consultant radiologist in DMCH blinded to the clinical data and to any hypothesis about this study. Following the above inclusion and exclusion criteria from them 30 patients with lacunar stroke were selected as Group-A patients and equal number of non-lacunar stroke same ages as group B were compared. The risk factors of stroke were defined as hypertension; diabetes mellitus ; hypercholesterolemia ; smoking ; history of transient ischemic attack; myocardial infarction; atrial fibrillation and carotid stenosis. Data was collected by face-to-face interview, physical examination and investigations in a data collection sheet.. On admission detailed history and thorough clinical examination including neurological assessment was carried out. Emphasis was given on risk factors especially hypertension and diabetes mellitus. Patients who presented with sudden onset of lateralizing signs especially in the presence of atrial fibrillation, rheumatic heart disease, recent myocardial infarction and carotid bruit were considered to be suffering from ischemic stroke. In addition to routine investigation fasting blood sugar, lipid profile, ECG and in some selected patient echocardiography and Duplex Ultrasound of carotid (extracranial) vessels were done. Study was intended to evaluate risk factors and clinical presentation in lacunar and non-lacunar strokes.

Statistical analyses related with this study were performed by use of SPSS 12 package program. The comparisons between patients with lacunar and non-lacunar stroke with the Student t test for normally distributed continuous variables and  $\chi^2$  tests for dichotomous variables. Test of performance were done to detect the sensitivity, specificity, positive predictive value, negative

predictive value and accuracy. Ethical clearance is taken from ethical committee of DMCH. Every patient and/or responsible family member will be asked for informed consent about the procedure and the study goal.

## Observation and Results:

**Table-I**  
*Frequency of patients with lacunar and non-lacunar stroke*

No of patients with Ischemic stroke	Group A Lacunar stroke	Group B Non-lacunar stroke
151	31(20.52%)	120(79.47%)

Table I shows, a total of 151 patients with ischemic stroke were included in this study. In Group A, 31(20.52%) patients were lacunar stroke and 120(79.47%) patients were non-lacunar stroke. In this study the incidence of non-lacunar strokes were more common than lacunar strokes.

**Table-II**  
*Age distribution of the study patients (n=60)*

Age (in years)	Group A (n=30)		Group B (n=30)		P Value
	N	%	N	%	
≤40	0	0.0	1	3.3	
41-50	3	10	7	23.3	
51-60	7	23.3	11	36.66	
61-70	13	43.33	8	26.66	
71-80	9	30	3	10	
>80	1	3.3			
Mean ±SD	60.9±10.2		56.2 ±11.8		0.104 <sup>ns</sup>
Range (min-max)	(41-85)		(38 – 80)		

ns=Not significant, P value reached from unpaired t-test.

A total of 60 patients were included in the study. They were divided into six groups according to age (Table II). Majority of the patients was found in the age group of 61-70 years in group A, which was 13(43.33%) and 51-60 years in group B, which was 11(36.66%). The mean age was found 60.9±10.2 years in Group A and 56.2±11.8 years in Group B. The mean age difference was not statistically significant ( $p>0.05$ ) between the patients with lacunar stroke and non-lacunar stroke in unpaired t-test.

**Table-III**  
Sex distribution of the study patients (n=60)

Sex	Group A (n=30)		Group B (n=30)		P Value
	N	%	N	%	
Male	19	63.33	23	76.67	0.259 <sup>ns</sup>
Female	11	36.67	7	23.33	

ns= Not significant ,P value reached from chi square test.

**Table-IV**  
Distribution of the respondents according to risk factors (n=60)

Risk Factors	Group A (n=30)		Group B (n=30)		P Value
	Lacunar stroke		Non-lacunar stroke		
	N	%	N	%	
Hypertension	27	90.0	19	63.3	0.014 <sup>s</sup>
Smoking	11	36.67	17	56.66	0.120 <sup>ns</sup>
Diabetes mellitus	17	56.70	9	30.00	0.037 <sup>s</sup>
Myocardial Infarction	5	16.70	13	43.30	0.024 <sup>s</sup>
Carotid artery stenosis(>50%)	7	23.30	17	56.70	0.008 <sup>s</sup>
Hypercholesterolemia	9	30.00	17	56.70	0.037 <sup>s</sup>
Previous TIA	5	16.66	7	23.33	0.518 <sup>ns</sup>
Atrial fibrillation	2	6.66	5	16.66	0.211 <sup>ns</sup>

\*Multiple responses . s=Significant, ns=Not Significant ,P value reached from chi square.

Table III shows, in Group A, 19(63.33%) patients were male and 11(36.67%) patients were female. In Group B, 23(76.67%) patients were male and 7(23.33%) patients were female. Not significant ( $p>0.05$ ) difference was found between patients with lacunar and non-lacunar stroke regarding sex distribution. Male female ratio was 2.3:1 in the whole study patients.

Regarding the risk factors hypertension was observed most common risk factor in the study patients having lacunar and non-lacunar strokes (Table IV). Hypertension and diabetes mellitus were common in lacunar stroke, and myocardial infarction, carotid artery stenosis and hypercholesterolemia were common in non-lacunar stroke which were statistically significant ( $p<0.05$ ) in chi square test. However, the percentage of

smoking, previous TIA and atrial fibrillation were not significantly ( $p>0.05$ ) different between lacunar and non-lacunar stroke.

#### Discussion:

This observational comparative study was carried out with an aim to compare risk factors (i.e. Hypertension, diabetes mellitus, smoking; dyslipidemia, previous transient ischemic attack, myocardial infarction and carotid stenosis) between lacunar and non-lacunar strokes as well as their partial demographic profile. The study was carried out in patients attending in inpatient and outpatient Department of Neurology and Department of Medicine in DMCH from September 2010 to August 2011. A total of 200 patients clinically diagnosed as stroke were selected. Detailed history, physical examination and CT scan of Head in every patient

was done by the investigator and findings were recorded. Out of them 151 patients were ischemic stroke and 49 patients were hemorrhagic stroke. MRI of brain was done in all patients with ischemic stroke. Lacunar stroke was found in 31 patients and nonlacunar stroke was detected in 120 patients. Based on the inclusion and exclusion criteria 30 patients with lacunar stroke were selected as Group-A from 31 patients and another 30 patients with age and sex matched patients having non-lacunar stroke were selected from 120 patients as Group-B .

In this current study (Table I), it was observed that out of 151 patients with ischemic stroke non-lacunar stroke was predominant than lacunar stroke, which was 79.47% in and 20.52% in respectively. Similarly, Kaul et al. (2000)<sup>14</sup> undertaken a study on 893 patients of ischaemic stroke in the stroke registry of Nizam's institute of Medical Sciences, Hyderabad and majority of patients with ischemic stroke were non-lacunar stroke (84%) and sixteen percent (16%) of them had lacunar infarction.

Cupini et al. (2002)<sup>11</sup> observed that of 292 adult patients with an acute first-ever ischemic stroke, 96(32.87%) were considered lacunar and 196(67.12%) were considered non-lacunar strokes in their study. The above findings strongly support the current study.

Khan et al (2009)<sup>15</sup> found the mean age of patients with ischemic stroke was 60.34 ±13.24 years ranging from 21- 103 years. Majority of patients (33%) were in the age of 7<sup>th</sup> decade, followed by patients in 6<sup>th</sup> decade<sup>14</sup>, which closely resembled with the current study, where the current study (Table II) found the mean age was 60.9±10.2 years in Group A and 56.2±11.8 years in Group B, which was almost similar between two groups (p>0.05). Singh et al. (2006)<sup>16</sup> observed in their study that the mean age of the patients was 58.6±12 years ranging from 25 to 85 years which closely resembled with the current study. On the other hand, Homurg et al. (2010)<sup>17</sup> has observed higher mean age in their study patients which were 64±13 years and 61±13 years in Group A and in Group B respectively, the higher age range may be due to increased life expectancy in their study patients.

In this current study (Table III) it was observed that male was predominant, which were 63.33% and 76.67% in group A and group B respectively. Male female ratio was 2.3:1 in the whole study which was slightly higher than those reported from elsewhere. May be this is a reflection of low tendency of female patients for seeking medical advice in tertiary hospital rather relying on treatment of rural doctors as in other parts of the developing world . Bejot et al. (2008)<sup>13</sup> reported that the incidence of lacunar infarcts was significantly higher in men than in women. Similarly, Mohammad et al. (2003)<sup>18</sup> observed that males were predominately affected than females from stroke. Ali et al. (1998)<sup>19</sup> found in their study that most of the stroke patients were male, and male female ratio was 2:1. All these observations closely resemble with the current study where male and female ratio was 2.3:1 and 3.2:1 in lacunar stroke and non-lacunar stroke respectively. The above findings strongly support the current study.

In this series (Table IV) it was observed that smoker was found in 36.67% patients with lacunar stroke and in 56.66% in nonlacunar stroke, which was not significantly (p>0.05) higher in patients having lacunar strokes. Cupini et al. (2002)<sup>11</sup> showed smoking among 35.4% and 33.2% of patients with lacunar and non-lacunar stroke respectively which was not significant (p>0.05), but was consistent with the current study. Similarly, Tejada et al. (2003)<sup>20</sup> showed smokers were almost similar between two groups.

In this current series it was observed that 90% and 63.33% patients were hypertensive in patients with lacunar and non-lacunar stroke respectively, which was significantly (p<0.05) higher in patients having lacunar strokes. Similarly, Khan et al. (2007)<sup>21</sup> have showed hypertension 88.6% in group A and 71.2% group B. Jackson and Sudlow (2005)<sup>22</sup> identified hypertension as a significant risk factor for lacunar stroke compared with non-lacunar ischemic stroke. Jackson and Sudlow et al. (2005)<sup>22</sup> mentioned in their study that the apparent excess of hypertension in lacunar infarction was confined to studies in which the presence of hypertension favored a diagnosis of lacunar infarction (pooled RR, 1.25; 95% CI, 1.21 to 1.28).

In this study it was observed that diabetes mellitus was significantly ( $p < 0.05$ ) higher in patients having lacunar strokes, which was 56.7% in group A and 30.0% in group B. Kaul et al. (2000)<sup>14</sup> reported that patients with lacunar infarction had higher frequency of diabetes and absence of significant (>50%) extracranial carotid artery disease. Similarly, Jackson and Sudlow et al. (2005)<sup>22</sup> mentioned that there was a significant excess of diabetes in lacunar versus nonlacunar infarction among studies using a classification in which diabetes favors a diagnosis of lacunar infarction (pooled RR, 1.25; 95% CI, 1.17 to 1.34). Jackson and Sudlow (2005)<sup>22</sup> suggested that the current trend of using the TOAST classification system could overestimate the role of hypertension and diabetes in lacunar stroke, as the criteria stipulate that a history of hypertension and diabetes may be useful indicators to the existence of SVD. All the above findings are consistent with the current study.

The atrial fibrillation of the present study patients was found 6.66% in group A and 16.66% in group B. In this study the incidence of atrial fibrillation was more in non-lacunar stroke than lacunar stroke that was not statistically significant ( $p > 0.05$ ). The frequency of atrial fibrillation was found to be higher in non-lacunar in some studies. Cupini et al. (2002)<sup>11</sup> showed atrial fibrillation was 4.2% in lacunar stroke and 23.5% in non-lacunar stroke. In another study Jackson and Sadlow et al. (2005)<sup>22</sup> demonstrated the association of AF with non-lacunar infarction was particularly pronounced among studies in which the presence of atrial fibrillation favored a diagnosis of non-lacunar infarction, which support the current study findings.

In this present series it was observed that myocardial infarction was found 16.7% patients having lacunar stroke and 43.3% patients having non-lacunar stroke, that was significantly ( $p < 0.05$ ) higher in patients having non-lacunar strokes. Similarly, Baumgartner et al. (2003)<sup>23</sup> myocardial infarction was 5.3% and 18.0% in lacunar and non-lacunar stroke respectively ( $p < 0.05$ ), which is consistent with the current study. In Khan et al. 2007 study myocardial infarction was significantly higher in patients with non-lacunar stroke<sup>27</sup>.

In this present series it was observed that carotid stenosis, was significantly ( $p < 0.05$ ) higher in

patients having nonlacunar strokes than patients having lacunar stroke, which was 23.3% in group A and 56.7% in group B. Similarly, Cupini et al. (2002)<sup>11</sup> have showed 16.7% and 24.5% patients had carotid stenosis in lacunar and nonlacunar stroke respectively. Several studies showed overall, there was an excess of ipsilateral carotid stenosis among patients with non-lacunar infarction<sup>24-27</sup>. The association was more pronounced in Jackson and Sudlow (2005)<sup>22</sup> study in which severe carotid stenosis favored a diagnosis of non-lacunar infarction and similar result was observed for contralateral stenosis. The above findings are comparable with the current study.

Previous TIA was found in 6.66% among group A and 16.66% among group B patients in this study. There was some difference of incidence of previous TIA between lacunar and non-lacunar strokes in this series, which was not significantly ( $p > 0.05$ ) higher in patients of both groups. In another study done by Cupini et al. (2002)<sup>11</sup> did not find a significantly different percentage of previous TIA between the 2 groups of patients having lacunar and non-lacunar stroke.

#### **Conclusion:**

To compare risk factors (i.e. Hypertension, diabetes mellitus, smoking, hypercholesterolemia, previous transient ischemic attack, myocardial infarction and carotid stenosis) between lacunar and non-lacunar strokes majority of the patients was found in 7<sup>th</sup> and 6<sup>th</sup> decade in lacunar and non-lacunar strokes respectively and male was predominant. Smoking status was almost similar between two groups. Hypertension and diabetes mellitus were significantly ( $p < 0.05$ ) higher in patients having lacunar strokes however, carotid stenosis, myocardial infarction, hypercholesterolemia were significantly ( $p < 0.05$ ) higher in patients having non-lacunar strokes. However, the percentage of smoking, previous TIA and atrial fibrillation were not significantly ( $p > 0.05$ ) different between lacunar and non-lacunar stroke.

#### **Study limitation:**

This study was based on data collected from Neurology ward and Medicine ward of a tertiary level hospital. As this study was based on a tertiary

level hospital so, the sample size was small, the findings may not represent overall population of our country. Majority of the stroke patients were not referred to such a tertiary care hospital and only the more severe cases were admitted. Further community based large sample studies are required to have an unbiased observation.

#### **Recommendation:**

Ischemic stroke management depends on stroke subtype. Cardio-embolic and artery to artery embolus are very uncommon cause of lacunar stroke and study suggests that patients with lacunar stroke may not require detailed evaluation of carotid artery or cardio-embolic sources. This study also strongly recommends that along with subtyping, determination of risk factors is essential for etiopathological correlation, management plan and outcome prediction both in lacunar and non-lacunar stroke. Risk factors should be studied to ensure better stroke care.

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