

# Frequency of Modifiable Risk Factors in Ischemic Stroke Patients at a Tertiary Care Hospital in Lahore Pakistan

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## Abstract

**Objective:** The objective was to find out the frequency of modifiable risk factors among patients of ischemic stroke at a tertiary care hospital in Lahore Pakistan.

**Study type, settings & duration:** This observational cross-sectional study was conducted at Medical Department Services Hospital, Services Institute of Medical Sciences, Lahore Pakistan from January 2019 to January 2020.

**Methodology:** After an informed consent 105 patients with ischemic stroke aged between 18-65 years from both sex was included in this study. Patients with trauma, tumor, arteriovenous malformations, unstable cardiopulmonary condition, psychiatric disease and hemorrhagic stroke were excluded. Demographic information and detailed history with physical examination was noted. Blood pressure and sugar levels were measured for all patients. All bloods test including fasting lipid profile were determined. SPSS version 17.0 was used for data analysis.

**Results:** A total of 105 patients of ischemic stroke were enrolled in the present study. Mean age of the patients was 51.2±8.4 years and 73 (69.5%) were male. Mean BMI was 29.3±2.9 kg/m<sup>2</sup>. Hyperlipidemia was the most frequent risk factor seen in 53 (50.5%) patients with ischemic stroke followed by obesity in 48 (45.8%) patients, smoking in 43 (40.9%), hypertension in 41 (39.1%) and diabetes mellitus in 41 (39.1%) patients.

**Conclusion:** Hyperlipidemia was the leading risk factor in ischemic stroke patients in the present study followed by obesity, smoking, diabetes mellitus and hypertension respectively.

**Key words:** Ischemic stroke, hypertension, hyperlipidemia, diabetes mellitus, smoking, obesity.

## Introduction

Stroke also called cerebrovascular accident (CVA) is an important health problem worldwide causing significant morbidity, disability and mortality. Stroke is defined as loss of function of

body part due to denervation caused by death of brain cells which results from sudden loss of central blood flow to the brain cells.<sup>1</sup> Stroke may occur as a result of brain cells death due to occlusion of brain vessels where it is called an ischemic stroke. Stroke can also occur because of rupture of blood vessel in brain where it is termed as hemorrhagic stroke. Overall around 85% strokes are ischemic and 15% strokes are hemorrhagic in origin.<sup>1</sup> Incidence of stroke is different in different parts of the world. According to American Heart Association (AHA) report, stroke is fifth leading cause of death in USA.<sup>1</sup> According to World Health Organization report, out of 5.5 million stroke related deaths, 20% were from South Asia.<sup>2</sup> As per Pakistan Stroke Society, stroke incidence is 250 cases per 100,000 people accounting for approximately 350,000 cases per annum.<sup>3</sup> The frequency of pathological types in stroke is variable in various ethnic populations with Asians having higher rates of intracerebral

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### Authors Contribution

HN, AA & SA conceptualized the project. HN, FA & MM did the data collection. NIB, FA & MM did the literature search. NIB performed the statistical analysis. Drafting, revision & writing of manuscript were done by all authors.

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hemorrhage which may be related to variation in exposure to environmental and genetic risk factors along with the differences in links of risk factors to pathological types.<sup>4</sup> Stroke is also a major cause of disability and financial burden on health care resources.<sup>1,5</sup> Various modifiable and non-modifiable factors increase risk for stroke e.g. smoking, diabetes mellitus, heart disease, atrial fibrillation, hypertension, obesity and hyperlipidemia. Management of modifiable risk factors is very crucial in prevention of subsequent recurrent stroke. Successful control of modifiable risk factors, stroke incidence may be decreased. Various studies have been done to determine prevalence of modifiable risk factors for stroke with varying results. These risk factors depend upon population being studied.

Smoking (45.1%) was the most common risk factor in ischemic stroke in a study conducted in Korea, followed by hypertension (28%) and diabetes mellitus (14.6%).<sup>4</sup> A study conducted in Egypt showed that modifiable risk factors for stroke included hypertension (62.3%) as the leading risk factor followed by dyslipidemia (58.1%), smoking (41.3%) and diabetes mellitus (34.7%).<sup>6</sup> Hypertension (60.8%), diabetes mellitus (35.7%) and tobacco use (32.2%) were reported as common risk factors in Indian patients with Ischemic Stroke.<sup>7</sup> In another Indian study, the most common risk factors in ischemic stroke were dyslipidemia (67.1%), metabolic syndrome (64.3%), hyperhomocysteinemia (58.9%), smoking (52%) and hypertension (44.2%).<sup>8</sup> From Bahawalpur, hypertension (58%), ischaemic heart disease (35%), smoking (27%) and diabetes mellitus (18 %) were reported as commonly associated with increased risk for stroke.<sup>9</sup> Hypertension (70.8%) was the most common risk factor for stroke followed by dyslipidemia (60.1%), diabetes mellitus (39.2%) and smoking (26.0%) in Islamabad.<sup>10</sup> Hypertension (65%) was the most common risk factor followed by smoking (32%), diabetes mellitus (36.3%), dyslipidemia (32.7%) and obesity (18%) at Karachi.<sup>11</sup> A study conducted at Jamshoro and Hyderabad showed that hypertension was present in 51.0%, diabetes mellitus and dyslipidemia in 30.0%, smoking in 22% in patients of ischemic stroke.<sup>12</sup> Hyperlipidemia (37.1%) was the most frequent risk factor in Multan, furthermore the frequency of hypertension (10.1%) and diabetes mellitus (9.6%) was quite less.<sup>13</sup> To look for differences in Northern and Southern Indian patients of ischemic stroke, 2066 patients were assessed to report that North Indian patients were significantly older with fewer men and had lower rates of diabetes (32.8% vs. 38.7%), dyslipidemia (3.5% vs. 25.7%) and tobacco smoking (27% vs. 38%).<sup>14</sup>

This study was conducted with the rationale that evaluation of modifiable risk factors for ischemic stroke is very important for prevention of recurrence of stroke. Prevalence of the different risk factors for stroke in different studies carried out on different study populations, both nationally and internationally is variable. It is not known whether ethnic differences play a role in pathogenesis of these risk factors and the subsequent development of ischemic stroke. Once modifiable risk factors are identified, physicians can treat and manage those factors to avoid further event. This will help in prevention of morbidity and mortality associated with this condition. Furthermore, estimation of modifiable risk is also important for primary prevention of stroke in patients who have multiple risk factors which can predispose to stroke.

## Methodology

This descriptive cross-sectional study was conducted at department of Medicine Services Hospital, Lahore from January 2019 to January 2020 with a sample size of 105 keeping 95% confidence level and 5% margin of error, with anticipated frequency of smoking (45.1%), hypertension (28%) and diabetes mellitus (14.6%).<sup>4</sup> Ischemic Stroke was defined as patients who presented with loss of function of one or more than one part of the body on clinical examination and radiologically assessed with CT brain scan at the time of admission. Hyperlipidemia was defined as (any of these): LDL >4.1mmol/L, HDL <2.08mmol/L, total cholesterol >5mmol/L or triglycerides >1.7mmol/L on fasting lipid profile analysis. Hypertension was defined as elevated blood pressure exceeding 140/90 mm of Hg on  $\geq 2$  different occasions or ambulatory blood pressure of greater than 130/85 mm of Hg at least 15 days apart, currently or on past history. Diabetes mellitus was diagnosed as fasting blood sugar level was >126 mg/dl, currently or on past history. Cigarette smoking was defined as  $\geq 5$  pack years. Obesity was defined as BMI  $\geq 30\text{kg/m}^2$ .

Patients with past history of stroke, patients with trauma or tumor, malignancy, arteriovenous malformations, unstable cardiopulmonary condition, psychiatric disease and hemorrhagic stroke as assessed by CT scan brain at admission were excluded from the study. Using non-probability consecutive sampling, 105 patients of ischemic stroke aged 18 to 65 years of both sexes were enrolled in this study after informed consent from the patient and/or attendant. Demographic particulars of patients including detailed history and physical

**Table 1: Stratification of modifiable risk factors with regards to age groups.**

Modifiable Variables	Non-modifiable risk factor: Age		p-value
	18-40 years (n=13)	41-65 years (n=92)	
Hypertension:			
Present	01 (7.6%)	40 (43.5%)	0.013
Absent	12 (92.4%)	52 (56.5%)	
Diabetes Mellitus:			
Present	05 (38.4%)	36 (39.2%)	0.963
Absent	08 (61.6%)	56 (60.8%)	
Smoking:			
Present	06 (46.2%)	37 (40.2%)	0.684
Absent	07 (53.8%)	55 (59.8%)	
Hyperlipidemia:			
Present	05 (38.4%)	48 (52.1%)	0.355
Absent	08 (61.6%)	44 (47.9%)	
Obesity:			
Present	08 (61.6%)	40 (43.4%)	0.883
Absent	05 (38.4%)	52 (56.6%)	

**Table 2: Stratification of modifiable risk factors with regards to sex.**

Modifiable Variables	Non-modifiable risk factor: Sex		p-value
	Male (n=73)	Female (n=32)	
Hypertension:			
Present	24 (32.8%)	17 (53.1%)	0.050
Absent	49 (67.2%)	15 (46.9%)	
Diabetes Mellitus:			
Present	32 (43.8%)	09 (28.1%)	0.129
Absent	41 (56.2%)	23 (71.9%)	
Smoking:			
Present	30 (41.1%)	13 (40.6%)	0.964
Absent	43 (58.9%)	19 (59.4%)	
Hyperlipidemia:			
Present	37 (50.7%)	16 (50.0%)	0.948
Absent	36 (49.3%)	16 (50.0%)	
Obesity:			
Present	27 (36.9%)	21 (65.6%)	0.609
Absent	46 (63.1%)	11 (34.4%)	

examination were assessed and entered on a pre-designed proforma. Blood pressure and blood sugar levels and all blood test including fasting lipid profile were measured. Patients were treated as per hospital protocol.

Data was entered in SPSS version 21.0 and analyzed. All quantitative variables were depicted as mean and SD. All qualitative variables were depicted as frequency and percentage. Data was stratified and chi-square test was applied to see effect modifiers by keeping *p*-value of <0.05 as significant.

The ethical approval was obtained from Institutional Review Board of Services Institute of Medical Sciences, Lahore.

## Results

Out of the 105 patients with ischemic stroke enrolled in our study, 73 (69.5%) were male and 32 (30.5%) were female. Mean age of the patients was 51.2±8.4 years. Ninety-two (87.6%) patients were

older than 40 years while 13 (12.4%) were aged 40 years or younger. Hyperlipidemia was the leading risk factor found in 53 (50.5%) ischemic stroke patients. Mean BMI of the patients was 29.3±2.9 kg/m<sup>2</sup> and 48 (45.8%) were obese. Smoking was reported in 43 (40.9%) followed by hypertension in 41 (39.1%) and diabetes mellitus in 41 (39.1%) ischemic stroke patients.

Stratification of outcome (modifiable risk factors) with respect to non-modifiable risk factors (age and sex) of the patients is shown in Table-1 and Table-2 respectively demonstrating that hypertension was significantly associated with both age (*p*-value 0.013) and sex (*p*-value 0.050) of the ischemic stroke patients.

## Discussion

There is a variable prevalence of the different risk factors in different studies carried out on different study populations, both internationally

and within Pakistan. It is not known whether ethnic differences play a role in pathogenesis of these risk factors and the subsequent development of ischemic stroke. Once modifiable risk factors are identified, physicians can treat and manage those factors to avoid further event.

In our study out of the 105 patients with ischemic stroke, 73 (69.52%) were male with male to female ratio of 2.3:1. Age of the patients ranged from 18 to 65 years. Mean age was 51.2±8.4 years with 92 (87.62%) patients aged between 41-65 years. Venugopalan et al.<sup>14</sup> assessed 2066 patients from north India and reported the significantly older patients and fewer men with ischemic stroke.

In the current study participants, hyperlipidemia was the most commonly seen modifiable risk factor found in 53 (50.5%) patients followed by obesity in 48 (45.8%) patients, Abid et al.<sup>13</sup> from Multan reported hyperlipidemia (37.1%) as the most frequent risk factor, furthermore the frequency of hypertension (10.1%) and diabetes mellitus (9.6%) was quite less. The association of stroke and dyslipidemia is complex as raised total cholesterol level increases risk while raised levels of high-density lipoprotein cholesterol lowers stroke risk.<sup>1</sup> Furthermore elevated cholesterol is significantly associated with large artery ischemic stroke as compared to other subtypes of stroke.<sup>4</sup> Additionally total cholesterol is inversely linked with risk of hemorrhagic stroke evidenced by hemorrhagic stroke risk rising as total cholesterol lowers.<sup>15</sup> Although various studies depicts inconsistent and contrasting link of dyslipidemia with risks of hemorrhagic and ischemic stroke, statin use appears to lower risk of ischemic stroke while having no definite elevation hemorrhagic stroke risk. Risk of ischemic stroke increased with rising values of total cholesterol and LDL.<sup>15</sup> MRFIT study showed that risk of ischemic stroke increased with cholesterol >200mg/dl, and the risk doubled with cholesterol >280 mg/dl. Spengos et al.<sup>16</sup> surveyed 253 ischemic stroke patients aged ≤45 years old and reported smoking in 59% and hyperlipidemia in 41%. People aged 15 to 45 years who smoke are at higher risk to suffer stroke as compared to non-smokers and the higher the duration and dose of smoking the higher the risk.

Hypertension and diabetes was seen in 41 (39.1%) patients however it has been reported as the major risk factor in ischemic patient by others. In the study conducted in Korea by Park et al.<sup>4</sup> it was seen that major risk factors for stroke were smoking (45.1%), hypertension (28%) and diabetes mellitus (14.6%). The frequency of hypertension in our study is less than 86.5% reported by Desalu et al.<sup>17</sup> and 76% by Eze et al.<sup>18</sup> Khan et al.<sup>11</sup> also reported

hypertension (65%) as the most common risk factor followed by smoking (32%), diabetes mellitus (36.3%), dyslipidemia (32.7%) and obesity (18%) at Karachi. Frequency of diabetes mellitus in our study was more than the 23.8% by Desalu et al.<sup>17</sup> The study conducted in Egypt by Soliman et al.<sup>6</sup> showed that modifiable risk factors for stroke included hypertension (62.3%), diabetes mellitus (34.7%), dyslipidemia (58.1%) smoking (41.3%). The study conducted at Jamshoro and Hyderabad by Kumar et al.<sup>12</sup> showed that hypertension was present in 51.0%, diabetes mellitus and dyslipidemia in 30.0%, smoking in 22% in patients of ischemic stroke. Kamal et al.<sup>19</sup> reported hypertension in 60%, diabetes mellitus in 20%, hyperlipidemia in 18%, smoking 16% and cardiovascular disease in 16% which is in contrast to our findings. In Karachi, Shaikh et al.<sup>20</sup> reported hyperlipidaemia in 19.65%. In India, Chethan et al.<sup>8</sup> reported the most common risk factors in ischemic stroke were dyslipidemia (67.1%), metabolic syndrome (64.3%), hyperhomocysteinemia (58.9%), smoking (52%) and hypertension (44.2%).

In ischemic stroke patients aged 18-45 years analyzed by Dash et al.<sup>21</sup> hypertension (34.4%) was the most frequent risk factor. Kumar et al.<sup>22</sup> reported hypertension in 79 (72.5%) ischemic stroke patients aged 15-45 years. Hypertension (70.8%) was the most common risk factor for stroke followed by dyslipidemia (60.1%), diabetes mellitus (39.2%) and smoking (26.0%) reported by Ahmed et al.<sup>10</sup> in Islamabad.

With regards to age, 01 (7.6%) of the 13 patients aged 18-40 years in our study had hypertension compared to 40 (43.5%) of the 92 patients aged 41-65 years having a statistical association (p-value 0.013) indicating that hypertension was a significant risk factor for stroke in older patients. With regards to sex, 24 (32.8%) of the 73 male patients had hypertension compared to 17 (53.1%) of the 32 female patients having a statistical association (p-value 0.05) indicating that hypertension was a significant risk factor for stroke in female patients. Ji et al.<sup>23</sup> showed the prevalence of hypertension (20%), diabetes mellitus (11%), dyslipidemia (38%) and smoking (34%) in young patients with stroke. Putaala et al.<sup>24</sup> studied 3,944 young patients with stroke and reported that commonly seen risk factors were smoking (49%), dyslipidemia (46%) and hypertension (36%).

There is a variable prevalence of the different risk factors in different studies carried out on different study populations, both internationally and within Pakistan. It is not known how ethnic differences play a role in pathogenesis of these risk factors and the subsequent development of ischemic stroke.

Modifiable risk factors have great significance because strategies to reduce them subsequently lower stroke risk, therefore prompt identification and modification of these factors is vital.<sup>23,25,26</sup> Hypertension has a continuous, linear and direct association with stroke risk.<sup>27</sup> According to INTERSTROKE,<sup>28</sup> by incorporating both a history of hypertension and blood pressure reading of 160/90 mmHg, the proportion of strokes attributable to hypertension was 54% but the effect of hypertension was higher for hemorrhagic stroke as compared to ischemic stroke. Blood pressure increases with rising age, thus elevating the lifetime probability of developing hypertension and more than two-third people aged  $\geq 65$  years have hypertension.<sup>29</sup> Along with medications, behavioral lifestyle changes including diet modification and regular physical activity help to lower the burden of hypertension and subsequently aid in lowering stroke risk. Recent studies depict intra-individual variations in blood pressure readings, or changes in blood pressure readings measured at various points in time, are linked with higher stroke risk as compared to raised mean blood pressure alone suggesting that blood pressure agents that lower variability (calcium channel blockers) have higher benefits than agents that reduce mean blood pressure only.<sup>29</sup> However, the Cardiovascular Health Study<sup>30</sup> showed no association of blood pressure variability with stroke risk, but had association with adverse cardiac events and all-cause mortality. Diabetes mellitus and pre-diabetes increases stroke risk 2-fold with poor diabetes control and long duration of diabetes significantly elevating the risk of stroke and up to 20% deaths in diabetics are attributed to stroke.<sup>31,32</sup> The rise of diabetes mellitus in younger patients can also help to explain increased risk of stroke in the young and reduction in stroke risk has been observed by using both medical therapy and lifestyle modifications.<sup>33</sup> Moreover, glycemic control by itself does not reduce risk to the extent that combined behavior modification and medical therapy does.<sup>34</sup> There are a few limitations of our study as well. Our study was a descriptive non-randomized cross-sectional study and therefore limited due to patient selection bias. A single center-based study having a relatively small sample size, our results may not be generalized to general population. Our study should be used as a stepping stone based on which further studies should be conducted to collect further evidence.

We concluded that hyperlipidemia was the leading risk factor seen in ischemic stroke in the present study conducted at a tertiary care hospital of Lahore Pakistan followed by obesity, smoking, diabetes mellitus and hypertension.

**Conflict of interest:** None declared.

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