



RISK FACTORS FOR ISCHEMIC STROKE- A CASE CONTROL STUDY

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Stroke is global health problem and is a leading cause of disability. It is one of the leading causes of mortality and morbidity worldwide. In rapid increase in burden of stroke in coming years and limited availability of stroke care in India, it would be better to study stroke prevention strategies. The current hospital based case-control study was undertaken with aim to identify the risk factors for ischemic stroke. A study was carried out in BLDEU's Shri B M Patil Medical College, Hospital & Research Centre. A prospective case-control, age matched study was designed to find the risk factors. Comparing the cases with controls, hypertension, diabetes mellitus, smoking, obesity and hypercholesterolemia were significant Risk factors, whereas Alcohol, Family history of stroke and Transient ischemic attack were not found to be statistically significant risk factors. The most significant risk factors was systemic hypertension, (OR=9.3) followed by diastolic (OR=6.19), Hypercholesterolemia (OR=4.115), Diabetes (OR=3.542), smoking and obesity (OR=2.333, OR=2.151 respectively). Current study found, Hypertension, Diabetes, Smoking, Obesity and Hypercholesterolemia were strong association with Ischemic stroke. Prevention of these modifiable risk factors can lead to decrease in the incidence of stroke.

KEYWORDS: Ischemic stroke, Risk factors, Univariate analysis and odds ratio.**INTRODUCTION**

Stroke is becoming an important cause of premature death and disability in low income and middle income countries like India, largely driven by demographic changes and enhanced by the increasing prevalence of the key modifiable risk factors. As a result, developing countries are exposed to a double burden of both communicable and non communicable diseases. The poor are increasingly affected by stroke, because of both the changing population exposures to risk factors and most tragically, not being able to afford the high cost for stroke care. Majority of stroke survivors continue to live with disabilities and the costs of ongoing rehabilitation and long term care are largely undertaken by family members, which impoverish their families^[1,2]. In spite recent advances in acute stroke treatment, effective prevention of stroke by means of improved control of risk factors have the greatest potential to reduce the burden of stroke. And also to reduce the economic burden of stroke, a better understanding of risk factors for prevention is mandatory. Numerous risk factors such as hypertension, cigarette smoking, diabetes mellitus, hyper-lipidemia and cardiac disease have been recognized as well-documented modifiable risk factors for ischemic stroke^[3,4]. Data from hospital –based studies offer important information for the design of future epidemiological studies on the risk factors of stroke patients. The purpose of this prospective hospital based study was to investigate risk factors in a group of first ever ischemic stroke patients.

METHODS

A present study was carried out at BLDEU's Shri B M Patil Medical College, Hospital & Research Centre, Bijapur, India. The study was designed as age matched case-control study.

Cases: The study consisted of 78 hospitalized CT scan proved cases of stroke. The recruitment of cases in the study was performed prospectively and only incident cases (first ever in the lifetime) were included. Hence we did not include cases that had a past history of any type of stroke.

Controls: The controls were selected from patients who attended the study hospital for conditions other than stroke (confirmed with CT scan). For each case of stroke, one control was selected. The controls were matched to cases in respect to age (± 5 years), sex. One hundred controls were selected in the same manner.

Sample size: A pilot study, using the methods described below, was performed to determine the sample size and for assessing the feasibility of the study. Six risk factors for stroke were determined in 30 randomly selected stroke cases admitted in medicine wards and equal number of age and gender matched controls admitted to diseases other than stroke in the same medicine wards.

The odds ratio of six risk factors was estimated. An average odds ratio 3.0 and prevalence of hypertension in general population 10%,^[21] allowing error of 5% and with 90% the power of study, sample size calculated was 93 (Lwanga, S.K. & Lemeshow, S.)^[22]. Hence a total of 100 stroke cases and equal number of controls were

selected. Further we classified the stroke cases as Ischemic and Hemorrhagic strokes. Out of 100 stroke cases, we found, 78 ischemic stroke cases and 22 hemorrhagic stroke cases. Hence, finally 78 ischemic stroke cases and 100 controls were included in the study to identify the risk factors for Ischemic stroke.

Risk Factors

Eight risk factors including hypertension, diabetes mellitus, cigarette smoking, serum cholesterol, smoking, alcohol consumption, waist to hip ratio, family history of stroke and transient ischemic attack were identified. Subject was considered to have hypertension if they had systolic blood pressure ≥ 140 mmhg or diastolic blood pressure ≥ 90 mm hg. Diabetes mellitus was diagnosed if a subject had fasting blood glucose level was ≥ 120 mm/dl. On admission we considered only those who currently smoked cigarettes, which was defined as smoking more than 10 cigerrates day for more than 6 months. We defined alcohol consumption as a person who has consumed alcohol at least once a day for a minimum period of 6 months. Transient ischemic attack defined as abrupt onset of focal neurological deficit lasting less than 24 hours. Subjects were considered to have obesity only when waist: hip ratio was ≥ 0.9 cm in males and ≥ 0.8 cm in females. And if participants had serum cholesterol ≥ 220 mg/dl, considered as hypercholesterolemia.

Statistical Analysis

Bivariate analysis on matched pairs was carried out. Odds ratio, their 95% confidence interval (CI), Chi square test was calculated for all the risk factors. The continuous data like Age, systolic and diastolic blood pressure, fasting blood sugar level, waist to hip ratio and serum cholesterol level were presented with mean \pm SD and were compared by using unpaired ‘t’ test and Mann Whitney ‘U’ test.

RESULTS

Table (1) and (2) shows the distribution of cases and controls according to age and gender. Among cases

65(84%) of patients were 50 years age group and among controls 83 (83%). The mean (\pm SD) age of cases was 62.02 (± 12.80) and that of control was 62.39 (± 12.27) years. There was no significant difference found between ages of cases and controls ($P=0.7420$).

TABLE 1: Distribution of cases and controls according to age

Age(years)	Cases (%)	Controls (%)
30-40	4 (5)	4 (4)
40-50	9 (11)	13 (13)
50-60	16 (22)	26 (26)
60-70	28 (36)	26 (26)
70-80	12 (15)	22 (22)
≥ 80	9 (11)	9(9)
Total	78	100

Among cases 48(62%) were males and 30(38%) were females; 59(59%) were males and 41(41%) were females in control group. Statistically no significant difference was found between cases and control regarding gender ($P=0.7315$) (Table (2)). The potential risk factors for ischemic stroke that are investigated are shown in Table (3).

TABLE 2: Distribution of cases and control according to gender

Gender	Cases (%)	Controls %
Males	48(62%)	59(59%)
Females	30(38%)	41 (41%)
Total	78	100

Both systolic blood pressure (156.461 ± 27.879 mmhg vs 127.73 ± 26.856 mmhg) and diastolic blood pressure (90.576 ± 14.801 mmhg vs 80.35 ± 13.68 mmhg) were higher among cases than among controls. Stroke victims had higher serum cholesterol levels (239.653 ± 47.451 mm/dl vs. 191.51 ± 40.209 mm/dl).

TABLE 3: Mean and standard deviation of selected Risk factors in cases and controls

Risk factors	Cases/Controls	Mean	S.D	t. Test/Mean Whitney U Test	P Value
Mean age (Years)	Cases	62.02	12.8	$t=0.3297$	$P=7420$
	Controls	61.39	12.27		
Mean systolic blood pressure (mmHg)	Cases	156.461	27.879	$U=1.6955$	$P<0.0001$
	Controls	127.73	26.865		
Mean diastolic blood pressure (mmHg)	Cases	90.576	14.801	$U=2185.5$	$P<0.0001$
	Controls	80.35	13.68		
Mean fasting blood sugar mm/dl	Cases	142.525	63.166	$U=2923.5$	$P=0.0042$
	Controls	109.19	31.658		
Mean serum cholesterol (mm/dl)	Cases	239.653	47.451	$U=1698.5$	$P<0.0001$
	Controls	191.51	40.209		
Waist – hip ratio (cm)	Cases	1.0316	0.1070	$U=3098.5$	$P=0.0189$
	Controls	0.9966	0.1247		

Fasting blood sugar higher controls (142.525 ± 63.166 mm/dl vs. 109.19 ± 31.658 mm/dl) and higher waist to hip ratio i.e. more abdominal obesity (1.0316 ± 0.9966 cm vs. 0.1070 ± 0.1274 cm) than controls group. The difference between cases and controls across all risk

factors found to be statistically significant ($P<0.05$). A univariate analysis was applied to find the association between risk factors and ischemic stroke. Table (4) describes comparison of cases and controls according to exposure to risk factors and results of univariate analysis.

TABLE 4: Bivariate Analysis of risk factors of stroke

Risk factors	Cases	Controls	OR	95% C.I.	X ²	P value
Hypertension						
Present	46	30	3.354	1.801-6.247	15.036	P=0.0001
Absent	32	70				
Blood Pressure						
SBP≥ 140	66	37	9.365	4.481-19.572	40.748	P<0.0001
SBP<140	21	63				
DBP≥ 90	60	35				
DBP<90	18	63	6.190	3.173-12.076	30.947	P<0.0001
Diabetes Mellitus						
Present(FBS≥120)	30	15	3.542	1.734-7.232	12.769	P=0.0001
Absent(FBS<120)	48	85				
Smoking						
Smokers	39	39	30	2.333	1.260-4.322	P<0.0066
Non-smokers	39	39	70			
Alcoholism						
Present	22	20	1.571	0.7840-3.150	1.636	P=0.2008
Absent	56	80				
Family History of stroke						
Present	17	16	1.463	0.6854-3.123	0.9744	P=0.3236
Absent	61	84				
Transient Ischemic attack						
Present	22	19	1.675	0.8299-3.380	2.094	P=0.1478
Absent	56	81				
Obesity						
Present	64	68	2.151	1.052-4.398	4.515	P=0.0336
Absent	14	32				

Hypertension

Among Ischemic stroke cases 46(59%) had hypertension, whereas among controls only 30(30%) had the diseases. The association was statistically significant ($X^2= 15.0216$, $P=0.0001$). And also it was found to be significant risk factor for ischemic stroke (OR = 3.354, 95% C.I. 1.801-6.247). On admission of the patients both systolic and diastolic blood pressure were recorded. Among cases 66(84%) had SBP 140 mmhg compared to 12(12%) among controls (OR=9.365, 95% C.I. 4.481-19.572) and 60(77%) had DBP 90 mmhg compared to 35(35%) among controls. (OR=6.190 95% C.I. 3.173-12.076). Thus SBP and DBP were found to be risk factors for ischemic stroke; also there was an association between ischemic stroke and SBP and DBP ($X^2 = 40.748$ $P<0.0001$ and $X^2= 30.947$, $P<0.0001$) respectively.

Diabetes Mellitus

The ischemic stroke cases had significantly higher proportion of diabetes mellitus 30(44%) than controls 15 (15%), It was found significant association between diabetes and risk of ischemic stroke ($X^2=12.769$, $P=0.0004$). The risk of ischemic stroke is three times more (OR=3.542, 95% C.I.1.734- 7.232)

Smoking

Out of 78 cases of ischemic stroke cases 39(42%) were smokers compared to 30(30%) of controls. There was a significant association between smoking and ischemic stroke ($X^2= 7.384$ $P=0.0066$). And habit of smoking doubled the risk of ischemic stroke (OR=2.333, 95% C.I. 1.260-4.322). In the present study 22(25%) were alcoholic in the ischemic stroke cases and 20(20%) among controls. No statistical association was found between alcohol and ischemic stroke. ($X^2= 1.636$, $P=0.2008$).

Family history of stroke

Among cases 17(22%) controls 16(16%) had family history of stroke. Significant association was not found between ischemic stroke and family history of stroke. ($X^2=0.974$, $P=0.3236$). The current study revealed that family history of stroke is not a risk factor ischemic stroke (OR=1.463, 95% C.I. 0.6854-3.123).

Transient Ischemic Attack (T.I.A); among cases 22(28%) had significant past history of TIA, among controls only 19(19%) had reported such a history. Our result suggested that TIA is not a risk factor ischemic stroke. (OR=1.675, 95% C.I. 0.8299 to 3.380).

Obesity

Among cases 64(95%) were obese whereas 68(68%) among controls. Obese is significantly associated with ischemic stroke ($X^2= 4.515$, $P=0.033$). The risk of an obese doubled the risk of ischemic stroke (OR=2.151, 95% C.I. 1.052-4.398).

Hypercholesterolemia

53(65%) of case had serum cholesterol level >220 mg/dl as against only 34 (34%) among controls. Extremely significant association was found between serum cholesterol and ischemic stroke ($X^2=20.212$, $P<0.0001$) the risk of ischemic stroke was 4 times higher with hyper cholesterol (OR=4.115, 95% C.I. 2.191-7.731).

DISCUSSION

The current study provides estimated of the odds ratio of Ischemic stroke associated with various risk factors. Our data indicate that hypertension, diabetes mellitus, smoking, obesity and hypercholesterolemia in univariate analysis were significantly associated with ischemic type of stroke. No significant association with the risk of

ischemic stroke was found for alcohol, family history of stroke and TIA. Hypertension is recognized as the most common risk factor of ischemic stroke in this study. The same result of hypertension replicate the same outcome in many studies^[3,4,7,8,9]. Our study found that smokers among cases were 39(42%), having $P=0.0066$, odds ratio of 2.33. Our study findings are in the near range of studies^[4,8,9,11]. During recent years, obesity (including waist to hip ratio) has received increased attention as a possible risk factor for stroke. Our findings of a significant association of waist to hip ratio with the risk of ischemic stroke suggest that obesity may be a more potent risk factor for ischemic stroke. The odds of ischemic stroke and diabetes mellitus were 3.5 in our study. But surprising result reported was the lack of association between diabetes and the risk of ischemic stroke^[7,8]. However other researchers reporting that those with diabetes mellitus were at greater risk for stroke from control subjects^[12, 13]. Serum cholesterol level is associated with ischemic stroke and is increased the risk of ischemic stroke. But the study by TengYeow Tan *et al.*, 2004 found that, serum cholesterol level is not a risk factor for ischemic stroke^[8]. The univariate analysis suggested that TIA was not associated with ischemic stroke. Similar finding was reported by Valery L. *et al.*, 1988^[7].

CONCLUSION

Our analysis indentified several risk factors that were significantly associated with risk of first ever ischemic stroke. Findings suggest that hypertension, hypercholesterolemia obesity, and diabetes are the biggest risk factors for ischemic stroke is important because like many other factors, these are modifiable risks that can be addressed by a proper medication and life style changes. Weight reduction, cessation of cigarette smoking and exercise. These simple treatments and life style alteration have a greater potential for ischemic stroke prevention. The most important message from this study for both clinicians and policymakers is that, adequate prevention measures of modifiable stroke risk factors may contribute to prevention of severe morbidity and mortality.

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