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FACTORS ASSOCIATED WITH STROKE AND ITS OUTCOME AMONG PATIENTS ATTENDING TERTIARY CARE HOSPITAL IN BANGALORE

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ABSTRACT

Introduction: Globally, cerebrovascular disease (stroke) is the second leading cause of death. Comprehensive information on stroke mortality, morbidity, risk factors and disability are required for planning and implementing programmes in prevention, management and rehabilitation. Due to demographic changes, strategies to reduce stroke burden and ensure adequate health resources are urgently needed. **Objective:** To study the factors associated with stroke and its outcome. **Material and Methods:** Case control approach for assessing risk factors and longitudinal study-follow up of 28 days for assessment of outcome. Pre designed, semi structured questionnaire was administered after validation by pilot testing. **Study Population**: **Cases:** All patients with first stroke diagnosed and confirmed with radiological investigations admitted to the hospitals. **Controls:** For each case two controls were selected (1:2) for whom gender and +5 year age class intervals was matched. **Sample Size**: Sample size worked out to be 60 cases and 120 controls. **Statistical analysis**: Frequency of various risk factors among the cases and controls was found out and tested for statistical significance employing chi-square/ Fischer exact test. Significant factors in the univariate analysis was included for multivariate logistic regression analysis to find out the independent risk factors related to the development of the disease. **Results:** Mean age of persons with stroke was 61.08+1.32. 27(45%) of cases had diabetes. 38 (63.3%) of cases had hypertension. Hypertension and family history were highly statistically significant (p=<0.001). 19(31.7%) of cases were either past or present smokers. 16(26.7%) of cases and 17(14.2%) of controls had history of alcohol intake. Functional outcome of stroke subjects was measured using Modified Rankin Scale at the time of admission and at the end of 28 days. Mean score was 23.95 at the time of admission and 17.95 at the 28 days time. This was statistically not significant (p=0.118). **Summary and conclusion:** Increasing age, male gender and family history of stroke are the non modifiable risk factors of stroke as seen in this study. Other important modifiable risk factors were diabetes, smoking, alcohol intake, increased central obesity, increased LDL levels which can be reduced using adequate preventive strategies. Severity of the disease is shown by 50% ICU admission, and severe disability in 16.7% of the patients and also by the presence of loss of consciousness and speech impairment and paresis.

KEYWORDS: Stroke, Risk factors, Outcome.

INTRODUCTION

Globally, cerebrovascular disease (stroke) is the second leading cause of death. It was estimated that stroke as the sixth most common cause of disability adjusted years of life lost (DALY) world- wide during 2000. It has been projected that it will become the fourth most common cause by 2020.[1] In addition to being a major cause of death many surviving stroke patients are disabled and need help in activities of daily living which must be provided by family members, the health system, or other social institutions. Comprehensive information on stroke mortality, morbidity, risk factors and disability are required for planning and implementing programmes in prevention, management and rehabilitation. Due to demographic changes, strategies to reduce stroke burden and ensure adequate health resources are urgently needed.

As it is evident that reduction of burden of stroke is mainly by risk factor modification we proposed to identify the most common risk factors and quantify them. As stroke causes disability in many affected persons we also measured outcome of stroke patients. Patients were also followed up for 28 days to know the outcome. This information would help in formulating policies for treatment and rehabilitation.

METHODS

Objective was to study the factors associated with stroke and its outcome in patients admitted to M S Ramaiah hospitals. Case control approach was used for assessing risk factors and longitudinal study - follow up of 28 days for assessment of outcome. Study was conducted in M S Ramaiah Medical college hospitals. M S Ramaiah Teaching hospital is a multi speciality hospital with 800 beds capacity. M S Ramaiah Memorial Hospital is again a multi speciality hospital with 400 bed strength. Cases constituted by all subjects with first stroke diagnosed and confirmed with radiological investigations admitted to these hospitals. For each case two controls were selected (1:2) for whom gender and +5 year age class interval was matched. Controls were from among patients admitted to medical wards and surgical wards for diseases not related to vascular pathologies.

Inclusion criteria

Cases

1. Development of sudden onset neurological deficit respecting a vascular territory with sustained deficit at 24 hours verified by a healthcare professional.
2. Evidence of stroke on MRI or non contrast CT scan confirmed by neurologist.

Controls

1. Patients from in-patient departments with minor complaints for example, refractive errors, cataracts and minor ear, nose and throat complaints.
2. Patients from surgical day care departments undergoing minor elective surgery for example, hernia repair, hemorrhoids, etc.

Exclusion criteria

Cases: Inability to consent due to disability and non-availability of a valid surrogate respondent. A valid surrogate respondent is defined as a spouse, a first degree relative living in the same house or an attendant self identified as aware of the patient's medical history, habits and behaviors.

Controls

1. Stroke or TIA phenotype or undefined prior neurologic event.
2. Admitted for myocardial infarction or coronary artery bypass and graft surgery.
3. Pregnancy.

Complete enumeration of the stroke patients admitted to both M S Ramaiah hospitals during study period.

Sample size was calculated on basis of study carried out by Nagaraj et al[2] indicated that prevalence of hypertension to be 48%. The various prevalence surveys carried out in the country amongst general population has revealed that the prevalence of hypertension to be 16%. To detect difference of 34% in the frequency of hypertension amongst the stroke cases the estimated sample size with power of 95% and alpha error of 2.5% works out to be nearly 60 patients and 120 controls. Study was carried out from 1st May 2012 to 30th April 2013.

Statistical analysis

Quantitative parameters such as age, biochemical investigation were expressed as mean and standard deviation. Qualitative variables are summarized with proportion and 95% confidence interval. Differences in mean values between cases and controls were tested for statistical significance by student's "t" test/ Mann Whitney U test.

Odd's ratios along with 95% of confidence interval were estimated. Analysis was carried out separately for ischemic and haemorrhagic stroke as well combined together. All the significant factors in the univariate analysis were included for multivariate logistic regression analysis to find out the independent risk factors associated with the development of the disease.

$P<0.05$ was considered as statistically significant. The analysis was carried out using SPSS Version 16.

Methodology

Necessary permission was sought from the concerned authorities in M.S.Ramaiah hospitals for the study. All stroke patients and controls were approached in the wards. Informed oral consent was taken from both the cases and controls before collecting information. For each case, two controls were selected. The cases and controls were sex and age matched with +5 yr age class interval. Pre designed, semi structured questionnaire was administered after validation by pilot testing. (Annexure-1).

Search for admissions of stroke cases in both the hospitals in different wards and in ICU was conducted daily. Patients diagnosed as stroke by physician or neurologists were enrolled in the study. Consent was taken from patient or valid surrogate respondent in case of inability of the patients to respond. Details were collected by interview using pre designed questionnaire adapted from WHO STEP Stroke. As subjects were from rural and urban area Sociodemographic status was classified using B. G. Prasad classification.

Use of alcohol was based on history. For assessment of alcohol use, Audit Questionnaire was used. History of smoking in the past or present collected. Assessment of tobacco consumption was done by Fagerstorm nicotine dependence questionnaire was used. History of vascular risk factors like hypertension, diabetes mellitus, and cardiac disease was obtained based on history and from medical records if available. The blood pressure recorded at the time of interview in supine position with sphygmomanometer. Reports of blood pressure at the time of admission were availed from record. Biochemical parameters like lipid profile, electrolytes, liver function tests, renal function tests, coagulation

profile etc was obtained from medical records. Waist circumference was measured with non stretchable measuring tape at the level at midpoint of lower border of rib cage and iliac crest (at the level of umbilicus) in standing position and in supine position if patient was not able to stand with minimal clothing. Modified Rankin scale was used for assessing the outcome in terms of daily activities before the discharge of patient from the hospital as well as during period of 28 days from date of stroke. Diagnosis was based on imaging techniques and confirmation by specialist. Diagnostic examinations, medical management, in- hospital assessment were taken from records. Duration of stay in hospital was confirmed by discharge records availed from medical records section. Follow up at 28 days was done by telephone/ in hospital assessment to measure the functional outcome using Modified Rankin Scale. Date of death was ascertained in case of death within 28 days.

RESULTS AND DISCUSSION

The 15 risk factors initially considered.

	Risk factors	Cases n(%)	Controls n(%)	OR(95% CI)	p value
	History Of Cardiac Disease	10(16.7)	13(10.8)	1.64(0.67-4.00)	0.269
	Diabetes	27(45.0)	36(30)	1.90(1.00-3.62)	0.047
	Hypertension	38(63.3)	41(34.2)	3.32(1.74-6.35)	<0.001
	History of Smoking	19(31.7)	16(13.3)	3.01 (1.14-6.42)	0.003
	History of alcohol intake	16(26.7)	17(14.2)	2.20(1.02-4.75)	0.041
	Family history of stroke	10(16.7)	2(1.7)	11.85(2.49-55.80)	<0.001
Lipid levels	Cholesterol levels(Mg/dl)>240	4(10.8)	5(8.5)	1.30(0.32-5.22)	0.702
	HDL (mg/dl) male <40	24(64.9)	26(57.8)	1.34(0.55-3.31)	0.513
	*HDL (mg/dl) female <50	12(85.57)	0		
	Triglyceride (mg/dl)>200	3(8.1)	8(13.8)	0.55(0.13-2.22)	0.398
	LDL (mg/dl)>160	4(12.5)	1(1.8)	7.857(0.83-73.66)	0.037
	Waist circumference (cms) Males >80	31(43.7)	40(56.3)	0.437(0.33-0.56)	0.028
	Waist circumference (cms) Females >90	32(91.4)	53(75.7)	3.421(0.92-12.59)	0.053

*None of the females in controls had HDL level measured

It was observed that 10(16.7%) of cases had history of cardiac diseases like atrial fibrillation, IHD, CHF. 13(10.8%) of controls had history of cardiac disease. The odds ratio of stroke among patients with history of cardiac disease is 1.64 compared to patients with no history of cardiac disease. However this difference was not statistically significant (p=0.26).

Different studies showed variation of prevalence of cardiac disease. Study done in Pakistan showed past history of MI in11.8% of persons with stroke and 5.6% of among controls.[3] Study done among Indian American showed 35.5% of cardiovascular diseases and 9.7% atrial fibrillation among persons with stroke.[4] Study done in Bangalore showed 9.7% of persons with stroke with history of stroke.[5]

It was observed that 27(45%) of cases and 36(30%) of controls had diabetes. The odds ratio of stroke among patients with diabetes was 1.90 compared to patients with no diabetes. The difference was statistically significant (p=0.04).

Study done in Bangalore[5] showed 23.1% of stroke Patients. A study conducted in South India showed 14% of prevalence of DM among stroke cases compared to 7% among controls.[6] Study conducted by Ayeesha Kamran Kamal et al showed prevalence of DM among persons with stroke as 30.3% and 17.4% among controls.[3] The Interstroke Study showed that prevalence of diabetes was 21% in ischaemic persons with stroke, 10% among hemorrhagic stroke patient compared to 12% among controls.[7]

Presence of diabetes in controls was also high (30%) which might indicate high prevalence of diabetes in population. It was observed that 38 (63.3%) of cases had hypertension and 41(34.2%) of controls had hypertension. The odds ratio of stroke among patients with hypertension was 3.32 compared to patients with no history of hypertension. The difference was statistically significant (p=<0.001).

Similar results were found in Strong Heart Study that showed that prevalence of hypertension among persons with stroke 55.7% compared to 38% among controls.[8] The Interstroke Study showed that prevalence of self reported hypertension among persons with stroke as 55% among ischaemic stroke, 66% among hemorrhagic stroke, compared to 32% among controls.[7] The study done in South India showed that prevalence of hypertension among persons with stroke was 36% compared to 25% among controls.[6] The study done by Ayeesha Kamran Kamal et al showed that prevalence of hypertension among persons with stroke was 63.9% compared to 47.7% among controls.[3]

It can be justified from the various studies as discussed above that hypertension is a major risk factor of stroke.

It was seen that 19(31.7%) of cases smoked either in the past or present. The odds ratio of stroke among patients

with history of smoking was 3.01 compared to patients with no history of smoking. The difference between the two groups was statistically significant (0.003).

Only one person with stroke consumed chewable tobacco. Hence analysis was not carried out.

Similar results seen in Interstroke study showed smoking among ischaemic stroke to be 37%, 31% among hemorrhagic persons with stroke compared to 24% among controls.[7] Study done in Pakistan showed prevalence of smoking among persons with stroke to be 21% compared to 28.9% among controls.[3] Study done in Bangalore showed that 32.6% persons with stroke used one of the tobacco products.[5] Risk profile from Framingham study showed smoking among persons with stroke to be 33.8% among men and 26.4% among women.[9] Study done by Salah et al showed 17% current smokers and 17% ex smokers among persons with stroke.[10]

It was observed from the table that 16(26.7%) of cases and 17(14.2%) of controls provided history of alcohol intake either in past or present. The odds ratio of stroke among patients with history of alcohol intake was 2.20 compared to patients with no history of alcohol intake. The difference between the groups was statistically significant (p=0.041).

Similar results were seen in study done in Bangalore.[5] 25.1% of persons with stroke used alcohol. The Interstroke study showed 15% of ischaemic persons with stroke taking 1-30 drinks per month compared to 18% among hemorrhagic stroke and control group. 16% of ischaemic patients were taking more than 30 drinks per month compared to 16% among hemorrhagic persons with stroke and 11% among control group.[7]

10(16.7%) stroke subjects had family history of stroke compared to 2(1.7%) of controls. This difference was statistically significant (p=<0.001).

Study done in Bangalore[5] showed 7.3% of stroke patients with family history. Study done in Pakistan[3] showed presence of family history of stroke or cardiovascular disease among 31.1% of stroke patients. Family history is a important risk factor which needs further evaluation.

4(10.8%) of cases had cholesterol levels more than 240 mg/dl compared to 5(8.5%) among controls. The odds ratio of stroke among patients with cholesterol levels more than 240 mg/dl was 1.30 compared to patients with cholesterol levels less than 240 mg/dl. The difference between the groups was not statistically significant (p=0.730).

Only 13(35.1%) of male stroke subjects had HDL level above 40mg/dl. Only 14 female stroke patients had reports for HDL. Only 2(14.3%) of female stroke subjects had HDL level above 50mg/dl.

Of the 37 stroke subjects having triglyceride levels measured 3(8.1%) had above 200 mg/dl. However this difference was not statistically significant (p=0.520).

LDL levels > 160 mg/dl was seen in 12.5% of cases and 1.8% of controls. This difference was statistically significant (p=0.057).

Strong heart study[8] showed statistically significant difference in LDL & Triglycerides among cases and controls. Similarly study done in South India showed statistically significant difference in HDL and triglyceride level among cases and controls.

Due to small number of study subjects the difference was not well defined.

It was observed that 91.4% of females among cases had waist circumference more than 90 cms. The difference among female patients was statistically significant (p=0.043).

Difference between male cases and controls showed a protective effect of waist circumference more than 80cms. This might be due to the method of measurement of waist circumference. In persons who were not able to stand up, waist circumference was measured in lying position. Because of relaxed abdominal muscles that would have altered the results.

Strong heart study[8] and study done in Pakistan[3] showed no statistical difference in waist circumference among persons with stroke and controls.

Modified Rankin Scale of persons with stroke

Modified Rankin Scale	At the time of interview n(%)	At 28 days n(%)
No symptoms	3(5.0)	7(14.0)
No significant disability despite symptoms	12(20.0)	9(18.0)
Slight disability	5(8.3)	10(20.0)
Moderate disability, able to walk without assistance	10(16.7)	10(20.0)
Moderate disability unable to walk without assistance	20(33.3)	12(24.0)
Severe disability	10(16.7)	2(4.0)
Total	60(100.0)	*50(100.0)

Wilcoxon test was used to compare the functional outcome of stroke subjects which was measured using Modified Rankin Scale at the time of admission and at the end of 28 days. Mean score was 23.95 at the time of admission and 17.95 at the 28 days time.

This was statistically not significant (p=0.11).

Table shows Modified Rankin Scale of persons with stroke at the time of interview and at 28 days follow up. 16.7% of the patients had severe disability. This was reduced to 4% at day28. At end of 28 days 14% were free from all symptoms.

Wilcoxon test was used to compare the functional outcome of stroke subjects which was measured using Modified Rankin Scale at the time of admission and at the end of 28 days. Mean score was 23.95 at the time of admission and 17.95 at the 28 days time.
This was statistically not significant (p=0.11).
Following study done in Bangalore shows similar results.[5]

The study showed 7.4% case fatality among stroke subjects within 28 days of stroke. 6 subjects could not be followed up for 28 days.

In worst case scenario assuming death of all the 6 subjects who were lost to follow up case fatality would be 16.6%. In case of best case scenario where all the subjects who were lost to follow up would give case fatality of 6.6.

The strong heart study showed that overall 30-day case fatality from first stroke was 18%, with a 1-year case-fatality rate of 32%.[8] The pooled data from the Framingham Heart Study, Atherosclerosis Risk in Communities Study, and Cardiovascular Health Study showed that 1-year case fatality after a first stroke was 21% for men and 24% for women whose age was >40 years.[11] One hundred forty-seven patients did not survive beyond the 28th poststroke day - fatality rate 27.2% (24.5% for urban and 37.1% for rural population.[4] The overall 30-day case fatality noted in the Kolkata study[12] is 41.08% (men, 38.18%; women, 43.24%), significantly higher than that seen in the Western industrialized and the inhabitants of Tbilisi I n Georgia (35.7%)countries (17% to 33%).15–18,20 Blacks in Manhattan (38%).[13]

Univariate and multivariate analysis of determinants of stroke among study participants

Variable	Level	Case	Control	Univariate analysis		Multivariate analysis	
				OR(95%CI)	P value	OR(95%CI)	P value
Diabetes	Present	27(45.0)	36(30)	1.90(1.00-3.62)	0.047		NS
	Absent	33(55.0)	84(70)	1			
Hypertension	Present	38(63.3)	41(34.2)	3.32(1.74-6.35)	<0.001	5.07(0.90-28.35)	0.06
	Absent	22(36.7)	79(65.8)	1			
Smoking	Present	19(31.7)	16(13.3)	3.01(1.14-6.42)	0.003		NS
	Absent	41(68.3)	104(86.7)	1			
Alcohol Intake	Present	16(26.7)	17(14.2)	2.20(1.02-4.75)	0.041	4.34(0.99-18.98)	0.05
	Absent	44(73.3)	103(85.8)	1			
Family history	Present	10(16.7)	2(1.7)	11.85(2.49-55.80)	<0.001		NS
	Absent	50(83.3)	118(98.3)	1			
LDL (mg/dl)	>160	4(12.5)	1(1.8)	7.857(0.83-73.66)	0.037		NS
	<160	28(87.5)	55(98.2)	1			
Waist circumference male	>90	32(91.4)	53(75.7)	3.421(0.92-12.59)	0.053		NS
	90	3(8.6)	17(24.3)	1			

All the variables which revealed statistical significance in univariate analysis were included for multivariate analysis to find out the independent factors associated with the development of stroke. Only two factors namely hypertension and alcohol turned out to be statistically significant at p=0.06 and 0.05 levels. All other factors did not turn out to be statistically significant in multivariate analysis.

All other factors of clinical importance, possibly due to small sample size the analysis did not reveal statistical significance.

SUMMARY AND CONCLUSIONS

A case control study was undertaken with the objective of assessing factors associated with stroke and outcome among the patients attending M S Ramaiah hospitals.

The following are the highlights of the study

- Mean age of persons with stroke was 61.08+1.32. 6(10.0%) of the patients were below the age of 40 i.e. stroke among the young. 58.3% of stroke cases were males.
- 10(16.7%) of cases and 13(10.8%) of controls had history of cardiac disease. Further odds ratio of

stroke among patients with history of cardiac disease was 1.64 compared to patients who had no history.

- 27(45%) of cases and 36(30%) of controls had diabetes. The odds ratio of stroke among patients with history of diabetes was 1.90 compared to patients with no history. The difference was statistically significant (p=0.047).
- 38 (63.3%) of cases and 41(34.2%) of controls had hypertension. The odds ratio of stroke among patients with history of hypertension was 3.32 compared to patients with no history which was statistically significant. (p=<0.001)
- 19(31.7%) of cases were either past or present smokers. The odds ratio of stroke among patients with history of smoking was 3.01 compared to patients with no history further difference between the two groups is statistically significant (p=0.003).
- 16(26.7%) of cases and 17(14.2%) of controls had history of alcohol intake either in past or present. The odds ratio of stroke among patients with history of alcohol intake was 2.20 compared to patients with no history and the difference between the groups is statistically significant (p=0.041).
- 10(16.7%) stroke subjects had family history of stroke compared to 2(1.7%) of controls. This difference was statistically significant (<0.001).
- LDL levels > 160 mg/dl was seen in 12.5% of cases and 1.8% of controls respectively. This difference was statistically significant. Other lipid levels were not statically significantly.
- Functional outcome of stroke subjects was measured using Modified Rankin Scale at the time of admission and at the end of 28 days. Mean score was 23.95 at the time of admission and 17.95 at the 28 days time. This was statistically not significant.(p=0.118)
- Case fatality of 7.4% was seen among stroke subjects within 28 days of stroke further 6 subjects were lost to follow up.
- Multivariate analysis showed hypertension and alcohol use as statistically significant factors associated with stroke.

Thus, from the above findings it can be concluded that

Increasing age, male gender and family history of stroke are the non-modifiable risk factors of stroke as seen in this study. Modifiable risk factors were hypertension, diabetes, smoking, alcohol intake, increased central obesity, increased LDL levels which can be reduced using adequate preventive strategies.

Severity of the disease is shown by 7.4% of case fatality, 50% ICU admission, and severe disability in 16.7% of the patients and also by the presence of loss of consciousness and speech impairment and paresis. Only 53.3% of the patients had first scan within 24 hours & & none before 3 hours. This shows lack of awareness among public.

There was definitive change in the functional outcome after the treatment at 28 days. But larger sample size is needed to see the difference between the outcomes. Overall it shows that with treatment there is reduction in functional disability.

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