Risk Factors and Stroke Outcome – An Indian Study

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Abstract

Stroke is the second leading cause of death and one of the commonest causes of disability in adults. It is potentially the most devastating consequence of vascular disease, causing serious long-term disability and incurring extremely high medical, emotional and financial costs.

In Chennai, we conducted the ICASS-II /WHO stroke surveillance study from Dec 2003 to Dec 2004. A total of 402 definite stroke patients were evaluated.

In this paper we evaluate the risk factors of stroke (such as age, hypertension, diabetes, ischemic heart disease, dyslipidemias and nicotine.) and stroke outcome. The stroke outcome was evaluated by the Modified Rankin Scale on the 28th day of illness. We found that hypertension was the commonest risk factor. Recovery depended essentially on the type, sub-type of stroke and its severity. The morbidity and mortality increased with a combination of risk factors. We found that there is a statistically significant trend which shows that in stroke patients age, diabetes, IHD and tobacco increases morbidity with severe disability and mortality.

Key words: stroke, risk factor, outcome, Modified Rankin Scale, hypertension, IHD, diabetes, tobacco, disability

Introduction

Stroke is a heterogeneous syndrome caused by many disease mechanisms, all of which result in disruption of cerebral blood flow and subsequent tissue damage. It is the second leading cause of death[1] and one of the commonest causes of disability in adults. In 2001, stroke accounted for 5.5 million deaths world wide which is equivalent to 9.6% of all deaths. Two-thirds of those deaths occurred in people living in developing countries.[1] While India is still struggling with the problems of communicable diseases, noncommunicable diseases are on the rise. Stroke is potentially the most devastating consequence of vascular disease, causing serious long-term disability and incurring extremely high medical, emotional and financial costs. Hypertension is the leading risk factor for stroke. Control of hypertension can decrease the morbidity and mortality due to stroke. Age is an important and independent risk factor for stroke (Wolf et al 1992)[2]. 20-30% of the hospital stroke population falls below the age of 40 years (Nagaraja and Taly 1988).[2]

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Objective

The objective of the study was to evaluate various risk factors of stroke and their outcome in India. The risk factors evaluated were age, hypertension, diabetes, ischemic heart disease, dyslipidemias and nicotine.

Materials and Methods

This ICASS-II /WHO Stepwise stroke surveillance study is a sequel to the ICASS - I study conducted in 2002. ICASS is the acronym for Indian Co-operative Acute Stroke Study done by the Indian Stroke Association. A total of 402 patients were evaluated at two stroke units in Vijaya Health Centre and Mercury Nursing Home in Chennai, India. The recommended standard WHO stroke definition is "a focal (or at time global) neurological impairment of sudden onset, and lasting more than 24 hours (or leading to death) and of presumed vascular origin". [3] The strokes were confirmed by CT or magnetic resonance scanning. The study duration was from Dec 2003- Dec 2004. A pilot study of 10 cases was evaluated before the actual study started in Dec 03. The WHO stroke surveillance part of the study focuses on hospitalized stroke patients only (STEP- 1). We did not undertake the evaluation of strokes in the community (STEP -2 and STEP-3) due to various reasons.

The epidemiological data of age, sex, occupation, socio-economic status, race and religion were also obtained for the surveillance study. The type and sub-type of strokes were established and analyzed. However in this paper we will focus on risk factors and stroke outcome as it is the result of our rehabilitation program. The severity of strokes was evaluated by international scales such as the modified NIH scale and the outcome by the Modified Rankin Scale.[4] The NIH scale was evaluated on admission and by 7-10 days. The MRS was evaluated after 4 weeks by physical evaluation or by telephonic interview of the attendant. In this study 4 week follow up was possible in 354 of the 402 patients. This was because some patients come from remote rural areas where communication links are inadequate and also due to illiteracy. The scoring of the Modified Rankin Scale is <2 where the patient is walking independently and requires no assistance for his/her ADL. MRS score of 3-4 is moderate disability where ADL assistance is required and 5 is severe disability where the patient is totally dependent for his/her ADL and a score of 6 refers to death.

The risk factors of age, hypertension, diabetes mellitus, ischemic heart disease, dyslipidemia, and nicotine intake were evaluated.

Risk factor inclusion criteria are as follows. Hypertension is diagnosed if BP is >140/90 on 2 independent readings or on anti-hypertensive treatment. Diabetes mellitus is defined if 2 independent reading of blood glucose is >180mg/dl (post-prandial – venous sample) or an elevated glycosylated hemoglobin or on anti diabetic treatment. Hyperlipidemia is defined if the total cholesterol was above 200mg/dl or LDL is more than 160mg/dl or triglycerides more than 150 mg/dl or VLDL is >26mg/dl.

The statistical analysis used p-value and odds ratio using multiple logistic regression (forward stepwise addition method) to infer the statistical significance of the various risk factors. Pearson correlation analysis was also done to look for linear association between single and combination of risk factors.

Observations and Results

Age

77.8% of our patients were between 50 and 79 years of age. The youngest patient was 17 years old and our oldest patient was 92 years. The morbidity with severe disability and death is maximum in the 6th to 8th decades as revealed by MRS scores of 5 and 6. The p-value is 0.04 which is statistically significant. Refer Table 1.

The mean age of stroke is 61.7. The standard deviation is 13.4.

Table 1 Patients Age vs MRS Score

| Age | Modified Rankin Scale Score | | | | p-value |
	Mild <2	Moderate 3-4	Severe 5	Death 6	
<29	5	2	0	2	
30-39	8	3	1	2	
40-49	17	2	1	1	0.04 (sig)
50-59	44	15	7	11	
60-69	55	31	26	12	χ^2 34.09
70-79	38	14	12	14	d.f. = 21
80-89	12	4	4	8	
90>	0	0	1	2	
Total	179	71	52	52	

Gender

We had 265(65.9%) male patients and 137(34.1%) female patients. The stroke outcome was evaluated in 354 patients and there was no statistical significance in the gender and stroke outcome. Refer Table 2 Gender vs MRS Score.

Table 2 Gender vs MRS Score

| Gender | Modified Rankin Scale Score | | | | p-value |
	Mild <2	Moderate 3-4	Severe 5	Death 6	
Male	119	44	32	37	0.67 (not sig)
Female	60	27	20	15	χ^2 1.56
Total	179	71	52	52	d.f. = 3

Modifiable Risk Factors

Hypertension was found to be a major risk factor of stroke in 72 percent of the patients. It was found separately and in combination with diabetes mellitus and IHD. 49.8% had diabetes mellitus and 33.8% had ischemic heart disease. Around 16% of the patients in this study had no significant risk factor detected with the present facilities and methods available. Refer to Table 3.

Table 3. Incidence of Modifiable Risk Factors

Risk Factor	No of cases	Percentage
Hypertension	289	71.9%
Diabetes mellitus	200	49.8%
Ischemic heart disease	136	33.8%
Atrial fibrillation	13	3.2%
Valvular heart disease	14	3.5%
Congenital heart disease	2	0.5%
Total Cholesterol	105	26.1%
HDL Low	159	39.6%
LDL High	30	7.5%
TGL High	117	29.1%
VLDL High	155	38.6%
Nicotine	95	23.6%
Anemia	40	10.0%

Hypertension

289 patients (72%) of the 402 were hypertensives. The 4 weeks follow up by modified Rankin scale was possible in 354 patients. Out of this 260 were diagnosed as stroke with hypertension as risk factor (HT alone or in combination with other risk factors). 140/90 mmHg and above was taken as hypertensive. 129 of them had a mild disability, 57 had moderate disability and 41 had severe disability and 33 patients died. The p – value is 0.15 which is statistically not significant.

Diabetes

173 patients were diabetic. Blood sugar (post prandial venous sample) >180 mg/dl were taken as diabetics. 76 were mildly disabled while 37 had moderate disability and 27 had severe disability and 33 expired. The p-value is 0.049 and is statistically significant. This means that diabetics definitely had higher morbidity and mortality

Ischemic heart disease

126 patients were found to have IHD. These were diagnosed by the electrocardiogram and ECHO findings and confirmed by a cardiologist. 53 patients had mild disability while 46 of them had severe morbidity and mortality (MRS 5 & 6). Hence the p-value was not significant.

Table 4 Modifiable Risk Factors vs Stroke Outcome

	Modified Rankin Scale Score				
Risk Factor	*Mild* *<2*	*Moderate* *3-4*	*Severe* *5*	*Death* *6*	*p-value*
Hyper-tension	129	57	41	33	0.15 NS
Diabetes mellitus	76	37	27	33	0.049 Sig
Ischemic heart disease	53	27	23	23	0.37 NS
Total cholesterol	96	37	24	19	0.21 NS
LDL	137	49	27	29	0.43 NS
TGL	87	33	21	22	0.26 NS
VLDL	71	23	19	14	0.15 NS
Nicotine	48	16	8	8	0.42 NS

Dyslipidemia

The individual components of the lipid profile such as total cholesterol, HDL, LDL, VLDL and TGL were 26.1%, 35.6%, 7.5%, 38.6% and 29.1%. On statistically analyzing the data the p-values were 0.21, 0.43, 0.15, 0.25 and 0.26. All of them are not significant in altering the outcome of stroke.

Tobacco

23.6 percent of the stroke patients consumed tobacco – either via smoking cigarettes or beedis, or chewing tobacco with betel leaves or nasal snuff. The quantity of tobacco consumed by the smokers was not estimated. The p-value was not significant in comparison with other risk factors (0.42) however on comparing the outcome of smokers and non-smokers there was a definite statistical significance. The p-value is 0.009.

Analysis of Results

On evaluating a combination of risk factors diabetes and hypertension - the number of patients with 5 &6 on the MRS showed severe morbidity and mortality than those with minimal disability <3. Refer to Table 4.

There were only 8 stroke patients with IHD alone as the risk factor and only 15 patients with Diabetes and Ischemic heart disease (out of 354) as the risk factors. This figure is too small to be statistically analysed. However though there is an association of DM and IHD in the multi-factorial etiology of stroke these risk factors independently do not add any additional risk to the stroke outcome.

When three or more risk factors (Hypertension, diabetes and ischemic heart disease) are involved the mortality (MRS 6) rises to one-fifth. Refer to Table 5.

Table 5. Modifiable Risk Factors alone and in Combination

	Modified Rankin Scale Score				
Risk Factor	*Mild* *<2*	*Moderate* *3-4*	*Severe* *5*	*Death* *6*	*Total*
Hyper-tension	42	14	10	4	70
Diabetes mellitus	10	1	1	4	16
Ischemic heart disease	4	2	0	2	8
HT +DM	42	20	12	13	87
HT+IHD	25	9	9	5	48
DM+IHD	4	2	4	5	15
HT + DM + IHD	20	14	10	11	55
No risk	32	9	6	8	55

Analysis of combination of DM, HT and IHD and outcome showed p value of .003 which is statistically significant.

There is a linear trend indicating that a combination of risk factors increase the disability, morbidity, and mortality of stroke. However a larger study would be required to establish a definite association.

Table 6   Regression Analysis Results

Independent risk factor	*Regression coefficient*	*S.E (6)*	*p-value*	*Odds ratio*
Age	0.31	0.16	0.045	1.37
Diabetes mellitus	0.71	0.31	0.02	2.02
IHD	0.69	0.31	0.03	1.98

The results of multiple logistic regression analysis (Table 6) shows, an increase in morbidity and mortality with the MRS scores more than 4 in the above risk factors of age, diabetes mellitus and ischemic heart disease. The non-significant variables are sex, hypertension and LDL (dyslipidemias). Hypertension is the most significant risk factor. However the stroke outcome is not affected as there are proportionate number of hypertensives with favourable outcome (MRS<4) as there are with increased morbidity and mortality (MRS 5&6).

Discussion

In our study the age group of maximum stroke incidence was 50-79 years with a mean age incidence of 61.7 ± 13.4 (SD). In the German Stroke Data Bank study by Armin J Grau et al[5] the age incidence was almost similar with 65.9 ± 14.1. The above mentioned study also used the Modified Rankin Scale to follow up the patients. A few other studies used the Barthel Index along with the Modified Rankin Scale. We used the Modified Rankin Scale because it is simple and easy to assess by the clinician and the attendant. It could be assessed over the phone and it was essentially part of the WHO Stroke Step questionnaire (version 1.1).

A study done in Karachi, Vohra EA[6] also shows similar results of increased mortality and morbidity due to advancing age and cardiac illness. This study from Pakistan has similar demographic data as the Indian subcontinent. Majority of their cases were between 4th and 6th decade. They had 50% hypertensives, 19% CAD and 18% diabetes and 17% were smokers.

Gender differences are present in the incidence of stroke in our study. 65.9% were men and 34.1% were women. However this could reflect the gender bias existing in Indian society. There is no statistically significant difference in the stroke outcome due to gender.

In our study elevated total cholesterol, LDL, VLDL, TGL and lower HDL values have not directly altered the outcome of stroke. Similar finding have been observed by Ross et al.[7]   Ross R found that elevated serum cholesterol has not been linked to an increased stroke incidence. However it indirectly increases stroke risk due to hypercholesterolemia and coronary artery disease. His study was a large prospective observational study of middle-aged men and found no relationship between plasma total cholesterol concentration and 16.8 year incidence of fatal or non-fatal stroke.

Another large 10-year prospective study in Britain[8] by Wannamethee SG (Stroke 2000), of 14,175 middle-aged men and women, free of clinical cardiovascular disease at the outset, found a weak inconsistent relationship between low density lipoprotein-cholesterol (LDL-c) or high density lipoprotein-cholesterol (HDL-c) and ischemic stroke.

23.6% of our patients used nicotine in the form of chewing tobacco, nasal snuff, cigarettes and beedis. Our figures show increased mortality and morbidity in nicotine consumers compared to those who do not. (p= 0.009 statistically significant) Smokers both current and past have a higher risk of developing stroke was earlier quoted by Ruth (Bonita et al 1986)[9].

In an Australian study Lefkovits[10] of Royal Melbourne Hospital found that stroke type, age, cardiac disease and diabetes all independently worsen acute stroke outcome – this is similar to the findings in our Indian study.

However, Katedry I Kliniki Neurologii et al[11] in a Polish study in 2003 found that diabetes has no effect on the course and outcome of ischemic stroke. In contrast we found that in our Indian subcontinent diabetes is an independent risk factor by itself in increasing the morbidity.

Conclusions

The outcome of stroke essentially depends on the type of stroke, the severity and sub-type. However the morbidity and mortality of stroke, determined by the outcome after 4 weeks by the Modified Rankin Scale, is significant in elderly patients with diabetes and ischemic heart disease and smokers. The sex of the individual also did not alter the outcome. Hypertension and dyslipidemias did not alter the stroke outcome directly. An increased public awareness of the risk factors and their management not only leads to primary prevention of stroke, but also leads to lesser disability.

Analysis of combination of DM, HT and IHD and outcome showed p value of .003 which is statistically significant.

There is a linear trend indicating that a combination of risk factors increase the disability, morbidity, and mortality of stroke. However a larger study would be required to establish a definite association.

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