

RISK FACTORS, MORTALITY AND RECOVERY OF STROKE: A prospective study on 1000 Patients

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ABSTRACT

Objective: To determine whether a single or multiple risk factors have a relative significance on the mortality and morbidity of stroke and whether previous treatment of major risk factors like hypertension and diabetes mellitus had any positive influence on the clinical outcome.

Methodology: One thousand consecutive cases of acute stroke were included in this prospective descriptive study conducted at the Dept. of Neurology, Jinnah Postgraduate Medical Centre, Karachi from Dec. 1985 to July 1988. A special proforma was designed to collect all the relevant clinical information. Functional status was assessed by using the Barthel Index activity score. Scores obtained at admission were compared with the scores obtained at six weeks follow-up. The results were then analyzed in the background of various risk factors present. Similar observations were made in assessing the mortality. The pre-stroke treatment status of major risk factors like hypertension and diabetes mellitus was also studied.

Results: Of the 1000 cases, 61% were male and 39% female. Majority of the cases were in the age group 60-69 years. Hypertension (HTN) alone was present in 58.3% followed by diabetes mellitus (DM) 5%, ischemic heart disease (IHD) 1.3%, whereas in 19.8% HTN, DM, IHD were present in various combinations, 1.5% had Valvular Heart Disease (VHD) while 14.1% had none of the above risk factors. Six-weeks follow-up was available on (673/1000) 67% cases. Gross mortality was 59% (396/673). Higher mortality was seen in cases with Glasgow Coma Scale (GCS) range 3-9/15. Risk factor profile in fatal cases showed that 221/379 (58%) had HTN, 21/32 (65%) had DM, 6/12 (50%) had IHD and 6/10 (60%) had Valvular heart disease (VHD). Some patients had multiple risk factors, among those 60/95 (63%) had HTN + DM, 19/41 (46%) had HTN + IHD, 5/7 (71%) had DM+ IHD, 11/16 (68%) had HTN + DM + IHD while 47/81 (58%) had none of the above risk factors. Relative influence of individual risk factor or in combination was not statistically significant. The functional recovery showed no significant relative difference among patients with different risk factors. There was no significant difference in the outcome among treated and untreated hypertensive and diabetic patients.

Conclusions: Individual or multiple risk factors do not have a relative influence on the higher morbidity and mortality in stroke. For poor prognosis severity of stroke at onset is more important than the type of risk factors. Furthermore, there was no difference in outcome in patients who got pre-stroke treatment compared to those who had no treatment.

KEY WORDS: Stroke , Risk factors, Mortality, Recovery.

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INTRODUCTION

Despite declining incidence of stroke in some countries^{1,2} cerebrovascular disease remains a major cause of death and disability worldwide.³ Stroke may be as a result of infarction due to thrombotic or embolic occlusion of a cerebral

vessel or as a result of cerebral hemorrhage. The effects may differ according to the nature of lesion, the type of risk factor and the possible role of treatment. Various risk factors for stroke have previously been identified.⁴⁻⁶ Epidemiological evidence indicates that hypertension is the most important cause of stroke in men and women of all ages.⁷

There can be little doubt that even hypertensive patients at high risk go untreated. On the other hand, not all vascular events associated with hypertension are reversed by the control of high blood pressure. How far this is true for stroke, very little has been reported.^{8,9} The objective of this study was to determine whether a single or multiple risk factors have a relative significance on the mortality and morbidity of stroke and whether previous treatment of a major risk factor such as hypertension and diabetes mellitus had any positive influence on the clinical outcome.

METHODOLOGY

One thousand consecutive patients with acute stroke were enrolled in the study at the Department of Neurology, Jinnah Postgraduate Medical Centre (JPMC), Karachi from December 1985 to July 1988. All relevant clinical information of patients was documented on a printed stroke study proforma especially designed for this purpose. Age ranged from 30 - 70 years and above. Majority of the cases were seen in the casualty as an emergency. All those with intracranial infections, cerebral tumors or other diseases presenting with neurological symptoms simulating stroke were excluded from the study. Investigations such as routine blood counts, blood sugar, urea, urine analysis were carried out in all patients. CT scan of brain was done whenever it was considered necessary as this facility was newly introduced at the JPMC and was available for a selected number of cases on a daily basis. Some patients died before intensive testing could be done.

All cases were assigned a different group according to the number of risk factors they carried such as those having one risk factor, two risk factors or multiple risk factors. Diagnosis

of hypertension and diabetes mellitus and other risk factors was based on a combination of findings such as medical history, checking previous prescriptions or other hospital discharge cards. Hypertension was defined as past history of hypertension requiring treatment based on a blood pressure of >160/90 at least on two separate occasions.¹⁰ Diabetes mellitus was defined as a past history of diabetes mellitus requiring oral hypoglycemic therapy. Some cases were not known diabetics but their random blood glucose levels were found to be higher than normal during preliminary investigations. In those cases a quick assessment was done and they were considered diabetics when their blood sugar levels were more than 200mg/100ml after one hour of taking 50grms of oral glucose. Evidence of cardiac abnormality was based on the past history of heart disease, present or past abnormal ECG¹⁰, or previous history of cardiac surgery. When in doubt, cardiac opinion was taken. History of medication for hypertension and diabetes mellitus was carefully recorded including the drugs in use at present or in the past, their dosage and the compliance. Subjects were grouped separately i.e. those with treated hypertension and diabetes mellitus and those with untreated hypertension and diabetes mellitus.

Stroke was defined as the sudden onset of focal or global neurological deficit lasting for more than 24 hours or leading to death with no apparent cause other than that of vascular origin.¹¹ Those lasting less than 24 hours were classified as Transient Ischemic Attacks (TIA). Reversible Ischemic Neurological Deficit (RIND) or 'minor stroke' was defined as the complete reversal of neurological symptoms within four weeks of onset. The diagnosis of cerebral hemorrhage and cerebral infarction was made either clinically or by the CT scan of brain when performed.

Patients discharged from the hospital were followed at home up to six weeks. The assessment of patient's activities of daily living was made by using the Barthel Index. The maximum score given was 105 and the minimum 0 (when in coma). The extent of recovery was judged by

comparing the initials scores at admission and scores obtained at six weeks. The recovery was classified according to the following four grades: Grade 1: score 0 (no recovery). Grade 2: score 1-50 (mild recovery). Grade 3: score 51-104 (moderate recovery). Grade 4: score 105 (complete recovery). Grade achieved by the individual patient at six weeks was compared with the grade achieved by the same patient at admission, thus giving rise to the net result.

Mortality was recorded in different age groups along with the various risk factors in order to determine the influence of any particular risk factor on the mortality. Statistical analysis was carried out by means of X² test and t-student test. P value <0.05 was considered as significant.

RESULTS

Demographic data on one thousand patients indicates that 61% (613) were male and 39%(387) were female. Stroke was maximally encountered in the 60-69 age group followed in frequency by >70 age group. Six-weeks follow-up wa available on 67%(673/1000). Overall mortality was 59%(396/673). Majority of the cases who expired had initial Glasgow Come Scale (GCS) between 3-9/15.

Hypertension alone was present in 58.3%, diabetes mellitus in 5%. HTN+DM in 11.9% of patients. Other details are shown in Table-1. Majority of the patients who expired 71%(128/180) were in the age group of seventy and above while least mortality was seen in patients below forty years of age. Increasing mortality

Table-I: Risk Factors N= 1000

	<i>No. of Patients</i>	<i>%</i>
HTN	583	58.3
DM	50	5.0
HTN + DM	119	11.9
HTN + IHD	51	5.1
DM + IHD	8	0.8
HTN + DM + IHD	20	2.0
IHD	13	1.3
VHD	15	1.5
None of the above	141	14.1

was seen with increasing age. (P<0.001) Table-II.

Details regarding type of stroke and mortality, mortality related to risk factors are given in Table III and IV. Out of 583 hypertensives, 379 were followed up of which 221 (58%) expired. The mortality in treated group was 50%(sixty three patients) as compared to 63%(158 patients) in the untreated group. Similarly out of fifty diabetics, thirty two were followed up and the overall mortality was twenty one patients (65%). Mortality in treated group eight patients was 57% as compared to 72% in the untreated group (thirteen patients).

Appendix A shows the recovery and mortality in different groups along with the various risk factors. The functional recovery assessed at 6 weeks revealed no significant relative difference among patients having different risk factors (p<0.05). The recovery and mortality was comparable in all groups irrespective of the type or the number of underlying risk factors.

DISCUSSION

We studied patients admitted to the hospital with acute stroke. Various risk factors were identified. The most common being the hypertension. There were patients who had a single risk factor and others who had multiple. We tried to study the relative significance of any one or more than one risk factor on the functional recovery and the mortality of stroke.

It was interesting to note that there were no differences in the recovery and the mortality of stroke irrespective of the type or the number of

Table-II: Mortality and Age Distribution

<i>Age Group Years</i>	<i>No. of Cases</i>	<i>Followed Up</i>	<i>Mortality No (%)</i>
<40	55	30	10 (33.3)
40 – 49	128	78	36 (46.2)
50 – 59	271	181	*99 (54.7)
60 – 69	290	204	*123 (60.3)
>/ 70	256	180	128 (71.1)
Total	1000	673	396 (59%)

*P <0.001

risk factors that an individual possessed. Some previous reports highlighting the same aspect show inconclusive results. In a regional hospital based study Jafari et al.¹² reported that patients with multiple risk factors (hypertension plus diabetes mellitus) had a poor clinical outcome compared to those who had hypertension alone. In another similar kind of study Basir et al.¹³ reported no differences in the recovery and outcome in patients who had diabetes mellitus compared to the hypertensives. These studies were based on a small sample size as such a reliable conclusion cannot be drawn. However in a large multi-centre study¹⁴ diabetes mellitus was associated with poor prognosis compared to the non-diabetics. This is inconsistent with our findings where no such differences were seen. A possible reason for this variable influence of risk factors on the outcome could be the differences in the severity of stroke at the time of admission. Recent reports indicate that the baseline disability is an important predictor for the subsequent outcome in stroke.^{15,16} Also, the severity of stroke and old age are associated with the dependency after stroke.^{17,18} and that the old age influenced stroke outcome because of poor compensatory ability.¹⁹ Majority of our cases were old (>70 years), their GCS score ranged from 3-9/15 at onset thereby reflecting much severity and the mortality was also higher in the older age group. That we believe, collec-

tively, accounted for a poor outcome in our patients rather than the influence of risk factors alone whether individual or multiple.

In our study, the pre-stroke treatment of hypertension and diabetes mellitus did not significantly improve the outcome either. The question arises whether this is really so or there are methodological errors. Repeated checking of the figures seems to have not changed them. The probable reason could be inadequate treatment and incorrect reporting of treatment. Also, it could be due to a treatment gap between the onset of stroke and the treatment sought by the patient which may have initiated pathological changes and hence are not entirely reversible. Black et al.²⁰ were the first to suggest that the pathological changes (atherosclerosis) that give rise to hypertension is already established at the time when treatment is actually begun and that the progression of these processes is unaffected by the treatment. We endorse this already published possibility. Thus treating a risk factor, in fact, is the forced lowering of its alarming levels that otherwise leads to an early catastrophe and the treatment at this stage is unlikely to help in arresting or reversing the progressive pathological changes to the original form.

In light of the recent advancement in the pre-stroke treatment of hypertension, a different perspective can be drawn from our study. Clinical trials like HOPE⁸ and PROGRESS⁹

Table-III: Type of Stroke and Mortality

Age Group Years	No. of Cases	Followed Up	Mortality No (%)
<40	55	30	10 (33.3)
TIA	74	46	5 (10.9)
RIND	62	32	1 (3.01)
CI	670	443	*263 (59.3)
CH	186	145	*125 (86.2)
SAH	8	7	2 (28.6)
Total	1000	673	396 (58.8)

* P <0.001

TIA: Transient Ischemic Attack

RIND: Reversible Ischemic Neurological Deficit

CI: Cerebral Infarction

CH: Cerebral Haemorrhage

SAH: Subarachnoid Haemorrhage

Table-IV: Risk Factors and Mortality

Risk Factors	Cases	Followed Up	Expired Total (%)
HTN	583	379	221 (58)
DM	50	32	21 (65)
I.H.D	13	12	6 (50)
V.H.D	15	10	6 (60)
HTN + DM	119	95	60 (63)
HTN + IHD	51	41	19(46)
DM + I.H.D	8	7	5 (71)
HTN + DM + I.H.D	20	16	11 (68)
None of the above	141	81	47 (58)
Total	1000	673	396 (59)

have shown stroke risk reduction by 22% and 28% respectively when the hypertension was treated with ACE-Inhibitors. Also, pre-stroke treatment with ACE-Inhibitors leads to a better functional outcome.⁻²¹ Furthermore, Angiotensin Type II Receptor Blockers (ARBs) provide greater protection against cerebrovascular

events.^{-22,23} It is of note that the hypertension at the time of this study was more often treated with the beta blockers. The effects of beta blockers in reducing the morbidity and mortality is less clear and remains questionable²⁴, whereas ACE-Inhibitors have shown better disease modifying effects compared to the other antihypertensives.²⁵ It is conceivable that our patients might have done better had they been adequately treated with ACE-Inhibitors or ARBs prior to the stroke. Needless to say, benefits of the newer therapies can be achieved only when our society becomes health conscious. Majority of the people in this part of the world do not seek early medical care nor they have an easy access to the available health care facilities. Those who go for medical treatment do not strictly follow the drug regime as prescribed by their physicians. The worst affected are the rural masses which constitute about 70% of the whole population. Whenever they feel any bodily distress they tend to get relief by taking some traditional medicines (herbs). When these do not work then they rush to a "Pir or fakir" the so called faith healers who subject them to various maneuvers. Consequently, most of the risk factors go undetected for many years. By the time they consult a qualified doctor, it is already too late. Then despite of scientific treatment, the chain of pathological events continue to progress and become irreversible.

Limitations and strengths: This study was done quite a long time ago (1985-1988). However, the authors feel that the ground realities particularly among the rural masses have not changed over these years. The submission of this material was not possible earlier, as this is part of the MD Neurology (University of Karachi) thesis work. According to the university rules, thesis work cannot be published before the award of the degree. CT scan of brain could not be done in all the cases as such the diagnostic uncertainty between the stroke sub-types cannot be ruled out in a certain number of cases. The major strength of this study being the largest series of cases ever reported from Pakistan. Complete cases ascertainment was done right from the admission till the 6-weeks follow-up by the

Appendix A

Initial Barthal Index	No Recovery	Mild Recovery	Moderate Recovery	Complete Recovery	Mortality
6 Weeks Barthal Index					
	0 Grade 1	1-50 Grade 2	51-104 Grade 3	105 Grade 4	
No risk factors: n = 81					
0 (44)	1	1	0	4	38 (86%)
1-50 (11)	0	1	3	0	6 (55 %)
51-104 (20)	0	0	9	8	3 (3%)
105 (6)	0	0	0	6	0
HTN: n = 379					
0 (216)	0	11	13	14	178 (82%)
1-50 (58)	0	6	17	9	26 (45%)
51-104 (84)	0	3	37	29	15 (18 %)
105 (21)	0	0	0	20	1 (5%)
DM: n = 32					
0 (16)	0	0	2	0	14 (88%)
1-50 (6)	0	0	2	0	4 (67%)
51-104 (7)	0	0	1	3	3 (43%)
105 (3)	0	0	0	3	0
HTN + DM: n = 95					
0 (48)	1	2	1	2	42 (80%)
1-50 (17)	0	1	4	1	11 (65%)
51-104 (22)	0	1	7	7	7 (32%)
105 (8)	0	0	0	8	0
HTN + DM. + IHD: n = 16					
0 (7)	0	0	0	0	7 (100%)
1-50 (1)	0	0	0	0	1 (100%)
51-104 (8)	0	0	3	2	3 (38%)
105 (0)					
HTN + IHD: n = 41					
0 (12)	0	0	1	0	11 (92%)
1-50 (13)	0	0	4	2	7 (54%)
51-104 (12)	0	0	5	6	1 (8%)
105 (4)	0	0	1	3	0
DM + IHD : n = 7					
0 (2)	0	0	0	0	2 (100%)
1-50 (3)	0	0	0	0	3 (100%)
51-104 (1)	0	0	1	0	0
105 (1)	0	0	0	1	0
IHD: n = 12					
0 (2)	0	0	0	0	2 (100%)
1-50 (3)	0	0	1	0	2 (67%)
51-104 (3)	0	0	0	1	2 (67%)
105 (4)	0	0	0	4	0
VHD: n = 10					
0 (5)	0	0	0	0	5 (100%)
1-50 (1)	0	0	0	0	1 (00%)
51-104 (4)	0	0	2	2	0
105 (0)	0	0	0	0	0

same neurologist so there was no inter-observer bias. The cases were unselected so there was no selection bias either. The results of this study will help the future researcher who wish to either repeat the study or conduct a longitudinal cohort study to see the benefits of prevention and early modification of risk factors in our population.

CONCLUSIONS

Individual or multiple risk factors do not have a relative influence on the higher mortality or morbidity in stroke. For poor prognosis, the severity of stroke at onset is more important than the type of risk factors. Furthermore, there was no difference in the outcome in patients who got pre-stroke treatment compared to those who had no treatment.

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REFERENCES

- Carandang R, Seshadri S, Beiser A. Trends in incidence, lifetime risk, severity, and 30-day mortality of stroke over the past 50 years. *JAMA* 2006;296(24):2939-2946.
- Sivenius J, Tuomilehto J, Immonen-Raiha P. Continuous 15-year decrease in incidence and mortality of stroke in Finland. The FINSTROKE Study. *Stroke* 2004;35:420-425.
- American Heart Association. Heart Disease and stroke statistics-2009 update. Dallas, Texas. USA
- Elkinad MS, Sacco RL. Stroke risk factors and stroke prevention. *Semin Neurol* 1998;(18):429-40.94.
- Banerjee TK, Mukherjee CS, Sarkhel A. Stroke in the urban population of Calcutta: An epidemiological study. *Neuroepidemiology* 2001;20(3):201-207.
- Khan SN, Vohra EA. Risk factors for stroke: A hospital based study. *Pak J Med Sci* 2007;23(1):17-22.
- Sehadri S, Wolf PA, Beiser A. Elevated midlife blood pressure increases stroke risk in elderly persons: The Framingham study. *Arch Intern Med* 2001;161:2343-2350.
- Heart Outcome Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med* 2000;342:145-153.
- PROGRESS Collaborative Group. Randomized trial of a perindopril-based blood pressure-lowering regime among 6105 individuals with previous stroke or transient ischemic attack. *Lancet* 2001;358:1033-1041.
- Bogousslavsky J, Melle GV, Regli F, The lausanne Stroke Registry: Analysis of 1000 consecutive patients with first stroke. *Stroke* 1988;19:1083-1092.
- Aho K, Harmsen P, Hatano S, Marquardsen J, Smirnov, Strasser T. Cerebro vascular disease in community: Results of a WHO collaborative study. *Bull. WHO.* 1980;58:113-130.
- Jafari FH, Ahmed SI, Qureshi HA. Presentation and prognosis of stroke in hypertensive, the diabetic and the normotensive normoglycemic. *J Rawal Med Coll* 2000;4(1-2):47-49.
- Basir F, Ali S, Aziz H. Stroke recovery and outcome in diabetes. *J Coll Physicians Surg Pak* 2001;11(12):736-738.
- Megherbi SE, Milan C, Minier D. Association between diabetes and stroke subtype on survival and functional outcome 3 months after stroke. *Stroke* 2003;34:688-699.
- Hankey GJ, Jamrozik K, Broadhurst RJ. Long-term disability after first-ever stroke and related prognostic factors in the Perth community stroke study. *Stroke* 2002;33:1034-1040.
- Hankey GJ, Spiesser J, Hakimi Z. Rate, degree, and predictors of recovery from disability following ischemic stroke. *Neurology* 2007;68:1583-1587.
- Appelros P, Nydevik I, Viitanen M. Poor outcome after first-ever stroke: predictors for death, dependency, and recurrent stroke within the first year. *Stroke* 2003;34:122-126.
- Kelly-Hayes M, Beiser A, Kase CS. The influence of gender and age on disability following ischemic stroke: The Framingham study. *J Stroke Cerebrovasc Dis* 2003;12:119-126.
- Kapral MK, Fang J, Hill MD. Sex differences in stroke care and outcome: Results from the registry of the Canadian Stroke Network. *Stroke* 2005;36:809-814.
- Black DG, Heagerty AM, Bing RF. Effects of treatment for hypertension on cerebral hemorrhage and infarction. *BMJ* 1984;289:156.
- Chitravas N, Dewey HM, Nicol MB. Is prestroke use of angiotensin-converting enzyme inhibitors associated with better outcome? *Neurology* 2007;68(20):1687-1693.
- Rupp H. Risk reduction by preventing stroke: Need for blockade of angiotensin II and catecholamines? *Curr Med Res Opin* 2007;23(5):S25-S29.
- Dowlathshahi D, Hill MD. Angiotensin receptor blockers and secondary stroke prevention: the MOSES study. *Expert Rev Cardiovasc Ther* 2009;7(5):459-464.
- Carlberg B, Samuelsson O, Lindholm LH. Atenolol in hypertension: Is it a wise choice? *Lancet* 2004;364:1684-1689.
- Bertrand ME. Provision of cardiovascular protection by ACE inhibitors: A review of recent trials. *Curr Med Res Opin* 2004;20(10):1559-1569.

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