

## Risk Factors and Outcome of Recurrent Ischemic Stroke-A Prospective Study in a Tertiary Care Hospital

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**Abstract:** Cerebrovascular disease CVD is the most common disease group among all the neurological diseases. The prevalence of strokes in India is increasing as found in community-based studies. We in the present study tried to evaluate the risk factors and outcomes of recurrent ischemic stroke in patients presented to our tertiary care hospital. Methods: This study was conducted at Prathima Institute of Medical Sciences a tertiary care hospital located in Nagunoor, Karimnagar. 100 consecutive cases admitted under Arogyasri scheme with first recurrent ischemic stroke are included in this study. A modified Rankin Scale was used to assess the outcome of the first recurrent ischemic stroke patients and also analyze various risk factors of recurrent ischemic stroke with reference to history, symptomatology, and investigations. Out of the 100 patients admitted during the study 22 were lost during follow up and 5 developed another recurrent stroke within three months of follow up and all these were excluded from the study and 73 patients were taken for evaluation and statistical analysis. Results: The mean age for men was 58.06 years women were 62.52 years the total number of the male in our study was 38 (52.1%) and the female was 35(47.9%). Out 73 studied Out of 73 16 (21.9%) were with hypertension and 6 (8.2%) were diabetic, 19(26%) were smokers and 9 (12.3%) were only alcoholic 7(9.5%) were both and 38 (52.1%) had no addictions. During the recurrent stroke 39(53.4%) patients had the weakness (hemiparesis or hemiplegia or monoparesis or monoplegia) as the only presentation, 10(13.6%) patients had both weakness and facial palsy as their presentation, 16(21.9%) of patients had both weakness and aphasia as their presentation. At the third follow up after second stroke every patient some disability (MRS 1-5) on comparison of the patients with their residual weakness and weakness at the third follow up 21(28.7%) patients had MRS 1 as their residual disability and 10(13.6%) patients had MRS 1 as their disability at follow up. Conclusion: it can be concluded that the risk factors and outcome of RIS in this study were comparable with other similar studies. The important risk factors were hypertension, diabetes mellitus, smoking, atrial fibrillation and decreased compliance with the treatment. Therefore an improvement in patient adherence to treatment is a single very important factor in addition to optimal treatment and follow-up in decreasing the incidence of RIS.

**Keywords:** Recurrent Ischemic Stroke, Risk factors, tertiary care Hospital.

### INTRODUCTION

Recurrent stroke is defined as a new focal neurological deficit "occurring at any time after index stroke" or an event that is clearly in another part of the brain after the preceding stroke [1, 2]. Recurrent stroke constitutes about one-quarter of all strokes and represents failed secondary prevention. The risk of stroke after a transient ischemic attack (TIA) or mild ischemic stroke was determined to be 10% within 1 week and 18% within the 3 months in a study in the UK in 2002-03 [3]. The substantial early risk is 3 folded

higher if the TIA or ischemic stroke is caused by large artery disease and 5 fold lower if the cause is small artery disease [4]. Globally each year 7.95 Lakh people experience a new or recurrent stroke of this approx 6.1 Lakh are due to first attack and 1.85 Lakhs are due to recurrent attacks [5]. Approximately 30% of strokes in population-based studies are recurrent events, and these recurrent strokes are more likely to be disabling or fatal than first strokes. The first 5-year cumulative incidence of stroke recurrent varies between 16 and 30% in western countries [5-9]. The incidence of stroke

recurrent is closely and significantly related to increased mortality and morbidity [10, 11] the recurrent risk varies depending on the CVD type and risk factors. The standard approach in preventing recurrence is by determining etiology and anticoagulant medications and non-pharmacological methods such as carotid endarterectomy and stenting procedures for occlusive vascular lesions. However, the effective treatment of the identified modifiable risk factors is another important factor in addition to the specific treatment methods. Prevention of recurrent stroke is therefore of considerable importance to both individual and public health. Reliable data are required on the absolute risk of recurrent stroke so that prevention services can be organized appropriately and the likely cost-effectiveness of preventive treatment can be assessed. In this hospital-based prospective study, we tried to evaluate the risk factors for recurrent ischemic stroke and its outcome based on the Modified Rankin Scale of the scoring system.

### **MATERIALS AND METHODS**

This study was conducted at Prathima Institute of Medical Sciences a tertiary care hospital located in Nagunoor, Karimnagar. Institutional Ethical Committee permission was obtained for the study. Written consent was obtained from all the participants of the study. 100 consecutive cases admitted under Arogyasri scheme with first recurrent ischemic stroke are included in this study. A modified Rankin Scale was used to assess the outcome of the first recurrent ischemic stroke patients and also analyze various risk factors of recurrent ischemic stroke with reference to history, symptomatology, and investigations. All the ischemic stroke patients were admitted within the above period and WHO satisfied set criteria were included in the present study. Inclusion criteria: patients with first recurrent ischemic stroke and aged above 18 years. Exclusion criteria were hemorrhagic strokes, first ischemic stroke, and age below 18 years. All the patients diagnosed to have the second ischemic stroke (first recurrent ischemic stroke) were thoroughly examined. Elaborate history, mode of presentation, past

history and TIA's and symptoms were sought and recorded. Symptoms of ischemic stroke like gait/language disturbances, headache, vomiting, and convulsions are recorded. Signs like hemiparesis, facial paresis, and hemianopia and altered levels of consciousness and diplopia and sensory deficits were recorded. A detailed history regarding the risk profile in the patients including systemic Hypertension, Smoking, Alcoholism, Dyslipidemia, Diabetes Mellitus, Coronary Artery Disease and RHD were noted for each patient. The details of previous stroke amount of disability, the time is taken for relief of symptoms and details of residual weakness before the onset of present stroke were recorded for each patient. Detailed examinations of neurological status of the patient with a comprehensive examination of other systems were recorded in the proforma. MRS was applied to all the patients before and after the onset of present stroke with five scores for each patient, on admission, at discharge, 10 days after discharge, 1 month after discharge and 3 months after discharge. All the patients were investigated for basic biochemical, hematological investigations including ECG, ECHO, CXR, CT brain, Carotid Doppler, lipid profile and HbA1c in cases of known diabetic patients. Serum homocysteine levels and ANA profile were done in selected patients. Out of the 100 patients admitted during the study 22 were lost during follow up and 5 developed another recurrent stroke within three months of follow up and all these were excluded from the study and 73 patients were taken for evaluation and statistical analysis.

### **RESULTS**

Out of the total 73 participants in the study, the majority of patients were found in the age group of 51-60 years 30 (41.09%) and 61-70 years of age group had 23(31.5%). The 41-50 years age group contributed 6(8.2%) and similarly, 71-80 years had 11(15%) and 2(2.7%) were of 20-30 years age. The mean age for men was 58.06 years women were 62.52 years the total number of the male in our study was 38 (52.1%) and the female was 35(47.9%) there was a greater risk of development of stroke in men as compared to women.

**Table-1: Age and sex wise distribution of the cases in the study**

Age Group years	Male	Female	Percentage
20 – 30	1 (1.36%)	1 (1.36%)	2 (2.7%)
31 – 40	0	0	0
41 – 50	3 (4.1%)	3 (4.1%)	6(8.2%)
51 – 60	14 (19.1%)	16 (21.9%)	30(41.09%)
61 – 70	16 (21.9%)	7 (9.58%)	23 (31.5%)
71 – 80	4 (5.4%)	7 (9.58%)	11(15%)
81 – 90	0	1 (1.3%)	1(1.3%)
Total	38 (52.1%)	35 (47.9%)	73(100%)

Out 73 studied 19(26%) were smokers and 9 (12.3%) were only alcoholic 7(9.5%) were both and 38 (52.1%) had no addictions. The risk factors involved were studied for the recurrent stroke carotid disease was

seen in 29(39.7%) of patients, and 21(28.7%) had hyperlipidemia cardiac disease was seen in 16(21.9%) and highest was due to non-drug compliance 36(49.3%) of patients.

**Table-2: Evaluation of Risk factors for recurrent stroke**

Risk Factor	Male	Female	Total
No DM or HTN	12 (16.4%)	4 (5.4%)	16 (21.9%)
DM only	2 (2.7%)	4 (5.4%)	6 (8.2%)
HTN only	12 (16.4%)	10 (13.6%)	22 (30.1%)
DM and HTN	12 (16.4%)	17 (23.2%)	29 (39.7%)
Total	38 (52.1%)	35 (47.7%)	73 (100%)

**Table-3: Time duration from first stroke in RIS patients**

Time duration	Male	Female	Total
< 1 year	16 (42.1%)	16(45.7%)	32(43.8%)
1 -2 year	10 (26.3%)	4(11.4%)	14(19.1%)
2 -3 year	6 (15.7%)	6(17.1%)	12(16.4%)
3 – 4 year	4(10.5%)	3(8.5%)	7(9.5%)
4 – 5 year	0	3(8.5%)	3(4.1%)
> 5 year	2(5.2%)	3(8.5%)	5(6.8%)
Total	38(100%)	35(100%)	73(100%)

In the study of symptoms we found 52(71.2%) had weakness (hemiparesis or hemiplegia or monoparesis or monoplegia) on their presentation during the first stroke, 9(12.3%) patients had only facial palsy as their presentation during the first stroke, 7(9.5%) patients had both weakness and facial palsy as presented during the first stroke. During the recurrent stroke 39(53.4%) patients had the weakness (hemiparesis or hemiplegia or monoparesis or monoplegia) as the only presentation, 10(13.6%)

patients had both weakness and facial palsy as their presentation, 16(21.9%) of patients had both weakness and aphasia as their presentation. In both first as well as second stroke most patients had the weakness (hemiparesis or hemiplegia or monoparesis or monoplegia) on their presentation. During the recurrent stroke, there was an increase in the number of cases with weakness and facial palsy, weakness, and aphasia which are clinically significant when compared to the first stroke (table 4).

**Table-4: Symptom presentation in RIS patients**

Symptom	Old stroke	New stroke
Weakness Only	52(71.2%)	39(53.4%)
Only Facial Palsy	9(12.3%)	3(4.1%)
Only Aphasia	4(5.4%)	2(2.7%)
Weakness and Facial Palsy	7(9.5%)	10(13.6%)
Weakness and Aphasia	1(1.3%)	16(21.9%)
Seizures	0	1(1.3%)
Giddiness and Vomiting	0	2(2.7%)
Total	73	73

The MRS scoring showed 36(49.3%) of patients had no residual weakness or disability (MRS 0) before the onset of the second stroke but at the third follow up after second stroke every patient some disability (MRS 1-5) on comparison of the patients with their residual weakness and weakness at the third follow up 21(28.7%) patients had MRS 1 as their

residual disability and 10(13.6%) patients had MRS 1 as their disability at follow up. There was no statistically significant difference noted between the sex wise distribution of stroke according to MRS score at their follow up both male and female tend to have the same severity of disability in the present study shown in (table 5).

**Table-5: Sex wise distribution of patients depending on the MRS scoring at third follow up**

Gender	3 <sup>rd</sup> follow up					Total
	1	2	3	4	5	
Female	1(10%)	8(66.6%)	8(57.1%)	12(48%)	6(50%)	35
Male	9(90%)	4(33.3%)	6(42.9%)	13(52%)	6(50%)	38
Total	10	12	14	25	12	73

The age wise and gender-wise distribution of cases shown in table 6 has 2(100%) patients were with a disability of MRS 1 and 6 patients of age group 41-50 2(33.3%) patients were the disability of MRS 1. Only 1 (16.6%) patient was with the disability of MRS 2 and 2(33.3%) patients with MRS 3 disability and 1 (16.6%)

was with MRS 4. Similarly, in 51-60 year, category 2(6.6%) patients were with disability MRS 1, 6(20%) were disability MRS 2 and MRS 3 respectively. 11 (36.6%) were with MRS 4 and 5 (16.6%) were with MRS 5.

**Table-6: Age wise distribution of patients based on MRS at third follow up**

	MRS 1	MRS 2	MRS 3	MRS 4	MRS 5	Total
< 40	2(100%)	0	0	0	0	2
41- 50	2(33.3%)	1(16.6%)	2(33.3%)	1(16.6%)	0	6
51- 60	2(6.6%)	6(20%)	6(20%)	11(36.6%)	6(16.6%)	30
61 – 70	2(8.6%)	4(17.3%)	6(26%)	7(30.4%)	4(17.3%)	23
> 70	2(16.6%)	1(8.3%)	0	6(50%)	3(25%)	12
Total	10	12	14	25	12	73

**DISCUSSION**

Recurrent ischemic stroke is an important public health concern [12]. Age is the most important un-modifiable risk factor for all stroke types and is also one of the significant independent predictors of recurrent stroke [12- 15]. The incidence of stroke rises more than twice for both men and women after the age of 55 years [14]. In the present study highest numbers of patients were found to be between the age group 51-60 years the mean age of men in the present study was 58.0 ± 6.86 and the mean age for women was 62.52 ± 8.28. In various studies, it has been shown that 65% of all strokes occur in individuals over the age of 65 years [12, 15, 16]. Hypertension is the most prevalent and important modifiable risk factor among all the stroke patients within the population [17-20]. According to the outcomes of a meta-analysis including 17 different studies a reduction of 38% in the total stroke risk may be provided by controlling hypertension alone [21]. A similar meta-analysis of seven randomized controlled trials including the PATS (indapamide, a diuretic), HOPE ramipril and PROGRESS [predinopril with or without indapamide] showed that antihypertensive drugs reduce stroke recurrence after TIA (RR 0.76 95% CI 0.63-0.92) [22-26]. Another study has reported that an effective antihypertensive treatment reduces the stroke recurrence by 50% [74]. In the present study, hypertension was present in 51(69.9%) of the 73 study patients. Diabetes mellitus is yet another cause for the development of stroke. Hyperglycemia is known to accelerate development of both microvascular disease and atherosclerosis throughout the body. Consequently diabetes mellitus increases the combined risk of stroke and myocardial infarction by 2.5 times [27]. In the present study, 35(47.9%) of the patients were diabetics and it was found that both sexes were equally affected with hypertension and diabetes. Smoking increases the risk of CVD and the effects are more when the patient is already suffering from diabetes mellitus or hypertension. In the present study, we found 26(35.6%) of the patients had a history of smoking at the time of RIS. Laloux et al; has found the rate of RIS in smokers to be 25% [28]. Elevated total cholesterol and altered

TC/HDL ratio are associated with myocardial infarction and similar rates were found for athero-thrombotic brain ischemia [29]. According to the AHA/ASA 2011 guidelines, statin treatment with intensive lipid-lowering effects is recommended to reduce the risk of stroke and cardiovascular events with Ischemic stroke or TIA [30]. In the present study, 21(28.8%) of 73 patients were having dyslipidemia. Atrial fibrillation accompanied with RHD and mitral stenosis is an important predisposing factor in etiology of stroke [27]. Warfarin treatment provides 64% relative risk reduction in the prevention of stroke [31]. In this study atrial fibrillation was seen in 10 (13.7%) of patients and cardiac regional wall motion abnormality was present in 16(21.9%) of patients. In the present study 36(49.3%) were non-compliant to their anti-platelet drugs. The improvement in adherence to treatment is very important in addition to the optimal treatment and follow-up strategy for decreasing incidence of RIS. Patients with a stroke recurrence are known to have an average poorer survival outcome compared to those with first stroke only. More than 50% of stroke survivors have the significant residual physical disability and functional impairment. In the present study considering MRS scores 0-2 as mild disability, MRS 3 as moderate disability and MRS 4 & 5 as severe disability, then out of the 73 patients 37(50.6%) patients had severe disability at third follow up in this 19(50%) of male had severe disability at third follow up and 18(51.4) female patients had severe disability at third follow up. The strengths of the present study were prospective designed and longitudinal follow up at regular intervals of 3 months however limitations included because it is a tertiary care hospital the results may not be generalized to all settings. The detailed history and treatment regarding their first stroke were found missing in some cases.

**CONCLUSION**

Within the limitations of the present study, it can be concluded that the risk factors and outcome of RIS in this study were comparable with other similar studies. The important risk factors were hypertension,

diabetes mellitus, smoking, atrial fibrillation and decreased compliance with the treatment. Therefore an improvement in patient adherence to treatment is a single very important factor in addition to optimal treatment and follow-up in decreasing the incidence of RIS.

#### REFERENCES

1. Hankey GJ, Jamrozik K, Broadhurst RJ, Forbes S, Burvill PW, Anderson CS Stewart-waynnel EG. Long-term risk of first recurrent stroke in the Perth community stroke study. *Stroke*. 1998;29:2491-00.
2. Burn J, Dennis M, Bamford J, Sandercock P, Wade D, Warlow C. Long-term risk of recurrent stroke after a first-ever stroke: the Oxford shire community stroke project. *Stroke*. 1994; 25:333-37.
3. Coull AJ, Lovett JK, Rothwell PM. Oxford vascular study. A population-based study of early risk of stroke after the transient ischemic attack or minor stroke: implications for public education and organization of services. *BMJ*. 2004; 328:326-28.
4. Lovett JK, Coull A, Rothwell PM. Early risk of recurrence by subtype of ischemic stroke in population-based incidence studies. *Neurology*. 2004;62(4):569-73.
5. Kolominsky Rabas PL, Weber M, Gefeller O, Neundoefer B, Heuschmann PU. Epidemiology of ischemic stroke subtypes according to TOAST Criteria: incidence, recurrence and long-term survival in ischemic stroke subtype: a population-based study. *Stroke*. 2001;32:2735-40.
6. Petty GW, Brown RD, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Ischemic stroke subtypes: population-based study of functional outcome, survival and recurrence. *Stroke*. 2000; 31:1062-68.
7. Mohan KM, Crichton SL, Grieve AP, Rudd AG, Wolfe CD, Heuschmann PU. Frequency and predictors for the risk of stroke recurrence up to 10 years after stroke: The south London stroke register. *J Neurol Neurosurg Psychiatry*. 2009; 80:1012-18.
8. Mohan KM, Wolfe CD, Rudd AG, Heuschmann PU, Kolominsky-Rabas PL, Grieve AP. Risk and cumulative risk of stroke recurrence: a systematic review and meta-analysis. *Stroke*. 2011;42:1489-94.
9. Modrego PJ, Pina MA, Mar Farj M, Llorens N. Type cause and prognosis of stroke recurrence in the province of Teruel Spain. A 5-year analysis. *Neuro Sci*. 2000;21:355-360.
10. Filippi A, Bignamini AA, Sessa E, Samani F, Mazzaglia G. Secondary prevention of stroke in Italy. A cross-sectional survey in family practice. *Stroke*. 2003;34:1010-14.
11. Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, Aboyans V. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *The lancet*. 2012 Dec 15;380(9859):2197-223.
12. Helgason CM, Wolf PA. American Heart Association Prevention Conference IV: prevention and rehabilitation of stroke: executive summary. *Circulation*. 1997 Jul 15;96(2):701-7.
13. World Health Organization (WHO) MONICA project (Monitoring trends and determinants in cardiovascular disease) a major international collaboration *J Clin Epidemiol*. 1988;41:1050-114.
14. Rothwell PM, Coull AJ, Silver LE, Fairhead JF, Giles MF, Lovelock CE, Redgrave JN, Bull LM, Welch SJ, Cuthbertson FC, Binney LE. Population-based study of event-rate, incidence, case fatality, and mortality for all acute vascular events in all arterial territories (Oxford Vascular Study). *The Lancet*. 2005 Nov 19;366(9499):1773-83.
15. Petty GW, Brown RD, Whisnant JP, Sicks JD, O'fallon WM, Wiebers DO. Survival and recurrence after first cerebral infarction: a population-based study in Rochester, Minnesota, 1975 through 1989. *Neurology*. 1998 Jan 1;50(1):208-16.
16. Lloyd-Jones D, Adams R, Carnethon M, De Simone G, Ferguson TB, Flegal K, Ford E, Furie K, Go A, Greenlund K, Haase N. Heart disease and stroke statistics—2009 update. A report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2008 Dec 15.
17. Leo T, Lindgren A, Peterson J, Von Arbin M. Risk factors and treatment at recurrent stroke onset. Results from the recurrent stroke quality and epidemiology (RESQue) study. *Cerebrovasc Dis*. 2008; 25:254-60.
18. Sacco RL. Identifying patient populations at high risk for stroke. *Neurology* 1998;51(suppl 3):27-30.
19. Lawes CM, Vander Hoorn S, Rodgers A. International society of hypertension. Global burden of blood pressure related diseases 2001. *Lancet* 2008;371:1513-18.
20. Bornstein N, Silvestrelli G, Caso V, Pranetti L. Arterial Hypertension and stroke prevention: an update *Clinic Exp Hypertens*. 2006;28:317-26.
21. Gueyffier F, Boissel JP, Boutitie F, Pocock S, Coope J, Cutler J, Ekblom T, Fagard R, Friedman L, Kerlikowske K, Perry M. Effect of antihypertensive treatment in patients having already suffered from stroke: gathering the evidence. *Stroke*. 1997 Dec 1;28(12):2557-62.
22. Rashid P, Leonardi BJ, Bath P. Blood pressure reduction and secondary prevention of stroke and other vascular events: a systematic review. *Stroke*. 2003;34:21741-48.
23. PATS CG. Post-stroke antihypertensive treatment study. A preliminary result. *Chinese medical journal*. 1995 Sep;108(9):710.
24. Yusuf S, Sleight P, Pogue JF, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular

- events in high-risk patients. *The New England journal of medicine*. 2000 Jan;342(3):145-53.
25. Bosch J, Yusuf S, Pogue J, Sleight P, Lonn E, Rangoonwala B, Davies R, Ostergren J, Probstfield J. Use of ramipril in preventing stroke: double blind randomised trial. *Bmj*. 2002 Mar 23;324(7339):699.
26. Progress collaborative group randomized trial of perindopril-based blood pressure lowering regimen among 6105 individuals with previous stroke or transient ischemic attack. *Lancet*. 2001; 358:1033-41.
27. Pencina MJ, D'Agostino RB, Larson MG, Massaro JM, Vasan RS. Predicting the 30-year risk of cardiovascular disease: the Framingham Heart Study. *Circulation*. 2009 Jun 23;119(24):3078-84.
28. Laloux P, Lemonnier F, Jamart J. Risk factors and treatment of stroke at the time of recurrence. *Acta Neurol Belg*. 2010;299-02.
29. Simons LA. Triglyceride levels and risk of coronary artery disease: a view from Australia. *Am J Cardiol*. 1992;70:14-18.
30. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo Jr JL, Jones DW, Materson BJ, Oparil S, Wright Jr JT, Roccella EJ. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. *Jama*. 2003 May 21;289(19):2560-71.
31. Whisnant JP, Wiebers DO, O'fallon WM, Sicks JD, Frye RL. A population-based model of risk factors for ischemic stroke Rochester, Minnesota. *Neurology*. 1996 Dec 1;47(6):1420-8.