Original Article

Clinicodemographic Profile Of Recurrent Stroke And Secondary Prevention At Tertiary Care Centre Of North-West India

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Abstract

Background and Aim: Stroke is a major public health problem worldwide. The risk of recurrence is highest in the first year after the stroke, majority of the recurrent cases are due to atherosclerosis of the large arteries.The present study was conducted to evaluate clinico-bio-demographic profile of recurrent stroke patient in respect of risk factor and secondary prevention of stroke.

Methods: A hospital-based cross-sectional study was conducted on 300 recurrent ischemic/hemorrhagic stroke (age 18-85 yrs.) from August 2015 to March 2017. Stroke mimic were excluded. Risk factors studied were hypertension, diabetes mellitus, hyperlipidemia, cardiac causes and cigarette smoking.

Results: Mean age of recurrent stroke was 60±13 years with male preponderance (M: F=5.3).Ischemic stroke was found in 93% cases. About one third (33%) patients had their first recurrence within three months of index stroke. Active smoking, uncontrolled hypertension and diabetes were found in 71%, 62%, and 65 % cases respectively. There was association between first ever stroke and recurrence showing P value > .05, <.001 and <.01 for uncontrolled hypertension, diabetes and active smoking respectively.Extra cranial stenosis (≥70%) was found in 29% of recurrent stroke. Out of all stroke cases 40% were drug defaulters.

Conclusions: In our study commonest cause of recurrent stroke was active smoking followed by uncontrolled diabetes, uncontrolled hypertension, poor drug compliance and symptomatic carotid stenosis. Frequency of recurrence was more within 3 months.

Keyword: Atherosclerosis, Drug adherence, Extra cranial stenosis, Risk factors, Recurrent stroke

Introduction:

Stroke is the second commonest cause of mortality and the third leading cause of disability after cardiac and gastrointestinal disease worldwide[1]. Globally 70% of stroke cases and 43% death are reported due to stroke in 1st three decades.In India recurrence rate of stroke varies from 14% to 21% in population and hospital based registries[2]. Recurrent stroke was defined as a focal neurological deficit occurring suddenly in a vascular territory, lasting more than 24 hours, and occurring at any time after one week from the index stroke either acute infarcts or hemorrhage on DWI/NCCT Head[3]. Recurrent stroke during the first year are in a mainly due to atherosclerosis of the large arteries[4]. During subsequent years the most important risk factors usually are hypertension, dyslipidemia, diabetes and cardiovascular risk factors including atrial fibrillation[5]. After the first year, the frequency of recurrent stroke is 4-5% per year[6]. Poor drug compliance jack of medicine and awareness about stroke prevention,cost of treatment are important barrierin low income-middle income countriec in secondary stroke prevention[7]. In present scenario there is need to identify risk factors in stroke, evaluate and implement intervention[8].Only few studies are available on recurrent stroke and risk factors in western world and most of them lack data on carotid stenosis and on the evaluation of secondary prevention. Therefore we proposed this study to find out epidemiology of recurrent stroke.

Aims : The aim of proposed study was to evaluate the clinical-bio-demographic profiles of the recurrent stroke patients in respect of risk factor and secondary prevention of stroke.

Material & Methods: A hospital-based cross-sectional study was conducted on clinically diagnosed cases of recurrent ischemic/haemorrhagic stroke (age 18-85 yrs ./either sex) admitted to the neurology department of a tertiary Centre from August 2015 to March 2017. Durations (10-day- 20 years) between first-ever stroke and recurrence were taken.

Sample size: We recruited all eligible cases of recurrent stroke during the study period of twenty months. So during this period total 1575 stroke cases were admitted and 300 clinically diagnosed recurrent strokes cases were eligible for study. Study was approved by the institutional ethical committee.

Inclusion Criteria: All eligible patients of recurrent stroke are taken as cases. Diagnosis of index stroke was as defined by World Health Organization, NCCT-Head consistent with ischemic stroke. Written informed consent was taken by all patients or their legal representative.

Exclusion criteria: Patients with malignancy, pregnancy, stroke mimics such as migraine, seizure, aneurysm, arteriovenous malformation (AVM) anxiety, trauma, surgery and chronic disease like liver disorder, renal disorder and HIV were excluded.

All eligible cases of recurrent stroke enrolled into stroke database after screening in consecutive manner. Screening included clinical history, general physical examination and review of previous available records. Recurrent stroke categorised as ischemic and

haemorrhagic after imaging (NCCT Brain *I* MRI Brain with DWI). All cases were grouped into first recurrence or subsequent.- Varios risk factors were classified as smoking (active/Ex-smoker), hypertension (HT), diabetes mellitus (DM), dyslipidemia and cardiac causes. Cardiac causes included atrial fibrillation (AF), coronary artery disease (CAD), valvular heart disease and patent foramen ovale. Complete hemogram,erythrocyte sedimentation rate, plasma glucose level, renal function test ,lipid profile, activated prothrombin time(aPTT),pro thrombin time tests, HbAic ,VDRL and HIV were performed .When further work up were needed tests for hypercoagulable state, lupus anticoagulant, ant phospholipid antibodies, homocysteine and transesophageal echocardiography were also performed . Electrocardiography (ECG) and two- dimensional echocardiography (2D- ECHO) were carried out in all the patients for cardiac evaluation. CT angiography of brain and neck vessels was also conducted in all patients. Definitions of variables were modified from the AHA/ASA[2014] guidelines[9,10] and according these newly detected hypertensive defined as systolic pressure ≥140 mm Hg OR diastolic ≥ 90 mm Hg or uncontrolled if systolic pressure ≥130 mm Hg OR diastolic ≥ 90 mmHg on antihypertensive medications on two or more occasions during the study evaluation.

If fasting blood sugar level was ≥126 mg/dl, HbAic ≥ 6.5% or random blood sugar level more than 200 mg/dl.It was uncontrolled if HbAic ≥ 7% or if fasting ≥130 mg/dl on anti diabetic medications.

If they either had LDL-C ≥190 mg/dl without other risk factors or with diabetes LDL-C 70 to 189 mg/ dl , triglycerides >150 mg /dl and LDL-C more than 100 mg/dl on statin therapy.

Cardiac causes are defined as documented history of acute myocardial infarction or presence of AF, valvular heart disease, regional wall motion abnormality (RWMA) by 2 DECHO and ECG changes

Regular smoker who smokes ≥1 cigarettes daily, Biris, Cigar for proceeding> 3 months.

Transient Ischemic Attack (TIA)who developed focal neurologic symptoms attributable to vascular etiology relating to focal cerebral, brain stem, or retinal ischemia with abrupt onset and complete resolution within 24 hours.

Symptomatic stenosis defined in case of amaurosis fugax, TIA, or hemispheric stroke as severe carotid stenosis (70-99%) and moderate stenosis (50-69%) by MR or CT angiography[11].

Statistical analysis: Outcomes in our study were the proportion of cases with various etiologies and risk factors. For outcome analysis, we used for Quantitative (mean ±SD) and for Qualitative data (% and proportion). For significant difference in proportion, Chi square test was used. P value < .05 was considered significance. Data analysis was performed by using the program SAS.

Results: Total 1575 cases of first ever stroke were screened to get 300 diagnosed cases of recurrent stroke during a period of 20 months from August 2015 to March 2017. Out of them 252 (84%) were male and rest of female. Male to the female ratio was 5.3.

The mean ages of all patients were 60±13 years, and 52% patients were more than 60 years. There were 48 (16%) patients in young age (< 45) group. Out of total recurrent stroke, ischemic stroke was found in 279 (93%) cases and 21(7%) cases were haemorrhagic (Table 1) .

(Table 1). Distribution of Study Population

S. No.	Variables	Results N (%)
1.	**Age (Mean± SD) in Years**	**60 ±13**
2.	**Sex (M/F) in (%)**	**252/48 (84, 16)**
3.	**Recurrent stroke**	**N=300**
	(a) Ischemic (%)	**279(93)**
	(b) Hemorrhagic (%)	**21(7)**
4.	**Total smoker (Onset of index event)**	**126(42)**
5.	**Ex- smokers**	**37(29)**
6.	**Active Smoker (%)**	**89(71)**
7.	**Total hypertensive (Onset of index event)**	**213(71)**
8.	**Controlled hypertension**	**81(38)**
9.	**Uncontrolled hypertension**	**132(62)**
10.	**Total Diabetic (Onset of index event)**	**60(20)**
11.	**Controlled diabetes**	**21(35)**
12.	**Uncontrolled diabetes**	**39(65)**

There were varied clinical presentation including motor weakness in 246 (82%) patients, speech disturbances 27 (9%), ataxia, vertigo and dysarthria 30 (10 %) and fifteen patients (5%) had sensory symptoms.

Hypertension was present in 213(71%) patients and other risk factor like chronic smoking,-diabetes,dyslipidemia and cardiac causes were present in 126 (42%), 60 (20%),72(24%) and 60 (20%) respectively at time of first ever stroke. (Table 2)

(Table 2). Comparision of various study on recurrent stroke

Variable	RESQUE study (71	Laloux et.al.fl5l	Kockman.et.al[14]	Present study
First ever stroke patients	-	532	500	1575
Recunent stroke patients (%)	889	168(32%)	91(18)	300(19)
Mean age of onset	77	72 ±13.3	71.55 ±10.45	60 ±13
Male / Female	504/385	89/79	55/41	252/48
% of recurrence after one yrs	-	60.7	-	68
Common risk factors in recunent stroke n (%)				
1.Hypertension	658(75)	133(79.2)	80(88)	213(71)
2. Chronic Smokers	114(13)	42(25)	13(14)	126(42)
3. Dyslipidemia	388(56)	72(42.8)	27(30)	72(24)
4. Cardiac causes	317(37)	41(24.4)	33(36)	60(20)
5 . Diabetes	212(24)	37(22)	39(43)	60(20)
5. Arterial Stenosis				105(35)
(a). Extracranial ≥ 70% < 70% (b). Intracranial				87(29) 63(21) 24(8) 18(6)
More than two risk factors	410(51)	94(55.9)	35(48)	141(47)

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All patients were advised to quit smoking at time of first ever stroke but only 37out of 126 patients stopped smoking and 89out of 126 patients (71%) were still continuing smoking.

A significant number 132(62 %) patients had uncontrolled hypertension and uncontrolled diabetes was present in 39(65%) patients (Figure 1).

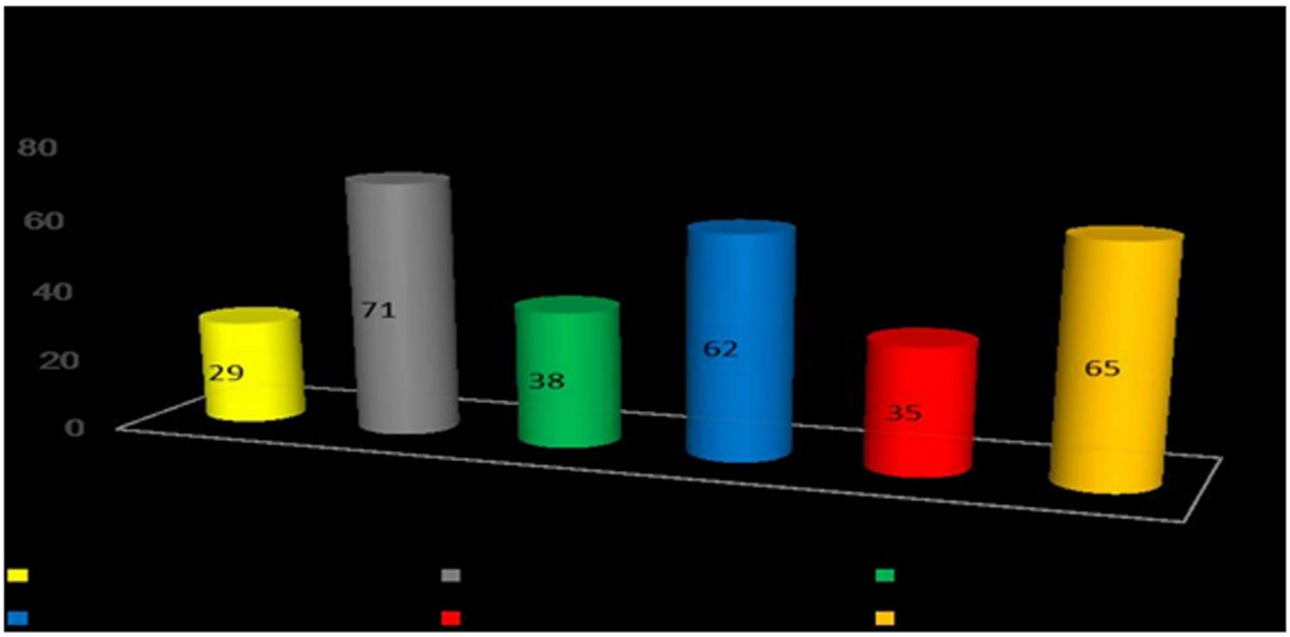

Figure 1, Showed comparison of various risk factors in recurrent stroke patients.

The statical analyses were performed between first- ever stroke and recurrence with respective to risk factors for uncontrolled hypertension^ .05), diabetes (<.001) and active smoking(<.01). Extra cranial stenosis was the cause of recurrence in 29% while intracranial only in 6% cases.

About one third patient had first recurrence within three months of index stroke . In this study 40% were drug defaulters. They left out the treatment after 2-3 months of the first ever stroke. Drug adherence for antihypertensive, antiplatelet and statins were 60%, 35% and 27% respectively.

Discussion:

Stroke is a major public health problem with various modifiable and non-modifiable risk factors. In present scenario, due to lack of exercise and education programs about stroke warning symptoms and various risk factors, frequency of recurrent stroke is increasing at a rapid pace in Indian population. Here 19% patients were admitted for recurrent stroke which were similar to kockman et al. study[12] and lower as comparison 32% in Laloux et. Study. This proportion was higher probably due to inclusion of recurring TIA cases.Cases of ischemic recurrent stroke was almost similar to 805(91%) RESQUE trial[5] and 279(93%) in present study.

Age is the important risk factor in stroke. The mean age of onset for fresh and recurrent stroke is higher in Western countries than India. In a Western study of recurrence stroke, 62.2% patients were > 60 years of age as compared to our study (52%). Stroke onset and recurrent stroke are common in younger Indian than the western. Hence loss of the peak of their productive life span is being now commonly seen developing countries like Industrialised nations.

Smoking flares the risk of recurrence. This increase is more pronounced with multiple co-existing risk factors. In our study, it was second most common risk factor after hypertension in first ever stroke.

The smoking-cessation rate was 29 % in the present study as compared to 21.7% in previous literature[15]. That's why we could find a significant association between first-ever stroke and recurrence with smoking (P <.01).

Uncontrolled hypertension is common risk factor in India as well as western countries. In a western study after one year follow up hypertension was uncontrolled in 66% patients on anti-hypertensive drugs and 57% were enrolled as newly detected hypertensive[16].It was more common(62%patients) in current study but we could not establish the static significance of hypertension in recurring stroke (p > .05) after the first - ever stroke. This may be debatable but we had multiple coexisting risk factors in large numbers of patients.

Diabetes is an independent risk factor. It was associated with increased risk of 60 % for recurrent ischemic stroke (RR-1.59: 95% CI, 1.07-2.37) and found in 25 to 45% of overt diabetes[17]. Near about two third had uncontrolled diabetes that had highly significant impact (P<.001) on first - ever stroke in causing recurrence.Reduction of low density lipoprotein cholesterol (LDL-C) is an important component in the secondary risk reduction strategy for an index event. High dose statin therapy in stroke patients with > 50% reduction in LDL-C had a reduction in recurrent stroke, which may be fatal and nonfatal[18].

The percentage of coronary artery disease and AF were 37 and 29 in RESQUE study. In our study AF was not an obvious finding like RESQUE trial and other western studies. In RESQUE study 21% patient with AF were on anticoagulant[5]. Anticoagulants are commonly used in cardio embolic strokes and their monitoring is necessary to prevent bleeding risk.

Most common etiological factor was large artery atherosclerosis (53%) in higher proportion because of coexisting of multiple risk factors mainly smoking,dyslipidemia and diabetes which increase atherosclerosis in ischemic stroke. Therefore we found a significant(29%) extracranial stenosis on imaging compare to 25 - 26 % stroke patients in previous[19].Intracranial stenotic lesions was also significantly associated up to 50% to 99% stenosis of the MCA, intra-cranial ICA, intra-vertebral artery, or basilar artery in western patient[20]. Stenotic lesions are the more common cause of recurrence in the younger age with higher incidence. That's why neuro intervention is a growing field to prevent ipsilateral recurrence due to extracranial or intracranial stenosis, but we lack behind performing intervention as compared to western countries because of lack of infrastructure facilities and training in intervention.

As we know that treatment drop out is a common problem in Indian with a burden 40% in this study, 30.9% Worldwide and 32 % in Indian subcontinent. These patients were neither taking anti platelets, statin or anti-hypertensive treatment at time of recurrence. Drug adherence for these medications was variable in this study, Worldwide and in Indian subcontinent. It was fair for antihypertensive and poor for statins.[21,22] (Figure 2).

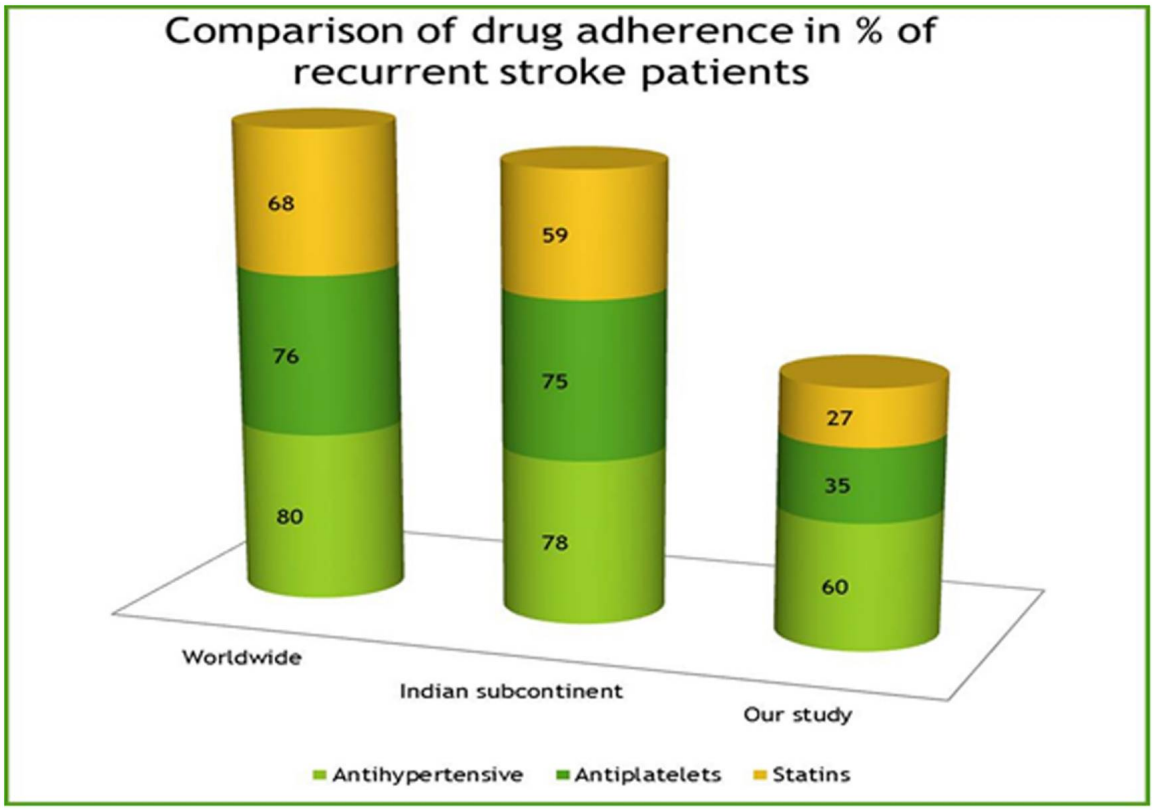

Figure 2 , Showed comparison of drug adherence in recurrent stroke patients.

In developing countries, including India an important reason for recurrence is poor drug compliance, treatment drop out after 2-3 month , lack of knowledge about stroke care and warning symptoms or myths in society.

Conclusions: The commonest cause of recurrent stroke in this study was active smoking followed by uncontrolled diabetes, uncontrolled hypertension, poor drug compliance and symptomatic carotid stenosis. Frequency of recurrence was more within three months. Strategy and planning should be formulated and are advised to prevent different modifiable risk factors, treatment dropouts, myths in society and promotion neuro intervention in stroke on cost effective rate. Hence a rapid and early action is required to control distinctive risk factors so that recurrence can be prevented in young Indian po pulation.

Hypertension ,diabetes and smoking are important treatable and modifiable risk factors. Strengths of the study: There are no published data from India and only very few studies were done on recurring stroke worldwide. Present study has taken with more risk actors with their drug compliance. Extracranial stenosis has never been evaluated in recurrence stroke before. Records and data were tracked for a long period average 7-9 years with index and recurrent stroke.

Limitations of study: First, site was not chosen at random but rather were chosen based on the existence of a recurring stroke admitted to neurology department or dedicated care for patients with recurrent stroke evaluated yearly during the study period. This suggests that either investigators overestimated their annual recruitment rate or

not all patients were included in study. Our study was biased toward more specialized stroke physician rather than a population-based study. Second, owing to resource constraints, we could audit only small size sample.

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