



DRUG UTILIZATION PATTERN AND RISK ELEMENTS OF STROKE PATIENTS IN A TERTIARY CARE HOSPITAL: A CROSS SECTIONAL STUDY.

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ABSTRACT **Background:** Stroke is not only one of the leading causes of morbidity and mortality worldwide but is also a topic of major public health concern in developing countries with a prevalence of 44 - 559 per 100,000 people. This study focuses on risk factors, socioeconomic distribution, drug utilization pattern, rehabilitation of patients and possible solutions to the encountered problems. **Methods:** Patients admitted to ESIC MC & PGIMSR, Bangalore were included in this cross-sectional study. A complete profile of patients diagnosed with stroke was obtained. **Results:** On analysing the data obtained from 51 patients under study, it was noted that ischemic stroke was the highest (84.31%), and stroke in males (70.59%) was higher than among females (29.41%) with highest occurrences between 55-70 years of age (41.18%). A large number of people were found to have ≥ 3 risk factors (72.54%), including hypertension (78.43%), alcoholism (50.98%), diabetes mellitus (49.02%), smoking (47.05%), and dyslipidemia (27.45%). It was found that an average patient is prescribed 3.01 drugs in generic name and 4.68 in brand name ($p < 0.05$). The study also highlighted the inadequacy of physiotherapy (39.21%), speech-therapy (11.76%) and occupational-therapy (0%). **Conclusion:** An understanding of risk factors and drug prescription strategies followed by physicians across different socioeconomic groups helps to fine tune management strategies in accordance with guidelines, to provide a better quality of life to patients.

KEYWORDS : drug utilisation, risk factor, stroke, ischemic, haemorrhagic.

INTRODUCTION

The World Health Organization definition of stroke is "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin".¹

Stroke is said to be one of the major neurological diseases affecting a vast number of the population across the globe. A nationwide survey in India proved that the disease prevalence ranges from 44 to 559 per 100,000 populations with region wise variations. The incidence and prevalence of stroke in India was found to be higher among the people belonging to high socio-economic groups.² Some of the major risk factors for the stroke are hypertension, diabetes, cardiovascular diseases, dyslipidemia, smoking, age, sex and race.

Appropriate treatment of these risk factors, early diagnosis and management of stroke is pivotal to improve the outcome. Some of the hurdles for appropriate drug utility can be low socioeconomic status, presence of disability and inappropriate counselling.^{3,4} As people with stroke are affected by most of the above factors meticulous follow up is required for the better adherent to the medications.

The appropriate analysis of drug utilization demands some of the basic questions to be answered. This includes, the reason for the prescription of drugs, compliance to the medication by patients, analysing the benefits and risks of drugs prescribed.⁵ Considering the magnitude of the disease, some solutions lie in an efficient drug utilization.⁶ Following guidelines and standardized prescription protocols can aid this step.

There is a profound need for such studies in developing countries to understand the factors and patterns in drug utility. This aids in better management of patients affected by stroke. This study focuses on inferring medical and non-medical determinants playing a role in drug utilization. Furthermore, by observing the prescribing attitude of physicians in stroke patients, appropriate interventions based on the type of problems associated with drug utilization can be framed. This results in preventing irrational use of drugs and minimizing the

economic burden posed by the disease.

MATERIALS AND METHODOLOGY.

The study was conducted on patients presenting to the Intensive Care Unit and In-patient services of ESIC MC & PGIMSR, Bangalore to access the risk factors, drug utilisation, investigations and interventions and to provide solution to the problems encountered. Clearance from the institutional ethical committee was obtained. A total of 51 subjects diagnosed with cerebrovascular accidents were enrolled in the study.

The inclusion criteria considered for the study was a) Patients of either gender aged more than or equal to 18 years. b) Patients who were diagnosed with stroke. c) Patients who volunteered to provide written informed consent. The exclusion criteria was a) Pregnant / lactating women b) Patients with renal or hepatic diseases.

After obtaining informed consent (consent was obtained from legally accepted representative when patient was unable to provide), socio-demographic details including patient's name, age, gender and past medical history was collected. Prescription details such as number of drugs, name of individual drugs, dosing schedule, number of drugs prescribed by generic and brand name were procured from patient notes and thorough clarification by the attending physician.

The descriptive and inferential analysis of the study was done using statistical tools such as frequencies, mean, standard deviation and percentage. Non-parametric variables were assessed using the chi-square. The data was analysed by excel office 2010. The p value of < 0.05 was considered significant.

RESULTS:

A total of 51 patients were enrolled in the study, among them 15 were females and 36 were males. Stroke was higher in the age group of 55-69 years (41.17%). Sociodemographic data showed that stroke was higher among those from an urban (58.82%) followed by rural (27.45%) and semi-urban background (13.72%). The demographic details of the patients are represented in table 1.

Table 1: Profile of patient demographics: age and sex distribution.

Sex/Age	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	Total
Female N	1	2	2	0	2	1	1	3	1	1	1	15
Male N	1	0	0	6	3	4	6	4	6	4	2	36

Weakness of the limbs was the most common presenting symptoms (80.39%) while the ocular symptoms was the least (11.76%). The details of presenting complaint is represented in table 2. Hypertension was the commonest risk factor followed by alcohol dependence, diabetes and tobacco use respectively. The percentage and corresponding number of patients with risk factor is represented in table 3.

Table 2: Details of presenting symptoms.

Symptoms	Female N (%)	Male N (%)	Total N (%)
Change in consciousness	4 (7.84%)	13(36.10%)	17(33.33%)
Speech difficulty	11(21.57%)	24(66.70%)	35(68.63%)
Weakness of limbs	14(27.45%)	27(75.00%)	41(80.39%)
Ocular symptoms	0(0%)	6(16.70%)	6(11.76%)
Vertigo	6(11.76%)	14(38.90%)	20(39.22%)
Sensory symptoms	5(9.80%)	7(19.40%)	12(23.53%)
Headache	10(19.61%)	11(30.60%)	21(41.18%)
Others	3(5.88%)	12(33.30%)	15(29.41%)

Table 3: Details on risk elements distribution.

Risk elements	Female N (%)	Male N (%)	Total N (%)
Hypertension	11(21.57%)	29(56.86%)	40(78.43%)
Diabetes Mellitus	6(11.76%)	19(37.25%)	25(49.02%)
Dyslipidemia	6(11.76%)	8(15.69%)	14(27.45%)
Transient ischemic attack	2(3.92%)	6(11.76%)	8(15.69%)
Ischemic heart disease	2(3.92%)	11(21.57%)	13(25.49%)
Angina	2(3.92%)	6(11.76%)	8(15.69%)
Peripheral vascular disease	1(1.96%)	1(1.96%)	2(3.92%)
Malaria	0(0%)	0(0%)	0(0%)
Migraine	0(0%)	0(0%)	0(0%)
Seizures	0(0%)	6(11.76%)	6(11.76%)
Sleep apnea	1(1.96%)	3(5.88%)	4(7.84%)
Fever in last 4 weeks	0(0%)	2(3.92%)	2(3.92%)
Past stroke	4(7.84%)	7(13.73%)	11(21.57%)
Tobacco	0(0%)	24(47.06%)	24(47.06%)
Alcohol	0(0%)	26(50.98%)	26(50.98%)
Oral contraceptive pills	3(5.88%)	0(0%)	3(5.88%)
Hormonal replacement therapy	1(1.96%)	0(0%)	1(1.96%)

All the patients underwent either CT or MRI for the diagnosis of stroke. CT and MR angiography was performed in 5(9.80%) and 12(23.53%) respectively. 37 patients underwent 2D echocardiography and 7 patients had cardiac monitoring. The incidence of ischaemic stroke was found to be 11(73.30%) in females and 32(88.90%) in males and the incidence of haemorrhagic stroke was found to be 5(33.30%) in females and 6(16.70%) in males. 17.6% of all patients in the current study were found to be using alternative medicine like Ayurveda and Unani in the past 6 months prior to stroke.

The detailed representation of utilisation of drugs and intervention received are shown in Table 4. Parenteral feeding, carotid stenting was not performed on any cases. Physiotherapy and speech therapy was provided in 20(39.22%) and 6(11.76%) respectively, but occupational therapy was not provided in any patients.

Table 4: Details on utilisation pattern of drugs and intervention.

Class of drugs and intervention	Female N (%)	Male N (%)	Total N (%)
Antiplatelet	10(19.61%)	30(58.82%)	40(78.43%)
Neuroprotective	1(1.96%)	3(5.88%)	4(7.84%)
Antibiotic	5(9.80%)	13(25.49%)	18(35.29%)
Osmotic	8(15.69%)	9(17.65%)	17(33.33%)
Low Molecular Weight Heparin	3(5.88%)	6(11.76%)	9(17.65%)
Oral Anti-coagulants	3(5.88%)	10(19.61%)	13(25.49%)
Calcium channel blocker	6(11.76%)	18(35.29%)	24(47.06%)
Beta blocker	4(7.84%)	7(13.73%)	11(21.57%)
ACEi/ARB	4(7.84%)	16(31.37%)	20(39.22%)
Diuretic	4(7.84%)	5(9.80%)	9(17.65%)

Statins	13(25.49%)	30(58.82%)	43(84.31%)
Oral hypoglycemic agents	0(0%)	6(11.76%)	6(11.76%)
Insulin	5(9.80%)	17(33.33%)	22(43.14%)
Nebulisation	1(1.96%)	0(0.00%)	1(1.96%)
Anti-depressants	0(0%)	5(9.80%)	5(9.80%)
Antiepileptic	3(5.88%)	8(15.69%)	11(21.57%)
Sedative	2(3.92%)	0(0%)	2(3.92%)
Anti-vertigo	1(1.96%)	1(1.96%)	2(3.92%)
Antiemetic	4(7.84%)	10(19.61%)	14(27.45%)
Analgesic	4(7.84%)	7(13.73%)	11(21.57%)
Nasogastric feeding	5(9.80%)	9(17.65%)	14(27.45%)
Physiotherapy	6(11.76%)	14(27.45%)	20(39.22%)
Speech therapy	2(3.92%)	4(7.84%)	6(11.76%)

DISCUSSION

The study evaluated patient characteristics and events surrounding stroke associated with drug utilization in adult patients diagnosed with stroke in a tertiary care centre in Bangalore, India. The mortality rate of stroke in India is 1.4 times that of tuberculosis and 22 times that of malaria.⁷ Drug utilization pattern is useful for identifying the pattern of drug use in the society so necessary protocols can be generated after analysing the merits and demerits.

Stroke can be divided into haemorrhagic and ischemic, including transient ischemic attack and silent stroke which usually go unnoticed. Ischemic variety contributes to 50-80% of stroke. However, few studies have reported even higher.^{8, 9, 10} In the present study, the incidence of ischemic, haemorrhagic and subarachnoid stroke was found to be 84.31%, 21.56% and 1.96% respectively.

The risk factors play a crucial role in the prevalence of stroke, which can be divided into modifiable and non-modifiable risk factors. The present study found that stroke was more common in men (70.59%) than women (29.41%) by 2.4 times and the incidence of haemorrhagic stroke was seen more commonly in women by nearly 2 times. A survey reported that male to female ratio of stroke was 1.7.¹¹ Similarly, study done in the Taiwan population revealed a male predominance in stroke with 63.39%.¹² This is attributed to protective effects of estrogen during reproductive life in women and the higher prevalence of uncontrolled hypertension, smoking and excessive consumption of alcohol in men compared to women.¹³

The strongest determinant factor for stroke is age.¹⁴ The present study showed a peak incidence of stroke between 55 to 69 years, made up of 41.17% of all stroke patients. The mean age for men and women was found to be 58.5 years and 51.1 years respectively. The incidence of stroke increases significantly with age and doubles every decade above 55 years as the duration of exposure to risk-factor increases. Wu et al. in his study showed that the 50-75 years age group made up 60.5% of all stroke patients. He also concluded that the mean age of stroke in men and women was 55.5 and 57.9 years respectively.¹⁵

Hypertension is one of the most important modifiable risk factors for stroke.¹⁶ The prevalence of hypertension in the present study was 78.43%. The risk of death due to stroke associated with hypertension increases with age.¹⁷ The Australian controlled therapeutic trial showed that there was a reduction in the incidence of TIA and stroke by 50% when treated with anti-hypertensives.¹⁸

Diabetes mellitus was present in 49.02% of stroke patients in present study. One-fourth of all strokes is attributed to diabetes. Patients suffering from diabetes with stroke have higher mortality rates along with poor prognosis and longer hospital stay.¹⁹ The risk of subsequent stroke increases by two times and risk of development of dementia increases by more than three times in diabetics compared to non-diabetics with stroke.^{20,21} The study by Gang Hu et al. and the Greater Cincinnati/Northern Kentucky Stroke Study concluded that risk of stroke independently increased with hypertension and diabetes but there was a drastic rise with the combination.^{22,23}

An 11-year prospective study on healthy women showed that there was a significant increase in risk of ischemic stroke associated with dyslipidemia.²⁴ In the present study, dyslipidemia was noted in 27.45%. The Asia Pacific Cohort Studies Collaboration concluded that for every 1mmol/L increase in total cholesterol there was a 25% increase in the risk of ischemic stroke.²⁵

Smoking and alcohol consumption was identified only in male patients

in the present study and accounted for 47.05% and 50.98% respectively. There is a significant increase in risk of stroke with passive and active smoking in both genders.²⁶ Smoking cessation in light smokers (<20 cigarettes/day) showed a significant and rapid decrease in the risk of stroke recurrence.²⁷ Alcohol contributes to hypertension, cardiac arrhythmias, platelet aggregation, activation of coagulation cascade and reduction of cerebral blood flow.²⁸ There is a decrease in risk with a small (20-40g/day) amount but risk increases with large amounts of alcohol intake suggesting a J-shaped relationship.^{29, 30, 31} There is a synergistic effect of hypertension and alcohol on stroke.³²

Use of oral contraceptives and hormone replacement therapy have shown to increase the risk of stroke. Stroke patients on HRT were found to have worse outcomes.^{33, 34, 35, 36} The prevalence of OCPs and HRT in women in the present study was 20% and 6.7% respectively.

Aggressive management of risk factors can slow the pace of the epidemic of stroke. Early recognition with history and physical examination followed by diagnosis using imaging tools can help decrease mortality as well as morbidity. In the present study, use of imaging modality (including CT and MRI) in the diagnosis of stroke was 100% while 33.33% of patients underwent both modalities. There is an association of cortical strokes and significant carotid artery stenosis warranting a carotid doppler ultrasound in every stroke patient.³⁷ Only 58.82% of patients underwent carotid doppler in the present study and 66.8% underwent either CT/MRI angiography.

Studies conducted previously in different populations have shown a wide disparity in medication use and adherence. It is difficult to decipher whether international recommendations are followed in Indian population. Prompt treatment in acute settings measures should be initiated as soon as the diagnosis is made. Any suspicion of stroke should be followed by CT scan, blood pressure and seizure control.

There has been no established primary treatment for acute haemorrhagic stroke. After securing airway, breathing and circulation, a non-contrast CT should be taken with door to CT time <20 minutes of emergency department arrival. Intubation is indicated in patients with severe respiratory distress or Glasgow coma scale ≤ 8 .³⁸ Nimodipine (calcium channel blocker) is found helpful in haemorrhagic stroke.³⁹ Reversal of coagulopathy with vitamin K and 3-factor/4-factor to be given when INR ≥ 1.4 on vitamin K antagonists. Mannitol or hypertonic saline or ventriculostomy should be done in case of brainstem herniation, decreased level of consciousness or mass effect.³⁸

Usage of thrombolytic agents (in-patient), antithrombotic and statins (at discharge) are recommended for ischemic stroke.⁴⁰ Only 3% of population receive thrombolytic agents⁴¹ There is proven benefit of thrombolytic therapy within 3 hours of symptom onset but a modest benefit is seen up until 4.5 hours with an improved clinical outcome.⁴² In the present study, none of the patients were treated with thrombolytic agents due to delay in hospitalization. Medical management for ischemic stroke includes blood pressure control, statins for dyslipidemia, antiplatelet therapy along with aspirin and reduction of raised intracranial pressure. In the present study, the use of antihypertensive drugs, statins and antiplatelets amounted to 78.43%, 84.31% and 78.43% respectively. 25.49% received two and 11.76% received three or more antihypertensive drugs. Secondary management including anticoagulation using warfarin and heparin, carotid endarterectomy (70-99% stenosis) and angioplasty can be pivotal in ischemic stroke.⁴³

India is experiencing a stroke epidemic like most low and middle income countries.⁴⁴ This could be due to lack of resources to combat stroke or uniformity in the drug prescribing pattern. Combinations of neuroprotective agents together have shown to lengthen the therapeutic time window, improve outcome and reduce the infarct volume.⁴⁵ Studies have shown to improve neurological outcomes with a combination of glutamate receptor antagonists and clenbuterol or muscimol.^{46,47}

Priority must also be given to prevent complications like DVT or seizures, prevent recurrence and mobilization of patients. Stroke survivors require a multidisciplinary approach to improve outcome. Depending on time of evaluation and diagnostic method. The incidence of DVT in immobilised patient secondary to stroke is 10-75%.⁴⁸ The present study was found to have an incidence of DVT of

3.9% as a post-stroke sequelae. The risk of death is around 15% for proximal DVT and most commonly due to pulmonary embolism.⁴⁹ Early initiation of low molecular weight heparin, physiotherapy and pressure stocking can greatly benefit the prognosis. Seizures secondary to stroke is estimated to be around 4% to 10%. It is more likely seen with haemorrhagic than ischemic stroke and cortical than subcortical strokes.

21.57% of patients with stroke had a recurrence in the present study. Cardiac embolism due to atrial fibrillation or other cardiac conditions and carotid atherosclerotic plaque can cause recurrence. It requires etiology specific management. Antiplatelets are the mainstay in prevention of secondary ischaemic stroke.⁵⁰

The burden of disability attributed to stroke is higher compared to other diseases.⁵¹ Rehabilitation should be initiated as soon as the patient is stabilised. A screening examination along with previous medical records and evaluation of mental status is needed to devise a patient-specific rehabilitation program. Only 39.21% of patients in the present study received physiotherapy, 11.76% received speech therapy and none received occupational therapy or psychotherapy. Physical rehabilitation should begin with exercises to improve range of motion and change of position in bed followed by increasing activity level. The American Heart Association has recommended aerobic training, resistance training and exercises for flexibility, coordination and balance in stroke survivors.⁵² Trials have shown an adequate improvement in strength and other activities when progressive resistance exercise was performed regularly for 1.5 to 3 months.⁵³

More than half the patients with stroke suffer from dysphagia which can cause aspiration.⁵⁴ Assessment of severity of dysphagia and techniques to facilitate swallowing or nasogastric tube should be planned. Speech rehabilitation targeting specific impairments correlates directly with the magnitude of improvement in aphasia.⁵⁵

Family support and education is vital. Bowel and bladder maintenance with the use of urinary catheters and diapers during acute care of stroke is important. Urinary catheters should be removed as soon as possible to prevent UTI. The prevention of fall, maintenance of nutrition, hydration, cleanliness and skin integrity is crucial. Due to long-term hospitalization and disability development of depression after stroke is common.⁵⁶ Identification and adequate treatment with counselling, encouragement, psychotherapy and pharmacotherapy is required.

Average number of drugs prescribed per patient in the present study was 7.72. 60.66% of all drugs prescribed was using brand names. It not only is expensive but can lead wrong prescription due to similarity in names and a potential ethical conflict arises. From the above analysis, middle and lower income countries need a systematic protocol to follow so as to improve the outcome.

CONCLUSION:

The study concludes that stroke increased with age. Hypertension was the commonest risk factor found in the present study. The use of neuroprotective agents was found to be very low and statins were the highest prescribed drugs. Prescription using brand name was highly prevalent. A minority of patients underwent rehabilitation and none underwent psychiatric counselling or assessment. There is a need for systematic protocol for physicians to follow in stroke management along with coordinated multidisciplinary approach with equal focus on physical rehabilitation and mental status assessment.

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