



STUDY OF PATTERN, ETIOLOGY, RISK FACTORS AND ITS OUTCOME ON DISCHARGE AND AFTER THREE MONTHS OF YOUNG STROKE IN A TERTIARY CARE HOSPITAL

General Medicine

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ABSTRACT

Background: Stroke is also the most common neurological disorder that leads to long-term disability and has enormous emotional and socioeconomic consequences in patients, their families and healthcare services. Stroke is a neurological injury that occurs when blood flow to the brain is disturbed, resulting in cell death and dysfunction in one or many parts of the brain. Stroke may result mainly from ischemia or hemorrhage. Another important aspect that differentiates the young stroke patients from the older ones is their social and vocational situation. They often have family to take care of, at the childbearing age, and their strokes often occur at a time of decisive career moves. Nevertheless, efficient acute treatment, rehabilitation, and stroke prevention can potentially lead to improved outcomes in individuals with young stroke. **Methods:** A prospective, descriptive and clinical study evaluated by detailed history, clinical examination and assessment of severity of stroke by National Institutes of Health Stroke Scale (NIHSS) Score was conducted in a tertiary care hospital. **Result:** Out of 76 stroke cases, 16 patients were less than 15 years. Among them 68.4% were males and 31.6% were females. All the 42 patients of Ischemic Stroke underwent extensive evaluation to determine the etiology. All of these patients presented Atrial Fibrillation with Rheumatic heart diseases. When the patients of hemorrhagic stroke underwent evaluation for etiology, the hypertension was the major cause in 32.3%(n=11) patients, followed by bleeding disorders in 23.5% of patients. **Conclusion:** There is an increase in the global prevalence and traditional risk factors of young stroke. Unfavourable behavioural patterns may cause and promote the development of well-documented risk factors.

KEYWORDS

Stroke in young, NIHSS, mRS, ischemic stroke, Hemorrhagic stroke.

INTRODUCTION

Stroke is the leading cause of disability in adults and second most common cause of death worldwide. About two-thirds of stroke patients belong to developing countries [1]. WHO defines stroke as an event caused by the interruption of the blood supply to the brain, usually because a blood vessel bursts or is blocked by a clot. It is also the most common neurological disorder leading to long-term disability and enormous emotional and socioeconomic consequences in patients, their families and healthcare services. Stroke burden has been rising in India as compared to the developed countries where it has reached plateau or decreased [2]. A greater proportion of strokes are due to subarachnoid hemorrhage and intracranial hemorrhage in young adults (40–55%) as compared to the general stroke population where cerebral infarction is most common [3]. Ischemic heart diseases and stroke are the world's biggest killers, accounting for a combined 15.2 million deaths in 2016. These diseases have remained the leading causes of death globally in the last 15 years [4]. Stroke occurs 15 years earlier and causes more deaths in people living in low and middle-income countries [5]. The lifetime risk of stroke after 55 years of age is 1 in 5 for women and 1 in 6 for men [6]. Despite its enormous impact on countries socio-economic development, this growing crisis has received very little attention to date.

The two main types of stroke include ischemic, due to lack of arterial blood flow to the brain, and hemorrhagic resulting from bleeding from a ruptured cerebral artery. Stroke may also occur in children, and its causes may be different from that in young adults and in individuals older than 65 years.

The average annual incidence rate of stroke in India currently is 145 per 100,000 population, which is higher than the western nations. But there is no strong evidence indicating higher incidence of stroke in young patients in India as compared to other countries. Age-specific incidence rates from recent population-based studies from India are comparable to the western populations [7]. As far as stroke in pediatric age group is considered, the etiology and outcome of pediatric stroke

differs in different geographical regions. The annual incidence of pediatric stroke is reported to range between 1.1 and 3.13/100,000 from the developed countries. The etiology of pediatric stroke depends on several factors such as prevalence of infection, malnutrition, genetic predisposition and health infrastructure. The non-specific clinical presentation, variable risk factors and pathogenesis leads to diagnostic uncertainty and management dilemmas in pediatric strokes, so stroke is under-recognized in children leading to marked delays in diagnosis. In the Asian countries, there is paucity of epidemiological data on pediatric stroke. Hospital based studies from Japan, Argentina, Hong Kong, Turkey, India, Thailand, China, Pakistan and Kenya have reported variable incidence of stroke and differing etiologies [8-15].

The young stroke patients have a different profile of risk factors and etiology as compared to older stroke patients. Common risk factors among young stroke patients include pregnancy and the postpartum period, genetic factors, migraine, illicit drug use, and patent foramen ovale. However, risk factors and causes that are commonly associated with older onset stroke can be present at younger ages as well.

Another important aspect that differentiates the young stroke patients from the older ones is their social and vocational situation. Although the chances of surviving a stroke at a young age is much better than when it occurs at an older age, they still have to face an increased risk of recurrent strokes for years after the first event. Nevertheless, efficient acute treatment, rehabilitation, and stroke prevention can potentially lead to improved outcomes in individuals with young stroke.

MATERIALS AND METHODS

A prospective, descriptive and clinical study was carried out in the tertiary care center of North India from July 2021 to June 2022 after approval from the Institutional Ethical Committee. A total of 76 patients in the age group of 15 to 45 years with acute stroke were enrolled in this study. Patients with subdural hemorrhage, head injury and Intra-cranial space occupying lesion (ICSOL) were excluded from the study.

All the enrolled patients were evaluated by detailed history, clinical examination and assessment of severity of stroke by National Institutes of Health Stroke Scale (NIHSS) Score. The detailed clinical history included all the symptoms pertaining to stroke with emphasis on all the risk factors attributable to stroke in young like smoking, alcohol consumption, diabetes, hypertension, obesity, dyslipidemia, previous history of stroke and valvular heart disease. The detailed clinical examination was conducted to identify the neurological deficits. Ischemic stroke and hemorrhagic stroke were defined by neurological examination and computed tomography (CT) of the brain. All the admitted patients were subjected to hematological investigations (Complete blood counts, kidney and liver function tests, prothrombin time, lipid profile, blood glucose), imaging of brain (CT, MRI), ECG and echocardiography at admission.

Other investigations like doppler of carotid vessels, angiography and venography of cerebral vasculature, serum homocysteine, Protein C and S, Antithrombin-III, antinuclear and other autoantibodies were done during the course of hospitalization to look for specific etiology of the acute stroke.

The patients were followed up during their hospital stay and three months after the discharge from the hospital. Disability at the time of discharge and after three months was determined by the Modified Rankin Scale (mRS) (Table 1). Modified Rankin Scale Score ≤ 2 was considered a better outcome.

Table 1: Modified Rankin Scale

Score	Description
0	No symptoms.
1	No significant disability. Able to carry out all usual activities, despite some symptoms.
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
3	Moderate disability. Require some help, but able to walk unassisted.
4	Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
6	Dead

RESULTS:-

A total of 76 patients admitted with stroke (aged between 15 to 45 years) between 2021 to 2022 were enrolled for the study. The mean age observed in the study 25.8 with the standard deviation of 13.3 years. Among them 52 (68.4%) were males and 24 (31.6%) were females. Ischemic stroke accounted for 42 patients. Smoking 22 (28.9%), alcohol consumption 21 (27.6%), hypertension 17 (22.6%) and Hyperhomocysteinemia 16 (21.1%) were more prevalent risk factors identified in this study. Other risk factors include Dyslipidemia 14.5%, diabetes mellitus 5.3% and Rheumatic heart disease 9.2% in their decreasing order of prevalence. (Table 2)

Table-2: Risk factors according to stroke subtype

Risk Factor	Total (n=76)	Ischemic Stroke (n=42)	Hemorrhagic Stroke (n=34)	P-Value	Odds Ratio (OR)
Type-2 Diabetes Mellitus	4 (5.3%)	4 (9.5%)	0	0.999	0.000
Hypertension	17 (22.4%)	4 (9.5%)	13 (38.2%)	0.005	5.881
Rheumatic Heart Disease	7 (9.2%)	6 (14.3%)	1 (2.9%)	0.123	0.182
Dyslipidemia	11 (14.5%)	6 (14.3%)	5 (14.7%)	0.959	1.034
CKD	3 (3.9%)	0	3 (8.8%)	0.999	0.000
Obesity	14 (18.4%)	6 (14.3%)	8 (23.5%)	0.305	1.846
Family History of Stroke	15 (19.7%)	9 (21.4%)	6 (17.6%)	0.681	0.786
Smoking	22 (28.9%)	13 (31.0%)	9 (26.5%)	0.669	0.803
Alcohol	21 (27.6%)	11 (26.2%)	10 (29.4%)	0.755	1.174

Hyperhomocysteinemia	16 (21.1%)	9 (21.4%)	7 (20.6%)	0.929	0.951
Pregnancy Related	3 (3.9%)	2 (4.8%)	1 (2.9%)	0.688	0.606

We subclassified ischemic stroke and Hemorrhagic stroke in the study population by using the NIHSS Score. All the 42 patients of Ischemic Stroke underwent extensive evaluation to determine the etiology. According to TOAST Classification, 23 patients (54.7%) were categorized other "Other determined etiology" which included vasculitic infarcts (n=8), prothrombotic states (n=9), Systemic Lupus Erythematosus (n=1), Pregnancy related (n=2), Moya-Moya Disease (n=1) and Infections/encephalitis (n=2). No etiology could be identified in 3 patients (7.1%) of Ischemic Stroke. Cardioembolic stroke was seen in 5 patients (11.9%). All of these patients presented Atrial Fibrillation with Rheumatic heart diseases. (Table 3)

Table-3: Etiology of Ischemic Stroke according to TOAST classification

Causes	No. of Ischemic Patients (n=42)	Percentage
Large Vessel Atherosclerosis (LAA)	4	9.5
Cardioembolism (CE)	5	11.9
Small Vessel Occlusion (SVO)	7	16.6
Other determined etiology (ODE)	23	54.7
Vasculitic Infarcts		
Tuberculous Meningitis	7	16.6
Takayasu Arteritis	1	2.3
Systemic Lupus Erythematosus	1	2.3
Pregnancy related	2	4.6
Prothrombotic states		
Protein-C deficiency	1	2.3
Protein-S deficiency	2	4.6
Hyperhomocysteinemia	4	9.2
Antiphospholipid Antibody Syndrome	2	4.6
Moya-Moya disease	1	2.3
Infections/Encephalitis	2	4.6
Stroke of Undetermined etiology (UD)	3	7.1

When the patients of hemorrhagic stroke underwent evaluation for etiology, the hypertension was the major cause in 32.3% (n=11) patients, followed by bleeding disorders in 23.5% of Patients. (Table 4)

Table-4: Etiology of Hemorrhagic stroke patients in the study

Causes	No. of Hemorrhagic Stroke Patients (n=34)	Percentage
Hypertension	11	32.3
Bleeding Disorders	8	23.5
A-V Malformations	3	8.8
Cortical vein thrombosis	2	5.8
Anticoagulants use	1	2.9
Cavernous Angioma	1	2.9
Others	4	11.7
Vasculitis	1	
Sepsis/ Meningoencephalitis	3	
Cryptogenic	4	11.7

In patients with ischemic stroke, 36 (85.7%) patients improved during the course of hospitalization and six patients expired. These 36 patients were followed up to three months regarding their functional outcome. Majority of them (30 patients) revealed improvement in the functional status according to mRS score and three patients expired. So, at the end of three months after discharge from the hospital, nine patients (21.4%) had expired out of 42 patients of Ischemic stroke in our study (Table 5).

Table-5: Functional outcome in ischemic stroke patients according to modified Rankin Scale (mRS) score

mRS Score	No. of Patients (n=42)		
	At Admission	At Discharge	After 3 months
0-2 (Good outcome)	6	21	30
3-5 (Poor outcome)	36	15	3
6 (Dead)	0	6	9

As far as the patients with hemorrhagic stroke (n=34) are concerned, 21 (61.8%) patients improved during the hospital stay and 13 (38.2%) patients expired. Among the patients who had expired, the majority of patients (53.8%) had uncontrolled hypertension at presentation. The discharged patients (n=21) were followed up to three months regarding assessment of functional outcome and it revealed that 16 (47.0%) patients had improved functional outcome and four more patients expired during this period. Thus, the total patients of hemorrhagic stroke that expired at the end of the three months were 17 (50%) (Table 6).

Table-6: Functional outcome according to Modified Rankin Scale Score among Hemorrhagic Stroke Patients

mRS Score	No. of Patients (n=34)		
	At	At Discharge	After 3 months
0-2 (Good outcome)	2	12	16
3-5 (Poor outcome)	32	9	1
6 (Dead)	0	13	17

When the combined data regarding outcome of both the ischemic and hemorrhagic stroke is taken into consideration, it reveals that 57 patients (75%) improved and were discharged and 19 patients (25%) expired. When the discharged patients were followed up to three months, 7 more patients expired during that period. At the end of three months, out of 76 patients, 50 patients (65.8%) improved and 26 patients (34.2%) expired.

An association was derived between NIHSS Score at admission and the outcome of patients at the time of discharge from the hospital. It revealed that mortality was higher in patients (71.4%) who were classified as "Severe Stroke" based on NIHSS Score at presentation and statistical analysis revealed it as highly significant (P-value 0.0001) (Table 7).

Table-7: Association between NIHSS Score and Outcome of Patients at Discharge

NIHSS Score	Stroke severity	Improved & discharged	Expired	P-value
0-4 (n=4)	Minor Stroke	4 (100.0)	0	
5-15 (n=37)	Moderate Stroke	36 (97.3%)	1 (2.7%)	
16-20 (n=14)	Moderate to Severe Stroke	11 (78.6%)	3 (21.4%)	
21-42 (n=21)	Severe Stroke	6 (28.6%)	15 (71.4%)	0.0001

A one-way repeated measure analysis of variance (ANOVA) was conducted to evaluate the null hypothesis that there is no change in participants' mRS score when measured at the time of admission, discharge and after three months of discharge in the patient group (n=76). The results of ANOVA indicated a significant time effect (Wilk's Lambda = 0.122, F (2, 94) = 266.42, P<0.01) which led to the rejection of the null hypothesis. Follow up comparisons indicated that each pairwise difference was statistically significant (P-value <0.01). Hence, there was significant decrease in mRS scores (MRSS) over time, suggesting that the treatment improved the functional outcome of the admitted patients.

DISCUSSION

In India, the prevalence of young stroke has been showing an increasing trend. Stroke in young adults is becoming a rising concern with the increase in vulnerability to traditional risk factors and changing lifestyles. Several studies have been conducted to analyze the risk and etiological factors of stroke in young, but considering its impact on younger generation, more studies are needed for identification and modification of risk factors. Stroke grows

exponentially from 30 years of age, and etiology varies with age [16,17]. Although two-thirds of strokes occur in those over the age of 65, it is observed now that the prevalence is becoming high among younger age group and low socioeconomic status [18]. Diabetes and dyslipidemia are found to have a very low association with the stroke among young individuals. In this study, in concordance with the other reviews in India, the stroke was predominant among males (52 out of 76) with the mean age observed was 15-45 years. With increasing age, there was an increase in mRS scores after 3 months, which was correlated with the persistence of disability even after 3 months.

The mean age of the patients enrolled in our study was 25.8±13.3 years with male predominance (males 68.4% and male to female ratio was 2.16). This was in concordance with Chandrashekhar et al. [19] where the mean age of the patients was 31.3 years and majority being males (64%) as compared to females (36%).

Out of 76 patients enrolled in our study, ischemic stroke was more common as compared to hemorrhagic stroke. 42 patients (55.3%) had ischemic stroke as compared to hemorrhagic stroke which was diagnosed in 34 patients (44.7%). This was in concordance with Hussain M et al. [20] in which cerebral infarction was present in 50.66% of patients.

In our study, etiology couldn't determine (Cryptogenic Stroke) in 7 out of 76 patients (9.2%). Previous published literature [21] has reported the incidence of cryptogenic stroke ranging from 25-40%. Due to increase in advanced diagnostic tools, the incidence of cryptogenic stroke is declining for the past few years.

If the outcome of ischemic stroke (n=42) is analysed separately, the mortality at time of discharge is 14.3% (6 patients), which is quite high as compared to study done on ischemic stroke subjects by Karri, Madhavi et al having mortality of 0.02% [22]. At the time of discharge in our study, 21 patients (50%) had good outcome (mRS Score 0-2) and other 50% had poor outcome (mRS Score 3-6). After 3 months of discharge, 3 more patients expired of ischemic stroke and 30 patients (71.4%) had good outcome (MRS 0-2).

As far as outcome in patients with hemorrhagic stroke (n=34) in our study is concerned, mortality was higher (38.2%) as compared to ischemic stroke (14.3%). This is in contrast with the study by Ruiz-Sandoval et al in which mortality was 8% [23]. On mRS, 12 patients (35.3%) had good outcomes while 22 patients (64.7%) had poor outcomes. After 3 months follow up, 4 more patients expired and 47% had good outcomes (mRS Score 0-2).

The association between NIHSS Score and outcome in young stroke was analyzed statistically and it revealed significantly that mortality was higher in patients (71.4%) who were classified as "Severe Stroke" based on NIHSS Score at presentation to the hospital. (P-value 0.000, highly significant). It is in concordance with study conducted by Fonarow GC et al [24].

When the trend of mRS was analysed over 3 months using analysis of variance (ANOVA), it revealed that there was a significant decrease in MRS Scores over time, suggesting that the treatment decreases the MRS Score of stroke patients.

CONCLUSION

Although there is an increase in the global prevalence of young stroke, we had a low prevalence rate, and hence low mortality was observed. Preventive measures could aid immensely in bringing down costs and emotional burden on the family. Stroke in young requires a different approach to investigate and treat. This is due to the different underlying etiology as compared to elders. Although traditional risk factors, such as hypertension, diabetes, and smoking, are associated with stroke in both elderly and young, our study shows that other modifiable risk factors such as alcohol consumption were also prevalent. Unfavorable behavioral patterns may cause and promote the development of well-documented risk factors. There is a need for population-based studies of stroke in young, which will provide information on underlying etiology and incidence rates, in different populations.

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