ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at: www.ijmacr.com

Volume – 4, Issue – 6, November – December - 2021, Page No. : 314 – 320

Risk factors for small and large artery ischemic stroke – A comparative study

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How to citation this article: Vatsal Himanshu, Soni Deep K, Rawal Divyant, Kumar Sunil, Grover Ankit, Johri Sharat, "Risk factors for small and large artery ischemic stroke – A comparative study", IJMACR- November – December - 2021, Vol – 4, Issue - 6, P. No. 314 – 320.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: The prevalence of Ischemic stroke in India demonstrates a massive variation of 147-922/100,000 through different community-based studies. According to the Indian ischemic stroke factsheet updated in year 2012, the projected age-adjusted frequency rate for the stroke fluctuated between 84/100,000 and 262/100,000 in rural area and between 334/100,000 and 424/100,000 in urban areas. Stroke is classified mainly into 2 categories, ischemic (80%-85% cases) and hemorrhagic (15%- 20% cases). Ischemic stroke was further classified and the most collective stroke subtype was the intracranial LAA, accounting for 29.4%. Risk factors profile revealed different arrangements of correlation with the subtypes. Therefore, current study was planned to the identify risk factors of ischemic strokes and their correlation with major subtypes.

Material And Methods: Cross sectional, hospital based, observational study involving 84 adult patients with acute ischemic stroke. Data were collected by face-to-face interviews, physical and neurologic examinations performed by neurologists using preformed, pretested questionnaires. Vital statistics and relevant lab investigations were carried out and noted in the patients proforma.

Results: 54.8% patients were found to be having Large Artery Atherosclerosis (LAA). Male predominance in ischaemic stroke but no correlation was found between age/ sex and subtypes of ischemic stroke. LAA patient had mean HbA1c of 9.3±3.7% while SAA had mean of 6.9±3.8%. Increased total

cholesterol levels were seen in 37.3%, Hypertriglyceridemia 58.2%, Increased LDL levels in 51.8% patients. 78.9% of patient with SAA had Hypertension as its risk factor. 73.9% of LAA had hypertension as its risk factor. 76.08% patient of LAA had dyslipidemia as its risk factor. 32.6% patient of LAA had diabetes as its risk factor while 39.5% of the patient of SAA had diabetes as its risk factor. On statistical analysis the correlation found between different subtypes and risk factor came out to be insignificant.

Conclusion: This study was done to identify importance of various risk factor in different subtypes of ischemic stroke. Majority patients had Large Artery Atherosclerosis (LAA). Hypertension, Dyslipidemia and Diabetes Mellitus and Smoking were important modifiable risk factors for all subtypes of ischemic stroke but no statistical relationship between the various risk factors and different subtypes of ischemic stroke. Larger cohort is required to validate the above observation.

Keywords: Ischemic stroke, large artery atherosclerosis, Small artery atherosclerosis, risk factors.

Introduction

WHO defines stroke as a clinical syndrome characterized by rapidly developing clinical symptoms and/or signs of focal and at times global loss of cerebral function, with symptoms lasting for more than 24 hours or leading to death, with no apparent cause other than that of vascular origin.[1] The prevalence of Ischemic stroke in India demonstrates a massive variation of 147-922/100,000 through different community-based studies.[2,3] According to the Indian ischemic stroke factsheet updated in year 2012, the projected age-adjusted frequency rate for the stroke fluctuated between 84/100,000 and 262/100,000 in rural area and between 334/100,000 and 424/100,000 in urban areas.[4] Stroke is classified mainly into 2 categories, Ischemic (80%-85% cases) and Hemorrhagic (15%-20% cases).[5] Ischemic stroke was classified further into 5 categories, Large-artery atherosclerosis (LAA)/macro-angiopathic, Small-vessel occlusion (SVO)/micro-angiopathic, Cardio-embolism (CE), stroke of other determined etiology and undetermined etiology. The specific feature was that the most collective stroke subtype was the intracranial LAA, accounting for 29.4% of the ischemic strokes. Risk factors profile revealed different arrangements of correlation with the subtypes: hyperlipidemia was powerfully associated with LAA and IHD with cardio-embolic strokes. The strongest relationship of HTN was with the SVO, and DM associated with both the SVO and LAA dependable with dominant reports.[6] Similarly, smoking and chronic alcoholism were additional frequently related with the extra-cranial LAA. Patients with LAA and CE also had a higher frequency of a prior stroke compared to SVO.

There are limited studies on stroke subtypes in India because smost health centers lack facilities for magnetic resonance imaging (MRI) and neck vessel Doppler scan. Often, if the facilities are available, the same are unaffordable. However, knowledge derived from clinical studies can help prevent the burden of stroke by means of risk factor modification. As such, current study was planned to identify risk factors of ischemic strokes and their correlation with major subtypes.

Material And Methods

This cross sectional, hospital based, observational study was performed in Department of General Medicine, at SRMS - IMS Bareilly, Uttar Pradesh from

January 2018 to April 2019. All adult patients with acute ischemic stroke (radiologically proven cerebral infarction) were included in the study after taking a written informed consentfrom the patient (if conscious) or a surrogate attendant (if unconscious). A total of 120 patients were screened, 36 were rejected based on inclusion/exclusion criteria and 84 patients were enrolled in the study.

Data were collected by face-to-face interviews; physical and neurologic examinations performed by neurologists using preformed, pretested questionnaires.

Large-artery atherosclerosis was labelled in patients having clinical and brain imaging findings of either significant (>50%) stenosis or occlusion of a major brain artery or branch of cortical artery, presumably due to atherosclerosis. Small-artery occlusion (lacunae) category included patients with lacunar infarcts where CT/MRI examination shows relevant brain stem or sub cortical hemispheric lesion with a diameter of less than 1.5 cm.

Vital statistics and relevant lab investigations were carried out and noted in the patients proforma.

Data were entered using Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS) version 23 for Windows. Data were summarized using means and percentages, and appropriate statistical tests used where applicable. Statistical significance was defined as two-tailed p-value <0.05.

Results

Table 1: Age distribution of the Study population

Age	SEX				Total	
	F		M			
	n	%	n	%	n	%
≤ 50	6	17.1	9	18.4	15	17.9
51 - 65	22	62.9	17	34.7	39	46.4
66 - 80	6	17.1	21	42.9	27	32.1
> 80	1	2.9	2	4.1	3	3.6
Total	35	100.0	49	100.0	84	100.0

Table 1 shows the distribution of studied patients on the basis their age and sex where the majority of patients were of age ranging 51 years to 65 years (46.4%) followed by 66 years to 80 years (32.1%) while the least were of age greater than 80years (3.6%). Most of our study subjects were males (54.8%).

Figure No. 1 shows the frequency of Ischemic Stroke subtype in the studied patient. 46 (54.8%) patients were Large Artery Atherosclerosis (LAA), followed by Small Artery Atherosclerosis (SAA) 38 (45.2%).

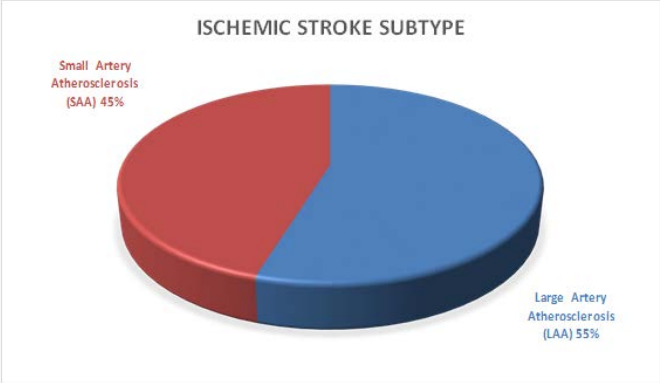

Figure 1: Ischemic Stroke subtype

Table 2: Non modifiable risk factors of ischemic stroke

Ischemic Subtypes		LAA (46)	SAA (38)	p-value
Age	Mean ± SD	61.28±11.9	62.5±12.5	0.6488
	≤40 years	5 (10.9%)	1 (2.6%)	0.1445
	>40years	41 (89.11%)	37 (97.4%)	
Sex	Male	30 (65.2%)	20 (52.6%)	0.2421
	Female	16 (34.8%)	18 (47.4%)	

Table 2 shows non modifiable risk factors of age and gender in correlation with different subtype of ischemic stroke. On statistical analysis there was no correlation found between age or gender and subtypes of ischemic stroke.

Table 3 shows the mean of the hemodynamic parameters of the patient at the time of presentation of stroke. The mean systolic blood pressure was 169.30±29.15 and 139.20±09.65 for LAA and SAA respectively while the mean diastolic blood pressure was 90.24±10.66 and 84.24±9.79 for LAA and SAA

respectively. The differences in mean were statistically significant with p-values 0.0001 and 0.0093 forSBP and DBP respectively indicating higher SBP and DBP in patients with LAA.

Table 3: Blood pressure at the time of presentation of stroke.

Blood Pressure	LAA N=46	SAA N=38	p-value
Systolic Blood pressure (mmHg)	169.30±29.15	139.20±09.65	0.0001
Diastolic Blood Pressure (mmHg)	90.24±10.66	84.24±9.79	0.0093

Table 4 shows the HbA1c level of recruited patients**.** 5.74±1.79 was the mean withrange of 4-14.2%. LAA patient had mean of 9.3±3.7% while SAA had mean of 6.9±3.8%. This difference in mean was found to be statistically significant with p- values 0.0045 thereby emphasizing on higher mean HBA1C in LAA.

Table 4: HBA1C distribution among stroke subtypes

HbA1C	Mean ± SD (Range) n=84	LAA n=46	SAA N=38	p-value
HbA1c (%)	5.74 ± 1.79 (4-14.2)	9.3 ± 3.7	6.9 ± 3.8	0.0045

Table 5 shows the lipid profile values in different subtypes of ischemic stroke. Total number of cases for Hypercholesterolemia was 37 of which 67.57% patient were having LAA. Total number of cases for hypertriglyceridemia were 56 and out of which 29(51.79%) were having LAA and 27(48.21%) patients had SAA. Low HDL patients were 53 in number of which 35(66.04%) cases were of LAA. High LDL patients were 41 out of which 27(65.85%) cases were of LAA. Differences in proportions were found to be statistically significant for hypercholesterolemia, low HDL and high LDL with p-values 0.0364, 0.0066 and 0.0461 respectively.

Table 5: Relation of different subtypes of strokes with lipid profile

	LAA (n=46)	SAA (n=38)	p-value
Hypercholesterolemia (n=37)	25(67.57%)	12(32.43%)	0.0364
Hypertriglyceridemia(n=56)	29(51.79%)	27(48.21%)	0.4381
Low HDL(n=53)	35(66.04%)	18(33.96%)	0.0066
High LDL(n=41)	27(65.85%)	14(34.15%)	0.0461

Table 6 shows the association of risk factors with Subtypes of Ischemic stroke. 78.9% of patient with SAA had Hypertension as its risk factor. 73.9% of LAA had hypertension as its risk factor. 76.08% patient of LAA had dyslipidemia as its risk factor. 32.6% patient of LAA had diabetes as its risk factor while 39.5% of the patient of SAA had diabetes as its risk factor. On statistical analysis the correlation found between different subtypes and risk factor came out to be insignificant.

Table 6: Risk Factors in Subtypes of Ischemic Stroke

	LAA (n=46)	SAA (n=38)	p-value
HTN	34 (73.9%)	30(78.9%)	0.5896
DM	15 (32.6%)	15(39.5%)	0.5135
Smoker	16 (34.7%)	17(44.7%)	0.3526
Dyslipidemia	35(76.0%)	24(63.1%)	0.1971
CAD	0 (0.0%)	3(7.8%)	0.0885
TIA	2(4.34%)	3(7.8%)	0.6543
Alcoholic	5(10.8%)	6(15.7%)	0.5342

Discussion

Stroke is one of the leading causes of death and disability in India. Accurate classification of ischemic stroke subtype and their risk factor is critical for guiding treatment decisions and prevention. The current study focuses on the risk factors associated with strokes subtypes. Stroke is the main cause of adult disability and the second most leading cause of death worldwide.7 It is widely known that incidence, prevalence and mortality of the stroke vary widely in different populations. Studies such as the World Health Organization's Monitoring of trends and determinants of cardiovascular disease project have

shown that relative to Caucasians, Asians have the higher prevalence of stroke.[8]

The present study "Risk factors for small and large artery ischemic stroke – A comparative study" was a prospective cross-sectional study of the patients of ischemic stroke admitted in SRMS – IMS a tertiary care center in Rohilkhand region, Bareilly, India from 1st January 2018 to 30th April 2019. Similar types of studies were performed by Manorenj S et al[9], Raghuvanshi S[10] and Tan KS et al[11].

In our study, the studied patients were distributed on the basis of age where the majority of patients were of age ranging from 51 years to 65 years (46.4%) followed by 66 years to 80 years (32.1%) while the least were of age greater than 80 years (3.6%). The mean age of the studied patients was 62.21±11.29 years. Our study was in accordance with Manorenj S et al[9] who has reported the mean age as 53.9±12.3 years, Renjen PN et al[8] has depicted the mean age at the time of stroke was 57.1 years, Chung JW et al[19] mean age as 67.3±12.5years.

This indicates that the prevalence of stroke is generally takes place in older age that is in 5th to 7th decade of human life. In our study the majority of patients were found to be male 49 (54.8%) followed by Female 35 (45.2%). Manorenj S et al[9] reported 65.4% males and 34.6% females in their study and the male to female ratio was 1.8: 1 which was similar to the present study. Renjen PN et al8 reported 67.6% were male and 32.4% were female. Also Raghuvanshi S10 depicted 74.28% males and 25.71% females in his study.

This shows that male sex is considered as an important risk factor for stroke. In our study the majority of the patients were Large Artery Atherosclerosis (LAA) (54.8%), followed by Small Artery Atherosclerosis (SAA) (45.2%). Our findings were in accordance with the studies performed by Manorenj S et al[9] who reported Large Artery Atherosclerosis (LAA) (46.4%) was highest (Extracranial: 41.1%, intracranial: 36.9%), followed by SVO (32.4%). Etiology of index acute ischemic stroke reported by Raghuvanshi S[10] that maximum numbers of patients, i.e., 72 cases (41.1%) had large vessel atherothrombotic disease, 27 cases (15.4%) had small vessel disease (lacunar infarcts).

Our findings were consistent with the available Indian data of ischemic stroke subtypes.[12] A hospital-based registry of Southern India has attributed 41% of strokes to large artery atherosclerosis and 18% to lacunar causes. In this study, age and gender with different subtype of ischemic strokes were analyzed. However, there was no significant statistical relation between age, gender and propensity to have a specific subtype of stroke. The study by Manorenj S et al[9] shows that there was significant association between SVO and gender (P value of 0.003 with odds ratio of 3.20); men were more likely than women. Wu et al[20] and Tan SK et al[11] reported similar findings as in the present study and found no statistical relation among age and stroke classification.

In the very old patient group, LAA was the common stroke subtype in a study in Spain.[13] . Zafar A et al[21] reported hypertension to be more frequent in SVO (84%) than LAA (78%), similar to what Yaqub et al14 reported in their study, i.e., the percentage of hypertension was 81% in patients with lacunar infarction; however, this finding is not in accordance to other studies.[15,16] Diabetes mellitus has been reported to be more closely associated with small

vessel disease than with the other subtypes. No statistically significant difference could be identified in the prevalence of dyslipidemia across IS subtypes. There was no significant association of the mean levels of Cholesterol with the different subtypes of ischemic stroke.

The role of dyslipidemia in the pathogenesis is less certain in cerebrovascular disease than for CAD; more consistent association has been noted with low high-density lipoprotein (HDL) cholesterol and high total cholesterol to HDL cholesterol ratio than with total cholesterol, low-density lipoprotein cholesterol and triglycerides.17 Yuan BB et al18 found that LDL-C and TC levels may be independent predictors for the occurrence of large-artery atherosclerotic stroke.

Conclusion

This study was done to identify importance of various risk factors in different subtypes of ischemic stroke. Hypertension, Dyslipidemia and Diabetes Mellitus and Smoking were important modifiable risk factors for all subtypes of ischemic stroke. There was no statistical relationship between the various risk factors and different subtypes of ischemic stroke. Larger cohort is required to validate the above observation.

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