

An observational study of clinico-etiological profile of stroke in young and elderly patients in P. R. M. Medical College and hospital, Baripada, Odisha

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Abstract

Background: The cerebrovascular stroke is one of the leading causes of morbidity & mortality in adult life. Indian studies have shown a stroke prevalence of 471.58/100000 population. Stroke mostly occurs in elderly people. Risk factors for stroke differ between young and elderly patients. The aim was to study the clinical presentation, risk factors, types, topography as per CT scan findings in ≤ 45 years and > 45 years patients from PRM medical college and hospital, Baripada. **Methods:** This is a retrospective study of all new patients managed for stroke in the medical ward of PRM medical college and hospital, Baripada, from June, 2018 to January, 2019. **Results:** Incidence of stroke in elderly (≥ 45 years) was than young (< 45 years) patients with male predominance in both the groups. Most common clinical presentation from both age groups was hemiplegia (84.88% in young vs. 84.69% in elderly). Common risk factors in were HT and dyslipidemia in both the groups. Most common type of stroke in both age groups was Hemorrhagic (65.66% in young vs. 51.02% in elderly), followed by ischemic. Common sites of hemorrhage in young and elderly were basal ganglia and ventricular. Most common infarction site in both age groups is MCA territory. **Conclusion:** The cerebrovascular stroke was more in elderly with hypertension and dyslipidemia. The most common type of stroke was haemorrhagic.

Keywords: Cerebrovascular stroke, Ischemic stroke, Young, Elderly

Date of Submission: 03-07-2019

ate of acceptance: 18-07-2019

I. Introduction

Stroke is a devastating and disabling cerebrovascular disease with significant amount of residual deficit leading on to economic loss. It has been defined as a rapidly developing signs of focal (or global) disturbance of cerebral function with symptoms lasting for ≥ 24 hours, or leading to death with no apparent cause other than vascular origin. [1] It is a collection of clinical syndromes resulting from cerebral ischemia to intracranial hemorrhage. In the west, it is the 3rd most common cause of morbidity and mortality. [2]

Some of the recent studies have elucidated the stroke pattern to considerable extent in our country with a prevalence rate of 471.58/100000 population. [3] Recent study identified that 7% of medical and 45% of neurological admissions were due to stroke with a fatality rate of 9% at hospital discharge and 20% at 28 days. [4]

In a recent study conducted in India, Latin-America and China, chronic diseases as a whole (stroke, heart disease, diabetes, chronic respiratory disease, and malignancy) accounted for the majority of death among the elderly. [5] Individual Indian studies have estimated that the prevalence rates increases from 0.1-0.3/1000 in the < 45 year age group to 12-20/1000 in the 75-84 year age group. [6] In India stroke in younger people is high (18-32% of all stroke cases) compared to high income countries. [7] Men are more likely to have a stroke than women: the male/female sex ratio for India is 7:1. [8] This may be due to differences in risk factors such as smoking and drinking which are more prevalent among men in India compared with women. [9]

In a recent study conducted in Gujarat, it was found that modifiable risk factors such as hypertension (40%), alcoholism (35%), smoking (28%) and hyperlipidemia (17%) are the commonest cause of stroke among the elderly; and smoking, alcoholism, increased BMI, diabetes and hypertension are significantly associated

with strokes among young people. [10] By 2050, the global number of old people (aged ≥ 65 years) will exceed the number of young people (aged < 65 years) for the first time since formal records began. [11]

This growth in the aged population, together with the influence of aging on stroke, suggests that the incidence and economic cost of this disease will rise. [12] One report estimates that the global occurrence of first-ever strokes will increase to 18 million by 2015, and to 23 million by 2030. [13] Moreover, this study estimates that the death toll from stroke will reach 6.5 million per year by 2015 and 7.8 million per year by 2030. [13]

Despite many studies prevail regarding stroke, still this major illness remain widely prevalent. Hence this study was undertaken to delineate the various aspects of stroke in our setup which shall be of immense use to the physicians who are required to manage the patients disabled by stroke. This study was conducted on acute cerebrovascular accidents (CVA) patients admitted to the Institute of Internal Medicine, Rajiv Gandhi Government General Hospital, Chennai, to assess and analyze the epidemiological, clinical and risk factor profile of these stroke victims with particular reference to < 45 years (young stroke) and > 45 years age groups.

II. Methods

This is a observational study of 589 cases managed for stroke in the medicine ward of PRM medical college and hospital Baripada, Odisha from June, 2018 to January, 2019. The relevant data were extracted from the case sheets of the admitted patients and analyzed. We have only CT scan machine in house, for MRI we have to send pts to higher centers. We divided patients in 2 groups. First group (Group-1) was consisting of young patients group (age < 45 years), second group (Group-2) was consisting of elderly patients (age > 45 years). We studied difference in clinical presentation, risk factors, neurological presentation, pattern of brain strokes, areas of brain affected as per CT scan findings in both the groups managed for stroke in the medical ward of PRM medical college and hospital Baripada, Odisha. Now onwards we will address young patients group as group-1 and elderly patient group as group-2 in this study.

Inclusion criteria

1) All pts above age 18 years & having clinical & CT confirmed diagnosis of stroke.

Exclusion criteria

- 1) Pts below 18.
- 2) Stroke due to trauma.
- 3) Pts' medical records which were not showing CT confirmed diagnosis.
- 4) Medical records in which patient sent for MRI brain with inconclusive CT scan findings.

Statistical analysis: -The data obtained were analyzed using SPSS version 21.0 software. Results were expressed in frequencies and percentages.

III. Results

589 cases of stroke case sheets (from 796 cases of stroke patients by exclusion criteria) managed in medical ward for stroke in the medicine ward of PRM medical college and hospital Baripada, Odisha during a period of June 2018 to January 2019 were studied & evaluated for clinical presentation, risk factors, neurological presentation, pattern of brain strokes, areas of brain affected as per CT scan findings in both the groups.

In this study youngest pt was 28 years & oldest was 98 years old. There were 99 patients from group-1 and 490 patients from group-2. Mean age in group-1 was 38.2 ± 7.7 year and mean age in group-2 was 63.6 ± 10.0 years. Incidence of stroke in group-1 was 16.81%; in group-2 it was 83.19% as shown in (Table 1).

Table 1: Frequency & percentage of cases according to age groups.

FREQUENCY & PERCENTAGE OF CASES ACCORDING TO AGE GROUP		
AGE GROUP	NUMBER OF CASES	%
Group-1	99	16.81
Group-2	490	83.19
TOTAL	589	100

Youngest age of the patient is 18 years. oldest age of the patient is 98 years. Average age of the patient in our group is 59.3 ± 13.5 .

Out of 589 pts, as shown in (Table-2) in group-1 there were 59 (59.6%) males and 40 (40.4%) were females. In group-1 male to female ratio was 1.47:1. In group-2 there were 291 (59.39%) males and 199 (40.61%) were females. In group-2 male to female ratio was 1.46:1.

Table 2: Sex wise distribution of stroke cases as per age groups.

GENDER WISE DISTRIBUTION OF STROKE PATIENTS						
GENDER	GROUP-1	%	GROUP-2	%	TOTAL	%
MALE	59	59.60	291	59.39	350	59.42
FEMALE	40	40.40	199	40.61	239	40.58
TOTAL	99	100	490	100	589	100

Type of stroke according to age groups

Table 3: Age group wise frequencies of different types of stroke

AGE GROUP WISE FREQUENCIES OF DIFFERENT TYPES OF STROKE						
TYPE OF STROKE	GROUP-1	%	GROUP-2	%	TOTAL	%
ISCHAEMIC	34	34.34	240	48.98	274	46.52
HAEMORRHAGIC	65	65.66	250	51.02	315	53.48
TOTAL	99	100	490	100	589	100

In our study (Table 3 & 4) most common type of stroke in both age groups was haemorrhagic stroke, in group-1 it was (65.66%) and in group-2 it was (51.02%), out of which there were (58.46%) males and (41.54%) females in group-1 and (59.2%) males, (40.80%) females in group-2.

Second most common type of stroke in both age groups was ischaemic stroke, in group-1 it was (34.34%) and in group-2 it was (48.98%), out of which there were (61.76%) males and (38.24%) females in group-1 and (59.58%) males and (40.42%) females in group-2.

Table 4: Gender wise frequencies of different types of stroke

GENDER WISE FREQUENCY OF DIFFERENT TYPES OF STROKES												
GENDER	GROUP-1						GROUP-2					
	ISCHAEMIC STROKE		HAEMORRHAGIC STROKE		TOTAL		ISCHAEMIC STROKE		HAEMORRHAGIC STROKE		TOTAL	
	No. OF CASES	%	No. OF CASES	%	No. OF CASES	%	No. OF CASES	%	No. OF CASES	%	No. OF CASES	%
MALE	21	61.76	38	58.46	59	59.60	143	59.58	148	59.20	291	59.39
FEMALE	13	38.24	27	41.54	40	40.40	97	40.42	102	40.80	199	40.61
TOTAL	34	100	65	100	99	100	240	100	250	100	490	100

Table 5: Quantitative parameters of patients included in study

QUANTITATIVE PARAMETERS OF PATIENTS INCLUDED IN STUDY			
	GROUP 1	GROUP 2	TOTAL
PARAMETERS	MEAN ± SD	MEAN ± SD	MEAN ± SD
SYSTOLIC BP	152.2 ± 30.8	152.5 ± 32.9	152.5 ± 32.5
DIASTOLIC BP	94.5 ± 17.8	91.1 ± 16.4	91.7 ± 16.6
HAEMOGLOBIN	11.7 ± 2.57	11.6 ± 5.3	11.6 ± 5.0
TOTAL CHOLESTEROL	181.7 ± 37.9	173.2 ± 39.1	174.6 ± 39.0
TRIGLYCERIDE	135.2 ± 58.8	119.6 ± 44.6	122.3 ± 47.6
HDL	55.24 ± 14.5	56.8 ± 12.8	56.5 ± 13.1
LDL	102.3 ± 22.9	101.6 ± 26.4	101.7 ± 25.8
SERUM UREA	37.5 ± 26.32	40.8 ± 24.9	40.3 ± 25.1
SERUM CREATININE	1.4 ± 0.9	1.4 ± 0.8	1.4 ± 0.8

In our study (Table 6) most common risk factors in group-1 were hypertension (76.77%), dyslipidemia (60.61%), tobacco chewing (28.28%), smoking (26.26%), CKD/ renal dysfunction (20.20%), alcohol (19.19%) and past h/o CVA (10.10%). Valvular heart disease is present in 2.02% cases.

In group-2 most common risk factor was hypertension ((77.96%), dyslipidemia (52.65%), tobacco chewing (34.29%), CKD/ renal dysfunction (24.69%), smoking (20.61%), alcohol (17.14%) and past h/o CVA (7.35%). Other heart diseases like CAD, DCM and atrial fibrillation were found in group-2 which were not found in group-1.

Hypertension, dyslipidemia, alcohol intake and renal dysfunction were more commonly associated with haemorrhagic stroke in both the groups.

Smoking was most commonly associated with ischemic strokes in group-1 (35.29%).

Past h/o CVA was more commonly associated with ischaemic strokes in both the groups.

Table 6: Prevalence of risk factors for stroke pts in both the age groups.

RISK FACCTORS FOR GROUP 1 STROKE PATIENTS							RISK FACCTORS FOR GROUP 2 STROKE PATIENTS					
RISK FEATURES	GROUP 1 ISCHAEMIC		GROUP 1 HAEMORRHAGIC		GROUP 1		GROUP 2 ISCHAEMIC		GROUP 2 HAEMORRHAGIC		GROUP 2	
	f	% (n=34)	f	% (n=65)	f	% (n=99)	f	% (n=240)	f	% (n=250)	f	% (n=490)
Hypertension	21	61.76	55	84.62	76	76.77	173	72.08	209	83.60	382	77.96
Diabetes	1	2.94	1	1.54	2	2.02	30	12.50	9	3.60	39	7.96
Dyslipidemia	20	58.82	40	61.54	60	60.61	121	50.42	137	54.80	258	52.65
Alcohol	5	14.71	14	21.54	19	19.19	29	12.08	55	22.00	84	17.14
Tobacco	6	17.65	22	33.85	28	28.28	79	32.92	89	35.60	168	34.29
Smoking	12	35.29	14	21.54	26	26.26	49	20.42	52	20.80	101	20.61
CKD/ renal dysfunction	4	11.76	16	24.62	20	20.20	47	19.58	74	29.60	121	24.69
RHD/ valvular heart disease	1	2.94	1	1.54	2	2.02	1	0.42	0	0.00	1	0.20
CAD	0	0.00	0	0.00	0	0.00	2	0.83	2	0.80	4	0.82
DCM	0	0.00	0	0.00	0	0.00	2	0.83	0	0.00	2	0.41
Atrial fibrillation	0	0.00	0	0.00	0	0.00	3	1.25	0	0.00	3	0.61
Past h/o of CVA	5	14.71	5	7.69	10	10.10	30	12.50	6	2.40	36	7.35

In our study (Table 7) most common clinical presentation from both age groups was hemiplegia (87.88% in group-1 vs. 84.69% in group-2), followed by speech involvement (62.63% vs. 68.16%) in group-1 and group 2 respectively.

3rd most common clinical feature was UMN facial palsy (61.62%) in group-1 and altered sensorium (55.31%) in group-2.

Other clinical features present in group-1 in order of frequency were altered sensorium (46.46%), convulsions (9.09%) and headache (6.06%).

Other clinical features present in group-2 in order of frequency were UMN facial palsy (44.69%), convulsions (8.16%), giddiness (10.2%), coma (7.55%), vomiting (4.9%) and headache (4.29%).

Table 7: Clinical presentation of stroke pts in both the age groups.

CLINICAL FEATURES OF STROKE PATIENTS				
PREDOMINANT PRESENTING CLINICAL FEATURE	GROUP 1		GROUP 2	
	FREQUENCY	%	FREQUENCY	%
HEMIPLEGIA	87	87.88	415	84.69
SPEECH INVOLVEMENT	62	62.63	334	68.16
UMN FACIAL PALSY	61	61.62	219	44.69
FASCIO BRACHIAL PALSY	0	0.00	1	0.20
ALTERED SENSORIUM	46	46.46	271	55.31
CONVULSION	9	9.09	40	8.16
INSTABILITY OF GAIT	1	1.01	9	1.84
SENSORY IMPAIRMENT	1	1.01	2	0.41
HEADACHE	6	6.06	21	4.29
VOMITING	6	6.06	24	4.90
GIDDINESS	5	5.05	50	10.20
COMA	4	4.04	37	7.55
VISUAL IMPAIRMENT	2	2.02	6	1.22

Topographic distribution of hemorrhage according to age groups

In our study (Table 8) most common site of hemorrhage in group-1 was basal ganglia (36.92%), followed by internal capsule (30.77%), ventricular (24.62%), external capsule (24.62%), thalamus (20.00%) and parietal (12.31%).

In group-2 most common site of hemorrhage was ventricular (38.4%), followed by thalamus (33.60%), external capsule (23.20%), basal ganglia (21.20%), internal capsule (13.2%), parietal (11.6%), temporal (4.80%), para ventricular (4.40%), SAH (4.40%), cerebellar (3.20%) and frontal (3.20%).

Table 8: Topographic distribution of cerebral hemorrhage.

TOPOGRAPHIC DISTRIBUTION OF CEREBRAL HAEMORRHAGE				
ALTERED AREAS OF BRAIN ON CT SCAN	GROUP 1		GROUP 2	
	FREQUENCY	%	FREQUENCY	%
FRONTAL	2	3.08	8	3.20
PARIETAL	8	12.31	29	11.60
TEMPORAL	2	3.08	12	4.80
BASAL GANGLIA	24	36.92	53	21.20
CAUDATE NUCLEUS	0	0.00	3	1.20
CENTRUM SEMIOVALE	0	0.00	0	0.00
VENTRICULAR	16	24.62	96	38.40
PARAVENTRICULAR	1	1.54	11	4.40
INTERNAL CAPSULE	20	30.77	33	13.20
EXTERNAL CAPSULE	16	24.62	58	23.20
MID BRAIN	0	0.00	1	0.40
THALAMUS	13	20.00	84	33.60
OCCIPITAL	1	1.54	5	2.00
PONS	0	0.00	1	0.40
BRAINSTEM	0	0.00	3	1.20
CEREBELLAR	1	1.54	8	3.20
SUB ARACHNOID HAEMORRHAGE	1	1.54	11	4.40

Topographic distribution of infarct according to age groups

In our study (Table 9) most common site of infarct in group-1 was parietal (29.41%), followed by para ventricular (26.47%), basal ganglia (14.71%), frontal lobe (11.76%), external capsule (11.76%), temporal lobe (8.82%), internal capsule (8.82%). In age group-2 most common area of infarct was also parietal (41.25%), followed by para ventricular (22.92%), occipital lobe (17.92%), basal ganglia (15.83%), frontal (11.67%), temporal (11.25%), internal capsule (6.67%) and cerebellar (5.0%).

Table 9: Topographic distribution of cerebral infarction.

TOPOGRAPHIC DISTRIBUTION OF CEREBRAL INFARCTION				
ALTERED AREAS OF BRAIN ON CT SCAN	GROUP 1		GROUP 2	
	FREQUENCY	%	FREQUENCY	%
FRONTAL	4	11.76	28	11.67
PARIETAL	10	29.41	99	41.25
TEMPORAL	3	8.82	27	11.25
BASAL GANGLIA	5	14.71	38	15.83
CAUDATE NUCLEUS	1	2.94	1	0.42
CENTRUM SEMIOVALE	1	2.94	2	0.83
PARAVENTRICULAR	9	26.47	55	22.92
INTERNAL CAPSULE	3	8.82	16	6.67
EXTERNAL CAPSULE	4	11.76	8	3.33
MID BRAIN	0	0.00	0	0.00
THALAMUS	1	2.94	9	3.75
OCCIPITAL	4	11.76	43	17.92
PONS	0	0.00	2	0.83
BRAINSTEM	0	0.00	1	0.42
CEREBELLAR	1	2.94	12	5.00

IV. Discussion

In group-1, incidence of stroke in group-1 was (16.81%), it correlates with the study done by P. Chitrabalam et al., [14] in which 20% patients were below 45 years. It also correlates with the study done by Baiju et al. [15] in which incidence of stroke in young was 18.5 percent. In group-2 it was (83.19%). The peak incidence of stroke is in ≥45 year’s age group. It also correlates with the study done by P. Chitrabalam et al. [14] in which 80% of patients was more than 45 years. Mean age of male in elderly age group was 64.21 years and in female it was 62.69 years. It correlates with the study done by Bhattachatya et al. [16] and study by Dalal et al., [17] in which it was mentioned that the mean onset of stroke for men in India ranges from 63-65 for men and 57-68 for women. In our study mean age in group-1 was 38.2 ± 7.7 year which correlates with the study done by Antonio et al., [18] in which Mean age was 35.7 ± 7.4 years. In group-1 male to female ratio was 1.47:1. It correlates with study done by Baiju et al., [15] in which it was 2.1:1. In group-2 male to female ratio was 1.2:1, which correlates with 1.46:1 ratio in study of P. Chitrabalam et al. [14]

Men are more likely to have a stroke than women. This may be due to differences in risk factors such as smoking and drinking which are more prevalent among men in India compared with women. [19] Though

majority of case (83.19%) were seen in the elderly, stroke in the young carries special importance as they form the most productive age group. Young stroke has increased in the recent times with changing lifestyles and better diagnostic modalities.

In our study most common type of stroke in both age groups was hemorrhagic stroke, in group-1 it was (65.66%) and in group-2 it was (51.02%), more young patients suffered hemorrhagic stroke than elderly counterpart. Owolabi MO et al [20] study says in low- and middle-income countries, 34% of strokes (versus 9% in high-income countries) are of haemorrhagic subtype and up to 84% of stroke patients in low- and middle-income countries (versus 16% in high income countries) die within three years of diagnosis. In this study, we found in young group there were more chances of hemorrhagic stroke contrary to the study done by Arindam Datta et al., [21] in which (22.2%) hemorrhagic stroke was in young patients and (77.7%) hemorrhagic stroke was in elderly age group.

In group-1 of hemorrhagic stroke there was male predominance which correlates with study done by Jose´ Luis et al., [22] in which (53%) were males and (47%) were females in young hemorrhagic stroke patients. In group-2 hemorrhagic stroke there was male predominance which correlates with study done by Arindam Datta et al. [21]

In our study most common risk factors in group-1 were hypertension (HTN) and dyslipidemia and third most common risk factor was tobacco chewing. In group-2 most common risk factor was hypertension followed by dyslipidemia and tobacco chewing; this observation correlates with the study done by Trilochan Srivastava et al., [23] in which hypertension and smoking were the most common risk factors in both young and elderly groups. In assessing the combination and their effects of risk factors, tobacco abuse and hypertension appear to act synergistically as stroke risk factors. [24] It was evident in study by P. Chitrambalam et al., [14] in which hypertensive tobacco abusers were 60.43% in contrast to only hypertensives without tobacco abuse were only 39.57%. In our study, we found CKD/ renal dysfunction in 24.69% of total stroke patients, with more common amongst hemorrhagic stroke patients, which could be explained due high prevalence of chronic kidney disease patients in the study area.

In study done by Hirotaka Shimizu et al., [25] it was found that most common risk factors were hypertension and smoking in both age groups. Other risk factors in group-1 in order of frequency were dyslipidemia and alcohol with similar percentage, past history of Coronary Artery Disease (CAD) and diabetes (DM) with similar percentage and 1 case was with rheumatic (RHD) valvular heart disease. These findings were consistent with study done by Kay Sin Tan et al., [26] in which hypertension was documented in 47.2% of the entire cohort of patients and was the most common risk factor. The risk factors in descending order were dyslipidemia, smoking, diabetes and alcohol excess. In study done by Prasad et al., [6] smoking, alcoholism, increased BMI, diabetes and hypertension are significantly associated with strokes among young people. Recurrent CVA was most commonly seen in <45 years (10.1%). Similar trend was seen in study done by P. Chitrambalam et al., [14] in which it was (10%). Recurrent CVA is much more common in ischemic stroke patients 14.71% in group-1 vs. 12.5% in group-2. In group-2 most common risk factor was hypertension followed by equal percentage of dyslipidemia and smoking past history of CVD, Diabetes, alcohol, past history of CAD and history of cancer in 2 cases. Similar trend was observed with study done by Hirotaka Shimizu et al., [25] in which older patients were having hypertension (46.7%) as most common risk factor followed by previous stroke (24.6%), hyperlipidemia (23.6%) and equal percentage (19.6%) of smoking and diabetes. In study done by R. P. Eapen et al., [10] it was found that modifiable risk factors such as hypertension (40%), alcoholism (35%), smoking (28%) and hyperlipidemia (17%) are the commonest cause of stroke among the elderly.

In our study most common clinical presentation from both age groups was hemiplegia (87.88% in group-1 vs. 84.69% in group-2), followed by speech involvement (62.63% vs. 68.16%) in group-1 and group-2 respectively, which correlates with study by P. Chitrambalam et al. [14] In that study also most common clinical presentation from both age groups was hemiplegia (93.3% in young vs. 89.2% in elderly), speech involvement was (43.3% vs. 30.8%) in young and elderly respectively.

In our study most common site of hemorrhage in group-1 was basal ganglia (36.92%), followed by internal capsule (30.77%), ventricular (24.62%), external capsule (24.62%), thalamus (20.00%) and parietal (12.31%). In group-2 most common site of hemorrhage was ventricular (38.4%), followed by thalamus (33.60%), external capsule (23.20%), basal ganglia (21.20%), internal capsule (13.2%), parietal (11.6%), temporal (4.80%), para ventricular (4.40%), SAH (4.40%), cerebellar (3.20%) and frontal (3.20%). Similar trend was seen in study done by P. K. Chhetri et al. [27] and Pipat Chiewvit et al [28]. In our study most common site of infarct in both group-1 and group-2 was area supplied by middle cerebral artery which was also seen in study done by Trilochan Srivastava et al., [23] and Baiju et al. [15]

V. Conclusion

To conclude stroke incidence of stroke in young (<45 years) patients is on rise. Peak incidence of stroke is in ≥ 45 years age group. Mean age of male in elderly age group was 64.21 years and in female it was 62.69 years. Mean age for young age group was 38.2 year. In young age group male to female ratio was 1.47:1. In elderly it was 1.46:1. Most common clinical presentation from both age groups was hemiplegia. Most prevalent risk factors in both the groups were hypertension, dyslipidemia and tobacco chewing. CKD/ renal dysfunction were associated with significant number of stroke patients (24.69%) in our study. Most common type of stroke in both age groups was hemorrhagic stroke with male predominance. Most common site of hemorrhage in young patients was basal ganglia hemorrhage. Most common site of hemorrhage in elderly was ventricular. Most common site of infarct in both age groups was area supplied by middle cerebral artery. More research is required to address stroke pattern in young and elderly to combat this deadly and disabling disease.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Bibhu P. Behera. " An observational study of clinico-etiological profile of stroke in young and elderly patients in P. R. M. Medical College and hospital, Baripada, Odisha." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, vol. 18, no. 7, 2019, pp 42-48.