

# A Study of Stroke in Individuals less than 45 Years of Age

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**Abstract-** To assess clinical features, risk factors and etiology of stroke in individual's age group of 15-45 years. All young patients in the age group of 15-45 years admitted to Kasturba hospital, Manipal with ischaemic strokes (based on CT or MRI Brain scan) from October 2018 to June 2020 were recruited in this prospective study after obtaining prior informed consent. Each patient was examined in detail and evaluated according to common proforma. Of 332 total ischaemic stroke patients admitted during the study period, 74 had stroke in young with smoking (40.5%), hypertension (33.8%), diabetes (17.6%) and existing heart disease (14.8%) were found to be the most common risk factors involved. Aetiology of young stroke patients in the present study could be identified in 46 (62.1%) of patients and no cause was found in 28 (37.8%). As majority constitutes modifiable risk factors, there is significant scope for primary and secondary prevention of ischaemic stroke in the young and a sincere attempt should be made to identify the risk factors and etiology in such cases.

**Index Terms-** cerebrovascular accident, cva, stroke, young stroke

## I. INTRODUCTION

Stroke is the most common life-threatening neurological disease. It is the second leading cause of death in the world (WHO)(1)(2). It is also a major cause of disability and morbidity. When stroke befalls a healthy young individual in the productive years of life, it can be particularly devastating. Young adults constitute 15-30% of all stroke patients in India(3). Many risk factors for stroke can be modified to reduce the incidence of stroke. Similarly, appropriate management of many of the aetiological factors can reduce the rate of recurrent strokes and morbidity and mortality. Considering the morbidity and mortality of stroke especially in the young population and the heavy burden it puts on the individual and family and society it is of paramount importance on part of the physician to evaluate the modifiable risk factors and aetiology in every young stroke patient and take appropriate measures in the primary and secondary prevention of stroke.

**Study methodology-** All young patients in the age group of 15-45 years admitted to Kasturba hospital, Manipal with ischaemic strokes (based on CT or MRI brain scan) from 1<sup>st</sup> October 2018 to 30<sup>th</sup> June 2020 were included in this prospective study. Each patient was examined in detail and investigated according to common proforma. Special investigations were done depending on clinical suspicion on an individual basis.

Type of study: Observational, Cross Sectional Study

Place of study: Kasturba hospital, Manipal

Study period: October 2018 - June 2020

Sample size: Time bound study

### **Inclusion criteria:**

All patients less than 45 years of age of both sexes who give informed consent

Proven cases of ischaemic stroke by the following criteria: -

Stroke causing measurable neurological deficit by means of History, Physical Examination and Imaging

### **Exclusion criteria:**

Strokes because of neuroendovascular procedures or coronary angiography

Blood glucose concentration <50 mg/dL (2.7 mmol/L)

Hemorrhagic stroke

Stroke due to venous occlusion

Transient Ischemic attack

Seizures

Syncope

**Statistical analysis-**

SPSS 22 software (IBM SPSS statistics, USA) - FOR DATA ANALYSIS

Categorical variables-frequency and percentage.

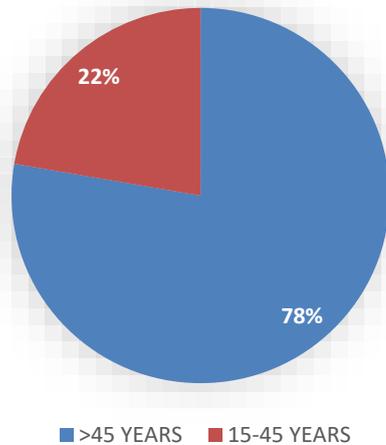
Continuous variables-mean and standard deviation and also as median and interquartile range, where required.

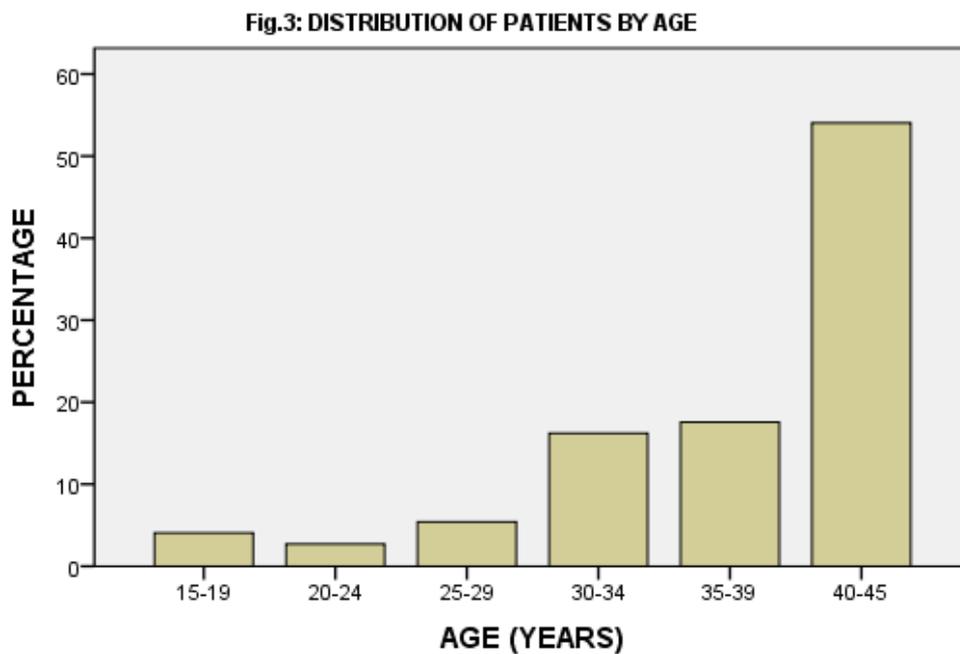
II. RESULTS-

**1. Demography**

The present study was undertaken in KMC, Manipal from October 2018 to June 2020 of ischaemic stroke patients of less than 45 years of age. During the study period a total of 332 ischaemic stroke patients were admitted. Out of this 74 (22.28%) patients were young (Fig 1). The age distribution is shown in Table 1 (Fig 3). The mean age at onset of stroke was 37.86 years (standard deviation = 7.248)

**Fig.1: INCIDENCE OF STROKE IN THE YOUNG**





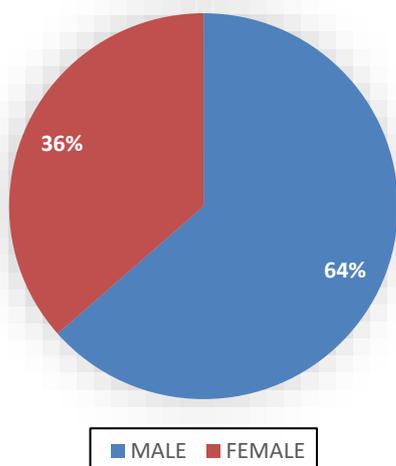
**Table 1: Distribution of patients by age**

Age group (years)	Number	Percentage
15-19	3	4.1
20-24	2	2.7
25-29	4	5.4
30-34	12	16.2
35-39	13	17.6
40-45	40	54.1

Most common age group in the present study was between 40 to 45 years of age group.

**Sex distribution-**

**Fig.2 SEX DISTRIBUTION**



There were 47 (63.5%) males and 27 (36.5%) females (Fig.2). Male to female ratio was 1.7:1

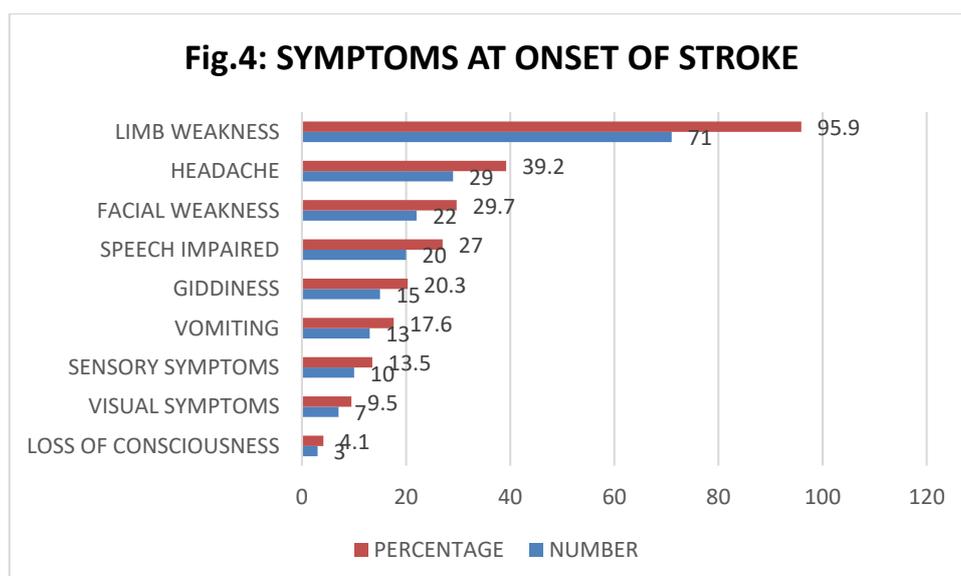
**2.Clinical presentation at onset of stroke**

The various symptoms at onset are shown in Table 2 (Fig.4)

**Table 2: symptoms at onset of stroke**

SYMPTOMS	NUMBER	PERCENTAGE
HEADACHE	29	39.2
VOMITING	13	17.6
GIDDINESS	15	20.3
VISUAL SYMPTOMS	7	9.5
LOSS OF CONSCIOUSNESS	3	4.1
SPEECH IMPAIRED	20	27
FACIAL WEAKNESS	22	29.7
SENSORY SYMPTOMS	10	13.5
LIMB WEAKNESS	71	95.9

**Fig.4: SYMPTOMS AT ONSET OF STROKE**



Apart from limb weakness (95.9%) the commonest symptoms were headache (39.2%), facial weakness (29.7%), speech impairment (27%) and giddiness (20.3%) (Table.2 & Fig.4). 17.6% of patients presented with vomiting and 13.5% of patients had sensory symptoms (all of them presented with tingling and numbness).

**General examination-**

Pallor was present in 18 (24.3%) patients, while suffused conjunctiva in 5 (6.7%) of patients. Tendon xanthomas was observed in 2 (2.7%) patients and xanthelesma in 4 (5.4%) patients.

**Vital signs-**

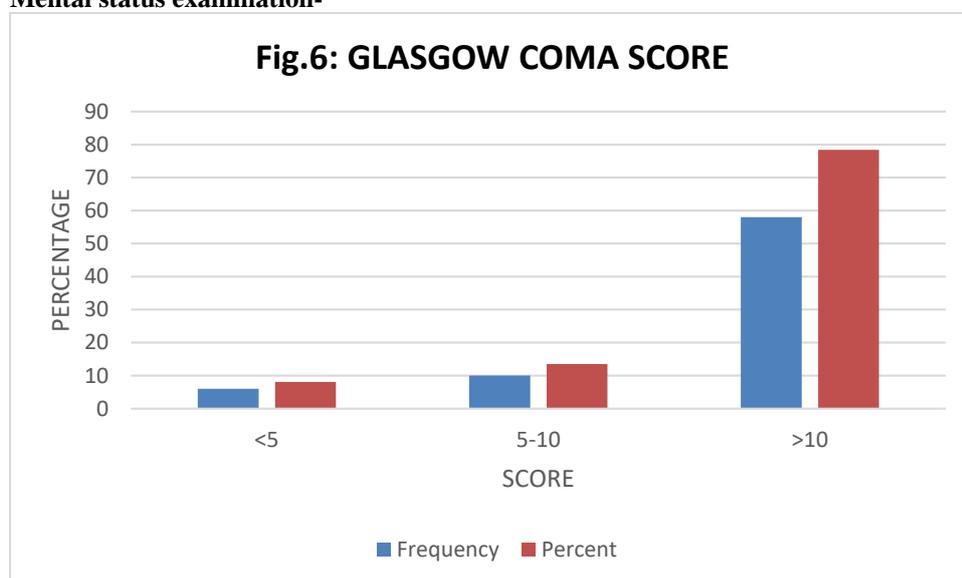
Pulse was irregularly irregular in 8 (10.8%) patients. Left carotid was absent in 3 (4.1%) patients. Blood pressure was high in 24 (32.4%) of patients at the onset of stroke with mean blood pressure being 163.79/94.95 mm of Hg

Systolic Blood pressure	Frequency
140-160 mm of Hg	7
160-180 mm of Hg	14
>180 mm of Hg	3

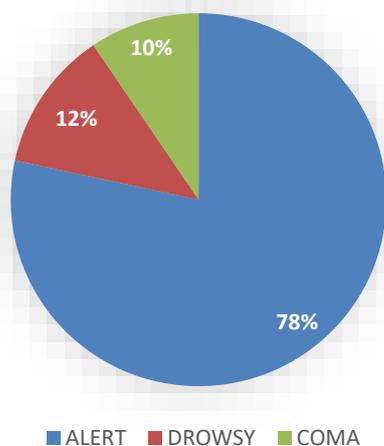
Respiratory rate and temperature was normal in all the patients.

**Neurological examination-**

**Mental status examination-**



**Fig.5: CONSCIOUSNESS LEVEL**



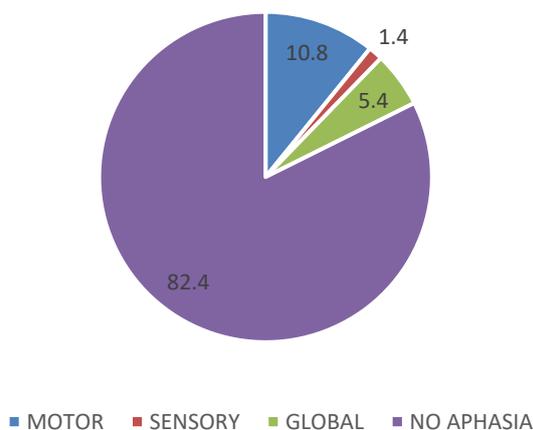
The scoring according to Glasgow coma scale is given in Table.3 (Fig.6). On examination 58 (78%) patients were conscious, 9 (12%) were drowsy and 7 (10%) were in comatose state (Fig.5)

**Table.3: Glasgow Coma Score**

GCS	Frequency	Percent
<5	6	8.1
5-10	10	13.5
>10	58	78.4

**Speech impairment-**

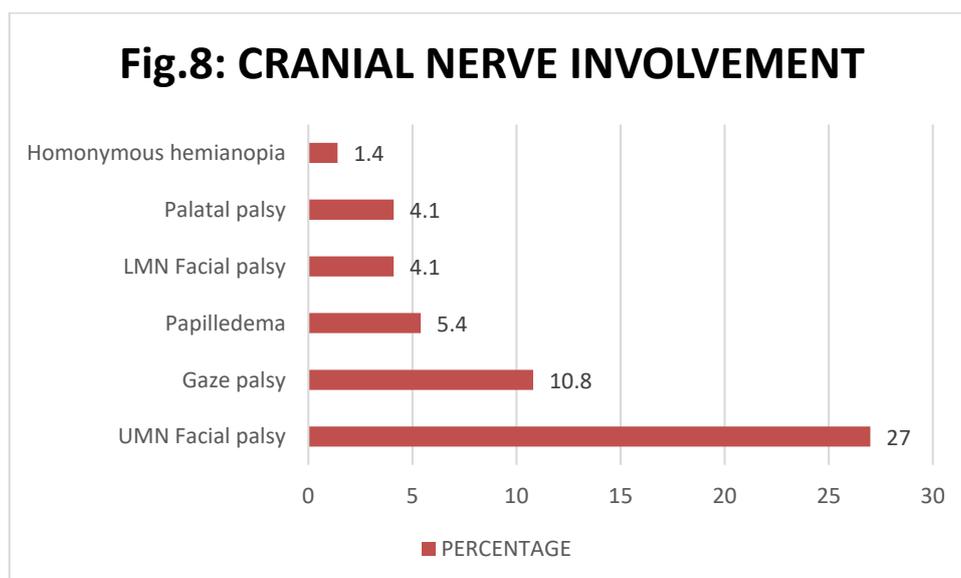
**Fig.7: SPEECH IMPAIRMENT**



Speech impairment (Fig.7) was noticed in 22 (29.7%) of patients. 13 (17.56%) of the patients had some form of aphasia, which 8 (10.8%) had motor aphasia, 1(1.4%) had sensory aphasia and 4 (5.4%) had global aphasia. 9 (12.2%) patients had dysarthria (due to facial nerve palsy and palatal palsy).

**Cranial nerve involvement-**

Table.4 shows the various cranial nerve abnormalities (also Fig.8)



**Table.4: cranial nerve involvement**

CRANIAL NERVE INVOLVEMENT	NUMBER	PERCENTAGE
Papilledema	4	5.4
Homonymous hemianopia	1	1.4
Gaze palsy	8	10.8
UMN Facial palsy	20	27
LMN Facial palsy	3	4.1
Palatal palsy	3	4.1

The common cranial nerve deficits observed other than upper motor neuron facial palsy (27%) were gaze palsy (10.8%), papilledema (5.4%), palatal palsy (4.1%) and lower motor neuron palsy (4.1%) (Table.4 & Fig.8). one patient had homonymous hemianopia.

**Motor system-**

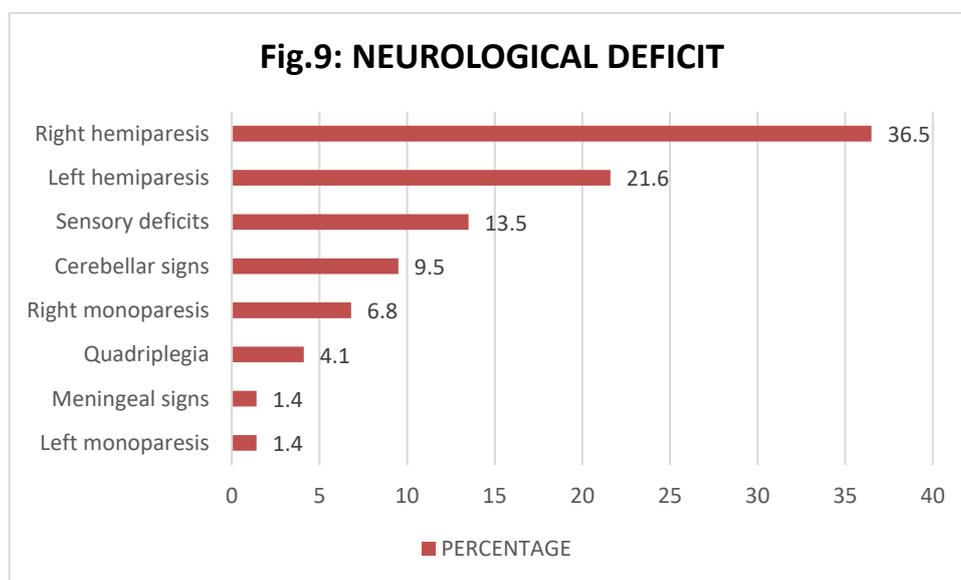
The most common motor deficit observed was hemiparesis of which right side constitutes 50% while left side constitutes 37.83% and right monoparesis is seen in 6.8% of patients while left monoparesis is seen in 1.4% of patients and involvement of all the four limbs is seen in 3 (4.1%) patients.

**Cerebellar signs-**

Impairment of finger-finger test, finger nose test, knee heel test was observed in 7 (9.5%) patients.

**Signs of meningeal irritation-**

One patient (1.4%) of tubercular meningitis had neck rigidity and kernigs test positive. Summarizing the Neurological deficits observed are shown in Table.5 (Fig.9).



**Table.5: Neurological deficit**

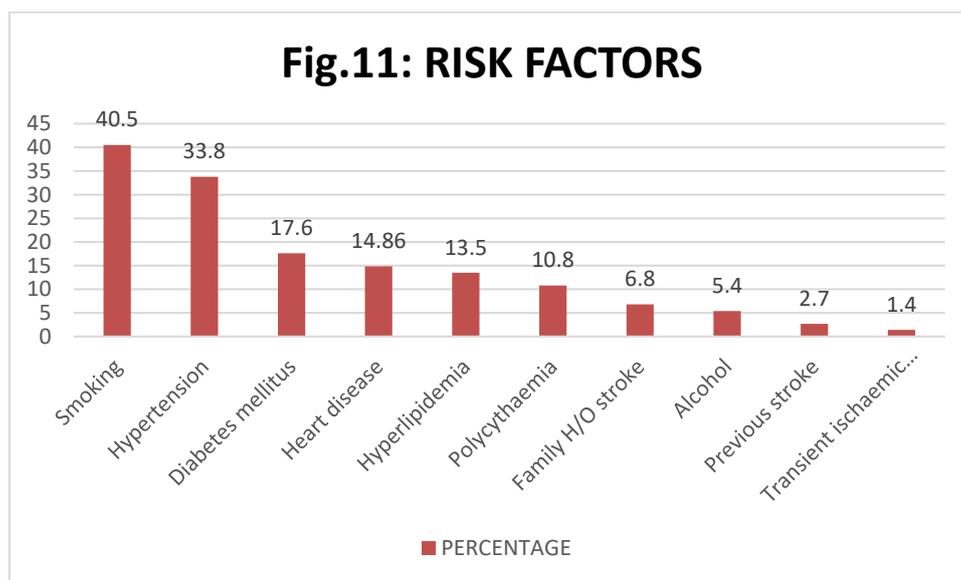
NEUROLOGICAL DEFICITS	FREQUENCY	PERCENTAGE
Right hemiparesis	37	50
Left hemiparesis	28	37.83
Right monoparesis	5	6.8
Left monoparesis	1	1.4
Quadriplegia	3	4.1
Sensory deficits	10	13.5
Cerebellar signs	7	9.5

Meningeal signs	1	1.4
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36.5% of the patients had right hemiparesis and 21.6% had left hemiparesis. (Table.5 & Fig.9). 10 (13.5%) of patients had sensory deficits (loss of all sensations), 3 (4.1%) of patients had quadriplegia, 6 (8.2%) of patients had monoparesis and 7 (9.5%) of patients had cerebellar signs. 1 (1.4%) patient had meningeal signs (associated with tubercular meningitis).

### 3. Risk factors

The various risk factors identified are shown in Table.7 (Fig.11)



**Table.7: Risk factors**

RISK FACTORS	FREQUENCY	PERCENTAGE
Hypertension	25	33.8
Diabetes mellitus	13	17.6
Smoking	30	40.5
Hyperlipidemia	10	13.5
Previous stroke	2	2.7
Transient ischaemic attack	1	1.4
Pre-existing heart disease	11	14.86
Alcohol	4	5.4
Polycythaemia	8	10.8
Family H/O stroke	5	6.8

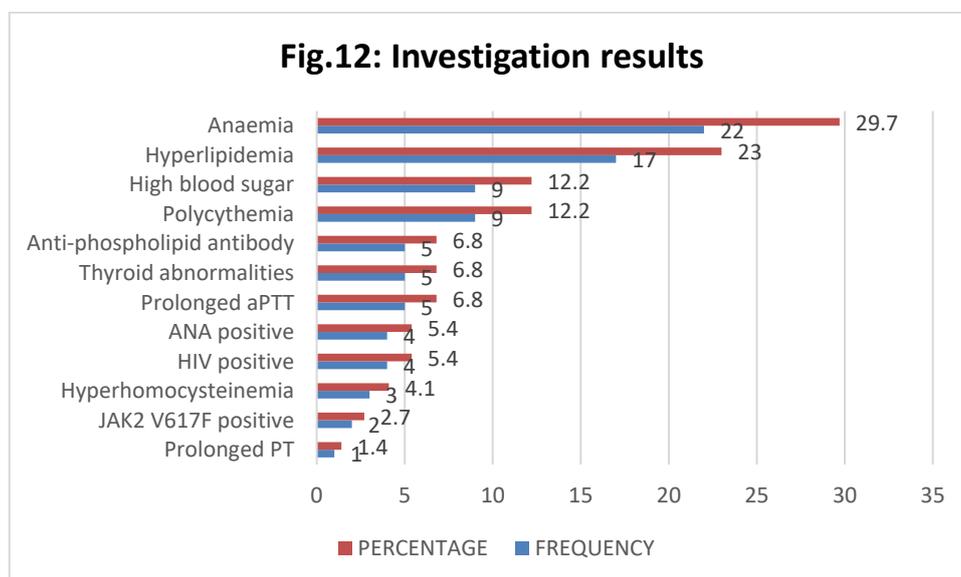
The common risk factors observed were smoking (40.5%), hypertension (33.8%), diabetes mellitus (17.6%), hyperlipidemia (13.5%), previous heart disease (14.86%), polycythemia (10.8%) (Table.7 & Fig.11).

### 4. Investigations

Table.8 shows the investigation results observed (Fig.12)

**Table.8: Investigation results**

INVESTIGATION	FREQUENCY	PERCENTAGE
Hematological	31	41.89
Anaemia	22	29.7
Polycythemia	9	12.2
Prolonged PT	1	1.4
Prolonged aPTT	5	6.8
Biochemical	49	66.21
Hyperlipidemia	17	23
High blood sugar	9	12.2
Thyroid abnormalities	5	6.8
Others	16	21.62
JAK2 V617F positive	2	2.7
HIV positive	4	5.4
Hyperhomocysteinemia	3	4.1
ANA positive	4	5.4
Anti-phospholipid antibody	5	6.8

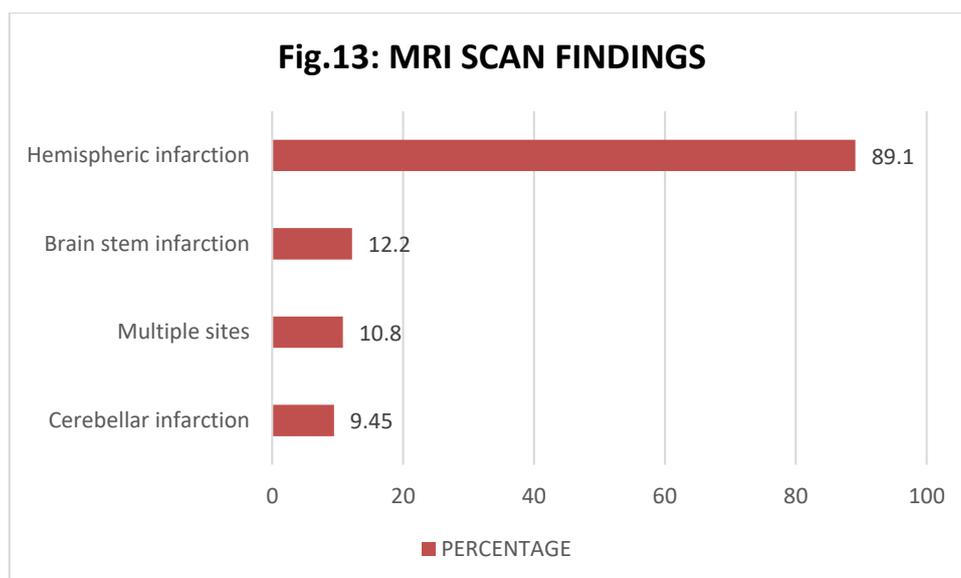


The common abnormalities observed were anaemia (29.7%), hyperlipidemia (23%), high blood sugars (12.2%) and polycythemia (12.2%). 6.8% of the patients had prolonged aPTT values and also positive for anticardiolipin antibodies.

### 5. Topography of cerebral infarction

The topography or site of the cerebral infarction was determined based on Magnetic resonance imaging (MRI) studies of the brain.

MRI scan findings are shown in Table.9 (Fig.13)

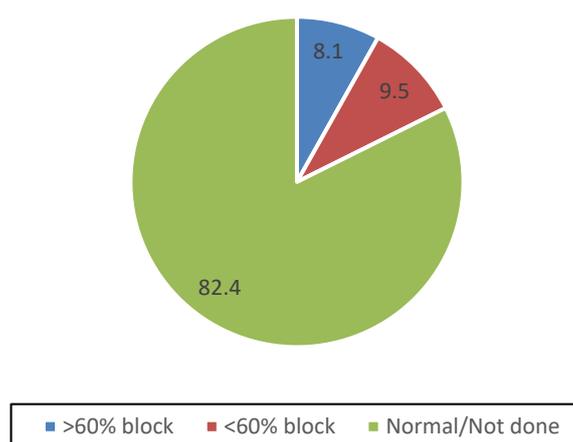


**Table.9: MRI scan findings**

MRI SCAN FINDINGS	FREQUENCY	PERCENTAGE
Hemispheric infarction	66	89.1
Brain stem infarction	9	12.2
Cerebellar infarction	7	9.45
Multiple sites	8	10.8

The most common observed was hemispheric infarction in 66 (89.1%) patients, followed by brain stem infarction in 9 (12.2%) patients and multiple sites in 8 (10.8%) patients.

**Fig.15: CAROTID DOPPLER STUDY**



Carotid Doppler studies showed evidence of atherosclerotic plaque in 13 (17.6%) of patients among which 6 (8.1%) of them having >60% block (Fig.15).

## 6. Aetiology

Aetiology (Table.12 & Fig.17) could be identified in 46 (62.1%) out of 74 patients. No cause could be identified in 28 (37.83%) patients.

The various subtypes were shown in Table.11 (Fig.16).

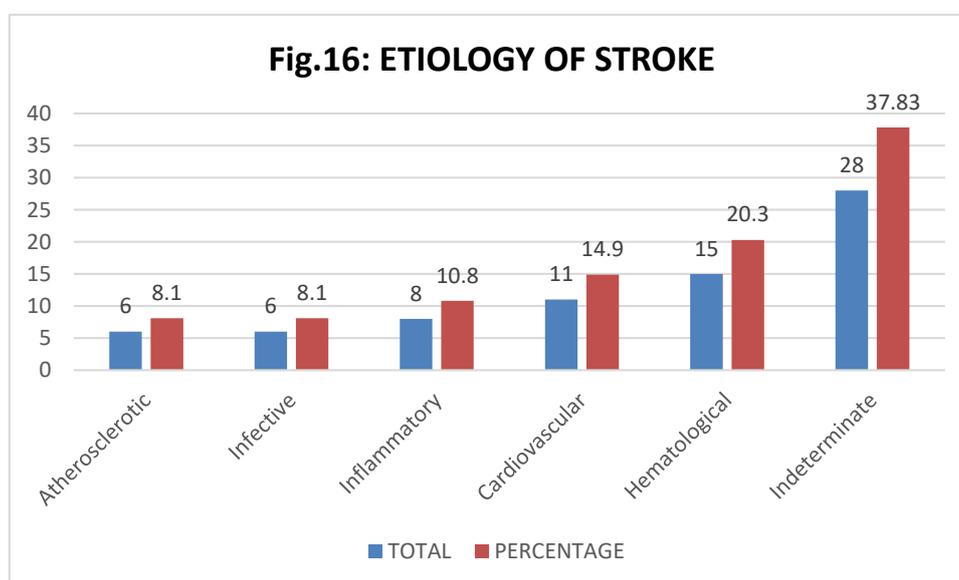
Among the atherosclerotic pathology, in carotid doppler study, 6 (8.1%) patients were found to have more than 60% stenosis and other 7 (9.45%) patients had less than 60% stenosis.

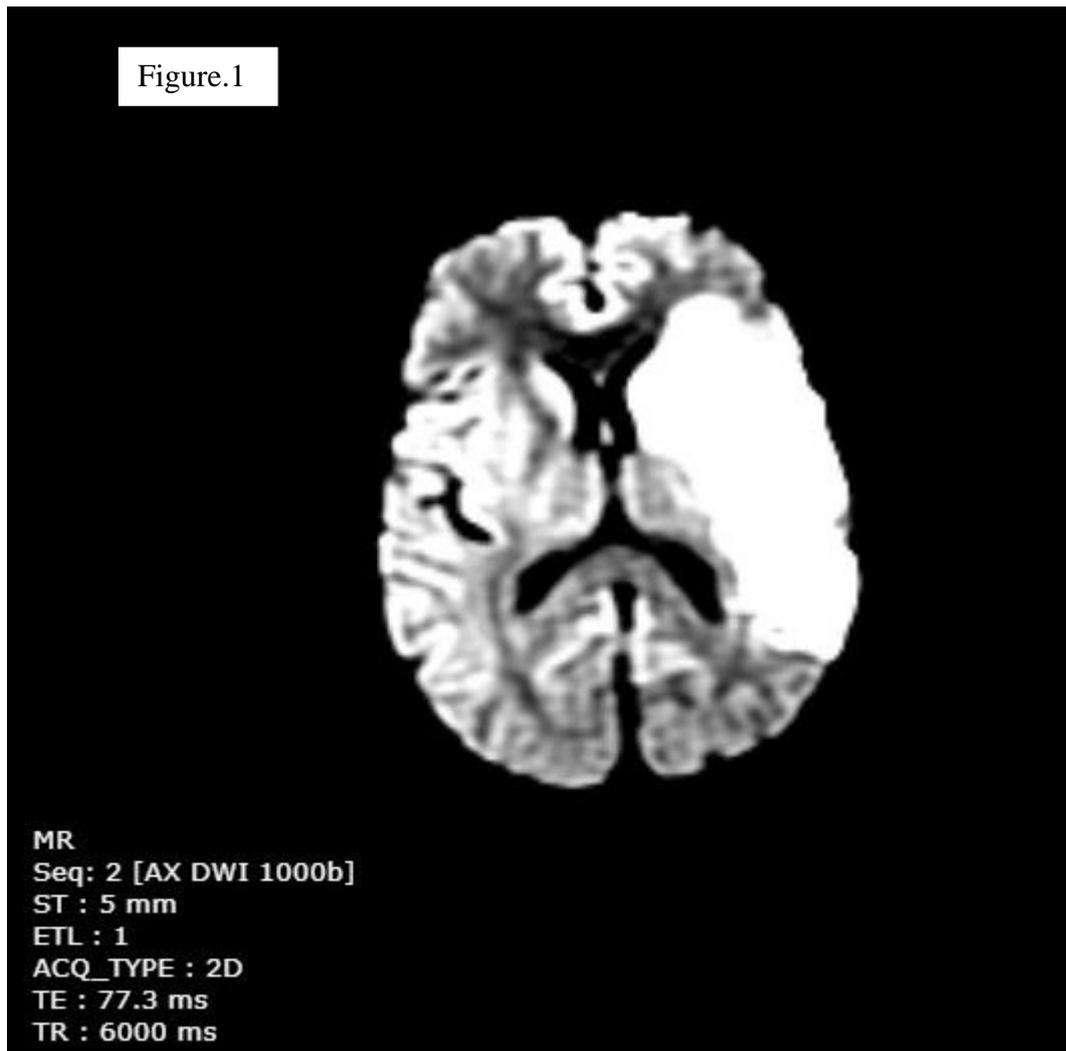
Among the non-atherosclerotic-

- a) infective etiology, that is infective arteritis, 2 (2.7%) patients were positive for tubercular, 2 (2.7%) patients were positive for HIV (of which 1 patient was found to be toxoplasmosis and other found to be cryptococcosis) and other 2 (2.7%) patients were positive for both.
- b) inflammatory vasculopathy, 3 (4.2%) patient each had systemic lupus erythematosus, 1 (1.4%) patient had mixed connective disorder, 1 (1.4%) patient had small vessel vasculitis with cANCA positive having lung involvement also in the form of interstitial lung disease, 1 (1.4%) patient had moya moya disease confirmed by angiography also has pANCA positive with renal involvement in the form of polycystic kidney disease, 1 (1.4%) patient had systemic sclerosis which ANA scl 70 positive, 1 (1.4%) patient had primary biliary cirrhosis and liver failure with pANCA positive and AMA M2 positive.
- c) haematological causes, 9 (12.1%) patients were diagnosed to be polycythemia (of which 2 patients were diagnosed as polycythemia vera and other 7 patients found to be secondary polycythemia related to smoking), 5 (6.75%) patients were positive for either lupus anticoagulant or IgG anticardiolipin antibody. We could not evaluate other patients for prothrombotic states like protein C, protein S and antithrombin III deficiency. Routine evaluation for these prothrombotic states is not practically feasible especially in developing countries due to the high cost factor and the non-availability of tests. They could be done only in selected group of patients.
- d) Cardiovascular pathology, total of 11 patients, 8 (10.8%) had rheumatic heart disease (associated with severe mitral stenosis along with atrial fibrillation), 3 (4.05%) patients had infective endocarditis (3 patients with mitral regurgitation).

**Table.11: Etiology of stroke**

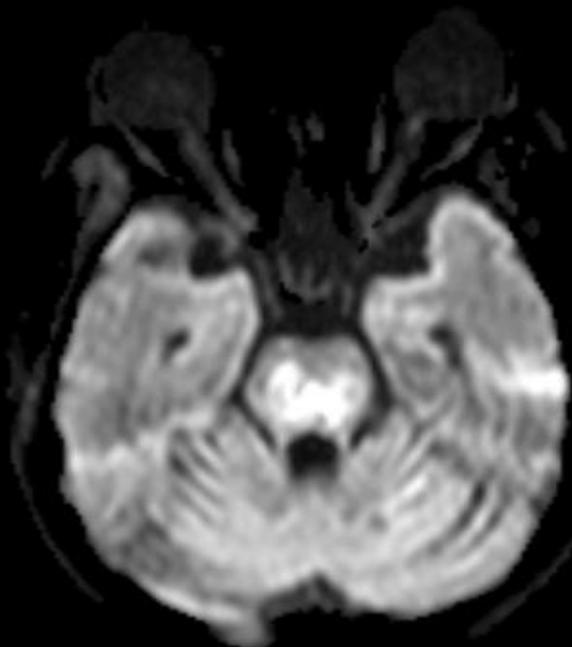
ETIOLOGY OF STROKE	TOTAL	PERCENTAGE
Atherosclerotic	6	8.1
Non-atherosclerotic	40	54.05
• Infective	6	8.1
• Inflammatory	8	10.8
• Haematological	15	20.3
• Cardiovascular	11	14.9
Indeterminate	28	37.83





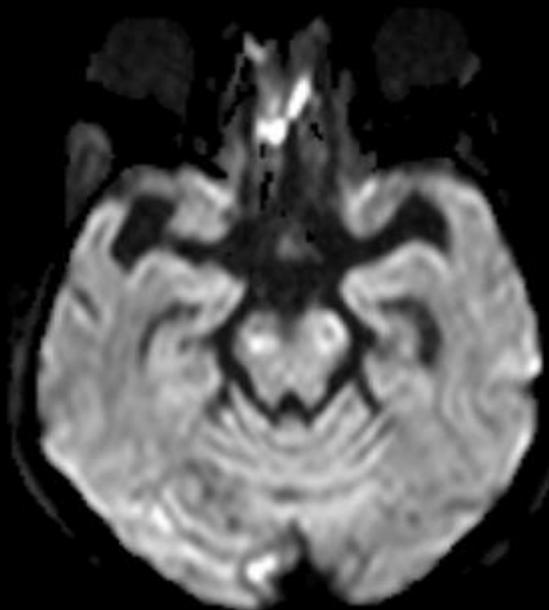
**Figure.17:** MRI showing Acute massive infarct of in the left frontal, temporal, parietal lobes, corona radiata, centrum semiovale, capsuloganglionic region and left insular cortex involving the left MCA territory where patient presented with right hemiparesis and global aphasia

Figure.18



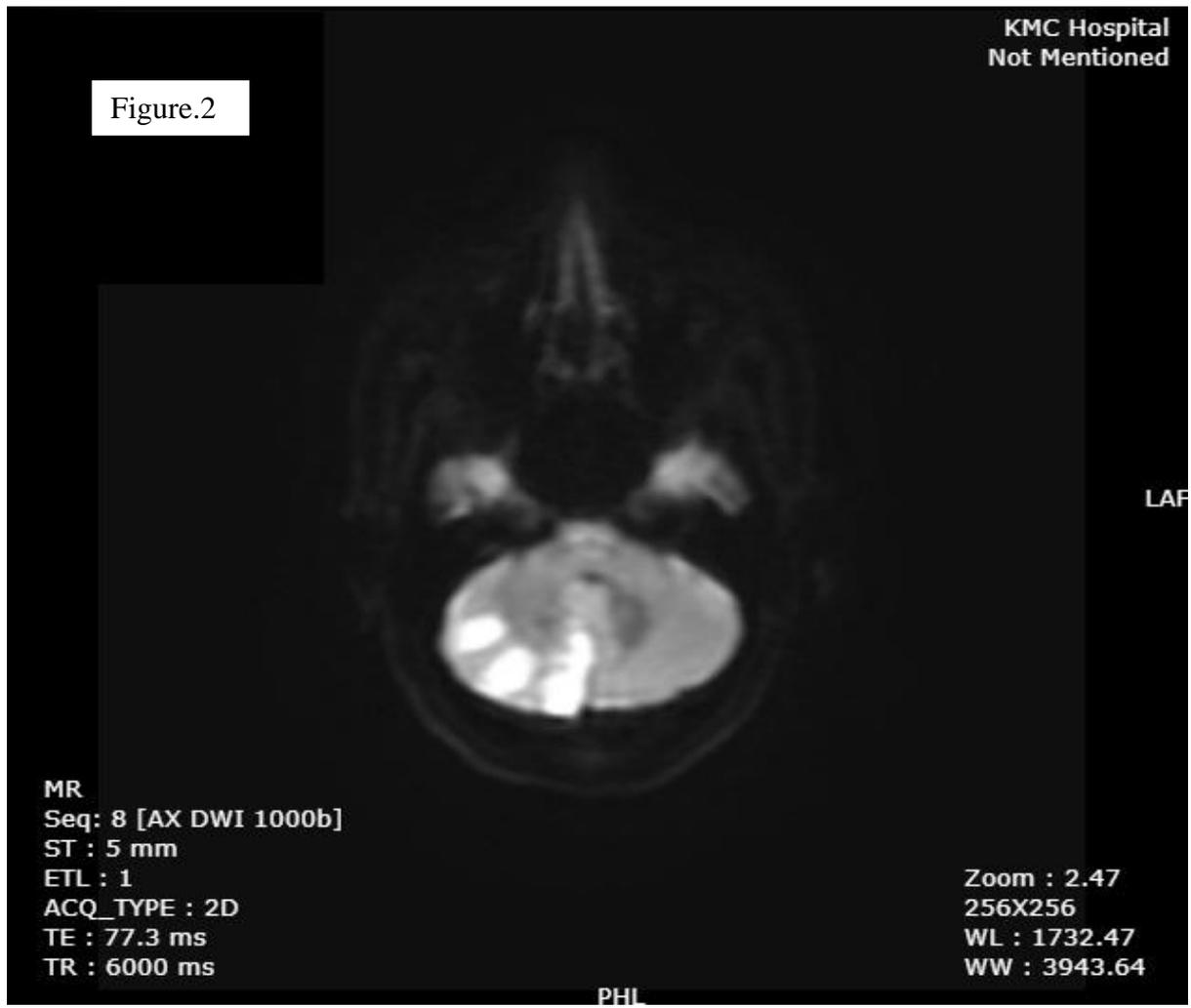
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Figure.19



MR  
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**Figure.18 & 19:-** MRI showing Subacute infarct with micro bleeds involving posterior circulation in midbrain, pons and right middle cerebellar peduncle and bilateral cerebellar hemispheres



**Figure.20:-** MRI showing Acute infarcts involving the right posteroinferior cerebellar lobe, part of right posterosuperior cerebellar lobe

### III. DISCUSSION

Stroke is the most common life-threatening neurological disease which causes disability and morbidity. When stroke befalls a healthy young individual in the productive years of life, it can be particularly devastating. Young adults constitute 15-30% of all stroke patients in India because of change in lifestyle pattern(3). Many risk factors for stroke in young can be modified to reduce the incidence of stroke. Similarly, appropriate management of many of the aetiological factors can reduce the rate of recurrent strokes and morbidity and mortality.

The present study was undertaken in KMC, Manipal from October 2018 to June 2020 of ischaemic stroke patients of less than 45 years of age. During the study period a total of 332 ischaemic stroke patients were admitted. Among the total number of ischaemic stroke patients 74 (22.28%) were young (Fig.1). This was comparable to other similar studies in India where young adults contributed 15-30% of all stroke patients(3). The mean age was  $37.86 \pm 7.24$  years. This was similar to that observed by Carolei et al(4) and Dinesh et al(3). Nearly 87% of the patients were in the 30-45 years age group as smoking, hypertension emerged as important risk factors (Table.1 & Fig.3). Previous studies have shown that the incidence of young stroke increases markedly after 30 years of age(5)(6)(7). Males outnumbered in our study as 30 out of 47 had smoking as the risk factor and male to female ratio was 1.7:1(Fig.2). Compared to other studies from India and abroad males outnumbered females in this study, the differences mainly in the other studies because of female specific risk factors like usage of oral contraceptive pills, pregnancy and puerperium(8)(9)(10). However, another similar study from south India has reported a male to female ratio was 3.2:1(3). Onset of stroke was sudden in most of the patients. This was similar to the pattern seen in the oxfordshire community stroke project(11) and the Framingham study(12).

The most common clinical presentations observed in the present study were limb weakness (95.9%), facial weakness (29.7%), and speech impairment (27%). These symptoms were mainly due to involvement of middle cerebral artery territory. Other symptoms observed are headache and vomiting because of acute onset of stroke leading to raised intracranial pressure (Table.2 & Fig.4). This is almost comparable to the previous Indian study(3)(13).

General examination in a patient of young stroke one should observe for the evidence for premature atherosclerosis, polycythemia, vasculitis, hyperlipidemia and pulse abnormalities like irregular pulse, vessel wall thickening including absence of peripheral pulses for finding the etiology of stroke. In the present study suffused conjunctiva was observed in 5 (6.7%) patients had the evidence of polycythemia. Polycythemia increases blood viscosity, which can impair blood flow, making individuals susceptible to vaso-occlusive events. This hyperviscous state leads to ischaemic stroke. Tendon xanthomas were observed in 2 (2.7%) patients and xanthesma in 4 (5.4%) patients and these patients had the evidence of hyperlipidemia and atherosclerosis with more than 60% of carotid stenosis. Atherosclerosis leads to hardening of blood vessels and forms an atherosclerotic plaque which leads to decreased cerebral perfusion and if plaque dislodges can lead to stroke.

Radial pulse was irregularly irregular in 8 (10.8%) patients as they had atrial fibrillation with rheumatic heart disease. Atrial fibrillation is significant risk factor for stroke as it produces cardioembolic event. Absent carotid pulse was observed in 3 (4.1%) patients as they had more than 60% of stenosis. This produces decreased cerebral perfusion and lead to cerebrovascular accident. Blood pressure was high in 24 (32.4%) patients with mean blood pressure of 163.79/94.95 mm of Hg, all these patients were known patients of chronic hypertension. Hypertension can lead to accelerated atherosclerosis and stroke. Therefore, a careful general examination is very important in young stroke patients as this may help in identifying the aetiology and further management of the patient.

Majority (78.4%) of the patients were conscious on admission while 9.5% of the patients were in coma (Fig.5) because of massive cerebral infarction. The cause of altered sensorium in stroke patients either due to massive cerebral infarction, brainstem infarction, hyponatremia due to syndrome of inappropriate anti diuretic hormone (SIADH). Speech impairment was noticed in 29.7% of patients among these 13 (17.56%) patients had aphasia as there was left sided involvement. The common cranial nerve deficits observed other than upper motor neuron facial palsy (27%) were gaze palsy (10.8%), papilledema (5.4%), palatal palsy (4.1%) and lower motor neuron facial palsy (4.1%) (Table.4 & Fig.8). One patient had homonymous hemianopia. Upper motor neuron facial palsy and homonymous hemianopia was due to involvement of supratentorial stroke and other cranial nerve deficits due to brainstem involvement. Papilledema observed in 5.4% of patients as they had raised intracranial pressure. 50% of the patients had right hemiparesis because of left sided involvement and 37.83% had left hemiparesis. (Table.5 & Fig.9). Right hemiparesis was more common in our present study which is comparable to other studies(14) 10 (13.5%) of patients had sensory deficits, 3 (4.1%) of patients had quadriplegia due to multiple infarcts, 6 (8.2%) of patients had monoparesis due to high cortical involvement and 7 (9.5%) of patients

had cerebellar signs due to involvement of cerebellum. 1 (1.4%) patient had meningeal signs had tubercular meningitis. Tubercular meningitis causes endarteritis obliterans and thrombosis and leads to ischaemic stroke.

The common risk factors observed were smoking (40.5%), hypertension (33.8%), diabetes mellitus (17.6%), hyperlipidemia (13.5%), preexisting heart disease (14.86%), polycythemia (10.8%) (Table.7 & Fig.11). The frequency of smoking, hypertension, diabetes mellitus, heart disease was found to be high in previous study done by Roger You et al(15). Tobacco smoking has been clearly linked to atherothrombotic stroke and several studies have documented that this is an important risk factor for stroke like P Subha et al(16), M George(17), Kapil Singhal(18). Among the 13 patients who had atherosclerotic vasculopathy as evidenced by carotid doppler 12 (92.3%) had abnormal lipid profile emphasizing the role of hyperlipidemia as a risk factor for development of atherosclerosis.

In the present study 5.4% patients had alcohol intake as a risk factor. A similar incidence of moderate to heavy alcoholism was observed in the present study compared to previous ones(3)(4)(17). Risk of stroke associated with alcohol consumption is related to the amount of alcohol consumed. Heavy alcohol use either habitual daily consumption or binge drinking seems to be related to stroke and death, however exact mechanism leading to stroke was not clear.

The abnormal blood investigations detected are shown in Table.8 (Fig. 12). The common hematological abnormalities observed were anaemia, polycythemia and prolonged aPTT. Anaemia was detected in 22 (29.7%) of patients. Role of anaemia in stroke is important as it can exacerbate hypoxia, causes reactive thrombocytosis and also can lead to borderline infarcts. Polycythemia was detected in 9 (12.2%) of patients leads to stroke because of increased viscosity and causing hypercoagulable state. Two patients were diagnosed to have primary polycythemia vera because of JAK2 mutation positivity and seven patients had secondary polycythemia related to smoking. 6.8% of the patients had prolonged aPTT values and also positive for anticardiolipin antibodies diagnosed to have anti phospholipid antibody syndrome characterized by hypercoagulable state which leads to stroke. The common biochemical abnormalities observed were Hyperlipidemia in 17 (23%) patients, high blood sugars in 9 (12.2%) patients leading to stroke because of associated atherosclerosis. Carotid ultrasound with Doppler studies showed evidence of atherosclerotic plaque in 13 (17.6%) of patients among which 6 (8.1%) of them having >60% block. Atherosclerosis causes decreased cerebral perfusion and predisposes to stroke. Carotid doppler is the screening modality of choice for the detection of extracranial carotid or vertebral artery disease and is probably the best modality available to visualize small atherosclerotic plaques(19)(20). The topography of cerebral infarction observed are given in Table.9 (Fig.13). In the present study majority of the patients had middle cerebral artery territory involvement. The topography of cerebral infarction in young ischaemic stroke patients was studied by Bogousslavsky et al, according to this study carotid artery territory was involved in 61% of all patients; vertebrobasilar territory in 34% and multiple territories in 5% cases. Though angiography is the final word in the identification of the occluded vessel, vascular territory can also be assessed with reasonable accuracy non-invasively based on the site of lesion by CT or MRI brain scan(21). The incidence of middle cerebral artery involvement is predominant in our study which is comparable to many other studies. 8 (10.8%) of patients had infarcts at multiple sites.

Aetiology of young stroke patients in the present study could be identified in 62.1% of patients and no cause was found in 37.8%. This was similar to the Baltimore-Washington cooperative young stroke study(27). The common causes observed were Hematological (20.3%), cardiovascular (14.9%), inflammatory (10.8%) (Table.11 & Fig.16). Kittner et al(27) have reported a similar incidence of hypercoagulable states. Incidence of non-atherosclerotic vasculopathy was more in the present study compared to Kittner et al(27). As per the observations made, the incidence of atherosclerotic vasculopathy in the present study was similar to Bogousslavsky et al(48) and Adams Jr.et al(52) study.

Among the cardiovascular pathology, total of 11 patients, 8 (10.8%) had rheumatic heart disease (associated with severe mitral stenosis along with atrial fibrillation, as proved by echocardiography), atrial fibrillation leads to irregular contraction of the heart and leads to a thromboembolic event which causes stroke. 3 (4.05%) patients had infective endocarditis (has mitral regurgitation in echocardiography). Infective endocarditis causes septic embolization which causes occlusion of cerebral arteries and leads to stroke. In a patient of young stroke, holter monitoring is an ideal investigation, as it can detect intermittent atrial fibrillation which causes cardioembolic stroke. In the present study it was not possible to do holter monitoring. Among the atherosclerotic pathology, 6 (8.1%) patients were found to have more than 60% block as detected by carotid doppler.

Among the inflammatory etiology, 3 (4.2%) patients had systemic lupus erythematosus with central nervous system involvement, 1 (1.4%) patient had mixed connective disorder with central nervous system involvement, 1 (1.4%) patient had small vessel vasculitis with cANCA positive having lung involvement also in the form of interstitial lung disease with central nervous system involvement, 1 (1.4%) patient had moya moya confirmed by angiography with renal involvement in the form of polycystic kidney disease and also with central nervous system involvement, 1 (1.4%) patient had systemic sclerosis which ANA scl 70 positive with central nervous system involvement, 1 (1.4%) patient had primary biliary cirrhosis and liver failure with pANCA positive and AMA M2 positive with central nervous system involvement.

Among the non-atherosclerotic, infective etiology, that is infective arteritis, 2 (2.7%) patients were positive for tubercular meningitis, 2 (2.7%) patients were positive for HIV (of which 1 patient was found to be toxoplasmosis of brain and other found to be cryptococcal meningitis) and other 2 (2.7%) patients were positive for both retrovirus and tubercular meningitis. Tuberculous meningitis is one of the most devastating presentations of the tuberculosis, which constitutes about 10% of all tuberculosis cases and is responsible for about 40% of deaths in the developing countries(22). The main complications of tubercular meningitis include stroke, hydrocephalus and tuberculoma formation(23). Stroke is a common complication of tubercular meningitis which causes irreversible brain damage and can result from endarteritis obliterans and thrombosis causing ischaemic stroke. The mortality is about 3 times higher in tubercular meningitis patients with stroke compared to those without stroke(24). 2 (2.7%) patients were positive for HIV (of which 1 patient was found to be toxoplasmosis of brain and other found to be cryptococcal meningitis). Toxoplasmosis occurs in advanced stages of human immunodeficiency virus (HIV) infection and especially occurs in those patients with a CD4+ count <200 cells/mm<sup>3</sup>(25). Headaches, focal neurological deficits and seizures are the most common clinical manifestations of cerebral toxoplasmosis in patients with HIV infection (25). Ischaemic stroke is a known complication in the acute stage of cryptococcal meningitis and is believed to be caused by infectious vasculitis, leading mainly to endarteritis obliterans (26). The increased risk of cerebrovascular disease is well known in HIV patients (27). With proposed mechanisms including increased prevalence of typical vascular risk factors, infectious vasculitis, HIV-associated vasculopathy and coagulopathy, pathophysiology is likely to be multifactorial(28).

Among the haematological causes, 9 (12.1%) patients were diagnosed to be polycythemia of which two patients were diagnosed to have primary polycythemia vera (JAK2 mutation positivity) and seven patients had secondary polycythemia related to smoking, 5 (6.75%) patients were positive for either lupus anticoagulant or IgG anticardiolipin antibody diagnosed to have anti phospholipid antibody syndrome characterized by hypercoaguable state which leads to stroke. Present study shows the majority of patients had non atherosclerotic etiology which is comparable to Baltimore Washington cooperative young stroke study(29). We could not evaluate other patients for prothrombotic states like protein C, protein S and antithrombin III deficiency. Routine evaluation for these prothrombotic states is not practically feasible especially in developing countries due to the high cost factor and the non-availability of tests. They could be done only in selected group of patients(30).

Despite extensive evaluation, the aetiology still remains obscure in a good number of young ischaemic stroke patients and a negative work up does not avert recurrent events. However, there is significant scope, if primary and secondary prevention implemented which also brings down the cost and emotional burden of the family of ischaemic stroke in the young and a sincere attempt should be made to identify the risk factors and aetiology in each case. Present study highlights the importance of clinical profile and need of aggressive evaluation for risk factors, investigations and etiology in patients presenting with stroke, as majority of them are correctable factors.

#### IV. CONCLUSIONS

- Young patients constituted 22.28% of all ischaemic strokes in the present study and males were more frequently affected compared to females.
- The common symptoms were limb weakness, headache, facial weakness, speech impairment and dizziness.
- The common risk factors were smoking, hypertension, diabetes mellitus, hyperlipidemia and heart disease.
- The common causes observed were non-atherosclerotic like polycythemia, anti-phospholipid syndrome (APLA).
- Cardiovascular diseases are also common risk factor for stroke in young in the form of rheumatic valvular heart diseases, atrial fibrillation, and infective endocarditis.
- Tuberculosis and HIV infection are also important etiological factors in a patients with young stroke.
- Atherosclerosis is a less common etiological factor in a patients of young stroke.

## V. LIMITATIONS OF THE STUDY

- The small number of stroke patient's make the statistical power quite small.
- Further prospective studies are needed to validate our findings in different population with larger sample size for better generalization.
- Strokes including hemorrhagic strokes and venous infarcts are not included in the present study.
- Angiographic studies are not performed in the present study.

### Appendix-

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## REFERENCES

- [1] 1. World Health Organization. WHO - The top 10 causes of death. 24 Maggio. 2018.
- [2] 2. Sacco RL, Wolf PA, Gorelick PB. Risk factors and their management for stroke prevention: Outlook for 1999 and beyond. *Neurology*. 1999.
- [3] 3. Nayak SD, Nair M, Radhakrishnan K, Sarma PS. Ischaemic stroke in the young adult: Clinical features, risk factors and outcome. *Natl Med J India* [Internet]. 1997; Available from: <https://www.ncbi.nlm.nih.gov/pubmed/9230597>
- [4] 4. Carolei A, Marini C, Ferranti E, Frontoni M, Prencipe M, Fieschi C. A prospective study of cerebral ischemia in the young. Analysis of pathogenic determinants. The National Research Council Study Group. *Stroke* [Internet]. 1993; Available from: <https://www.ncbi.nlm.nih.gov/pubmed/8446970>
- [5] 5. Bogousslavsky J, Regli F. Ischemic Stroke in Adults Younger Than 30 Years of Age: Cause and Prognosis. *Arch Neurol*. 1987;
- [6] 6. Hilton-Jones D, Warlow CP. The causes of stroke in the young. *J Neurol*. 1985 Jul;232(3):137-43.
- [7] 7. Adams HP, Butler MJ, Biller J, Toffol GJ. Nonhemorrhagic Cerebral Infarction in Young Adults. *Arch Neurol*. 1986;
- [8] 8. G. L, A. A, G. DP, S. U, P. L, A. S, et al. Etiopathogenesis and prognosis of cerebral ischemia in young adults. A survey of 155 treated patients. *Acta Neurol Scand*. 1991;
- [9] 9. Adams HP, Kappelle LJ, Biller J, Gordon DL, Love BB, Gomez F, et al. Ischemic stroke in young adults. Experience in 329 patients enrolled in the Iowa Registry of stroke in young adults. *Arch Neurol*. 1995;
- [10] 10. Boot E, Ekker MS, Putaala J, Kittner S, De Leeuw FE, Tuladhar AM. Ischaemic stroke in young adults: A global perspective. *Journal of Neurology, Neurosurgery and Psychiatry*. 2020.
- [11] 11. Wroe SJ, Sandercock P, Bamford J, Dennis M, Slattery J, Warlow C. Diurnal variation in incidence of stroke: Oxfordshire community stroke project. *Br Med J*. 1992;
- [12] 12. Kelly-Hayes M, Wolf PA, Kase CS, Brand FN, McGuirk JM, D'agostino RB. Temporal patterns of stroke onset: The framingham study. *Stroke*. 1995;
- [13] 13. Bansal BC, Prakash C, Jain AL, Brahmanandam KRV. Cerebrovascular disease in young individuals below the age of 40 years. *Neurol India*. 1973;
- [14] 14. Bindawas SM, Mawajdeh HM, Vennu VS, Alhaidary HM. Functional recovery differences after stroke rehabilitation in patients with uni- or bilateral hemiparesis. *Neurosciences*. 2017;
- [15] 15. You RX, McNeil JJ, O'Malley HM, Davis SM, Thrift AG, Donnan GA. Risk factors for stroke due to cerebral infarction in young adults. *Stroke*. 1997;
- [16] 16. Subha P, Pillai Geethakumari S, Athira M, Nujum Z. Pattern and risk factors of stroke in the young among stroke patients admitted in medical college hospital, Thiruvananthapuram. *Ann Indian Acad Neurol*. 2015;
- [17] 17. George MG. Risk factors for ischemic stroke in younger adults a focused update. *Stroke*. 2020;
- [18] 18. Prasad K, Singhal K. Stroke in young: An Indian perspective. *Neurol India* [Internet]. 2010 Jul 1 [cited 2020 Feb 7];58(3):343. Available from: <http://www.neurologyindia.com/text.asp?2010/58/3/343/65531>
- [19] 19. Martin PJ. Causes of ischaemic stroke in the young. *Postgraduate Medical Journal*. 1997.
- [20] 20. Carroll BA. Carotid ultrasound. *Neuroimaging Clinics of North America*. 1996.
- [21] 21. Damasio H. A Computed Tomographic Guide to the Identification of Cerebral Vascular Territories. *Arch Neurol*. 1983;
- [22] 22. Wasay M, Farooq S, Khowaja ZA, Bawa ZA, Ali SM, Awan S, et al. Cerebral infarction and tuberculosis in central nervous system tuberculosis: Frequency and prognostic implications. *J Neurol Neurosurg Psychiatry*. 2014;
- [23] 23. Thwaites GE, van Toorn R, Schoeman J. Tuberculous meningitis: More questions, still too few answers. *The Lancet Neurology*. 2013.
- [24] 24. Zhang L, Zhang X, Li H, Chen G, Zhu M. Acute ischemic stroke in young adults with tuberculous meningitis. *BMC Infect Dis*. 2019;
- [25] 25. Philip-Ephraim EE, Charidimou A, Williams E, Kajogbola G. Stroke-like presentation of cerebral toxoplasmosis: Two HIV-infected cases. *Cerebrovasc Dis Extra*. 2015;
- [26] 26. G. M-B, P. D, A. B, P. M, B. M, R.S. L, et al. Pathogenesis of the immune reconstitution inflammatory syndrome affecting the central nervous system in patients infected with HIV. *Brain*. 2011;
- [27] 27. Benjamin LA, Corbett EL, Connor MD, Mzinganjira H, Kampondeni S, Choko A, et al. HIV, antiretroviral treatment, hypertension, and stroke in Malawian adults. *Neurology*. 2016;
- [28] 28. Benjamin LA, Bryer A, Lucas S, Stanley A, Allain TJ, Joekes E, et al. Arterial ischemic stroke in HIV: Defining and classifying etiology for research studies. *Neurology: Neuroimmunology and NeuroInflammation*. 2016.
- [29] 29. Kittner SJ, Stern BJ, Wozniak M, Buchholz DW, Earley CJ, Feeser BR, et al. Cerebral infarction in young adults: The Baltimore-Washington Cooperative Young Stroke Study. *Neurology* [Internet]. 1998 Apr 1 [cited 2018 Dec 4];50(4):890-4. Available from: <http://www.neurology.org/cgi/doi/10.1212/WNL.50.4.890>
- [30] 30. Bogousslavsky J, Pierre P. Ischemic stroke in patients under age 45 [Internet]. *Neurologic Clinics*. 1992. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/1556998>

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