SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY
THIRUVANANTHAPURAM, KERALA

Risk Factors, Outcome and Predictors of Outcome in Young Patients with Ischemic Stroke

Thesis submitted in partial fulfilment of the rules and regulations for DM Degree Examination of Sree Chitra Tirunal Institute for Medical Sciences and Technology

By

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Month and Year of Submission: October 2013
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THIRUVANANTHAPURAM
2011-2013

INTRODUCTION

Introduction

The incidence of stroke rises exponentially with age and is therefore low in young adults.[1] But, ischaemic stroke in young adults is a common cause of admission to stroke units and referral to neurology departments or tertiary hospitals. [2,3 1]

While a specific definition of “young stroke” is lacking, the vast majority of studies consider “young stroke” to pertain to individuals 15-45 years of age.

Traditional risk factors for stroke such as hypertension and diabetes are not very frequent in young adults; however, some other permanent or transient risk factors such as smoking, use of oral contraceptives, migraine, trauma, use of illicit drugs, and pregnancy or puerperium have a more important role in this age group than in older adults.

The main clinical challenge in management of a young adult with acute stroke is the identification of its cause. Although large extracranial and intracranial atheroma, small-vessel disease, and atrial fibrillation [2,3] have a major role in cases of stroke in older adults, these disorders are much less frequent in young adults. Though a change in life style pattern led to epidemic of traditional risk factors at younger population also.

Stroke in a young person can be devastating in terms of productive years lost and impact on a young person’s life. Ability to establish a definite cause for stroke in young people has improved in the past decades because of advances in the noninvasive imaging of the brain vessels, heart cavities, and valves, and cardiac electrophysiology and genetic diagnostic instruments. Advances in medical and surgical field led to improvement in outcome after stroke in all age group especially in younger population.

In this study we tried to analyse whether change in risk factor profile and outcome in Indian scenario is same or different from the western population.

Review of Literature

Review of Literature

Incidence, prevalence, and demographics

In a hospital-based study in Finland, the yearly incidence of stroke increased from 2·4 per 100 000 for people aged 20–24 years, to 4·5 per 100 000 for people aged 30–34 years, and to 32·9 per 100 000 for people aged 45–49 years. Stroke is slightly more frequent in women aged 20–30 years and in men older than 35 years in younger population.

The proportion of strokes of undetermined or rare causes is much higher for young adults than for older patients.[5] In young adults the etiological subgroups also vary with age: the proportion of strokes of undetermined cause decreases with age, whereas the proportion of strokes caused by large artery atherosclerosis and small-vessel disease increases after the age of 35–40 years.[2,7]

Causal data for stroke in young adults come mainly from registries of reference hospitals in developed and few developing countries and are therefore prone to ascertainment and referral biases. The incidence of stroke in young adults in developing countries is higher than in developed countries because of the higher incidence of strokes related to infections, rheumatic heart disease, and undetected or uncontrolled vascular risk factors [8-11]

Risk factors for ischaemic stroke in young adults

Understanding of risk factors for ischaemic stroke in young adults is based mainly on hospital-based case-control studies and less often on population-based studies. The proportion of young adult patients with stroke who have classic risk factors increases with age. [2,3,7]

In different series, a variable proportion of women (7%- 45%) [2-3] were on oral contraceptives. Alcohol misuse is also an independent risk factor for ischaemic stroke in young and middle-aged adults. [12]

Smoking

Cigarette smoking is an important risk factor for stroke in young adults[13] which has been replicated in a population-based case-control study (odds ratio [OR] 2·6 [95% CI 1·9–3·6]).[14]

The risk increased with the duration and dose [13,14] of the exposure, from an OR of 2·2 (1·5–3·3) for one to ten cigarettes per day up to 9·1 (3·2–26·0) for 40 or more cigarettes per day. The large proportion of smokers among young adults with stroke in countries with a high prevalence of smokers[15], particularly in some developing countries, is of concern. [16,17]

Migraine

Findings from a meta-analysis[18] showed that the risk of ischaemic stroke in people who had migraine with aura was doubled compared with people without migraine. An age of less than 45 years, smoking, and oral contraceptive use further raised the risk. However, migraine without aura did not seem to affect the risk. The mechanism by which migraine with aura increases the risk of ischaemic stroke is unknown. They mostly affect the posterior cerebral artery territory, but single and multiple infarcts of any size and location have been reported. The incidence of migrainous stroke is too low to explain the increased risk of stroke in people with migraine. Other potential mechanisms include association of migraine with known or unknown causes or risk factors for stroke (e.g. PFO, dissection). Other mechanism includes increased platelet activation, release of serotonin and increased adhesion of platelet during acute attack.[18,19] Additionally infarcts induced by drugs (e.g. ergotamine) might also be a contributing factor. Several disorders such as mitochondrial encephalopathy with lactic acidosis

and stroke-like episodes (MELAS), cerebral autosomal dominant arteriopathy with subcortical ischaemic strokes and leucoencephalopathy (CADASIL), or essential thrombocythaemia can cause stroke and are also associated with migraine. Cerebral infarcts in patients with migraine should be investigated in the same way as any cerebral infarcts in young people and, the label of migrainous stroke is a diagnosis of exclusion.

Pregnancy and puerperium

The risk of ischaemic stroke for pregnant women rises in the last trimester, and the 6 weeks post-partum but overall pregnancy-related stroke is rare.[20,21]

Although some disorders can be triggered by pregnancy (eg, peripartum cardiomyopathy)., in many patients, the cause of the stroke cannot be identified. Whether a hyper-coagulable state and changes in vessel walls associated with pregnancy have a role in the occurrence of these otherwise unexplained ischaemic strokes.[21,22]

Eclampsia is the main pregnancy-specific disorder that might be associated with reversible cerebral vasoconstriction syndrome (RCVS) and with non-haemorrhagic stroke-like episodes.

The diagnostic approaches to stroke during pregnancy should proceed as in the non-pregnant state, while taking into account the welfare of the fetus[21–23] and a history of pregnancy related stroke should not be a contraindication for subsequent pregnancy.[24]

Oral contraceptives

The role of OCPs as a risk factor for ischaemic stroke remains controversial. According to the results of a meta-analysis[25], the risk of stroke is increased by about four times for women who take pills with a high content of

oestrogen, and is doubled for those who take pills with low oestrogen content. Pills composed of progesterone alone do not seem to increase the risk of stroke.[25]

Overall, the excess risk due to oral contraceptives is low (four incident strokes per 100 000 women per year of oral contraceptive use).[27], however, in women with migraine, oral contraceptives are associated with an increased risk of ischaemic stroke[28,29]. Women who have prothrombotic genetic variants are also at increased risk.[30]

Illicit drugs

Stroke is one of the complications of recreational drug use[31]. The frequency of illicit drug use in young adults with stroke can be as high as 12%.[32] Therefore, toxicology screening for illicit drugs should be done in young patients with stroke with no obvious cause, or if suggested by history or examination. The intravenous use of drugs can produce embolisation of foreign material or endocarditis. Drugs with a sympathomimetic effect (amphetamine, cocaine, crack) can cause ischaemic stroke through several mechanisms such as acute hypertension, enhanced platelet aggregation, and rarely vasculitis (mainly related to amphetamine and cocaine intake).

Cardioembolism

The etiology includes disease of valves, congenital heart disease, cardiomyopathies, PFO with paradoxical embolism and rhythm disorder.

ECG, TTE, TEE, Holter monitoring and cardiac MRI may reveal specific etiology in majority of patients, correction of which can reduce future stroke risk.

In young adults, high-risk sources of embolism detected by echocardiography include mechanical prosthetic valves, mitral stenosis,

endocarditis (infective and non-infective)[53,54] dilated cardiomyopathies, intracardiac thrombus, and cardiac tumours such as myxoma and fibroelastoma.[55]

The most common uncertain sources of embolism are patent foramen ovale and atrial septal aneurysm, akinetic or dyskinetic segments of the ventricular wall, and redundant mitral valve prolapse. Transcranial doppler monitoring of both middle cerebral arteries after injection of agitated saline in the antecubital vein can be used to detect a right-to-left shunt and to grade its intensity.[56]

Small-vessel disease

Small-vessel single perforator disease can produce small (<15 mm diameter) deep hemispherical or brainstem lacunar infarcts in young adults, usually in patients with hypertension and diabetes and in those older than 35 years.[2]

Infections, vasculitis, Fabry's disease, and CADASIL can also cause lacunar infarcts. Patients often have additional imaging evidence of small-vessel disease such as old silent lacunar infarcts, leukoaraiosis on CT, deep or periventricular white matter lesions on T2-weighted and FLAIR MRI, or microbleeds on GRE/SWI sequences. [40]

When classifying a patient in the subgroup of small-vessel disease, two potential pitfalls should be avoided: (1) proximal arterial or cardiac embolic source that can cause a small deep infarct should not be missed and (2) atheroma of the wall of a large vessel (eg, basilar artery) impinging on the ostium of the perforator as the cause of the lacunar infarct should be excluded.

Detection of multiple acute small infarcts, suggesting embolism, can be achieved by doing acute MRI with DWI. High-resolution MRI and MRA can

be used to distinguish between atheroma plaques of a large vessel and penetrating vessel disease. [57]

Other identifiable causes

First-line tests (complete blood and platelet count; erythrocyte sedimentation rate; C-reactive protein; serum electrolytes, glycaemia, lipid profile, renal, and hepatic functions; activated partial thromboplastin time; and prothrombin time)[58] can detect biological risk factors and can provide insight into rare causes of ischaemic stroke such as coagulation disorders (e.g. thrombocythaemia) or systemic diseases (e.g. lupus).

Extracranial or intracranial large-vessel arterial disease

Though large artery atherosclerotic disease is an uncommon cause of stroke in young but other possibilities like arteritis (especially Takayasu arteritis) is not an uncommon etiology especially in Asian population. In addition Moya-Moya disease is also an important etiological consideration.

Depending on local availability and experience, DSA,MRA, CTA, or neck vessel Doppler combined with TCD [34,35,12] can be used to confirm or rule out extracranial or intracranial arterial disease or an occlusion.

Arterial dissection

Spontaneous arterial dissection[59] is one of the most common causes of stroke in young adults[59]. This disorder often affects the extracranial ICA, with dissection starting a few centimetres after the common carotid bifurcation, or the vertebral artery as it enters the intervertebral canal or as it leaves it before piercing the dura. Extracranial dissection is multiple in about a quarter of the cases. Dissection is usually subintimal and the resulting haematoma causes a long, irregular stenosis or even an occlusion. Sometimes, the dissection is subadventitial, forming a pseudoaneurysm. Intracranial

dissection (e.g. of the intracranial vertebral artery) might rupture into the subarachnoid space. The etio-pathogenesis of dissection is still unclear. Often dissection is preceded hours to weeks by minor trauma to the head or neck, but only a few of the many young people who sustain minor neck injuries have an arterial dissection. The role of other vascular risk factors, genetic factors, and minor connective tissue abnormalities sometimes detected in skin biopsy samples of patients with arterial dissection are unknown. [60–62]

The occurrence of multiple concomitant dissections[63] and the finding of many clustered early recurrences[64] contrast with the rarity of late recurrences and indicate a transient vasculopathy, which might be triggered by infections. [59]

Clinical features that are suggestive of dissection include a history of head or neck trauma (even minor), headache or neck pain, and local signs (such as Horner's syndrome or cranial nerve palsies), with or without symptoms of cerebral ischaemia.

The diagnosis of arterial dissection can be made with ultrasound, MRI, CT, or catheter angiography. The risk of early recurrence is low (<1%), although very early multiple recurrence (usually asymptomatic) might occur. The risk of recurrence is higher in patients with stroke or transient ischaemic attack than in those with local signs. Most recurrent strokes happen during the first month, and long-term risk of recurrent dissection (0·3–1·4%), stroke (0·3–3·4% per year), and vascular death are low.[68] Stenotic lesions resolve in about 70% of patients, whereas recanalisation of completely occluded arteries is less frequent and occurs mainly within the first 6 months.[69] Carotid aneurysms persist in about two-thirds of cases, whereas vertebral aneurysms frequently resolve. Because complications of persistent aneurysms are rare, the main issue in cervical arterial dissection is the severity of the initial stroke rather than the risk of recurrence.

Patent foramen ovale (PFO)

The foramen ovale is a remnant of the fetal circulation that remains patent in about 25% of the general population. TEE with a bubble contrast study is the most sensitive diagnostic test.

TCD can also be used to identify other causes of a right-to-left shunt—namely, a pulmonary arteriovenous fistula. Many case-control studies have established a statistical association between PFO and cryptogenic stroke.[71,72]

In a meta-analysis of these studies,[72] the summary OR for PFO in cryptogenic stroke versus controls was 2·9 (95% CI 2·1–4·0). The corresponding OR was 5·1 (3·3–7·8) for younger patients (<55 years) and 2·0 (>1·0–3·7) for older patients (>55 years). The association has also been reported to be stronger in patients with large right-to-left shunts and in those who have an atrial septal aneurysm in addition to a PFO.[71,72] Results from a population-based study[73] suggest that selective referral of cases and under recognition of PFO in comparison groups of patients referred for echocardiography might have led to an overestimation of its role in cryptogenic strokes.

In contrast with case-control studies, longitudinal studies have been unable to show an increased risk of first[74] or recurrent stroke[75] in patients with PFO. In a meta-analysis of 15 studies,[75] the pooled absolute rate of recurrent stroke in medically treated patients with cryptogenic stroke and PFO was 1·6 events per 100 person-years (95% CI 1·1–2·1).

The mechanism of stroke in patients with a PFO is not well defined. A shunt via a PFO might allow passage of thrombotic material from the venous bed into the arterial circulation (paradoxical embolism) .Other potential stroke mechanisms, such as direct embolisation of thrombi formed in situ and paroxysmal arrhythmia, remain unproven. This uncertainty suggests that

other mechanisms unrelated to PFO might be operant in many cases. In this respect, it should be kept in mind that PFO is a common finding in the normal population and must coexist by chance alone in about a third of patients with ischaemic stroke.[72] Consequently, for some patients, stroke is erroneously attributed to a PFO.

Primary and secondary vasculitis and connective tissue disorders

In primary vasculitis like SLE[88]and Takayasu's disease in which stroke is common and might even be the presenting manifestation. Other vasculitic causes of stroke include Churg-Strauss, Wegener's vasculitis, polyarteritis nodosa, cryoglobulinaemia, and Behçet's disease, vasculitis associated with inflammatory bowel disease, and sarcoidosis. Sneddon's syndrome refers to a rare disorder featuring widespread generalised livedo reticularis and multiple strokes[90] and it can be isolated or associated with antiphospholipid syndrome. Stroke is a rare manifestation in patients with primary angiitis of the CNS.[91]

Most patients present with encephalopathy, cognitive decline and headache. Lumbar puncture usually shows lymphocytic pleocytosis, and cerebral angiography either shows signs that suggest vasculitis or is normal. A meningeal brain biopsy should be done to confirm the [91] diagnosis, however, the biopsy can be negative or inconclusive, although its sensitivity is moderate (50–60%).[92] Cerebral vasculitis should be distinguished from RCVS in which various segmental narrowings of the intracranial vessels disappear on repeat angiograms after few weeks and the CSF is usually normal. [93,94]

Other rare non-inflammatory arteriopathies

Other arteriopathies include radiation arteriopathy, fibromuscular dysplasia, and moyamoya syndrome[95,96]. The rarest causes of stroke in young adults are the retinocerebral or retinocochlearcerebral arteriopathies, such as Eales

disease (retinopathy with neovascularisation), Susac's syndrome (encephalopathy, hearing loss, andretinal artery branch occlusions), and acute posterior multifocal placoid pigment epitheliopathy (multiple cream coloured lesions of the retinal pigment epithelium).

Haematological disorders

Apart from sickle-cell anaemia,[98] other haematological diseases affecting young adults can be occasionally complicated by arterial stroke. Examples are paroxysmal nocturnal haemoglobinuria, thrombotic thrombocytopenic purpura, erythrocytosis, leukaemias, and intravascularlymphoma.

Monogenic diseases

There are more than 50 monogenic diseases that can cause stroke, but they account for a very low percentage of strokes. Subcortical vascular dementia, depression and other psychiatric disorders, migraine with aura, and recurrent strokes are the main clinical features of CADASIL. The diagnosis is suspected if there is a family history (autosomal dominant) and if MRI shows the characteristic confluent subcortical white matter changes extending to the temporal lobes. The diagnosis is confirmed by skin biopsy and genetic testing (Notch 3 mutations)[100] .The estimated prevalence of CADASIL in young patients with stroke is very low (0·5% of lacunar strokes; 2% in patients younger than 65 years with white matter changes). [101]Hypertension and smoking are associated with an increased probability of stroke in patients with CADASIL, suggesting that vascular risk factors might modulate the clinical expression of this disorder. [102]

The availability of an effective enzyme (α-galactosidase) substitution therapy has led to a renewed interest in Fabry´s disease as a cause of stroke in young adults. Fabry´s disease is a systemic disorder affecting mainly the kidney, skin (angiokeratoma), and eye (corneal opacities). It causes a painful neuropathy. The diagnosis in symptomatic men can be confirmed by a deficit

in serum α galactosidase, but usually needs genetic testing, particularly in women, who can have normal concentrations of α galactosidase.[103] Vertebrobasilar dolicoectasia and the coexistence of large-vessel and small-vessel disease are suggestive of Fabry's disease. Fabry's disease is more frequent in young patients with cryptogenic ischaemic stroke.[104] In two large multicentre studies of young patients with stroke, α galactosidase pathogenic mutations were recorded in 2·4% [3] of 493 and 1% [105] of 1000 patients with strokes, more often in those with ischaemic stroke (both cryptogenic and non-cryptogenic). Of importance is the fact that stroke frequently arises before diagnosis of Fabry's disease and in the absence of other clinical findings. [106]

In *COL4A1* mutations—namely, in hereditary angiopathy, nephropathy, aneurysm, and muscle cramps (HANAC) syndrome—the cerebral vascular phenotype involves an association between a subcortical small-vessel disease and aneurysms of the carotid siphon. [107]

Hereditary endotheliopathy with retinopathy, nephropathy, and stroke (HERNS) is associated with mutations of the *TREX1* gene and its phenotype includes psychiatric symptoms, dementia, subcortical strokes, and leucoencephalopathy.

Cryptogenic stroke

In about 30% of patients, the cause of stroke cannot be identified despite the detailed and comprehensive aetiological work up described previously. Some of these patients might have classic vascular risk factors, but they do not show evidence of large atherosclerotic or small vessel arterial disease. Minor atherosclerotic lesions might be missed by current diagnostic and imaging techniques. A frequent mistake is the diagnosis of cryptogenic stroke in patients with incomplete or delayed aetiological investigation.[108] This misdiagnosis is of particular importance in dissection, which can resolve

quickly, and in intracardiac thrombus, which can either resolve or fragment and embolise. Results of some biological diagnostic tests (eg, APLA syndrome) can fluctuate, and therefore repeated assessment is needed. Repeated or extended Holter monitoring might be necessary if paroxysmal arrhythmias are suspected. Repeated angiography might also be necessary to distinguish between reversible cerebral vasoconstriction syndrome, in which the various segmental arterial narrowings are reversible, and vasculitis, atherosclerosis, or other vasculopathies of intracranial arteries, in which the narrowing persist or even progress.

AIMS AND OBJECTIVES

Aims and objectives

1. To analyse risk factors in young patients with stroke.

2. To evaluate etiology of stroke in young population.

3. To analyse outcome of stroke in young population and factors influencing it.

Materials and methods

Materials and methods

SUBJECT/PARTICIPANT SELECTION

All consecutive patients admitted or visited the department of neurology/stroke clinic, aged 15 to 45 years with ischemic stroke from January 2007 to December 2012.

Inclusion criteria

All ischemic strokes/TIA patients between15-45 years age group.

Exclusion Criteria

Age < 15 years and > 45 years.

Hemorrhagic stroke and Subarachnoid Hemorrhage.

Traumatic Stroke.

Stroke due to infective causes

"Gender, class, caste, ethnicity and race were not used as Inclusion and/or Exclusion criteria"

Methods:

In the present study, we included all consecutive patients aged 15 to 45 years with ischemic stroke from January 2007 to December 2012,with clearly defined inclusion and exclusion criteria. Information regarding clinical data, imaging and treatment were obtained from case records. Stroke severity was measured by using the National Institute of Health Stroke Scale (NIHSS) score and the Glasgow Coma Scale (GCS) and modified Rankin's

Scale (mRS) scale. If a NIHSS score is not available from the medical records, it's assessment was based on documented patient examination (Retrospective assessment of NIHSS score has been validated and suggested to be reliable and unbiased). [129] Based on NIHSS, stroke severity was classified as mild (NIHSS score 0 to 6), moderate (7 to 15), or severe (>15).

Stroke etiology was classified according to the TOAST criteria. The short term and intermediate functional outcome was evaluated by means of the mRS and NIHSS at discharge, 3months,6 months and 1 year.

Design :

Retrospective observational analytical study from hospital based records.

Statistical Analysis:

Statistical analysis was done by standard software. Ordinal data were assessed by non-parametric test. Dichotomous and categorical variables were compared with the chi-square test and continuous variables were compared with the unpaired t-test.

In addition univariate and multivariate analysis was be performed to detect variables influencing outcome in young patients with ischemic stroke.

Results

Results :

In our study we enrolled total 125 patients (91 Males and 34 females). (Figure 1) Mean age of study population was 36.032 (S.D. 7.89, range 16-45). Mean age in male patients were 37.12(S.D. 7.514) while in female patients were 33.12 (S.D. 8.242). (Figure 2)

Figure 1

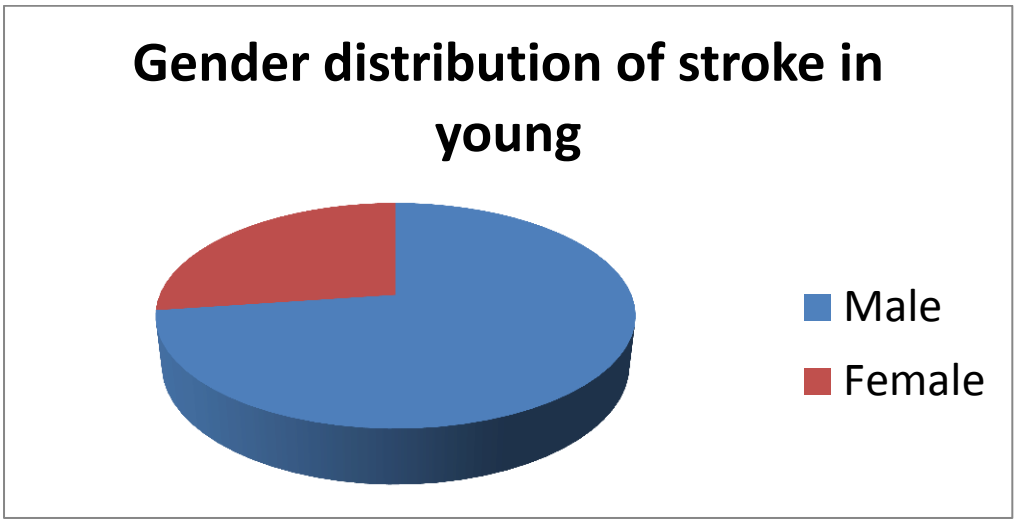
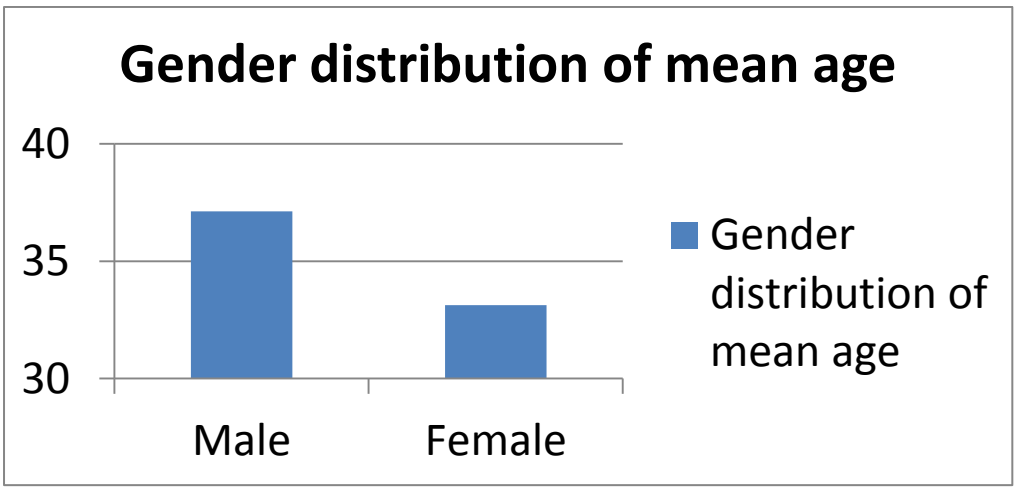


Figure2

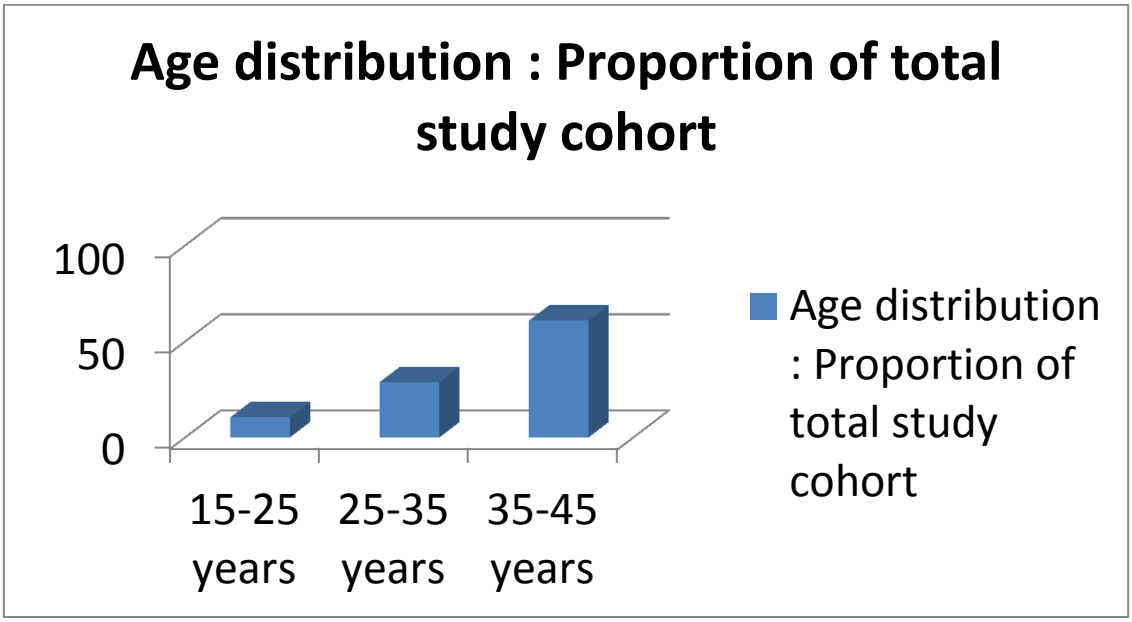


We classified population in 3 age groups (15-25, 25-35 and 35-45 years). Majority of patients (60.8%) were between 35-45 years. (Table 1, Figure 3)

Table 1: Age group distribution is shown in Table 1 :

Age group	Frequency	Percent
15-25	13	10.4
25-35	36	28.8
35-45	76	60.8
Total	125	100

Figure3



We studied various risk factors including smoking, alcoholism, illicit drug abuse, oral contraceptive exposure, hypertension, diabetes mellitus, presence of cardiac illness, prior history of TIA and stroke. The relative frequencies of which is shown in Table 2 and graph 4-6.

Table 2: **Risk factor profile of Patients:**

Risk Factor	**Yes**	**Percent (%)**	**No**	**Percent (%)**
Hypertension	34	27.2	91	72.8
Diabetes	26	20.8	99	79.2
Smoking	35	28.2	89	71.8
Alcohol	26	21	98	79
Migraine	8	6.4	117	93.6
OCPs/Exposure to any hormone	1	0.8	114	99.1
Cardiac disease	24	19.2	101	80.8
History of Prior Stroke	20	16	105	84
History of prior TIA	17	13.6	108	86.4

Figure 4

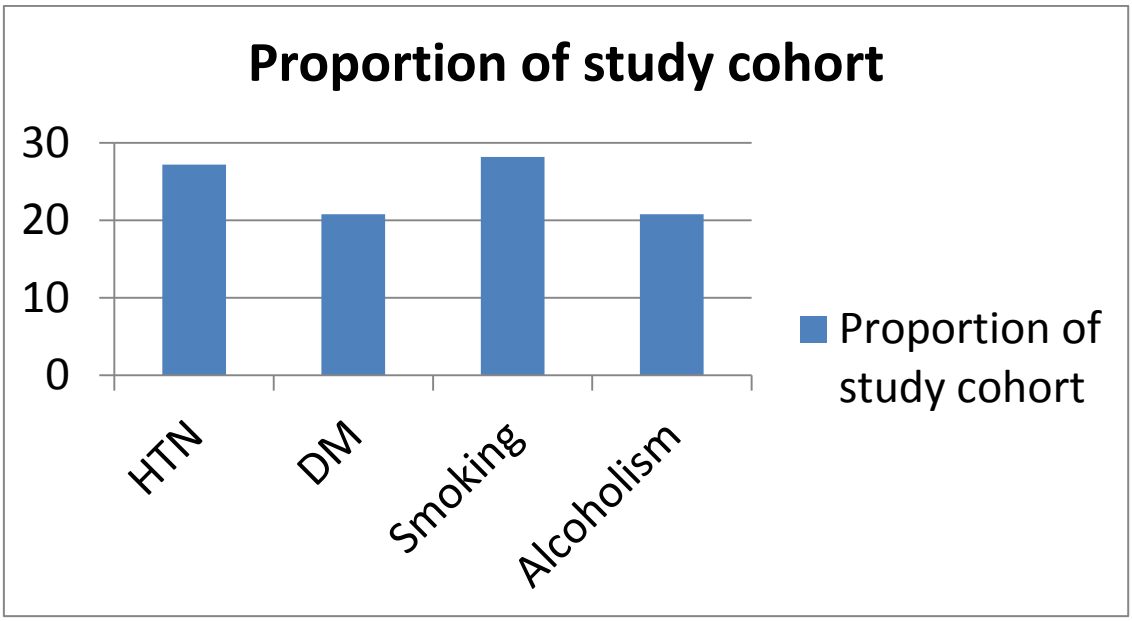


Figure 5

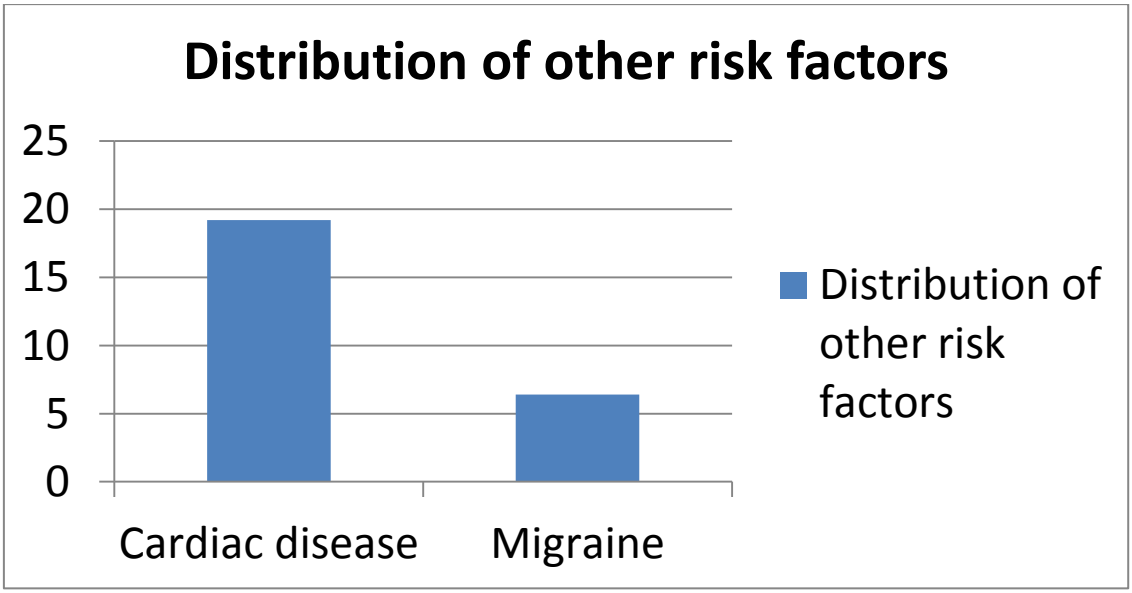
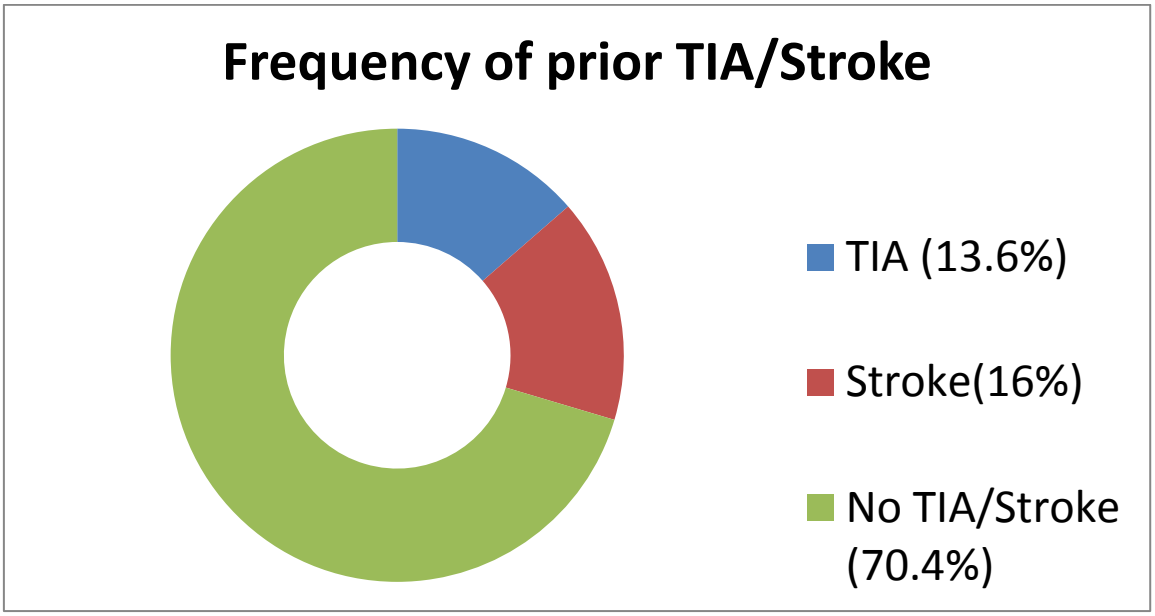


Figure 6



At presentation 8 patients (6.4%) had irregularity of pulse which was a clue to an etiology of stroke.

105 patients required hospital admission while rest (n=20) were treated on OPD basis. Mean duration of hospital stay was 8.533 days (s.d.5.04, range 1-25).

Other important observation at admission is shown in Table 3

Table 3: Observations at presentation

Observation	Mean	Median	S.D	Range
SBP	135.184	130	24.14	90- 250
DBP	82.752	80	11.99	60-120
RBS	121.067	106	51.94	57-326
GCS	14.488	15	1.6	4-15
NIHSS	7.576	6	6.32	0-32
m-RS	2.928	3	1.35	0-5

All patients underwent routine cardiac evaluation including ECG, Transthoracic Echo. Transesophageal Echo and Holter monitoring were performed if clinically indicated. ECG and Echo findings are mentioned in Table 4, Fig 7,8.

In 84% patients ECG was normal while other abnormality found in ECGs were LVH, Left atrial enlargement, recent or old MI. Echocardiogram was normal in ~70% of patients while LV Dysfunction(6.4%), Thrombus(0.8%), Valve disease(9. 6%), IE(1.6%) were noticed in rest which were important clue for diagnosis and management point of view. In addition PFO was noticed in 11.2%, out of which a clinically significant PFO defined as presence of atrial septal aneurysm and right to left shunt on valsalva with in first 3 breath was demonstrable in only 3 patients who underwent successful PFO closure. Holter monitoring was performed in 30% of patients but diagnostic yield of was poor, only 3 patients had significant abnormality leading to change in treatment modality. (Fig 9)

Table 4: ECG abnormalities at presentation

ECG Changes	Number	Percent (%)
Normal	105	84
LVH	4	3.2
LAE	8	6.4
Old MI	6	4.8
Recent MI	2	1.6

Figure:7

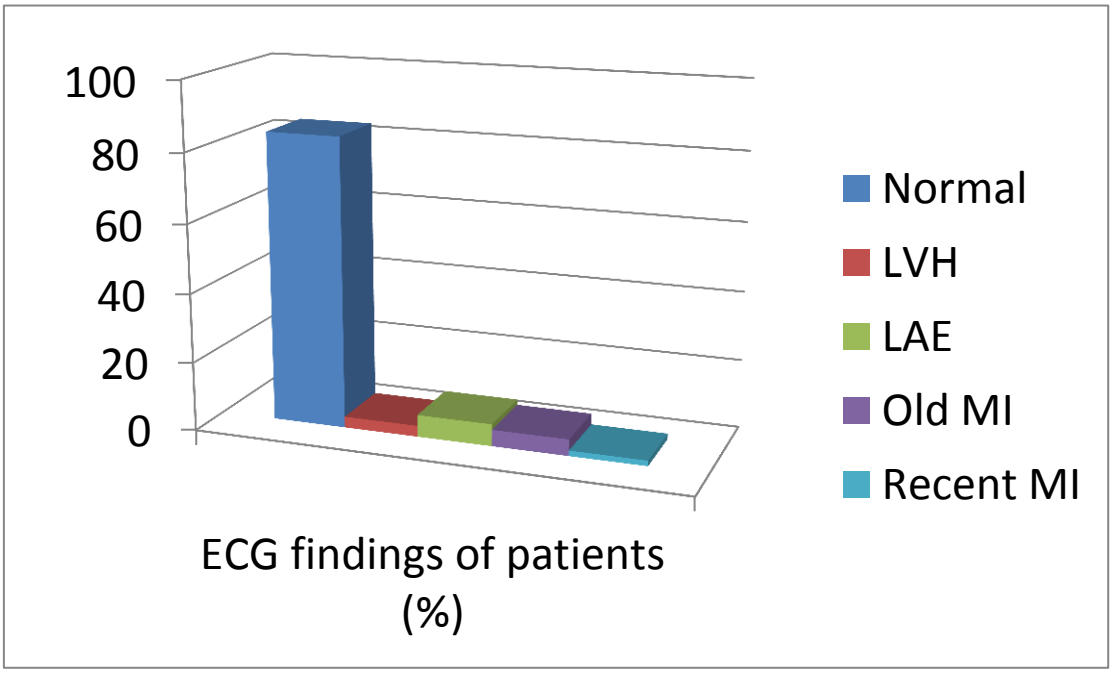


Figure 8.

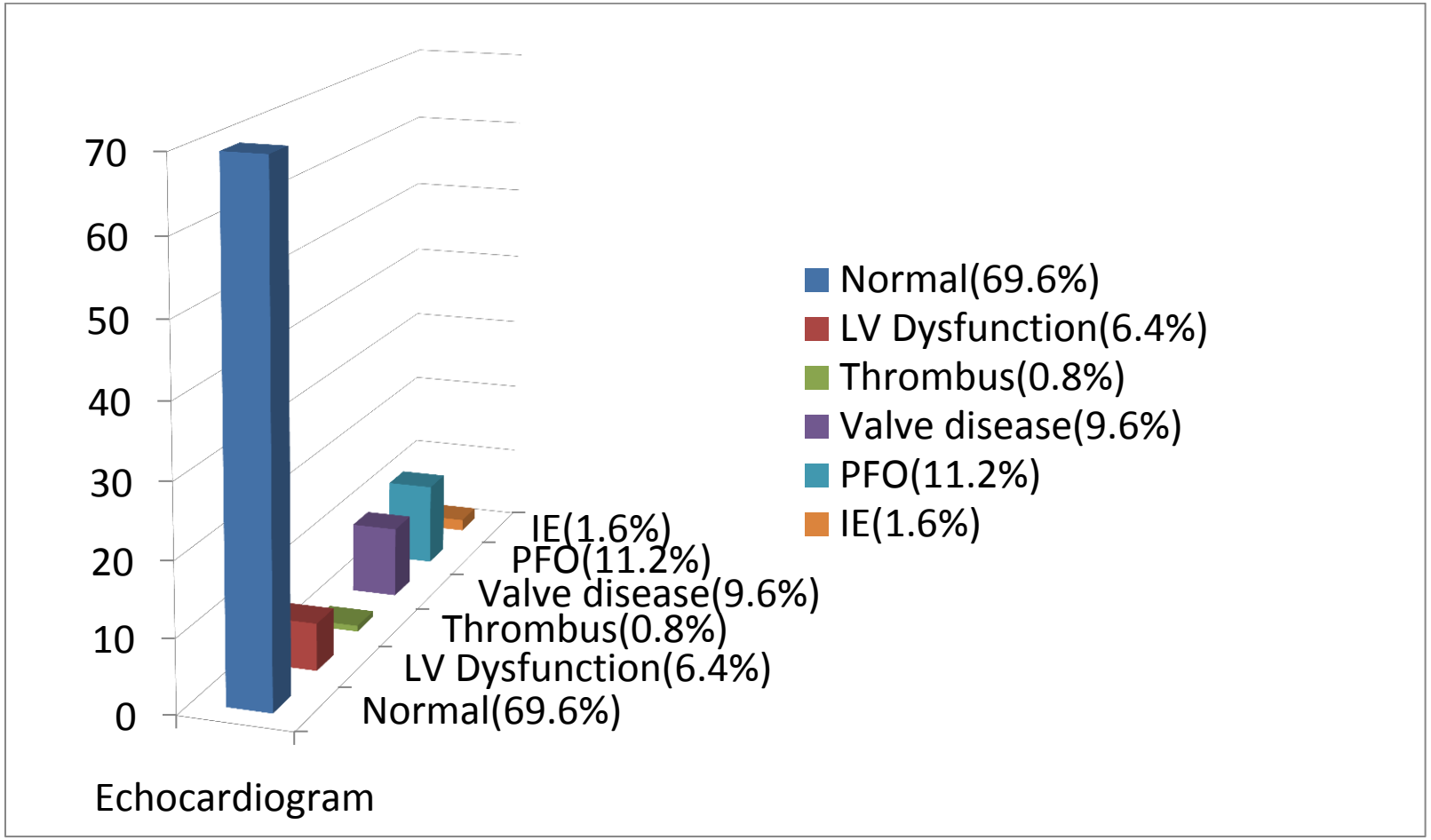

70
60
50
40
30
20
10
0
IE(1.6%)
PFO(11.2%)
Valve disease(9.6%)
Thrombus(0.8%)
LV Dysfunction(6.4%)
Normal(69.6%)
Normal(69.6%)
LV Dysfunction(6.4%)
Thrombus(0.8%)
Valve disease(9.6%)
PFO(11.2%)
IE(1.6%)
Echocardiogram

Fig 9

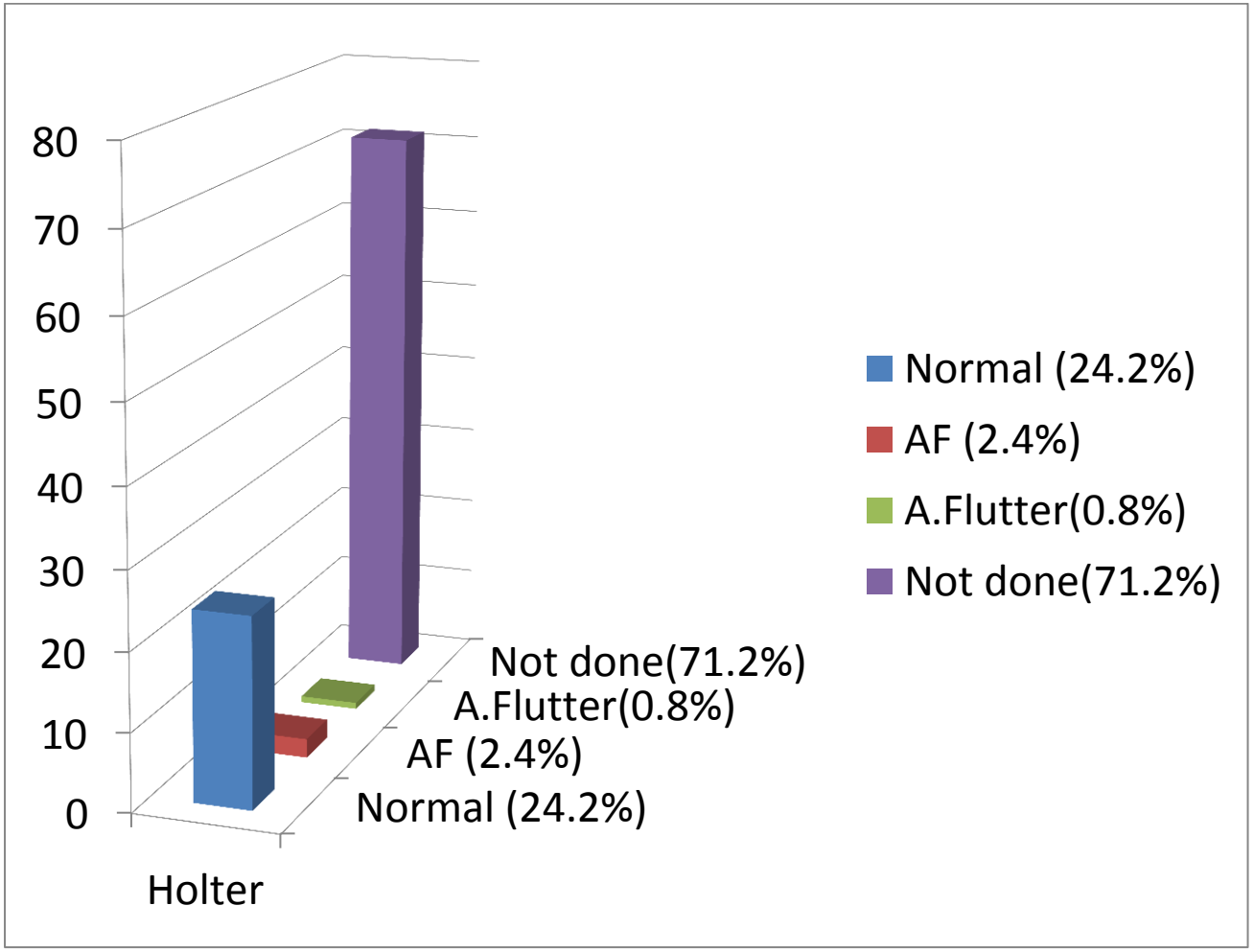
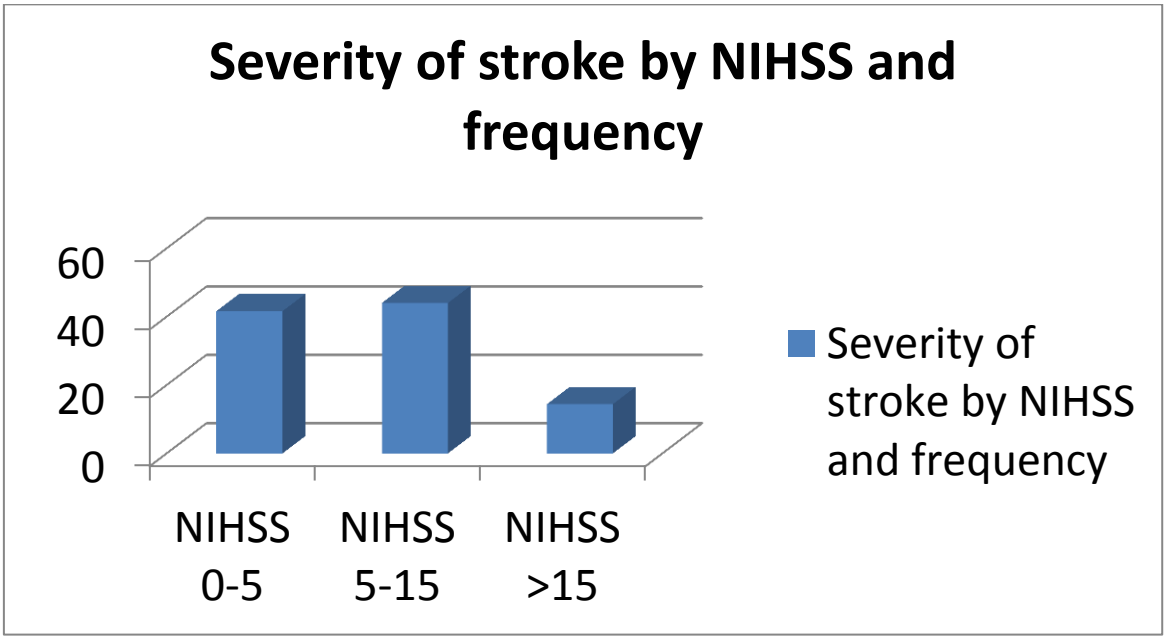

80
70
60
50
40
30
20
10
0
Holter
Not done(71.2%)
A.Flutter(0.8%)
AF (2.4%)
Normal (24.2%)
Normal (24.2%)
AF (2.4%)
A.Flutter(0.8%)
Not done(71.2%)

Table 5: Severity at presentation by NIHSS

NIHSS	frequency	Percent (%)
0-5	52	41.6
5-15	55	44
>15	18	14.4

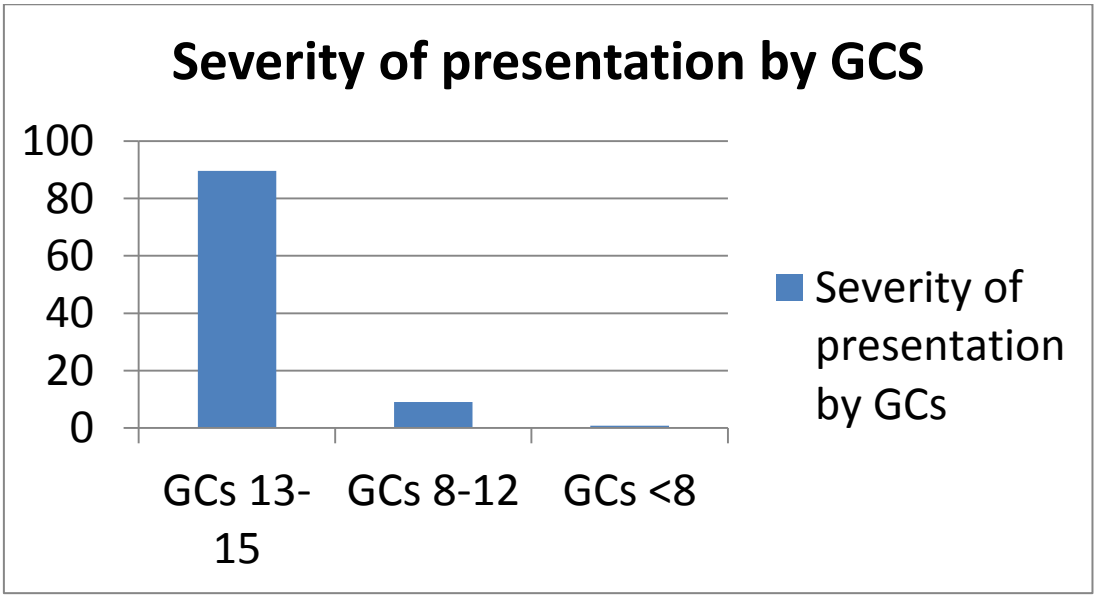
Fig 10



As shown in Table 5 and fig 10 majority of stroke were minor or moderate in severity while a major stroke defined as NIHSS >15 was observed in ~15% of total patients. Disability defined as mild, moderate and severe (based on m-RS) were more or less equally distributed (~33%) in each group despite the majority of patients presenting with good GCs except for one whose presentation GCs was very poor (<8).(Table 6, Fig 11,12)

Table 6 : Severity at presentation : GCs and m-RS

GCS	**GCS 13-15**	**GCS 8-12**	**GCS<8**
	112(89.6%)	**11(9%)**	**1 (0.8%)**
m-RS	**m-RS 0-2**	**m-RS 3**	**m-RS 4-5**
	39(31.2%)	**43(34.4%)**	**43(34.4%)**
Fig 11,12			



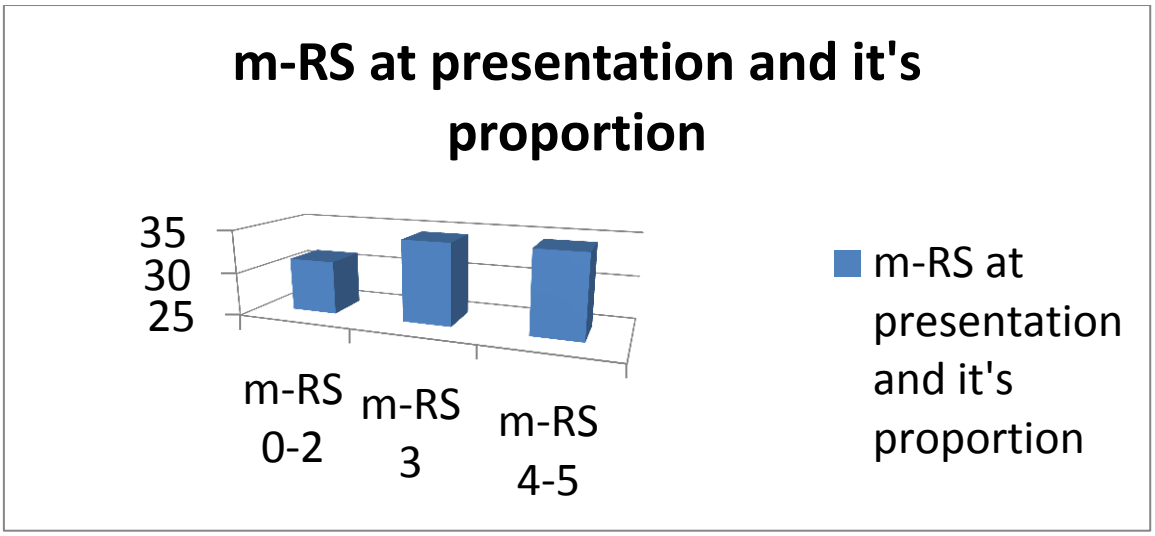
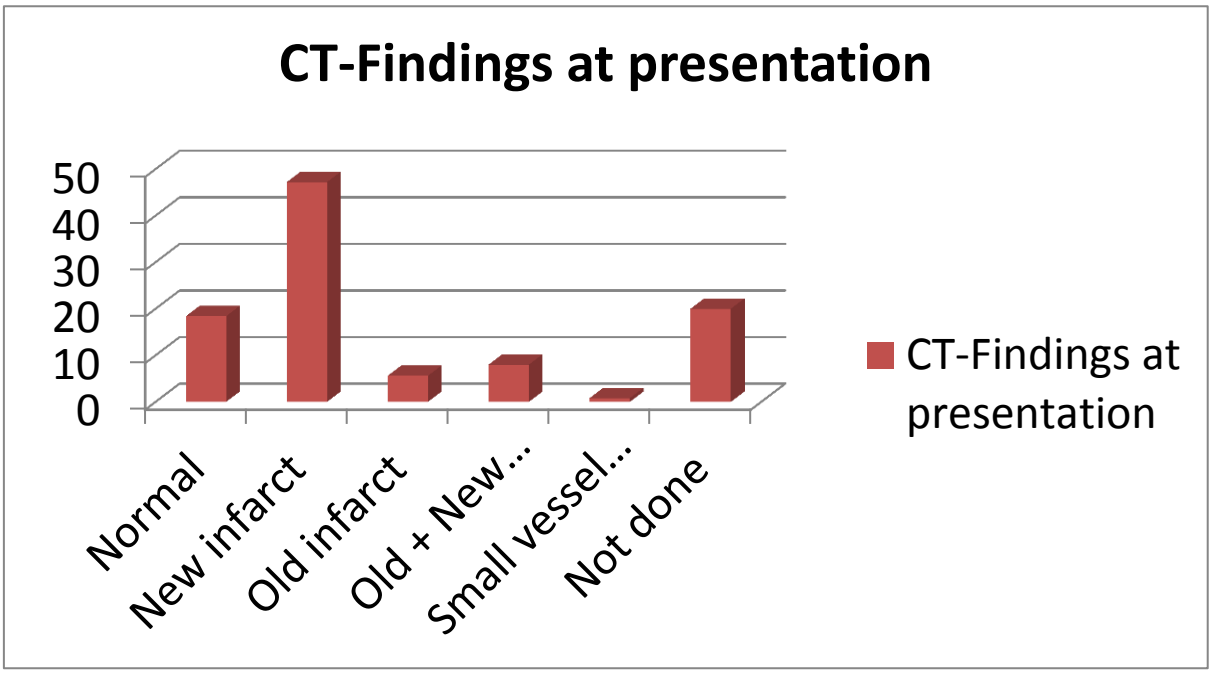


Table 7: CT findings at presentation

CT Finding at Presentation	Percentage
Normal	18.4
New infarct	47.2
Old infarct	5.6
Old + New infarct	8
Small vessel ischemic changes	0.8
Not done	20

Fig13



At presentation CT-Brain was done in 80% of cases [In rest MRI was performed at presentation due to suspicion of posterior circulation stroke and stroke mimicker]. New infarcts were seen in 50% of cases while in 18% it was normal.

Fig14

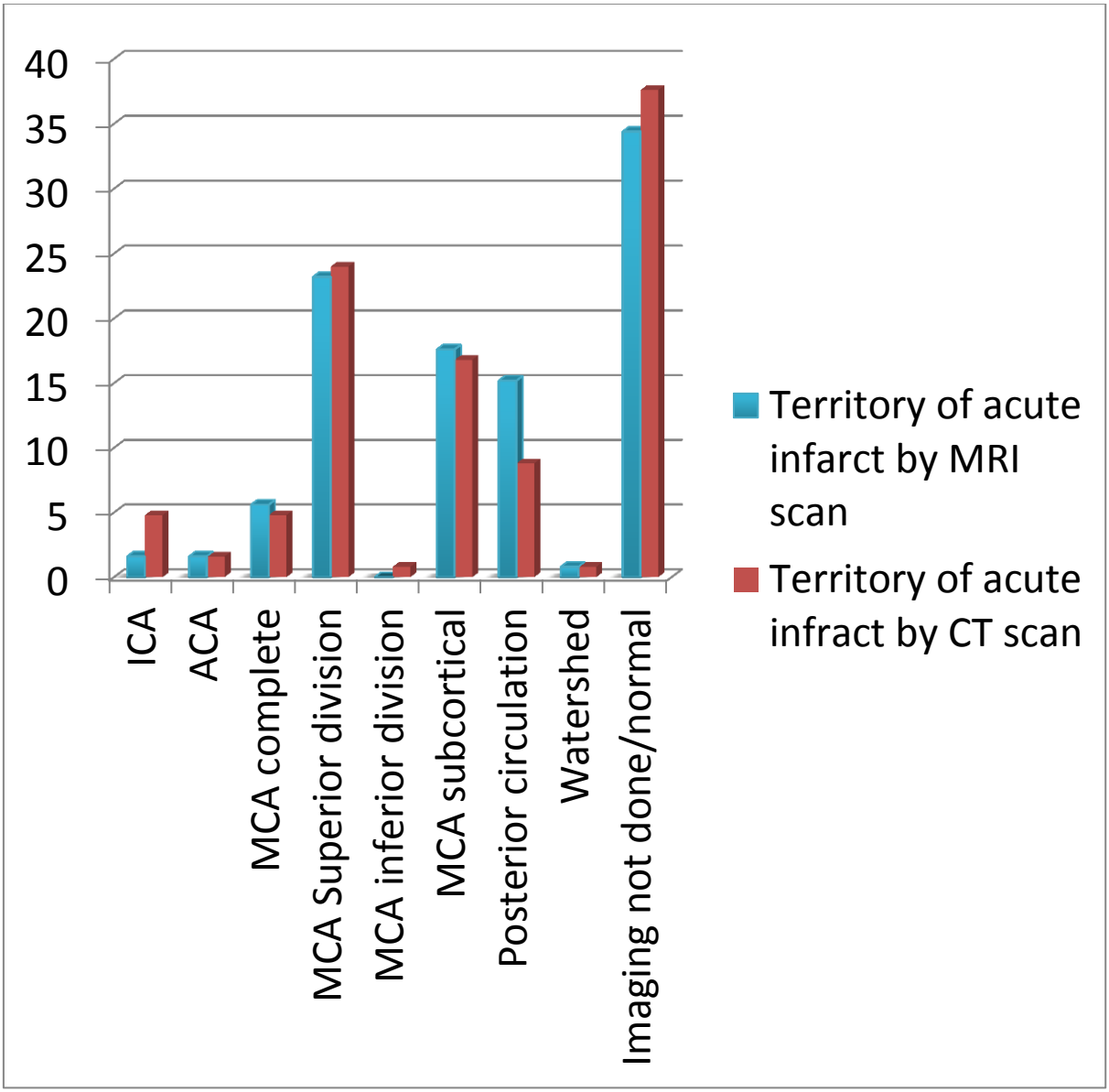

40
35
30
25
20
15
10
5
0
ICA
ACA
MCA complete
MCA Superior division
MCA inferior division
MCA subcortical
Posterior circulation
Watershed
Imaging not done/normal
Territory of acute infarct by MRI scan
Territory of acute infract by CT scan

Table 8: Territory of acute infarct on CT Scan

Territory of acute infract by CTscan	Percentage
ICA	4.8
ACA	1.6
MCA complete	4.8
MCA Superior division	24
MCA inferior division	0.8
MCA subcortical	16.8
Posterior circulation	8.8
Watershed	0.8
Imaging not done/Normal	37.6

The territory of stroke in majority of patients were in anterior circulation (91%) while posterior circulation stroke accounted by 9%. In anterior circulation the frequency of stroke in descending order is as follows: MCA superior division, MCA subcortical, MCA complete, ICA, ACA and MCA inferior division. Almost similar findings were observed on MRI also. Dense – artery-sign which signify an occlusion of affected artery was seen in 10% of case, out of which majority were in MCA followed by basilar and ICA. Branch artery occlusion was not included in this.

Fig 15

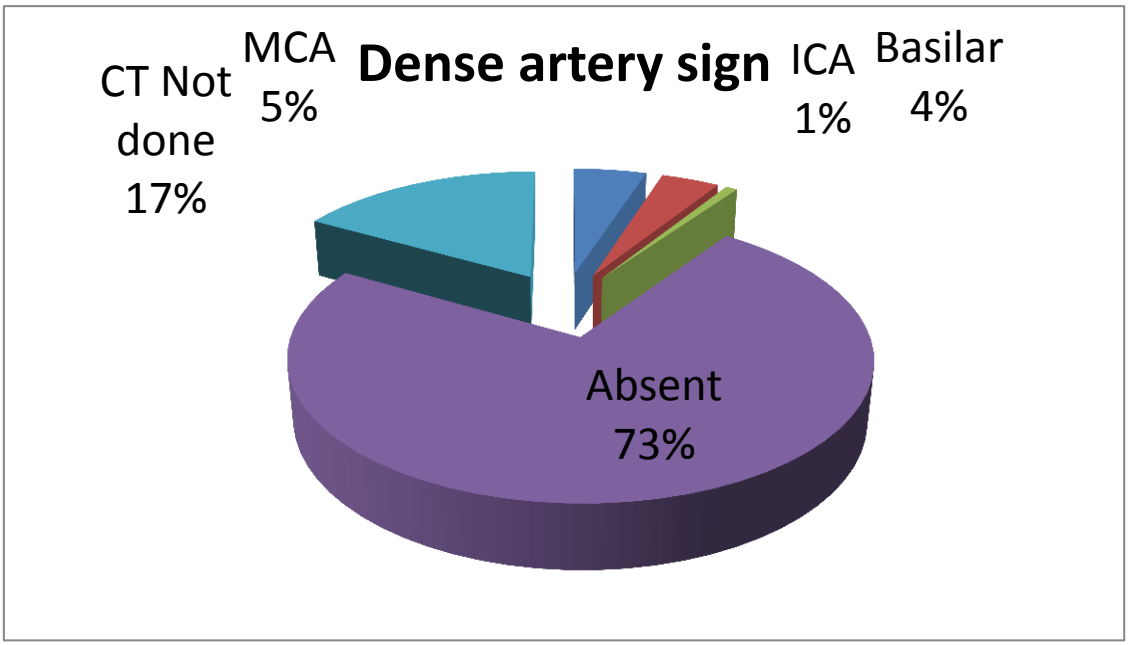


Table 9 : Angiographic abnormality

	CT Angiogram Extracranial	CT-Angio Intracranial	MR Angio Extracranial	MR Intracranial	DSA
Normal	31.2	33.6	8.2	23.2	8
Abnormal	21.6	18.4	3.2	23.2	17.6
Not done	47.2	48	1.4	53.6	74.4

Fig 15

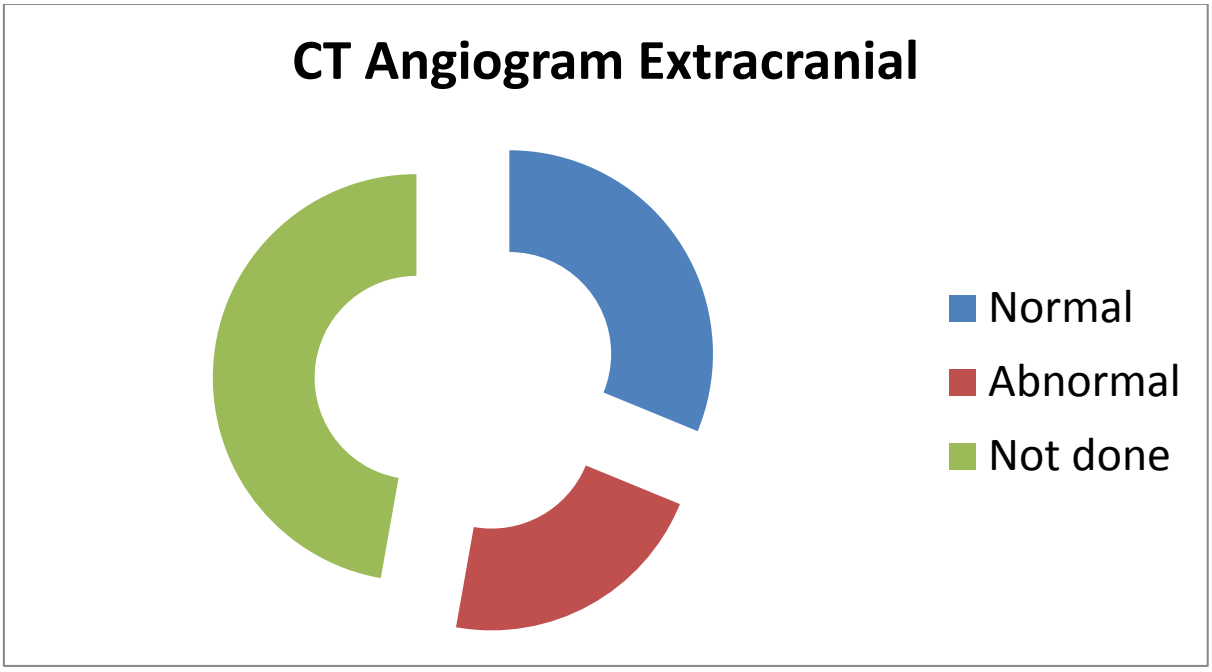

CT Angiogram Extracranial
Normal
Abnormal
Not done

Fig 16

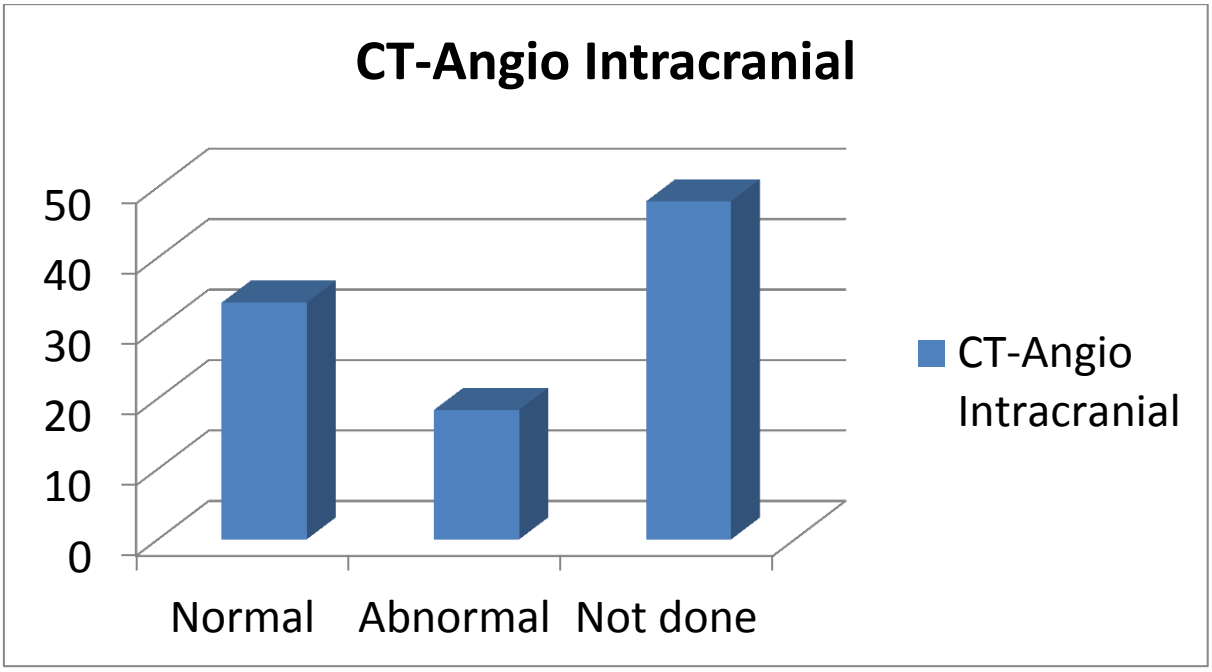

CT-Angio Intracranial
50
40
30
20
10
0
Normal
Abnormal
Not done
CT-Angio Intracranial

Fig 17


MR Angio Extracranial
Normal
Abnormal
Not done

Fig 18

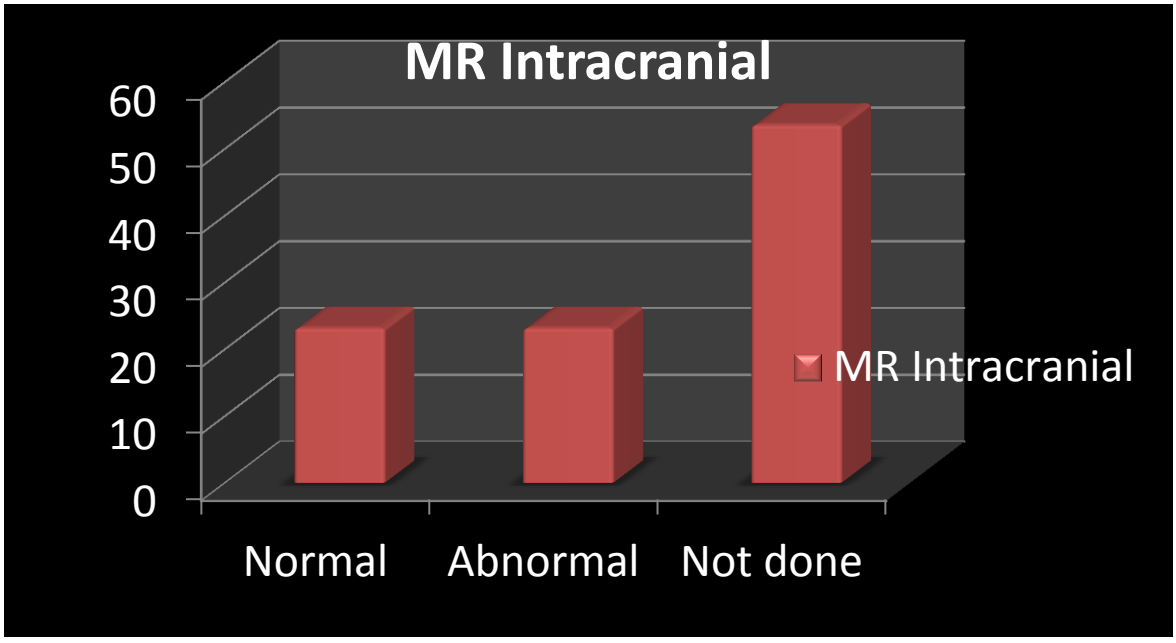
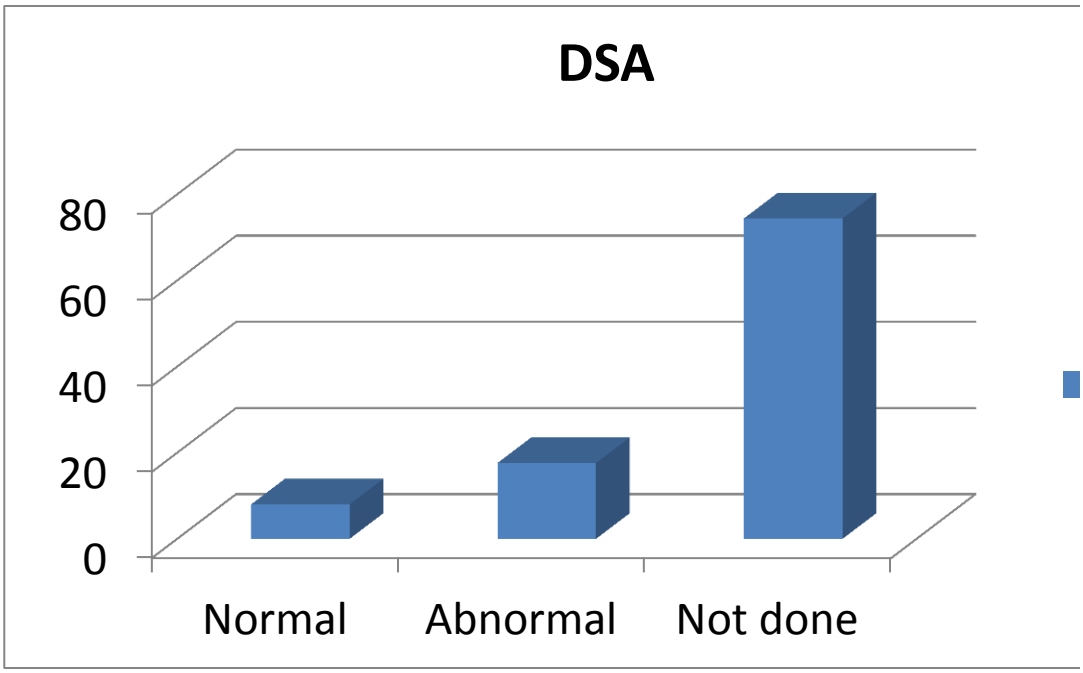

MR Intracranial
60
50
40
30
20
10
0
Normal
Abnormal
Not done
MR Intracranial

Fig 19



All patient underwent some form of angiogram either CT-Angio, MR Angio or DSA. Few patients received more than one modality for diagnosis , if it was not clear from one modality. A self explanatory table 9 had shown different modality used and abnormality of intra and extracranial circulation which includes occlusion, dissection, stenosis, vasculitis, vasculopathy including moya moya collaterals and helped in etiological diagnosis and treatment plan.

Fig 20: DWI abnormality at presentation

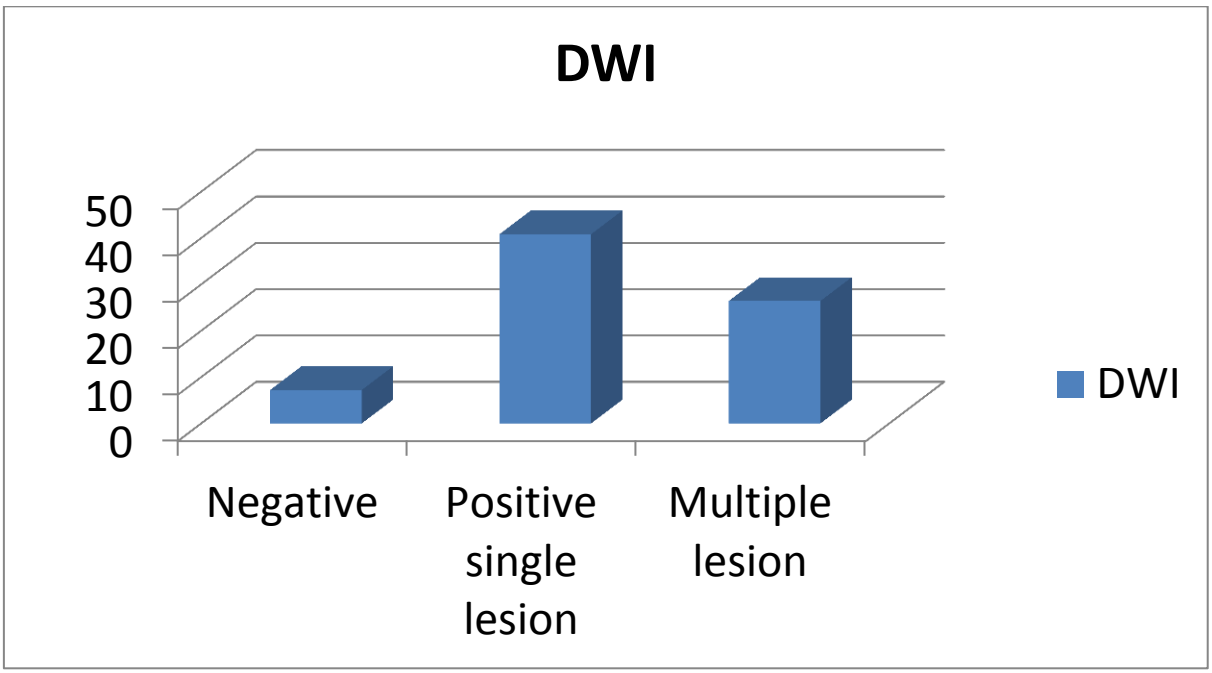
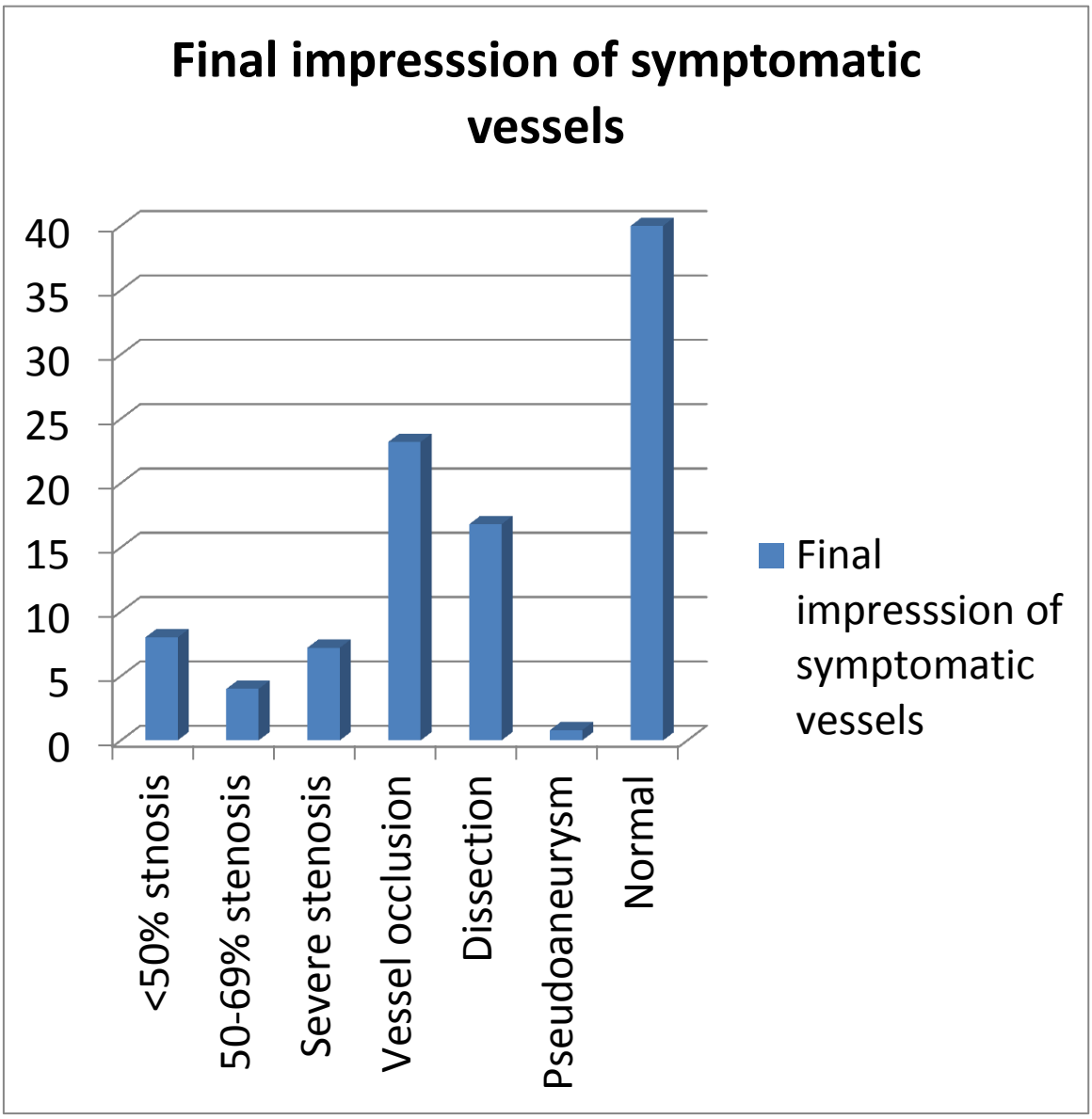


Fig:21.



As mentioned in figure 21, symptomatic vessel were completely normal in aprox. 40% of cases. The major abnormality noticed were vessel occlusion followed by dissection. Rest of the vessels showed mild to moderate or severe stenosis.

An important aspect of our study was to evaluate the etiology (Table 10 and figure 22,23). Despite extensive evaluation , etiology remained undetermined in 33.6%. Among determinable etiology, other specific etiology group was the most common subgroup(27.2%) as per TOAST

criteria followed by cardioembolic(16.8%). Large artery atherosclerotic disease accounted for 14.4% etiologies while lacunar strokes were seen in 8%. In specific etiology group, major etiology comprised of dissection of extracranial vessels, while other etiologies included prothrombotic conditions like APLA syndrome, vasculitis and haematological disorder like polycythemia. One new finding in our study was delayed vasculopathy after atrial myxoma resection and other vasculopathy of undetermined etiology (affecting MCA bifurcation without recent varicella infection) which had been recognised as a separate entity by AHA in 2013.

Table 10 : Etiology of stroke and it's proportion

Etiology of Stroke	Percentage of all Etiology
Large artery atherosclerotic disease	**14.4**
Cardioembolic	**16.8**
RHD including mechanical valve	4.8
PFO	3.2
RWMA	2.4
Atrial fibrillation	2.4
Infective Endocarditis	1.6
Endomyocardial fibrosis	0.8
Other specific causes	**27.2**
Dissection	18.4
Prothrombotic	4.8
Vasculitis	3.2
Moya Moya	0.8
Hematological	0.8
Myxoma associated vasculopathy	0.8
Other vasculopathy	0.8

RCVS		0.8
Undetermined	**33.6**	
Lacunar	**8**	

Fig 22

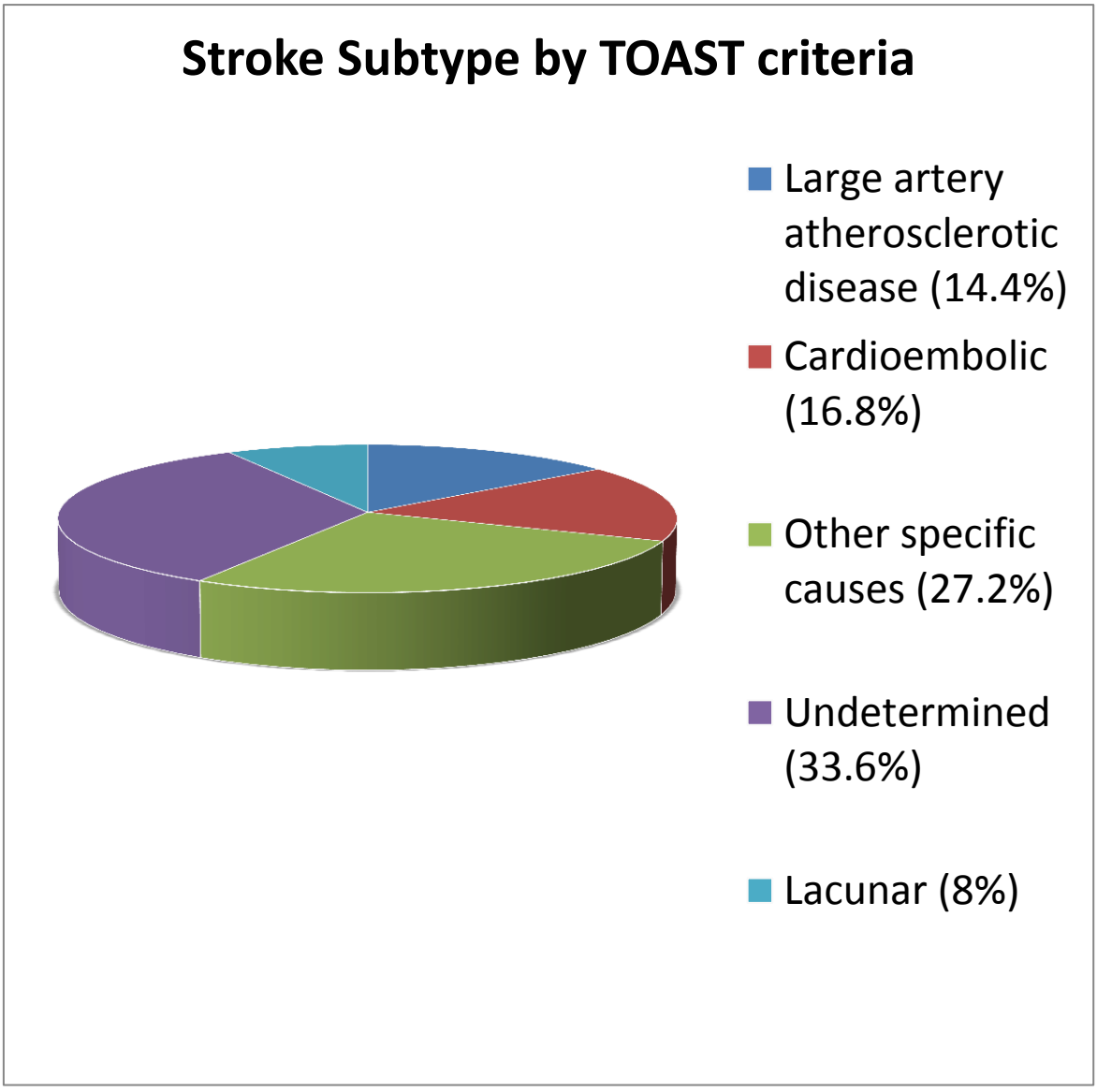
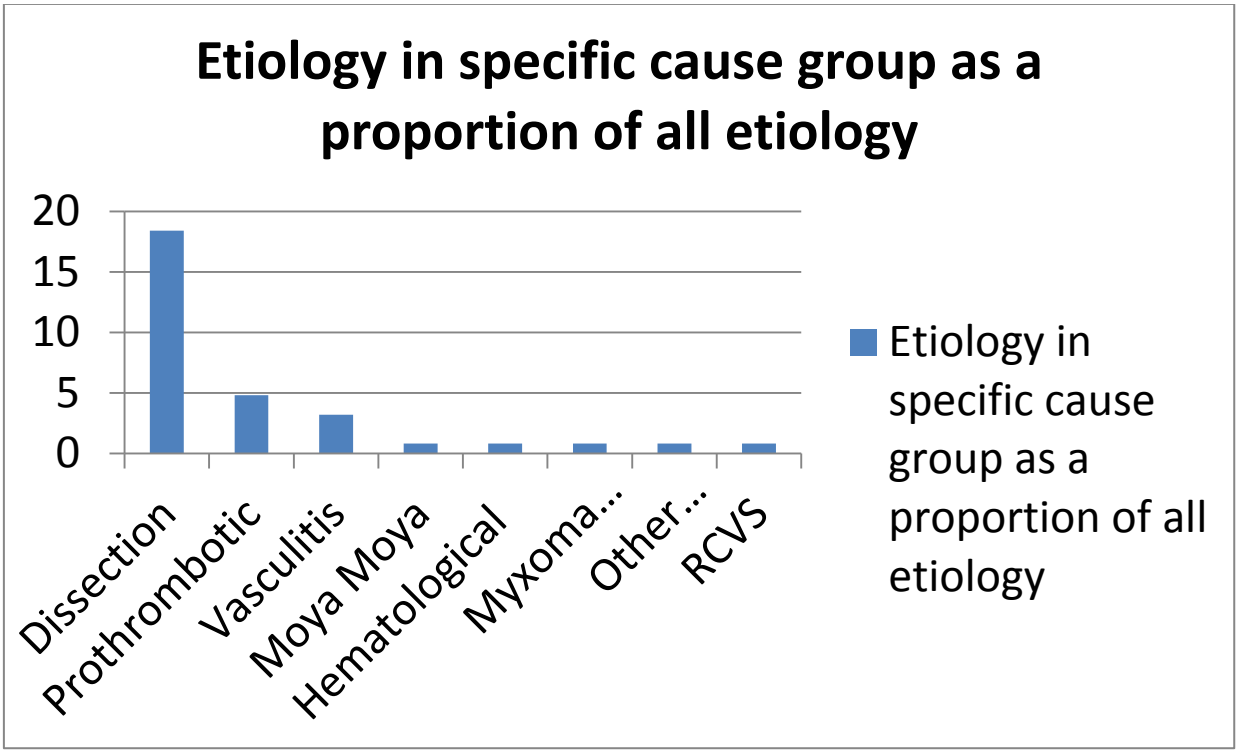


Fig23



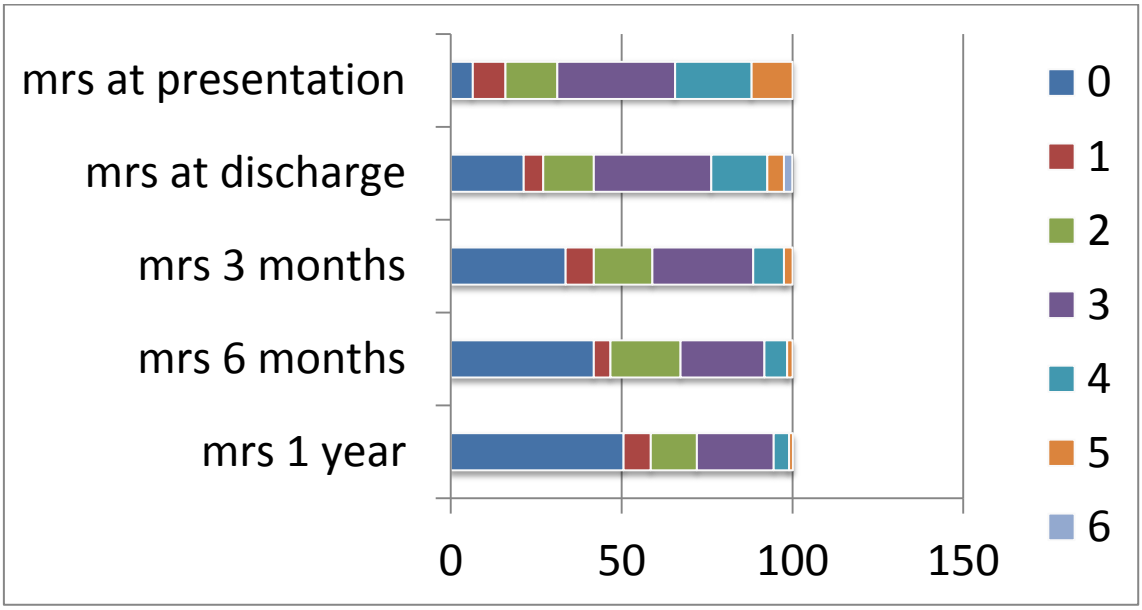
Among three patients succumbed due to severity of stroke, two were due to cardioembolic etiology while one was due to dissection.

We followed our patient at 3 months, 6 months and 1 year. Follow up m-RS and NIHSS were documented in all patients. In addition, any new events if happened were also recorded. New event on follow up was noticed in 8 patients. In 6 patients it was new infract while in 2 patients a delayed hemorrhagic transformation was noticed.

Table 11: m-RS at admission and follow up :

m-RS	0	1	2	3	4	5	6
At presentation	6.4	9.6	15.2	34.4	22.4	12	
At discharge	21.3	5.7	14.8	34.4	16.4	4.9	2.4
3 months	33.6	8.2	17.2	29.5	9	2.5	
6 months	41.8	4.9	20.5	24.6	6.6	1.6	
1 year	50.6	7.9	13.5	22.5	4.5	1.1	

Fig24



As shown in Table 11 and fig 24 there was progressive improvement in m-RS from admission to discharge except in 3 patients, who died after 1st event, for whom m-RS 6 was considered. At the end of 1 year, 50% patient

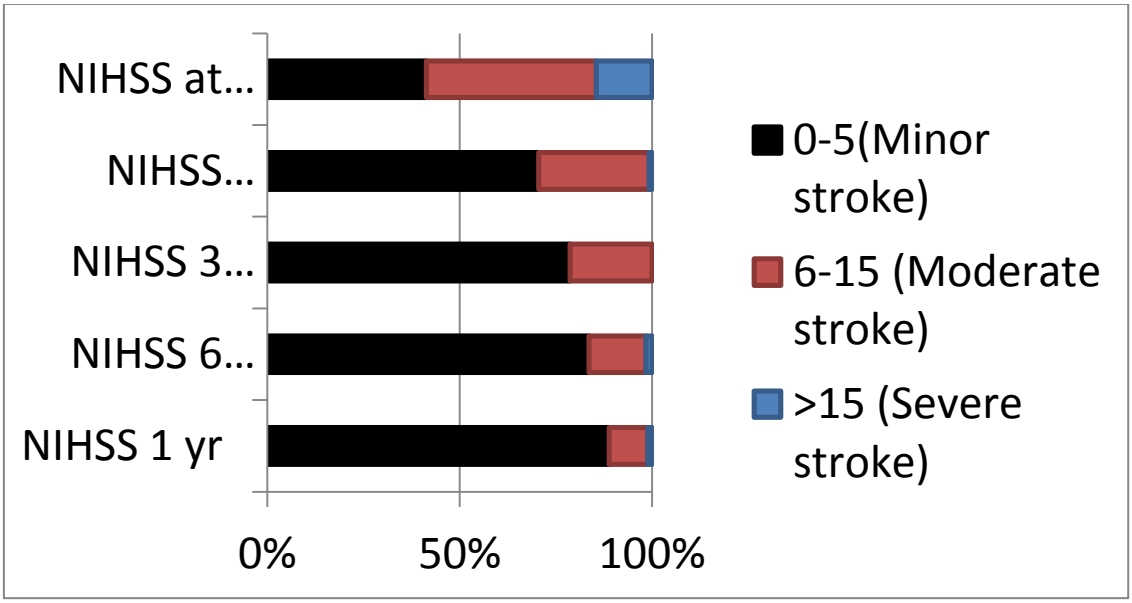
achieved m-RS of 0 which is an ideal goal, while only 5.6% patients remained as m-RS 4 and 5 at 1 year while this grade of m-RS was present at admission in 34.4%. This data suggests an excellent recovery in younger population with continuous rehabilitative measures.

Similarly if we look at NIHSS, a score of >15 which is a marker of severe stroke was present in 14.4% of patients which improved to 0% at 3 months but due to recurrence of events in few patients, the proportion of patients with this severe stroke at 6 months and 1 year is 1.6% and 1.1% respectively. NIHSS of <5 was achieved in 88% of patients at the end of 1 year which is in parallel with improvement in m-RS.

Table 12: NIHSS at presentation and follow up :

NIHSS	0-5(Minor stroke)	6-15 (Moderate stroke)	>15 (Severe stroke)
At admission	41.1	44	14.4
At Discharge	70.5	28.7	0.8
3 months	78.7	21.3	0
6 months	83.6	14.8	1.6
1 yr	88.8	10.1	1.1

Fig25



As far as treatment is concerned 43.8% patients received Ecospirin alone, 4.8% clopidogrel, while 33.8% received dual antiplatelet agents. Warfarin was prescribed to 17.6% patients; in majority it was due to valvular heart disease or atrial fibrillation. In one patient with cervical artery dissection who had recurrence of stroke while on dual antiplatelet agents, warfarin was given for 6 months. 4 patients received IV thrombolysis with good outcome. A separate analysis was not performed for patients who received thrombolysis due to very less number of patient in this group. Only 10 patients reached in the window period for thrombolysis, out of which only 4 patients were eligible for thrombolytic therapy. The most important reason for delayed presentation was delayed recognition of symptoms by patient or relatives as well as delayed referral from 1st health care center encountered. One patient who developed in- hospital stroke while receiving treatment for infective endocarditis underwent mechanical thrombectomy and retrieved clot demonstrated presence of gram positive cocci on microscopy. This patient had an excellent outcome and had NIHSS of 0 and m-RS of 0 at discharge underscoring the need for decision making beyond guidelines in

selected patients. Moya-Moya revascularization by STA-MCA bypass was performed in two patients who had recurrence of stroke while on conservative management and had an excellent course following surgery. PFO closure was done in 3 patients with high risk PFO and all had no recurrence in 3 years of follow up. Two patients required hemicraniectemy due to malignant MCA stroke with etiology being cardioembolic in both. In hemicraniectemy group one patient achieved m-RS of 3 while the other one was dependent on last follow up available. None of the patient underwent any stenting/endarterectemy.

Univariate analysis showed that the outcome by means of m-RS and NIHSS at 3 months, 6 months and 1 year was significantly influenced by severity of stroke($p<0.005$) and etiology being cardioembolic ($p=0.01$) and dissection ($p=0.02$). While other factors like gender, age groups, smoking, alcoholism, hypertension, diabetes mellitus, prior history of TIA/Stroke, presenting SBP/DBP, random blood sugar at presentation, side of involvement, anterior Vs posterior circulation stroke and vessel status did not influence the outcome in our study.

Multivariate analysis also showed findings similar to univariate analysis.

Discussion

Discussion

Risk Factor Pattern: A comparison of previous studies from India Vs western studies Vs Present study :

The prevalence of various risk factors in stroke in young has been analysed in two studies from India. In a case control study of young stroke patients by Lipska et al[8](age group15–45 years) with age and sex matched hospital and community controls, prevalence of various risk factors were studied. In the study of Lipska et al, 214 South Indian patients with first acute ischemic stroke and 99 hospital and 96 community controls were included. There was higher prevalence of smoking (odds ratio [OR] 7.77), systolic blood pressure (OR 1.88) and fasting blood glucose (OR 4.55) in patients. High density lipoprotein (HDL) was low and total cholesterol/HDL ratio was high in cases when compared with both hospital and community controls.

A unit increase in the ratio of total cholesterol to HDL was associated with doubling of stroke risk. More than three components of metabolic syndrome were present in 12.6% cases when compared to 6% of community controls. Presence of three components of metabolic syndrome was also strongly associated with stroke (OR 4.76).

In another study in 1997 by Nayak et al[116],177 patients with first ever ischemic stroke (age group 15–45 years) were included retrospectively based on hospital data, with 76% male and 24% female patients. Hypertension was present in 18% of the patients, whereas diabetes mellitus was present in 7% only. 69% of male patients were smokers. Dyslipidemia in the form of elevated cholesterol was present in 17% and increase in triglycerides was observed in 42% patients.

In a study of stroke in the young from Southeast Asia by Lee et al [126], the most common risk factors observed were hyperlipidemia (53.1%), smoking

(49.8%), hypertension (45.8%) and a family history of stroke (29.3%). The presence of hyperlipidemia and hypertension was more commonly seen in patients with small vessel occlusion, large artery atherosclerosis and stroke due to unknown etiology, whereas hyperlipidemia was less commonly associated with cardioembolic stroke.[126]

Analysis of prevalence of risk factors in studies of stroke in young from the west reveals prevalence of hypertension from 20 to 60%. In Baltimore Washington Cooperative Young Stroke Study[128] examining 296 incident stroke cases in Black and White adults, hypertension was present in 61% of Black patients. Prevalence of smoking was 40-57%.

In Helsinki Young Stroke Registry which included 1008 patients with first ever ischemic stroke in the age group of 15–49 years, hypertension, smoking and dyslipidemia with high total cholesterol emerged as important risk factors. The prevalence of hypertension increased with increasing age and was seen in 28.3% of patients in 15–44year age group[128], whereas it was prevalent in 51.7% of patients in 45–49 year age group. Similarly, 38.4% of patients in 15–44 year age group and 54.5% in 45–49year age group had increased level of cholesterol. Low HDL was present in 15.3 and 23.9% of the patients, respectively. Increased LDL was also present in 38.4%patients in 15–44 year age group and in 54.5% patients in 45–49 year age group. Smoking as a risk factor was observed in around 47% patients in both the age groups.

With above mentioned studies it appears that the risk factor profile becomes similar to older population with increasing age, the change becoming more apparent at around 44 years of age. In a study of 203 patients of stroke in age group of 15–45 years from Switzerland, hypercholesterolemia(39%) and smoking (46%) were important risk factors, however, hypertension was present in 19% patients only. Increased C reactive protein level was observed in 36% patients.[128]

In our study , we noticed prevalence of Hypertension in 27.2 %, Diabetes 20.8%, Smoking 28.2%, and Alcoholism in 21% cases. Prevalence of migraine was 6.4% and OCPs was 0.8%, which seems to be negligible and did not influence risk of stroke in our cohort. In our cohorts, the classical risk factors are more common than the previous study of Nayak et al but less than the western populations. It may be because of influence of pattern of industrialisation and effect of change in life style pattern in south Asian countries.

Etiology of Stroke in Young : A comparison of previous studies from India Vs western studies Vs Present study :

In a study on stroke in young from our institute by Nayak et al, the patients of ischemic stroke were classified based on Trial of ORG 10172 in Acute Stroke Treatment(TOAST) criteria; 25.2% patients had cardioembolic[116] stroke, 12.6% had large artery atherosclerosis and 7.5% had lacunar infarcts. Strokes due to other determined etiology were 11. 2% (7.0% arterial dissection, and one patient each with SLE, APLA syndrome and protein S deficiency). Four patients had stroke due to other causes (one each of Moya moya disease, Takayasu's arteritis,fibromuscular dysplasia and nephritic syndrome).

While data from several western studies indicate that 21–48% of strokes in the young are caused by atherosclerotic large artery occlusive disease, 10–33% are due to non-atherosclerotic large artery occlusive disease (dissections have comprised 10–20% in some studies), 13–35% are caused by cardioembolism, 3–18% by penetrating artery disease, 8–15% by prothrombotic states and 4–15% by miscellaneous causes. Cryptogenic stroke comprises 7–40% of the cases.

Cervical artery dissection was one of the relatively common causes of stroke in young in western series, various studies reported that around 6–15% of

the patients had carotid artery dissection. Carotid and vertebral artery dissection were seen with a variable frequency. In one study, 24patients had arterial dissection among 170 patients who underwent angiographic studies, with carotid dissection in 13 and vertebral dissection in 11.

Putaala *et al.*[2] in a study of stroke in young from Helsinki, reported that 59% of patients with stroke of other determined etiology had cervical or intracranial artery dissection. Out of 155 patients with dissection, 80 had vertebral artery dissection and 67 had internal carotid artery dissection. Other causes of stroke like APLA syndrome, factor V Leiden mutation, proteins C and S deficiency, ANA positivity, SLE, fibromuscular dysplasia, migraine-related stroke andother vasculitis were observed in 1–2% of patients.

The different subtypes of ischemic stroke in different studies are outlined in Table 16.

In our study we noticed Large artery atherosclerotic disease in 14.4%, Cardioembolic 16.8% [RHD including mechanical valve 4.8%, PFO 3.2%, RWMA 2.4%, Atrial fibrillation 2.4%, Infective Endocarditis 1.6%, Endomyocardial fibrosis 0.8%], Other specific causes 27.2% [Dissection 18.4, Prothrombotic4.8, Vasculitis 3.2, Moya Moya 0.8%, Hematological 0.8%, Myxoma associated vasculopathy 0.8%, other vasculopathy 0.8%, RCVS 0.8%], Lacunar 8% and etiology remained undetermined in 33.6%.

Therefore, if we compare our study with previous study done by Nayak et al, the proportion of patients with undetermined etiology had reduced while number of patients with other specific etiology had increased. This change is observed in same institute and in similar population, which could be due to advancement in diagnostic modalities. In addition, there is significant reduction in proportion of patients with cardioembolic stroke which is

possibly due to reduction in number of cases with RHD which was seen in last 15 years due to better preventive strategies.

Table 16 : Comparative analysis of present studies Vs previous studies

Study	**Age group**	**Patient no**	**LAA**	**SVO**	**CE**	**ODE**	**UDE**
Adams et al[121], (Iowa, USA) 1995	**15–44**	**329**	**21.6**	**8.2**	**19.5**	**24.5**	**25.7**
Nayak et al[116] (India) 1997	**15–45**	**177**	**12.6**	**7.5**	**25.2%**	**11. 2%**	**43**
Kittner *et al.,* **1998 (Baltimore, USA)[122]**	**15–44**	**428**	**2**	**10**	**15**	**35**	**38**
Leys *et al.,* **(France) 2002[127]**	**15-45**	**287**	**8.4**	**1.7**	**5.2**	**22.3**	**62.5**
Lipska *et al.,* **(India) 2007[8]**	**15–45**	**214**	**12.6**	**7.5**	**25.2**	**11.2**	**43.5**
Putaala *et al.,* **(Finland) 2009** Helsinki Young Stroke Registry [2]	**15-49**	**1008**	**7.5**	**13.8**	**19.6**	**26**	**31**
Wasay M., Kaul S Et al 2010[130]	15–45	958	24%	15%	19%	**NM**	**NM**
Present study Mandliya et al	15-45	125	14.4	8	16.8	**27.2**	**33.6**

LAA : Large artery atherosclerotic disease, SVO : Small vessel occlusive disease, CE: Cardioembolic, ODE : Other determined etiology, UDE: Undetermined etiology.

Outcome of Stroke in Young : A comparison of previous studies from India Vs western studies Vs Present study :

In comparison to etiology and risk factors which are predominantly determined by race, genetic factors and individual habits, the outcome is predominantly determined by severity of stroke, quality of care provided, rehabilitative measures and risk factor reduction. Hence the outcome may vary between countries and within the countries. and even within same institute/hospital over the time.

Many of the previous studies did not follow a uniform pattern of outcome measurement, some of the studies used functional dependence Vs independence, some used back to work strategies, while a few reported outcome based on m-RS. None of the large studies used NIHSS also as a marker for outcome.

In the study of Nayak et al at a mean follow up of 7 months (range 1-62 months), 75%of the patients were independent or only mildly disabled.

In the study of Varona et al[37] with a study of 272 patients, reported at mean duration of follow up of 12.3 years, 90% of the followed patients were independent for ADL and 53% returned to work, although adjustments were necessary for 23 % of them, m-RS 0 was achieved in 27% cases.

In another study of Leys et al [128] comprising 272 consecutive patients, the functional independence defined as m-RS 0-2 was noticed in 94%.

Our study is one of the systematic study which was planned to evaluate outcome measures by both NIHSS and m-RS. Patients were followed up at fixed interval (3 months, 6 months, 1 year and 2 years). All of the patients had 1 year follow up while 2 year follow was done in minority, hence 2 year follow up was not included for final analysis.

There was progressive improvement in m-RS from admission to discharge except in 3 patients who died after 1st event; hence m-RS 6 was considered for them. At the end of 1 year, 50% patients achieved m-RS of 0 which is an ideal goal, while only 5.6% patients remained as m-RS 4 and 5 at 1 year while this grade of m-RS was present at admission in 34.4%. It suggests an excellent recovery in younger population with aggressive management and continuous rehabilitative measures . Similarly, if we look at NIHSS, an score of >15 which is a marker of severe stroke was present at admission in 14.4% of patients while none of the patient had NIHSS of >15 at 3 months but due to recurrence of events in few patients , the proportion of patients with this severe stroke at 6 months and 1 year was 1.6% and 1.1% respectively. NIHSS of <5 was achieved in 88% of patients at the end of 1 year which is in parallel with improvement in m-RS.

Conclusion

Conclusion:

1. Males are at increased risk for stroke in comparison to female in young population.
2. Peak incidence in younger population is between 35-45 years.
3. Traditional risk factors like hypertension, Diabetes Mellitus, Smoking and alcoholism are important risk factors in younger population and are progressively increasing in Indian population in comparison to previous studies the reason could be change in life style, industrialisation and dietary habits.
4. Migraine and possibly OCPs are probably not significant risk factors for stroke in young.
5. Prior TIA and strokes are not uncommon and can be seen in 13.6% and 16% of cases.
6. Proportion of severe stroke is less (14.4%) in comparison to mild (41.6%) and moderate stroke (44%) in young population. The majority of stroke in young population were in anterior circulation (91%) while posterior circulation stroke are less frequent and accounted by 9%.
7. In anterior circulation , the frequency of stroke in descending order is as follows : MCA superior division, MCA subcortical, MCA complete, ICA, ACA and MCA inferior division.
8. Dense-artery-sign was seen in 10% of cases, majority being in MCA followed by basilar and ICA distributions.
9. Etiology of Stroke: Undetermined (33.6%) > other specific cause (27.2%) > cardioembolic(16.8%) > Large artery atherosclerotic disease(14.4%) > lacunar (8%).
10. In other specific cause, dissection of extracranial vessels is the most important cause (18.4% of all stroke etiologies) outweighting the cardioembolic causes.

11. Minority of young stroke (<10%) reach with in window period, which needs to be improved for better outcome. An emphasis for awareness in youth needs to be implemented.
12. Mortality is uncommon and accounted for 2.4% of all ischemic stroke.
13. Young population have excellent outcome with m-RS 3 or less achieved in 95% cases including m-RS 0 in 50.6% cases at 1 year follow up.

Limitation of Study :

1. Hospital based study hence referral bias and admission bias cannot be eliminated.
2. It is a retrospective study hence problems associated with retrospective study cannot be eliminated.

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ANNEXURE –I

1a. Level of Consciousness:

0 = **Alert;** keenly responsive.

1 = **Not alert**; but arousable by minor stimulation to obey, answer, or respond.

2 = **Not alert**; requires repeated stimulation to attend.

3 = Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, and areflexic.

1b. LOC Questions:

0 = **Answers** both questions correctly.

1 = **Answers** one question correctly.

2 = **Answers** neither question correctly.

1c. LOC Commands:

0 = **Performs** both tasks correctly.

1 = **Performs** one task correctly.

2= **Performs** neither task correctly.

2. Best Gaze:

0= **Normal.**

1= **Partial gaze palsy;**

2= **Forced deviation,**

3.Visual:

0 = **No visual loss.**

1 = **Partial hemianopia.**

2 = **Complete hemianopia.**

3= **Bilateral hemianopia** (blind including cortical blindness).

4.Facial Palsy:

0 = **Normal** symmetrical movements.

1 = **Minor paralysis** (flattened nasolabial fold, asymmetry on smiling).

2 = **Partial paralysis** (total or near-total paralysis of lower face).

3= **Complete paralysis** .

5.Motor Arm:

0 = **No drift;**

1 = **Drift;**.

2 = **Some effort against gravity;** .

3 = **No effort against gravity;**

4 = **No movement.**

UN = **Amputation** or joint fusion

6.Motor Leg:

0 = **No drift;**

1 = **Drift;** .

2 = **Some effort against gravity;**

3 = **No effort against gravity;**

4 = **No movement.**

UN = **Amputation** or joint fusion

7. Limb Ataxia:

0 = **Absent.**

1= **Present in one limb.**

2= **Present in two limbs.**

8.Sensory:

0 = **Normal;** no sensory loss.

1= **Mild-to-moderate sensory loss;**

2= **Severe to total sensory loss;**

9.Best Language:

0 = **No aphasia;** normal.

1 = **Mild-to-moderate aphasia;**

2 = **Severe aphasia;**

3 = **Mute, global aphasia;**

10.Dysarthria:

0 = **Normal.**

1 = **Mild-to-moderate dysarthria;**

2 = **Severe dysarthria;**

11.Extinction and Inattention (formerly Neglect):

0 = **No abnormality.**

1 = **Visual, tactile, auditory, spatial, or personal inattention**

2 = **Profound hemi-inattention or extinction to more than one modality**

ANNEXURE –II

MODIFIED RANKIN SCALE (mRS)

Score Description

0 = No symptoms at all

1 = No significant disability despite symptoms; able to carry out all usual duties and activities

2 = Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance

3 = Moderate disability; requiring some help, but able to walk without assistance

4 = Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance

5 = Severe disability; bedridden, incontinent and requiring constant nursing care and attention

6 = Dead

ANNEXURE –III

TOAST Classification of Subtypes of Acute Ischemic Stroke

(TOAST, Trial of Org 10172 in Acute Stroke Treatment.)

1. Large-artery atherosclerosis
2. Cardioembolism
3. Lacunar
4. Stroke of other determined etiology
5. Stroke of undetermined etiology

ANNEXURE –IV

APLA : Antiphospholipid antibody syndrome

CT : Computed Tomography

DM: Diabetes Mellitus

DSA : Digital Subtraction Angiogram

HTN : Hypertension

m-RS : Modified Rankins Scale

MRI : Magnetic Resonance Imaging

MRA : MR Angiogram

NIHSS : National institute of Health Stroke Scale

OCPs: Oral contraceptive pills

RHD : Rheumatic Heart Disease

SLE : Systemic Lupus Erythematosus

TCD : Transcranial Doppler

TIA : Transient Ischemic Attack

TOAST:Trial of Org 10172 in Acute Stroke Treatment

DECLARATION

I, **Dr.Alok Mandliya**, hereby declare that the projects in this book were undertaken by me under the supervision of the faculty, Department of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

Thiruvananthapuram
Date: 11/10/2013

Dr. Alok Mandliya

Forwarded

The candidate, **Dr. Alok Mandliya**, has carried out the minimum required project.

Thiruvananthapuram
Date: 11/10/2013

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ACKNOWLEDGEMENT

I take this opportunity to express my sincere gratitude to **Dr. Abraham Kuruvilla**, Additional Professor of Neurology, SCTIMST, my guide for the study, for his expert guidance, constant review, kind help and keen interest at each and every step during the completion of the study.

I am thankful to **Dr. Muralidharan Nair**, Professor and Head, Department of Neurology for his guidance, encouragement and valuable suggestions during the period of the study.

I express my sincere thanks to **Dr.Sankara Sarma,** Professor, Achutha Menon Centre for Health Science Studies for helping me with the statistical analysis of this study.

Last but not the least, I extend my gratitude's to all my patients and their primary caregivers who participated in this study as well as my colleagues without whose help this study was not possible.

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