

POSTERIOR CIRCULATION STROKE

CHARACTERISTICS

[POCSTROCH STUDY] -

AN OBSERVATIONAL COHORT STUDY

Determination of prevalence, demographic characteristics, comorbidities, clinical profile, radiological profile, outcomes and complications in posterior circulation stroke.



**A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE
REQUIREMENT FOR THE M.D. BRANCH I (GENERAL MEDICINE)
EXAMINATION OF THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY,
CHENNAI, TO BE HELD IN MAY 2018**

DECLARATION

This is to declare that this dissertation entitled "An observational cohort study to determine the prevalence, demographic characteristics, comorbidities, clinical profile, radiological profile, outcomes and complications in posterior circulation stroke in a tertiary care centre in South India [POCSTROCH STUDY]", is my original work done in partial fulfillment of the rules and regulations for the MD General medicine examination (Branch I) of the Tamil Nadu Dr. M.G.R Medical University, Chennai, to be held in May 2018.

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POSTERIOR CIRCULATION STROKE CHARACTERISTICS [POCSTROCH STUDY] - AN OBSERVATIONAL COHORT STUDY Determination of prevalence, demographic characteristics, comorbidities, clinical profile, radiological profile, outcomes and complications in posterior circulation stroke.

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INTRODUCTION

Cerebrovascular accident is the leading cause of acquired disability and the second most common cause of death worldwide. Global burden of disease programme under the World Health Organization showed that the mortality due to stroke is different in different countries with the low income countries being affected the most. Major part of the resource consumption by stroke patient occurs in terms of loss of manpower and financial burden. Studies in stroke neurology is an exquisite process, whereby a link is attempted from the

This is to certify that this dissertation work titled "An observational cohort study to determine the prevalence, demographic characteristics, comorbidities, clinical profile, radiological profile, outcomes and complications in posterior circulation stroke in a tertiary care centre in South India [POCSTROCH STUDY]", of the candidate Dr. Anju Susan Jacob, with registration number 201511452 in the branch of General Medicine has been submitted for verification. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows 2% percentage of plagiarism in the dissertation.

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ABBREVIATIONS

AC stroke: Anterior Circulation stroke

ACA: Anterior Cerebral Artery

ADC: Apparent Diffusion Coefficient

AICA: Anterior Inferior Cerebellar Artery

ASA: Anterior Spinal Artery

AUC: Area Under Curve

BA: Basilar Artery

BAO: Basilar Artery Occlusion

BP: Blood Pressure

CAD: Cervical Artery Dissection

CDC: Centers for Disease Control and Prevention

CE: CardioEmbolic

CT: Computed Tomography

CVA: Cerebrovascular Accident

DALY: Disease-Adjusted Life Year

DAMA: Discharged Against Medical Advice

DBP: Diastolic Blood Pressure

DWI: Diffusion-Weighted Imaging

ECASS: European Cooperative Acute Stroke Study

ECVA: Extra Cranial Vertebral Artery

ED: Emergency Department

FIM: Functional Independence Measure

FLAIR: Fluid-Attenuated Inversion Recovery

GCS: Glasgow Coma Scale

HDL: High Density Lipoprotein

HSR: Hallym Stroke Registry

ICA: Internal Carotid Artery

ICD-10-CM: International Classification of Diseases, Tenth Revision, Clinical

Modification

ICH: Intra Cranial Hemorrhage

ICP: IntraCranial Pressure

ICVA: Intra Cranial Vertebral Artery

IHD: Ischemic Heart Disease

IQR: Inter Quartile Range

IST: International Stroke Trial

LAA: Large Artery Atherosclerosis

LACS: Lacunar Stroke

LDL: Low Density Lipoprotein

MELAS: Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-like episodes

MCA: Middle Cerebral Artery

mm Hg: millimeter of Mercury

MRI: Magnetic Resonance Imaging

MRA: Magnetic Resonance Angiography

mRS: modified Rankin Scale

NEMC-PCR: New England Medical Centre-Posterior Circulation Registry

NG: Nasogastric

NIHSS: National Institute of Health Stroke Scale

ODE: Other Determined Etiology

OPD: OutPatient Department

PACS: Partial Anterior Circulation Stroke

PAR: Population Attributable Risk

pc-ASPECTS: posterior circulation- Acute Stroke Prognosis Early CT Score

PC stroke: Posterior Circulation stroke

PCA: Posterior Cerebral Artery

PICA: Posterior Inferior Cerebellar Artery

POCS: Posterior Circulation Stroke

PRES: Posterior Reversible Encephalopathy Syndrome

PSA: Posterior Spinal Artery

PWI: Perfusion-Weighted Imaging

RCVS: Reversible Cerebral Vasoconstriction Syndrome

REACH programme: Remote Evaluation of Acute Ischemia Stroke programme

ROC: Receiver Operating Characteristics

ROSIER scale: Recognition Of Stroke In Emergency Room scale

SBP: Systolic Blood Pressure

SCA: Superior Cerebellar Artery

SD: Standard Deviation

SVO: Small Vessel Occlusion

SWI: Susceptibility-Weighted Imaging

TIA: Transient Ischemic Attack

tPA: tissue-type Plasminogen Activator

TACS: Total Anterior Circulation Stroke

TOAST: Trial of Org 10172 in Acute Stroke Treatment Classification

UDE: UnDetermined Etiology

VA: Vertebral Artery

VBD: VertebroBasilar Dolichoectasia

WHO: World Health Organization

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INTRODUCTION

Cerebrovascular accident is the leading cause of acquired disability and the second most common cause of death worldwide. Global burden of disease programme under the World Health Organization showed that the mortality due to stroke is different in different countries with the low income countries being affected the most. Major part of the resource consumption by stroke patient occurs in terms of loss of manpower and financial burden.

Studies in stroke neurology is an exquisite process, whereby a link is attempted from the anatomical localization to the evolving knowledge of the function. The understanding of clinicopathological study of the posterior circulation of brain reached its zenith in the era of Kubik and Adams. (1)

Good history taking and careful clinical examination precedes the posterior circulation investigations. Posterior circulation stroke seldom have the extensive cardiac or vascular evaluation done, compared to the anterior circulation stroke, leading to a lag in the clinical information. (2) Prior to the New England Medical Center study, there was a lacuna in the understanding of vertebrobasilar territory ischemia. New England Medical Center Posterior Circulation Registry (NEMC-PCR) thoroughly evaluated 407 posterior circulation ischemia patients, from 1988 to 1996. This has served as the database for many other subsequent reports. Among 407 (NEMC-PCR) patients, 59% had strokes without TIAs, 24% had TIAs then strokes, and 16% had only TIAs. Posterior circulation strokes account for approximately 20% of all strokes.

Once diagnosed a posterior circulation stroke, etiopathogenesis is provided by the extensive imaging of the brain and other investigations, which aids in classification based on TOAST criteria. Categorization of the severity of the disease is essential for further management and prognostication of the stroke. Scoring systems such as Modified Rankin Scale [mRS] and National Institute of Health Stroke Scale [NIHSS] are the commonly used ones. Incidence of such strokes being low, there is scarce data regarding these, in India. Major contribution to the data regarding mortality and morbidity of posterior circulation [PC] stroke was based on retrospective evaluation. Correct and justified management relies on rapid diagnosis and treatment through investigations and rehabilitation. Cumulative information on demographic characteristics, clinical profile, radiological profile, etio-pathogenesis and complications needed to be looked into.

As there is a lacunae in the knowledge of the above factors that predict long term outcomes following posterior circulation stroke, this study was planned, predominantly in a specific South Indian population.

AIM AND OBJECTIVES

- **Aim:**

To study characteristics of Posterior circulation stroke among patients above 18 years age, presenting to Christian Medical College Vellore, over a period of 3 years.

- **Objectives:**

Primary outcome:

To determine prevalence of posterior circulation stroke among stroke patients presenting to our hospital, during January to December, 2016.

Secondary outcomes:

1]To determine comorbidities associated with posterior circulation stroke

2]To determine clinico-radiological profile of patients presenting with posterior circulation stroke

3] To determine outcomes of posterior circulation stroke

4] To determine complications of posterior circulation stroke

Hypothesis:

We estimate 20% prevalence of posterior circulation stroke among patients presenting with stroke

REVIEW OF LITERATURE

History of stroke

Advanced learning about nature, cause, clinical and imaging findings in patients with cerebrovascular diseases continue to happen, as the knowledge, personnel, and technology had been evolving during the past 200 years. (3)

In 1543, Andreas Vesalius, father of modern human anatomy, depicted anatomy of the human brain for the first time, in his book, *De humani corporis fabrica* [On the fabric of the Human Body] and in 1628, William Harvey described in detail the systemic circulation to the brain.

Sir Thomas Willis of the 17th century was the first person to use the term, neurology. There was a relative lull in the activity regarding brain anatomy and function till the 19th century when case studies were reported from European countries.

Most of the classic brain syndromes were named after the original describers of the syndromes. (4) Few of the midbrain syndromes named are Weber,(5) Benedikt,(6) Claude,(7) Millard-Gubler,(8) Foville, (9) Wallenburg,(10) Babinski-Nageotte(11) and Dejerine-Roussy.(12) Charles Foix contributed to studies on thalamic syndromes and lateral medullary syndrome. (13)

Willis described the vascular composition of the Circle of Willis. (14) During the 20th century, Charles Miller Fisher, a neuropathologist, a colleague of Raymond Adams, was one of the most responsible for furthering information about stroke pathology. Fisher along with Kubik and Kames described the occlusions of the vertebral artery in the neck (15) and lateral medullary infarcts. (16) He stated that intra-arterial embolism was an important mechanism of stroke. (17) Derek Denny-Brown introduced the term cerebrovascular insufficiency, to explain the TIAs and the fluctuating nature of brain ischemia.

Till the mid-1980s, clinical information regarding management of patients with posterior circulation had lagged behind that of anterior circulation ischemia along with difficulty in the precise definition of brain lesions during life before magnetic resonance imaging [MRI]. (18) New England Medical Center Posterior Circulation Registry [NEMC-PCR], a prospective computerized registry, from 1988 to 1996, thoroughly evaluated 407 posterior circulation ischemia patients using the brain imaging and vascular studies, which involved angiography initially, and later magnetic resonance angiography [MRA], extracranial and transcranial ultrasound, along with cardiac and hematological investigations. NEMC-PCR later served as the database for further case studies and reports. (19)

Global epidemiology:

The burden of stroke affects individuals living in resource-poor countries much more than individuals of a higher income group. Truelsen et al not only showed that developing countries attribute to 80 % of the global population living with stroke. They also found from 2000 to 2008 over a period of 8 years, that the overall stroke incidence rated in developing countries, exceeded by 20 % from high-income countries.(20)

Among 407 New England Medical Center Posterior Circulation registry (NEMC-PCR) patients, 59% had strokes without transient ischemic attacks (TIAs), 24% had TIAs then strokes, and 16% had only TIAs. Posterior circulation strokes account for approximately 20% of all strokes.(19)

Feigin et al studied population-based data on stroke since 1970 to 2008. Data regarding stroke incidence in high-income countries were available from 35 centers in 18 countries and low to middle-income countries were available from 12 centers in 10 countries. On studying stroke incidence rates over last 4 decades, their study showed a 42 % decrease in stroke incidence in high-income countries. However, the same study showed more than 100% increase in stroke incidence in low to middle-income countries.(21)

Indian Scenario

In 1969-71, the first community-based study on stroke was carried out in South India, followed by another study conducted in Rohtak, North India, during 1971-1974 .(22)

Abraham et al surveyed 258,576 people in both urban and rural area in and around the

town of Vellore. (23) They found prevalence rate of 68.5 in males and 44.8 in females per 100,000 population. This study also showed 25% of all strokes were under the age group of 40 and an annual incidence of 13 per 100,000.

In 1998, Saha et al surveyed a population of 20842 rural residents over in 2 phases over 1 year and found an incidence of 124/100,000 of stroke in the rural community of West Bengal.(24) Banerjee et al surveyed a population of 50,291 in the next year and showed incidence and prevalence of 36 per 100,000 and 147 per 100,000 in the urban community. (25)

The crude prevalence rate was found to be 4.72 per 1,000, in a community study conducted in the metropolitan city of Kolkata during 2003-2004. (26)

In India, the incidence of strokes have been persistently increasing and have doubled over the past 40 years. Around 1.5 million new cases of stroke were reported in 2010. With an incidence of 145 per 100,000 people, it is the third most common etiology behind neurological debility. (27)

20% of all strokes had been accounted by posterior circulation strokes, with high morbidity and mortality, (1) with a contribution of 6 to 10% of ischemic strokes by the basilar artery occlusion [BAO]. (28)

DEFINITIONS

The common term used by Hippocrates in 400 B.C. to describe acute non-traumatic brain injuries was "apoplexy". (29) Willaim Cole had first introduced the word "stroke" in 1989 in a 'Physico-Medical Essay Concerning the Late Frequencies of Apoplexies. (30)

Stroke has been defined as "a rapid onset of the focal neurological deficit, resulting from the disease of the cerebral vasculature and its contents". (31) Cerebral infarction, stroke, and cerebrovascular accident were given the code 434.91 by CDC. (32)

Transient Ischemic attack [TIA]:

2017 ICD-10-CM G45.9 describe TIA as a brief reversible episode of focal, non-convulsive ischemic dysfunction of the brain, for a duration of less than 24 hours, and usually less than one hour, which is caused by transient thrombotic or embolic vascular occlusion or stenosis.(33) A literature review from 1990 to 2007 showed that 33% of patients were misdiagnosed as TIA, where MRI with diffusion rated imaging showed restriction of diffusion, based on which American Heart of Association redefined TIA as a transient episode of focal neurological dysfunction without acute infarction and lasting less than 1 to 2 hours. (34)

Posterior circulation stroke[PCS]:

Posterior circulation stroke is defined by ischemia or hemorrhage within the vascular territory supplied by the vertebrobasilar arterial system.(35)Posterior circulation ischemic stroke is a clinical syndrome associated with ischemia related to stenosis, in situ

thrombosis, or embolic occlusion of posterior circulation arteries, which includes innominate and subclavian arteries in the chest, vertebral arteries in the neck, and intracranial vertebral, basilar, posterior cerebral arteries and their branches. (36)

Wake-up stroke which provides a therapeutic dilemma, is a phenomenon where a patient goes to sleep normally but awakens with stroke symptoms. (37)

POSTERIOR CIRCULATION VASCULATURE

Vertebrobasilar arterial system (35)

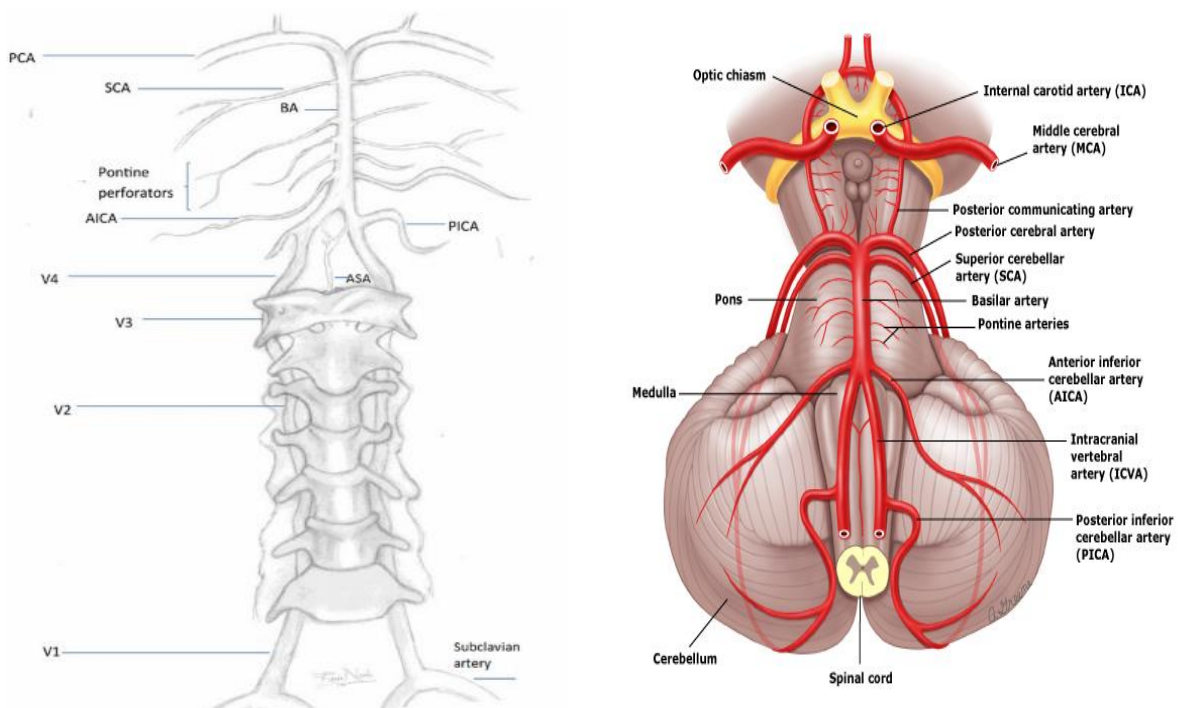


Figure 1: Figure showing the vertebrobasilar arterial system

Course:

Right and left subclavian arteries give rise to the vertebral arteries V1 [preforaminal], which traverse the transverse foramina of cervical vertebrae V2 [foraminal], reach foramen magnum and pierce dura mater V3 [extradural or atlantic], to start the intracranial course V4 [intradural or intracranial], join at the pontomedullary junction, forming the basilar artery, which travels rostrally along the ventral medulla and basis pontis, until it bifurcates into the right and left posterior cerebral arteries at pontomesencephalic junction. (35)

Branches:

Vertebral artery [VA] gives off numerous muscular, radicular, meningeal and spinal branches. V4 segment gives rise to anterior spinal artery [ASA], posterior spinal artery [PSA] and the largest branch of the vertebral artery, posterior inferior cerebellar artery [PICA], which is one of the three main arteries supplying the cerebellum. Basilar artery [BA] arising from the confluence of two vertebral arteries, before bifurcating into two posterior cerebral arteries [PCA], provides the paired branches of anterior inferior cerebellar artery [AICA], labyrinthine artery, pontine arteries and superior cerebellar artery [SCA]. The posterior cerebral artery is divided into four segments [P1 to P4], which provides the posterior communicating artery, medial and lateral posterior choroidal arteries, perforators and cortical branches.

TERRITORIAL CLASSIFICATION

Caplan described the topographic classification for localization of infarcts in NEMC - PCR by subdividing intracranial vertebrobasilar system into proximal, middle and distal territories. (19)

Intracranial vertebral arteries-supplied regions, medulla oblongata and posterior inferior cerebellar artery-supplied cerebellum, constitute the proximal intracranial posterior circulation territory.

Brain supplied by basilar artery upto its superior cerebellar artery branches, pons, and anterior inferior cerebellar artery-supplied cerebellum, constitute the middle intracranial posterior circulation territory.

All the territories supplied by the rostral basilar artery, superior cerebellar artery, posterior cerebral arteries and penetrating branches of these arteries to the midbrain and thalamus, constitute the distal intracranial posterior circulation territory. (38)

Posterior circulation stroke can have diverse presentations that differ from anterior circulation stroke in relation to etiology, clinical features, and prognosis. The poorest prognosis was seen in the embolic mechanism, distal territory location, and basilar artery occlusive disease. The best outcome was in patients with multiple arterial occlusive sites and had position-sensitive TIAs during months to years.(19)

SOURCE OF ISCHEMIA

TOAST [trial of ORG 10172 in acute stroke treatment] criteria divides ischemic stroke into five subtypes, which was formulated in a landmark trial in 1993. (39)

- 1) Large-artery atherosclerosis
- 2) Cardioembolism
- 3) Small-artery occlusion (lacunar)
- 4) Stroke of other determined etiology
- 5) Stroke of undetermined etiology, which are categorized as:
 - a. Two or more causes identified
 - b. Negative evaluation
 - c. Incomplete evaluation

Large-artery atherosclerosis included clinical or imaging findings of >50% stenosis or occlusion of any of the major cerebral arteries. The etiology for the same was attributed mostly to atherosclerosis.

Cardioembolism subtype included patients with arterial occlusions which were attributed to an embolus arising in the heart.

Small-artery occlusion included strokes or syndromes that were classified as lacunar infarcts.

Acute stroke of other determined etiology included rare causes of stroke-like non-atherosclerotic vasculopathies, hypercoagulable states, or hematologic disorders.

Stroke of undetermined etiology essentially included strokes with two or more causes identified, where no etiology was found or for strokes where the evaluation was incomplete.

A modified version of the existing TOAST classification, incorporating the advances in imaging and epidemiology, was put forth in 2005. The so-called Stop Stroke Study SSS – TOAST further divided the previous five subtypes into three categories- “evident,” “probable,” or “possible”. This brought down the number of patients under unclassified subtypes from 40% to 4%.

There have been other classifications like Causative Classification System (CCS)(40) and A-S-C-O. A-S-C-O (41) which is self-explanatory (A for atherosclerosis, S for small vessel disease, C for a cardiac source, O for other cause) is a promising classification in vogue.

STROKE MECHANISMS

Atherosclerosis, embolism, and dissection are the most common causes of posterior circulation large artery ischemia.

Atherosclerosis

Large vessel atherosclerotic disease causes 35% and small vessel disease accounts for 13% of PC strokes. (42) Large vessel atherosclerotic disease within the posterior circulation can cause thromboembolism or hemodynamic failure leading to ischemia. (43) Vertebral artery atherostenosis is most commonly located in the V1 and V4

segments. (44)Caucasian men more commonly have extracranial atherosclerosis and also the evidence of concomitant coronary and peripheral vascular disease. (45)Steno-occlusive atherosclerotic disease as an embolic source most commonly affects the PICA territory, distal BA, SCA and PCA branches. (46) Similar to AC strokes, the severity of ischemic presentation in the PC, correlate with the thrombogenic plaque characteristics such as lesion irregularity and plaque morphology. (47) The most common intracranial site of atherostenosis is the BA, followed by the ICAs, MCAs, VAs, PCAs, and ACAs.

“Misery perfusion” is the failure of the compensatory mechanism of the reflex vasodilation due to collateral circulation to increase the cerebral blood volume and to preserve the normal cerebral blood flow and the oxygen extraction fraction. (48)

“Tandem extracranial and intracranial lesions”, found in patients with the vertebral artery atherosclerosis and posterior circulation stroke, more often suffer clinical effects of the hemodynamic changes.(46)

Embolism to brain of cardiac or aortic origin(49)

Since approximately 40% of the cerebral blood flow goes to each ICA and only 20% goes to the posterior circulation, one-fifth of the cardiac emboli may end up within the PC by chance. (19) Embolism was the commonest stroke mechanism, in 407 patients in the NEMC-PCR (40% of patients including 24% cardiac origin, 14% intraarterial, 2% cardiac and arterial sources). Distal PC territory infarctions were most common followed by the middle territory infarcts. In contrast, in Hallym stroke registry (HSR), with 591 PC stroke Korean patients, only 11% had the potential cardiac sources of embolism, large

artery stenosis in nearly half and intrinsic small vessel disease in a third. Middle territory infarction occurred in 36.5% of patients followed by the distal territory in 28.1%. The commonly recognized cardiac sources of embolism are sinoatrial disorders, acute myocardial infarction, infective endocarditis, cardiac tumors and valvular disorders.(50)

Vertebrobasilar dolichoectasia (VBD)

VBD refers to the dilatation, elongation, and tortuosity of the Basilar artery and major risk factors include male gender, increasing age, hypertension, smoking and history of a myocardial infarction. (51)

Arterial dissection

CADISP study states that the cervical artery dissections (CADs) which occur spontaneously or from cervical trauma, (52)accounts for approximately 15% of the strokes in young adults. ECVA dissections are most commonly found to involve the V2 and V3 segments. 50 % patients present with posterior neck pain and two-thirds of the patients develop an occipital headache. Vertebral artery dissection has a delayed diagnosis and frequently present with ischemic vestibulocerebellar symptoms (>90%), which include dizziness, vertigo, veering to one side, loss of balance and PICA territory strokes (lateral medullary and/or cerebellar). (53)

Other etiologies and associations(54)

Rotational vertebral artery occlusion, due to dynamic compression of one (dominant) vertebral artery by bony elements of the cervical spine, triggered by turning of head, is an uncommon cause of transient posterior circulation ischemia with symptoms, which mainly includes paroxysmal vertigo or nonspecific dizziness, which may be accompanied by nausea, or vomiting, blurred vision, syncope, tinnitus or downbeat nystagmus. (55)

Other less common causes of ischemia with a predilection for the PC circulation include the subclavian steal syndrome, migraines, giant-cell arteritis, Fabry disease, MELAS (Mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes), and PRES (posterior reversible encephalopathy syndrome). As reversible cerebral vasoconstriction syndrome (RCVS) may mimic PCA embolus presentation, it should be considered in the differential diagnosis of sudden onset headache and focal neurological deficits.

VASCULAR OCCLUSIVE LESIONS

Among 32% of the NEMC-PCR patients, large artery occlusive lesions caused hemodynamic brain ischemia. Infarcts most often included the distal posterior circulation territory (rostral brainstem, superior cerebellum and occipital and temporal lobes); the proximal (medulla and posterior inferior cerebellum) and the middle (pons and anterior inferior cerebellum) posterior circulation territories were equally involved.

Severe occlusive lesions (>50% stenosis) in the study, involved more than one large artery in 148 patients, with more than half the patients having 2 occlusive large artery lesions. 134 patients had one artery site involved unilaterally or bilaterally, in the study.

The commonest occlusive sites were the extracranial vertebral artery (52 patients, 15 bilateral), the intracranial vertebral artery (40 patients, 12 bilateral) and the basilar artery (46 patients). The commonest mechanism of brain infarction in patients with vertebral artery occlusive disease was intra-arterial embolism. 30-day mortality was found to be 3.6%. (19) About one-third of the posterior circulation strokes were caused by occlusive disease of the vertebral arteries in the neck and the intracranial arteries, with the atherosclerotic occlusive disease most commonly located in the proximal portion of the vertebral artery in the neck. Most infarcts occurring in the posterior cerebral artery territory are due to embolism.

Extracranial artery disease

Innominate and subclavian arteries with atherostenotic lesions, do cause arm ischemia, can also cause reduction of the vertebral artery flow and transient ischemic attacks, but seldom cause strokes. (56)

The vast majority of occlusive lesions of the proximal vertebral arteries are atherosclerotic. Among a series of 100 patients with angiographically documented vertebral artery lesions, 92% were atherosclerotic in origin. (57) Infarction in ECVA lesions is primarily caused by the artery-to-artery embolism.

Proximal vertebral artery disease can cause sudden-onset strokes or transient ischemic attacks (TIAs). Dizziness is the most frequently reported symptom during TIAs. These TIAs are indistinguishable from those described by patients with a subclavian steal, except that the vertebral artery TIAs are not precipitated by effort or by arm exertion. Dizziness being the most common symptom may seldom be the only neurologic symptom. Usually, in at least some attacks, dizziness is accompanied by other signs of hindbrain ischemia. Diplopia, oscillopsia, numbness, weakness of legs and hemiparesis are often reported. In patients with proximal ECVA disease, a bruit can often be heard over the supraclavicular region. Proximal ECVA disease is diagnosed with the aid of an imaging, which includes a doppler or angiogram.

Intracranial vertebral artery disease

Proximal territory infarcts were mostly the lateral medullary infarcts and were attributed to atherosclerotic ICVA disease. PICA infarct if limited to the cerebellum, was most often secondary to the cardiac-origin embolism and artery-to-artery embolism from the ECVAs, than focal atherostenotic lesion.(58)

Basilar artery disease

Basilar artery territory infarcts were mostly in the middle intracranial posterior circulation territory and nearly all had atherosclerotic lesions. Distal territory infarcts were secondary to mostly spread of the atherosclerotic disease or embolism to the rostral

basilar artery and its distal branches, and hence usually seen along with the middle territory infarcts. (59)

Penetrating and branch artery disease

14% of the 407 NEMC posterior circulation infarcts were attributed to penetrating or branch artery disease, which was labelled so, when the brain infarcts were limited to the distribution of single branch penetrating arteries, and clinical features were explained by involvement of this region alone, with no significant compromise of the feeding parent artery, in a vascular imaging.

Posterior cerebral artery territory infarcts

PCA infarcts were mostly emboli from cardiac, ECVA, ICVA or BA disease. Patients with lateral thalamic infarction or PCA occlusion before the thalamo-geniculate pedicle, presented with somatosensory findings. (60) Motor signs if present was slight, and contralateral, and might also develop cognitive and behavioral abnormalities. (61)

RISK FACTORS

Assessment of risk factor association is important to guide the selection of targets at risk for population-based programs. Global variations in the prevalence of ischemic and hemorrhagic stroke can be explained by the recorded differences in the risk factor profile. (62)

Risk factors are divided into 2 categories. Non modifiable and modifiable risk factors. Non-modifiable stroke risk factors include, age, sex, low birth weight, ethnicity, genetic factors and modifiable risk factors include smoking, hypertension, diabetes mellitus and high cholesterol.

In the INTERSTROKE study, a standardized case-control study in 22 countries worldwide, over 3 years, between March 2007 and April 2010, O'Donnell et al studied 3000 cases and 3000 controls, and calculated odds ratios [OR] and population-attributable risks [PAR] for the association of all stroke, with the selected risk factors. (63)80% of the global risk of all stroke was attributed to five risk factors: hypertension, current smoking, abdominal obesity, diet and physical activity. Overall PAR as found to be consistent with the INTERHEART study and it rose to 90% with the addition of five other risk factors: diabetes mellitus, alcohol intake of more than 30 drinks per month or binge drinking, psychosocial factors, cardiac causes and ratio of apolipoproteins B to A1. Hypertension was found to be the most important risk factor in all stroke subtypes, in most of the studies, (64) and most amenable to change in low-income settings. (65)

A multicenter, prospective, Web-based registry, in 2012, was performed on atherosclerotic strokes, using diffusion-weighted resonance imaging and magnetic resonance angiography,(66) which showed that posterior circulation atherosclerosis was more associated with hypertension, diabetes, and metabolic syndrome, while cigarette smoking and alcohol consumption were seen more prevalent in anterior circulation diseases.

A Prospective Study in a North Indian Population by Mehndiratta et al 2012, showed following table of comparison of risk factors among various studies on Posterior circulation stroke.(38)

Table 23 Table showing the risk factors among various studies

Risk factors	Mehndiratta(3 NEMC-PCR(19)	Leeetal(67)	Umaetal(68)	Kora(69)
Hypertension	51	61	69.9	21 37
Diabetes	24	25.4	30.2	35.5 05
Smoking	25	35.7	32.4	35.5 –
Alcohol	05	31.1	–	19.7 21
Dyslipidemia	17	24.7	24.2	44.4 10
CAD	14	34.7	–	17.1 05
RHD	02	–	–	10.5 05
Cardiomyopathies	02	–	–	– –
Atrial fibrillation	01	–	–	– –
Obesity	08	17.3	–	–
Migraine	0	11.5	–	11.8 –
Oral contraceptive	0	12.5	–	39.1 –

CLINICAL PRESENTATIONS

In clinical practice, not all Posterior circulation stroke presentations are classic. PC is rich in potential collateral support and clinical manifestations of Basilar artery ischemia may be highly variable, presenting with signs and symptoms of multifocal PC infarctions. PC strokes have fewer cortical findings and relatively small lesions can cause significant

deficits as compared to AC stroke due to the other symptoms of posterior circulation stroke, which aid in localization, (70) along with the close proximity of major afferent and efferent tracts and cranial nerve nuclei in the brainstem.

Common symptoms include motor deficits such as weakness, clumsiness or paralysis of any combination of limbs, up to quadriplegia. Sensory deficits are numbness, including loss of sensation or paresthesia. Homonymous hemianopia, alteration in consciousness, ataxia, imbalance, unsteadiness, disequilibrium, vertigo, diplopia, dysphagia or dysarthria are the other symptoms.

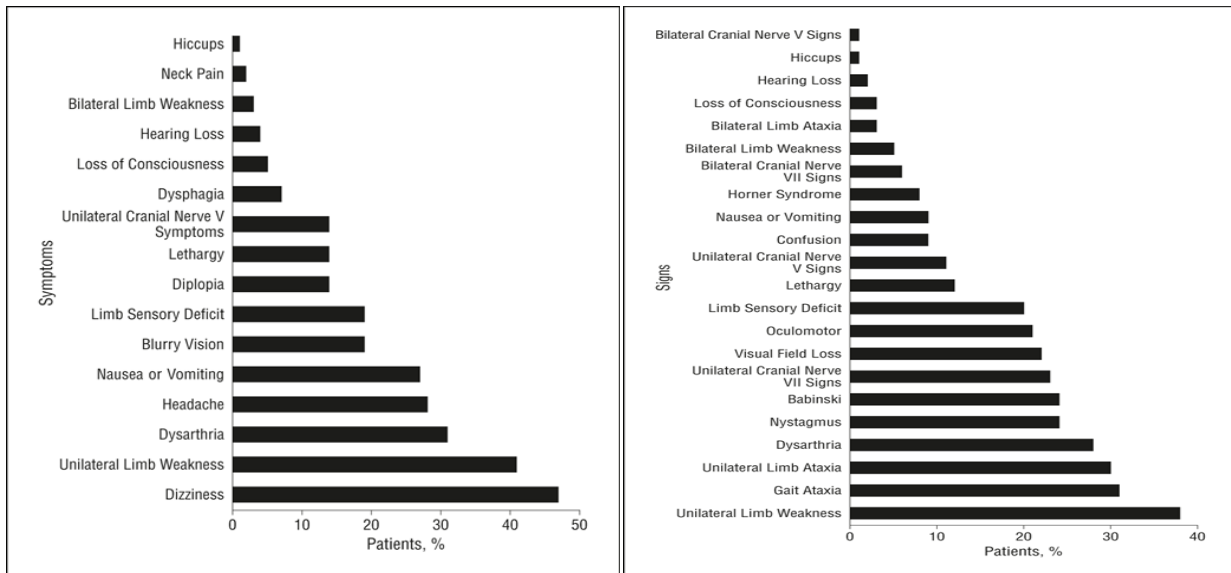


Figure 2 Figure showing symptom and sign frequencies of posterior circulation ischemia in NEMC-PCR (71)

Clinical syndromes(4)

Crossed syndromes involve ipsilateral cranial nerve function and contralateral long motor or sensory tract dysfunction.(72)A most common syndrome related to intracranial vertebral artery occlusion is the lateral medullary infarction (Wallenberg syndrome) in which blood flow through perforating branches to lateral medulla is impaired, with diagnostic signs including a reduced contralateral hemisensory loss to pain temperature. Medial medullary infarcts cause hemisensory loss to touch and proprioception and contralateral hemiparesis. Complete pontine infarction causes "locked-in syndrome" with quadriplegia, anarthria, and preserved consciousness. Distal basilar occlusion causes symptoms of either thalamic or bilateral occipital infarction. Full PICA territory infarcts cause ipsilateral occipital headache or neck pain along with the ataxia and vertigo. Combination of contralateral hemianopia and ipsilateral hemisensory loss on the same side without paralysis is diagnostic of posterior cerebral artery territory infarction. (73)

DIAGNOSIS

Diagnosis of posterior circulation stroke is based on rapidly developing clinical signs of focal or occasionally global disturbance of the cerebral function with no apparent cause other than that of vascular origin and is assisted by imaging.(74)In the initial assessment phase, it is important to establish onset and tempo of symptoms and establish whether the patient has experienced typical or characteristic PC stroke symptoms.(75) Diagnostic tools such as recognition of stroke in emergency room (ROSIER) scale, (76) ABCD2 score, (77) and HINTS, (78) may help medical staff in the emergency department to

rapidly recognize acute strokes. Assessment by specialist stroke team with a stroke thrombolysis protocol in place, during admission to an emergency department, is the optimum approach. Along with the clinical assessment, demographics, risk factor profile, stroke assessment scales and necessary investigations are carried out. (79) Ischemic strokes can be sub-classified using Oxford Community Stroke Project classification and Toast criteria will be assessed.

STROKE SCALES

Several stroke scales had been used extensively for assessing the extent of neurological deficit, the severity of a stroke, to plan on intervention and to predict the outcome as well. Some of the commonly used stroke scales to measure neurologic impairment are National Institute of Health Stroke Scale [NIHSS], Canadian Neurological Scale, European Stroke Scale, Scandinavian Stroke Scale. (80)

NIHSS is being used commonly for assessing functional impairment among stroke patients. (81) NIHSS score can be useful for triage purposes, especially in smaller hospitals with limited accessibility to emergency vessel imaging, so as to administer intravenous or endovascular strategies as early as possible. NIHSS score had been used in thrombolysis trials to exclude the patients from active treatment.

In NIHSS, 15 distinct variables are scored in each stroke patient. NIHSS was designed and validated in 1989 and had minimal inter-observer variability. (82) A study including 1,281 patients which compared baseline National Institute of Health Stroke Scale score as

predictor of outcomes, showed that a score of >16 at admission was strongly predictive of death and disability compared to that of a score of < 6 being a good predictor of recovery.(83)

The Remote Evaluation of Acute Ischemic Stroke[REACH] programme has been developed in order to evaluate NIHSS in a rural setup in the US using telephone and broadband and has been found to have strengthened stroke care in rural hospitals.(84) But the same is not practical in underdeveloped and developing countries. Olavarria et al had found a time-dependent association which was poor after 6 hours from the symptom onset. (85) Also, owing to high scores for cortical findings and motor deficits, and low scores for symptoms like vertigo, visual abnormalities, and ataxia, NIHSS score was unable to predict the severity of posterior circulation stroke. As no study was powered to assess the validity of NIHSS in posterior circulation stroke, the role of NIHSS in predicting the outcome, recovery and as a tool for serial assessment of disease course, is doubtful.

There have been several scales for measuring disability like Barthel index and Functional Independence Measure [FIM] and commonly used handicap scales have been modified Rankin Scale [mRS] and Oxford Handicap Scale.

mRS score with 6 grades has been used since 1988 for grading handicap with a good inter-observer agreement. (86) In MRS score, 0 implies no symptoms and score 5 indicates severe disability. In a systematic review of 8 studies which had used mRS to interpret outcome, it was observed that MRS of >3 was associated with a poor outcome

and mRS of 0-2 was associated with good outcome.(87) This score owing to its simplicity has been used in various Indian studies as well. A recent study, using a independent clinical trials dataset, had compared and confirmed the differences in the prognostic accuracy of acute stroke prognosis scales, and mentioned that it is not sufficient as a basis for clinical decision-making. (88)

NEUROIMAGING

Computed Tomography [CT]

"Time is brain", in the evaluation of acute stroke. CT is easy, fast, widely available and less expensive. Non-contrast CT of the brain is often the initial imaging modality used, by which hemorrhage is ruled out and can also detect early ischemic signs such as subtle hypodensities, loss of gray-white matter differentiation and sulcal effacement.(89)But recent studies have proven that CT has high inter-rater variability in interpretation and is less sensitive to acute infarct as well as intracranial hemorrhage when compared to MRI. (90) Suboptimal visualization of posterior fossa structures in CT maybe attributed to the relatively dense smaller area interpreted {Citation} and also obscuration by artifacts due to the cranial bony base. (91)Posterior Circulation Acute Stroke Prognosis Early CT Score (pc-ASPECTS) is sensitive for early ischemic change detection and unfavorable functional outcome prediction in patients with basilar artery occlusion, despite recanalization. (92)Though conventional catheter cerebral angiogram is the gold standard for intracranial and extracranial vascular imaging, non-invasive modalities such as CT angiography and MR angiography are more often used, (93) with contrast-enhanced MR

angiography having the highest sensitivity and specificity, for visualization of entire vertebrobasilar arterial tree and detection of stenosis. (94)

Magnetic Resonance Imaging [MRI]

Magnetic resonance imaging with diffusion-weighted imaging has 80-95% sensitivity (95) in the diagnosis of acute ischemic stroke but can have 12-19% false-negative rate with an early MRI in a PC stroke and in case of hyper-acute hemorrhages. (96) MRI Acute Stroke Protocol which involves T1-weighted, T2-weighted, FLAIR, DWI, SWI and MRA sequences, is put together to achieve a narrow time window for early thrombolytic therapy. (97)DWI images when combined with the apparent diffusion coefficient [ADC], helps in the distinction of infarct duration. (98) DW imaging lesion patterns [single versus multiple and unilateral versus bilateral] and stroke subtype classifications by TOAST criteria was found to have a significant overall association, and hence providing important information about the stroke etiology. (99)In view of close proximity of vital tracts and nuclei, location site than the infarction size correlate more and a better critical functional outcome predictor. (98)pc-ASPECTS score applied to MRI-DWI is proven to be a powerful predictor of functional outcome of PC stroke. (100)

MANAGEMENT

Baseline investigations

Optimum preventive treatment of stroke is achieved by identification of the underlying mechanism. Modifiable risk factors should be identified and secondary prevention

strategies implemented with the help of investigations recommended by the International stroke guidelines. (101) Basic tests include full blood count, renal and liver function tests, and measurement of glucose, lipid levels, electrolytes, bleeding parameters, and electrocardiography. (102) Cardiac rhythm monitoring and echocardiography are recommended in stroke with a cardioembolic source, (103) specifically in isolated posterior cerebral artery infarction and top of the basilar syndrome. In patient with no clear cause identified, a detailed evaluation for systemic diseases predisposing to the arterial thrombosis might be needed.

General measures

Patients with posterior circulation stroke need to be stabilized and resuscitated at admission. Airway, breathing, and circulation should be assessed and stabilized during transfer and on arrival.

Management of acute posterior circulation stroke

Comorbid diseases and time of onset of stroke primarily govern the acute management of stroke. NIHSS which assess the stroke severity, play a crucial role within the narrow therapeutic window of anterior circulation stroke but has limitations in posterior circulation strokes. Ataxia and cranial nerve deficits in PC strokes, carry fewer NIHSS points than the cortical findings and motor deficits, and hence undermining the unfavorable 3-month outcome despite the relatively low NIHSS scores.(104)

Intravenous thrombolysis

US and European guidelines, based on NINDS and ECASIII study, recommend intravenous tissue-type plasminogen activator [IV-tPA] as first-line therapy for ischemic strokes, within 4.5 hours of symptom onset and satisfying the eligibility criteria.(105) The IST 3 trial showed improvement in functional outcome and quality of life when treated with IV-tPA within 6 hours of symptom onset, but all trials were underpowered for PC stroke, in view of less than 10 % of the strokes studied. (106) Basilar artery occlusion [BAO] with >80% fatality rate, when treated with IV-tPA and heparin, was found to have good outcome independent of time to treatment. (107)

Intra-arterial fibrinolysis

Intra-arterial [IA] thrombolysis has shown favorable outcomes in patients with basilar artery occlusion when associated BA recanalization was achieved. A prospective observational study, the basilar artery international cooperation study [BASICS] found no evidence of the superiority of IA-thrombolysis over IV-thrombolysis when compared outcomes of patients with BAO. (108) AHA/ASA recommends IA-rt-PA in select MCA occlusion within 6 hours of symptom onset but not in posterior circulation stroke including BAO. (109)

Endovascular mechanical thrombectomy

A systematic review on the outcome of BAO after TA-rt-PA or IV-rt-PA, had only 2% of 420 patients with a good outcome, in absence of BA recanalization. (110) Recanalization was found to have a strong association with good clinical outcome, with mechanical thrombectomy achieving higher recanalization rate for all target vessels in reported device trials, (111) especially with stent retrievers.(112) Posterior circulation territory infarcts were thought to have salvageable tissue existing longer, in view of a probable higher proportion of white-matter and better collateral rendering resistance to ischemia, and hence reasonable to consider thrombolysis or thrombectomy up to 24 hours of symptom onset.(113) Posterior circulation strokes were under-represented or excluded in most of the studies, including MERCI trial, SYNTHESIS trial, and MR RESCUE trial, and had discouraging conclusions and unproven benefits.

Neurosurgery

Extensive cerebellar infarction with drop in sensorium attributable to raised intracranial pressure or acute hydrocephalus might benefit from a neurosurgical intervention, such as extra-ventricular drainage or decompression. (114) Edema in a large infarction can cause a delayed rapid progression of loss of brainstem function, secondary to brainstem compression and decompression can be life-saving. , which is substantiated by only case-series. In a case series study, twenty-one of the 30 patients with an advanced clinical state

who underwent decompressive surgery recovered, compared with none of the sixteen patients treated medically alone. (115)

Medical management

Secondary prevention with lifestyle modification and drugs, including antiplatelet agents, lipid-lowering drugs and blood pressure control to a target of less than 140/80mm Hg, is recommended by the current international guidelines.(102) Once hemorrhage excluded and if thrombolysed, after a 24 hours lapse, antiplatelets are initiated. Long-term secondary prevention of thromboembolic events is achieved by clopidogrel alone (or aspirin and dipyridamole). In patients with acute ischemic stroke with underlying indications for anticoagulation(such as atrial fibrillation), treatment should be started about 2 weeks later, when the potential benefit outweighs the risk of harm by hemorrhagic transformation of infarct. (116) Dual antiplatelet treatment is recommended in patients at high risk of ischaemic strokes, such as those with symptomatic vertebrobasilar stenosis. (117) In view of reduced recurrent non-fatal and fatal stroke, high-dose statin is recommended in all ischaemic stroke subtypes in SPARCL randomised controlled trial. (118) Treatment modalities and targets for comorbid diseases should be in accordance with the guidelines set for the same. 28% relative risk reduction for stroke was shown in the PROGRESS study, a randomised controlled trial, when treated with a perindopril-based regimen, substantiating the use of antihypertensives in stroke patients. (119)

Management of adverse outcomes

Patients can develop extension of infarct or hemorrhage and malignant infarcts can develop hemorrhagic transformation. Posterior circulation stroke patients can rapidly worsen due to extensive infarction or cytotoxic edema within the tight constraints of posterior fossa. The patient is clinically monitored for symptoms or signs of raised intracranial pressure. The patient will manifest symptoms such as a headache, vomiting, lethargy, disorientation or neurologic deterioration. Signs of hypertension, bradycardia or irregular respiratory pattern is observed for. Medical management is initiated to delay the progression and includes hyperventilation, head-end elevation, osmotherapy, antiepileptics, blood pressure control and sedation. Definitive surgical decompression in such patients was found to have a better functional outcome and lesser mortality. (120)

Like any stroke, posterior circulation stroke can develop acute complications such as dysphagia, infection, seizures, myocardial infarction or longterm complications including post-stroke pain, contractures, bedsores and recurrent stroke. The patient is given symptomatic treatment along with nursing care, and rehabilitative measures including NG feeds, catheter care and physiotherapy, speech therapy and swallowing therapy. Patients are closely followed up for addressing the complications and to ensure secondary prevention strategies.

OUTCOMES

Global measurements undertaken by WHO revealed an up to ten-fold difference in age-adjusted and sex-adjusted mortality rates and burden (measured in disability-adjusted life year loss rates (DALYs)) among countries. Both were considerably higher in low-income countries (North Asia, Eastern Europe, Central Africa, and South Pacific) compared to high-income countries (Western Europe, North America).

Posterior circulation ischemia had a more benign outcome in NEMC registry than previously thought. Most patients (n=284 [78.7%]) had no or minor disability. Death attributed to cerebrovascular disease was 1.9%, and total mortality at 30 days was 3.6%. Mortality and major disability were present in approximately one-fifth of patients (21.3%). Mortality (n=3 [4%] at 3 weeks) was similar in a series of 70 patients with acute posterior circulation infarcts who had MRI/MRA in the Lausanne Stroke Registry, but others estimated that >50% of patients with vertebra-basilar territory ischemia died or became severely disabled. Series of patients with poor outcomes invariably selected only patients with severe neurological signs for angiography and for inclusion in their series.⁽¹⁹⁾ Risk of recurrent stroke was 25% in the first 90 days, in patients with symptomatic vertebra-basilar stenosis. (121)

Embolism (especially cardiogenic) was the major contributor to poor outcome, as it has been in patients with AC infarcts. Poorest outcomes occurred in patients with distal territory infarcts, especially if both middle and distal territories were involved. Basilar artery disease (n=27 [7.7%]) and ICVA disease (n=19 [5.2%]) were the vascular

occlusive lesions that accounted for most instances of death or major disability. (122)
Acute BAO patients were found to have 41 to 95% mortality rate in natural history studies and were highest when there is poor recanalization, with survivors having a severe disability. (113)

Justification

Due to lack of skilled personnel and technology, diagnosis and management of posterior circulation stroke are missed or delayed. Very few studies had been published from India on outcome of posterior circulation stroke including mortality. Indian data available on assessing the risk factors and the clinico-radiological profile was also found to be very scarce. As there is a lacuna in the factors that predict long-term outcomes following posterior circulation stroke, we are planning this study.

Incorporating high risk-prediction score to clinical features like vertigo, visual symptoms and ataxia and substituting the vertebrobasilar stenosis, might refine the prediction of posterior circulation stroke and its characteristics. The ABCD2 clinical prediction score for TIA has not been specifically validated in VB territory TIA. The established NIHSS stroke score is accurate for anterior circulation scores while not so for posterior circulation strokes. Hence the need for this study. It is crucial to identify patients at highest risk of early recurrent stroke for prompt triaging and optimum management. This is a hospital-based study, with a good sample size, conducted mostly on South-Indian population, assessing the demographics, associated comorbidities, clinicoradiological presentations and adverse outcomes, to cater to the above-mentioned gap in literature.

MATERIALS AND METHODS

FUNDING AND APPROVAL

The study protocol was approved by the Institutional review board (IRB Number 9822). [Appendix I] The study was funded by the FLUID research grant of the Institution (Number 22 Y 967). [Appendix II]

SETTING

This was a single center cohort study, done in patients who presented to our hospital with a posterior circulation cerebrovascular accident (stroke).

The Christian Medical College is a University teaching hospital in South India that predominantly caters to low and middle income patients from southern and eastern India. The study was conducted in the departments of Internal Medicine, Emergency, Neurology and Physical Medicine & Rehabilitation at our hospital.

Consecutive patients, who presented with a clinical diagnosis of posterior circulation stroke, were enrolled. Recruitment was from January 2014 to December 2016. Data for the patients who were recruited from 2014 to 2015 was available in the hospital electronic medical records. They were prospectively followed up in the hospital or telephonically. All patients from 2016 onwards all data from presentation to follow up was prospective.

Diagnostic criteria assessed, prognostic scores, mRS (123) and NIHSS (124) calculated, and morbidity and mortality was followed up at discharge, at 3 months and 6 months. Data was collected after informed consent being taken from patient or patient relatives.

(Informed consent form in Annexure IV).

PATIENT POPULATION

Inclusion criteria:

1. Age 18 years or older
2. Clinical profile and radiological finding suggestive of acute posterior circulation stroke
3. Informed consent provided to participate in the study

Exclusion criteria:

1. Age less than 18 years
2. All patients who did not provide consent
3. Patients with diagnostic criteria not satisfied with both clinical and radiological profile

DEFINITION OF A CASE

Diagnostic criteria (19)

Clinical: Acute neurological symptoms and signs such as sensorimotor deficits, homonymous visual field defects, eye movement or pupil abnormalities, ataxia, vertigo, diplopia, dysarthria, dysphasia and dysphagia.

Radiological: Involvement of the posterior circulation territory [vertebra-basilar arterial system] on a CT/MRI brain with or without diffusion weighted imaging.

PROCEDURE:

Data sources:

Electronic Medical Records of the Hospital (Clinical workstation) and the study Clinical research form.

Data measurement:

The extra important data collected at admission, discharge 3 and 6 months were the modified Rankin Scale (mRS), and National Institute of Health Stroke Scale (NIHSS).

Data collection:

All data was collected on a predesigned clinical research form (CRF). (CRF in Annexure V). The CRF was designed to collect demographic characteristics, risk factors, aetiology, clinical profile, laboratory investigations and imaging features, was filled up for all the patients. The Modified Rankin Score and National Institute of Health Stroke scale data were also collected.

STROBE FIGURE:

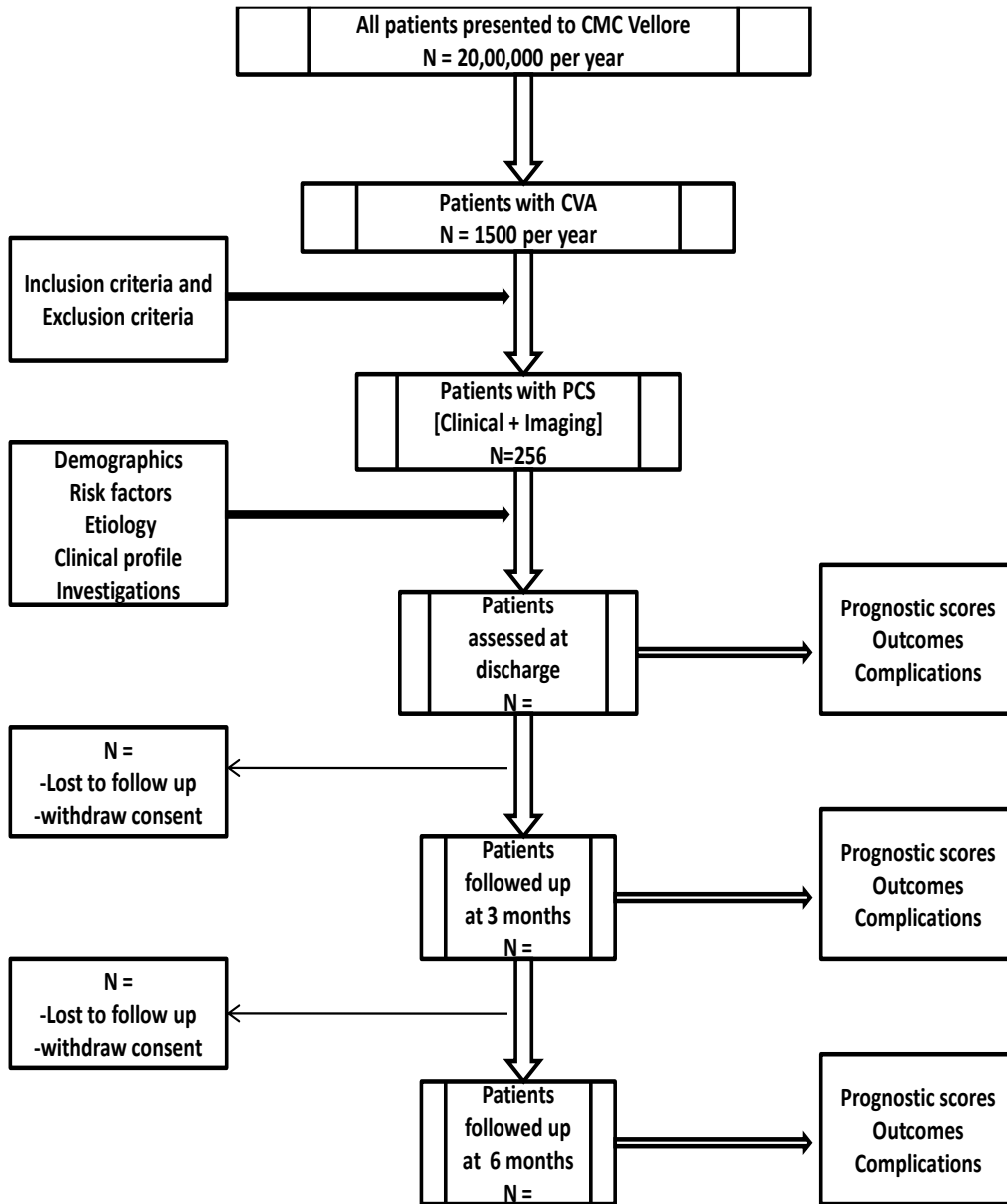


Figure 3 STROBE FIGURE of the POCSTROCH study [methodology section]

STATISTICAL ANALYSIS

Sample size calculation:

Sample size calculation was done using the N-Master-2 software. The sample size was based on the formula described by Lemeshow et al (125).

$$n = \frac{Z_{1-\alpha/2}^2 p(1-p)}{d^2}$$

Where,

p : Expected proportion

d : Absolute precision

$1 - \alpha/2$: Desired Confidence level

Based on the study by Labropoulos et al (42) using estimated 20% poor outcome with a precision of 5% and alpha error of 5% we planned to study 256 subjects.

The table below shows the sensitivity analysis done for the sample size calculation

Table 24: N master table for sample size calculation

Proportion	Precision	Q	sample size
10	5	90	144
10	7.5	90	64
20	10	80	64
10	6	90	100
15	7.5	85	90.66667
10	2.5	90	576
20	5	80	256
10	3.5	90	293.8776

Statistical methods:

All data from the CRF was entered in the epidata entry 3.1 software. This was then exported to the SPSS software version (21) for analysis. All analysis was done by a trained bio-statistician (Dr Visalakshi Jeyaseelan).

Prevalence of posterior circulation ischemic stroke was calculated as the proportion of those subjects who have posterior circulation ischemic stroke among those who were screened and this was expressed as percentages. The 95% CI for the prevalence was also calculated.

Demographic data was analysed with descriptive statistics such as mean with SD or median with IQR as mentioned above. All the quantitative variables were summarized using mean with SD or median with PQR depending on the distribution of each of the variable. The comparison of outcome for each quantitative variable was done using independent t-test or Mann whitney U test. Independent t-test was used if the distribution of the variables was approximately and if not, Mann Whitney test was done. All those variables which were significant at 0.2 level, were considered for multivariable analysis, which was a logistic regression and the OR with 95% CI was obtained. Categorical variables were expressed using frequencies and percentages. These categorical variables were associated with outcome (presence or absence of posterior circulation ischemic stroke) using chi-square test or Fisher's exact test. All those categorical variables which were significant at 0.2 level will be considered for multiple Logistic regression analysis.

The Hosmer Lemeshow goodness of fit was calculated to see which variables provided a good fit.

Median Survival time was calculated using Kaplan Meier estimate. The risk factors for survival time was done using Cox Proportional Hazards model. This assumption was checked using Log log survival plot for each variable.

This dissertation complies with **2007 STROBE GUIDELINES** for observational studies
[Annexure X]

RESULTS

STROBE FIGURE

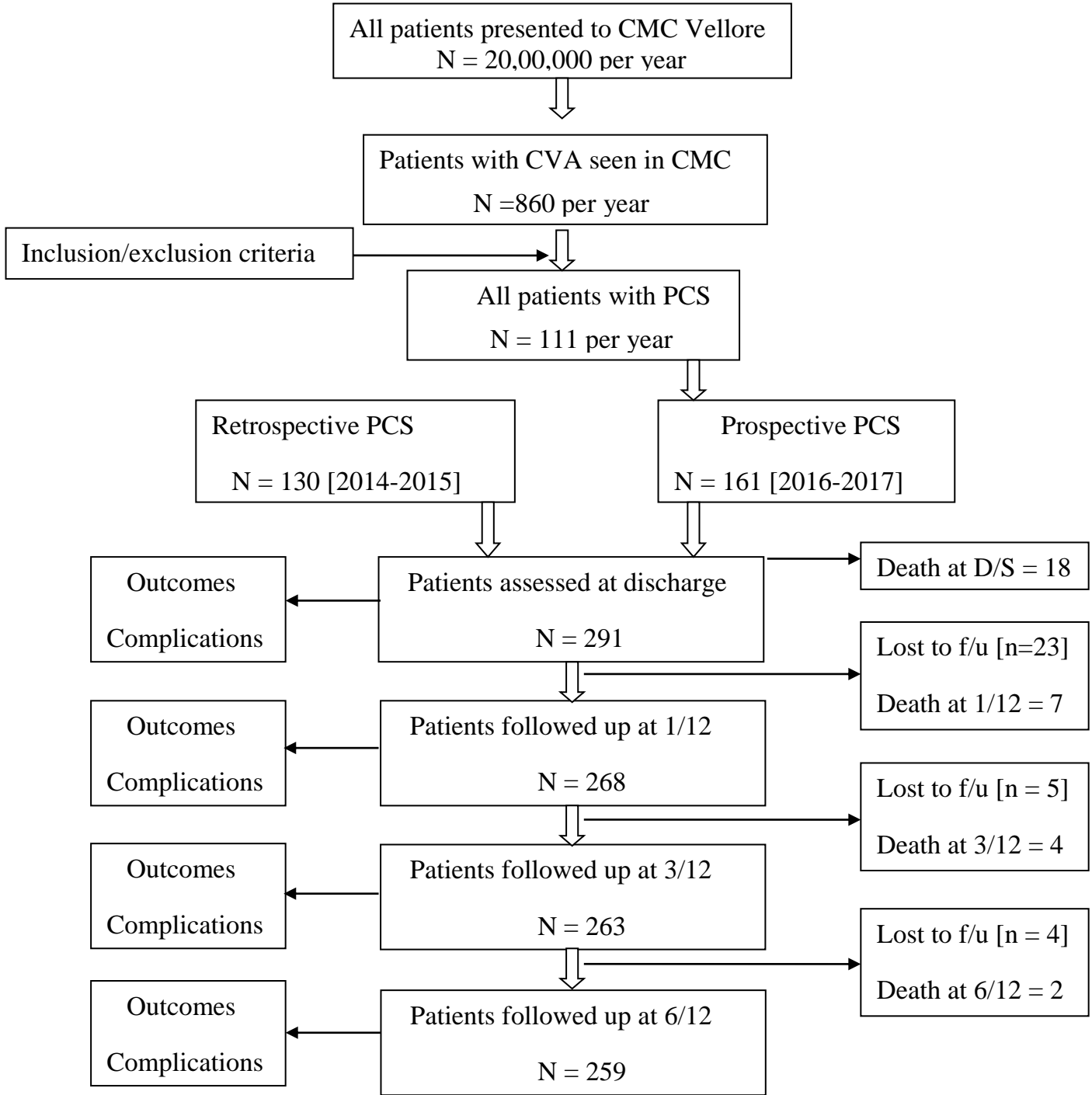


Figure 4 STROBE figure showing the flowchart of the POCSTROCH study

BASELINE CHARACTERISTICS

Baseline characteristics of the study population was divided into following categories:

A. Demographic details

B. Comorbidities

C. Clinical Features

D. Laboratory parameters

Demographic details:

Gender distribution of the patients:

Of the 291 patients studied, three-fourth were males. There were 222 males [76.3%] and 69 females [23.7%]. The male to female ratio was 3.21:1. The gender distribution is depicted below in figure 1.

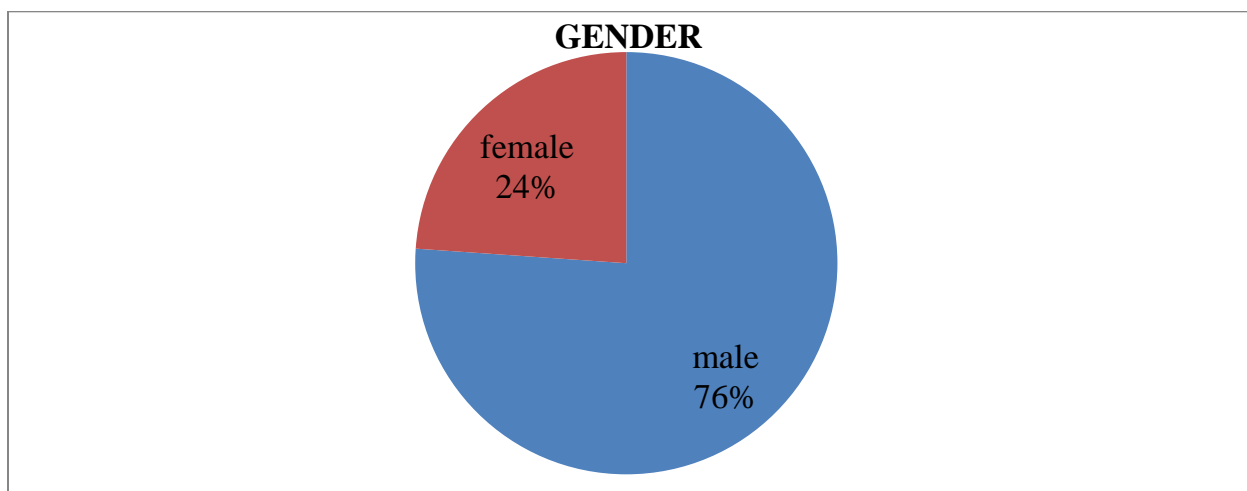


Figure 5 Pie chart showing the distribution of patients based on gender

Age distribution:

The mean age of the study population was 53.34 years with a standard deviation of +/-13.34 years and the median was 54 years, with an interquartile range of 19 [54 to 63]. The youngest patient included was 18 years old and the oldest was 94 years of age. The recruited patients had been further stratified into 5 age groups.

- 1. < 30 years of age
- 2. 30 to 45 years of age
- 3. 46 to 55 years of age
- 4. 56 to 75 years of age
- 5. > 75 years of age

The age distribution of the patients in shown below in figure 2.

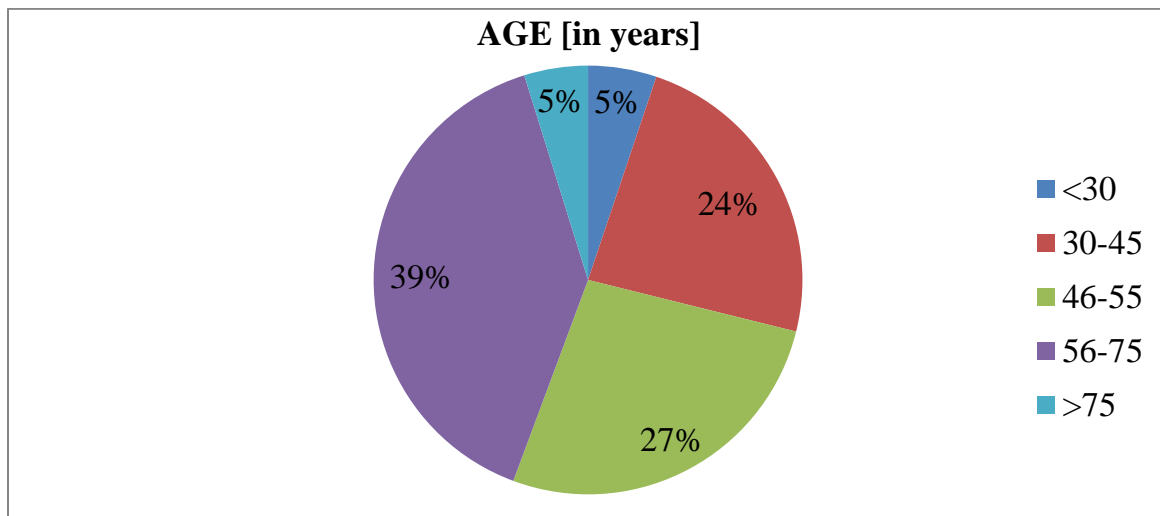


Figure 6 Pie chart showing distribution of patients based on age stratification

Patients, with respect to the definition of young stroke, were also analysed based on the age group of 45 years or below, which comprised 28.8 % [N=84] of the study population. Major part of the population were of the fifth and sixth decade.

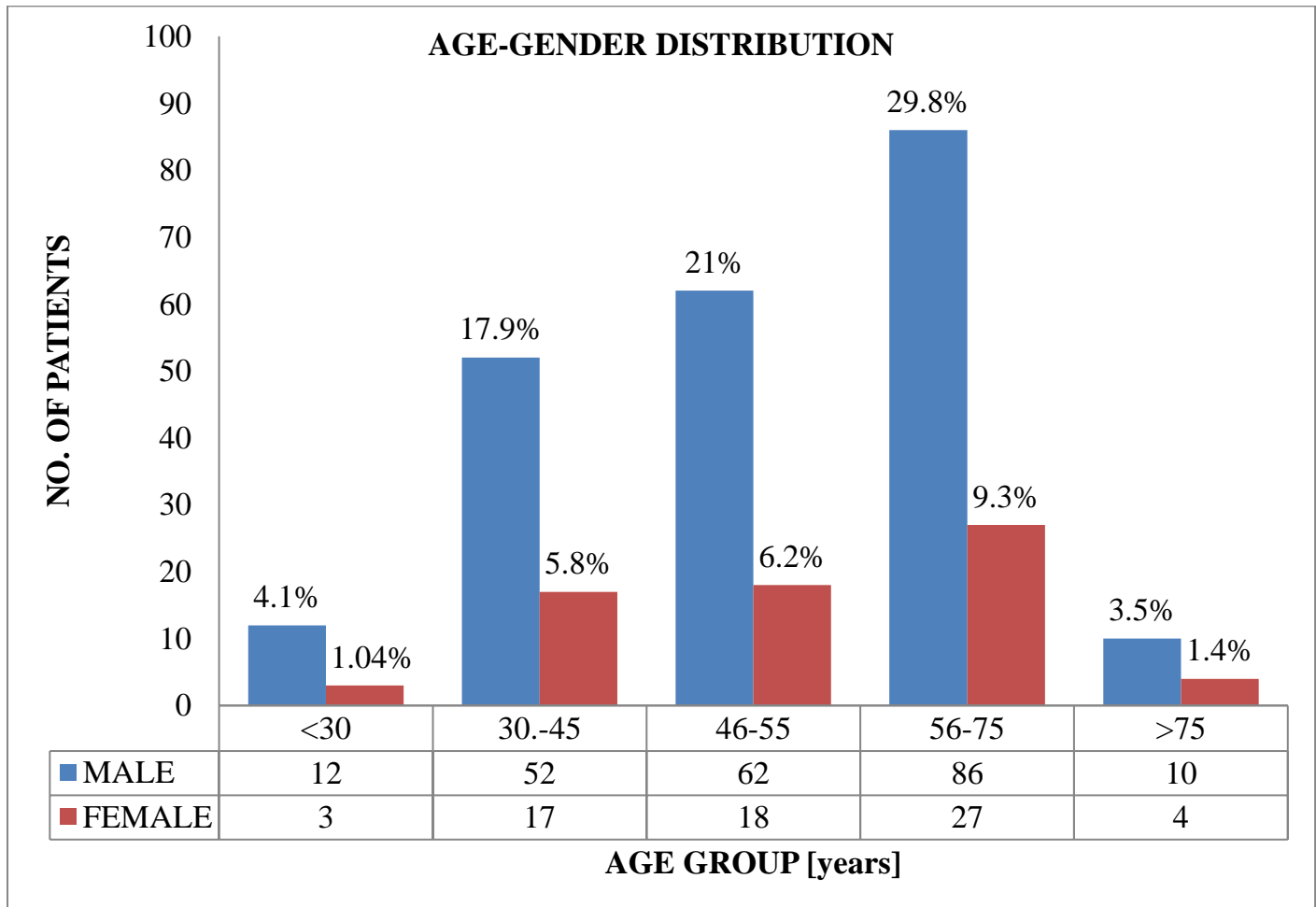


Figure 7 Bar graph showing age-gender distribution of the study population

Posterior circulation strokes was found to be more common among males [76%] and a similar trend was present in all the age groups. Maximum number of males with stroke

belonged to the age group of 56 to 75 years and was 30 % of the total PC strokes [86/291].

Similarly, maximum number of females who presented with stroke belonged to the age group of 56 to 75 [27/291], though they presented with relatively less than half the number of strokes in each age group.

Region of Residence:

Overall 80.1 % [N= 233] of the patients belonged to the local area of residence, which included the districts of Vellore, Chittoor and Tiruvanamalai. The remaining 19.9 % [N=58] were from elsewhere.

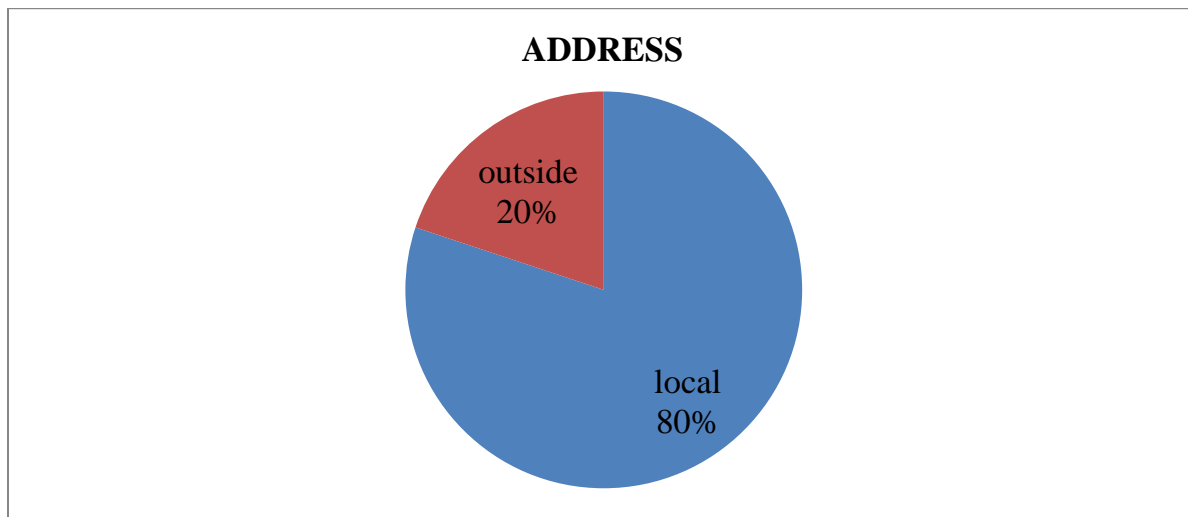


Figure 8 Pie chart showing the patient distribution based on their area of residence

Arrival location:

Three-fourths of patients with features of posterior circulation stroke, presented to the emergency department [N=224], suggesting early presentation to the hospital with

significant debilitating symptoms, but diagnosis can be missed out and treatment delayed with respect to the non-specific symptoms.

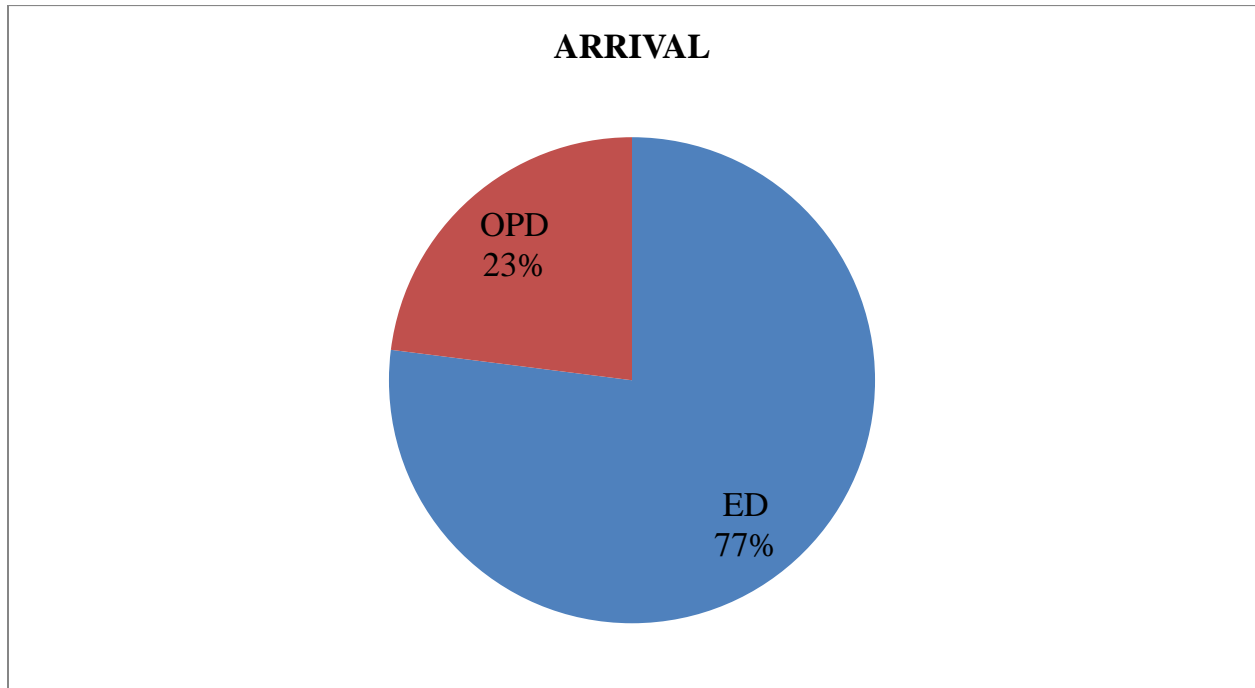


Figure 9 Pie chart depicting the distribution of the arrival location of patients

First Medical Contact:

Patients were initially managed either in a local hospital and later referred to our tertiary care centre, or had been brought directly to our centre, based on accessibility and need for higher care. More than two-thirds [69.4%, N = 195] of the patients presented to the local physician, before being referred to CMC. Therapeutic interventions in terms of thrombolysis, which depended on the onset-to-door time and door-to-needle time, was less feasible, due to the above presentation. First point of contact to our centre, was noted in 30%, with varying time intervals, from symptom onset to first presentation.

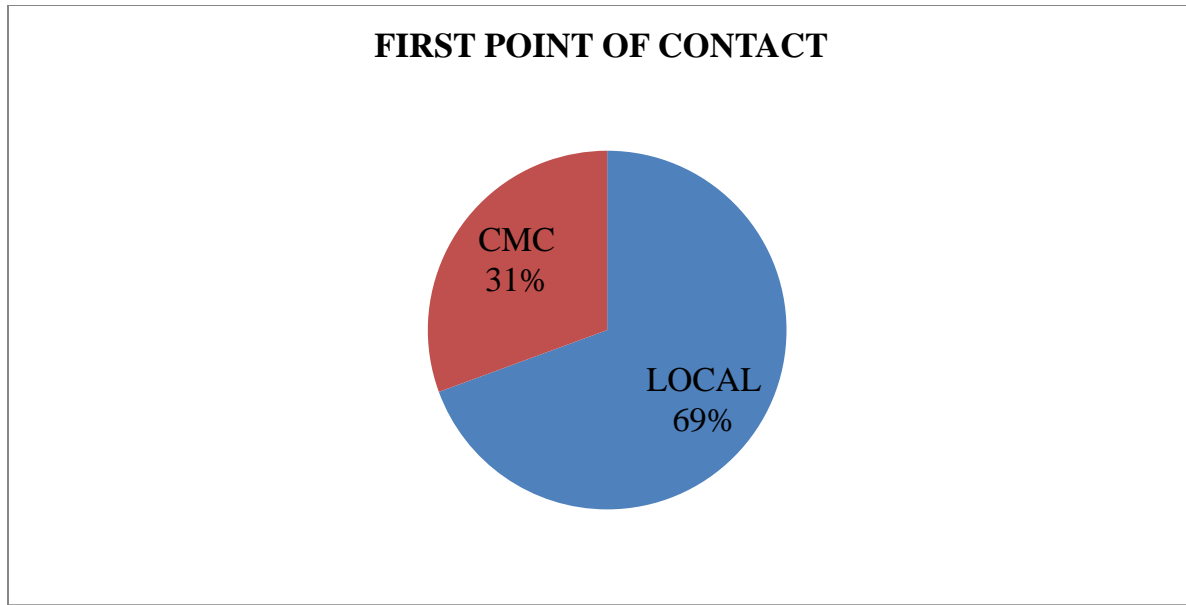


Figure 10 Figure Pie chart showing the distribution of first point of contact of care

Discharging departments:

In our centre, patient was initially seen in emergency department, from where patient get admitted under any one of the 5 units of General Medicine department, Neuromedicine or other units such as PMR. 68% [N=198] of the total study population [N=291] were admitted and managed in the ward. 13.1% [N=38] of the patients were discharged against medical advice from emergency department. Patients were later followed up in the out-patient departments including the stroke clinic. The distribution of patients based on the departments that managed them, has been shown below [figure 7]:

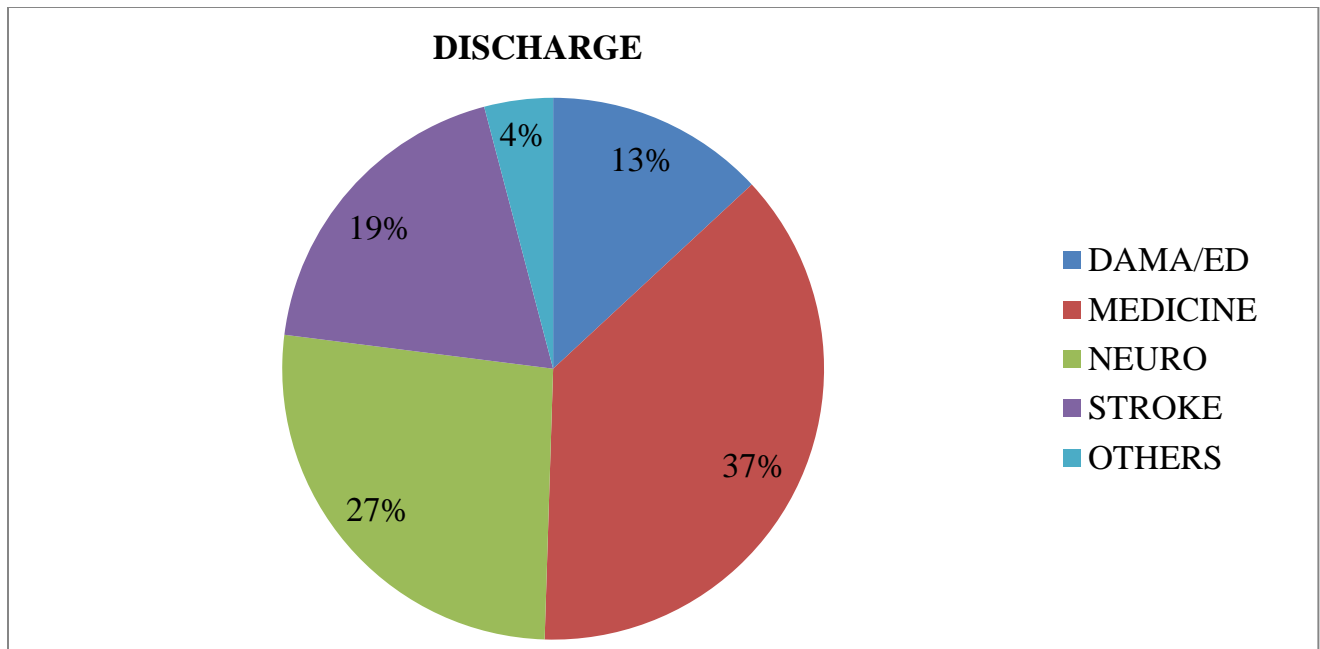


Figure 11 Pie chart depicting the department based distribution of the patients

Wake-up stroke:

The stroke presentation of patient, who was normal prior to sleep, but awakens with stroke symptoms, poses a therapeutic dilemma. Patient who presented with wake up stroke, constituted 15 % [N=43/291] of the total study population.

TIA before stroke:

10.3% [N= 30] of the patients presented with the history of transient ischemic attack, prior to the onset of posterior circulation stroke, suggesting the need to increase patient awareness about red flag symptoms and to emphasis on early intervention to prevent stroke.

In-hospital stroke:

5 patients [1.7%] developed posterior circulation stroke, while being admitted in hospital for other medical reasons.

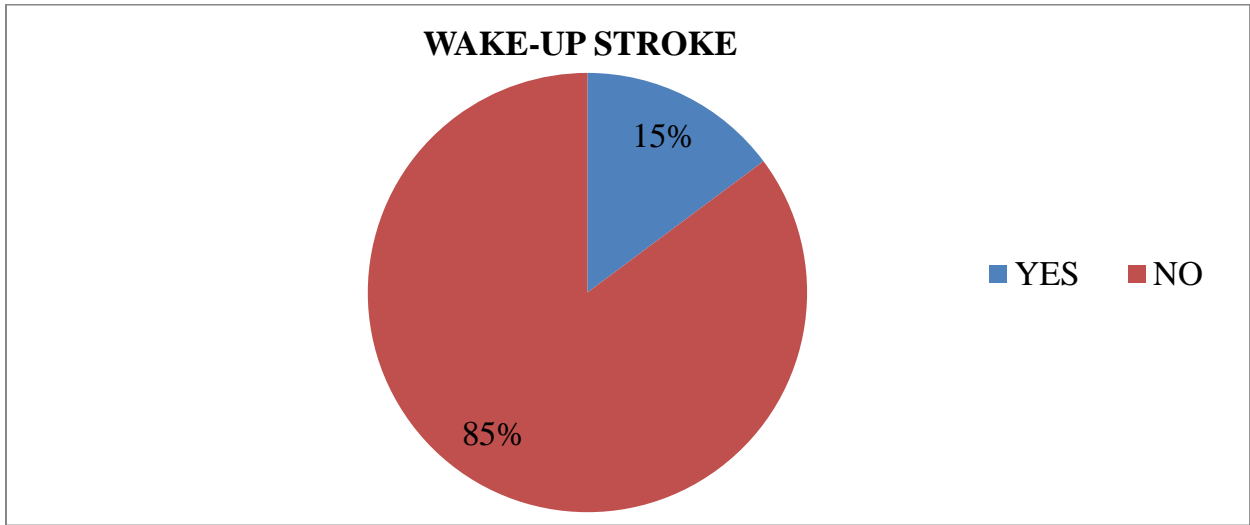


Figure 12 Pie chart showing the distribution based on wake-up stroke

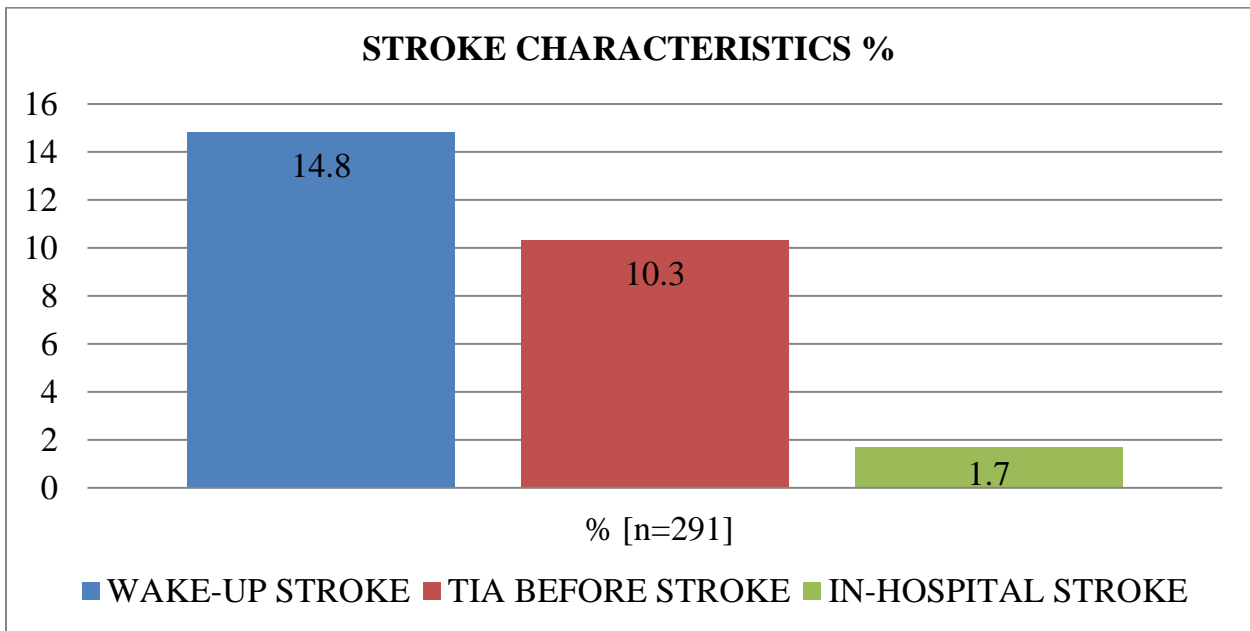


Figure 13 Bar chart depicting the various stroke characteristics

COMORBIDITIES

The study population was evaluated for the comorbidities, which was assessed to find the correlation as a possible risk factor contributing to the etiology of the posterior circulation stroke.

Hypertension was found to be the most common comorbidity and was present in 71.8% [N= 209] of the patients, with a high blood pressure [Systolic BP \geq 160mmHg or Diastolic BP \geq 100 mmHg] recorded at admission, in 55% [N= 159] of the patients.

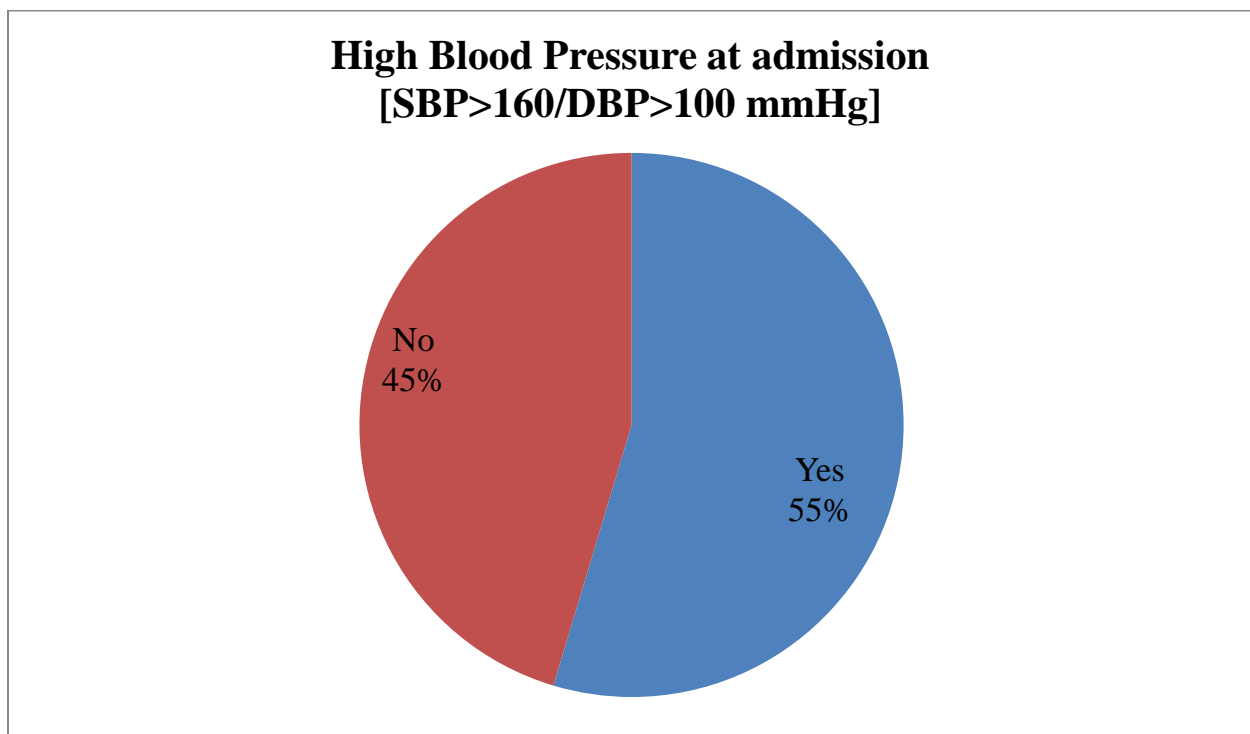


Figure 14 Pie chart showing distribution of patients with high BP at admission

153 patients had Diabetes mellitus [52.6%], with HbA1C of ≥ 7 g/dl in 77 patients. History of smoking was present in 38.5% of the patients [N= 112], and one-third of the patients had dyslipidaemia [N=95]. Fasting lipid profile was done which showed one-fifth of the patients [N=42/206] with total cholesterol level more than 200mg/dl, 18% with high triglycerides level of more than 200mg/dl. 40% of 206 patients had HDL < 35 g/dl and LDL level more than 100g/dl was found in about 50% of 207 patients.

Alcohol consumption was present in 22.3% of the patients [N=65]. 40% patients with ischemic stroke underwent 4-vessel colour doppler and significant stenosis was found in 82 patients. History of previous cerebrovascular accident or transient ischemic attacks was found in 50 patients [17.2%].

Other comorbidities assessed include previous history of valvular [4.8%] or ischemic heart disease [12.4%], cardiomyopathy, arrhythmia, and patent foramen ovale or shunt. Management of a cardioembolic stroke and in presence of large intracranial artery atherosclerosis included anticoagulation.

Hyperhomocysteinemia and low vitamin B12 levels were found in about 11% of patients. When no significant above comorbidities were diagnosed on initial evaluation, patients were further evaluated for evidence of vasculitis, dissection, malignancy, polycythemia, migraine, obstructive sleep apnea, chronic kidney disease, and infections including tuberculosis, and each of them was found to be present in less than 5 % of the study population.

Table 25: Distribution of comorbidities by their percentages

COMORBIDITIES	N	%
Hypertension	[209]	71.8%
Diabetes mellitus	[153]	52.6%
Dyslipdaemia	[95]	32.6%
High triglycerides	[24]	8.2%
Smoking	[112]	38.5%
Alcohol	[65]	22.3%
Carotid disease	[82]	28.2%
Ischemic heart disease	[36]	12.4%
Arrhythmia	[3]	1%
Valvular heart disease	[14]	4.8%
Recent MI	[8]	2.7%
Cardiomyopathy	[5]	1.7%
PFO/shunt	[12]	4.1%
Hyperhomocystinemia	[34]	11.7%
Low VitaminB12	[32]	11%
Migraine	[8]	2.7%
Tuberculosis	[2]	0.7%
Dissection	[7]	2.4%
Obstructive sleep apnea	[8]	2.7%
Malignancy	[4]	1.4%
Polycythemia	[6]	2.1%
Chronic kidney disease	[15]	5.2%
Recurrent stroke	[50]	17.2%

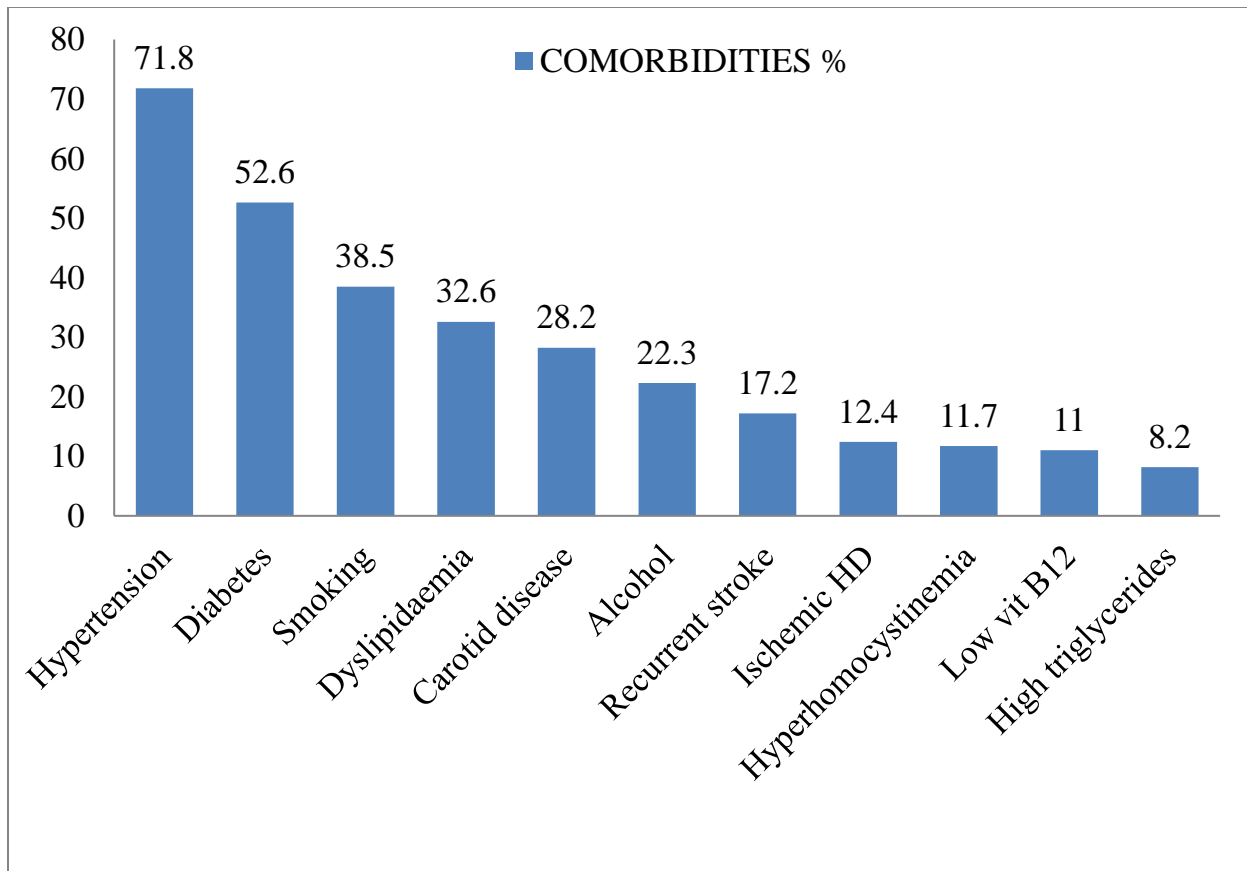


Figure 15 Bar graph showing distribution of patients with comorbidities

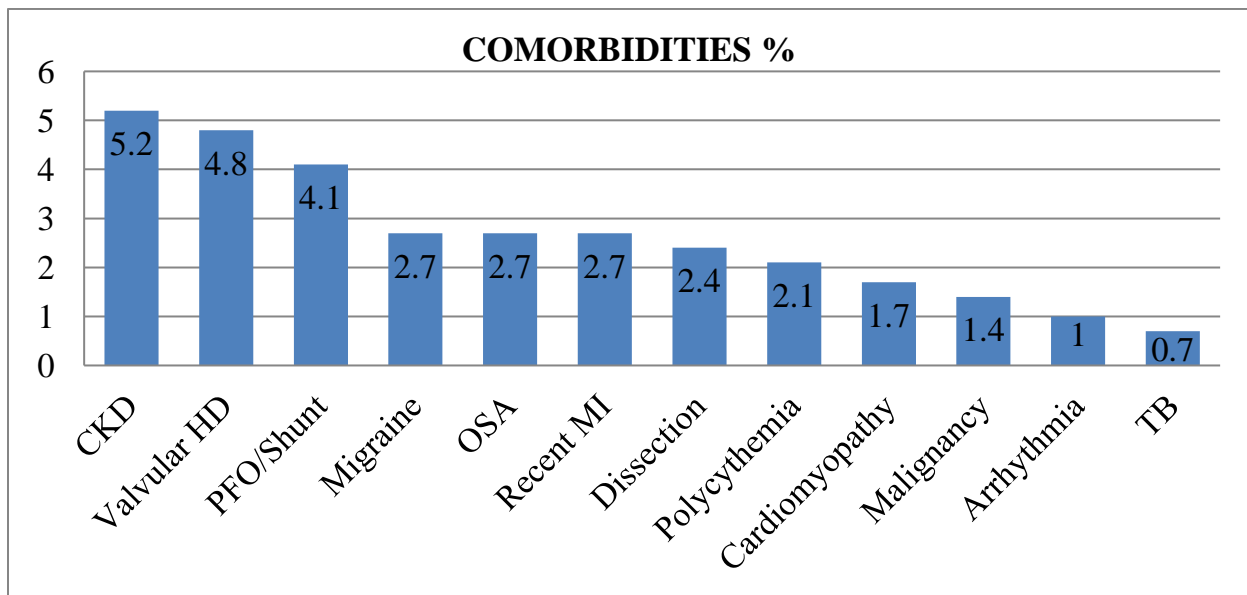


Figure 16 Bar graph showing distribution of patients with comorbidities [contd...]

CLINICAL PROFILE

Unlike in anterior circulation stroke, patients with posterior circulation stroke had predominantly non-specific symptoms. Three-fourths of the patients diagnosed with PC stroke, presented with symptoms of giddiness and feeling of unsteadiness [N=219], and ataxia was seen in 56 % of the patients N=163]. One-fifth of the patients[N=60] had altered sensorium, masking the other possible symptoms. Motor deficits was a predominant clinical feature in 48.8% of the patients [N= 142]. Nausea or vomiting was a very common symptom [43%, N= 143] alongwith gidiness, in patients with PC strokes.

Slurring of speech was one of the main symptom in one-fourth of the patients and dysphagia was seen in one-fifth of the patients, and was started on NG feeds.

Table 26: Percentages of clinical features in patients with PC stroke

CLINICAL FEATURES	N	%
Low consciousness	[60]	20.6%
Motor deficits	[142]	48.8%
Sensory deficits	[34]	11.7%
Crossed syndromes	[22]	7.6%
Ataxia	[163]	56%
Unsteadiness	[219]	75.3%
Vertigo	[230]	79%
Nausea/ vomiting	[125]	43%
Dysarthria	[74]	25.4%
Dysphagia	[61]	21%
Diplopia	[24]	8.2%
Visual abnormalities	[44]	15.1%
Bowel involvement	[1]	0.3%
Bladder involvement	[2]	0.7%

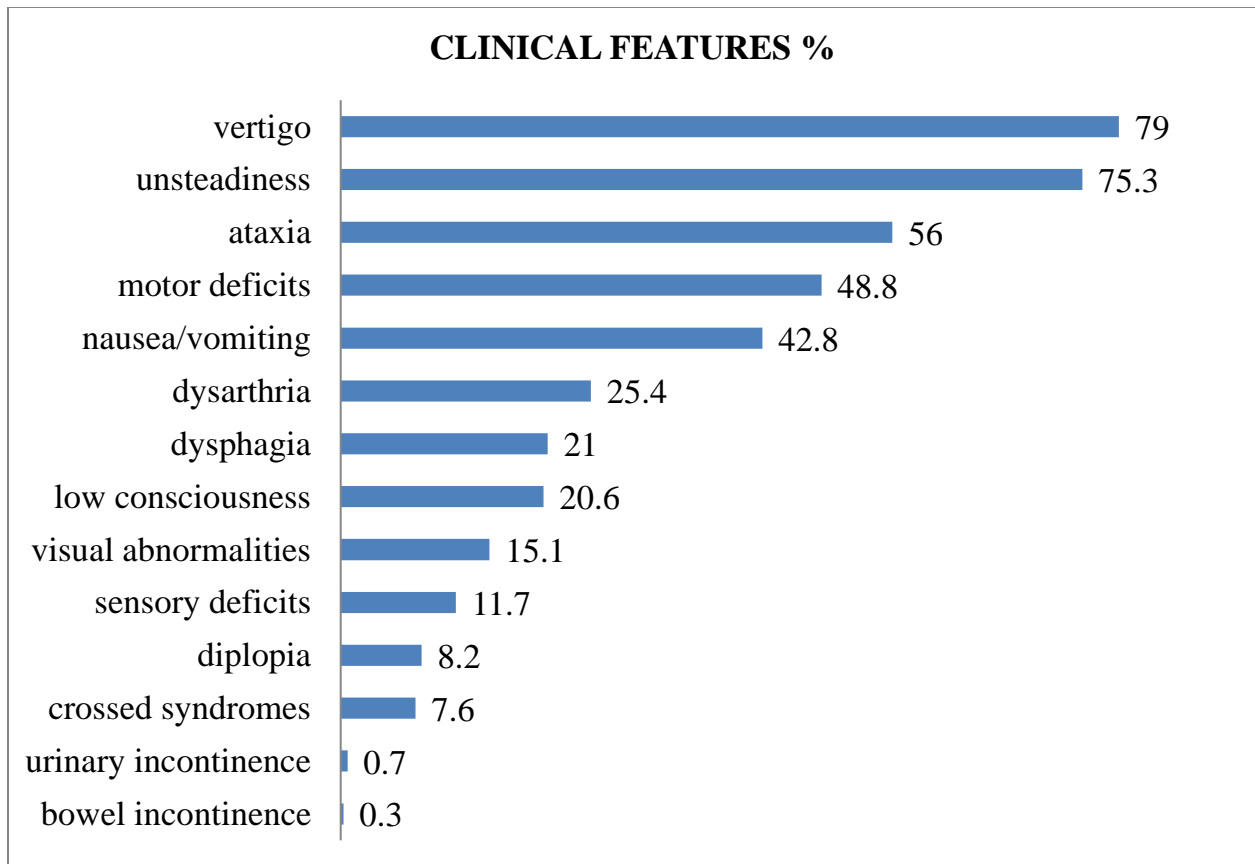


Figure 17 Bar chart showing percentages of clinical features in patients with PC stroke

Stroke scales:

National Institute of Health Stroke scale [NIHSS] and Modified Rankin Scale [mRS] scores were calculated for each patient at admission, and patients were followed up at discharge, at one month, at three month and at six months, with mRS score.

NIHSS scores of the patients at admission was divided into four categories of mild [1-7], moderate [8-14], severe [15-25], very severe [>25], and the patient distribution was shown in the figure below. Based on NIHSS score, 13.4% [N = 29] of the patients had severe stroke at the time of presentation.

Table 27: Distribution of patients based on NIHSS at admission

BASELINE NIHSS SCORE	N= 291	%
Mild [1-7]	176	60.5%
Moderate [8-14]	76	26.1%
Severe [15-25]	28	9.6%
Very severe [>25]	11	3.8%

Table 28: Mean and median value of NIHSS at admission

N =291	Mean	S.D.	Minimum	0.25	Median	0.75	Maximum
NIHSS	7.3	6.74	1	3	5	8	34

mRS score of the patients was calculated to assess the stroke severity at admission and followed up till 6 months. mRS score was further categorised, with score 1 to 3 considered as good outcome, found in 79% of the patients [N=205] and score 4 to 6 as bad outcome in 21% [N=54]. Score 4 or 5 was considered as morbid state, and 6 was death.

Table 29: Mean and median value of mRS at admission

N=291	Mean	S.D.	Minimum	0.25	Median	0.75	Maximum
mRS	2.71	1.12	0	2	2	3	5

Correlation between mRS and NIHSS at admission:

A good linear correlation was found to exist between the two scoring systems, in this study population, and was found to be highly significant with statistical methods.

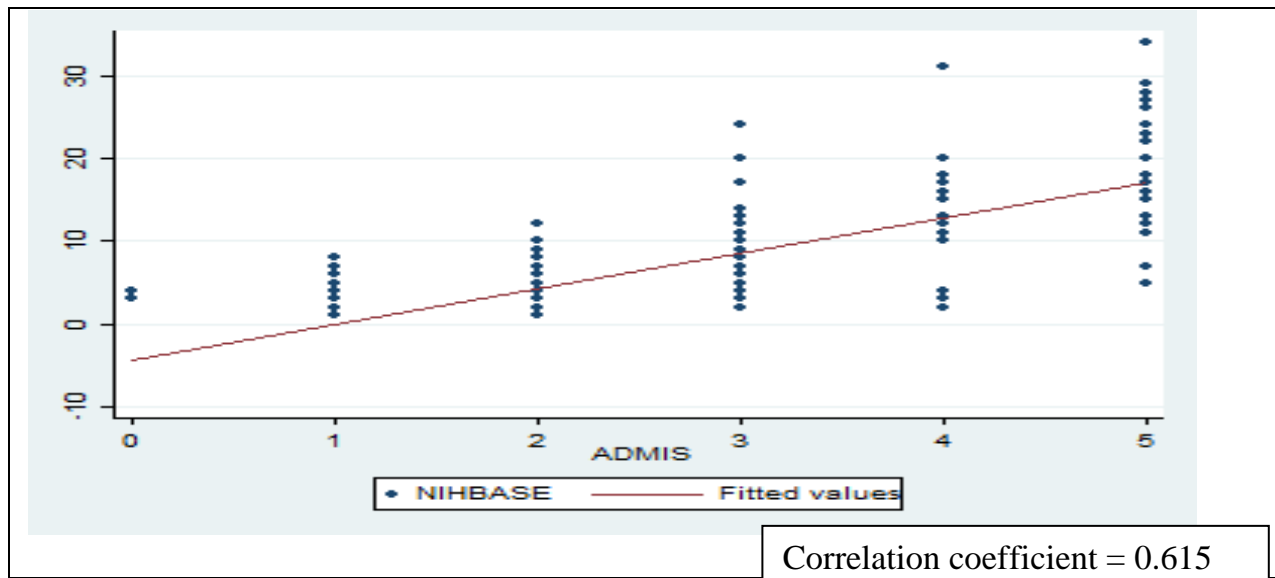


Figure 18 Scatter plot showing correlation between NIHSS and mRS at admission

Diagnostic imaging modality

85 % [N = 248] of the posterior circulation stroke was diagnosed with MRI, of which MRI with Acute Stroke Protocol comprised 35% [N = 101]. Many patients with plain CT brain done initially to rule out an intracranial bleed, had later on underwent a detailed MRI with an MR angiogram, to delineate the etiopathogenesis of the stroke.

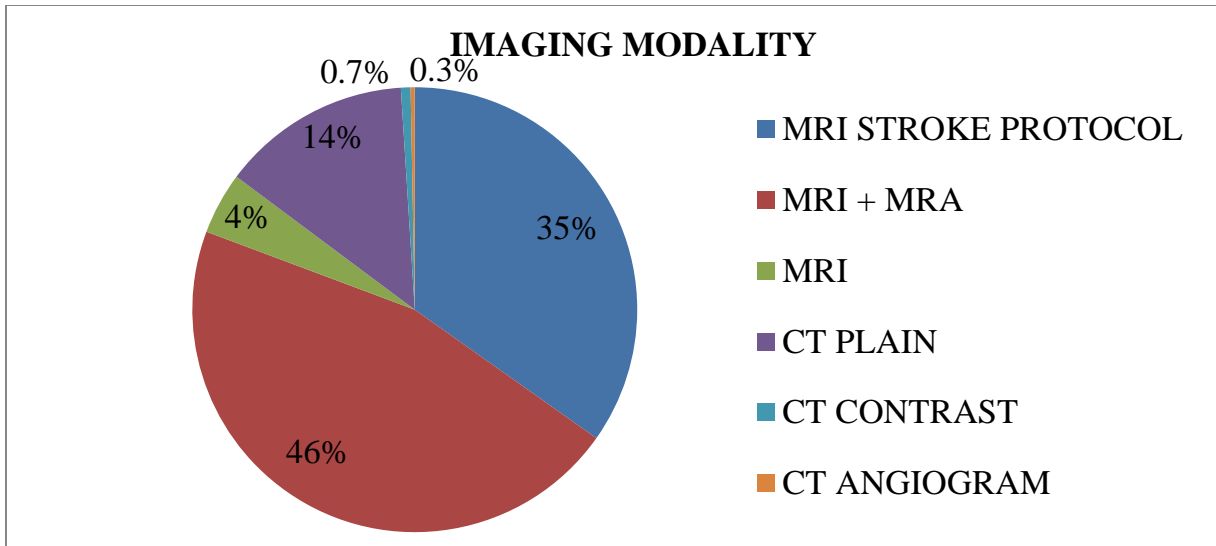


Figure 19 Pie chart showing patient distribution based on imaging modality used

STROKE CHARACTERISTICS

Stroke presentation:

Acute presentation of posterior circulation stroke was found in 67% of the patients [N= 195], while 32.6% [N= 95] had late presentation to our centre.

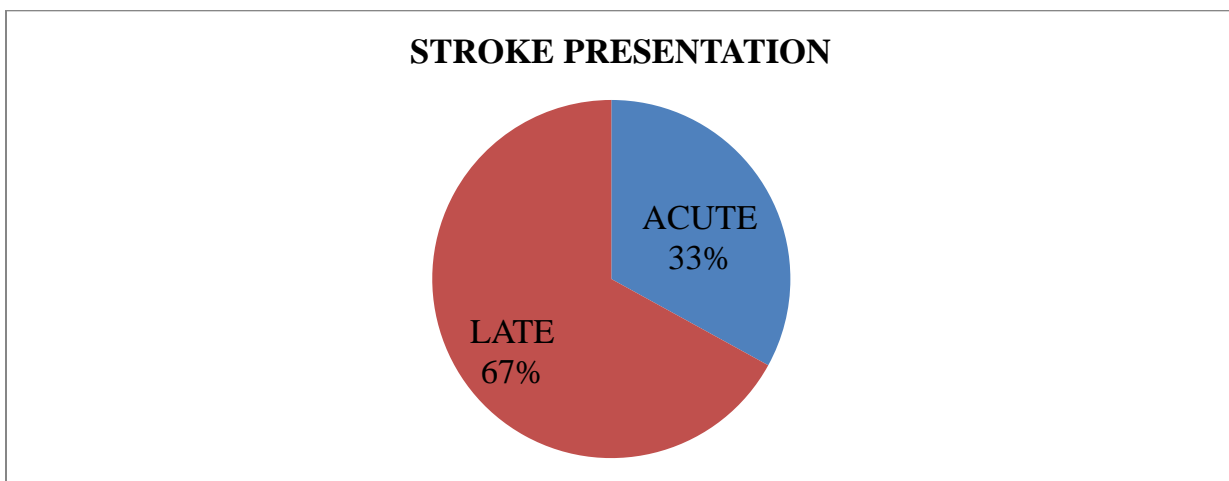


Figure 20 Pie chart showing distribution of type of stroke presentation among patients

Stroke pathology:

All the patients included in the study population belonged to the class of posterior circulation stroke under the Oxfordshire classification.

Pathological type of stroke was crucial to be identified in the earliest possible time, to decide on further intervention. 39 out of the 291 patients [13.4%] observed had hemorrhagic stroke. Among the ischemic strokes [86.5%, N=252], 15 patients had hemorrhagic transformation of the infarct at presentation. Patients were monitored for other complications including raised intracranial pressure, infarct extension, hydrocephalus, and seizure.

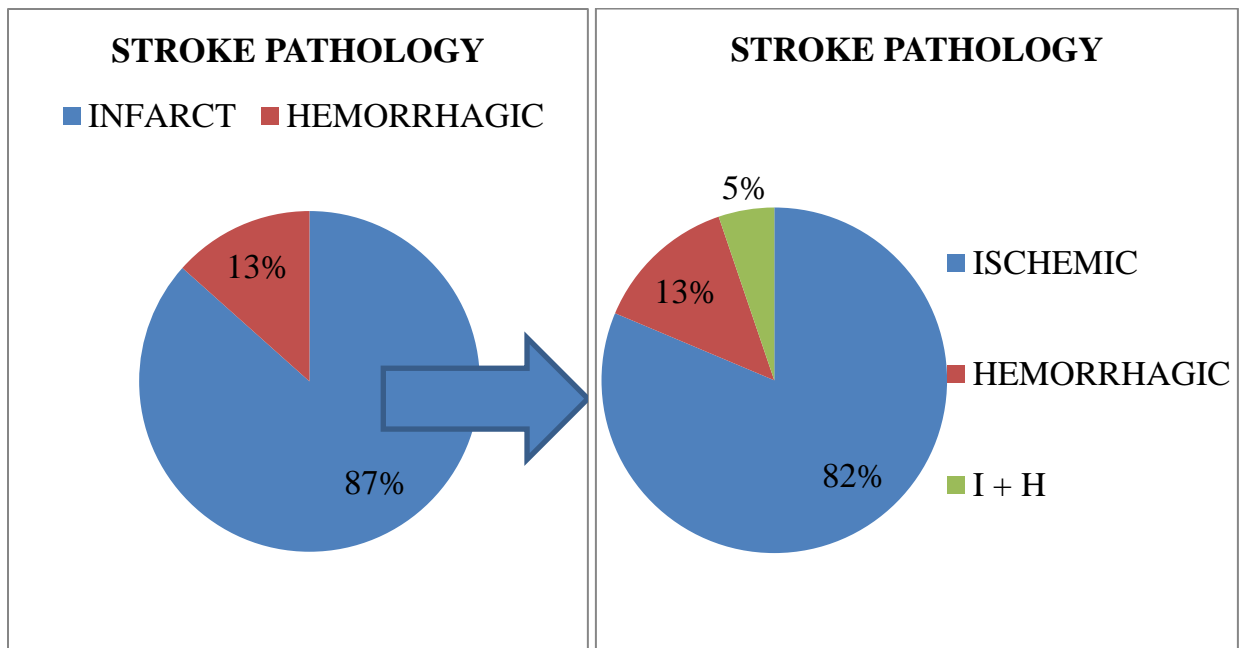


Figure 21 Pie chart showing the distribution based on pathological type of stroke

Characteristics of Arterial territory:

While 29 % [N=85] of the patients had bilateral arterial territory involvement, 39% [N=112] had predominantly left side involvement.

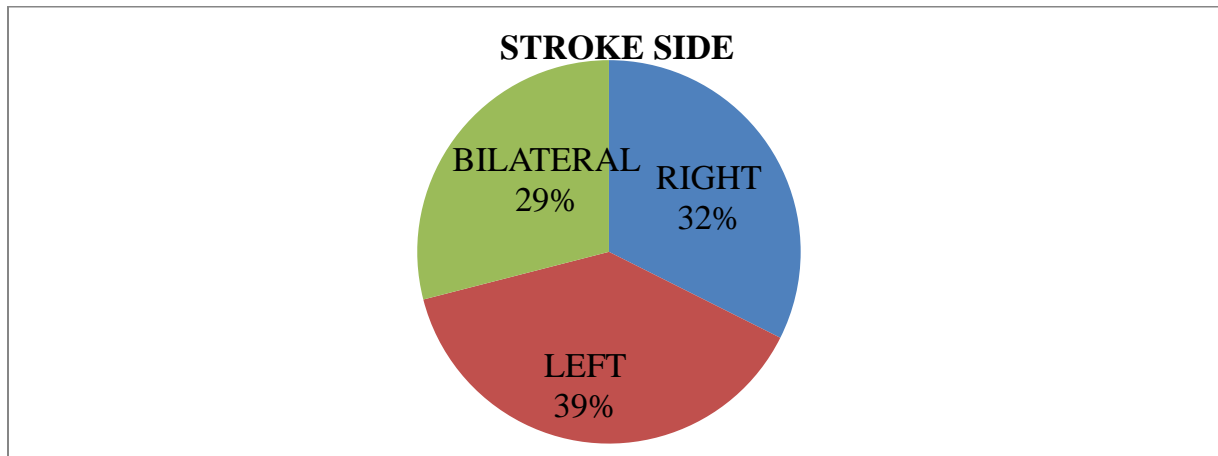


Figure 22 Pie chart depicting the side of arterial involvement

Arteries involved:

Radiological imaging had been evaluated in detail to assess the arteries of the vertebrobasilar system, involved in the posterior circulation stroke. There was a predominant involvement of the distal arterial system. Posterior cerebral artery was involved in 45 % of the patients, which also included the thalamic artery and other branches. The next common involvement was that of the posterior inferior cerebellar artery [38%], which was a branch of the vertebral artery. Basilar artery occlusion was found in about one-fifth of the patients. Vertebral artery dissection was found in 7 patients [2.4%].

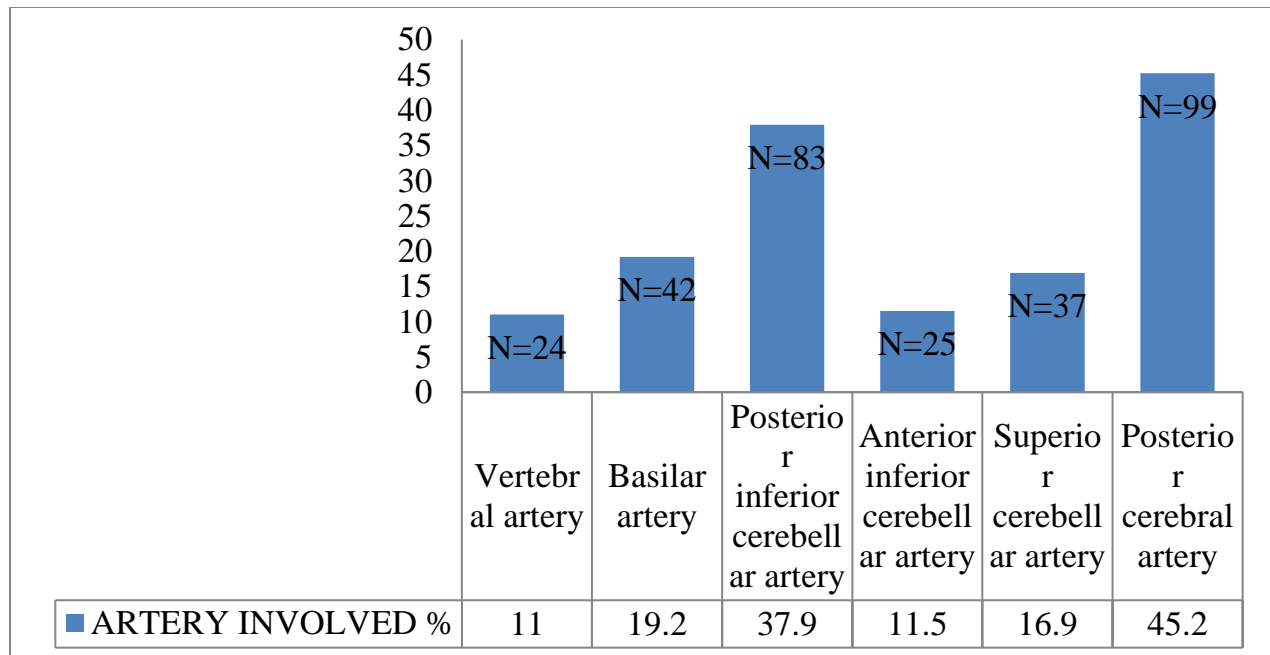


Figure 23 Bar chart showing distribution based on vertebrobasilar arterial system involvement

Stroke etiology- TOAST criteria:

According to the TOAST criteria [Trial of Org 10172 in Acute Stroke Treatment Classification], ischemic strokes were classified into seven categories based on the etiology. Clinical features, imaging findings, underlying comorbidities and laboratory parameters, aided in identifying the possible etiology of the patients who presented with the posterior circulation ischemic strokes.

Table 30: Distribution of ischemic stroke based on TOAST criteria

ETIOLOGY-TOAST	N	%
LAA	[128]	50.8%
CE	[36]	14.4%
SVO	[36]	14.4%
ODE	[17]	6.8%
UDE 2 OR >	[12]	4.8%
UDE –VE ETIO	[14]	5.6%
UDE INCOMPLETE	[9]	3.3%

51% of the patients [N = 128] had Large artery atherosclerosis, as the etiological cause for PC stroke. Cardioembolic stroke was found in 36 patients [14.4% of ischemic strokes] involved stroke secondary to valvular heart disease [4.8%], recent myocardial infarction [2.7%] with left ventricular systolic dysfunction, patent foramen ovale or right-to-left shunt [4.1% cumulatively], and arrhythmia [1%]. Lacunar strokes in the posterior circulation territory was included in the small vessel occlusion, which comprised same proportion of ischemic strokes as cardioembolic strokes. Other and un-determined etiology included hyperhomocystinemia, low vitamin B12, primary CNS vasculitis, systemic vasculitis, migraine, malignancy, and infection as underlying etiological causes.

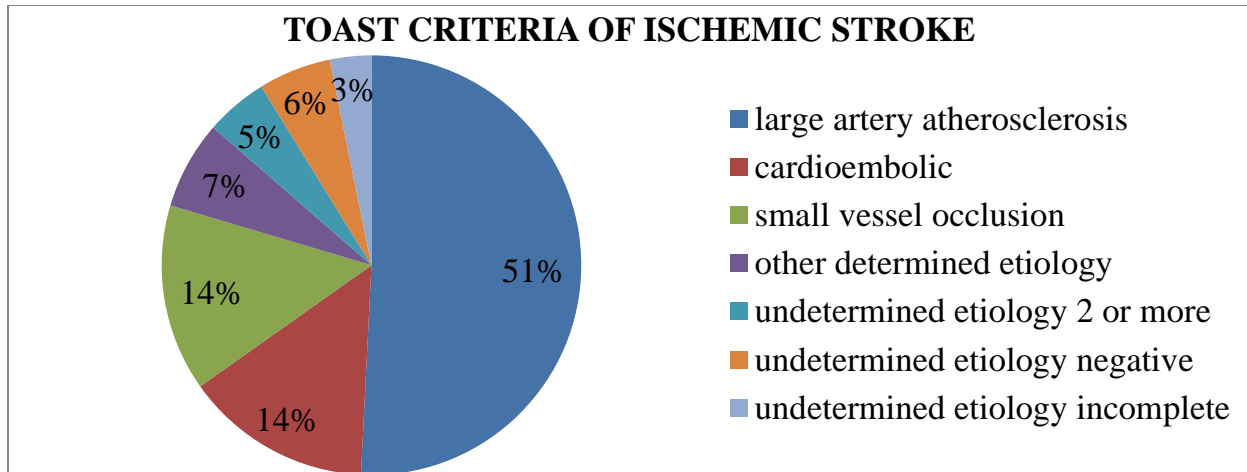


Figure 24 Pie chart showing distribution among ischemic strokes based on TOAST

MANAGEMENT

Management of posterior circulation stroke in the study population was categorized into:

1. Conservative
2. Thrombolysis
3. Surgical decompression

About 94% [N=273] of the total 291 patients had conservative management, which was mainly medical therapy. This category included those patients who opted for discharge against medical advice [5%]. Minority of patients, that is, around 5% underwent any therapeutic medical or surgical intervention. Among the 12 patients [4.1%] with raised intracranial pressure, and 6 patients [2.1%] with hydrocephalus, 10 patients underwent surgical decompression. 4 patients [1.4%] who fulfilled all the necessary criteria, underwent thrombolysis.

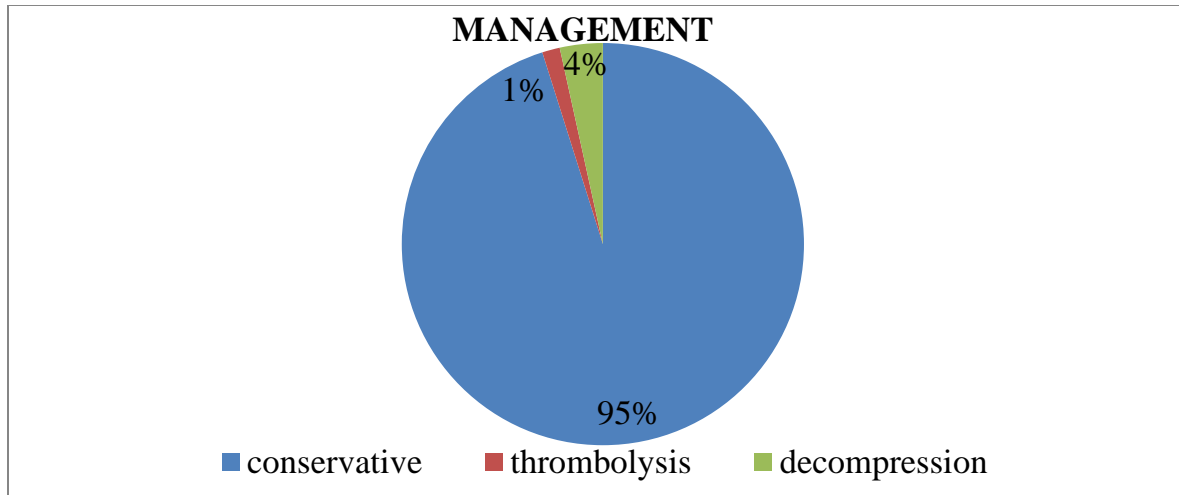


Figure 25 Pie chart showing distribution of patients based on the management

Medication:

50% of the patients [N=141] received single antiplatelet, mostly aspirin, as a part of the medical management of the stroke, to prevent recurrent stroke. One-fifth of the patients were initiated on dual antiplatelet, which was mostly changed to single antiplatelet in 3 months, in those patients with no underlying ischemic heart disease. Cardioembolic stroke and large intracranial artery atherosclerosis was given anticoagulation.

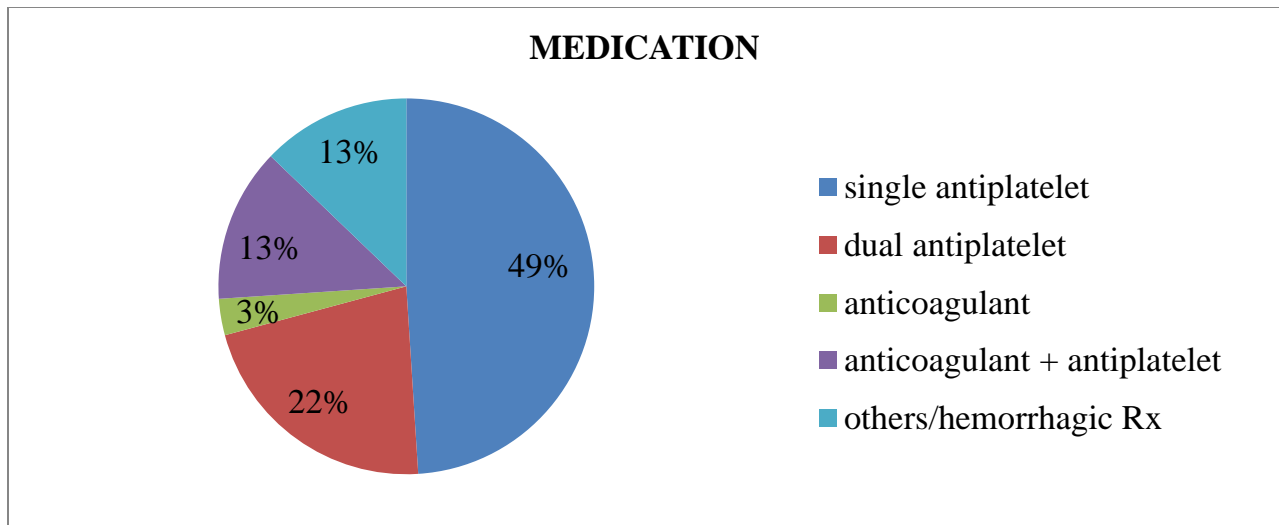


Figure 26 Pie chart showing distribution based on the medication received

Vitals and GCS of the patient was monitored. Antihypertensive dosages were optimised and patients were also evaluated and managed for the underlying comorbidities.

Patients were followed up in outpatient department including the stroke clinic for further drug optimisation, etiological work up and to manage the complications.

COMPLICATIONS

Mortality and mRS score at discharge:

18 patients died during the hospital stay, secondary to extensive stroke and due to complications which predominantly included sepsis. 31 patients had significant morbidity with a poor mRS score of 4 or 5 at discharge.

Patients were evaluated and managed the complications, which included the acute complications while admitted, and the late complications, which was addressed on outpatient basis, and readmitted, if warranted.

Most common acute complication was dysphagia [33%, N= 95]. One-third of patients were put on nasogastric feeds, whom were later reassessed for swallowing function and reinitiated on oral feeds, if tolerated. One-fifth of the patients [N= 56] had sepsis, while admitted with stroke, which was predominantly lower respiratory tract infection and urinary tract infection. About 8 % patients [N=23] with airway compromise, secondary to stroke or complications, required invasive ventilation, and some on prolonged ventilation underwent tracheostomy. 10 [3.4%] patients had seizure, either at presentation or later during the hospital stay, who were initiated on antiepileptics. 3 patients had myocardial infarction, while admitted with posterior circulation stroke.

Post-stroke pain was noted commonly [23%, N=67] during follow-up and often required pharmacotherapy to alleviate the neuropathic pain. 10% of patients [N=30] had cognition decline or extrapyramidal symptoms. Bedsores were found in patients [4.5%, N=13] with poor mRS score who were bedbound. Depression was another complication found significantly in about 4% patients, especially in those with high mRS score during follow-up, who are morbid and dependent. Acute coronary syndrome was seen in 4 patients during follow-up. Recurrent stroke 3.1%, N=9], especially in patients who were non-compliant to medication was noted.

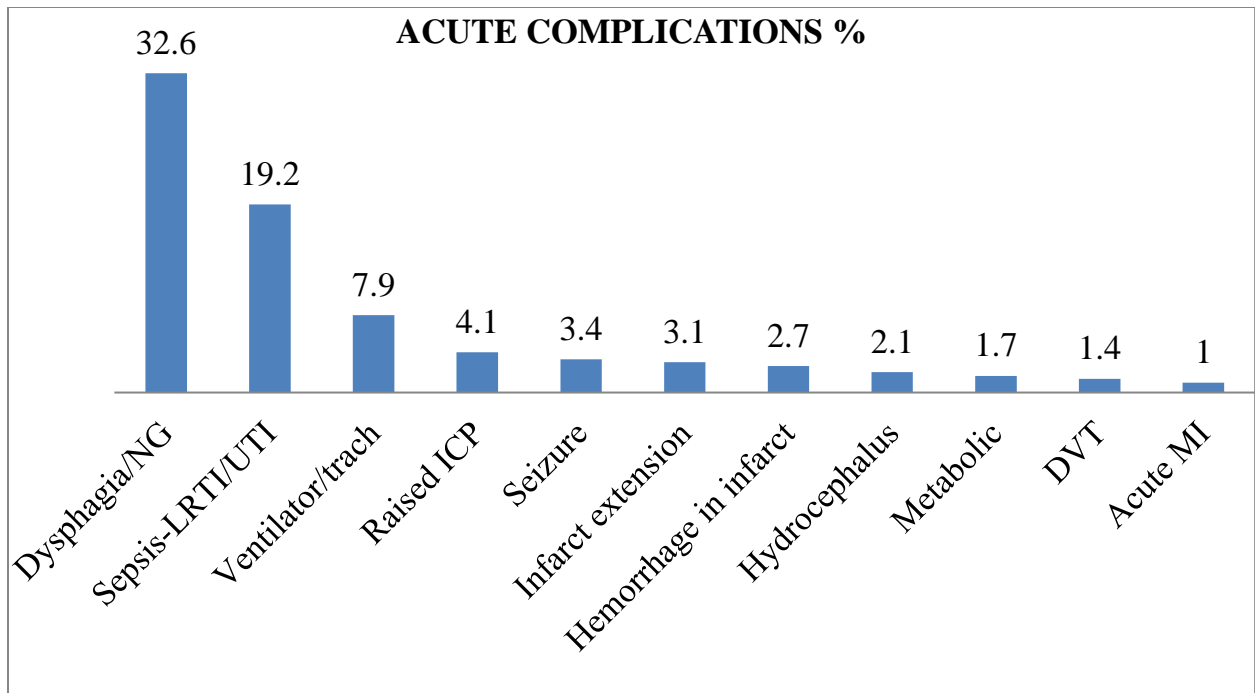


Figure 27 Bar graph showing the distribution of patients with acute complications

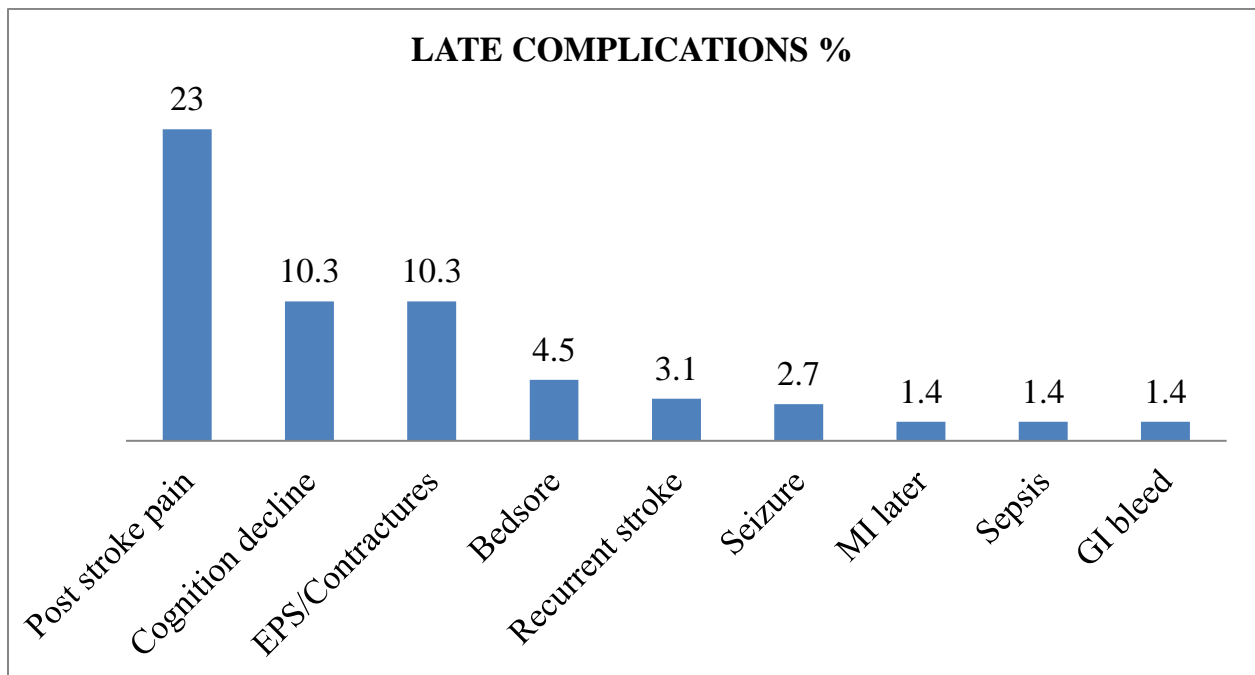


Figure 28 Bar graph showing late complications in the study population on follow-up

OUTCOMES

Occupation status:

Since most of the patients were more than 45 years of age [70%], with significant symptoms in the initial few months, 50% of the patients had no job on follow-up. 76% of the patients were males, and this posed a major economic and psychological burden to the family, as most of the patients were the main earning member of the family.

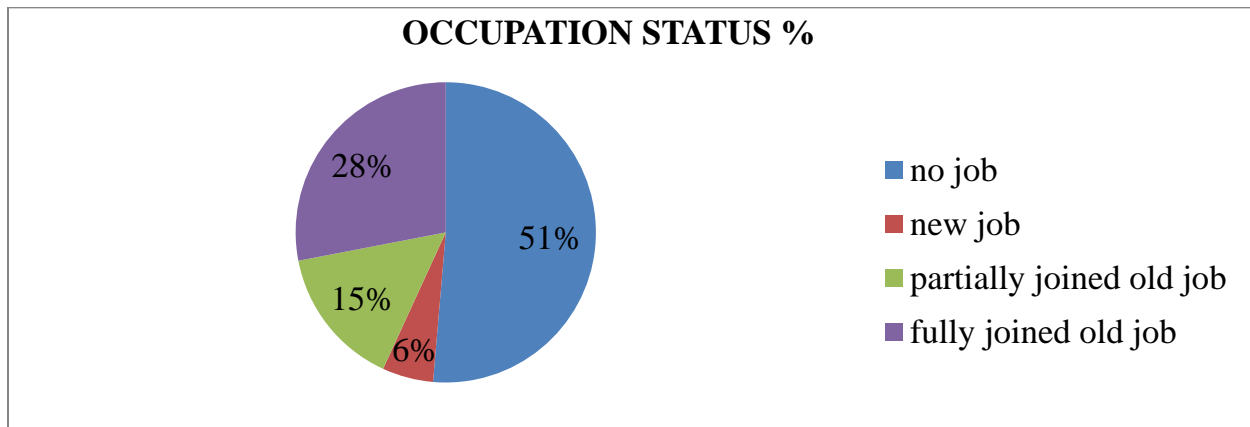


Figure 29 Pie chart showing distribution of patients with occupation status at follow-up

Kaplan-Meier graphs

Kaplan-Meier curves show that mortality following PC strokes, in our cohort was small, and staggered over 6 months. Similarly, when we analysed mRS score 4 to 6 as bad outcomes, we see that relatively small percentage have bad outcomes and these happen gradually over 6 months.

Kaplan-Meier graphs

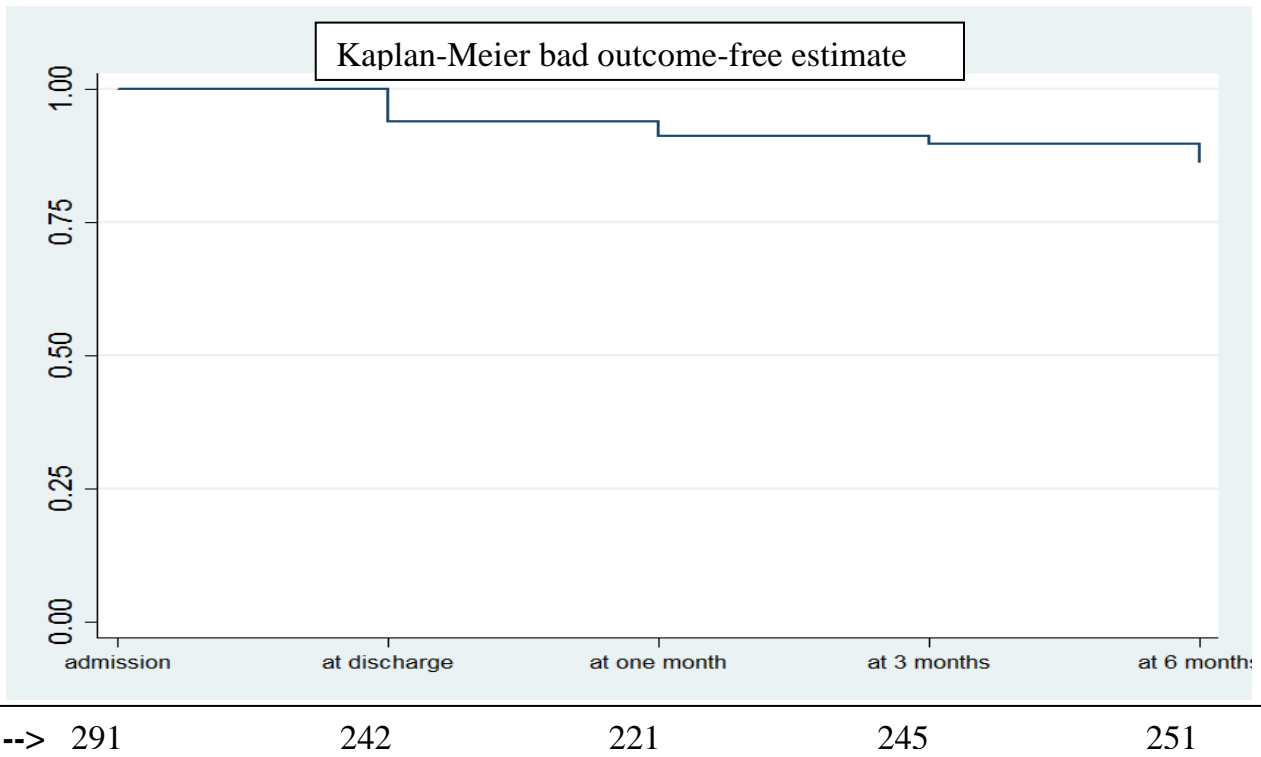
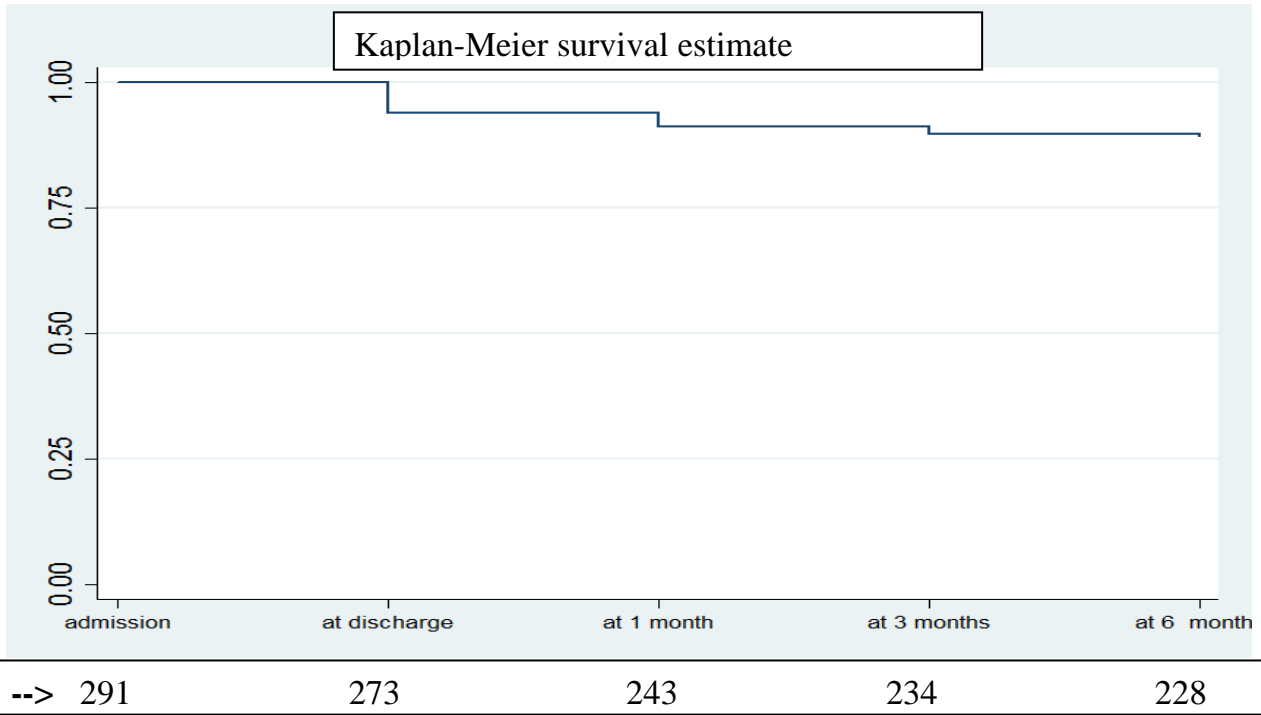


Figure 30 Kaplan-Meier graphs showing survival and bad outcome-free analysis

UNIVARIATE ANALYSIS

The outcome variable, 'bad outcome at 6 months', was defined as the mRS [Modified Rankin Scale] score of 4 or 5 or 6, on follow-up at 6 months. Other outcome variables, defined were 'morbidity', which was a mRS score of 4 or 5, and 'mortality', with mRS score of 6.

Correlation of the univariates with the outcome variable, bad outcome at 6 months [6/12] was done, and the results are given below: There was a lost to follow-up of 32 patients [12%] at 6 months, and the analysis is done as per protocol analysis.

Comparison of baseline characteristics of bad outcome versus good outcome at 6/12

Comparison of demographics:

Elderly age group [age above 55 years] had higher percentage of bad outcome, with a p-value of 0.07, and odds ratio [OR] of 1.29 with a confidence interval [CI] of 0.59-2.79]. Bad outcome did not have a significant correlation with the young stroke [age below 45 years]. Female gender was found to have a higher correlation with the bad outcome at 6 months, but was not statistically significant. Less than 50% of the study population belonged to the female gender as well as the age group above 55 years, at admission.

Table 31: Comparison of demographics of bad and good outcome at 6/12

Demographics	Bad outcome-6/12		Good outcome-6/12		OR [CI]	P value
	N [40]	%	N [219]	%		
Age >45 years	30	75%	153	69.9%	1.29[0.59-2.79]	0.512
<=45 years	10	25%	66	30.14%		
Age>55 years	23	57.50%	93	42.47%	1.83[0.92-3.62]	0.079
<=55 years	17	42.50%	126	57.83%		
Gender-Female	11	28.2%	47	21.6%	1.43[0.66-3.08]	0.361
-Male	28	71.8%	171	78.4%		

Admission details:

Patients who presented to the tertiary centre from the nearby residence had a relatively higher probability of bad outcome, but was not statistically significant. Patients from distant places, were of lesser proportion in the study, and would have had been stabilized in a nearby hospital and received the first aid, which would contribute to a better outcome.

Patients admitted through emergency department and those who got discharged from the emergency department [mostly discharged against medical advice], on follow-up, was found to have significant correlation with bad outcome.

Patients who had the first point of contact in CMC had higher incidence of bad outcome which was statistically significant and with a good correlation. This could be attributed to

the prolonged time interval from onset of symptoms to the first point of contact, compared to the others, who would have been stabilized in a local hospital.

Table 32: Comparison of admission details in bad and good outcome at 6/12

Admission details	Bad outcome-6/12		Good outcome-6/12		OR [CI]	P value
	N [40]	%	N [219]	%		
Address-Local	36	90%	173	79%	2.39[0.81-7.07]	0.105
-Outside	4	10%	46	21%		
Arrival-ED	36	90%	181	82.65%	1.89[0.64-5.62]	0.246
-OPD	4	10%	38	17.35%		
First medical contact-cmc	18	45%	60	27.4%	2.1[1.09-4.32]	0.028
First medical contact-local	22	55%	159	72.6%		
Discharge-ED	9	22.5%	17	7.8%	3.45[1.41-8.41]	0.003
-Medicine	20	50%	80	36.5%		
-Neurology	4	10%	64	29.2%		
-Stroke clinic	4	10%	47	21.5%		
-Others	3	7.5%	11	5.1%		

Comparison of comorbidities:

Hypertension was found to have a high correlation with bad outcome, but the confidence interval crossed below 1 and was not statistically significant. Dyslipidemia had a negative correlation with the bad outcome, which was statistically significant.

Alcohol consumption and smoking though had a correlation, had a wide confidence interval and was not statistically significant. Carotid disease had a p-value of 0.05, with a negative correlation.

Ischemic heart disease [IHD], valvular heart disease [VHD] and chronic kidney disease [CKD], though had an OR >1, was not statistically significant. Dissection had a good correlation, but had wide CI and p-value of 0.9. Hyperhomocystinemia and low vitamin B12 levels were found to have a negative correlation with the bad outcome.

Comorbidities like arrhythmia, recent myocardial infarction, migraine, malignancy, infection, obstructive sleep apnea and polycythemia, had very low prevalence in the study population, and hence with no bad outcome found at 6 months. Therefore, odd's ratio had been unable to calculate in the above variables.

Since cardiomyopathy and patent foramen ovale/shunt had a non-significant p value and a very wide confidence interval [0.78-41.77], was not included in the results.

Table 33: Comparison of comorbidities of bad vs good outcome at 6/12

Comorbidities	Bad outcome-6/12		Good outcome-6/12		OR [CI]	p value
	N [40]	%	N [219]	%		
Hypertension	32	80%	154	70.3%	1.69[0.74-3.86]	0.211
Diabetes	21	52.5%	115	52.5%	0.99[0.51-1.96]	0.999
Dyslipidaemia	6	15%	79	36.1%	0.31[0.13-0.78]	0.009
High TG	1	2.5%	21	9.6%	0.24[0.03-1.85]	0.139
Smoking	14	35%	88	40.2%	0.80[0.39-1.62]	0.537
Alcohol	10	25%	53	24.2%	1.04[0.48-2.28]	0.914
Carotid disease	7	17.5%	72	32.9%	0.43[0.18-1.03]	0.052
IHD	5	12.5%	26	11.9%	1.06[0.38-2.95]	0.910
VHD	2	5%	9	4.1%	1.23[0.26-5.91]	0.680
Hyperhomocyst	2	5%	29	13.2%	0.35[0.08-1.51]	0.140
Low vit B12	1	2.5%	26	11.9%	0.19[0.03-1.45]	0.074
CKD	3	7.5%	10	4.6%	1.69[0.45-6.45]	0.435
Dissection	1	2.5%	5	2.3%	1.09[0.13-9.65]	0.933

Comparison of lab parameters between bad and good outcome at 6 months:

Table 34: Comparison of lab parameters of bad vs good outcome at 6/12

Lab parameters [Total N]	Bad outcome-6/12		Good outcome-6/12		OR [CI]	P value
	N[40]	%	N[219]	%		
Hb<10 [250]	7/36	19.4%	15/214	7%	3.20[1.20-8.52]	0.015
Cr>=1.5 [253]	6/36	16.7%	12/217	5.5%	3.42[1.19-9.79]	0.016
HbA1C>=7 [219]	8/20	40%	62/199	31.2%	1.47[0.57-3.79]	0.419
T.Chol>=200 [189]	2/14	14.3%	37/175	21.1%	0.62[0.13-2.90]	0.542
TG>=200 [189]	3/14	21.4%	29/175	16.6%	1.37[0.36-5.23]	0.641
HDL<=35 [189]	8/14	57.1%	71/175	40.6%	1.95[0.65-5.87]	0.226
LDL>=100 [190]	6/14	42.9%	85/176	48.3%	0.80[0.27-2.41]	0.695
VitB12<=300 [104]	1/11	9.1%	22/93	23.7%	0.32[0.04-2.66]	0.271
Hcysteine >=20[97]	1/6	16.7%	20/91	22%	0.71[0.08-6.43]	0.760

Laboratory parameters, hemoglobin of less than 10g/dl, and serum creatinine of more than 1.4g/dl, was found to have a high correlation with the bad outcome at 6 months, with an OR>3 and was statistically significant. This was suggestive of probable underlying anaemia and azotemia contributing to the bad outcome. Among the parameters in fasting lipid profile, serum triglyceride level above 200mg/dl and HDL less than 35mg/dl , alongwith HbA1C of more than 7g/dl, had a positive correlation with bad outcome, but was not statistically significant. As mentioned earlier, high serum homocysteine level and low vitamin B12 level had a negative correlation, which was not significant.

Comparison of blood pressure and GCS at admission between bad and good outcome at 6/12:

Though high blood pressure [systoloc BP >160 or diastolic BP />100 mmHg] at admission had an OR>1, the p-value was not statistically significant.

Low GCS [Glasgow coma scale] of less than 10 [E+V+M] at admission, suggesting a poor baseline NIHSS and mRS score, had a statistically significant [p value <0.001] correlation [OR 35.5 with CI 12.79-98.55] with the bad outcome at 6 months.

Table 35: Correlation of admission BP and GCS in bad and good outcome at 6/12

Vitals [N =259]	Bad outcome-6/12		Good outcome-6/12		OR [CI]	p value
	N [40]	%	N [219]	%		
GCS[E+V+M]<=10	20/40	50%	6/219	2.7%	35.5[12.8-98.6]	<0.001
BP >160/100mmHg	24/40	60%	122/219	55.7%	1.19[0.60-2.37]	0.615

Patients who had a wake-up stroke or a transient ischemic attack [TIA] before stroke was found to have a statistically non-significant positive correlation with the bad outcome at 6 months. Recurrent stroke was found to have no significant correlation.

In-hospital stroke in patients with a pre-morbid illness, admitted for other medical reasons, was found to have a statistically significant correlation with the bad outcome [OR 8.79, CI 1.42-54.45], with a p-value of 0.005.

Table 36: Comparison of stroke characteristics of bad outcome vs good outcome at 6/12

Stroke characteristics	Bad outcome-6/12		Good outcome-6/12		OR [CI]	p value
	N[40]	%	N[219]	%		
Recurrent stroke	8	20%	46	21%	0.94[0.41-2.18]	0.886
TIA before stroke	5	12.5%	24	11%	1.16[0.42-3.25]	0.776
Wake-up stroke	9	22.5%	28	12.8%	1.98[0.85-4.59]	0.106
In-hospital stroke	3	7.5%	2	0.9%	8.79[1.42-54.45]	<0.001

Correlation of etiopathogenesis of stroke with the bad outcome at 6 months:

Patients with hemorrhagic stroke was found to have correlation with the bad outcome at 6 months. OR of comparison of ischemic stroke, in good versus bad outcome was 0.24, with a CI of 0.11-0.54, and was statistically significant with p-value of <0.001. Similar finding was seen on comparing MRI against CT for imaging a stroke patient, where OR was 0.09 with CI 0.05-0.21, and p-value of <0.001, suggesting the hemorrhagic stroke detected by CT imaging, which had a bad outcome.

Table 37: Comparison of stroke etiopathogenesis of bad vs good outcome at 6/12

	Bad outcome-6/12		Good outcome-6/12		OR [CI]	p value
	N[40]	%	N[219]	%		
Stroke imaging-						
MRI	19	47.5%	198	90.41%	0.09[0.05-0.21]	<0.001
CT	21	52.5%	20	9.13%	Ref.	
Stroke pathology-						
Infarct	27	67.50%	196	89.50%	0.24[0.11-0.54]	<0.001
Hemorrhage	13	32.50%	23	10.5%	Ref.	
Stroke etiology- TOAST criteria						
LAA	14	56%	100	51.02%	0.58[0.20-1.67]	0.426
CE	2	8%	28	14.29%	0.29[0.05-1.61]	
SVO	2	8%	31	15.82%	0.26[0.05-1.44]	
ODE	1	4%	12	6.12%	0.35[0.04-3.21]	
UDE >=2	2	8%	9	4.59%	Ref.	
UDE -VE	2	8%	12	6.12%		
UDE INCOMPLETE	2	8%	4	2.04%		

Comparison of arteries involved:

Basilar artery occlusion [BAO] was found to have a statistically significant correlation with the bad outcome at 6 months. BAO had OR of 3.93 with CI 1.41-10.96, and a p-value of 0.006. Occlusion of superior cerebellar artery was also found to have a positive correlation with bad outcome, with a p-value of 0.03. Occlusion of vertebral artery, anterior and posterior inferior cerebellar artery, though had a good correlation with bad outcome, was not statistically significant. Posterior cerebral artery which also included the thalamic artery, had non-significant negative correlation with bad outcome.

Table 38: Comparison of arteries involved in bad vs good outcome at 6/12

Arteries involved [Total N=196]	Bad outcome-6/12		Good outcome-6/12		OR [CI]	p value
	N/17	%	N/179	%		
Vertebral artery	3	17.65%	18	10.06%	1.92[0.50-7.31]	0.334
Basilar artery	8	47.06%	33	18.44%	3.93[1.41-10.96]	0.006
Posterior inferior cerebellar artery	9	52.94%	65	36.31%	1.97[0.73-5.36]	0.177
Anterior inferior cerebellar artery	3	17.65%	19	10.73%	1.78[0.47-6.77]	0.391
Superior cerebellar artery	6	35.29%	27	15.08%	3.07[1.05-9.00]	0.033
Posterior cerebral	6	35.29%	82	45.81%	0.65[0.23-1.82]	0.405

Comparison of management:

Patients who underwent surgical decompression, [mostly for raised intracranial pressure in a large stroke] had a significant correlation with bad outcome, suggesting that stroke severity have a major impact on long term outcome of the patient. Patient who underwent thrombolysis had no bad outcome at 6 months.

Table 39: Comparison of management in bad and good outcome at 6/12

Management	Bad outcome-6/12		Good outcome-6/12		OR [CI]	P value
	N[40]	%	N[219]	%		
Conservative	32	84.2%	210	96.8%	Ref.	<0.001
Thrombolysis	0	0%	4	1.8%	-	
Surgical decompression	6	15.8%	3	1.4%	12.47[2.97-52.23]	

Table 40: Comparison of medication between bad and good outcome at 6/12

Medication	Bad outcome-6/12		Good outcome-6/12		OR [CI]	P value
	N[40]	%	N[219]	%		
Single/dual antiplatelets	23	57.5%	157	71.69%	Ref.	<0.001
Anticoagulation/ anticoagulant+antiplatelet	2	5%	40	18.26%	0.34[0.08-1.50]	
Others	15	37.5%	22	10.05%	4.65[2.12-10.24]	

Comparison of medication used between bad and good outcome at 6 months:

Patients in the group others, were those with hemorrhagic stroke, who were not given any antiplatelet or anticoagulant at discharge, who on follow-up was found to have significant correlation with the bad outcome at 6 months.

Comparison of complications of bad outcome versus good outcome at 6 months

Table 41: Comparison of complications of bad outcome vs good outcome at 6/12

Complications	Bad outcome-6/12		Good outcome-6/12		OR [CI]	p value
	N[40]	%	N[219]	%		
Infarct extension	4	10%	4	1.83%	5.97[1.42-24.95]	0.006
Dysphagia/NG	22	55%	62	28.31%	3.09[1.55-6.16]	0.001
DVT	2	5%	2	0.91%	5.71[0.78-41.78]	0.054
Sepsis-LRTI/UTI	23	57.5%	28	12.79%	9.23[4.39-19.38]	0.000
Seizure	5	12.5%	4	1.83%	7.68[1.97-29.99]	0.001
Acute MI	1	2.5%	2	0.91%	2.78[0.25-31.43]	0.397
Ventilator/trach	16	40%	4	1.83%	35.8[11.07-115.92]	0.000
Raised ICP	8	20%	3	1.37%	18[4.54-71.39]	0.000
Hydrocephalus	5	12.5%	1	0.46%	31.14[3.53-274.53]	0.000
Post-stroke pain	6	15%	56	25.57%	0.51[0.21-1.29]	0.150
Recurrent stroke	1	2.5%	8	3.65%	0.68[0.08-5.56]	0.714
Cognition decline	9	22.5%	19	8.68%	3.06[1.27-7.36]	0.010
Seizure	3	7.5%	5	2.28%	3.47[0.79-15.14]	0.079
Bed sores	7	17.5%	5	2.28%	9.08[2.72-30.29]	0.000
Contractures	4	10%	10	4.57%	2.32[0.69-7.81]	0.162

Complications at discharge, or during follow-up were found to have high correlation with bad outcome at 6 months, and the statistically significant variables included infarct extension, dysphagia, sepsis, seizure, invasive ventilation +/- tracheostomy, raised intracranial pressure[ICP], hydrocephalus, cognition decline and bed sores. Though complications can be secondary to bad outcome, it can be considered as a significant contributor to the bad outcome.

Comparison of stroke scales:

NIHSS Stroke scale scoring was done at baseline which showed a mean value of 20.2 with SD of 7.41 among patients with bad outcome, while patients with good outcome had NIHSS baseline score of 5.24 with SD of 3.45. This was statistically significant. Mean value of mRS among patients at admission was 4.85 with SD 0.361 in bad outcome and 2.39 with SD of 0.773, respectively and was significant statistically.

6.39% [N=14] of patients among good outcome had poor mRS score at baseline [4 to 5] who improved with time. None of the patients with bad outcome [5 to 6] had a good mRS score at baseline. But 17.5% [N=7] of patients with baseline mild to moderate NIHSS [score<15] had a bad outcome at 6 months.

Table 42: Comparison of stroke scales of bad versus good outcome at 6/12

Stroke scales [N=259]	Bad outcome at 6/12 [N=40]	Good outcome at 6/12 [N=219]	p value		
NIHSS at admission					
Mean	20.2	5.24	<0.001		
Median	21	4			
Standard deviation SD	7.41	3.45			
95% CI	[17.83-22.56]	[4.78-5.70]			
mRS at admission					
Mean	4.85	2.39	<0.001		
Median	5	2			
Standard deviation	0.361	0.773			
95% CI	[4.73-4.96]	[2.29-2.50]			
<hr/>					
Stroke scales Baseline grading	Bad outcome-6/12		Good outcome-6/12		p value
	N[40]	%	N[219]	%	
Mild [1-7]	3	7.5%	153	69.86%	<0.001
Moderate [8-14]	4	10%	61	27.85%	
Severe [15-25]	22	55%	5	2.28%	
Very severe [>25]	11	27.5%	0	0%	
Good mRS [1-3]	0	0%	205	93.61%	<0.001
Bad mRS [4-5]	40	100%	14	6.39%	

MULTIVARIATE LOGISTIC REGRESSION ANALYSIS

Table 21: MODEL I [Baseline NIHSS included]

Table 43: Multivariate logistic regression analysis of significant univariates

Variables	OR	CI	p value
Age >45years	0.89	[0.03-23.39]	0.946
Female gender	0.61	[0.03-13.21]	0.755
Discharge from ED	1.71	[0.09-33.85]	0.724
Hypertension	2.05	[0.06-71.21]	0.689
Dyslipidemia	0.60	[0.04-9.89]	0.722
Carotid disease	0.28	[0.02-5.39]	0.399
Hyperhomocystinemia	3.82	[0.13-110.01]	0.435
Low vitamin B12	2.33	[0.12-46.79]	0.582
Hb<=10 g/dL	1.12	[0.03-488.32]	0.948
Cr>=1.5 mg/dL	1.72	[0.01-257.24]	0.832
HDL<=35 mg/dL	4.49	[0.36-55.41]	0.242
Infarct pathology	1.77	[0.02-199.10]	0.812
Dysphagia	0.54	[0.03-8.48]	0.664
Sepsis	0.85	[0.02-29.71]	0.926
Ventilator	2.66	[0.01-1652.66]	0.765
NIHSS at admission	1615.59	[27.64-94447.7]	<0.001

Table 22: MODEL II [Baseline NIHSS excluded]

Table 44: Multivariate logistic regression analysis of significant univariates

Variables	OR	CI	p value
Age >45years	1.61	[0.26-10.05]	0.612
Female gender	0.65	[0.10-4.22]	0.655
Discharge from ED	2.31	[0.28-19.14]	0.439
Hypertension	0.07	[0.89-5.01]	0.693
Dyslipidemia	1.67	[0.32-8.66]	0.545
Carotid disease	0.78	[0.16-3.86]	0.758
Hyperhomocystinemia	2.01	[0.22-18.85]	0.540
Low vitamin B12	1.01	[0.07-15.07]	0.996
Hb<=10 g/dL	1.93	[0.23-16.45]	0.546
Cr>=1.5 mg/dL	3.00	[0.39-22.80]	0.288
HDL<=35 mg/dL	2.62	[0.61-11.30]	0.195
Infarct pathology	1.05	[0.11-9.93]	0.965
Dysphagia	1.09	[0.23-5.16]	0.909
Sepsis	7.77	[1.57-38.43]	0.012
Ventilator	17.22	[1.45-204.08]	0.024

Table 23: MODEL III. [Arteries included and baseline NIHSS excluded]

Table 45: Multivariate logistic regression analysis of significant univariates

Variables	OR	CI	p value
Age >55years	7.95	[0.37-170]	0.185
Hypertension	0.363	[0.01-11.80]	0.568
Carotid disease	0.543	[0.56-5.22]	0.597
Cr>=1.5 mg/dL	3.49	[0.11-113.52]	0.482
HDL<=35 mg/dL	3.47	[0.30-40.03]	0.319
Dysphagia	1.61	[0.14-18.85]	0.706
Ventilator	49.17	[1.33-1810.52]	0.034
Superior cerebellar artery occlusion	1.68	[0.09-29.50]	0.723
Posterior inferior cerebellar artery occlusion	3.36	[0.36-31.20]	0.286
Basilar artery occlusion	19.98	[1.67-238.81]	0.018

Receiver Operating Characteristic [ROC] Curve

The results of the ROC analysis that had bad outcomes at 6 months (mRS 4-6) and compared with NIHSS score at baseline are shown below. They show an area under the curve [AUC] of 94%. Score above 13 in NIHSS seem to have nearly 100 percent specificity for bad outcomes while scores 0 to 5 suggest good outcomes.

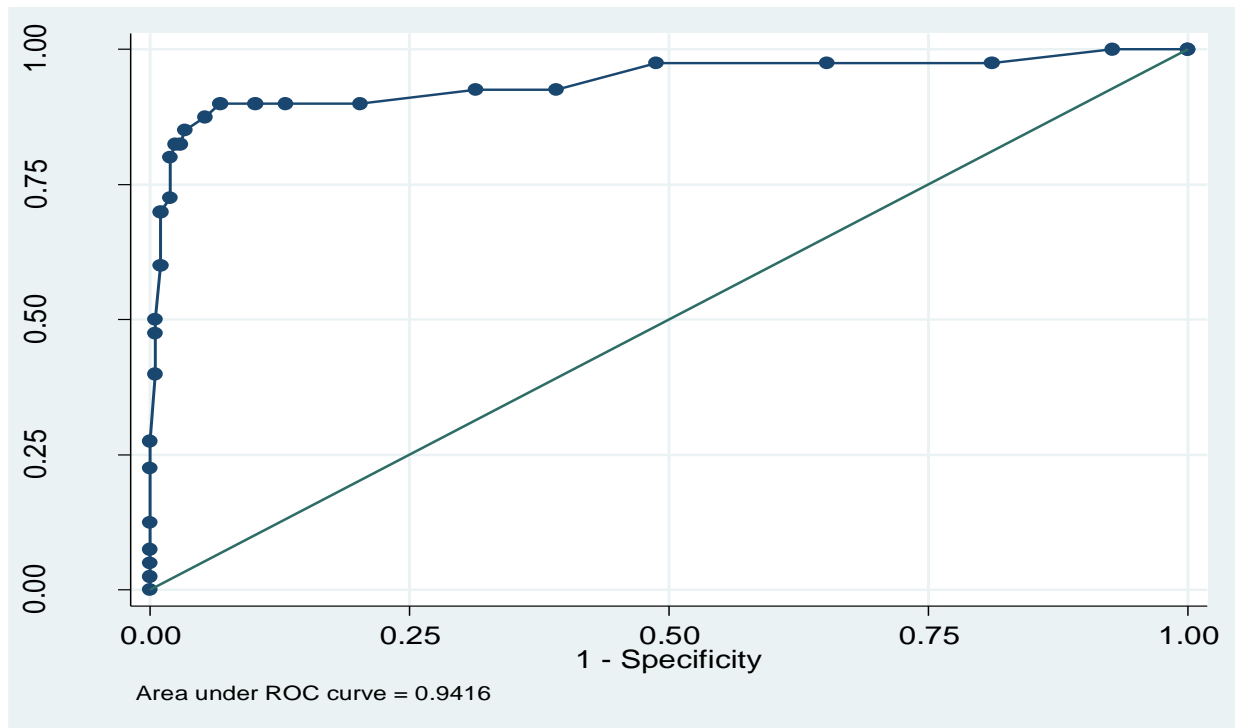


Figure 31 Figure showing the ROC analysis along with the AUC comparing bad outcome at 6 months with the baseline NIHSS

Obs.	Area [AUC]	S.E.	95% CI
247	0.9416	0.0268	[0.88917-0.99405]

Table 24: ROC analysis comparing bad outcomes at 6 /12 with baseline NIHSS

NIHSS Cutpoint	Sensitivity	Specificity	Classified	LR+	LR-
>=1	100%	0%	16.19%	1.0000	
>=2	100%	7.25%	22.27%	1.0781	0.000
>=3	97.5%	18.84%	31.58%	1.2013	0.1327
>=4	97.5%	34.78%	44.94%	1.4950	0.0719
>=5	97.5%	51.21%	58.70%	1.9983	0.0488
>=6	92.5%	60.87%	65.99%	2.3639	0.1232
>=7	92.5%	68.60%	72.47%	2.9458	0.1093
>=8	90%	79.71%	81.38%	4.4357	0.1255
>=9	90%	86.96%	87.45%	6.9000	0.1150
>=10	90%	89.86%	89.88%	8.8714	0.1113
>=11	90%	89.86%	92.71%	13.3071	0.1073
>=12	87.5%	93.24%	93.52%	16.4659	0.1320
>=13	85%	94.69%	94.74%	25.1358	0.1552
>=14	82.5%	96.62%	94.74%	28.4625	0.1802
>=15	82.5%	97.10%	95.14%	34.1550	0.1793
>=16	80%	97.58%	95.14%	41.4000	0.2039
>=17	72.5%	98.07%	93.93%	37.5188	0.2804
>=18	70%	98.07%	94.33%	72.4498	0.3029
>=20	60%	99.03%	92.71%	62.0998	0.4039
>=22	50%	99.52^%	91.50%	103.4997	0.5024
>=23	47.5%	99.52%	91.09%	98.3247	0.5275
>=24	40%	99.52%	89.88%	82.7997	0.6029
>=26	27.5%	100%	88.26%		0.7250
>=27	22.5%	100%	87.45%		0.7750
>=28	12.5%	100%	85.83%		0.8750
>=29	7.5%	100%	85.02%		0.9250
>=31	5%	100%	84.62%		0.9500
>=34	2.5%	100%	84.21%		0.9750
>34	0%	100%	83.81%		1.0000

DISCUSSION

Cerebrovascular accidents have severe consequences for patients and their families. As predominant CVA are in the anterior circulation most studies concentrate on them.

The clinical features, risk factors, short and long term outcomes of posterior circulation CVA (PCS) are not very well documented in India.

The clinical features of PCS can be non-specific and differ from that of ACS, leading to miss- diagnosis, causing delay in initiation of treatment and increased rate of complications. Our study included majority of the local population [80%], in and around Vellore, and hence tried to conduct a study which was representative of our community. The 3 year study constituted the retrospective data of 2 years, and prospective data of 1 year, with both the groups followed up prospectively for 6 months.

Prevalence of posterior circulation stroke:

The prevalence of the posterior circulation strokes, calculated as the proportion of the posterior circulation stroke to the total strokes in the year 2016, was 12.9% [111/860], which correlated with the INTERSTROKE study which showed the prevalence of posterior circulation stroke to be 14%.

Demographic details:

In our study, posterior circulation stroke was higher among males, who constituted 76% of the study sample. This was in accordance with the previous studies, where a male predominance of stroke was found. The mean age was found to be 53.3 years, with

majority of stroke in the age-group of 56 to 75 years [40%]. 65% of the stroke occurred in the age-group of 46 to 75 years. Our study was similar to BASICS study in terms of the elderly age group [mean age of 63years] and male predominance [65%], but had a higher value of the same.

Young stroke was found in about 28.8% of patients in our study, which was higher compared to the previous studies, including the INTERSTROKE study which showed 14%. Majority of the study sample was from local area [80%], which included patients from the districts of Vellore, Tiruvanamalai and Chittoor.

Three- fourth of the patients presented to the emergency department and 30.6% of patients had first medical contact in our centre. Optimal management in terms of prompt neuroimaging and thrombolysis was delayed due to poor awareness about the symptoms and delayed accessibility to a centre with the above facilities, which lead to delay in onset of symptoms to door time.

10% of the patients had TIA before stroke, which was missed by the patients due to lack of awareness. BASICS study had 18% of the patients with history of minor stroke/TIA. Wake-up stroke was found in 15 % of the ischemic stroke, which was comparable with other studies [8-28%]. 5 patients in the study sample had in-hospital stroke, which was predominantly cardioembolic stroke, and the infarct involved mainly the watershed territory.

Comorbidities among the patients:

Most common comorbidity associated with posterior circulation stroke was hypertension. 72% of the patients had a diagnosis of hypertension, and 55% of the patients presented with high blood pressure at admission. On-half of the patients had diabetes mellitus, and one-third had dyslipidaemia. BASICS study also had hypertension as the commonest comorbidity associated [60%], and diabetes mellitus and dyslipidaemia was seen in 23% and 29% patients, respectively.

About 40% of the patients had history of smoking and 22% gave history of alcohol consumption. Recurrent stroke was seen in 50 of the 291 patients [17%]. One-tenth of the patients had hyper-homocystinemia and low vitamin B12 levels. Ischemic heart disease was found in 12% of patients, with cardiomyopathy in 2% patients. The main etiological causes in patients with cardio emboli- stroke were valvularheart disease and patent foramen ovale or shunt, each of which was present in about 5% of the study sample. Unlike our study [1%], there were 21% of patients with atrial fibrillation, in the BASICS group.

Vertebral artery dissection was found in 7 patients. Rests of the comorbidities assessed were seen in less than 10% of the patients. Proportion of comorbidities were similar to those found in the studies of Mehndiratta et al, and other studies, as mentioned in the table in review of literature. (126)

Clinical and radiological profile of the patients and etio-pathogenesis of PC stroke:

The most common symptom at presentation was giddiness and sense of imbalance, which was seen in about three-fourth of the patients. Nausea and vomiting was the other common non-specific symptom [43%]. Motor deficits were seen in about one-half of the patients. Ataxia was the commonest sign at presentation of PC stroke in our study, which was difficult to elicit in acute settings, with debilitating symptoms of low sensorium [20%] and giddiness. Dysphagia and dysarthria were the other common findings, seen in about 21% and 25% of our patients.

Though plain CT brain was the primary choice of imaging, especially in patients with hemorrhagic stroke, many of the patients, later underwent MRI brain with MR angiogram [45%], which further delineated the pathology, volume of infarct and artery involved. MRI acute stroke protocol was done in about 35% of the patients, who had acute presentation to CMC. 40% of the patients with ischemic stroke later underwent a 4-vessel neck doppler, to characterize any carotid or vertebral artery stenosis.

30% of the patient had bilateral extensive or brainstem involvement, while 39% and 32% had predominantly left or right -sided involvement of the posterior circulation territory, respectively. 39 patients [13%] had hemorrhagic stroke, which was and majority was managed conservatively.

In our study, posterior cerebral artery alongwith its branch thalamic artery, which supplies the distal territory, was most commonly involved, and about 45% of the patients

was found to have significant involvement of the same. This was similar to the finding in NEMC-PCR. Significant basilar artery occlusion was found in one-fifth of the patients. Posterior inferior cerebellar artery, a branch of vertebral artery was involved in about 38% of the patients. Many patients had multiple vascular involvement, and also findings of hypoplastic vertebral artery was seen.

Etiological classification of the posterior circulation ischemic stroke was done, based on the TOAST criteria. 50% of the patients were found to have large artery atherosclerosis. Unlike in other studies, where cardioembolic stroke was found in 17% [TOAST study] to 24% [NEMC-PCR] of the PC ischemic strokes, only 14.4% of the patients were classified under the etiology of cardioembolic stroke. This was attributed to the patients probably lost to follow up and with incomplete evaluation. Young patients and patients with no history of hypertension, diabetes mellitus, dyslipidaemia, patent foramen ovale/shunt, ischemic or valvular heart disease, were evaluated in detail for other etiologies, which included vasculitis, vertebral artery dissection, migraine, polycythemia, low vitamin B12 levels and polycythemia.

Majority of the patients were managed conservatively with medical management and optimisation of treatment for underlying comorbidities. About 50% of the patients received single antiplatelet therapy. Anticoagulation was started after ruling out contraindication, predominantly in patients with cardioembolic stroke and large intracranial artery atherosclerosis. 4 patients with acute ischemic stroke, fulfilling the

inclusion criteria, underwent thrombolysis. 10 patients with raised intracranial pressure underwent surgical decompression.

Complications of posterior circulation stroke:

One-third of the patients had dysphagia and was initiated on NG feeds. One-fifth of the patients had sepsis, predominantly due to aspiration pneumonia, secondary to absent gag reflex and low sensorium, and also urosepsis, secondary to instrumentation and elderly with altered sensorium. 8% of the patients had invasive ventilation and few of them underwent tracheostomy, in view of prolonged ventilatory support required. 18 patients had seizures, either at presentation, during admission or during follow-up. One of the most common OPD symptom of follow-up PC stroke patients with motor deficits, was poststroke neuropathic pain [23%], which mostly required pharmacotherapy. 10 % of the patients had cognition decline during follow-up. About 50% of the patients had no job on follow-up during the initial 6 months

Stroke scales and outcomes of PC stroke:

NIHSS score at baseline was a mean of 7.3 (SD 6.7) and median 5(IQR 3-8). Unlike our study, BASICS study had high baseline NIHSS score, with a median of 21 [IQR 11-30]. 60% of the patients had a low NIHSS score of less than 7, and another one-fourth of the patients had score within 8 to 14. About 30 patients had high baseline NIHSS score of more than 14, which correlated well with the mRS score at baseline. Scatter plot between and baseline NIHSS and mRS score showed a correlation coefficient of 0.615. (figure 18)

The discharge from hospital data 10% of the patients had high morbidity [mRS of 4 or 5] and 18 patients died [mRS 6] at discharge. This 17% bad hospital outcome was attributed to both the PCA stroke and its complications mentioned above.

At one month follow up 25 patients (9.3%) had a mRS score 6 and 48 [18%] in our had mRS score of 4 to 6 .

On follow-up, 31 patients were found to have succumbed to death in total at 6 months, and predominantly constituted those patients with high morbidity at discharge. Combined with high morbidity mRS score [4 or 5] of 9, the bad outcome was found to have gone up to 40 patients, at 6 months follow-up.

Our study was compared with the BASICS study done by Rangaraju et al, (80) which identified independent predictors of poor outcome at 1 month, which, like in our study, was defined as mRS score of 4 to 6.

Univariate analysis of factors contributing to bad outcome at 6 months:

The significant factors with good correlation to bad outcome at 6 months, during univariate analysis, included elderly age, patients discharge against medical advice from ED, first medical contact to CMC, in-hospital stroke, anemia, azotemia, low GCS, hemorrhagic stroke, distal artery involvement, basilar artery occlusion, complications like infarct extension, dysphagia, sepsis , seizures, raised ICP, hydrocephalus, invasive ventilation, cognition decline, high baseline NIHSS and mRS score.

Basilar artery occlusion was also found to have a significant bad outcome. (127) 6 to 10% of ischemic strokes was attributed to basilar artery occlusion in BASICS study, and was associated with a higher morbidity and mortality. In our study, basilar artery involvement was seen in 19%, with 47% of bad outcome associate with BAO, which was found to statistically significant, with high odds ratio.

Of the predictors of poor outcome identified during univariate analysis in BASICS study, those similar to our study included age, time to treatment, intubation at 24 to 48 hours, and high baseline NIHSS score. Other predictors identified in BASICS study were smoking, dyslipidemia, history of minor stroke and 24 to 48 hour NIHSS. BASICS study did not include postdischarge variables influencing the longterm outcome, and outcome at 3 or 6 months was not looked into, thus limiting its generalizability.

BASICS study had highlighted the prognostic importance of 24 to 48 hours NIHSS, with a score ≤ 4 suggesting favorable early outcome and ≥ 22 suggesting poor early outcome, at 1 month. But in our study, 17.5% of patients with bad outcome at 6 months had a low baseline NIHSS score [< 15] suggesting a poor correlation of the same. 100% of bad outcome at 6 months had a poor baseline mRS score [4 to 5], suggesting a better prognostic value of mRS score compared to NIHSS.

Independent predictors of bad outcome at 6 months:

In the multivariate analyses factors that independently predicted a bad outcome at 6 months, was baseline NIHSS score [OR 1615.59, CI 27.64-94447.7] in Model 1. In

Model II invasive ventilation [OR 7.77, CI 1.57-38.43] and sepsis [OR 17.22, CI 1.45-204.08] were independent predictors of bad outcome at 6 months. In Model III Basilar artery occlusion [OR 19.98, CI 1.67-238.81] was found to be a significant independent predictor of the bad outcome at 6 months.

This data compares well with the one month outcome following PCA with the BASICS study which found that NIHSS score is a good predictor of poor 1 month outcome. However our outcomes were followed up to 6 months. The Analysis of the ROC curve we have done suggests that the NIHSS score at baseline has a good ability to differentiate between good and bad 6-month outcomes. We also note that a score more than 13 suggest a very poor outcome and scores 0-5 a good outcome. These can be clinically useful for clinicians in the future.

LIMITATIONS

A] All patients who were included into this study were those who had access to healthcare at a tertiary medical centre, which may under estimate the burden of disease.

B] Though majority of the recruited patients resided in and around Vellore, the hospital-based population selection has its inherent biases of extrapolation of the results to the community. However, doing a community based study of stroke was not feasible.

C] The mRS scores at follow up was calculated based on the subjective information received from patients or relatives, which can have reporter bias and recall bias. However, mRS score using the telephonic method has been widely used and accepted.

D] Significant number of patients were lost to follow up [11%], as the outpatient visits, telephonic method and chart viewing were the modes used, to which there was poor response. Since follow up of patients with stroke was found to be poor in most of the developing countries, the above modes were the only and possible method for follow up.

CONCLUSIONS

A] Prevalence

Prevalence of posterior circulation stroke to the total strokes in our center in 1 year was 12.9% [111/860].

B] Demographic characteristics

Mean age of presentation was 53.34 years (SD 13.34 years). Young strokes constituted 28.8% [N=84].

C] Comorbidities

Hypertension was found in 72%, diabetes mellitus in 52.6%, smoking in 38.5% and dyslipidemia in 32.6%.

D] Clinical profile

The most common symptoms were giddiness [79%], unsteadiness [75.35%], ataxia [56%], motor deficits [48.8%] and nausea & vomiting [43%].

E] Radiological profile

Ischemic stroke was 86.5%. Involvement of posterior cerebral artery was 45%, posterior inferior cerebellar artery was 38% and basilar artery was 19.2%.

F] TOAST classification of etiology

Among ischemic strokes, large artery atherosclerosis was 50.8%, cardio embolism and small vessel occlusion were 14.4% each.

G] Complications

Dysphagia was seen in 32.6%, sepsis in 19.2% and invasive ventilation in 8% . Post stroke pain, a late complication was seen in 23%, followed by cognition decline in 10.3%.

H] Outcomes

Mortality [mRS 6] was 6.2% at discharge, 2.4% at 1-month follow-up, 1.7% at 3-months and 0.7% at 6 months.

Poor outcomes we called morbidity [defined as mRS 4 or 5] was 10.7%at discharge, 7.9% at 1 month, 4.1% at 3 months and 3.1% at 6 months.

Bad outcome [defined as mRS 4 to 6] was 16.8% at discharge, 16.4% at 1 month, 14.4% at 3 months and 13.8% at 6 months.

I] Independent predictors of bad outcomes at 6-months

1. Baseline NIHSS score [OR 1615.59 with CI 27.64-94447.7]
2. Invasive ventilation [OR 7.77 with CI 1.57-38.43]
3. Sepsis [OR 17.22 with CI 1.45-204.08]
4. Basilar artery involvement [OR 19.98 with CI 1.67-238.81]

5. The NIHSS score at baseline has an area under the curve of 94% showing good ability to discriminate between the good and bad outcomes.

6. NIHSS scores at baseline of 0 to 5 suggest a good outcome at 6 months while scores more than 13 suggest a bad outcome at 6 months.

Cerebrovascular accidents especially posterior circulation strokes will continue to burden the community with a great deal of morbidity and mortality. This study was an attempt to help the clinicians for prompt diagnosis of posterior circulation strokes and to identify the predictors of bad outcome, which can prevent the delay in appropriate therapy and occurrence of unacceptable consequences.

This dissertation complies with the 2007 STROBE GUIDELINES for observational studies [Annexure X]

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ANNEXURE I: ACCEPTANCE LETTER BY INSTITUTIONAL REVIEW BOARD



**OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA**

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

Dr. Nihal Thomas,
MD, MNAMS, DNB (Endo), FRACP (Endo), FRCP (Edin), FRCP (Glasg)
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

January 14, 2016.

Dr. Anju Susan Jacob,
PG Registrar,
Department of General Medicine,
Christian Medical College,
Vellore – 632 004.

Sub: Fluid Research Funding: New Proposal

Determination of the prevalence, demographic characteristics, risk factors, clinic-radiological profile, outcomes and complications in posterior circulation stroke, among patients in Christian Medical College Vellore, a tertiary care hospital, over a period of three years.

Dr. Anju Susan Jacob, Emp. No: 29426, PG Registrar, Medicine, Dr. Thambu David, Emp. No: 30008, Prof. & Head, Dept. of Medicine 2, Dr. Sanjith Aaron, Emp. No: 14391, Dept. of Neurology, Dr. Sunithi Mani, Emp. No: 28244, Dept. of Radio diagnosis, Dr. Abhilash KPP, Emp. No: 28585, Emergency Dept. Dr. Dr. Ajay Kumar Mishra, Emp. No: 29814, Dr. Samuel George Hansdak, Emp. No: 30829, Dept. of Medicine 4, Dr. Ramya Iyyadurai, Emp. No: 31571, Dept. of Medicine 5, Dr. Alice Joan Mathuram, Emp. No: 28529, Dept. of Medicine 1, Dr. Sheena Ebenezer, Emp. No: 29038, Dept. of Medicine 3, Dr. Mahendri NV, Emp. NO: 30173, Dept. of Dietetics, Dr. Visalakshi Jeyaseelan, Emp. No: 31093, Dept. of Biostatistics.

Ref: IRB Min. No. 9822 dated 07.01.2016

Dear Dr. Anju Susan Jacob,
The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Determination of the prevalence, demographic characteristics, risk factors, clinic-radiological profile, outcomes and complications in posterior circulation stroke, among patients in Christian Medical College Vellore, a tertiary care hospital, over a period of three years" on January 07th 2016. I am quoting below the minutes of the meeting.

The Committee raises the following queries:

- a) How do you get certification?
- b) Are you planning to use chronic or acute strokes? What about those in stroke OPDs?
- c) You can keep the cutoff age as 18 years.

1 of 2



**OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA**

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

Dr. Nihal Thomas,
MD, MNAMS, DNB (Endo), FRACP (Endo), FRCP (Edin), FRCP (Glasg)
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Drs Anju Susan Jacob and Thambu David were present during the presentation of the proposal and satisfactorily responded to the queries raised by the Members. After discussion, it was resolved to **ACCEPT the proposal after receiving the suggested modifications and answers to the queries.**

- Note:
1. Kindly HIGHLIGHT the modifications in the revised proposal.
 2. Keep a covering letter and point out the answer to the queries.
 3. Reply to the queries should be submitted within 3 months duration from the time of the thesis/ protocol presentation, if not the thesis/protocol have to be resubmitted to the IRB.
 4. The checklist has to be sent along with the answers to queries.

Email the details to research@cmcvellore.ac.in and send a hard copy through internal dispatch to Dr. Nihal Thomas, Addl. Vice-Principal (Research), Principal's Office, CMC.

Yours sincerely,

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr. NIHAL THOMAS
MD, MNAMS, DNB (Endo), FRACP (Endo), FRCP (Edin), FRCP (Glasg)
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

Cc: Dr. Thambu David, Department of Medicine, CMC Vellore.



**OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA**

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

Dr. Biju George, MBBS., MD., DM
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

May 23, 2016
Dr. Anju Susan Jacob,
PG Registrar
Department of General Medicine-2,
Christian Medical College,
Vellore 632 004.

Sub: Fluid Research Funding: New Proposal

Determination of the prevalence, demographic characteristics, risk factors, clinic-Radiological profile outcomes and complications in posterior circulation stroke, among patients in Christian Medical College Vellore, a tertiary care hospital, over a period of three years.

Dr. Anju Susan Jacob, Emp. No: 29426, PG Registrar, Medicine, Dr. Thambu David, Emp. No: 30008, Prof & Head, Dept. of Medicine 2, Dr. Sanjith Aaron, Emp. No: 14391, Dept. of Neurology, Dr. Sunithi Mani, Emp. No: 28244, Dept. of Radio diagnosis, Dr. Abhilash KPP, Emp. No: 28585, Emergency Dept. Dr. Dr. Ajay Kumar Mishra, Emp. No: 29814, Dr. Samuel George Hansdak, Emp. No: 30829, Dept. of Medicine 4, Dr. Ramya Iyyadurai, Emp. No: 31571, Dept. of Medicine 5, Dr. Alice Joan Mathuram, Emp. No: 28529, Dept. of Medicine 1, Dr. Sheena Eben ezer, Emp. No: 29038, Dept. of Medicine 3, Dr. Mahendri NV, Emp. NO: 30173, Dept. of Dietetics. Dr. Visalakshi Jeyaseelan, Emp. No: 31093, Dept. of Biostatistics

Ref: IRB Min No: 9822 [OBSERV] dated 07.01.2016

Dear Dr. Anju Susan Jacob,

I enclose the following documents:-

1. Institutional Review Board approval
2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,


Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

Cc: Dr. Thambu David, Professor Dept. of Medicine 2, CMC

1 of 5



**OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA**

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

Dr. Biju George, MBBS., MD., DM
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

May 23, 2016

Dr. Anju Susan Jacob,
PG Registrar
Department of General Medicine-2,
Christian Medical College,
Vellore 632 004.

Sub: Fluid Research Funding: New Proposal

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Dr. Visalakshi Jeyaseelan, Emp. No: 31093, Dept. of Biostatistics

Ref: IRB Min No: 9822 [OBSERV] dated 07.01.2016

Dear Dr. Anju Susan Jacob,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Determination of the prevalence, demographic characteristics, risk factors, clinic- Radiological profile outcomes and complications in posterior circulation stroke, among patients in Christian Medical College Vellore, a tertiary care hospital, over a period of three years." on January 07th 2016.

The Committee reviewed the following documents:

1. IRB Application format
2. Information Sheet and Informed Consent Form 9English, Tamil, Hindi)
3. Proforma

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**OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA**

Dr. E.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

Dr. Biju George, MBBS., MD., DM
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

4. Cvs of Drs. Dr. Anju Susan Jacob, Dr. Thambu David, Emp. No: 30008, Dr. Sanjith Aaron, Emp. No: 14391, Neurology, Dr. Sunithi Mani, Emp. No: 28244, Radiodiagnosis, Dr. Abhilash KPP, Dr. Dr. Ajay Kumar Mishra, Dr. Samuel George Hansdak, Emp. No: 30829, Medicine 4, Dr. Ramya Iyyadurai, Medicine 5, Dr. Alice Joan Mathuram, Emp. No: 28529, Medicine 1, Dr. Sheena Ebenezer, Medicine 3, Dr. Mahendri NV, Dietetics. Dr. Visalakshi Jeyaseelan, Biostatistics,
5. No. of documents 1- 4

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on January 07th 2016 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Name	Qualification	Designation	Affiliation
Dr. Nihal Thomas	MD, MNAMS, DNB(Endo), FRACP (Endo) FRCP(Edin) FRCP (Glasg)	Professor & Head, Endocrinology. Additional Vice Principal (Research), Deputy Chairperson(Research Chairperson), Member Secretary (Ethics Committee), IRB. CMC, Vellore	Internal, Clinician
Dr. RV. Shaji		Professor, Heamatology, CMC, Vellore	Internal, Basic Medical Scientist
Dr. Mathew Joseph	MBBS, MCH	Professor, Neurosurgery, CMC, Vellore	Internal, Clinician
Rev. Joseph Devaraj	BSc, BD	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist
Dr. Balamugesh	MBBS, MD(Int Med), DM, FCCP (USA)	Professor, Pulmonary Medicine, CMC, Vellore	Internal, Clinician
Dr. Visalakshi. J	MPH, PhD	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Dr. Rajesh Kannangai	MD, PhD.	Professor, Clinical Virology, CMC, Vellore	Internal, Clinician
Dr. Niranjan Thomas	DCH, MD, DNB (Paediatrics)	Professor, Neonatology, CMC, Vellore	Internal, Clinician

IRB Min No: 9822 [OBSERV] dated 07.01.2016

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**OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA**

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho,
Chairperson, Research Committee & Principal

Dr. Biju George, MBBS., MD., DM
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay Person
Dr. B. J. Prashantham	MA(Counseling Psychol MA(Theology), Dr. Min(Clinical Counselling)	Chairperson, Ethics Committee, IRB. Director, Christian Counseling Cent Vellore	External, Social Scientist
Dr. Ratna Prabha	MBBS, MD (Pharma)	Associate Professor, Clinical Pharmacology, CMC, Vellore	Internal, Pharmacologist
Dr. Anand Zachariah	MBBS, PhD	Professor, Medicine, CMC, Vellore	Internal, Clinician
Mrs. Emily Daniel	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
Dr. Vivek Mathew	MD (Gen. Med.) DM (Neuro) Dip. NB (Neuro)	Professor, Neurology, CMC, Vellore	Internal, Clinician
Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert
Dr. Simon Pavamani	MBBS, MD	Professor, Radiotherapy, CMC, Vellore	Internal, Clinician
Dr. Inian Samarasam	MS, FRCS, FRACS	Professor, Surgery, CMC, Vellore	Internal, Clinician
Dr. Thomas V Paul	MD, DNB(Endo), Phd(Endo)	Professor, Endocrinology, CMC, Vellore	Internal, Clinician

We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of withdrawals for the study entitled: "Determination of the prevalence, demographic characteristics, risk factors, clinic- Radiological profile outcomes and complications in posterior circulation stroke, among patients in Christian Medical College Vellore, a tertiary care hospital, over a period of three yearsn" on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in)

IRB Min No: 9822 [OBSERV] dated 07.01.2016

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ANNEXURE II: FUNDING APPROVAL BY INSTITUTIONAL REVIEW BOARD



**OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA**

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

Dr. Biju George, MBBS., MD., DM
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Fluid Grant Allocation:

A sum of 14,500/- INR (Rupees Fourteen Thousand Five Hundred Only) will be granted for 3 Years.

Yours sincerely


Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

DR. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

IRB Min No: 9822 [OBSERV] dated 07.01.2016

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ANNEXURE III: INFORMATION SHEET

Christian Medical College, Vellore - Department of Medicine

PREVALENCE, DEMOGRAPHIC CHARACTERISTICS, COMORBIDITIES, CLINICO-RADIOLOGICAL PROFILE, OUTCOMES AND COMPLICATIONS OF POSTERIOR CIRCULATION STROKE, AMONG PATIENTS IN CHRISTIAN MEDICAL COLLEGE, VELLORE

Information sheet

You are being requested to participate in a study to see how common is a posterior circulation stroke in a tertiary care centre. In our study we would also like to see the risk factors contributing to this event. NIH stroke scale and modified ranking score are two scoring systems in place to determine the extent of involvement and prognosis in a stroke. These scoring systems will be administered to you at your presentation, at discharge and at follow up after 6 months.

If you take part what will you have to do?

If you agree to participate in this study, your base line data including dietary habits, will be collected. You will also be administered two scoring systems for stroke, namely NIHSS and MRS at presentation, at discharge and at follow up after 6 months. When the scoring system is administered to you, you will be requested to carry out simple commands as instructed by the examiner. All other treatments that you are already on, will be continued and your regular treatment will not be changed during this

study. You will be expected to come for routine reviews as advised by your physician. As per study guidelines, you are requested to review with us after 3 months and 6 months. Before starting the study, you will be asked questions about specific risk factors. Your vitals including temperature, oxygen saturation, heart rate, respiratory rate, blood pressure will be recorded at admission and at each visit. No additional procedures or blood tests will be conducted routinely for this study. If at any time you experience any problems, you will be expected to report this to the doctor. You will also be contacted by telephone or by post in case you do not follow up as advised.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

We do not expect any injury to happen to you because of taking part in this study, as we are only observing and no intervention done.

Will you have to pay anything extra to take part in the study?

You will not incur any extra charges for taking part in this study. Any other treatment that you usually take will continue and the usual arrangements that you have with the hospital will decide how much you pay for this.

What happens after the study is over?

You may or may not benefit from the study that you are a part of. However the conclusions drawn from this study will be useful to manage similar patients in future.

Will your personal details be kept confidential?

The results of this study may be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask Dr. Anju Susan Jacob

Phone No : 9994882355 // Email id : anjususanjacob@gmail.com

ANNEXURE IV: INFORMED CONSENT FORM

Informed Consent form to participate in a (OBSERVATIONAL COHORT) Research study [POCSTROCH STUDY]

Study Title: PREVALENCE, DEMOGRAPHIC CHARACTERISTICS, COMORBIDITIES, CLINICAL PROFILE, RADIOLOGICAL PROFILE, OUTCOMES AND COMPLICATIONS OF POSTERIOR CIRCULATION STROKE, AMONG PATIENTS IN CHRISTIAN MEDICAL COLLEGE VELLORE.

Study Number: _____

Subject's Initials: _____

Subject's Name : _____

Date of Birth / Age: _____

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____

for the above study and have had the opportunity to ask questions. []

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. []

(iii) I understand that the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it,

even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. []

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). []

(v) I agree to take part in the above study. []

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: ____/____/____

Signatory's Name: _____

Signature: Or

Representative: _____

Date: ____/____/____

Signatory's Name: _____

Signature or thumb impression of Witness: _____ Signature of the Investigator:

Date: ____/____/____ Date: ____/____/____

Name & Address of Witness: _____ . Study Investigator's Name:

ANNEXURE V: CLINICAL RESEARCH FORM

CLINICAL RESEARCH FORM- POCSTROCH STUDY

DATE OF STROKE [_ / _ / _] STUDY NO:

PREVALENCE, DEMOGRAPHICS, RISK FACTORS, CLINICO-RADIOLOGICAL PROFILE, OUTCOME, COMPLICATIONS OF POSTERIOR CIRCULATION STROKE IN CMCH VELLORE '14-'16

HOSPITAL NO.	NAME	AGE	M/F	ARRIVAL ED/OP/IP	D/S DAMA/ED/MED1/2/3/4/5/ NEURO/STRK/PMR/OTHER	ADDRESS - LOCAL/OUTSIDE	OCCUPATION	CONTACT

RISK FACTORS [DURN, IF YES]	NO	NEW	ON Rx	OFF Rx	NO RF	N/A	RISK FACTORS [DURN, IF YES]	NO	NEW	ON Rx	OFF Rx	NO RF	N/A
Hypertension							Takayasu,s						
Diabetes							Giant cell						
Dyslipidemia							Kawasaki						
Hi Triglycerides							Primary CNSA						
Smoking							PAN						
Alcohol (daily)							Wegener's						
Carotid disease							Churg- Strauss						
IHD							Microscopic poly						
Arrhythmia							Henoch-Schönlein						
Valvular Heart Disease							Cryoglobulinemic						
Recent MI							Cut Leukocytoclastic						
Cardiomyopathy							Undiff smalvessel						
PFO / L-R Shunt							Undiff med vessel						
Hyperhomocystinemia							Dissection						
Low B12							Moya moya						
Mitochondrial							Amyloid Angio						
Marfans							Dolichoectasia						
CADASIL							Fibromuscular D						
P AVF Syndromes							Burgers						
Vascular anomaly							Misc:						
SLE							APCR						
Rheut arthr							OCP Use						
Sjogren's							PNH						
Inflam myositis							OSA						
Behçet's							Protein S						
Sarcoidosis							MTHFRhmo/hetr						
Drug induced							Haemat malign						
Toxin induced							Malignancy solid						
Infective encrditis							Sickle cell						
Tuberculous							Hormone Rx						
Rickettsial							FVL hmo/hetr						
Bacterial							Factor 8						
HIV							Poly cythemia						
Viral							PT hmo/hetr						
Neurosyphilis							AT3						
HBSAG positive							CRF/ CKD						
HCV positive							Obesity						
RCVS							Prev TIA/Stroke						
Migraine							Aortic Dissectio						
RT Induced							Preg / Puperium						
Post procedure							Misc						

PAST MEDICATIONS	Y	N	LIFESTYLE	BASELINE PARAMETERS
ASPIRIN			EXERCISE- DURN/FREQ	BLOOD SUGARS
CLOPIDOGREL			DIET [0 - VEG / 1 - NV]	HAEMOGLOBIN
ANTICOAGULANT			24-HOUR RECALL	CREATININE
ANTIARRHYTHMICS			FOOD FREQUENCY	HBA1C
STATIN			FRUIT PORTION	T.CHOLESTEROL
BETA BLOCKER			VEG PORTION	TRIGLYCERIDES
ACEI			FIBRE INTAKE	HDL
ARB			ANTIOXIDANTS	LDL
CCB			DAILY SALT INTAKE	VITAMIN B12 ASSAY
ANTIPLATELETS D/C			TYPE/AMOUNT OF OIL	S. HOMOCYSTEINE

	CLINICAL SYMPTOMS	Y	N	CLINICAL SIGNS	Y	N
GCS /15 [E_V_M_]	CONSCIOUSNESS			LEVEL OF CONSCIOUSNESS		
BLOOD PRESSURE	MOTOR DEFICITS			MOTOR DEFICITS		
	SENSORY DEFICITS			SENSORY DEFICITS		
PT/REL. AWARENESS ABOUT A)STROKE B)GOLDEN PERIOD	CROSSED SYNDROMES			CROSSED SYNDROMES		
GOLDEN PERIOD	VISUAL ABNORMALITIES			VISUAL ABNORMALITIES		
FIRST MEDICAL CONTACT LOCAL/CMC	ATAXIA			ATAXIA		
TIME INTERVAL B/W 1ST SYMPTOM & MEDICAL CONTACT	UNSTEADINESS			UNSTEADINESS		
TIME INTERVAL B/W 1ST SYMPTOM & BEING SEEN IN CMC	VERTIGO			VERTIGO		
RECURRENT STROKE	DIPLOPIA			DIPLOPIA		
TIA BEFORE STROKE	DYSPHAGIA			DYSPHAGIA		
WAKE UP STROKE	DYSARTHRIA			DYSARTHRIA		
IN-HOSPITAL STROKE	NAUSEA/VOMITING			BOWEL INV.		
CAROTID STROKE	URINARY INCONTINENCE			BLADDER INV.		

DIAGNOSIS- TYPE	ACUTE/LATE	RIGHT/LEFT/BILATERAL	ISCHEMIC/HEMORRHAGIC/ I+H
IMAGING MODALITY	MRI-ASP/MRI+MRA / MRI / CTC- / CECT / CTA / ANGIO / DOPPLER		
IMAGING DESCRIPTION			

TOAST	Oxfordshire
LAA	TACS
CE	PACS
SVO	POCS
ODE	LACS
UDE 2 Or >	NA
UDE -ve Eti	
UDE Incomp	

Treatment	Medications
Conservative	Single antiplatelet
Thrombolysed	Double antiplatelets
Surgery:	Anticoagulants
CEA/Stent	Anticoagplus antiplatelet
Poor Prognosis	Triple therapy
DAMA	Others

NIH Stroke Scale Date & time	BASELINE	D/5	1/12	3/12	6/12
1a level of consciousness					
1b LOC Questions					
3 Visual					
4 Facial palsy					
5a Motor arm RUL					
5b LUL					
6a Motor leg RLL					
6b LLL					
7 Limb Ataxia					
8 Sensory					
9 Best Language					
10 Dysarthria					
11 Extinction & Inattention					
Total NIH Score					

OCCUPATION	NO JOB	NEW JOB	PARTIALLY JOINED OLD JOB	FULLY JOINED OLD JOB

MODIFIED RANKIN SCALE	PRE-STROKE	ADMISSION	D/5	1/12	3/12	6/12
SCORE						

COMPLICATIONS DURING ACUT PHASE	COMPLICATIONS DURING FOLLOW UP
INFARCT EXTENSION	POST STROKE PAIN
H'GE IN INFARCT	DEPRESSION
DYSPHAGIA/NG	REC. STROKE
DVT/PE/GI BLEED	MI
LRTI/UTI/SEPSIS	SEPSIS
METABOLIC IMB.	SEIZURE
SEIZURE	BED SORES
MI	DVT/GI BLEED
VENTILATOR/TRACH	CONTRACTURES
OTHERS	COGNITION DECLINE

ANNEXURE VI: NATIONAL INSTITUTE OF HEALTH SCALE [NIHSS SCORE]

NIH Stroke Scale		
Instructions	Scale Definition	Score
<p>1a. Level of consciousness: The investigator must choose a response, even if a full evaluation is prevented by such obstacles as an endotracheal tube, language barrier, orotracheal trauma/bandages. A "3" is scored only if the patient makes no movement (other than reflexive posturing) in response to noxious stimulation.</p>	<p>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, or is obtunded and requires strong or painful stimulation to make movements (not stereotyped) 3 = Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, areflexic</p>	_____
<p>1b. LOC Questions: The patient is asked the month and his/her age. The answer must be correct - there is no partial credit for being close. Aphasic and stuporous patients who do not comprehend the questions will score "2." Patients unable to speak because of endotracheal intubation, orotracheal trauma, severe dysarthria from any cause, language barrier or any other problem not secondary to aphasia are given a "1." It is important that only the initial answer be graded and that the examiner not "help" the patient with verbal or non-verbal cues.</p>	<p>0 = Answers both questions correctly 1 = Answers one question correctly 2 = Answers neither question correctly</p>	_____
<p>1c. LOC Commands: The patient is asked to open and close the eyes and then to grip and release the non-paretic hand. Substitute another one-step command if the hands cannot be used. Credit is given if an unequivocal attempt is made but not completed due to weakness. If the patient does not respond to commands, the task should be demonstrated to them (pantomime) and score the result (i.e., follows none, one or two commands). Patients with trauma, amputation, or other physical impediments should be given suitable one-step commands. Only the first attempt is scored.</p>	<p>0 = Performs both tasks correctly 1 = Performs one task correctly 2 = Performs neither task correctly</p>	_____
<p>2. Best Gaze: Only horizontal eye movements will be tested. Voluntary or reflexive (oculocephalic) eye movements will be scored but calorie testing is not done. If the patient has a conjugate deviation of the eyes that can be overcome by voluntary or reflexive activity, the score will be "1." If a patient has an isolated peripheral nerve paresis (CN, III, IV or VI) score a "1." Gaze is testable in all aphasic patients. Patients with ocular trauma, bandages, pre-existing blindness or other disorder of visual acuity or fields should be tested with reflexive movements and a choice made by the investigator. Establishing eyes contact and then moving about the patient from side to side will occasionally clarify the presence of a partial gaze palsy.</p>	<p>0 = Normal 1 = Partial gaze palsy. This score is given when gaze is abnormal in one or both eyes, but where forced deviation or total gaze paresis are not present 2 = Forced deviation, or total gaze paresis not overcome by the oculocephalic maneuver</p>	_____
<p>3. Visual: Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting or visual threat as appropriate. Patient must be encouraged, but if they look at the side of the moving fingers appropriately, this can be scored as normal. If there is unilateral blindness or enucleation, visual fields in the remaining eye are scored. Score 1 only if a clear-cut asymmetry, including quadrant anopia is found. If patient is blind from any cause, score "3." Double simultaneous stimulation is performed at this point. If there is extinction, patient receives a "1" and the results are used to answer question #11.</p>	<p>0 = No visual loss 1 = Partial hemianopia 2 = Complete hemianopia 3 = Bilateral hemianopia (blind, including cortical blindness)</p>	_____

NIH Stroke Scale - Continued

<p>4. Facial Palsy: Ask, or use pantomime to encourage the patient to show teeth or raise eyebrows and close eyes. Score symmetry of grimace in response to noxious stimuli in the poorly responsive or non-comprehending patient. If facial trauma/bandages, orotracheal tube, tape or other physical barrier obscures the face, these should be removed to the extent possible.</p>	<p>0 = Normal symmetrical movement 1 = Minor paralysis (flattened nasolabial fold, asymmetry on smiling) 2 = Partial paralysis (total or near total paralysis of lower face) 3 = Complete paralysis of one or both sides (absence of facial movement in the upper and lower face)</p>	<p style="text-align: center;">_____</p>
<p>5 & 6. Motor Arm and Leg: The limb is placed in the appropriate position: extend the arms (palms down) 90 degrees (if sitting) or 45 degrees (if supine) and the leg 30 degrees (always tested supine). Drift is scored if the arm falls before 10 seconds or the leg before 5 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic arm. Only in the case of amputation or joint fusion at the shoulder or hip may the score be "9" and the examiner must clearly write the explanation for scoring as a "9".</p>	<p>0 = No drift, limb holds 90 (or 45) degrees for full 10 seconds 1 = Drift, Limb holds 90 (or 45) degrees, but drifts down before full 10 seconds; does not hit bed or other support 2 = Some effort against gravity, limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity 3 = No effort against gravity, limb falls 4 = No movement 9 = Amputation, joint fusion explain: _____</p> <p>5a. Left Arm..... _____</p> <p>5b. Right Arm..... _____</p>	<p style="text-align: center;">_____</p> <p style="text-align: center;">_____</p>
	<p>0 = No drift, leg holds 30 degrees position for full 5 seconds. 1 = Drift, leg falls by the end of the 5 second period but does not hit bed. 2 = Some effort against gravity; leg falls to bed by 5 seconds, but has some effort against gravity. 3 = No effort against gravity, leg falls to bed immediately. 4 = No movement 9 = Amputation, joint fusion explain: _____</p> <p>6a. Left Leg..... _____</p> <p>6b. Right Leg..... _____</p>	<p style="text-align: center;">_____</p> <p style="text-align: center;">_____</p>
<p>7. Limb Ataxia: This item is aimed at finding evidence of a unilateral cerebellar lesion. Test with eyes open. In case of visual defect, insure testing is done in intact visual field. The finger-nose-finger and heel-shin tests are performed on both sides, and ataxia is scored only if present out of proportion to weakness. Ataxia is absent in the patient who cannot understand or is paralyzed. Only in the case of amputation or joint fusion may the item be scored "9", and the examiner must clearly write the explanation for not scoring. In case of blindness test by touching nose from extended arm position.</p>	<p>0 = Absent 1 = Present in one limb 2 = Present in two limbs</p>	<p style="text-align: center;">_____</p>
<p>8. Sensory: Sensation or grimace to pin prick when tested, or withdrawal from noxious stimulus in the obtunded or aphasic patient. Only sensory loss attributed to stroke is scored as abnormal and the examiner should test as many body areas [arms (not hands), legs, trunk, face] as needed to accurately check for hemisensory loss. A score of 2, "severe or total," should only be given when a severe or total loss of sensation can be clearly demonstrated. Stuporous and aphasic patients will therefore probably score 1 or 0. The patient with brain stem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic score 2. Patients in coma (item 1a=3) are arbitrarily given a 2 on this item.</p>	<p>0 = Normal; no sensory loss 1 = Mild to moderate sensory loss; patient feels pinprick is less sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick but patient is aware he/she is being touched 2 = Severe to total sensory loss; patient is not aware of being touched in the face, arm and leg</p>	<p style="text-align: center;">_____</p>

NIH Stroke Scale - Continued

<p>9. Best Language: A great deal of information about comprehension will be obtained during the preceding sections of the examination. The patient is asked to describe what is happening in the attached picture, to name the items on the attached naming sheet, and to read from the attached list of sentences. Comprehension is judged from responses here as well as to all of the commands in the preceding general neurological exam. If visual loss interferes with the tests, ask the patient to identify objects placed in the hand, repeat, and produce speech. The intubated patient should be asked to write. The patient in coma (question 1a=3) will arbitrarily score 3 on this item. The examiner must choose a score in the patient with stupor or limited cooperation but a score of 3 should be used only if the patient is mute and follows no one step commands.</p>	<p>0 = No aphasia, normal 1 = Mild to moderate aphasia; some obvious loss of fluency or facility of comprehension, without significant limitation on ideas expressed or form of expression. Reduction of speech and/or comprehension, however, makes conversation about provided material difficult or impossible. For example in conversation about provided materials examiner can identify picture or naming card from patient's response. 2 = Severe aphasia; all communication is through fragmentary expression; great need for inference, questioning and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response. 3 = Mute, global aphasia; no usable speech or auditory comprehension</p>	<p style="text-align: center;">_____</p>
<p>10. Dysarthria: If patient is thought to be normal an adequate sample of speech must be obtained by asking patient to read or repeat words from the attached list. If the patient has severe aphasia, the clarity of articulation of spontaneous speech can be rated. Only if the patient is intubated or has other physical barrier to producing speech, may the item be scored "9", and the examiner must clearly write an explanation for not scoring. Do not tell the patient why he/she is being tested.</p>	<p>0 = Normal 1 = Mild to moderate; patient slurs at least some words and, at worst, can be understood with some difficulty 2 = Severe; patient's speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/anarthric 9 = Intubated or other physical barrier, explain</p>	<p style="text-align: center;">_____</p>
<p>11. Extinction and Inattention (formerly Neglect): Sufficient information to identify neglect may be obtained during the prior testing. If the patient has a severe visual loss preventing visual double simultaneous stimulation, and the cutaneous stimuli are normal, the score is normal. If the patient has aphasia but does appear to attend to both sides, the score is normal. The presence of visual spatial neglect or anosagnosia may also be taken as evidence of abnormality. Since the abnormality is scored only if present, the item is never untestable.</p>	<p>0 = No abnormality 1 = Visual, tactile, auditory, spatial, or personal inattention or extinction to bilateral simultaneous stimulation in one of the sensory modalities 2 = Profound hemi-inattention or hemi-inattention to more than one modality. Does not recognize own hand or orients to only one side of space.</p>	<p style="text-align: center;">_____</p>
Total NIHSS Score:		<p style="text-align: center;">_____</p>
<p>Time of NIHSS Assessment: _____</p> <p>Date of NIHSS Assessment: _____</p> <p>Physician/NIHSS Certified Individual Signature: _____</p>		

ANNEXURE VII: MODIFIED RANKIN SCALE [mRS]

MODIFIED RANKIN SCALE (MRS)

Patient Name: _____
 Rater Name: _____
 Date: _____

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

TOTAL (0-6): _____

References

Rankin J. "Cerebral vascular accidents in patients over the age of 60." *Scott Med J* 1957;2:200-15

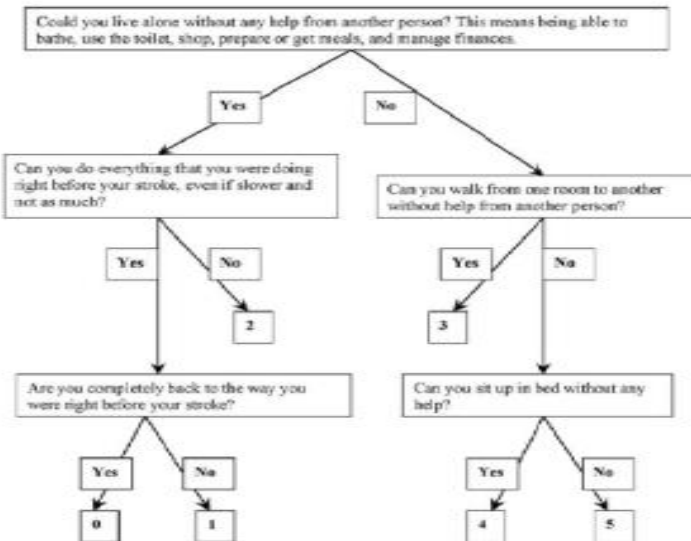


Figure. Slightly revised simplified modified Rankin Scale questionnaire.

American Stroke Association

Simplified Modified Rankin Scale Questionnaire: Reproducibility Over the Telephone and Validation With Quality of Life

Askiel Bruno, Abiodun E. Akinwuntan, Chen Lin, Brian Close, Kristin Davis, Vanessa Baute, Tia Aryal, Desiree Brooks, David C. Hess, Jeffrey A. Switzer and Fenwick T. Nichols

Stroke. published online June 16, 2011;

ANNEXURE VIII: ABSTRACT

POSTERIOR CIRCULATION STROKE CHARACTERISTICS

[POCSTROCH STUDY] - AN OBSERVATIONAL COHORT STUDY

Introduction: Cerebrovascular accident is among the leading causes of acquired disability and death worldwide. Posterior circulation stroke [PCS] with its difficulty in early diagnosis, seldom have the appropriate evaluation or management done. Studies are scarce which looked into the independent predictors of long term bad outcomes of PCS.

Our study aimed to characterize PCS among patients above 18 years age, presenting to Christian Medical College Vellore, over a period of 3 years. We wished to determine the short and long term outcomes of PCS.

Methods: We conducted a prospective observational cohort study in consecutive PCS patients who presented to our hospital. All patients from January 2014 to May 2017 were recruited, diagnostic criteria assessed and prognostic scores calculated. Morbidity and mortality at discharge, at 3 months and 6 months was studied.

Results: We recruited 291 PCS patients who were followed up in our cohort. Prevalence of posterior circulation stroke to the total strokes in our center in 1 year was 12.9% [111/860]. Mean age of presentation was 53.34 years (SD 13.34 years). Young strokes constituted 28.8%. The common co-morbidities were hypertension 72%, diabetes mellitus 52.6%, smoking 38.5% and dyslipidemia 32.6%. The common presenting symptoms were giddiness 79%, unsteadiness 75.35%, ataxia 56%, motor deficits 48.8%

and nausea & vomiting 43%. Most were Ischemic strokes 86.5%. Among the arteries involved, posterior cerebral artery 45%, posterior inferior cerebellar artery 38% and basilar artery 19.2%. Among ischemic strokes, large artery atherosclerosis was 50.8%, cardio embolism and small vessel occlusion were 14.4% each. Dysphagia was seen in 32.6%, sepsis in 19.2% and invasive ventilation in 8% . Post stroke pain, a late complication was seen in 23%, followed by cognition decline in 10.3%. Mortality was 6.2% at discharge, 2.4% at 1-month, 1.7% at 3-months and 0.7% at 6 months, following discharge. Morbidity [modified Rankin Scale (mRS) 4 or 5] was 10.7% at discharge, 7.9% at 1 month, 4.1% at 3 months and 3.1% at 6 months. Bad outcome [mRS 4 to 6] was 16.8% at discharge, 16.4% at 1 month, 14.4% at 3 months and 13.8% at 6 months. Independent predictors of bad outcomes at 6-months were baseline National Institute of Health Stroke Scale (NIHSS) score [OR 1615.59 with CI 27.64-94447.7], invasive ventilation [OR 7.77 with CI 1.57-38.43], sepsis [OR 17.22 with CI 1.45-204.08], basilar artery involvement [OR 19.98 with CI 1.67-238.81]. Baseline NIHSS score has an area under the curve 94% showing good ability to discriminate between good and bad outcomes. NIHSS scores between 0 to 5 suggest a good outcome while scores more than 13 suggest a bad outcome at 6 months. Our cohort follow-up of 6 months is among the largest to date.

Conclusion: The prevalence of PCS in our study was similar to the other studies in India and the West. Clinical features and co-morbidities were also similar to previous studies.

Survival analysis suggest good survival at 3 and 6 months following PCS. The baseline NIHSS score is an independent predictor of bad outcomes at 6 months.

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. . .	4 5 6	170	70	2	1	2 1 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 2	2	2	2	1 1 1	1	LACUNAR INFRACT	3	3	1 2 2 2 2 2 1	2 2	
. . .	4 5 6	180	90	2	1	2 2 2 2 2 2 2 2 2 2 2 1 1 2 1 2 2	2	2	2	1 3 1	4	B/L PCA INFRACT R OCC AND PICA	1	3	1 2 2 2 2 2 1	2 2	
14.8	4 5 6	130	80	2	1	1 2 2 2 2 2 2 2 2 2 2 2 1 2 2 1 2	2	2	2	1 3 1	2	R P1 INFRACT	1	3	1 2 2 2 2 2 2	2 2	
. . .	4 5 6	150	80	2	1	2 2 2 2 2 2 1 2 2 2 2 1 2 1 2 2 2 1	2	2	2	1 1 1	1	R PICA INFRACT	1	3	1 2 2 2 2 2 1	2 2	
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. . .	4 5 6	144	80	.	1	2 2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 1	2	2	2	1 1 1	2		3	3	1 2 2 2 2 2 1	2 2	
. . .	4 5 6	180	80	.	1	2 2 1 2 2 2 2 2 2 2 2 1 1 1 2 2 1 2	2	2	2	1 3 2	1	VERMIAN BLEED	.	3	1 2 2 2 2 2 6	2 2	
. . .	4 5 6	170	100	.	1	2 2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 2	2	2	2	1 1 1	1	R PCA THALAMUS INFRACT	1	3	1 2 2 2 2 2 1	2 2	
. . .	4 5 6	140	80	2	1	2 2 2 2 2 2 2 2 2 2 2 1 1 2 2 2 2	2	2	2	1 2 1	4	INFRACT L MEDULLARY	1	3	1 2 2 2 2 2 1 1	2 2	
. . .	4 2 5	170	90	.	1	2 2 1 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1	1	1	1 3 1	4	BASULAR ARTERY THROMBOSIS	1	3	1 2 2 2 2 2 6	2 2	
850	10.7	4 5 6	140	100	.	1	2 2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 1	2	2	2	2 1 2	1	R PICA HAEMORAGE	.	3	1 2 2 2 2 2 6	2 2
687	.	4 5 6	150	100	.	1	2 1 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 2	2	2	2	1 2 2	4	INTRA PARENCHYMAL HAEMORAG	1	3	1 2 2 2 2 2 6	2 2
2000	10	3 2 3	110	80	.	1	2 2 2 2 2 1 1 2 2 2 1 1 1 1 2 2 2 2	2	2	2	1 1 3	1	R CEREBELLAR PICA SICA INFRAC	1	3	2 2 2 2 2 2 1	2 2
. . .	4 5 6	160	90	2	1	2 2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 2	2	2	2	1 2 1	1	INF-MED L CEREBELLUM INF VERM	1	3	1 2 2 2 2 2 1 1	2 2	
889	.	4 5 6	190	86	.	2	2 1 2 2 2 1 2 2 2 2 2 1 1 2 2 2 2	2	2	2	1 1 1	2	R CEREBELLAR INFRACT-R SBCLA	1	3	1 2 2 2 2 2 2 2	2 2
415	.	4 5 6	186	75	.	1	1 1 2 2 2 1 2 2 2 2 1 2 2 2 1 2 2	2	2	2	1 1 1	2	L CHRONIC,R PONS,R SIDE INPERF	2	3	1 2 2 2 2 2 4	2 2
587	11.2	2 3 4	185	65	.	1	2 2 2 2 2 1 2 2 2 1 1 1 1 2 1 1 2	2	2	2	1 3 1	1	PONTINE INFRACT BASILLAR ARTE	1	3	1 2 2 2 2 2 1	2 2
. . .	1 2 2	180	90	2	2	2 2 2 2 1 2 2 2 2 2 2 2 2 2 2 2	2	2	2	1 3 2	4	B/L CEREBELLAR H'GE	.	3	1 2 2 2 2 2 1 6	2 2	
148	.	4 5 6	144	80	2	1	2 2 2 2 2 1 1 2 2 2 1 1 1 2 2 2 2	2	2	2	2 2 1	1	INFRACT L THALAMUS	1	3	1 2 2 2 2 2 2 2	2 2
. . .	17.7	4 5 6	180	100	.	1	2 2 1 2 1 1 1 2 1 2 2 1 1 2 1 1 2	2	2	2	1 3 1	2	SUBCLAVIAN STEAL, L AICA R PICA	1	3	1 2 2 2 2 2 1	2 2
. . .	4 5 6	160	90	2	1	2 2 2 2 2 2 2 2 2 2 2 1 1 2 2 2 2	2	2	2	1 2 1	1	L CEREBELLAR HEM.%PONS,BA TH	3	3	1 2 2 2 2 2 2 2	2 2	
92	5.5	4 5 6	169	79	.	2	2 2 2 2 2 1 2 1 1 1 1 1 2 2 2 2	2	2	2	1 1 1	2	R SICA INFRACT	2	3	1 2 2 2 2 2 2 3	2 2
. . .	4 5 6	180	85	.	1	2 2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 1	2	2	2	1 2 1	4	INFRACT L CEREBELLAR HEMISPH	1	3	1 2 2 2 2 2 1 1	2 2	
456	9.7	4 5 6	.	2	1	2 2 2 2 1 1 2 1 2 2 2 2 2 2 2 2	2	2	2	2 3 1	2	Infarct pons,b/l cereb.hemisph.,LOCKE	2	3	1 2 2 2 2 2 2 4	2 2	
111	18	4 5 6	176	85	.	1	1 2 2 2 2 1 2 2 2 2 1 1 2 1 2 2	2	2	2	1 1 1	2	R INFRACT,R PCA,MCA,PERFORAT	1	3	2 1 2 2 2 2 2 2	2 2
. . .	4 5 6	197	82	.	1	2 2 2 2 2 2 2 2 2 2 2 1 1 2 1 2 1	2	2	2	1 2 1	4	L CEREBELLAR,L PCA	1	3	1 2 2 2 2 2 1	2 2	
515	9.7	4 5 6	185	75	.	1	1 2 2 2 1 2 2 2 2 1 1 1 2 2 2 2	2	2	2	1 3 1	2	L POST WATERSHED,L PCA,B/L CE	1	3	1 2 2 2 2 2 1	2 2
. . .	4 5 6	185	90	.	1	2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 2	2	2	2	2 2 1	2	R VA	4	3	1 2 2 2 2 2 4	2 2	
. . .	4 5 6	190	90	2	1	1 2 2 2 2 1 2 2 2 1 2 1 2 1 2 1	2	2	2	1 3 1	1	POSTERIOR MEDULLA RIGHT CERB	1	3	1 2 2 2 2 2 1	2 2	
. . .	27.5	4 5 6	146	90	2	1	2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 1	2	2	2	1 1 1	2	RIGHT PCA INFRACT	1	3	1 2 2 2 2 2 1	2 2
. . .	4 5 6	185	90	2	1	2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 1	2	2	2	1 1 1	2	INFRACT R MEDULLA,R VA NOT VIS	7	3	1 2 2 2 2 2 1	2 2	
. . .	4 5 6	187	76	.	1	2 2 2 2 2 1 2 2 2 1 1 1 2 1 2 2	2	2	2	1 3 1	2	B/L PICA/SCA TERRITORY	1	3	1 2 2 2 2 2 1	2 2	
. . .	5.3	4 5 6	190	85	.	1	2 2 2 2 1 2 2 2 2 2 1 1 2 1 2 1	2	2	2	1 3 1	2	MULTI INFRACT POST R VA,ATENU	1	3	1 2 2 2 2 2 .	2 2
. . .	4 5 6	195	84	.	1	2 2 2 2 2 2 2 2 2 2 1 1 2 2 2 1	2	2	2	1 2 1	4	INFRACT L TEMP,L OCCIPTL LOBES,	1	3	1 2 2 2 2 2 1	2 2	
337	10.6	1 1 1	122	80	.	1	2 2 1 2 1 1 2 2 2 1 1 1 2 1 2 2	2	2	2	1 1 1	2	THROMBSIS OF BASLR ARTRY RV47	7	3	2 2 1 2 2 2 .	2 2
. . .	20.1	4 5 6	188	74	.	2	2 2 2 2 2 2 2 2 2 2 2 1 2 2 2 2	2	2	2	1 3 1	2	ISCHMIC INFRACT B/L OCCIPITAL LG	1	3	1 2 2 2 2 2 1	2 2
235	19	4 5 6	195	84	.	1	2 2 2 2 2 2 2 2 2 2 1 2 2 2 2 2	2	2	2	1 1 1	2	A/C R THALAMIC INFRACT	3	3	1 2 2 2 2 2 1	2 2
1306	.	4 5 6	180	110	2	2	2 2 1 2 2 1 1 2 2 1 1 1 2 2 2 2	2	2	2	1 1 1	1	R PCA INFRACT	1	3	1 2 2 2 2 2 2 2	2 2
. . .	4 5 6	196	73	.	1	1 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 2	2	2	2	1 3 1	2	INFRACT L OCCIPTL,ATTENUATIO	1	3	1 2 2 2 2 2 1	2 2	
456	12	4 5 6	130	80	.	1	2 2 2 2 2 2 2 2 2 2 1 1 2 2 2 1	2	2	2	2 1 1	2		6	3	1 2 2 2 2 2 1	2 2
. . .	4 5 6	175	83	.	1	2 2 2 2 2 1 2 2 2 1 1 1 2 1 2 2	2	2	2	1 3 1	2	CUT OFF MCA PLEXOUS SEGMENT	1	3	1 2 2 2 2 2 2 2	2 2	
. . .	1 2 1	100	50	2	2	2 1 1 2 1 1 2 2 2 2 1 1 2 2 2 1	2	2	2	1 3 1	2	INFRACTB/L THALAMI,TEMPORAL,	1	3	1 2 2 2 2 2 1	1 2	
2000	9.5	4 5 6	174	75	.	1	2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 1	2	2	2	1 2 1	2	L CERBELAR,MEDULA L PICA TER	1	3	1 2 2 2 2 2 4	2 2
. . .	4 5 6	188	74	.	1	1 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 1	2	2	2	2 3 1	1	AIC INFRACT CERBELLAR B/L PICA,	1	3	1 2 2 2 2 2 1	2 2	
. . .	4 5 6	186	74	.	2	2 1 2 2 1 2 2 2 2 2 1 1 2 2 2 1	2	2	2	1 3 1	1	R CEREBRAL HEMISPR,PONS,THR	1	3	1 2 2 2 2 2 1	2 2	
208	10.2	4 5 6	186	84	.	1	2 1 2 2 2 2 1 2 2 1 1 1 2 2 2 1	2	2	2	1 3 1	1	B/L CEREBELR,L INFER,R POSTR,	2	3	1 2 2 2 2 2 4	2 2
149	30.4	4 5 6	185	68	.	1	2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 1	2	2	2	1 2 1	1	R CEREBELLAR INFRACT,R PICA INF	5	3	1 2 2 2 2 2 1	2 2
. . .	4 5 6	195	84	.	1	2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 1	2	2	2	1 1 1	1	INFRACT R MEDULA,MRA-R VA,PIC	1	3	1 2 2 2 2 2 1	2 2	
2000	.	4 5 6	180	82	.	1	2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 1 1	2	2	2	1 3 1	1	B/L PCA INFRACT,BA THROMBOSIS	1	3	1 2 2 2 2 2 1	2 2
. . .	4 5 6	170	68	.	1	2 2 2 2 2 1 2 1 2 2 1 1 2 2 2 2	2	2	2	1 1 1	2	wedge infrcr l pons,R cerebrl,MRA-R	3	3	1 2 2 2 2 2 1	2 2	
2000	17.5	4 5 6	188	84	.	1	2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 1	2	2	2	1 1 1	2	R CEREBELLAR&BRAINSTEMS,PIC	6	3	1 2 2 2 2 2 2 2	2 2
1376	.	4 5 6	187	65	.	1	2 2 2 2 2 1 2 2 2 2 2 2 2 2 2 2	2	2	2	1 2 2	4	L GANGLIOTHALAMIC HAEMORRAC	1	3	1 2 2 2 2 2 3	2 2
2000	13.3	4 5 6	190	86	.	2	2 2 2 2 2 2 2 2 2 2 1 1 1 2 1 2 2	2	2	2	1 1 1	1	R CEREBELAR INFRACT,R VA THR	1	3	1 2 2 2 2 2 2 2	2 2
3330	23.1	4 5 6	195	83	2	1	2 2 1 2 2 2 2 2 2 2 1 1 1 2 2 2 1	2	2	2	1 1 1	2	R CEREBELR L MEDIAL OCCIPTL R	1	3	1 2 2 2 2 2 2 2	2 2
. . .	4 5 6	190	82	.	2	2 2 2 2 2 2 2 2 2 2 2 1 1 2 2 2 1	2	2	2	1 2 1	1	ALC INFRACT CERBELR L-R PICA AL	1	3	1 2 2 2 2 2 2 2	2 2	
2000	.	4 5 6	186	68	.	1	2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 2	2	2	2	1 3 1	2	MULTPL INFRACT-SCA,LPCA FOCL	1	3	1 2 2 2 2 2 4	2 2
346	46	4 5 6	190	76	.	1	2 2 2 2 2 2 2 2 2 2 2 1 2 2 2 1	2	2	2	1 2 1	3	INFRACT-ANTERIOR ASPECT OF L TH	5	3	1 2 2 2 2 2 2 2	2 2
. . .	4 5 6	190	72	.	1	2 2 1 2 2 2 2 2 2 2 1 1 1 2 2 2 2	2	2	2	1 1 1	1	INFRACT R THALAMUS,R PCA,R FUS	2	3	1 2 2 2 2 2 1	2 2	
1164	18	4 5 6	190	82	.	1	2 2 2 2 2 1 2 2 2 1 1 1 2 2 2 2	2	2	2	1 3 1	2	MULTPL INFRACT B/L OCCIPTL L COR	1	3	1 2 2 2 2 2 3	2 2
. . .	4 5 6	188	84	.	1	2 2 2 2 2 1 2 2 2 2 2 2 2 2 2 1	2	2	2	1 3 1	1	INFRACT DEEP WHITE B/L,WATERSH	1	3	1 2 2 2 2 2 4	2 2	
. . .	4 5 6	190	86	2	2	2 2 2 2 2 1 2 2 1 2 1 1 1 2 2 1	2	2	2	1 3 1	2	INFRACT L PONS,R CEREBELR HEM	1	3	1 2 2 2 2 2 4	2 2	
. . .	4 5 6	175	78	.	1	1 2 2 2 2 1 1 1 1 1 1 1 1 2 2 2	2	2	2	1 3 1	4	INFRACT N POST CIRCLU TERITORY	1	3	1 2 2 2 2 2 1	2 2	
. . .	4 5 6	190	68	.	1	2 2 2 2 2 1 2 2 2 2 2 1 2 2 2 2	2	2	2	1 3 1	2	INFRACT MEDULLA	3	3	1 2 2 2 2 2 1	2 2	
846	.	4 5 6	190	85	.	1	2 2 2 2 2 2 2 2 2 2 2 1 1 2 2 2 1	2	2	2	1 3 1	2	BRAINSTEM, L THALAMIC R MEDIA	1	3	1 2 2 2 2 2 2 2	2 2
. . .	4 5 6	188	82	.	1	2 2 2 2 2 2 2 2 2 1 1 1 1 2 2 1	2	2	2	1 2 1	1	All infarct in LPICA territ.&nonvisualise	2	3	1 2 2 2 2 2 2 3	2 2	
. . .	4 5 6	160	90	.	1	2 1 2 2 2 2 2 2 2 2 1 2 2 2 2 1	2	2	2	1 1 1	2		2	3	1 2 2 2 2 2 1	2 2	
. . .	3 5 6	170	90	2	2	2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 2	2	2	2	2 2 2	1	R PCA THALAMUS AND OCCIPITAL	1	3	1 2 2 2 2 2 2 2	2 2	
. . .	4 5 6	164	80	.	1	2 2 2 2 2 2 2 2 2 2 2 1 2 2 2 1	2	2	2	1 2 1	2		1	3	1 2 2 2 2 2 1	2 2	
. . .	4 5 6	144	90	.	2	2 2 2 2 2 2 2 2 2 2 1 1 1 2 2 2 1	2	2	2								

ANNEXURE X: STROBE CHECK LIST

STROBE Statement

—checklist of items that should be included in reports of observational studies

	Item	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection

Participants

6 (a) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants.

Describe methods of follow-up

Case-control study—Give eligibility criteria, and sources and methods of case ascertainment and control selection.

Give the rationale for the choice of cases and controls

Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants

(b) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed

Case-control study—For matched studies, give matching criteria and the number of controls per case

Variables

7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable

Data sources/
measurement

8* For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group

Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	<p>(a) Describe all statistical methods, including those used to control for confounding</p> <p>(b) Describe any methods used to examine subgroups and interactions</p> <p>(c) Explain how missing data were addressed</p> <p>(d) <i>Cohort study</i>—If applicable, explain how loss to follow-up was addressed</p> <p><i>Case-control study</i>—If applicable, explain how matching of cases and controls was addressed</p> <p><i>Cross-sectional study</i>—If applicable, describe analytical methods taking account of sampling strategy</p> <p>(e) Describe any sensitivity analyses</p>

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram

Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)

Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure
		<i>Cross-sectional study</i> —Report numbers of outcome events

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% CI). Make clear which confounders were adjusted for and why they were included
		(b) Report category boundaries when continuous variables were categorized
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results

Other information

Funding 22 Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.