A DISSERTATION ON

"SERUM CORTISOL LEVELS IN ASSESSING SEVERITY OF ACUTE STROKE – A CROSS SECTIONAL STUDY IN CHENGALPET MEDICAL COLLEGE AND HOSPITAL"

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M.D DEGREE IN GENERAL MEDICINE

BRANCH – I

CHENGALPET MEDICAL COLLEGE AND HOSPITAL

CHENGALPET – 603001

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BONAFIDE CERTIFICATE

This is to certify that this dissertation titled **"SERUM CORTISOL LEVELS IN ASSESSING SEVERITY OF ACUTE STROKE – A CROSS SECTIONAL STUDY IN CHENGALPET MEDICAL COLLEGE AND HOSPITAL"** is the bonafide original work of **Dr.G . N I S H A N T H I** in partial fulfillment of the requirements for M.D Branch I (GENERAL MEDICINE) Examination of the TamilNadu Dr.M.G.R.Medical University to be held in May 2023.The period of study was from November 2021 to October 2022.

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This is to certify that dissertation **"SERUM CORTISOL LEVELS IN ASSESSING SEVERITY OF ACUTE STROKE – A CROSS SECTIONAL STUDY IN CHENGALPET MEDICAL COLLEGE AND HOSPITAL"** is a bonafide work performed by **Dr. G. NISHANTHI .**, postgraduate student of General Medicine , Chengalpattu Medical College , under my guidance and supervision in partial fulfillment of regulations of The Tamil Nadu Dr. M.G.R Medical University for the award of M.D. Degree during May 2023 exams.

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DECLARATION

I **Dr.G.NISHANTHI** solemnly declare that the dissertation titled "**SERUM CORTISOL LEVELS IN ASSESSING SEVERITY OF ACUTE STROKE – A CROSS SECTIONAL STUDY IN CHENGALPET MEDICAL COLLEGE AND HOSPITAL**"is a bonafide work done by me at Chengalpattu Medical College and Hospital during 2021 – 2022 under the guidance and supervision of **Prof. Dr. R. NARMADHA LAKSHMI M.D.,DCH.,**The dissertation is submitted toTheTamilnadu Dr.M.G.R.MedicalUniversity towards The partial fulfillment of requirements for the award of M.D.Degree (BranchI) in General Medicine May 2023.

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ABSTRACT

INTRODUCTION

The stress response that occurs after the event of acute stroke causes the activation of the hypothalamo–pituitary–adrenal (HPA) axis. Certain studies have found that increased serum cortisol level in patients with acute stroke is related to greater stroke severity. Whether the stress response is just an epiphenomenon to stroke severity or independently contributes to prognosis remains uncertain. But there is a immense need to detect a biomarker for predicting the outcome of acute stroke.[15]

OBJECTIVE OF THE STUDY

The aim of the study was to investigate if a single serum cortisol determination was related to severity of acute stroke.

METHODS

A cross sectional study was conducted in 120 patients with acute stroke presenting within 24hours of stroke onset after getting informed consent. The patients were studied from medical wards and IMCU in Chengalpattu government hospital. Scandinavian Stroke Scale (SSS) was used to study severity of acute stroke. Diagnosis of Acute Ischemic or Hemorrhagic stroke was based on CT imaging in all patients.Blood samples are taken for assessing serum cortisol levels.Data was entered in MS excel analyzed using SPSS

software for appropriate descriptive and inferential statistics.

RESULTS

The mean age group is 50 to 59 years with 50% males and 50 % females. The mean cortisol level was 637nmol/L. Of the 120 cases 98 had acute ischemic stroke and 22 had acute hemorrhagic stroke.The mean SSS score was 20.85 and mean time duration was 9.5 hours.The correlation coefficient for SSS and serum cortisol was -0.984 which had significant correlation indicating high serum cortisol levels had low SSS score and also the P value being < 0.001 which was statistically significant.

CONCLUSION

Acute stroke severity related to increasing serum cortisol levels.Serum cortisol was associated with stroke severity and markers reflecting stroke severity.

ABBREVIATIONS

HPA - Hypothalamo pituitary axis

ICH - Intracerebral Hemorrhage

LDL - Low density lipoprotein

NMDA - N methyl D aspartate

AMPA - Amino methyl propionic acid

FLAIR - Fluid attenuated inversion recovery

CT – Computed tomography

MRI – Magnetic resonance imaging

TIA – transient ischemic attacks

ECG – Electro cardio gram

MRA – Magnetic resonance Angiography

ACA – Anterior cerebral artery

MCA – Middle cerebral artery

PCA – Posterior cerebral artery

RT-PA – Recombinant Tissue plasminogen activator

ACTH –Adrenocorticotropic hormone

CONTENTS

INTRODUCTION

The stress response that occurs after the event of acute stroke causes the activation of the hypothalamo–pituitary–adrenal (HPA) axis. Certain studies have found that increased serum cortisol level in patients with acute stroke is related to larger infarct volume, greater stroke severity and poor outcome, including death. Whether the stress response is just an epiphenomenon to stroke severity or independently contributes to prognosis remains uncertain.

There are many clinical variables like symptom severity and advanced age which are identified as potential predictors of outcome in patients with acute stroke. But there is a immense need to detect a biomarker for predicting the outcome of acute stroke.

In acute stroke the first measurable alterations are the endocrine changes because of the alteration in HPA axis. One of the HPA axis-related hormone is cortisol which has a robust circadian rhythm wherein the levels peak typically in the early hours of the day and decline later on.It has also been observed that the normal circadian rhythm of cortisol is suspended during acute stroke as equal levels of cortisol were found round the clock[15]

OBJECTIVE OF THE STUDY

1. The aim of the study was to investigate if a single serum cortisol determination was related to severity of acute stroke.

REVIEW OF LITERATURE

A stroke is defined as rapid development of clinical symptoms and/or signs of focal and at times global loss of brain function,with symptoms lasting more than 24hours or leading to death, with no apparent cause other than that of vascular origin17.If all neurological symptoms and signs resolve within 24 hours, the condition is termed as Transient Ischemic Attack. Focal ischemia is caused by either a emboli from a arterial source which is proximal or from heart or because of thrombosis of major cerebral vessels. Intracranial hemorrhage is caused by bleeding into brain parenchyma and producing mass effects leading to manifestation of various neurological signs and symptoms.

EPIDEMIOLOGY

Stroke is one of the leading causes of death and disability in India. The estimated adjusted prevalence rate of stroke range, 84-262/100,000 in rural and 334-424/100,000 in urban areas. The incidence rate is 119-145/100,000 based on the recent population based studies. A population-based study in Tianjin, China, from 1992 to 2014 showed that the age-standardized first-ever stroke incidence was 297 per 100,000 persons, which significantly increased across sex and strokes subtypes: increase of 6.3% overall, 5.5% for men and 7.9% for women, 4.6% for HS, and 7.3% for IS. Although the majority of strokes occur beyond the fifth decade, ≈10%–15% of strokes occur in patients 18–50 years of age.[11] The age at stroke onset tends to be lower in low- and middle-income countries, accounting for a relatively higher proportion of strokes (19%–30%), adding to the higher burden of disability and DALYs lost in the developing world.

According to the TOAST[1] classification, there are four main types of ischemic strokes. These are large vessel atherosclerosis, small vessel diseases (lacunar infarcts), cardio embolic strokes, and cryptogenic strokes. Each of these has different causes and pathophysiology. Regardless o the type of stroke, it is important to know that with each minute of large vessel ischemic stroke untreated, close to two million neurons die. This is the most important "time is brain" concept in understanding acute stroke and its treatment. There are numerous causes of stroke, such as prolonged hypertension, arteriosclerosis, and emboli that have formed in the heart as a result of atrial fibrillation or rheumatic heart disease. In younger patients, the possible list of causes may be broadened to include clotting disorders, cervical arterial dissection, and various forms of vasculitis. In the event of a possible stroke presentation, a precise history and physical must be performed alongside emergent neurological imaging before administering any form of treatment. With early, focused treatment based on the stroke etiology, rehabilitation programs, and long-term lifestyle changes, one can maximize his/her chances for a meaningful recovery.

ETIOLOGY

There is a multitude of etiologies that can lead to a stroke. Some of the most common risk factors include hypertension, diabetes mellitus, hypercholesterolemia, physical inactivity, obesity, genetics, and smoking. Cerebral emboli commonly originate from the heart, especially in patients with preexisting heart arrhythmias (atrial fibrillation), valvular disease, structural defects (atrial and ventricular septal defects), and chronic rheumatic heart disease.

Emboli may lodge in areas of preexisting stenosis.[3] Alcohol intake has a J-shaped relationship with ischemic stroke. Mild to moderate drinking carries a slightly lower risk of ischemic stroke yet heavier drinking increases the risk drastically. Alcohol intake increases the risk of hemorrhagic stroke in a near linear relationship. Strokes that occur in small vessels(lacunar infarcts) are most commonly caused by chronic, uncontrolled hypertension resulting in the pathological entity of lipohyalinosis andarteriolosclerosis. These strokes occur in the basal ganglia, internal capsule, thalamus, and pons. Uncontrolled hypertension in these areas can also lead to hypertensive intracerebral hemorrhages (ICH).[4]About 15% of all strokes are classified as hemorrhagic, with the etiology being the most commonly uncontrolled hypertension. Other causes of hemorrhagic strokes include cerebral amyloid angiopathy, a disease in which amyloid plaques deposit in small and medium vessels, which causes vessels to become rigid and more vulnerable to tears. Deposition can occur anywhere, but they occur most commonly on the surfaces of the frontal and parietal lobes. The structural integrity of vessels is another important consideration in hemorrhagic stroke etiology, with aneurysms, arteriovenous malformations,

cavernous mal formations, capillary telangiectasias, venous angiomas, and vasculitis being more common reasons for stroke.

Risk factors

- Age (more common in elderly)
- Male gender
- Hypertension
- Smoking(more pack years=more severity)
- Hyperlipidemia
- Diabetes mellitus
- Increasing plasma fibrinogen
- High factor VII coagulant activity
- High tissue plasminogen activator antigen
- Low blood fibrinolytic activity
- Raised vonWillebrand factor
- Atria fibrillation
- Alcohol dependence
- Obesity and diet
- Physical Inactivity
- Raised white blood cell count
- Recent Infection
- Hyperhomocysteinaemia
- Snoring

- Arcus senilis
- Psychological factors
- Vasectomy
- Low serum albumin
- Family history of stroke
- Social deprivation
- Evidence of pre-existing vascular disease
- Myocardial infarction

NON MODIFIABLE RISK FACTORS:

AGE:**-** Age is the most important determining risk factor for stroke .The rate of stroke doubles in men and women , for every successive 10 years after the age of 55years.

SEX: The incidence of stroke is 1.25 times more in men when compared to women. However because women live longer than men, more women die of stroke than men.

RACE:- The mortality rate of stroke is higher in blacks20 than whites. Mortality rates are 4 to 5 times higher for African – Americans when compared with whites, between the age group of 45 and 55 years. This difference decreases as the age advances. Asians especially Japanese and Chinese have very high incidence rates of stroke, also the intracranial atherosclerosis is more common in Chinese.

HEREDITY:- There is a increased tendency of stroke to run in families because of genetic tendency of stroke, genetic determination of risk factors for stroke, common familial exposure to lifestyle and environmental risks

MODIFIABLE RISK FACTORS:

HYPERTENSION: The relative risk of stroke is 4 when an individual is said to have a hypertension. The hypertension is strong risk factor for stroke14-16.The odds ratio for the age of 50 is 4 whereas for the age of 90 is 1.In a study of 50000 patients around the world with 17 treatment trials of hypertension, there is 40 % reduction of fatal stroke and 38% reduction in all stroke, favoring treatment of hypertension. Treatment of systolic hypertension with antihypertensives in elderly persons is very effective in preventing stroke CARDIAC DISEASE**:** Atrial fibrillation is one of the powerful risk factor of stroke. With increase in age the incidence and prevalence of atrial fibrillation increases. It was proved in Framingham study that the attributable risk of AF for

stroke increased from 1.5% in individuals who are aged 50 to 59 years to 23.5% in subjects of age 80 to 89 years. It is proved that nearly half of the cardio embolic strokes occur due to atrial fibrillation. In a pooled analysis of AF trials warfarin anticoagulation reduces the stroke risk by 68%. Cardiac valve abnormalities like mitral valve prolapse and mitral stenosis increases the risk of incidence of stroke. Another risk factor for stroke is mitral annular calcification. The risk of stroke increases fivefold with both AF and mitral annular calcification. For every 10 mm rise in left atrial size the age adjusted risk of stroke double in men and women , was shown in Framingham study. Another important finding related with stroke is valvular strands. These are filamentous process attached to mitral and aortic valves . Two preliminary studies showed that these valvular strands predisposes to stroke, but more prospective studies are needed.Patent foramen ovale and myocardial disease are also a risk factor for stroke. The risk ofstroke is 0.2% to 0.3% after cardiac catheterization and angioplasty. Radio frequency ablation,pacing, electrophysiological procedures and cardioversion , all can lead to embolic complications.

DIABETES MELLITUS: Because of increased preponderance for atherosclerosis andatherogenic risk factors like obesity , hyperlipidemia, hypertension, prospective epidemiological studies showed that the relative risk of stroke in diabetic individuals ranges from 1.8 to 3.0.In Framingham study, individuals with glucose intolerance , there is double the risk of stroke in diabetic patients when compared to non-diabetics.Hyperinsulinemia and increased insulin resistance causes diabetes to play a major role as risk factor for stroke. LIPIDS**:** There is a positive correlation between LDL and total cholesterol and incidence of stroke19, and protective role of HDL

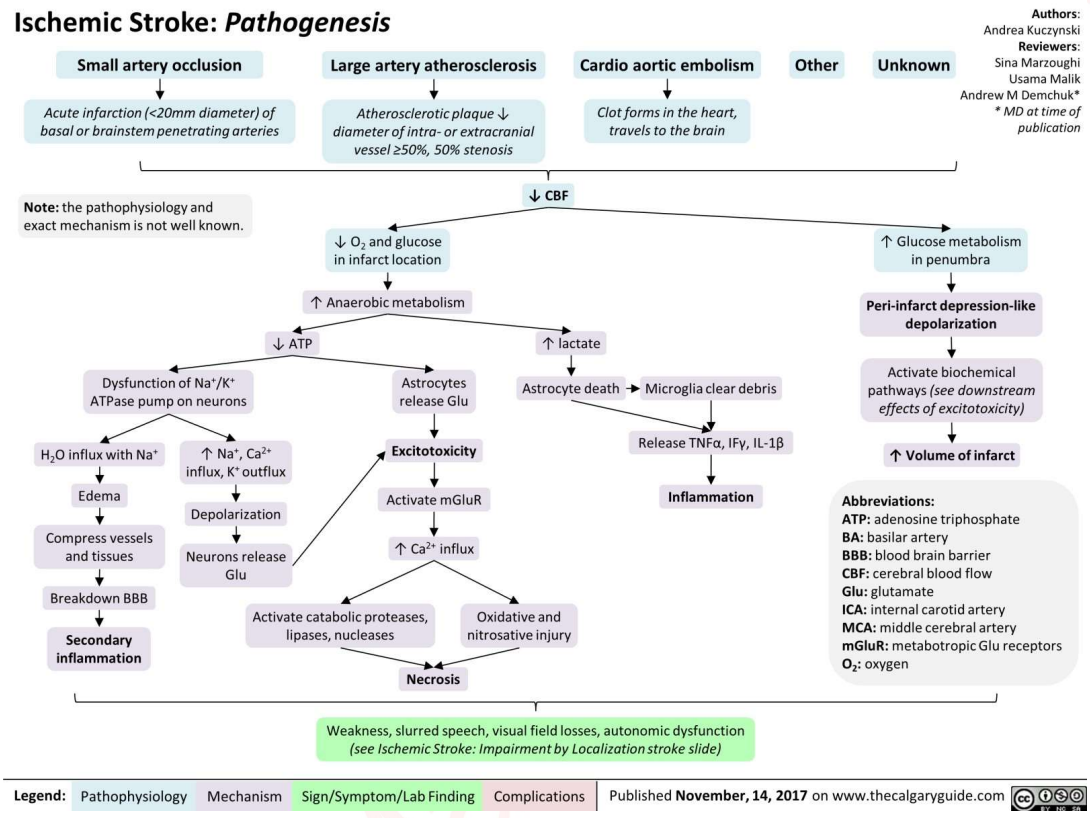
cholesterol in extracranial atherosclerosis.Asymptomatic carotid artery plaque study showed fewer strokes in lovastatin versus placebo group. SMOKING: There is clear dose response relation between smoking and stroke. The relative risk (RR) of smoking in causing stroke is2.In Framingham study there is a prompt reduction in stroke risk after cessation of smoking.

ALCOHOL: A J – shaped association curve was established in a overview analysis of stroke studies, for the relation of moderate consumption of alcohol and ischemic stroke. There is increased risk for brain hemorrhage with increasing alcohol consumption. DRUG ABUSE: The drugs that are linked to stroke are amphetamines, heroin, LSD and marijuana. ORAL CONTRACEPTIVES**:** There is a high risk for stroke with oral contraceptives containing estrogen content > 50 micrograms. However low dose estrogens disclosed no increased risk of stroke.

HOMOCYSTEINE**:** There is a strong relation of homocysteine levels to stroke shown recently in British Regional Heart Study, among middle aged men. There is a high level of biological plausibility that high levels of homocysteine are both prothrombotic and atherogenic21.Vitamin B3,B6, B12, Folic acid though reduces the homocysteine levels , there is less evidences to prove that this intervention will reduce the incidence of stroke. SEDENTERY LIFE STYLE**:** There are evidences to support the fact that moderate physical activity reduces the incidence of stroke. It exerts a protective effect against atherosclerotic disease by reducing weight, blood pressure23 , pulse rate, lowering LDL, raising HDL,increasing insulin sensitivity and decreasing platelet aggregability Obesity is associated with high levels of glucose, blood pressure and atherogenic lipids in serum which are serious risk factors to stroke ,.incidence. In men aged 35-64 years and women aged 65 – 94 years , obesity which is defined as Metropolitan Life chart relative weight more than 39% above average is a significant contributor to incidence of stroke, shown in Framingham study. Food habits like increased consumption of fish, milk, green tea are protective against stroke. Diets which are rich in fats and cholesterol are deleterious. MIGRAINE**:** There is a good association between stroke andmigraine23. The presence of migraine increased the stroke incidence from10 in 1 lakh woman-years to 19 in 1 lakh woman-years. However the magnitude of the risk of stroke associated with migraine is small. ASYMPTOMATIC CAROTID STENOSIS**:** On routine screening, presence of carotid bruit indicates the presence of stenosis of carotid artery. The rate of stroke is 1% to 2%annualy in persons who are diagnosed with cervical bruit which is asymptomatic. With progressing and more severe bruit , the risk of stroke also

increases. Risk factors increase the probability of stroke independently, however they also can interact with each other to increase the risk of stroke.

Pathophysiology



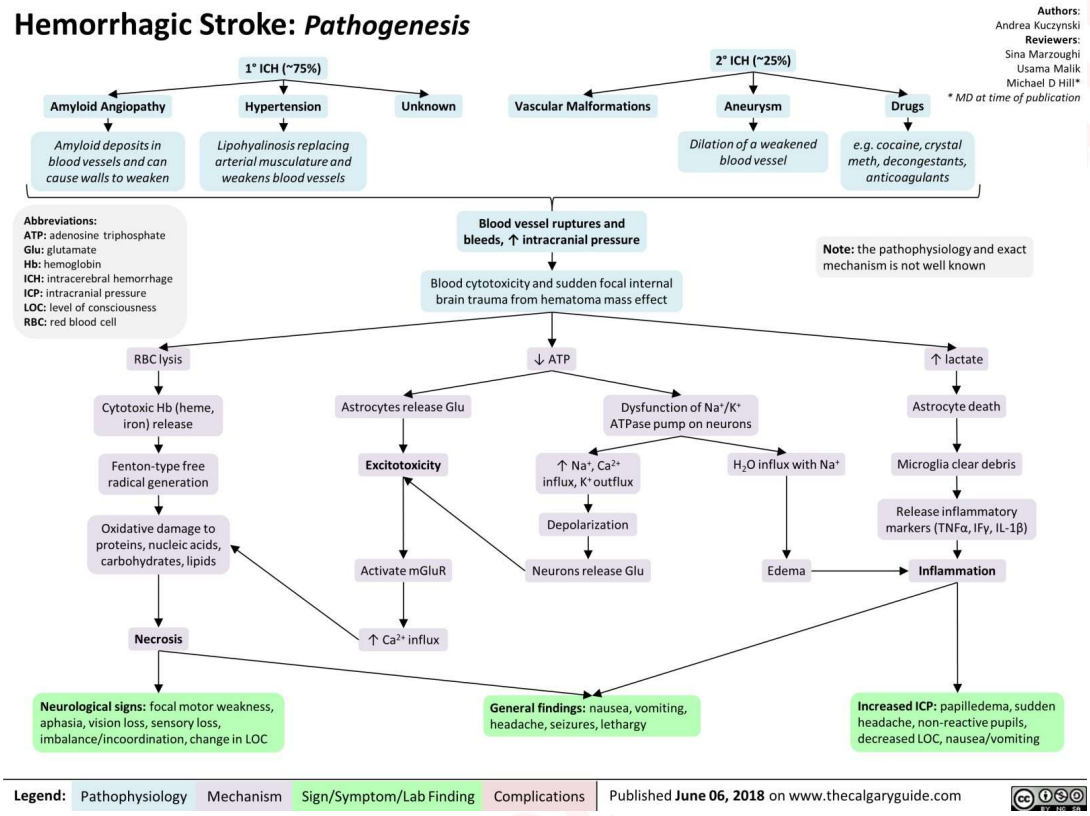
Atherosclerosis is the most common and important underlying pathology which leads to the formation of an atherothrombotic plaque secondary to low-density lipoprotein cholesterol (LDL) build up in the arteries supplying the brain. These plaques may block or decrease the diameter of the neck or intracranial arteries resulting in distal ischemia of the brain. More commonly they may also rupture. Plaque rupture leads to exposure of the underlying cholesterol crystals which attract platelets and fibrin. Release of fibrin-platelet rich emboli causes strokes in the distal arterial territories via an artery-to-artery embolic mechanism.

The nature of the cardiac source of emboli depends on the underlying cardiac problem. In atrial fibrillation, clots tend to be formed in the left atrium. These are red blood cell rich clots. There may be tumor emboli in left atrial myxoma and bacterial clumps from vegetations when emboli arise during infective endocarditis. When an arterial blockage occurs, the immediately adjacent neurons lose their supply of oxygen and nutrients. The inability to go through aerobic metabolism and produce ATP causes the Na+/K+ ATPase pumps to fail, leading to an accumulation of Na+ inside the cells and K+ outside the cells.

The Na+ ion accumulation leads to cell depolarization and subsequent glutamate release. Glutamate opens NMDA and AMPA receptors and allows for calcium ions to flow into the cells. A continuous flow of calcium leads to continuous neuronal firing and eventual cell death via excitotoxicity. In the first 12 hours, there are no significant macroscopic changes. There is cytotoxic edema related to energy production failure with neuronal cellular swelling. This early infarction state can be visualized by diffusion-weighted MRI which shows restricted diffusion as a result of neuronal cellular swelling. Six to twelve hours after the stroke, vasogenic edema develops.

This phase may be best visualized with FLAIR sequence MRI. Both cytotoxic and vasogenic edema causes swelling of the infarcted area and an increase in intracranial pressure. These are followed by the invasion of phagocytic cells which try to clear away the dead cells. Extensive phagocytosis causes softening and liquefaction of the affected brain tissues, with peak liquefaction occurring 6 months post-stroke. Several months after a stroke, astrocytes form a dense network of glial

fibers mixed with capillaries and connective tissue.



Hemorrhagic strokes lead to a similar type of cellular dysfunction and concerted events of repair with the addition of blood extravasation and resorption.

ISCHEMIC STROKE:

Ischemic stroke is caused by three major mechanisms

1. Thrombosis

2. Embolism

3. Global ischemia

However not all ischemic stroke fall into these categories

THROMBOSIS:

The most important pathological feature of vascular obstruction is atherosclerosis. Atherosclerotic plaque can undergo pathological changes like

a) Ulcerations,

b) Thrombosis,

c) Calcification and

d) Intra plaque hemorrhage

The structure, consistency and composition of the plaque decides the susceptibility of the plaque to ulcerate, disrupt and fracture. This causes disruption of endothelium activating many vasoactive enzymes. Then follows the platelets adherence and aggregation forming platelets and fibrin. Within 1 hour the leukocytes initiates the inflammatory process. Apart from atherosclerosis other conditions that causes thrombotic occlusion are, Hypercoagulable state, Fibromuscular dysplasia, Arteritis and Dissection of vessel wall 46 Lacunar infarcts36,37 ,occur as a result of deep penetrating artery occlusion .

As a result of long standing hypertension and diabetes mellitus the small arteriole becomes tortuous and subintimal dissections and microaneurysms develops. This makes the arteriole susceptible to occlusion from micro thrombi. The underlying pathological mechanisms is ‗lipohyalinosis due to fibrin deposition'.

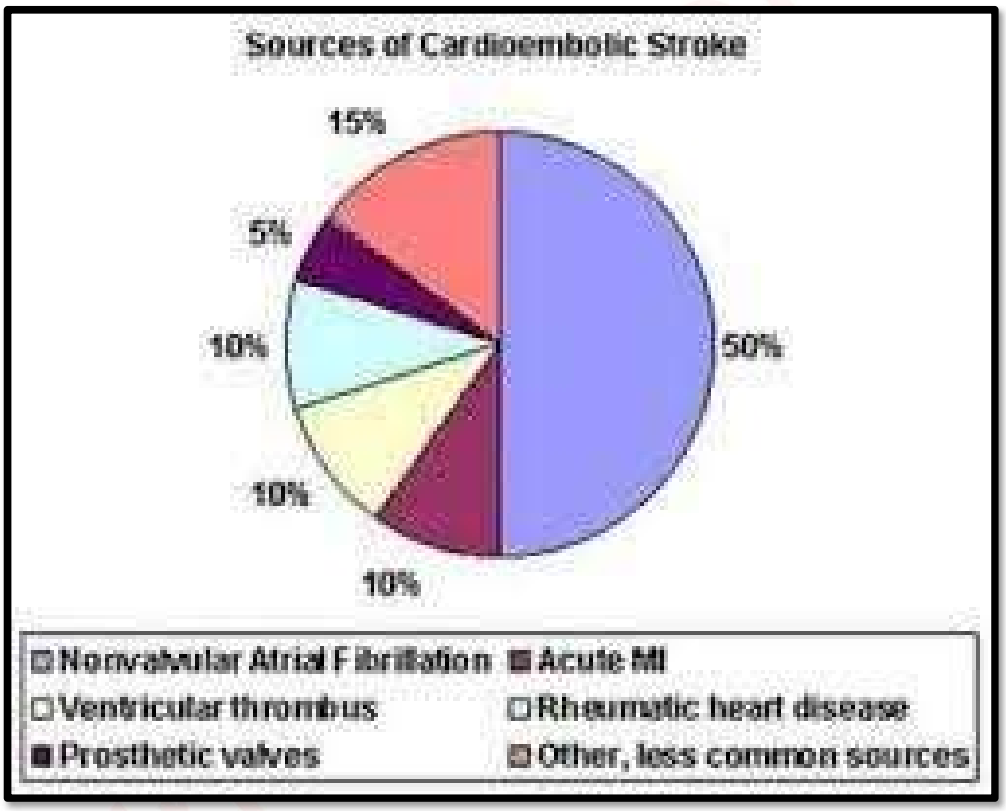
EMBOLISM:

Embolic stroke occurs as a result of embolisation from a variety of sources of an artery of central circulation. Materials that can embolize are atheromatous plaque pieces, fibrin, clot air, fat, tumor or metastases,foreign bodies, bacterial clumps. The most frequent targets are the superficial branches of superior cerebellar and cerebral arteries. As nearly 80 % of the blood carried by the large neck arteries flow in the middle cerebral artery, most of the emboli lodge in the distribution of middle cerebral artery.

CARDIO EMBOLIC STROKE:

20% of all ischemic stroke is due to cardio embolism. The thrombotic material attached to the atria, left ventricle or the valves detach and embolize into the circulation. The thrombi may only lyse or fragment so quickly to produce a TIA.If the occlusion lasts longer it 47 produces stroke. Embolic stroke is of sudden onset with maximum neurological deficit at the time of presentation. With reperfusion petechial hemorrhage tend to occur at the site of ischemic territory. However it is of no neurological significance and it must be distinguished from hemorrhage into the ischemic area, which can produce mass effect and cause decline in the neurological function. The order of involvement of vessels due to embolism from the heart are, Middle cerebral artery, posterior cerebral artery or its branches, and infrequently

anterior cerebral artery. The most important causes of cadioembolism are non rheumatic atrial fibrillation, myocardial infarction, rheumatic heart disease and ischemic cardiomyopathy. Paradoxical embolisation occurs when a venous thrombi migrate via patent foramen ovale or ASD into the arterial circulation. Even fat, air, amniotic fluid, bacterial endocarditis an be responsible for paradoxical embolization other than venous clot.



ARTERY TO ARTERY EMBOLIC STROKE:

A thrombus can form over an atherosclerotic plaque which can embolise into intra cranial artery ,causing artery to artery embolic stroke. Most common source of artery to artery embolic stroke is the atherosclerosis of carotid bifurcation. The dominant mechanism of brain ischemia is artery to artery embolism rather than local thrombosis unlike in myocardial vessels.Other causes of artery to artery embolic

stroke are intracranial atherosclerosis and dissection of internal carotid or vertebral arteries or even the vessels beyond the circle of willis. The outcome of the embolic stroke depends on the ability of the -embolus to initiate vasospasm by acting as vascular irritant. It tends to occur more commonly in young patients because of the more pliable and less atherosclerotic vessels. When a bleeding develops in the necrotic cerebral tissue it is called as hemorrhagic transformation of an ischemic infarct.When a embolus is lysed spontaneously and restoration of blood flow occurs causing reperfusion, hemorrhagic transformation ensues. In the presence of persistent arterial occlusion, reperfusion can occur from collateral circulation from leptomeningeal vessels. The major factors associated with the hemorrhagic infarcts are the

1. Size of the infarct
2. Collateral circulation
3. Use of anticoagulants
4. Interventional therapy with thrombolytic agents

GLOBAL – ISCHEMIC OR HYPOTENSIVE STROKE:

Hypotensive stroke occurs due to profoundly reduced systemic blood pressure due to any cause.The viable neurons are

1. Pyramidal cell layer of the hippocampus,
2. Purkinje cell layer of the cerebellar cortex and
3. Cerebral gray matter

It is the more abundant glutamate in these neurons which makes them more vulnerable to global ischemia. The greatest damage also occurs to the ―water shed areas‖ or the ―boundary zone‖ formed by the territories of the cerebellar and cerebral arteries. The most commonly affected area is the parieto-temporo-occipital triangle ,which is formed at the junction of anterior,posterior and middle cerebral arteries. Water shed infarction of this area causes a clinical syndrome which consists of sensory loss and paralysis of arm but speech and face are 50% spared. Nearly 10 % of all the ischemic strokes are water shed infarcts and 40% of the watershed infarct occurs due to carotid occlusion or stenosis. Causes of dissection of the extra- and Intracranial arteries

Traumatic Penetrating injury Non-penetrating Injury

Spontaneous Fibromuscular dysplasia Cystic medial necrosis Marfan's syndrome Ehlers-Danlos syndrome Pseudo xanthoma elasticum Inflammatory arterial disease Infective arterial disease(e.g. syphilis) Spontaneous intracranial haemorrhage Spontaneous intracranial haemorrhage occurs within the brain (primary intracerebral haemorrhage), into the subarachnoid space (subarachnoid haemorrhage),sometimes into the ventricles (intraventricularhaemorrhage) ,and rarely into the subdural space(subdural haemorrhage).

The exact site of origin may not Necessarily be immediately obvious because, for example, a saccular aneurysm can rupture into the brain as well as into the subarachnoid space or disruption of a small perforating artery. Causes of spontaneous Intracranial haemorrhage. Hypertension Aneurysms Saccular Atheromatous Mycotic Myxomatous Dissecting Cerebral amyloid angiopathy

Intracranial vascular malformations Arteriovenous Venous Cavernous Telangiectasis Haemostatic failure Paraproteinaemias Disseminated intravascular coagulation Renal failure Liver failure Snakebite Inflammatory vascular disease Haemorrhagic transformation of cerebral infarction Intracranial venous thrombosis Sickle-cell disease/trait

Moyamoya syndrome Carotid endarterectomy Posterior fossa and other intracranial surgery post-traumatic Alcoholic Wernicke's encephalopathy Vascular tumours Melanoma Choriocarcinoma Malignant astrocytoma Oligodendroglioma Medullobiastoma Haemangioblastoma Choroidplexus papilloma Endometrial carcinoma Bronchogenic carcinoma Infections Herpes simplex Leptospirosis Anthrax Chronic meningitis

Primary Intracerebral haemorrhage Primary intracerebral haemorrhage is more common than subarachnoid haemorrhage, the incidence increases with age. It is most commonly due to intracranial small vessel disease associated with hypertension, cerebral amyloid angiopathy, and intracranial vascular malformations, but there is usually a combination of different factors operating in any one individual, e.g. hypertension and cerebral amyloid angiopathy, therapeutic thrombolysis and vascular malformation,etc.[43]Less common causes include saccular aneurysms; haemostatic defects, particularly induced by anticoagulation[44], therapeutic thrombolysis, perhaps with cerebral amyloid angiopathy, and possibly antiplatelet drugs;cerebral vasculitis and drug abuse.

Spontaneous subarachnoid haemorrhage The incidence of spontaneous subarachnoid haemorrhage increases with age and is about 5/100 000 population/annum, being somewhat more frequent in women than men. A ruptured saccular aneurysm is by far the most common cause[45].Some SAHs are due to bleeding from an intracranial vascular malformation, a few are due to rarities, and depending on the intensity of investigation in about 15 per cent no cause can be identified in life [46].Primary intraventricular haemorrhage is very unusual, except in premature babies. In adults, a cause is not always found. Some may be due to avascular malformation in the ventricular wall[47].

The clinical features are so similar to SAH that it can only be differentiated on CT or at postmortem.Subdural haemorrhage is more often traumatic,or due to ventricular decompression for hydrocephalus, than spontaneous rupture of a vascular malformation in the dura or of a very peripheral aneurysm, haemostatic defect (particularly therapeutic anticoagulation),or a peripheral cerebral tumour can be responsible. It is also a very rare complication of lumbar puncture. Transient ischaemic attacks About 15 percent of first stroke patients had earlier TIAs.The incidence of TIAs presenting to medical attention (about 0.5 per 1000 population per annum) must be an underestimate of the real situation[18,48].

By definition, the symptoms lasting less than 24 hours,but few patients have residual neurological signs of no functional significance, e.g. reflex asymmetry.About 25percent have focal hypodensity on CT, relevant to the symptoms in about half and therefore perhaps srepresenting recent infarction[49].An even higher proportion has focal lesions on MRI[50]. However, the diagnosis depends

not on either neurological signs or imaging but essentially on the nature and duration of the symptoms in the right 'vascular' milieu (elderly, vascular risk factors,absentpulses,andbruits,etc.).Fortunately,in general,there is less inter observer disagreement about symptoms, which are remembered, than signs which are likely to attenuate and disappear[51].T

he main use of brain imaging is to rule out the very occasional structural lesion causing 'transient focal neurological attacks'. Causes of transient focal neurological attacks Focal cerebral ischaemia Migraine Partial epileptic seizures Structural intracranial lesions Tumour subdural haematoma AV malformations Giant aneurysm Multiple sclerosis Labyrinthine disorders Peripheral nerve root lesion Metabolic Hypoglycemia Hyperglycemia Hypocalcaemia Hyponatremia Psychological Diagnosis It is important to rule out other causes, such as metabolic or drug-induced etiologies, which can present with symptoms similar to that of TIA. The following tests are considered on an emergency basis:

A finger stick blood glucose for hypoglycemia Complete blood count Serum electrolyte levels Coagulation studies 12-lead electrocardiogram (ECG) with rhythm strip The following tests typically are helpful and often can be performed on an urgent basis: Erythrocyte sedimentation rate Cardiac enzymes Lipid profile Additional laboratory tests, ordered as needed and on the basis of the history, include the following: Screening for hypercoagulable states (particularly in younger patients with no known vascular risk factors) [1] Syphilis serology Antiphospholipid antibodies Toxicology screens Hemoglobin electrophoresis Serum protein electrophoresis Cerebrospinal fluid examination Imaging of the brain should be

performed within 24 hours of symptom onset, as follows [1, 4] : Magnetic resonance imaging (MRI) with diffusion-weighted imaging (preferred) Noncontrast computed tomography (CT; ordered if MRI is not available) The cerebral vasculature should be imaged urgently, preferably at the same time as the brain. Vascular imaging for TIA includes the following: Carotid Doppler ultrasonography of the neck CT angiography (CTA) Magnetic resonance angiography (MRA)

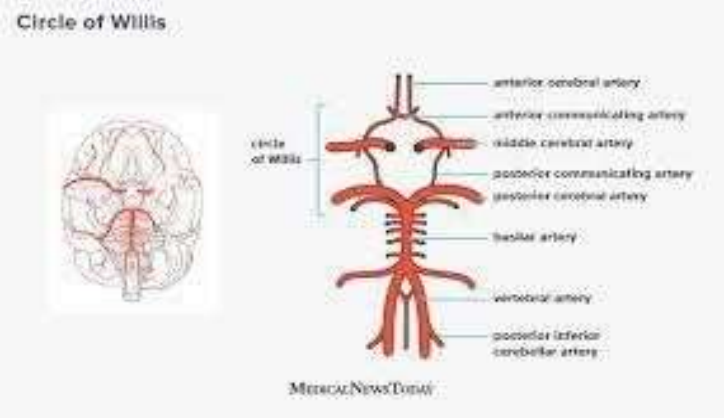
CLINICAL FEATURES.

Features of middle cerebral artery stroke: Contralateral hemiparesis and hypesthesia Gaze preference towards side of the lesion Ipsilateral hemianopsia Receptive or expressive aphasia (if the dominant hemisphere is affected) Agnosia Inattention, neglect

Features of anterior cerebral artery stroke: Speech is preserved but there is disinhibition Mental status is altered Judgment is impaired Contralateral cortical sensory deficits Contralateral weakness greater in legs than arms Urinary incontinence Gait apraxia

Posterior cerebral artery stroke: Cortical blindness Contraletarl homonynous heminopsia Altered mental status Visual agnosia Memory impairment

Vertebral/basilar artery stroke: Nystagmus Vertigo Diplopia and visual field deficits Dysarthria Dysphagia Syncope Facial hyperesthesia Ataxia



Total anterior circulation syndrome A large haematomainone cerebral hemisphere, or an infarct large enough to affect the cortex, basal ganglia, and internal capsule, causes a characteristic clinical syndrome of contralateral hemiparesis, with or without a sensory deficit, involving the whole of atleast two of the three body areas (face, upper limb, lower limb), a homonymous visual field defect, and new higher cerebralor 'cortical' dysfunction (dysphasia, neglect, visuospatial problems, etc., depending on cerebral dominance). Total anterior circulation infarcts. (TACIs) are usually due to acute occlusion of the internal carotidartery or embolicocclusion of the proximal middle cerebralartery from acardia corproximalarterialsource. **Partial anterior circulation syndrome** A lobar haemorrhage, or a cortical infarct, causes a more restricted clinical syndrome consisting of only two of the three components of the total anterior circulationsyndrome;orjustisolatedhighercorticaldysfunctionsuchasdysphasia;orapre-dominantly proprioceptive deficit in one limb; or a motor/ sensory deficit restricted to one body area or part of one body area[59]. If the 'cortical' signs are rather subtle (dressing apraxia, neglect, dysphasia mistaken for dysarthria, etc.). Partial anterior circulation o r cortical infarcts (PACIs) are caused by occlusion of a branch of the middle cerebralartery, orrarely the trunk of the anterior cerebralartery,_ usually as a consequence of embolism from the heart or proximal atherothrombosis, in the same ways as TACIs. Anterior cerebral artery infarcts cause contralateral weakness, predominantly of the lower limb, perhaps with some cortical sensory loss, and aphasia if in the dominant hemisphere. **Lacuna syndrome** Lacunar syndromes are defined clinically and are highly predictive of small, deep lesions affecting the motor

and/or sensory pathways, i.e. in the corona radiata, internalcapsule, thalamus, cerebralpeduncle ,andpons[59,60]. The four main lacunar syndromes are most reliably defined if there has been no previous stroke and if the patients are examined at the time of the irmaximaldeficit 1.puremotorstroke 2. pure sensory stroke 3.sensorimotarstroke4.ataxichemiparesis

Posterior circulation syndrome Brainstem, cerebellar, thalamic, oroccipital lobe signs normally indicate infarction in the distribution of the vertebrobaslar (i.e.posterior)circulation[61],or a localized haemorrhage A combination of brainstem and occipital lobe signs is highly suggestive of infarction due to thromboembolism within the basilar and posterior cerebral artery(PCA)territories. Occasionally, proximal PCA occlusion causes enough temporal, thalamic and perhaps midbrain infarction to cause some contralateral hemiparesis and sensory loss. A marked cognitive deficit such as aphasia, as well as the expected homonymous hemianopia, and so be confused with occlusion of the middle cerebral artery or one of its branches[62]; this is the so-called 'walking total anterior circulation syndrome (TACS)' because although it fulfils the definition of a TACS, the motor loss is mild. The causes of infarction in the vertebrobasilar territory are heterogeneous.[52].

If there is doubt about the speed of onset of a focal deficit, then the diagnosis is rather more likely to be an intracranial mass lesion, such as a tumour or chronic subdural haematoma. If the onset was clearly sudden, but there was no obvious focal deficit, then brain imaging may show a thalamic or cerebellar infarct or haemorrhage. Clinical clues to an intracranial tumour are recent headaches, seizures, papilledema, a worsening deficit over days or weeks, and any suggestion of a primary tumour out

with the brain. Clues to a chronic subdural haematoma are head injury in the previous few weeks; more drowsiness, confusion and headache than anticipated from the severity of the neurological deficit; a fluctuating course; and a patient on anticoagulants. Other diagnoses are usually but not necessarily obvious: multiple sclerosis (young age); peripheral nerve or root lesion (clinical signs); post-seizure hemiparesis (history);metabolic encephalopathy (global rather than focal neurological features); somatization and hysteria (young age,signs);encephalitis(fever, clinical symptoms and signs, diffusely abnormal EEG); and intracranial abscess (fever and predisposing cause such as sinusitis, congenital heart lesion, etc.)[53].

Haemorrhagic strokes causing a fall and so head injury can be equally confusing if the CT scan shows ‘primary intracerebral haemorrhage' or 'subarachnoid haemorrhage' and the circumstances at the onset are unclear[54]. If there are persisting signs from a previous stroke, and the patient then falls ill for some other reason such as an infection, or has an epileptic seizure, the old signs may appear to worsen and so mimic stroke recurrence. Determining the site of the lesion depends on classical clinic anatomical correlation[55].A Simple system, which does not require great neurological skill, divides stroke patients first into four main clinical syndromes: total anterior circulation syndrome (TACS), partial anterior circulation syndrome (PACS),lacunar syndrome(LACS),and posterior circulation syndrome(POCS). Occasionally one has to put the patient in an uncertain category.This division depends entirely and Only on symptoms and signs,which are accessible to everyone, irrespective of the availability or Standard of any technology.

Next, based on brain CT or perhaps MRI, patients with primary intracerebral haemorrhage are separated off. The rest, where the scan is either normal or shows infarction in a relevant area, can then be divided into: total anterior circulation infarct,about 15 percent of the total in community-based studies(TACI);partial anterior circulation infarct, 35 per cent (PACI); lacunar infarct, 25 per cent (LACI); and posterior circulation infarct,25percent(POCI)[56].These categories provide some prognostic information for survival, residual disability, and recurrence, and an indication of the cause of the stroke. Symptoms alone are not specific enough to distinguish ischemic from hemorrhagic stroke. However, generalized symptoms, including nausea, vomiting, and headache, as well as an altered level of consciousness, may indicate increased intracranial pressure and are more common with hemorrhagic strokes and large ischemic strokes. Seizures are more common in hemorrhagic stroke than in the ischemic kind. Seizures occur in up to 28% of hemorrhagic strokes, generally at the onset of the intracerebral hemorrhage or within the first 24 hours.

Focal neurologic deficits The neurologic deficits reflect the area of the brain typically involved, and stroke syndromes for specific vascular lesions have been described. Focal symptoms of stroke include the following: Weakness or paresis that may affect a single extremity, one half of the body, or all 4 extremities Facial droop Monocular or binocular blindness Blurred vision or visual field deficits Dysarthria and trouble understanding speech Vertigo or ataxia Aphasia Symptoms of subarachnoid hemorrhage may include the following: Sudden onset of severe headache Signs of meningismus with nuchal rigidity Photophobia and pain with eye

movements Nausea and vomiting Syncope - Prolonged or atypical Imaging studies Emergent brain imaging is essential for excluding mimics (SAH, ICH, masses) and potentially confirming the diagnosis of ischemic stroke. Noncontrast CT scanning is the most commonly used form of neuroimaging in the acute evaluation of patients with apparent acute stroke. A lumbar puncture is required to rule out meningitis or subarachnoid hemorrhage when the CT scan is negative but the clinical suspicion remains high. Multimodal CT imaging with the addition of CT angiography and CT perfusion to NCCT has the potential to identify large vessel occlusions and areas of salvagable tissue.

MRI with magnetic resonance angiography (MRA) has been a major advance in the neuroimaging of stroke. MRI not only provides great structural detail but also can demonstrate early cerebral edema. In addition, MRI has proved to be sensitive for detection of acute intracranial hemorrhage. However, MRI is not as available as CT scanning is in emergencies, many patients have contraindications to MRI imaging (eg, pacemakers, implants), and interpretation of MRI scans may be more difficult. Carotid duplex scanning is one of the most useful tests in evaluating patients with stroke.

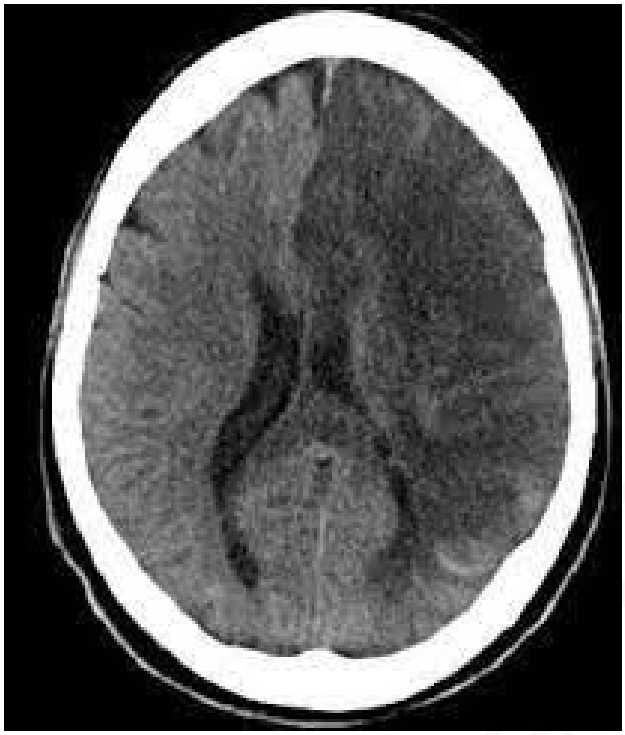
Increasingly, it is being performed earlier in the evaluation, not only to define the cause of the stroke but also to stratify patients for either medical management or carotid intervention if they have carotid stenoses.Digital subtraction angiography is considered the definitive method for demonstrating vascular lesions, including occlusions, stenoses, dissections, and aneurysms. ISCHEMIC STROKE-WORKUP Laboratory studies Extensive laboratory testing is not routinely required before

decisions are made regarding fibrinolysis. Testing can often be limited to blood glucose, plus coagulation studies if the patient ison warfarin, heparin, or one of the newer antithrombotic agents (eg, dabigatran, rivaroxaban). A complete blood count (CBC) and basic chemistry panel can be useful baseline studies.

Additional laboratory tests are tailored to the individual patient and may include the following: Cardiac biomarkers Toxicology screen Fasting lipid profile Erythrocyte sedimentation rate Pregnancy test Antinuclear antibody (ANA) Rheumatoid factor Homocysteine level Rapid plasma reagent (RPR) A urine pregnancy test should be obtained for all women of childbearing age with stroke symptoms.

The safety of the fibrinolytic agent recombinant tissue-type plasminogen activator (rt-PA) in pregnancy has not been studied in humans. Laboratory Studies Laboratory tests should include a complete blood count, a metabolic panel, and—particularly in patients taking anticoagulants—coagulation studies (ie, prothrombin time or international normalized ratio [INR] and an activated partial thromboplastin time). [1]

Imaging Studies



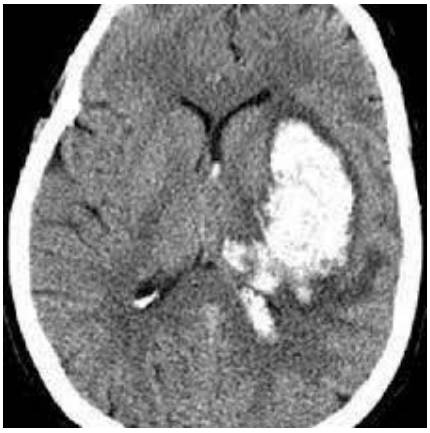
Brain imaging is a crucial step in the evaluation of suspected hemorrhagic stroke and must be obtained on an emergent basis. Brain imaging aids diagnosing hemorrhage, and it may identify complications such as intraventricular hemorrhage, brain edema, or hydrocephalus. Either non contrast computed tomography (NCCT) scanning or magnetic resonance imaging (MRI) is the modality of choice. Computed tomography (CT)-scan studies can also be performed in patients who are unable to tolerate a magnetic resonance examination or who have contraindications to MRI, including pacemakers, aneurysm clips, or other ferromagnetic materials in their bodies.

HEMORRHAGIC STROKE-WORKUP

Laboratory Studies

Laboratory tests should include a complete blood count, a metabolic panel, and—particularly in patients taking anticoagulants—coagulation studies (ie, prothrombin time or international normalized ratio [INR] and an activated partial thromboplastin time).

Imaging Studies



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MRI, magnetic resonance angiography (MRA), or magnetic resonance venography. [1] Conventional angiography is the gold standard in evaluating for cerebrovascular disease and for providing less-invasive endovascular interventions. This modality can be performed to clarify equivocal findings or to confirm and treat disease seen on MRA, CTA, transcranial Doppler, or neck ultrasonograms. However, Zhu et al found that in patients with spontaneous intracranial hemorrhage, angiographic yield was significantly lower in patients older than 45 years and those who had preexisting hypertension. Although the traditional approach to excluding underlying vascular abnormalities in patients with spontaneous intracerebral hemorrhage is to use digital subtraction angiography (DSA) in the acute and subacute phases, Wong et al found that MRA was able to detect most structural vascular abnormalities in the subacute phase in most patients. Consequently, they recommend MRA as the screening test.

MANAGEMENT

Initial Treatment

The goal for the acute management of patients with stroke is to stabilize the patient and to complete initial evaluation and assessment, including imaging and laboratory studies, within 60 minutes of patient arrival. [1] Critical decisions focus on the need for intubation, blood pressure control, and determination of risk/benefit for thrombolytic intervention. Thrombolytic Therapy Current treatments for acute ischemic stroke include IV thrombolytic therapy with tissue-type plasminogen activator and endovascular therapies using stent retriever devices. [5] .

A 2015 update of the American Heart Association/American Stroke Association guidelines for the early management of patients with acute ischemic stroke recommends that patients eligible for intravenous t-PA should receive intravenous t-PA even if endovascular treatments are being considered and that The Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE)trial suggested that there might be benefit of administering IV t-PA within 3-6 hours of stroke onset in patients with small ischemic cores on diffusion-weighted magnetic resonance imaging (MRI) and larger perfusion abnormalities (large ischemic penumbras). [7]patients should receive endovascular therapy with a stent retriever if they meet criteria. [5Studies have demonstrated that blood pressure typically drops in the first 24 hours after acute stroke, whether or not antihypertensives are administered.

Furthermore, studies have revealed poorer outcomes in patients with lower blood pressures, with these outcomes correlating with the degree of pressure decline.

The consensus recommendation is to lower blood pressure only if systolic pressure is in excess of 220 mm Hg or if diastolic pressure is greater than 120 mm Hg. [19] However, a systolic blood pressure greater than 185 mm Hg or a diastolic pressure greater than 110 mm Hg is a contraindication to the use of thrombolytics. Therefore, the management of elevated blood pressure in acute ischemic stroke may vary, depending on whether the patient is a candidate for thrombolytic therapy.

Hypertension control in non–rt-PA candidates

For patients who are not candidates for thrombolysis with recombinant t-PA (rt-PA) and who have a systolic blood pressure of less than 220 mm Hg and a diastolic blood pressure of less than 120 mm Hg in the absence of evidence of end-organ involvement (ie, pulmonary edema, aortic dissection, hypertensive encephalopathy), blood pressure should be monitored (without acute intervention) and stroke symptoms and complications (eg, increased ICP, seizures) should be treated.For patients with a systolic blood pressure above 220 mm Hg or a diastolic blood pressure greater than 120 mm Hg, labetalol (10-20 mg IV for 1-2 min) should be the initial drug of choice, unless a contraindication to its use exists. Dosing may be repeated or doubled every 10 minutes to a maximum dose of 300 mg.

Alternatively, nicardipine may be used for blood pressure control. Nicardipine is given intravenously at an initial rate of 5 mg/h and titrated to effect by increasing the infusion rate 2.5 mg/h every 5 minutes, to a maximum of 15 mg/h. Lastly, nitroprusside at 0.5 mcg/kg/min IV infusion may be used in the setting of continuous blood pressure monitoring. The goal of intervention is a reduction in blood pressure of 10-15%.

Hypertension control in rt-PA candidates

For patients who will be receiving rt-PA, systolic blood pressure greater than 185 mm Hg and diastolic blood pressure greater than 110 mm Hg require intervention. Monitoring and control of blood pressure during and after thrombolytic administration are vital, because uncontrolled hypertension is associated with hemorrhagic complication. [28]

The initial drug of choice, labetalol (10-20 mg IV for 1-2 min), may be repeated (maximum dose 300 mg). One to 2 inches of transdermal nitropaste may also be used. As an alternative to these choices, nicardipine infusion at 5 mg/h, titrated up to a maximum dose of 15 mg/h, can be used. [19]

Monitoring of blood pressure is crucial; for the first 2 hours, blood pressure should be checked every 15 minutes, then every 30 minutes for 6 hours, and finally, every hour for 16 hours. The goal of therapy should be to reduce blood pressure by 15-25% in the first day, with continued blood pressure control during hospitalization.

For patients with systolic blood pressure of 185-230 mm Hg or diastolic blood pressure of 110-120 mm Hg, labetalol is given at a dose of 10-20 mg IV over 1-2 minutes; the dose may be repeated every 10-20 minutes, up to 300 mg total, or an infusion rate of up to 2-8 mg/min may be used. [1]

For systolic blood pressure of greater than 230 mm Hg or diastolic blood pressure of 121-140 mm Hg, labetalol at the above doses can be considered. However, nicardipine infusion administered at a rate of 5 mg/h, to a maximum of 15 mg/h, might be a better first choice. For difficult-to-control blood pressure, sodium nitroprusside can be considered. [1]

The use of sublingual nifedipine to lower blood pressure in the ED is discouraged, since extreme hypotension may result. Trials of nimodipine, initially thought to be beneficial given its vasodilatory effect as a calcium-channel blocker, have failed to demonstrate any beneficial outcome in comparison with placebo. [18]

Consensus agreement is that these blood pressure guidelines should be maintained in the face of other interventions to restore perfusion, such as intra-arterial thrombolysis. [1]

SERUM CORTISOL

Cortisol is the main adrenal glucocorticoid and plays a central role in glucose metabolism and in the body's response to stress. Adrenal cortisol production is regulated by adrenocorticotropic hormone (ACTH), which is synthesized by the pituitary gland in response to hypothalamic corticotropin-releasing hormone (CRH). Serum cortisol in turn inhibits the production of both CRH and ACTH (negative feed-back loop), and this system self-regulates to control the proper level of cortisol production. The coordinated stimulatory and inhibitory connections between CRH, ACTH, and cortisol are referred to as the hypothalamic-pituitary-adrenal (HPA) axis.Most cortisol circulates bound to cortisol-binding globulin (CBG-transcortin) and albumin. The most common cause of increased CBG is estrogen. Therefore, higher levels are found in women, pregnant women, and women undergoing estrogen therapy.

Normally, less than 5% of circulating cortisol is free (unbound). The "free" cortisol is the physiologically active form. Free cortisol is filterable by the renal glomerulus.

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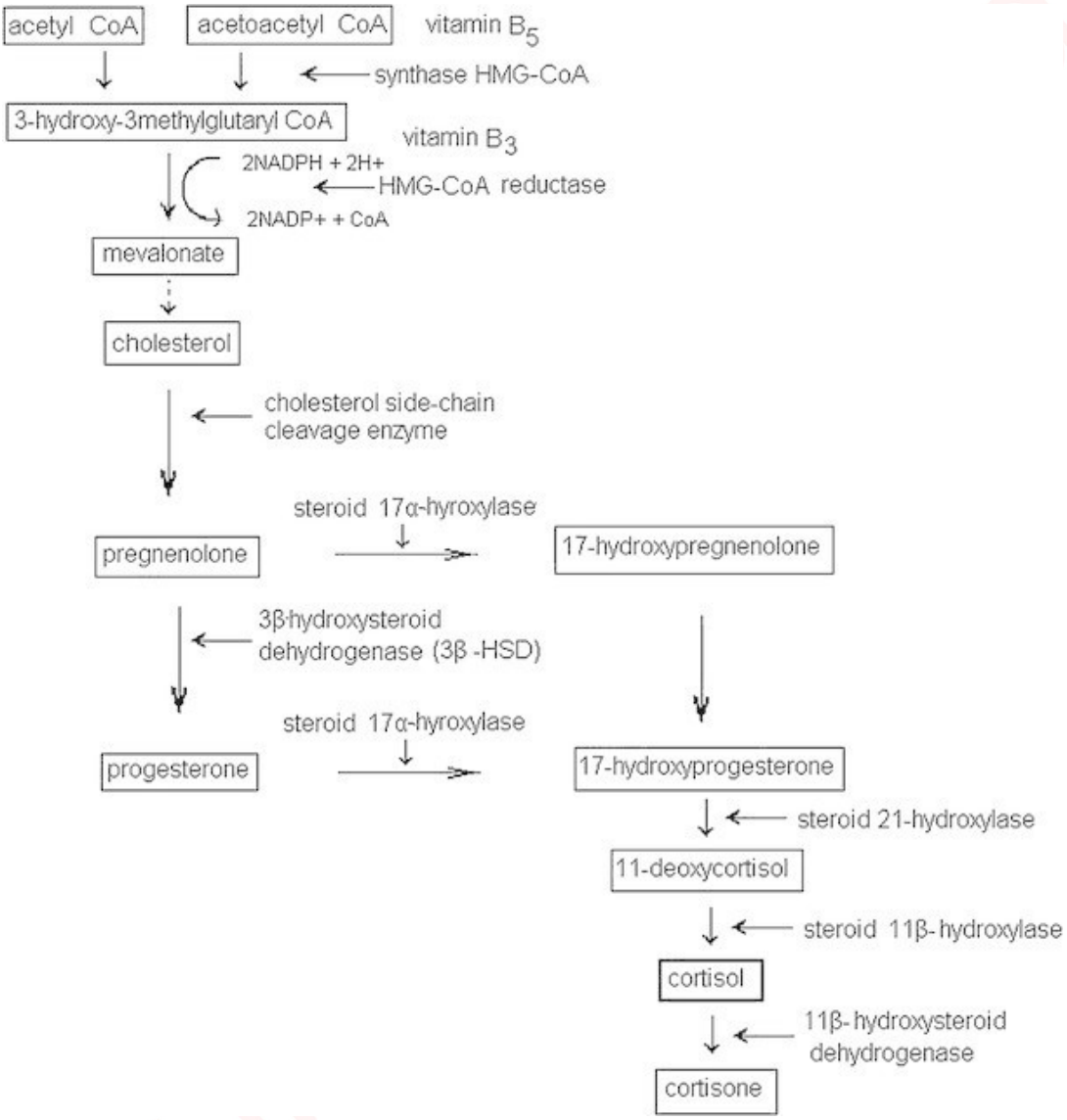
METABOLISM

Cortisol, a steroid hormone, is synthesized from cholesterol. It is synthesized in the zona fasciculata layer of the adrenal cortex. Adrenocorticotropic hormone (ACTH), released from the anterior pituitary, functions to increase LDL receptors and increase the activity of cholesterol desmolase, which converts cholesterol to pregnenolone and is the rate-limiting step of cortisol synthesis.[1] The majority of glucocorticoids circulate in an inactive form, bound to either corticosteroid-binding globulin (CBG) or albumin.[2] The inactive form is converted to its active form by

11-beta-hydroxysteroid dehydrogenase 1 (11-beta-HSD1) in most tissues, while 11-beta-HSD2 inactivates cortisol back to cortisone in the kidney and pancreas.[2]



Glucocorticoid receptors are present in almost all tissues in the body. Therefore, cortisol is able to affect nearly every organ system:[3]

Nervous

Immune

Cardiovascular

Respiratory

Reproductive

Musculoskeletal

Integumentary

Cortisol has many functions in the human body, such as mediating the stress response, regulating metabolism, the inflammatory response, and immune function.[4]

Immune Response

Glucocorticoids have a number of actions in the immune system. For example, they induce apoptosis of proinflammatory T cells, suppress B cell antibody production, and reduce neutrophil migration during inflammation.[3]

Stress Response

The human body is continually responding to internal and external stressors. The body processes the stressful information and elicits a response depending on the degree of threat. The body's autonomic nervous system is broken down into the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS). In times of stress, the SNS gets activated. The SNS is responsible for the fight or flight response, which causes a cascade of hormonal and physiological responses.

The amygdala is responsible for processing fear, arousal, and emotional stimuli to determine the appropriate response. If necessary, the amygdala sends a stress signal to the hypothalamus.[5] The hypothalamus subsequently activates the SNS, and the adrenal glands release a surge of catecholamines, such as epinephrine. This results in effects such as increased heart rate and respiratory rate. As the body continues to perceive the stimuli as a threat, the hypothalamus activates the HPA axis. Cortisol is released from the adrenal cortex and allows the body to continue to stay on high alert. Acutely, cortisol's catabolic mechanisms provide energy to the body.[6]

Glucose and Protein Homeostasis

Blood glucose levels drive key systemic and intracellular pathways. The presence of glucocorticoids, such as cortisol, increase the availability of blood glucose to the brain. Cortisol acts on the liver, muscle, adipose tissue, and pancreas. In the liver, high cortisol levels increase gluconeogenesis and decrease glycogen synthesis.[7] Gluconeogenesis is a metabolic pathway that results in the production of glucose from glucogenic amino acids, lactate, or glycerol 3- phosphate found in triglycerides. Gluconeogenesis reverses glycolysis, a cytoplasmic pathway used to convert glucose into pyruvate molecules. This pathway is used to release energy through substrate-level phosphorylation and oxidation reactions. Unlike glycolysis, gluconeogenesis becomes active when the body needs energy. Muscles have their own internal glycogen supply that allows them to respond to changes in ATP requirements rapidly. In the presence of cortisol, muscle cells decrease glucose uptake and consumption and increase protein degradation; this supplies gluconeogenesis with glucogenic amino acids.[8] In adipose tissues, cortisol

increases lipolysis. Lipolysis is a catabolic process that results in the release of glycerol and free fatty acids. These free fatty acids can be used in B oxidation and as an energy source for other cells as they continue to produce glucose. Lastly, cortisol acts on the pancreas to decrease insulin and increase glucagon. Glucagon is a peptide hormone secreted by the pancreatic alpha cells to increase liver glycogenolysis, liver gluconeogenesis, liver ketogenesis, lipolysis, as well as decreases lipogenesis. Cortisol enhances the activity of glucagon, epinephrine, and other catecholamines.

MECHANISM

The release of cortisol is under control of the hypothalamus-pituitary-adrenal (HPA) axis. Corticotropin-releasing hormone (CRH) is released by the paraventricular nucleus (PVN) of the hypothalamus.[2] It then acts on the anterior pituitary to release adrenocorticotropic hormone (ACTH), which subsequently acts on the adrenal cortex. In a negative feedback loop, sufficientcortisol inhibits the release of both ACTH and CRH. The HPA axis follows a circadian rhythm. Thus, cortisol levels will be high in the morning and low at night [2].

Steroid hormones, such as cortisol, are primary messengers. They can cross the cytoplasmic membrane because of their fat-soluble properties. Cell membranes are composed of phospholipid bilayers; these prevent fat-insoluble molecules from passing through. Once cortisol passes through the cell membrane and enters into the cell, it binds to specific receptors in the cytoplasm. In the absence of cortisol, the glucocorticoid receptor binds to an Hsp90 chaperone protein in the cytosol. The binding of cortisol to the glucocorticoid receptor dissociates the Hsp90. The cortisol-receptor complex then enters the nucleus of the cell and affects gene transcription.

EFFECT OF CORTISOL ON CNS

There are two major classes of adrenal corticosteroid hormones, glucocorticoids and mineralocorticoids. Both of these hormone classes are essential for life; however, excess activity of either one can cause hypertension and other symptoms of cardiovascular disease in humans and experimental animals. These steroids also can contribute to the development and/or maintenance of other manifestations of cardiovascular disease, including arrhythmia and heart failure; The brain plays an established role in mediating mineralocorticoid-induced hypertension , while participation of the central nervous system (CNS) in the aetiology of glucocorticoid-associated hypertension is supported by recent evidence but remains controversial.

Endogenous glucocorticoids (corticosterone and cortisol) and, to a lesser extent, mineral-ocorticoids (aldosterone) cross the blood–brain barrier to access corticosteroid receptors within the CNS . There are two major classes of corticosteroid receptors: mineralocorticoid receptors (MR) and glucocorticoid receptors (GR) . Activation of MRs within the CNS triggers hypertension, sympathetic activation and salt ingestion , whereas the effects of CNS GR activation on cardiovascular control are poorly understood. Glucocorticoid receptors are found throughout the CNS, while MRs are located in select regions that include limbic structures and brainstem nuclei associated with the autonomic nervous system, such as the nucleus of the solitary tract . The GR is selective for glucocorticoids, although the binding affinity of glucocorticoids for the GR is about 10 times lower compared with the binding affinity for MR. Mineralocorticoids and glucocorticoids bind to MR with approximately equal affinity and, even at the diurnal minimum, glucocorticoid

concentrations in the plasma are 100 times greater than normal plasma aldosterone concentrations. Therefore, in the absence of mechanisms to confer mineralocorticoid ligand specificity to the MR, these receptors would be largely occupied by glucocorticoids, as is the case for MRs located within the hippocampus. However, some neurons express the enzyme 11β-hydroxysteroid dehydrogenase 2 (11βHSD2), which catalyses the conversion of endogenous glucocorticoids to inactive metabolites, allowing aldosterone to occupy a larger number of MRs. Also, endogenous glucocorticoids can occupy MRs without triggering receptor activation . The relative contribution of endogenous cortisol, corticosterone and aldosterone to the central cardiovascular effects of MR activation remains a substantive area of investigation.Several additional critical unanswered questions regarding the CNS actions of corticosteroids on blood pressure regulation arise from the current fundamental understanding of corticosteroid actions within the brain and from the growing interest in the CNS actions of these hormones on cardiovascular regulation, as follows. (1) What mechanisms in addition to 11βHSD2 confer ligand specificity to the MR? (2) What is the effect of GR occupation within the CNS on cardiovascular regulation? (3) What are the cellular mechanisms mediating central effects of MR activation on the cardiovascular system, and in what circumstances are these important? The data and ideas presented at this symposium represent current understanding and investigation of these questions, whose answers are complex and are likely to depend on the physiological status of the organism and the region of the brain being studied.

Cortisol

Cortisol is the predominant corticosteroid secreted from the adrenal cortex in humans.In a healthy,unstressed person,cortisol is secreted according to a diurnal pattern under the influence of corticotropin released from the pituitary gland. Corticotropin secretion inturn is under the influence of hypothalamiccorticotropin-releasing hormone and both hormones are subject to negative feedback control by cortisol itself.Circulating cortisol is bound to corticosteroid binding globulin, with less than 10percent in the free,bioavailable form.With severe infection, trauma, burns, illness, or surgery, there is an increase in cortisol production by as much as a factor, of six that is roughly proportional to the severity of the illness[68]. Diurnal variation in cortisol secretion is also lost. These effects are due to increased production of cortisol secretion is also lost. These effects are due to increased production of corticotropin-releasing hormone[69].Stimulation of the hypothalamic-pituitary-adrenal axis in this context is caused by elevated levels of circulating cytokines,among other factors[70].Adrenal responsiveness to exogenous corticotropin is normally maintained during acute illness[71].Inaddition,during critical illness,levels of corticosteroid binding globulin decrease rapidly[72], leading to increase at sites of inflammation owing to the cleavage of corticosteroid - binding globulin by neutrophil elastate, an effect that liberates cortisol[75].In addition to having systemic actions, inflammatory metabolism[10] and can increase the affinity of glucocorticoid receptors for cortisol[11]. These changes in cortisol action appear to be important adaptive mechanisms regulating the inflammatory response[70].During severe illness, many factors can impair the normal corticosteroid response.These factors include preexisting conditions affecting the hypothalamic - pituitary -adrenal axis[76], but

corticosteroid insufficiency can also occur during the course of acute illness. Responses involving corticotropin releasing hormone and corticotropin can be impaired by head injury,central nervous system depressants,or pituitary infarction[77].Adrenal cortisol synthesis can be impaired by multiple meachanisms[71,76]. The anesthetic agent etomidate and the antifungal agent ketoconazole inhibit the activity of enzymes involved in cortisol synthesis[78]. Adrenal hemorrhage can occur in sick patients especially those with septicemia and underlying coagulopathy, and adrenal insufficiency can occur when there is extensive destruction of adrenal tissue caused by tumors orinfection. The high levels of inflammatory cytokines in patients with sepsis can also directly inhibit adrenal cortisol synthesis.Ischaemic stroke is a stress factor triggering a complex defensive reaction called"alarm reaction" by Selye. Stress gives rise to liberation of catecholamines, dopamine beta-hydroxylase in the blood, cerebro-spinal fluid and urine. Patients with ischaemic stroke were found to have increased adrenaline,noradrenaline,and3-metoxy-4-hydroxymandelicacid level in urine and increased cortisol level in blood serum.Patients,especially those with severe ischaemic stroke have increased concentrations of glucose metabolites in blood and cerebro-spinal fluid: pyruvate acid, lactic acid, acetylacetic acid and hydroxybutyricacid.

In acute illness, cortisol secretion increases whereas that of the adrenal androgens,and dehydroepiandrosterone sulfate declines. The period following ischemic stroke can be considered as a reaction to a stressful event. Changes in cortisol secretion are one of the indicators of stress reaction.

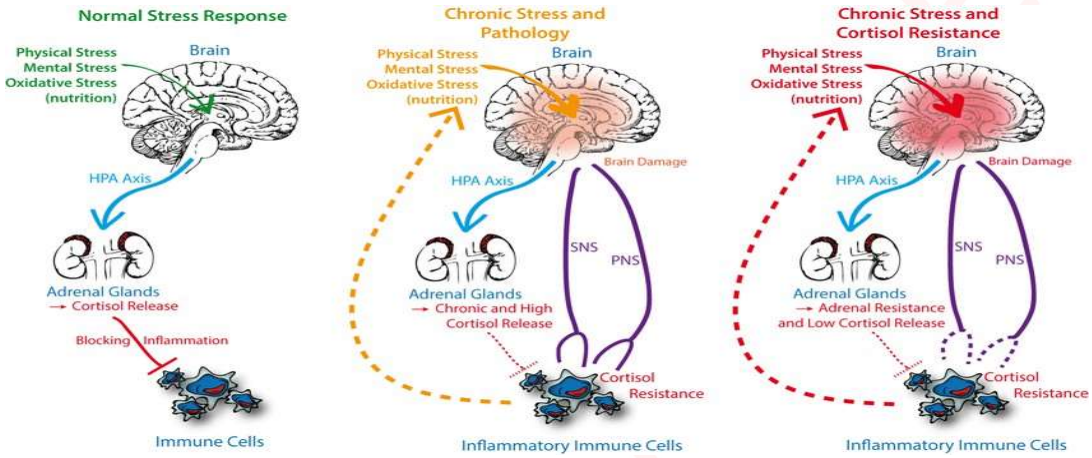
Increased levels of glucocorticoids (GCs) released from the adrenal cortex

during stress have negative effects on many organ systems and may impair the immune system,myocardial function and affect carbohydrate, protein and fat metabolism. *In vitro* and *invivo* studies have demonstrated neurotoxic effects of GCs,including exacerbation of hypoxic injury to neurons[80].Experimental ischaemic injury to neurons is thus potentiated by high physiological levels of GCs and attenuated after adrenalectomy[81-83]of corticosteroid receptors[85,86]. However, adrenalectomy *per se*can also induce neuron.Prolonged sustained exposure to GCs may also influence cognition and mood[84].Central for these effects is the hippocampal formation,important for mood and cognition and with a high density al injury and adequate circulating GC levels are essential formaintainingbodyhomeostasis[87].

Acute stroke is associated with increased activity in the hypothalamic-pituitary-adrenal axis resulting in increased cortisol production and elevated circulating cortisol level[88-90]. Previous research have shown that excessive cortisol levels after stroke is associated with cognitive dysfunction[89-91], severity of hemiparesis[89,92] and may predict stroke outcome and the later development of depression[93] . In contrast, low circulating cortisol levels have been associated with poor outcome after burns and septicemia[94-97],stressing the importance of cortisol for the maintenance of vital functions.

During the first few days after stroke, there is an initial rise of ACTH and cortisol but a subsequent, rapid decline of ACTH with a persisting increase of cortisol. This dissociation between ACTH and cortisol is most likely due to a cortisol-induced depression of ACTH levels combined with an increased responsiveness at the adrenal levels[88,90].

Increased cortisol levels may induce cognitive dysfunction[101] and in experimental studies GCs in conjunction with ischemia exert a toxic effect on neurones, especially those in the hippocampus[81,102], where it can induce hippocampal pyramidal neuron degeneration.



Hippocampal stimulation during surgery in man is known to inhibit the cortisol axis, and the hippocampus is suggested to be important for the feedback regulation for the cortisol axis[84,103].Hippocampal dysfunction may thus lead to hypercortisolism that, in turn, may aggravate existing damage, resulting in a vicious circle.

MATERIALS AND METHODS

The study included 120 patients with acute stroke presenting within 24hours of stroke onset after getting informed consent. The patients were recruited from medical wards and IMCU in Chengalpattu government hospital.

Exclusion criteria

1. Pregnancy
2. Hepatic impairment
3. Age<18 years
4. Patients who are on following drugs

a.phenytoin

b. rifampicin

c. ketaconazole

d. steroids

Methodology

Scandinavian Stroke Scale (SSS) was used to study severity of acute stroke in all patients presenting to the hospital. Diagnosis of Acute Ischemic or Hemorrhagic stroke was based on CT imaging in all patients.Blood samples are taken for assessing serum cortisol levels.

ScandinavianstrokeScale

The **Scandinavian Stroke Scale** was designed for ease of use by physicians[1]. It is simpler than the NIHSS and has comparable performance in predicting death or dependence after stroke. The degree of neurological impairment measured by the Scandinavian Stroke Scale has been shown to correlate with ASPECTS score severity in acute stroke [3].

CLASSIFICATION

- consciousness: 2 (reacts to verbal commands but not fully conscious) to 6 (fully conscious)
- eye movements: 0 (conjugate eye deviation) to 4 (no gaze palsy)
- arm motor power on affected side: 0 (paralysis) to 6 (raises arm with normal strength)
- hand motor power on affected side: 0 (paralysis) to 6 (normal strength)
- leg motor power on affected side: 0 (paralysis) to 6 (normal strength)
- orientation: 0 (completely disoriented) to 6 (correct for time, place and person)
- speech: 0 (only answers yes/no or less) to 10 (no aphasia)
- facial palsy: 0 (present) to 2 (none)
- gait: 0 (bedridden/wheelchair) to 12 (walks 5 m without aids)

INTERPRETATION

Stroke severity has been graded using this scale as [4]:

mild: 43-58

moderate: 26-42

severe: 0-25

Serum cortisol

Serum cortisol is estimated by competitive immune enzymatic calorimetric method(Dia Metra kit).The analyzing laboratories were blinded to all clinical information about patients.

Cortisol (antigen) in the sample competes with horseradish peroxidase-cortisol(enzyme labeled antigen) for binding on to the limited number of anti-cortisol (antibody) sites on the microplates(solidphase).After incubation,bound/free separation is performed by a simple solid phase washing.The enzyme substrate(H2O2) and the TMB-substrate are added. After an appropriate time is elapsed for maximal color development,the enzyme reaction is stopped and absorbances are determined.Cortisol concentration in the sample is based on a series by a set of standard. The color intensity is inversely proportional to the cortisol concentration in the sample.

Statistical analysis

Mean values of the parameters are calculated by Independent sample – t test. Correlation between serum cortisol levels and stroke scales are assessed by Chi – Square Test. All statistical analysis are performed using SPSS (software package used for statistical analysis) package. A p- value of less than 0.05 is considered to be statistically significant.

OBSERVATIONS

PATIENT CHARACTERISTICS

Patient Characteristics N=120	Percentage (or) Median
Age	58.5 (40 – 88)
Sex (Male)	50%
H/O Hypertension	58.3%
H/O Diabetes	58.3%

PATIENT PROFILE ON ADMISSION

Patient Indicators	Mean	Standard Deviation
SBP	146.58	25.553
DBP	93.92	13.553
Serum Cortisol	637.15	79.399
SSS	20.85	6.339
Time duration	9.53	3.130

LEVELS OF CORRELATION WITH SSS

Factor	Correlation Coefficient	Significance P value
SBP	0.136	0.140
DBP	0.110	0.233
Serum Cortisol	-0.984	<0.001*

LEVELS OF CORRELATION WITH SERUM CORTISOL

Factor	Correlation Coefficient	Significance P value
SBP	-0.121	0.186
DBP	-0.116	0.207
SSS	-0.984	<0.001*

CT Brain in patients

CT Brain	Frequency
Hemorrhage	22
Infarct	98
Total	120

Age (in yrs)	Frequency
40 – 49	15
50 – 59	46
60 – 69	39
More than 70	20
Total	120

Gender	Frequency
Male	60
Female	60
Total	120

Duration of presentation to the hospital

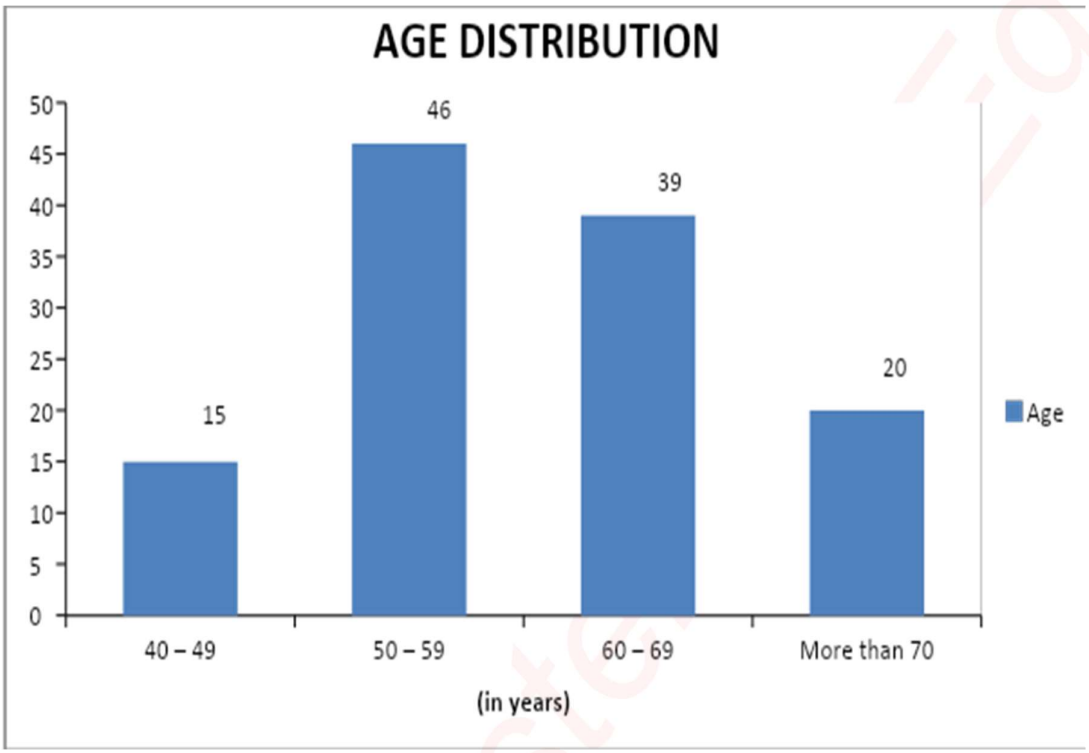
Duration	Frequency
Less than 8hrs	63
9 – 15hrs	49
16 – 12hrs	8
Total	120

SSS

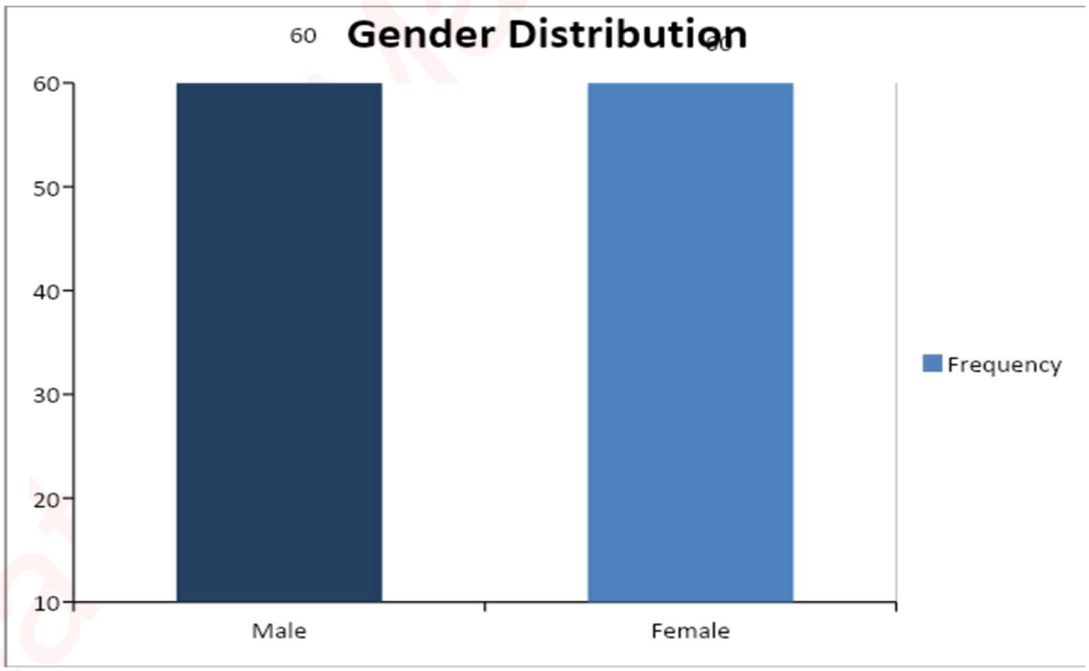
SSS	Frequency
Less than 15	20
16 – 30	89
More than 30	11
Total	120

CHARTS AND GRAPHS

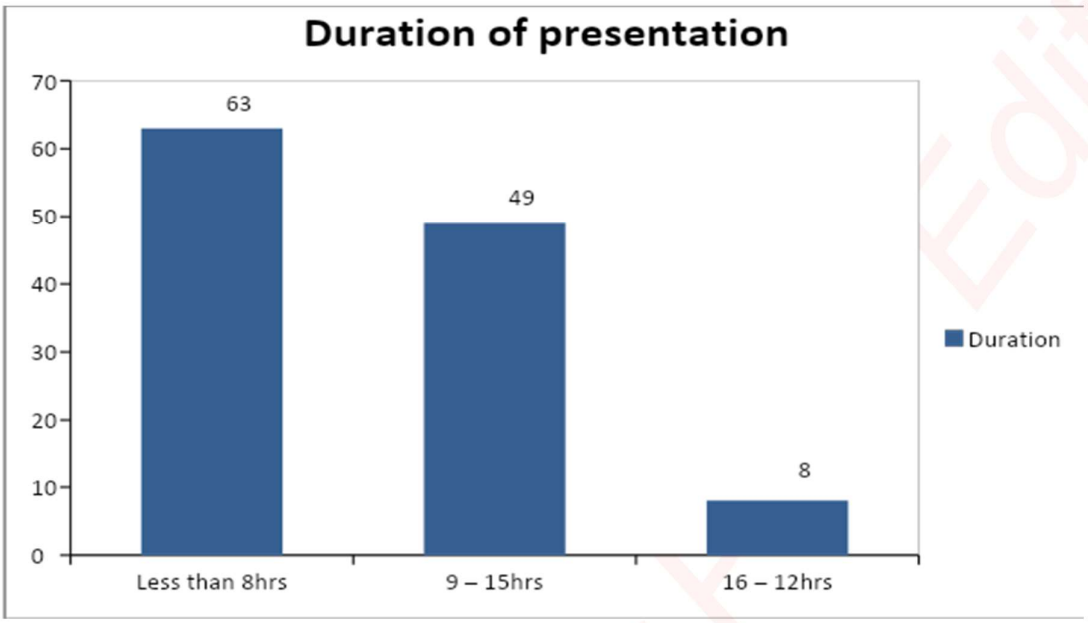
Age distribution



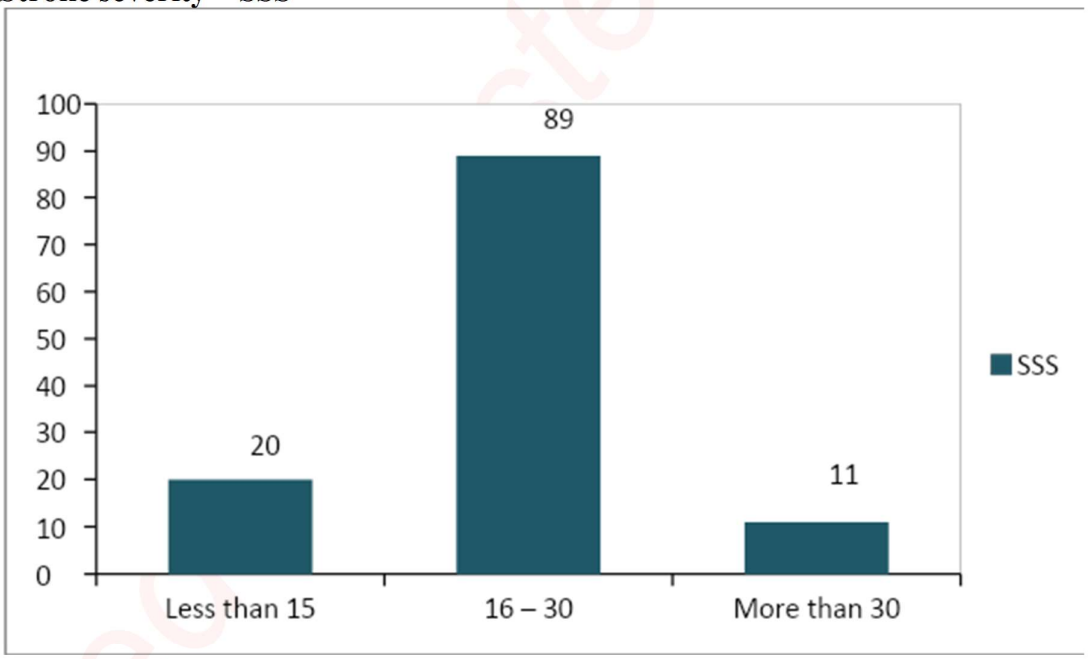
Gender Distribution



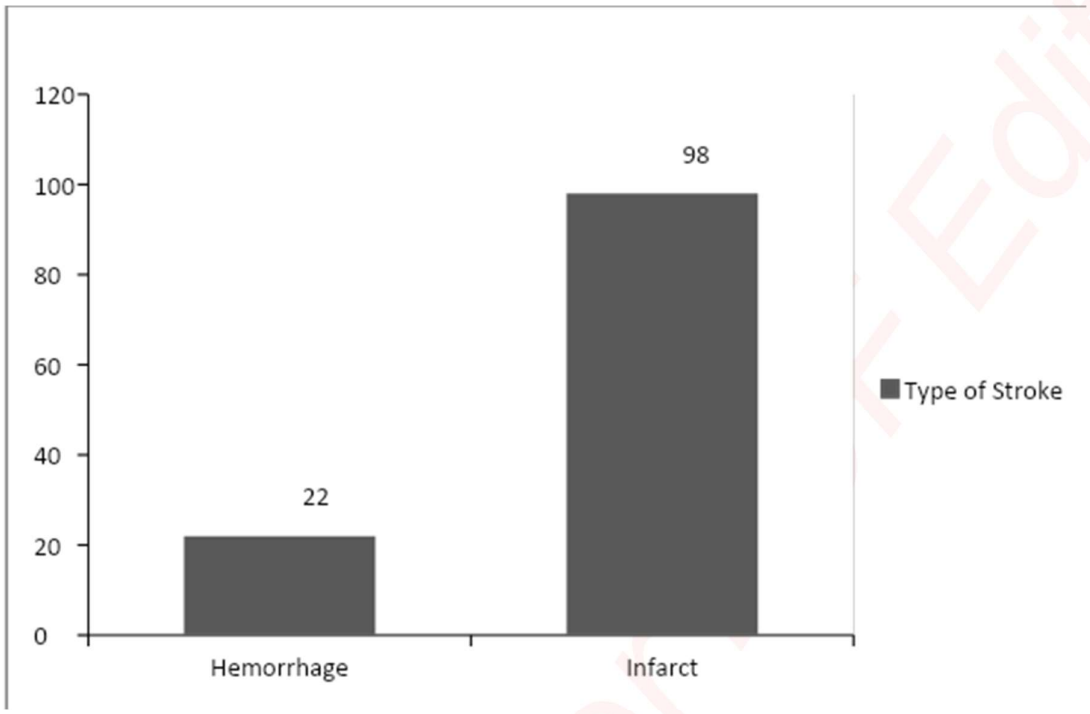
Duration of presentation

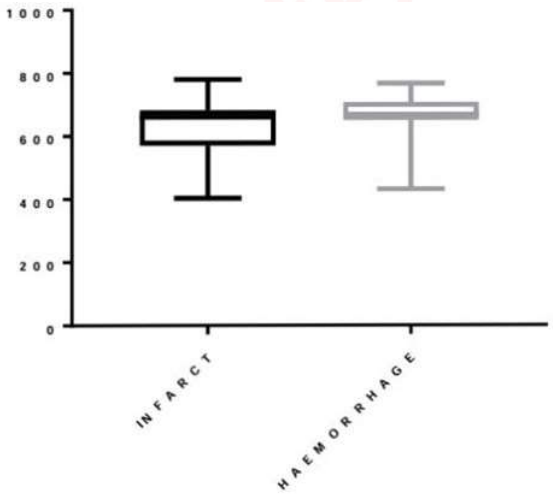


Stroke severity – SSS



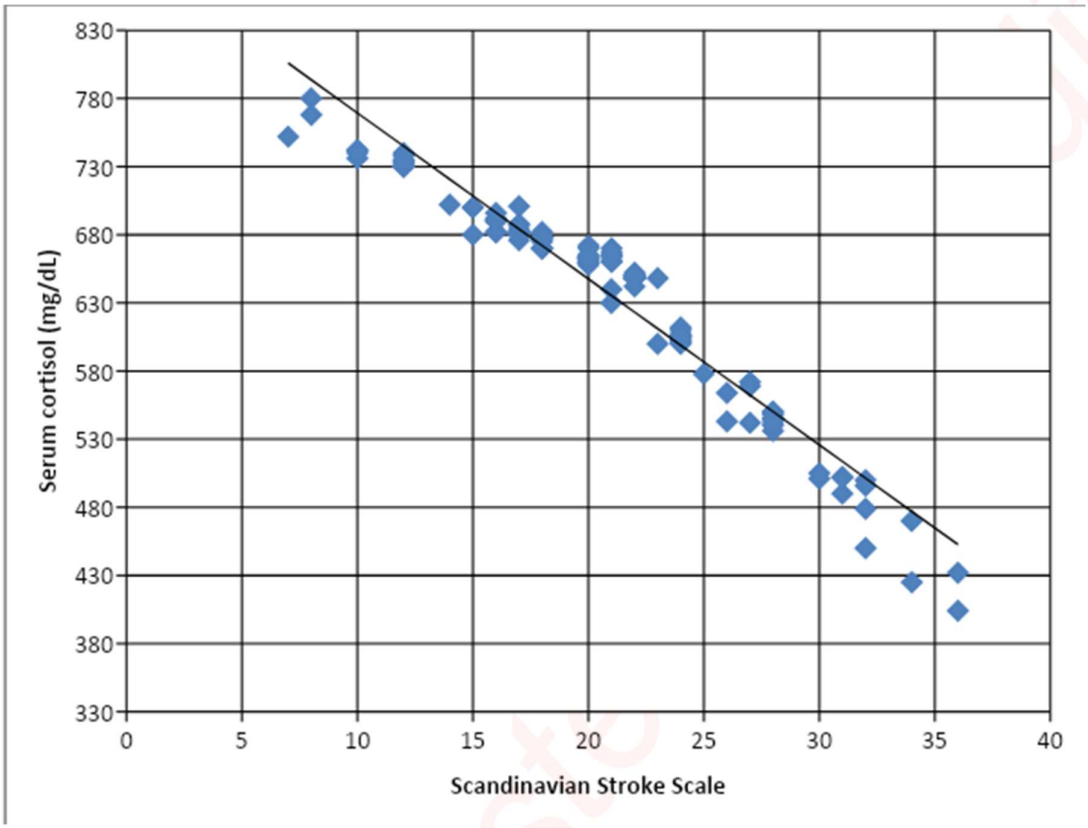
Types of stroke



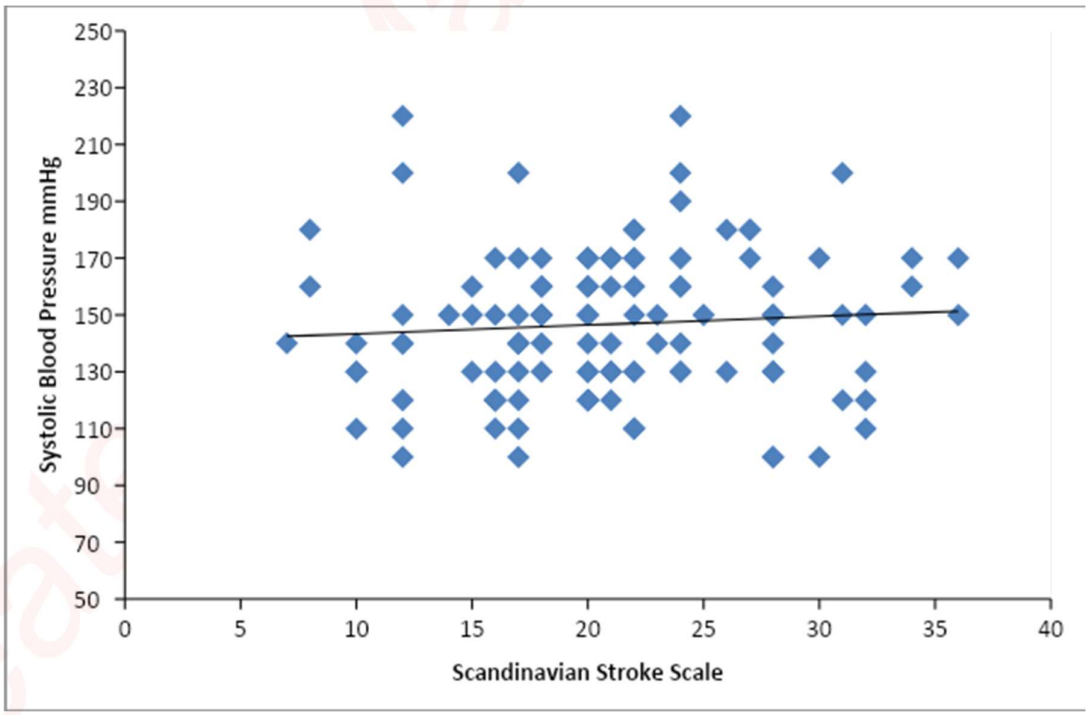


Mean cortisol value for infarct is 630 and hemorrhage is 665; standard deviation being 7.99 for infarct and 16.7 for hemorrhage.P value is 0.067.Hence in unpaired t test it is found that serum cortisol levels correlation in infarct and hemorrhage is not significant.

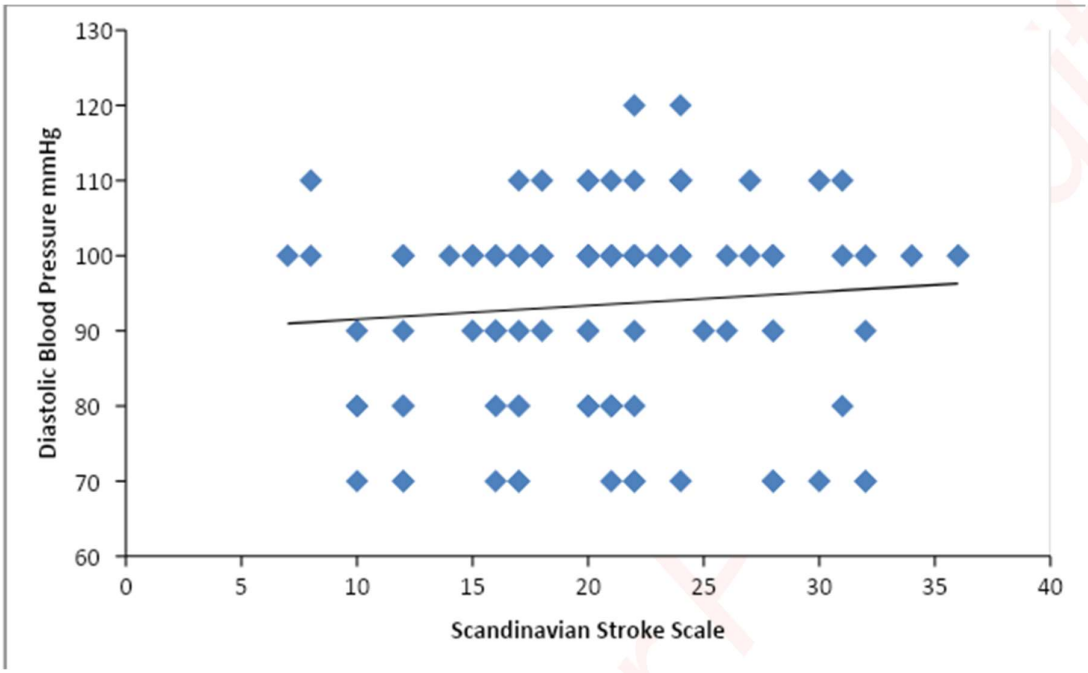
Correlation between SSS and Serum cortisol levels



Correlation between Systolic blood pressure and SSS



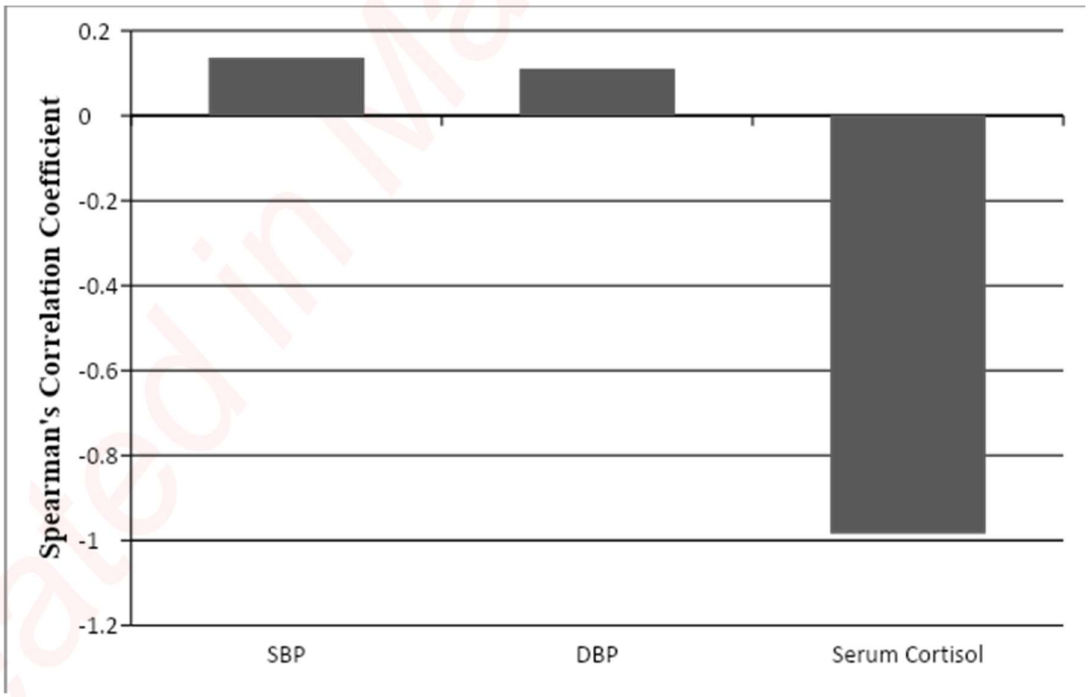
Correlation between Diastolic blood pressure and SSS



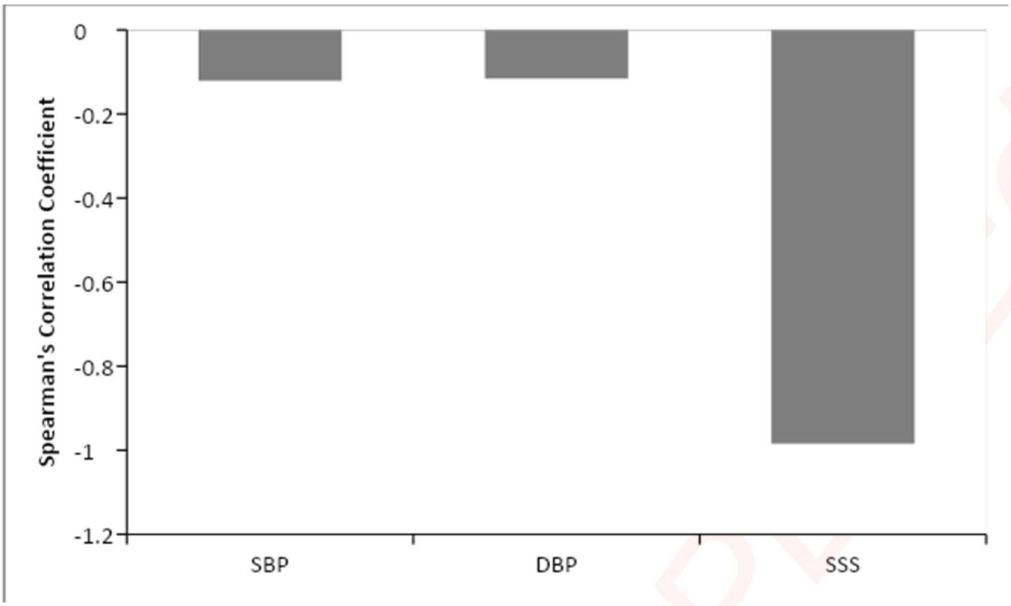
Correlation coefficients compared for SSS

Type : Spearman's rho

Correlation Coefficient



Correlation coefficients for Serum Cortisol



Type : Spearman's rho Correlation Coefficient

DISCUSSION

A total of 120 patients were enrolled in the study who were proven to have Acute Stroke by CT Brain which was taken at the time of admission. The minimum age of the patients is 43 years and the maximum age was 88 years. Among the 120 patients ,46 % of the acute stroke occurred in the age group of 50 to 59 years. And about 50%were males and 50 % were females. The mean cortisol level was 637nmol/L.Of the 120 cases, 58% were diabetics and 42% were non diabetics. 58 percent were hypertensives and 42 percent were normotensives. Of the 120 cases the mean systolic BP was 146mmhg and mean diastolic BP was93mmhg. Of the 120 cases 98 had acute ischemic stroke and 22 had acute hemorrhagic stroke. Among 98 acute ischemic stroke 28had infarct in the Anterior cerebral artery territory and 57 had infarct in the middle cerebral artery territory and 13 had infarct in the posterior cerebral artery territory.

Among 22 acute hemorrhagic stroke 21 had hemorrhage in MCA territory and 1 had ACA territory hemorrhage. It is clear that majority of the cases had MCA territory infarct and hemorrhage. The mean SSS score was 20.85 and mean time duration was 9.5 hours. Among 120 patients 63 patients presented less than 8 hours and 49 patients within 9 to 15 hours and 6 between 16 to 24 hours Among 120 patients SSS score was less than 15 in 20 patients.

In 89 patients score was between 16 to 30 and 11 patients had score more than 30 and the mean SSS score was 20 which comes under severe category. Among 15 patients with score less than 15 serum cortisol levels were more than 700nmol/L and those with score more than 30 serum cortisol levels were less than 500nmol/L.The

correlation coefficient for SSS and serum cortisol was -0.984 which had significant correlation indicating high serum cortisol levels had low SSS score and also the P value being < 0.001 which was statistically significant.

SIMILAR STUDIES:

A study done by H Christensen et al showed high cortisol levels predicts poor stroke outcome.(N=41; mean serum cortisol 649 nmol/L ; 95% CI ; P=0.03) Similar to the above study our study also showed positive correlation between serum cortisol levels and SSS score in predicting the severity of the acute stroke which is found to be statistically significant($P<0.001$). Hence it was very clear that acute ischemic stroke was very severe in patients with high serum cortisol levels.

CONCLUSION

The following conclusion was derived from our study

- ✓ High serum cortisol correlated with severity of stroke.

CLINICAL SIGNIFICANCE AND SCOPE OF FUTURE STUDIES

Cortisol is an independent short term marker of prognosis of functional outcome and death in patients with acute stroke..Elevated cortisol after the onset of stroke is clearly associated with high severity.A combined model including other stress hormones like ACTH , cytokines and paraclinical parameters can however add significant information to the clinical score. Since early prediction of stroke outcome is very important for therapeutic strategies, serum cortisol level measurement can add significant predictive information to the existing SSS score.

Although serum cortisol has been proved as an independent indicator of stroke severity, the exact pathophysiological mechanism of relationship has to be elucidated by further studies.

MASTER CHART

S.No	NAME	AGE	SEX	DM	SHTN	SYSTOLIC BP(MMHG)	DIASTOLIC BP(MMHG)	Time duration	CT brain	SSS scale	Sr.cortisol (NMOL/L)
1	Mahendran	68	Male	yes	yes	130	80	6hours	MCA infarct	12	730
2	Balaraman	75	male	yes	no	110	70	16hours	ACA infarct	16	690
3	Rajagopalan	48	male	no	no	120	80	8hours	MCA infarct	21	640
4	Gokulakannan	55	male	yes	yes	170	100	20hours	MCA hemorrhage	20	660
5	vijaya	58	female	no	no	130	70	7hours	MCA infarct	24	606
6	sridevi	51	female	no	yes	160	100	10hours	MCA hemorrhage	15	680
7	rajan	65	male	yes	yes	140	100	12hours	ACA infarct	23	600
8	lakshmi	56	female	yes	no	130	80	12hours	MCA infarct	10	740
9	arulsamy	85	male	no	no	110	70	5hours	MCA infarct	22	648
10	anbalagan	73	male	no	no	120	90	8hours	PCA infarct	16	682
11	raniammal	63	female	yes	no	130	90	10hours	ACA infarct	15	700
12	Prema	59	femlae	yes	no	120	80	12hours	MCA infarct	20	662
13	Selvi	49	female	yes	yes	150	100	15hours	MCA infarct	20	660
14	santhanammal	68	female	yes	yes	170	100	12hours	MCA hemorrhage	7	752
15	Baskaran	62	male	no	no	110	70	7hours	ACA infarct	12	732
16	Boopathy	61	male	no	no	120	80	8hours	MCA infarct	20	665
17	Sweetlin	57	female	yes	no	200	120	16hours	MCA hemorrhage	10	742
18	Sakunthala	55	female	yes	yes	160	110	6hours	MCA infarct	20	665
19	Panchanathan	63	male	no	no	130	70	8hours	ACA infarct	21	670
20	Chandra	65	female	yes	no	110	80	7hours	MCA infarct	10	736
21	Ravivarman	54	male	no	no	120	80	9hours	MCA infarct	12	738
22	Kanchana	60	female	yes	no	130	70	12hours	MCA infarct	32	479
23	Revathi	45	female	yes	no	130	80	16hours	MCA infarct	22	648

24	Amalanathan	58	male	yes	yes	150	100	8hours	PCA infarct	28	545
25	Chakravarthy	68	male	no	no	120	90	11 hours	MCA + PCA infarct	32	450
26	ramila devi	88	female	no	yes	170	100	7hours	ACA infarct	34	425
27	Prabhakar	48	male	yes	yes	180	110	8hours	MCA infarct	27	569
28	Anjalamma	88	female	no	yes	150	100	16hours	MCA infarct	36	404
29	Sulendran	53	male	no	yes	170	100	10hours	ACA hemorrhage	20	672
30	vaishnavi rani	65	female	yes	no	130	90	8hours	MCA infarct	28	536
31	Prema mani	58	female	no	no	100	70	12hours	MCA infarct	30	505
32	Jansi	51	female	no	yes	120	90	10hours	PCA infarct	16	692
33	Mohana	43	female	yes	yes	140	100	12hours	ACA infarct	21	664
34	Shanthi	48	female	no	yes	170	100	7hours	MCA infarct	24	607
35	Deviga	74	female	no	yes	150	100	8hours	MCA infarct	32	500
36	Muthu	68	male	yes	no	150	100	10hours	MCA infarct	31	502
37	Selvi	54	female	no	no	130	90	8hours	MCA infarct	28	545
38	pragathishwari	55	female	yes	yes	150	100	10hours	MCA hemorrhage	15	700
39	Renuga	75	female	yes	yes	140	100	7hours	MCA infarct	24	603
40	Kanan	66	male	no	yes	170	110	8hours	MCA infarct	30	501
41	Velmurugan	64	male	no	yes	160	100	10hours	ACA infarct	34	470
42	Shankari	63	female	no	no	140	100	12hours	MCA infarct	28	550
43	Vijayalakshmi	70	female	yes	yes	180	110	4hours	MCA infarct	27	542
44	Arthi	58	female	yes	no	130	90	10hours	ACA infarct	26	543
45	Uma	80	female	no	yes	160	100	6hours	MCA hemorrhage	18	678
46	Prasad	78	male	yes	yes	130	100	8hours	MCA +PCA infarct	24	601
47	Latha	65	female	no	no	110	70	8hours	ACA infarct	32	496
48	Ramesh	60	male	no	yes	170	100	9hours	MCA hemorrhage	36	432
49	Rajini	67	male	yes	no	130	80	20hours	ACA infarct	21	661

50	Rajeshwari	56	female	no	yes	170	110	7 hours	MCA infarct	24	600
51	Malliga	58	female	yes	no	100	70	8hours	MCA infarct	28	548
52	Veerapan	65	male	yes	no	130	80	12hours	ACA infarct	21	660
53	Govindan	61	male	no	yes	190	120	7hours	PCA infarct	24	610
54	mohid basha	75	male	yes	yes	150	100	10 hours	MCA hemorrhage	23	648
55	Saranraj	70	male	no	no	130	70	6hours	MCA infarct	28	550
56	Chinapan	63	male	yes	no	120	70	10hours	ACA infarct	17	680
57	Vijaya	71	female	no	yes	170	100	8hours	PCA infarct	22	648
58	Senthil	63	male	yes	no	120	80	8hours	MCA infarct	31	490
59	Paulraj	58	male	no	yes	140	100	11 hours	ACA infarct	17	682
60	Nasreen	70	female	yes	yes	150	100	7hours	MCA infarct	18	670
61	Padma	57	female	yes	yes	170	100	10 hours	MCA hemorrhage	21	665
62	Tulasiram	46	male	yes	no	150	100	16hours	MCA infarct	22	648
63	Sundar	52	male	no	yes	200	110	7hours	ACA infarct	17	684
64	Prabha	56	female	yes	yes	170	100	10hours	MCA infarct	21	667
65	moeiden b	60	male	yes	yes	180	100	6hours	ACA infarct	26	564
66	Sridevi	55	female	no	no	170	110	6hours	PCA infarct	18	670
67	Renuga	80	female	no	yes	200	110	12hours	MCA hemorrhage	31	502
68	Kumaran	40	male	yes	no	110	80	6hours	ACA infarct	17	682
69	sheik beevi	58	female	yes	yes	170	100	7hours	MCA infarct	21	665
70	Ushanandini	52	female	no	yes	180	100	8hours	MCA infarct	22	650
71	Rajesh	63	male	yes	yes	140	90	7hours	MCA infarct	12	734
72	Satyalekha	58	female	no	yes	150	100	8 hours	MCA infarct	18	670
73	Nasreen	54	female	yes	yes	160	100	20hours	ACA infarct	20	664
74	Kanmani	58	female	no	no	110	70	6hours	PCA infarct	22	650
75	Devakumar	67	male	yes	no	100	70	14hours	ACA infarct	28	545
76	Shanthi	58	female	yes	no	130	90	10hours	MCA infarct	18	675

77	Irudhayam	66	male	yes	yes	140	100	8hours	MCA infarct	12	730
78	Rajkumar	60	male	yes	yes	200	110	7hours	MCA hemorrhage	24	612
79	Krishna bai	45	female	no	no	140	100	12hours	ACA infarct	18	682
80	Kalaivani	52	female	yes	yes	160	100	8hours	MCA infarct	22	648
81	Raji	70	male	no	yes	150	100	10hours	MCA hemorrhage	20	660
82	saheed ali	68	male	no	yes	160	100	12hours	MCA infarct	24	605
83	Mary	63	female	yes	yes	170	110	8hours	MCA hemorrhage	22	652
84	selvi S	53	female	no	no	120	80	10hours	MCA infarct	20	670
85	Raghupathy	50	male	yes	yes	160	100	7hours	ACA+MCA infarct	8	780
86	Levine	52	male	yes	no	140	90	8hours	MCA infarct	17	701
87	Chitra	55	female	yes	no	130	90	10hours	MCA infarct	20	663
88	Thangaraj	66	male	yes	yes	180	120	8hours	MCA hemorrhage	22	650
89	Krishnaraj	82	male	no	yes	180	110	14hours	MCA hemorrhage	8	768
90	Ambedkar	48	male	yes	no	120	80	7hours	ACA infarct	16	696
91	Suresh	53	male	yes	no	100	70	10hours	PCA infarct	17	676
92	ram babu	52	male	yes	yes	150	100	8hours	ACA infarct	18	678
93	Prakash	61	male	yes	yes	170	110	7hours	MCA hemorrhage	20	662
94	Ellamal	55	female	no	yes	200	100	10hours	MCA hemorrhage	12	732
95	Velmurugan	44	male	yes	yes	160	100	6hours	MCA infarct	28	540
96	Ragavan	54	male	no	no	100	70	12hours	PCA infarct	12	740
97	Ragavendran	49	male	yes	yes	140	100	8hours	ACA infarct	17	680
98	Lalitha	53	female	yes	yes	150	90	14hours	MCA infarct	25	578
99	Sundaram	62	male	no	yes	160	100	8hours	MCA infarct	20	660
100	Thangarasi	65	female	yes	yes	160	110	9hours	MCA infarct	21	630

101	Dhanasekar	67	male	yes	yes	150	100	10hours	MCA infarct	28	542
102	Saravanan	76	male	yes	yes	170	100	7hours	MCA infarct	27	572
103	Veeramal	82	female	yes	no	130	80	14hours	ACA infarct	17	682
104	Rekha	45	female	no	yes	150	100	8hours	MCA infarct	14	702
105	Vedalakshmi	55	female	yes	no	120	80	8hours	PCA infarct	20	662
106	Sridevi	62	female	yes	no	140	90	15hours	MCA infarct	10	742
107	Karikalan	54	male	no	yes	170	100	10hours	MCA hemorrhage	20	658
108	Gopalan	62	male	yes	yes	160	110	8hours	MCA infarct	24	605
109	Rajalakshmi	54	female	no	no	130	90	7hours	ACA infarct	22	642
110	Maheshwar	65	male	yes	no	140	100	8hours	ACA infarct	20	664
111	Balakumaran	70	male	yes	yes	170	100	10hours	MCA hemorrhage	17	688
112	Suganthi	50	female	no	yes	220	110	6hours	MCA + PCA infarct	24	603
113	Santhanam	67	female	yes	yes	130	90	8hours	MCA infarct	16	690
114	Ragavan	55	male	no	yes	160	100	10hours	ACA infarct	18	677
115	Maryjohn	54	female	yes	yes	170	100	8hours	MCA hemorrhage	16	682
116	Ramadevi	55	female	no	no	150	100	10hours	MCA infarct	17	687
117	Mohamed R	46	male	yes	yes	150	100	8hours	MCA infarct	12	735
118	Shanthi	45	female	no	yes	150	100	15hours	ACA infarct	16	691
119	Rajagopal	55	male	yes	no	130	90	8hours	MCA infarct	20	664
120	Pandurangan	65	male	yes	yes	220	140	9hours	MCA hemorrhage	12	738

Proforma

Name: Age&Sex: IPNo.

Timeduration: Presenting complaints:LOC:

Seizures: Fever: Others:

History

HTN	DM	PT	BA	IHD
CVA	Seizures	Smoking	Alcoholism	

GeneralExamination

GCS:	BP:	PR:	JVP:

Temperature:Cranialnerves:VII

CNS examinationSSS:

1. Consciousness
2. Orientation
3. Speech
4. Eyemovements
5. Facialpalsy
6. Gait
7. Armpower
8. Handpower
9. Legpower
10. Footparesis

Investigations:

Blood Hb:	TC:	DC:	ESR:
BloodSugar:	Urea:	Creatinine:	

Electrolytes:Lipidprofile:

Serum cortisol:USG abdomen:ECG:

ECHO:

CT Brain:

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INFORMATION SHEET

We are conducting a study on "Serum cortisol levels in assessing severity of acute stroke-

A cross sectional study in Chengalpet medical college and Hospital. We are selecting patients who satisfy our inclusion criteria

and they are included in the study. The privacy of the patients will be maintained throughout the study,

in the event of any publication or presentation resulting from the research, no personally identifiable

information will be shared.

Participation depends on patients decision. Their decision will not result in any loss of benefits to which you are otherwise entitled.

Signature of Investigator Signature of the Participant

Dr.G.Nishanthi

Date :

Place :

INFORMED CONSENT FORM

(This is only a guideline – Relevant changes to be made as per the study requirements)

Title of the Study : " Serum cortisol levels in assessing severity of acute stroke- A cross sectional study in Chengalpet medical college and hospital".

Name of the Participant : _____ .

Name of the Principal (Co-Investigator):_____ .

Name of the Institution: Chengalpattu Medical college and Hospital.

Name and address of the sponsor / agency (ies) (If any) : _____ _____ .

Documentation of the informed consent

I _____have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in the study "Serum cortisol levels in assessing severity of acute stroke-

A cross sectional study in Chengalpet medical college and hospital".(title of the study).

1. I have read and understood this consent form and the information provided to me.

2. I have had the consent document explained to me.

3. I have been explained about the nature of the study.

4. I have been explained about my rights and responsibilities by the investigator.

5. I have been informed the investigator of all the treatments I am taking or have taken in the

past _____months including any native (alternative) treatment.

6. I have been advised about the risks associated with my participation in this study.*

7. I agree to cooperate with the investigator and I will inform him/her immediately if I suffer

unusual symptoms.*

8. I have not participated in any research study within the past _____month(s).*

9. I have not donated blood within the past _____months----add if the study involves

extensive blood sampling.*

10. I am aware of the fact that I can opt out of the study at any time without having to give any

reason and this will not affect my future treatment in this hospital.*

11. I am also aware that the investigator may terminate my participation in the study at any

time, for any reason, without my consent.

12. I hereby give permission to the investigators to release the information obtained from me

as result of participation in this study to the sponsors, regulatory authorities, Govt. agencies, and IEC. I understand that they are publicly presented.

13. I have understand that my identity will be kept confidential if my data are publicly presented .

14. I have had my questions answered to my satisfaction.

15. I have decided to be in the research study.

I am aware that if I have any question during this study, I should contact the investigator. By

signing this consent form I attest that the information given in this document has been clearly

explained to me and understood by me, I will be given a copy of this consent document.

signature of the investigator :

signature of the participant :

SELF DECLARATION

I **Dr.G.Nishanthi,** Second year post graduate, Department of Internal Medicine, Government Chengalpet Medical College and hospital, hereby declare that I will bear the entire expenditure of my post graduate dissertation study on **"Serum cortisol levels in assessing severity of acute stroke-A cross sectional study in Chengalpet medical college and hospital".**

PLACE: CHENGALPET

DATE: 6/10/2020

Signature of the post graduate student

(Dr.G.Nishanthi)

சுயஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு : "ெீரம் கார்டிொல் அளவுகள் லவத்து

பக்கவாதத்தின் தீவரத்லத மதீப்பீடு செய்தல்- செங்கற்பட்டு மருத்துவகல்லூரி மருத்துவமலையில் ஒரு குறுக்குசவட்டு ஆய்வு"

ஆய்வு செய்யப்படும் இடம்:

பங்கு சபறுபவரின் சபயர்:

பங்கு சபறுபவரின் வயது:

பங்கு சபறுபவரின் எண் :

மமமை குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் ளைக்கு விளக்கபட்டுள்ளது. நான்

இவ்வாய்வில் தன்ிச்லெயாக பங்மகற்கின்மறன். எந்த காரணத்திாமை, எந்த

ெட்டிெக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விகிக்சகாள்ளாம் என்றும்

அறிந்துசகாண்மடன்.

இந்த ஆய்வு ெம்பந்தமாகமவா, இலத ொர்ந்து மமலும் ஆய்வுமமற்சகாள்ளும் மபாதும் இந்த

ஆய்வில் பங்குசபறும் மருத்துவர், என்னுலடய மருத்துவ

அறிக்லகககலள பார்ப்பதற்கு என்

அனுமதி மதலவ இல்லை ளை அறிந்துசகாள்கிமறன். இந்த

ஆய்வின் மூைம் கிலடக்கும்

தகவலைமயா,முடிலவமயா பயன்படுத்திக்சகாள்ள

மறுக்கமாட்மடன்.

இந்த ஆய்வில் பங்குசகாள்ள ஒப்புக்சகாள்கிமறன். இந்த

ஆய்லவ மமற்சகாள்ளும் மருத்துவ

அணிக்கு உண்லமயுடன் இருப்மபன் என்று உறுதியளிக்கிமறன்.

பங்மகற்பவரின் லகசயாப்பம்:

ொட்ெியாளரின் லகசயாப்பம்:

இடம்:

மததி:

பங்மகற்பவரின் சபயர் மற்றும்

விைாெம்: ஆய்வாளரின் லகசயாப்பம்

:

இடம்:

மததி: