HIGHLY SENSITIVE C-REACTIVE PROTEIN AND TROPONIN T – MORBIDITY PREDICTOR IN ISCHEMIC STROKE

Dissertation submitted in partial fulfillment of the

requirement for the award of the Degree of

DOCTOR OF MEDICINE

BRANCH I - GENERAL MEDICINE

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CHENNAI, TAMILNADU

CERTIFICATE

This is to certify that the dissertation entitled "**HIGHLY SENSITIVE C-REACTIVE PROTEIN AND TROPONIN T – MORBIDITY PREDICTOR IN ISCHEMIC STROKE"** is the bonafide work of **Dr. U. NAGARAJAN** in partial fulfillment of the university regulations of Tamilnadu Dr. M.G.R. University, Chennai, for MD (Branch I) General Medicine examination to be held in April 2016.

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DECLARATION

I, **Dr. U. NAGARAJAN,** hereby declare that, I carried out this work entitled "**HIGHLY SENSITIVE C-REACTIVE PROTEIN AND TROPONIN T – MORBIDITY PREDICTOR IN ISCHEMIC STROKE"** at Kanyakumari Government Medical College Hospital, Asaripallam, under the guidance of **Prof. PRINCE SREEKUMAR PIUS, MD,** Professor of Medicine, during the period of October 2014 to September 2015. I also declare that this bonafide work has not been submitted in part or full by me or any others for any award, degree or diploma to any other University or Board either in India or abroad

This is submitted to the Tamilnadu Dr. M.G.R. Medical University, Chennai, in partial fulfilment of the university rules and regulations for MD (Branch I) General Medicine examination to be held in April 2016.

Place: Asaripallam Dr. U. NAGARAJAN

Date:

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INTRODUCTION

INTRODUCTION

CVD is an important health problem world wide, with annual incidence of 0.2 to 2.5 per 1000 population. CVD of ischemic origin is one of the major causes for disability and death. Parameters of ischaemic stroke for predicting outcome in the disease process, such patients have not been clearly identified in the Indian population. Various studies proved that CRP and Troponin T at admission was found to predict the poor functional disability in ischemic stroke.

Acute occlusion of a cerebral vessel causes reduced blood flow to the region in the brain it supplies. stroke syndrome are divided in to

1. Large vessel stroke involving anterior cirulation
2. Large vessel stroke involving posterior circulation.
3. Small vessel diseases

STROKE IN THE ANTERIOR CIRCULATION

Anterior circulation comprises of internal carotid artery and its branches. These vessels can be occluded by embolic or atherosclerosis and dissection occlusion from a proximal source.

MIDDLE CEREBRAL ARTERY (MCA):

Proximal MCA occlusion or its branches are cuased by an embolus of cardiac origin or of some unknown origin rather than intra cranial thrombosis. Because atherothrombosis of middle cerebral artery will be slowly progressive by the time it is significant in size effective collaterals would have developed which prevents MCA insufficiency from becoming apparent and symptomatic.

MCA branches that supply the supero medial border of the parietal and frontal lobes that is on its lateral surface supplied by the Anterior cerebral arteries (ACA). The lower occipital and temporal lobe convolutions. The M1 segment , proximal part of MCA, gives rise to the penetrating branches to the brain called lenticulostriate arteries supplying the posterior limb of the internal capsule, putamen, outer globus pallidus, most of the caudate nucleus and corona radiate.

The MCA after M1 segment, divides into inferior and superior divisions in the sylvian fissure, called M2 branches. The superior division supplies the frontal cortex and superior parietal cortex and the inferior division supplies the temporal and inferior parietal cortex.

In entire occlusion of MCA, the clinical findings are hemianesthesia homonymous hemianopia, and a gaze preference to ipsilateral side for a day or two along with contralateral hemiplegia. Global aphasia constructional apraxia,

anosognosia may also be present. Dysarthria is common becaue of facial nerve weakness.

Lenticulostriate arteries are small vessels when occluded stroke within the internal capsule may produce sensory motor stroke or pure motor stroke on the contralateral side. When genu of the internal capsule involved causes facial weakness primarily followed by arm then leg weakness as the ischaemia progresses posteriorly within the internal capsule.

ANTERIOR CEREBRAL ARTERY (ACA)

ACA is divided into

1. Precommunal circle of Willis A1 (proximal to anterior communicating artery)
2. Postcommunal A2 (distal to the anterior communicating artery)

A1 supplies the internal capsule – its anterior limb, anterior hypothalamus, anterior perforate substance, head of the caudate nucleus in its inferior part and amygdala. A1 branch occlusion is tolerated well because of the presence of anterior communicating artery. But occlusion of A2 results in contra lateral symptoms of urinary incontinence, motor involvement of leg arm. When both A2 are occluded profound abulia occurs.

ANTERIOR CHOROIDAL ARTERY:

Anterior choroidal artery arises from internal carotid artery that supplies the posterior limb of internal capsule with the white matter posterior to it and some geniculocalcarine fibres. Occlusion of anterior choroidal artery results in contalateral hemiplegia, hemianesthesia and homonymous hemianopia

INTERNAL CAROTID ARTERY:

Clinical pattern of occlusion of internal carotid artery varies depending upon the cause of ischaemia – low flow, embolism or propagated thrombus. MCA territory is most affected.

COMMON CAROTID ARTERY:

In common carotid artery occlusion all the clinical features of occlusion of internal carotid artery will be present along with claudicating of jaw because of occlusion of external carotid artery. Bilateral common carotid artery occlusion may occur in Takayasu's areteritis.

POSTERIOR CIRCULATION STROKE:

Posterior circulation includes

1. Vertebral arteries on both sides
2. Basilar artery is formed by joining of vertebral arteries on both sides.

3. And two posterior cerebral arteries formed by division of basilar artery in to two.

VERTEBRAL AND POSTERIOR INFERIOR CEREBELLAR ARTERIES:

The vertebral artery consists of four different segments, V1 from origin to its entry in to the vertebra foramenat C6 or C5, V2 from C6 to C2, V3 from winds around the arch of Atlas to pierce the duramater at foramen magnum entering brain and V4 runs uptwrads and joins to form basilar artery. Occlusion of V4 causes lateral medullary syndrome - the ishaemia of lateral part of medulla and causes vertigo, numbness of ipsilateral face and contralateral limbs, diplopia, ipsilateral Horner's syndrome. Hemiparesis will not occur in vertebral artery occlusion but quadriparesis can occur because of anterior spinal artery occlusion. Rarely medial medullary syndrome can occur. When cerebellum is involved sudden respiratory paralysis may occur.

BASILAR ARTERY:

Supplies the superior cerebellum and base of pons. There are 3 groups paramedian, short circumferential, and long circumferential bilaterally (anterior inferior and superior cerebellar) arteries. Complete basilar artery occlusion causes bilateral long tract sign with signs of cranial nerve palsies with cerebellar dysfunction. Occlusion of superior cerebellar artery results in severe cerebellar ataxia, nausea and vomiting, dysarthria and contralateral hemianesthesia over

the extremities, body and face. Occlusion of anterior inferior cerebellar artery produces facial weakness, vertigo, nausea, and vomiting, tinnitus, ipsilateral deafness, nystagmus, cerebellar ataxia, Horner's syndrome and conjugate lateral gaze palsy, contralateral hemianesthesia.

POSTERIOR CEREBRAL ARTERY:

In posterior cerebral artery occlusion two clinical syndrome can be seen

1. P1 syndrome:

   Proximal segment of the PCA occlusion causes infarction in the medial thalamus and ipsilateral subthalamus, midbrain and in the ipsilateral cerebral peduncle. A 3rd nerve palsy with contralateral ataxia called Claudes's syndrome can occur or with contralateral hemiplegia called Weber's syndromecan occur.

2. P2 syndrome:

   Distal PCA occlusion causes infarction in the occipital and medial temporal lobes. Contralateral homonymous hemianopia with macular sparing is the ususal presentation.

Inflammation plays an important role in the pathogenesis of cerebro vascular, cardiovascular acute athero thrombotic events it also activates the production of the many acute phase proteins like C-reactive protein(CRP), serum amyloid A and fibrinogen.

The CRP concentration in serum, may increase more than thousand times upon inflammation and with a half life of 19 hrs and it is an independent predictor of risk of cardiovascular events, atherosclerosis, atherothrombosis, myocardial infarction and hypertension.

Of many kinds of inflammatory markers, studies show CRP may be the most powerful inflammatory predictor of poor prognosis in cardiovascular and cerebrovascular events.

Also patient with elevated CRP levels within 72 hrs of stroke have an increased risk of mortality.

CRP in ischemic stroke predicts outcome and identifies patients who are at risk for future vascular events and early mortality.

CRP has also been found to be elevated in patients with ischemic stroke, correlating with the size of the infarct as evidenced by ct scan atherosclerosis is a multifactorial disease ,caused by the underlying inflammation. This inflammatory process also contributes to the pathogenesis of acute thrombotic events. CRP is an acute phase reactant and its level in the body is directly

proprortional to the level of inflammation in the body. Increased levels of CRP are consistently associated with increased cardiovascular disease and predict poor prognosis in myocardial infarctions and stroke.

Thus CRP is useful and reliable predictor of cerebrovascular events. Also cardiac activity is also affected by stroke. Particularly stroke involving insular cortex causes dysrythmia and also there are theories many micro emboli occluding the coronary arteries causeing myocardial damage which gives rise to elevated levels of serum cardiac specific troponin T. this myocardial injuty associated with ischemic stroke have a profound impact on the outcome of the morbidity in stroke patients. Thus troponin T and CRP (hsCRP) can be used as predictor of morbidity in cerebrovascular events

AIMS AND OBJECTIVES

AIMS AND OBJECTIVES

AIM OF THE STUDY

1. To evaluate the role of hsCRP and troponin T as a morbidity predictor in acute ischemic stroke
2. To study the CRP level pattern and troponin T level pattern in ischemic stroke.
3. To study the correlation between severity level of stroke and CRP and troponin T level individually and in combination of both values.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

STROKE

DEFINITION

Stroke or CVD is a acute onset of clinical symptoms and signs of focal or global (from just facial palsy or arm weakness to complete paralysis or coma) loss of cerebral function, with lasting for more than 48 hours and leading to death with no obvious cause, other than that of atherogenic vascular occlusion.

Cerebral infarction accounts for apparently 80% of stoke as opposed to 10% due to primary intra cerebral bleed, 5% due to sub arachnoid hemorrhage and 5% of uncertain etiology.

PATHOLOGICAL TYPE	%
CEREBRAL INFARCTION	
1. Large vessel occlusion 2. Small large vessel occlusion(lacunar infarct) 3. Cardiac emboli 4. Hematological disorder vasculitides 5. Vasculopathy	80%
PRIMARY INTRACEREBRAL HAEMORRHAGE	
1. Hypertensive bleeds 2. Vascular malformation 3. Bleeding diathesis anticoagulation	10%
Non traumatic SAH Aneurysm vascular malformation Non aneurysmal SAH	5%
Other causes	5%

CAUSES OF CEREBRAL ISCHAEMIA AND INFARCTION

1.	Arterial wall disorders	Athero thrombo embolism intra cranial small vessel disease (lipohyalinosis, micro atheroma) trauma, dissection, fibro muscular dysplasia, congenital altered wall anomalies, moyo-moyo disease, embolism, inflammatory, Binswanger's disease, irradiations and infections
2.	Embolism from heart	
3.	Hematological	
4.	Miscellaneous	Pregnancy, peripartum, OCP, drug abuse, cancer, IBD,homocystinemia, hypoglycemia, mitochondrial cytopathy, epidermal nerves, snake bite, fat embolism, nephrotic syndrome

RELATIVE IMPORTANT CAUSE OF ISCHEMIC STROKE

Athero thrombo embolism of cerebral arterial supply	50%
Lipohyalinosis / micro atheroma	25%
Embolism from heart	20%
Miscellaneous	5%

From above tables the following points are evident

1. Cerebral infarction accounts for 80% of all strokes.
2. Athero thrombo embolism of cerebral arterial supply is the cause of 50% of causes of cerebral infarction.

RISK FACTORS FOR ISCHEMIC STROKE

I. Non modifiable risk factors

Age

Sex

Race

Family history

II. Modifiable risk factors

Blood pressure

Diabetes mellitus

Hyper cholesterolemia

Smoking

Cardiovascular diseases

TIA

Carotid artery diseases

Drugs

Obesity

Diet

Exercise

Other risk factors

III. Newer risk factors

1. Infection / inflammation.

   Both acute and chronic inflammation play a role in development and stability of atheromatous plaques. There is now evidence of association between stroke and serum CRP and Troponin T levels.

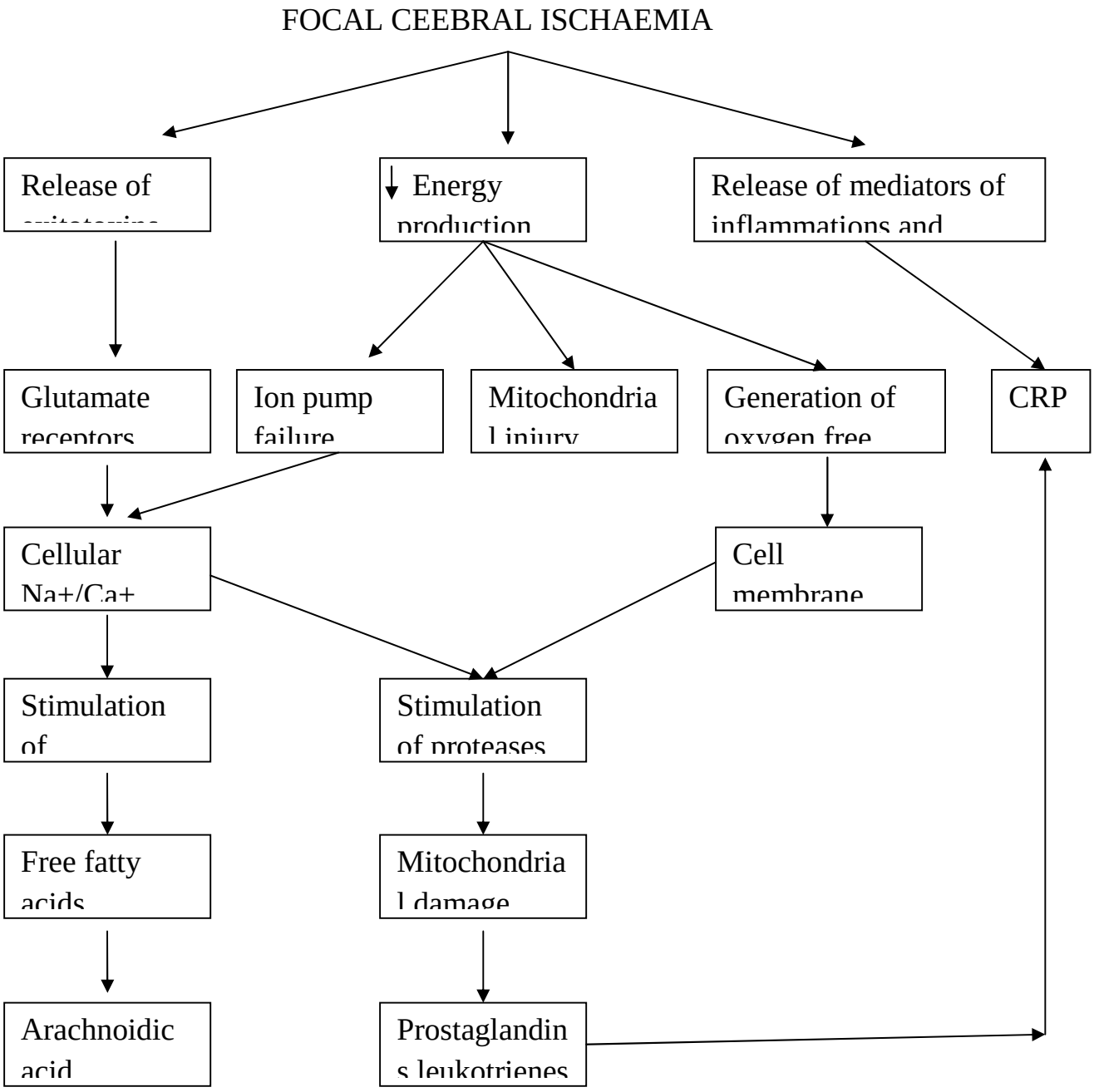
2. Haemostatic variables

Homocystinemia

PATHOPHYSIOLOGY OF ISCHEMIC STROKE

There are two patho physiological process.

1. A loss of supply of oxygen and glucose secondary to vascular occlusion.
2. An variety of changes in intracellular metabolism as a result of the loss of energy producing processes leading to disintegration of cell membrane


FOCAL CEEBRAL ISCHAEMIA
Release of
Energy
production
Release of mediators of
inflammations and
Glutamate
receptors
Ion pump
failure
Mitochondria
l injury
Generation of
oxygen free
CRP
Cellular
Na+/Ca+
Cell
membrane
Stimulation
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Stimulation
of proteases
Free fatty
acids
Mitochondria
l damage
Arachnoidic
acid
Prostaglandin
s leukotrienes

PREDICTORS OF STROKE OUTCOME

Although there are promising therapies for acute ischemic stroke with high expectation for rapid recovery and good outcome, poor outcome can still occur.

This is so because; ischemic stroke is a heterogenous condition. Whose outcome is influenced by many factors. The extent of brain injury and the result of outcome from ischaemia is largely dictated at a physiological level by the severity and duration of the insult. Demographic variables, risk factors, clinical examination findings, lab test result and imaging studies provide important insight regarding outcome.

DEMOGRAPHIC FACTORS:

1. Age:

    One of the major factors that negatively influence the outcome for patients with ischemic stroke. Older patients are less likely to improve comparing to the younger patients with similar size infarcts. Poor outcome can be explained by increased incidence of secondary complications among elderly stroke patients and having high incidence of other systemic diseases that preclude recovery.

2. Temperature:

Body temperature predicts and influences stroke outcome for each 10 Celsius increase in body temperature. The relative risk of poor outcome raised two fold. One explanation for this is and increased concentration of excitotoxic neurotransmitter.

While demographic and clinical findings have an established ray in the predictors and prognostic indicator, lab findings have also been found to play an important role.

3. I. high serum and CSF glutamate are common in patients with progressive stroke. High level of glutamate or glycine, both of which are excitotoxic neurotransmitters have strongly been related to large infarct size and severe neurological deficit. CNS specific proteins have been evaluated in blood, at the acute phase of ischemic stroke such as S100 and neuron specific enolase.

   II. prognostic value of acute phase reactant such as ESR and

   Two inflammatory markers also provide prognostic information.

   1. ESR erythrocyte sedimentation rate
   2. CRP

and a serum level of Troponin T also have a prognostic information.

4. Gender:

Some studies have shown male sex associates with poorer outcome, while some other studies have shown no difference. Probably hormonal protection could be the reason as experiments on animals showed improving stroke.

5. Cerebro Vascular Risk Factors:

Previous stroke and AF:

These are 2 major risk factors. Previous h/o stroke has been consistently associated with higher likelihood of death or dependence probably due to lower prestroke level of function and more advanced cardio vascular disease. Stroke in patients with atrial fibrillation are usually more severe, more disability and associated with high mortality.

6. Clinical Findings:

Level of consciousness and gaze deviation is generally associated with poorer outcome.

7. Blood Pressure:

Abnormal BP may influence outcome. Clinical studies of BP reduction have shown a decrease in cerebral blood flow to infarction area. On the other

hand, highly elevated BP has adverse long term effects in blood – brain barrier. Hypertension has been found to play a role in haemorrhagic transformation.

8. ESR: erythrocyte sedimentation rate independently predicted shor term outcome with increased level predicting poor outcome.

9. CRP:

an acute phase reactant has been found to predict outcome. concentrations measured in 72 hours of stroke, independently predicted survival after ischaemic stroke.

Inflammation plays an important part in the initiation, development and progression of atherosclerosis and other systemic blood markers of inflammation (i.e.) acute phase reactants such as and fibrinogen have emerged as powerful predictors of coronary and cerebrovascular events.

10. Troponin T: Serum levels of Troponin T was found to be an independent predictor of morbidity in patients with acute ischaemic stroke.

PATHOGENESIS OF INFECTION / INFLAMMATION ASSOCIATED WITH STROKE INVOLVES THE FOLLOWING

1. Increased fibrinogen.
2. Elastase released by activated granulocytes.
3. Inhibition of anticoagulation pathway involving with
    a. Protein C
    b. Protein S
    c. Anti thrombin III
4. Release of inflammatory cytokines
    a. TNF alpha
    b. IL 1B
    c. IL B
5. Increased CRP
6. Elevated Troponin T enzyme level

I. INFLAMMATION

Inflammation has an important part in the pathogenesis of acute athero thrombotic events, cardiovascular events and atherosclerosis. It also controls the production of many of the acute phase proteins such as fibrinogen, serum amyloid A and CRP. The serum concentration of CRP can increase more than thousand fold up on inflammation and with half life 19 hours, is a very stable maker of the inflammatory

process because it is a very sensitive indicator of the underlying inflammatory process, that it has been studied extensively, whether plasma levels of CRP and other inflammatory proteins in circulation (ex. Fibrinogen, IL 6) have a very high predictive value in the pathogenesis and progression of CVD.

II. COMPONENTS OF THE ATHERSCLEROTIC LESION

Endothelial dysfunction is the first step in development of atherosclerosis. These endothelial cells (EC's) express the vascular cell adhesion molecules (VCAM1). Intracellular adhesion molecule (ICAM1) and the endothelial leucocyte adhesion molecule (ELAM1) on the cell surface leucoytes, especially T lymphocytes (CD 8 cytotoxic T cells, CD 4 cells cross the endothelial cell barrier by diapedesis. These cells take up the lipoproteins and form foam cells. This causes proliferation of smooth muscle cells and induces the extracellular matrix to form a thick fibrous cap over the atherosclerotic vascular lesion.

The cells involved in the formation of atherosclerotic plaques stimulate many inflammatory mediators . These mediators contribute to the development, instability of the atherosclerotic palques and its eventual rupture.

III. CRP

CRP is one of the many acute phase reactants, present in the atherosclerotic vascular lesion and more specifically in the vascular intimal layer of the vessel. This localization makes it a major player directly in the development of atherosclerotic process (32). CRP is a phylogenetically highly conserved plasma proteins belong to a member of the pentraxin family. This protein was originally observed to 1930 in the plasma of patients with acute infection, where it react with the C-polysaccharide of pneumococcus and hence the name C reactive protein..

CRP present in plasma is produced by liver where the synthesis of regulated by IL 6 which in turn is controlled by other inflammatory cytokines such as IL 1 and TNF alpha.

NITRIC OXIDE EXPRESSION

CRP has been known to affect the expression and bio activity of endothelial NO synthase. Its increased serum level causes decreased activity of endothelial NO synthase which results in reduced bioavailability of Nitric Oxice (NO) and hence a decreased vasodilatory effect. This makes CRP a pro atherogenic and prothrombotic . CRP induces platet adhesion to endothelial cells. CRP is also chemotactic for human blood monocytes.

EXPRESSION OF INFLAMMATORY MEDIATORS OF CYTOKINES, CHEMOKINES AND ADHESION MOLECULES:

CRP causes elevation of inflammatory cytokines in relation to its level. Hence a high level of CRP induces a more increase in inflammatory cytokines. CRP induces release of IL 6 and IL 1 and TNF alpha. All three cytokine were detected 4 hours after CRP elevation with maximum level of TNF alpha at 8 hours and IL 1 & 6 at 16 hours. In atherosclerotic lesions CRP directly upregulates mRNA expression of the macrophage marker CD 2B and HLA DR as well as their protein products.

FRAMINGHAM STUDY(15)

To study the correlation between the baseline CRP level and risk of subsequent stroke events, CRP assay was done in member of Framingham study, original cohort, who were free of stroke or TIA at the time of 1980 to 1982 clinical examination and studied the baseline CRP plasma concentration to the incident of first ever stroke or TIA in their subjects during 12-14 years follow up. The date derived from the outcome of this study demonstrated a progressive increase in the incidence of TIA and ischaemic stroke with increased level of CRP.

CRP levels are known to be greater in smokers, obese individuals with (BMI>130% of ideal) and individuals with subclinical atherosclerosis. All of these afore mentioned aee individual risk factor of adverse cerebrovascular or cardiovascular events. But in a trend analysis, showed the relationship between the increased TIA and incidence of stroke with increased level of CRP persisted even after adjusting for a number of potential confounder.

In the Framingham study the data were obtained in a elderly cohort of men and women and led to the conclusion that the elevated level of CRP significantly predicted the greater risk of ischaemic stroke or TIA in elderly men and women.

PROGNOSTIC INFLUENCE OF INCREASED CRP AFTER FIRST EVER ISCHAEMIC STROKE

In their study Ridler and colleagues found an association between evidence of inflammation after myocardial infarction and increased risk of recurrent cerebral events.

This encourages Mario Di Nepoli and Co to conduct a study (7)

On the role of CRP level in short term prognosis after first ever ischaemic stroke. About 30 ischaemic stroke patient of either gender (combined) with age

group 49-90 years were studies within 4 weeks of the occurrence of the first ever CVD ischaemic events. No patients with evidence of acute infections were included in the series CRP was collected with in a medium of 14 days from stroke event. It was foud that patient with highest CRP level >5mg/dl at study entry died or had severe complications after stroke such as pulmonary embolism or had no evidence of recovery during the two months follow up.

This study concluded that CRP was increased in patients with cerebral ischaemia, the higher level correlating with significant neurological deficit and relevant disability and appear to provide additional information regarding prognosis after ischaemic stroke, as it appears to do after myocardial infarction.

PROGNOSTIC INFLUENCE OF INCREASED CRP AND FIBRINOGEN IN ISCHAEMIC STOKE

Mario Di Napoli and co also did a study to investigate and compare the influence of fibrinogen and CRP level in the prognosis of ischaemic stoke in one year. This led two conclusions.

1. Increased level of CRP are clearly related with poor prognosis in patients with ischaemic stroke and
2. Increased risk related with elevated CRP and prognostic influence of the fibrinogen are independent of one another.

INFLAMMATION AND STROKE, THE LEIDEN 85 PLUS STUDY (21)

All citizens of Leiden, Netherlands, who were 85 years old were visited at their residence (response rate was 87%) and their levels of the anti inflammatory cytokines IL 10 were assessed in a whole blood assay. In this study lipopolysaccharide was used as a stimulation. CRP serum level was also used as a marker of inflammation. A history of stroke was obtained at base line (prevalence 10%). The number of fatal stoke was prospectively obtained for a median follow up of 2.6 years (incidence 1.8/100 persons yearial rule). Subject with a history of stroke has significantly lower median IL 10 production level at base line done subject without stroke. They also had higher median CRP concentration. High CRP plasma concentration are directly related with an increased risk of stroke.

CRP AND OUTCOME AFTER FIRST EVER ISCHAEMIC STROKE(9)

Dr. Keith W. Muir, department of neurology, institute of neurological science,southern general hospital Glasgow, conducted a study in which Patients admitted to an acute stroke unit serving a catchment population of 2,26,000 were taken and the survival time and cause of death for upto 4 years after the index stroke were assessed and related to CRP concentrations assayed within 72 hours of stroke and prognostic variables by a COX proportional hazards regression model. Ischaemic stroke was diagnosed in 228 of 283 consecutive

admissions. Median follow up was 959 days geometric mean, CRP concentration was 10.1mg/L. survival window with CRP >10.1mg/L was significantly worse than with CRP < 10.1mg/L. higher CRP concentration was an independent predictor of mortality and morbidity together age and stroke severity on the national institute of health stroke scale.

CRP MORBIDITY PREDICTOR IN ISCHAEMIC STROKE(23)

Dr. H.N. Panicker, M. Thomes and Co conducted a prospective hospital based study of 105 patients of ischemic stroke in department of neurology. The focal neurological and functional core was assessed along with the CRP serum level. Then the patients were followed up ad 5 days and after 6 months and the outcome was studied. The functional status was assessed by Barthel Index by activities of daily living. Based on this the patients were divided in to two groups. Barthel Index <41 are brought under severly disabled group, 41-60 are grouped under moderately disabled and > 60 are grouped under mildly disabled. The results showed that if there is aphasia or the upper limb power of grade 4 along with elevated CRP level these patients showed higher di ability and belonged to severely disabled group. If there is no aphasia or upper limb power grade 3 or more with no elevation of CRP, these patients belonged to mildly disable dgroup at 6 months. Conclusion was patient can be stratified according to the predicted prognosis.

CRP AND INFARCT SIZE

In patients with ischaemic stroke the extent of necrosis is major factor but not then only determinant of morbidity. Various prognostic studies showed that CRP concentration were increased (>5mg/dl) in patients with large infarct size with worst outcome. Similarly with smaller infarct the elevatins of CRP were also smaller.

The strong association of elevated levels of serum CRP is clinically supported with quantitative analysis of cerebral infarction by CT scan of brain. This infarction is an acute phase response to inflammatory stimulus and is directly proportional to the inflammatory stimulus.

TROPONIN T AND ISCHAEMIC STROKE

The connection between brain and heart was highlited in early 20th century when Levy et al showed that ischemic changes in central nercous system and its metabolism influenced cardiac fuction. Later this report was supported by many other reports that have been published regarding the importance of the hypothalamus in controlling cardiac activity especially function of the sinus node and rythm. Morphological ECG canges of

repolarization type occur when the hypopthalamus and other related parts of the brain are stimulated experimentally.

In 1947 the first clinical study on ECG changes in brain dysfunction was published and in 1950s and 60s several reports regarding the same findings in intracerebral hemorrhage, subarachnoid haemorrhage, and ischaemic strokes were published.

Dysarhythmias and repolarisation disturbances occurring in stroke may be caused by catecholamines released into the systemic circulation secondary to direct neuronal effects mediated from CNS via neurons ending on the heart or co existing heart diseases. These may cause elevated levels of cardiac specific troponin T. Infact it has been clear that in many stroke cases there is concomitant increase in the serum concentrations of troponins in serum indicating coronary disease.

TROPONINS

Troponins are intracellular proteins in all muscle cells. In cardiac muscles also there are troponins proteins. These proteins are released into circulation when there is any injury to the muscle cells. Measuring these proteins may be useful in evaluating the extent of injury. Most useful of these proteins are troponin T and Troponin I. measuring these cardiac specific troponins gives a picture of the extent of injury to cardiac muscles. Of this we are measuring the Troponin T for this study.

This troponin T begins to elevate in 8 – 12 hours reaches peak in 1 – 2 days and remain elevated for 7 – 10 Days of cardiac injury. According to one school of thought, in ischaemic stroke there may be many micro emboli which may cause micro infarct in myocardium causing elevation of troponin T. In studies worldwide troponin T values more than 0.01ng/L is considered positive for troponin T.

FUNCTIONAL OUTCOME SCALE

Various functional outcome scale attempts to quantify the patients functional status are measured by ability to perform the task of daily living.

GLASGOW OUTCOME SCORE

It is 5 point scale with 1 = dead and 5 = good recovery.

MODIFIED RANKINS SCALE

5 points global assessment categorization of a patients function based on the ability to perform activities of day living.

ACTIVITIES OF DAILY LIVING SCALE

1. BARTHEL INDEX

Barthel index is a widely used increase of functional outcome.

A score of 100 indicates functional inadequacy, a score of 0 total dependence. If so if below 40 after 3 months of stroke despite rehabilitation procedures, the chances of patients being independent is remote. Although it is a measure of alround disability, it takes no account of vision, hearing and speech.

2. ACTIVITY INDEX

Activity index includes 4 mental capacity items, 6 measures of motor functions and 5 mesures of activites of daily living. There is a strong correlation between the activity index and Barthel index.

MATERIALS AND METHODS

MATERIALS AND METHODS

The study of hs CRP and troponin T in ischaemic stroke was carried out in the department of medicine, kanyakumari medical college.

SETTINGS

Medical wards

STUDY DESIGN

Single centre observational prospective hospital based study.

PERIOD OF STUDY

October 2014 to September 2015

Kanyakumari government medical college is a tertiary care centre and referral care centre. All stoke patients admitted in the above period and who are satisfied set criteria were included.

1. Stroke as define by WHO as a rapidly developing clinical signs of focal and at times global disturbances of cerebral function lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin.
2. All patients with CT proven cse of ischaemic stroke.
3. First episodes of ischaemic stroke.

4. Do not satisfying any of exclusion criteria.

EXCLUSION CRITERIA

1. Age >75 or <15
2. Patients with TIA
3. Patient with previous h/o stroke, TIA
4. Patients with haemorrhagic stroke, tumour, sub arachnoid haemorrhage.
5. Patients with head injury within 3 months.
6. CT negative stroke.
7. Patient who received aspirin treatment outside.
8. Patient with h/o hypertension, diabetes, heart disease, collagen disorders, hyperlipidemia, T.B., arteritis were excluded.
9. Smokers were excluded
10. Patients with obesity (BMI >30kg/M2)
11. Patients with major renal, hepatic, cancerous disease.
12. Patients with meningitis, brain abscess, or any chronic infection that affected CRP value.
13. Those with signs and symptoms of a clinical infection during the last 4 weeks before onset of stroke.
14. Those with signs and symptoms and clinical evidence of hospital acquired infection.

METHODOLOGY

After obtaining verbal consent from either patient or relatives, all patients in the study group were evaluated by complete medical history, full neurological examination standardized blood tests and imaging studies.

HISTORY

Clinical history was recorded from either the patient or his/her relatives. Special emphasis was given to presenting complaint, mode of onset, presence or absence of serizures, loss of consciousness, headache, vomiting etc. presence or absence of risk factors, for stroke was also noted. Past history of TIA, hypertension, diabetes, coronary artery disease, rheumatic heart disease, collagen disease, tuberculous etc were carefully sought. Personal history regarding dietary habits, smoking, alcoholic status were noted.

GENERAL EXAMINATION

Apart from routine observations, markers of atherosclerosis like carotid arteries, status of peripheral vessels, carotid thrill and BP were noted.

CNS EXAMINATION

Each of the patient were examined and assessed according to a predefined protocol developed for the study. The patients were evaluated thrice during the course of the disease.

The first evaluation was 24 -72 hours after the onset of stoke. A detailed clinical evaluation was done and recorded. The extent of neurological defect, cranial nerve palsies, aphasia, gaze palsies, sensory impairment, cerebellar dysfunction, heminaopia were all recorded along with computed tomography of brain and levels of hsCRP and troponin T were measured and recorded. Functional score was assessed based on Barthel Index. HsCRP was measured using immunoturbidimetry method and Troponin T was done using standard card test of Roche diagnostics. The patients was again assessed on the 5^{th} day and condition was reviewed. Proper treatment as according to the protocol was given along with nursing care and physiotherapy in indicated cases.

Third evaluation was done 4 weeks after the onset of stroke. Any improvement or worsening of the condition was recorded and functional status was recorded based on Barthel Index. Any doubts and apprehension of the patients or the relatives were addressed and importance of proper nursing care and physiotherapy was emphasised.

Based on the Barthel Index patients were divided into 3 groups.

Barthel index <41 severly disabled.

Barthel index 41 – 60 moderately disabled.

Barthel index >60 mildly disabled.

BARTHEL INDEX OF ACTIVITY OF DAILY LIVING

1. Feeding	10 = independent.
	5 = needs help i.e forcutting
	0 = inferior performance
2. Bathing	5 = performs without assistance
	0 = inferior performance
3. Personal toilet	5 = washes face, combs hair, brushes teeth
	0 = inferior performance
4. Dressing	10 = independent
	5 = needs help
	0 = inferior performance
5. Bowel control	10 = no accidents
	5 = occasional accidents
	0 = inferior performance
6. Bladder control	10 = no accidents
	5 = occasional accidents
	0 = inferior performance

7.	Toilet transfer	10 = independent with toilet or bed pan
		5 = needs help for balance
		0 = inferior performance
8.	Chair / bed transfers	15 = independent
		10 = minimum assistance
		5 = able to sit, needs assistance to transfer
		0 = inferior performance
9.	Ambulation	15 = independent for 50 yards
		10 = with help for 50 yards
		5 = independent with wheel chair
		0 = inferior performance
10.	Stair climbing	10 = independent
		5 = needs help or supervision
		0 = inferior performance

Maximum disability = 0

Minimum disability = 100

PRINCIPLES AND METHODS

In our study hs-CRP was determined by immunoturbidimetric method

PRINCIPLES OF IMMUNOTURBIDIMETRY:

This method is based on the principle that when an antigen and antibody is allowed to react they agglutinate and form a precipitate in the sample which is measured by a laser and the exact value of the antigen can be estimated. Here the antigen is CRP and the anti CRP antibody that is sensitized with latex particles are used. The agglutinated is pounded upon with a laser beam of 570nm. The magnitude of change in penetration of the laser is directly proportional to the quantity of CRP in the sample. The actual concentration then determined from a predefined calibration curve prepared by the calibrators with known concentration.

INTERPRETATION OF VALUES:

<1mg/L = Mild elevation of CRP

1 – 3 mg/L = moderate elevation of CRP

>3mg/L = high elevation of CRP.

TROPONIN T:

For the estimation of Troponin T, standard card test by Roche diagnostics, COBAS card is used.

METHOD:

Patients blood dample is collected by phlebotomy and mixed with EDTA. The EDTA mixed blood about 100 microliter is taken using a micro pipette and placed in the well provided in the card and wait for 15 minutes.

The result should be read exactly at 15 min. positivity is indicated by two lines – control and test. Negativity is indicated by single line. If the card reads positive, the value of Troponin T is >0.1ng/ml and if the card reads negative, the serum value of troponin is <0.1ng/ml.

After obtaining all the necessaryparameters, a detailed analysis of date was performed. Univariate analysis was done by chi square test and multivariate analysis by logistic regression.

TABLES AND CHARTS

TABLES AND CHARTS

AGE

Age		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	35	1	1	1	1
	40	1	1	1	2
	44	1	1	1	3
	45	2	2	2	5
	46	1	1	1	6
	49	2	2	2	8
	50	2	2	2	10
	52	4	4	4	14
	53	3	3	3	17
	54	1	1	1	18
	55	6	6	6	24
	56	5	5	5	29
	57	2	2	2	31
	58	10	10	10	41
	59	3	3	3	44
	60	4	4	4	48

	61	1	1	1	49
	62	5	5	5	54
	63	4	4	4	58
	64	2	2	2	60
	65	11	11	11	71
	66	3	3	3	74
	67	2	2	2	76
	69	1	1	1	77
	70	3	3	3	80
	72	5	5	5	85
	73	3	3	3	88
	74	3	3	3	91
	75	2	2	2	93
	77	1	1	1	94
	78	1	1	1	95
	79	2	2	2	97
	82	1	1	1	98
	85	2	2	2	100
	Total	**100**	**100**	**100**	

SEX

.SEX					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	E	1	1	1	1
	F	35	35	35	36
	M	64	64	64	100
	Total	100	100	100	

APHASIA

APHASIA					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	65	65	65	65
	2	35	35	35	100
	Total	100	100	100	

APHASIA

APHASIA					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	-	62	62	62	62
	+	38	38	38	100
	Total	100	100	100	

CONJUGATE DEVIATION

CONJUGATE GAZE DEVIATION					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	62	62	62	62
	1	38	38	38	100
	Total	100	100	100	

CONJUGATE DEVIATION

CONJUGATE GAZE DEVIATION					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	-	62	62	62	62
	+	38	38	38	100
	Total	100	100	100	

HSCRP +VE

.HSCRP+ve					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	62	62	62	62
	1	38	38	38	100
	Total	100	100	100	

HSCRP -VE

.HSCRP-ve					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	-	56	56	56	56
	+	44	44	44	100
	Total	100	100	100	

TROP T +VE

TROT T +VE					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	56	56	56	56
	1	44	44	44	100
	Total	100	100	100	

TROP T -VE

TROP T -VE					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	<41	44	44	44	44
	>60	8	8	8	52
	41-60	48	48	48	100
	Total	100	100	100	

BARTHEL INDEX

BARTHEL INDEX					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	<41	44	44	44	44
	>60	8	8	8	52
	41 to 60	48	48	48	100
	Total	100	100	100	

FREQUENCY TABLE

AGE

Particular	**No.of respondents (n=100)**	**Percentage (100%)**
Below 40yrs	2	2.0
41 to 50yrs	8	8.0
51 to 60yrs	38	38.0
61 to 70yrs	32	32.0
71yrs & above	20	20.0

SEX

Particular	**No.of respondents (n=100)**	**Percentage (100%)**
Male	64	64.0
Female	36	36.0

APHASIA

Particular	**No.of respondents (n=100)**	**Percentage (100%)**
Negative	62	62.0
Positive	38	38.0

CONJUGATE GAZE DEVIATION

Particular	**No.of respondents (n=100)**	**Percentage (100%)**
Negative	62	62.0
Positive	38	38.0

HSCRP

Particular	**No.of respondents (n=100)**	**Percentage (100%)**
Negative	56	56.0
Positive	44	44.0

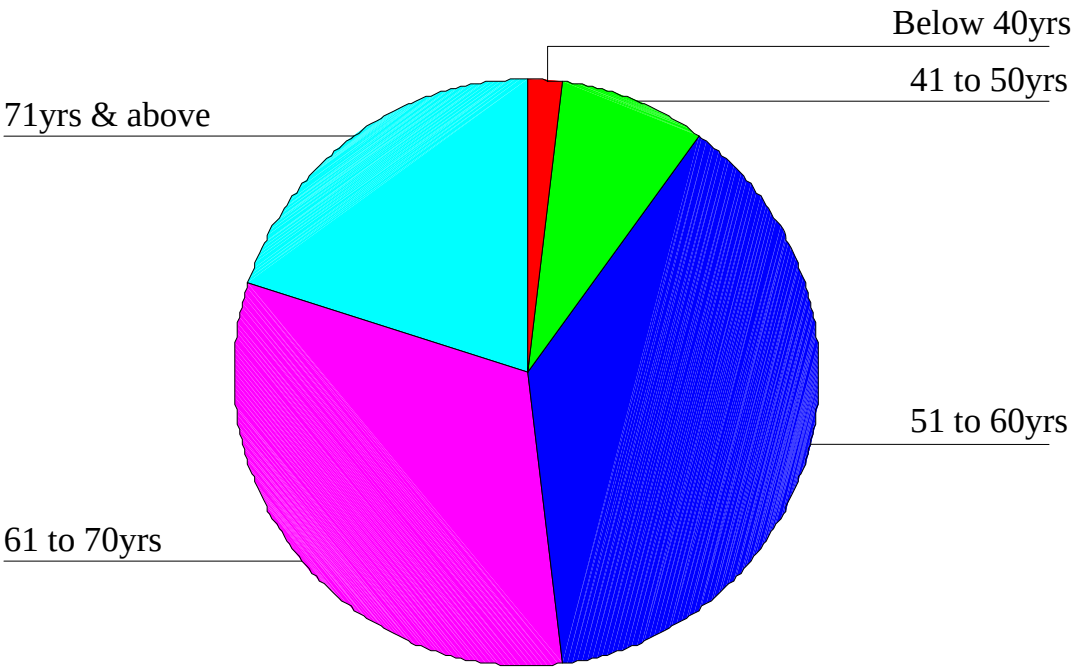
TROP T

Particular	**No.of respondents (n=100)**	**Percentage (100%)**
Negative	81	81.0
Positive	19	19.0

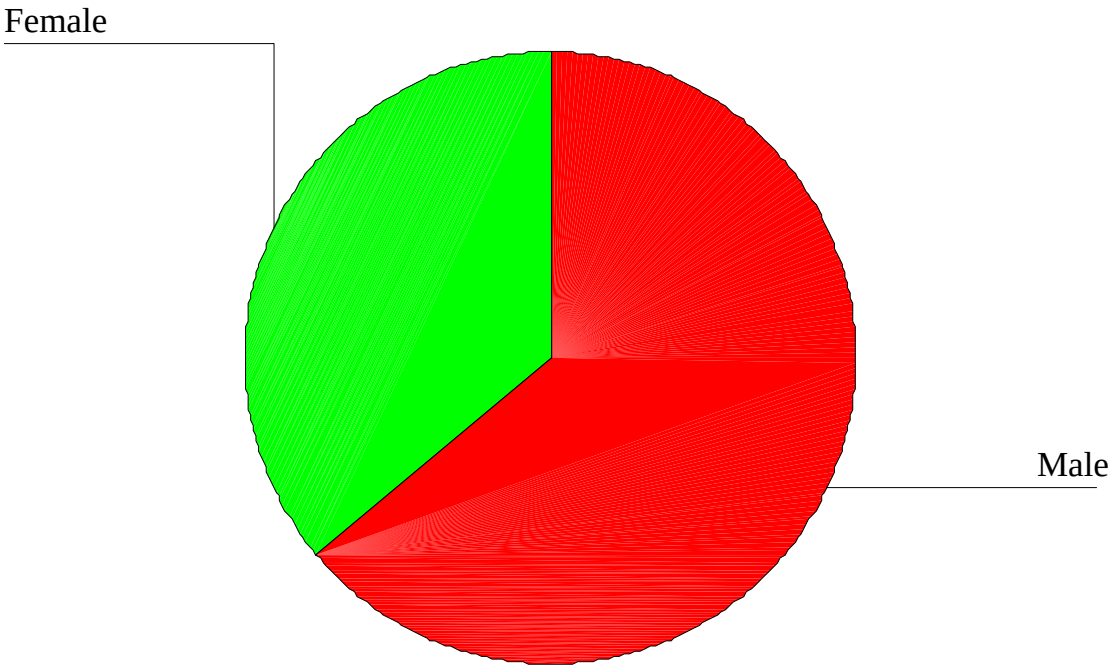
BARTHEL INDEX

Particular	**No.of respondents (n=100)**	**Percentage (100%)**
Below 41	44	44.0
41 to 60	48	48.0
61 & above	8	8.0

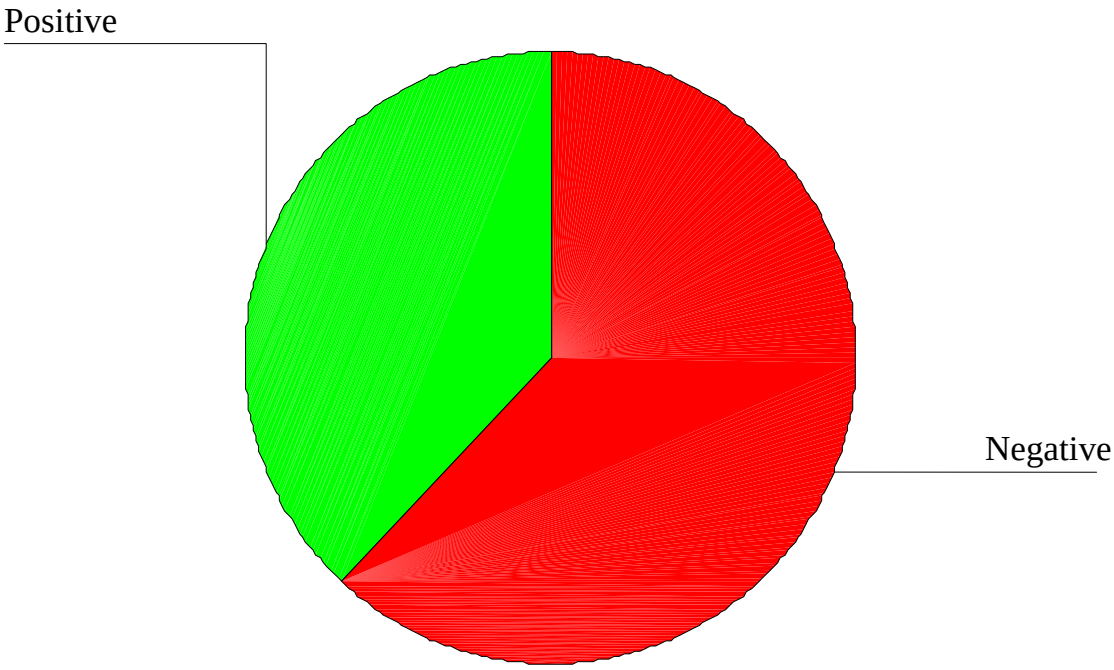
AGE



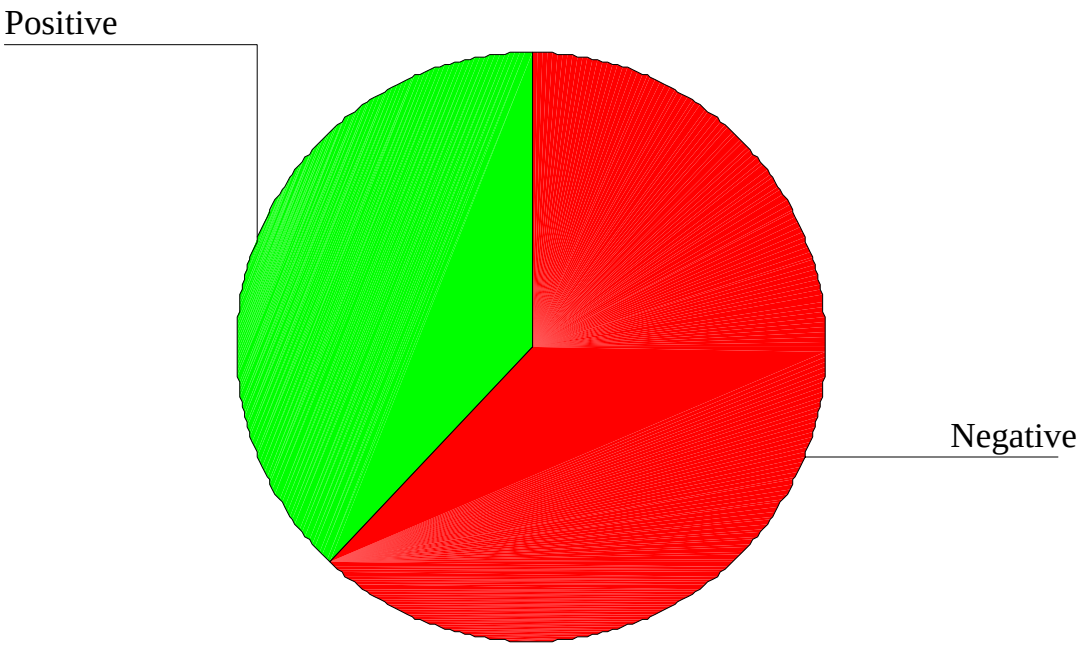
SEX



APHASIA



CONJUGATE GAZE DEVIATION



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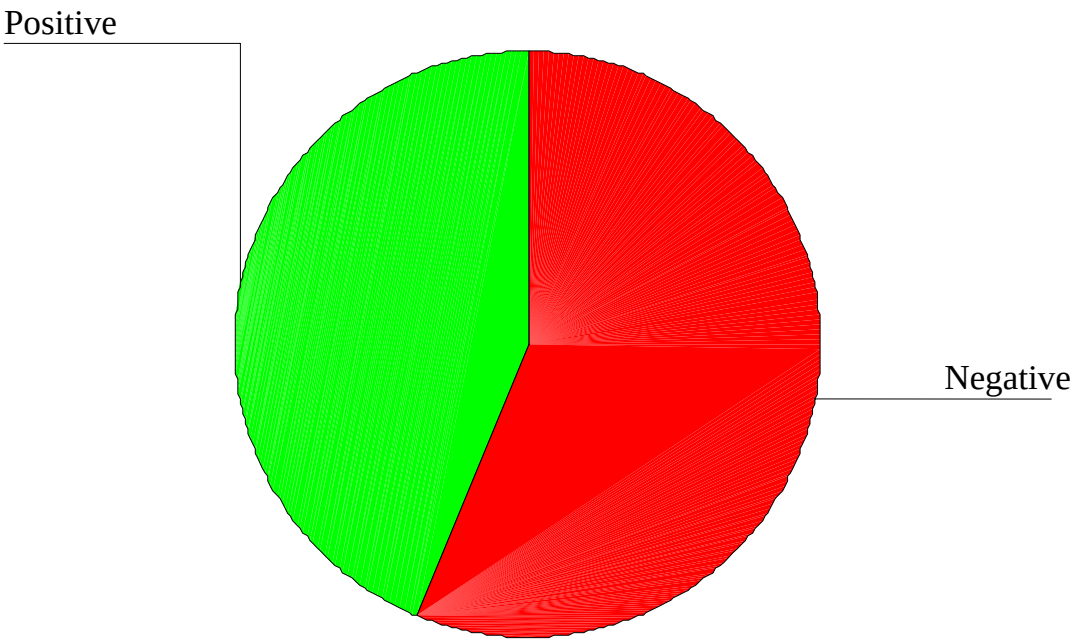
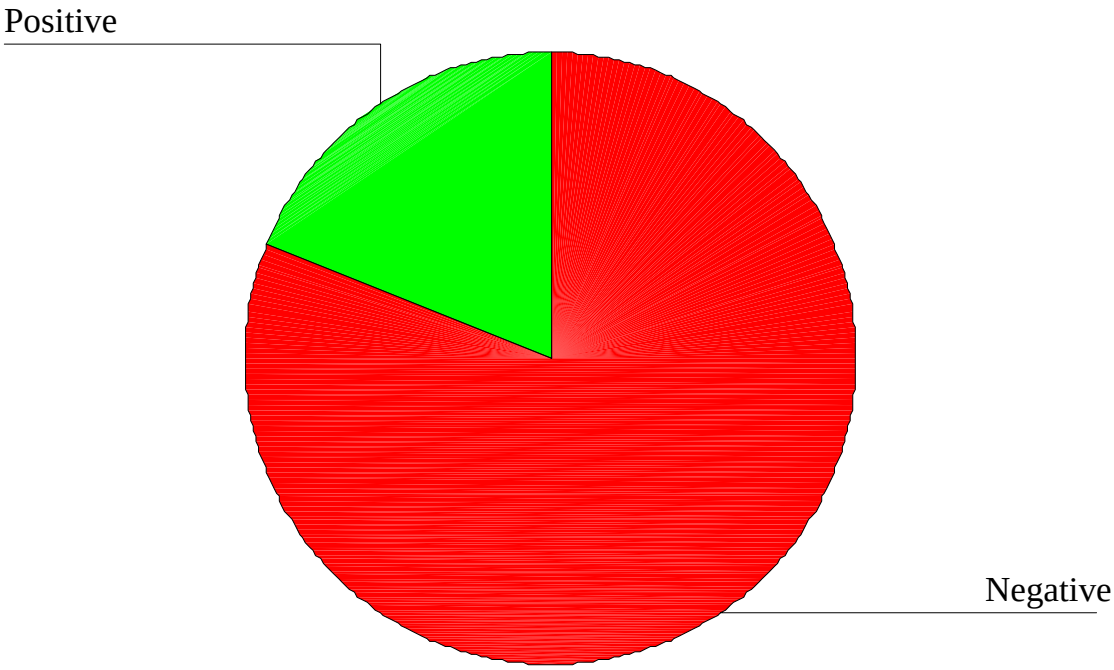
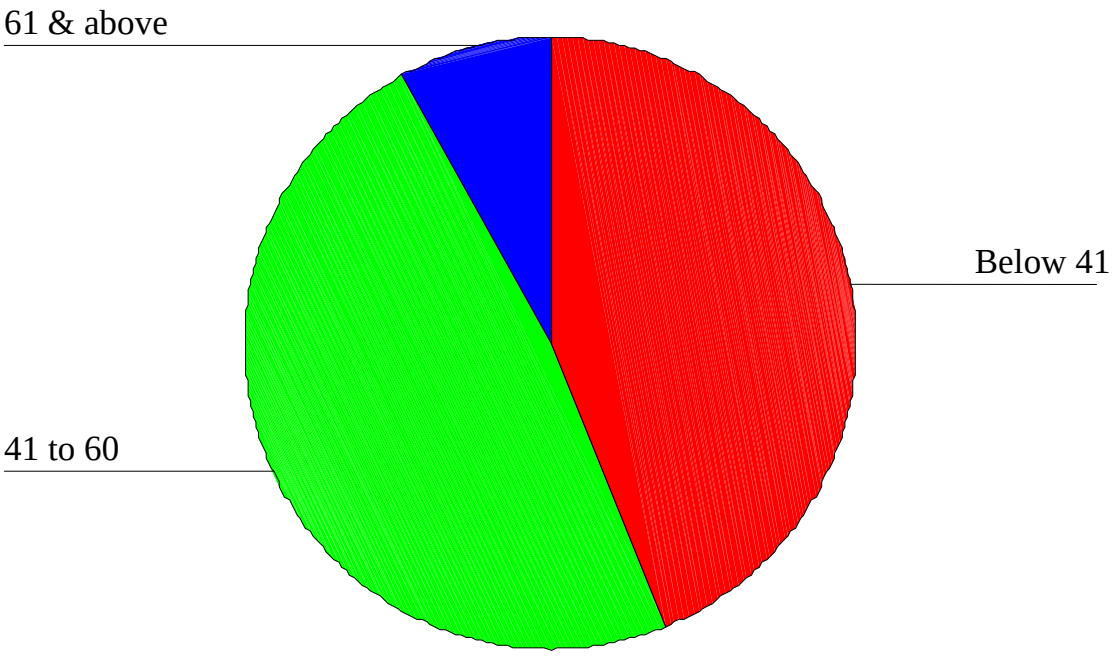


TROP T (+Ve/-Ve)



BARTHEL INDEX



Chi-Square Tests

	SEX						**Statistical inference**
	Male		**Female**		**Total**		
	(n=64)	**(100%)**	**(n=36)**	**(100%)**	**(n=100)**	**(100%)**	
APHASIA							
Negative	40	62.5%	22	61.1%	62	62.0%	X^2=.019
Positive	24	37.5%	14	38.9%	38	38.0%	Df=1 .891>0.05 Not Significant
CONJUGATE GAZE DEVIATION							
Negative	40	62.5%	22	61.1%	62	62.0%	
Positive	24	37.5%	14	38.9%	38	38.0%	X^2=..019 Df=1 .891>0.05 Not Significant

HSCRP							
Negative	35	54.7%	21	58.3%	56	56.0%	X^2=..124 Df=1 .724>0.05 Not Significant
Positive	29	45.3%	15	41.7%	44	44.0%	
TROP T (+Ve/-Ve)							
Negative	53	82.8%	28	77.8%	81	81.0%	X^2=..379 Df=1 .538>0.05 Not Significant
Positive	11	17.2%	**8**	**22.2%**	19	19.0%	
BARTHEL INDEX OUTCOME AFTER 4 WEEKS							
Below 41	28	43.8%	16	44.4%	44	44.0%	X^2=..831 Df=2 .660>0.05 Not Significant
41 to 60	32	50.0%	16	44.4%	48	48.0%	
61 & above	4	6.3%	4	11.1%	8	8.0%	

Chi-Square Tests

	BARTHEL INDEX								Statistical inference
	Below 41		41 to 60		61 & above		Total		
	44	**100.0%**	**48**	**100.0%**	**8**	**100.0%**	**100**	**100.0%**	
APHASIA									
Negative	14	31.8%	40	83.3%	8	100.0%	62	62.0%	X^2=31.188 Df=2 .000<0.05 Significant
Positive	30	68.2%	8	16.7%	0	.0%	38	38.0%	
CONJUGATE GAZE DEVIATION									
Negative	14	31.8%	40	83.3%	8	100.0%	62	62.0%	X^2=31.188 Df=2 .000<0.05 Significant
Positive	30	68.2%	8	16.7%	0	.0%	38	38.0%	

HSCRP									
Negative	14	31.8%	34	70.8%	8	100.0%	56	56.0%	X^2=21.014 Df=2 .000<0.05 Significant
Positive	30	68.2%	14	29.2%	0	.0%	44	44.0%	
TROP T (+Ve/-Ve)									
Negative	35	79.5%	38	79.2%	8	100.0%	81	81.0%	X^2=18.042 Df=2 .019<0.05 Significant
Positive	9	20.5%	10	20.8%	0	.0%	19	19.0%	

BARTHEL INDEX OUTCOME AFTER 4 WEEKS

BARTHEL INDEX	<41	>41	Total	ChiSquare test
hsCRP +ve	30	14	44	P = 0.11846
Trop T +ve	9	10	19	>0.05
Total	39	24	63	

Statistics

AGE	**Mean**	**Median**	**S.D**	**Mini.**	**Max.**
	61.88	62.00	9.551	35	85

DISCUSSION

DISCUSSION

100 patient s satisfied all the above criteria were included

Males 64

Females 36

The following observations were made out of the 100 patients

44 were hsCRP +ve

19 were trop T +ve

1. % level of hsCRP + in males is 45.3

   % level of hsCRP + in females 41.7

   For the above data we did Chi square test

   X2 = .724 p value > 0.05. So sex does not influence the hsCRP value of the patient.

2. There is no association between the age of patient and hsCRP x2= 0.674 here also P value >0.05. So age factor does not influence the group pattern.
3. Severe disability is more in hsCRP +ve compared to – ve group.
4. All patients who had aphasia at the time of admission were hsCRP +ve

5. All patients who had conjugate gaze deviation were hsCRP +ve and belong to severely disabled group. Follow up was done at the end of 4 weeks and the following observation made during follow up. Barthel index at day 1 was found to correlate with that at 4 weeks.
6. During the follow up 68.2% of the hsCRP +ve belonged to severely disabled group. 29.2% of the hsCRP +ve belonged to moderately disabled group.
7. All the persons in mildly disabled group were hsCRP –ve.
8. If at admission the uperlimb power is less than MRC grade 4 or aphasia or conjugate gaze deviation was present, these patients belonged to the severely diabled group.
9. If at admission the upperlimb or lower limb power was greater than MRC grade 3 or no aphasia or hsCRP – ve, then at 6 months these patients belonged to the mildly disabled group.
10. % level of Trop T + in males is 17.2

% level of Trop T + in females 22.2

For the above data we did Chi square test

X2 = .538 P VALUE > 0.05. So sex does not influence the trop t value of the patient

11. There is an association between the age of patient and Trop T x2= 0.0 here also P value >0.05. So age factor does influence the group pattern.
12. Severe disability is more in Trop T +ve compared to – ve group.
13. 50% of patients who had aphasia at the time of admission were Trop T +ve
14. 50% patients who had conjugate gaze deviation were Trop T +ve and belong to severely disabled group. Follow up was done at the end of 4 weeks and the following observation made during follow up. Barthel index at day 1 was found to correlate with that at 4 weeks.
15. During the follow up 20.5% of the Trop T +ve belonged to severely disabled group. 20.8% of the Trop T +ve belonged to moderately disabled group.
16. All the persons in mildly disabled group were Trop T –ve.
17. If at admission the uperlimb power is less than MRC grade 4 or aphasia or conjugate gaze deviation was present, these patients belonged to the severely diabled group.
18. 68.2% of the severely disabled group are hsCRP +ve and 20.5% of the severly disabled group are Trop T +ve and doing the Chi square test for these values show P 0.1185 which is >0.05 and hence either hsCRP or Troponin T test have no better significance in predicting the morbidity outcome in ischaemic stroke.

CONCLUSION

CONCLUSION

1. hsCRP & Trop T+ve is increased in a significant fraction of ischaemic stroke.
2. Increase in hsCRP & Trop T is independent of age.
3. Increase in hsCRP is independent of sex.
4. But Trop T is dependent on age elevated in old age.
5. Patients with increased hsCRP & Trop T+ve had invariably more deficit during admission.
6. Patients with low hsCRP & Trop T –ve had mild deficit during admission and have good prognostic outcome at 4 weeks after onset of stroke.
7. Patients with increased hsCRP & Trop T+ve had severe disability when compared with patients with normal levels, 4 weeks after onset of stroke.
8. hsCRP and Trop T has no better advantage over one another in predicting the morbidity in ischaemic stroke, but Trop T card test is cheaper the hsCRP assay can be taken into consideration.

PROFORMA

PROFORMA

Name: Ward:

Age: Unit:

Sex: IP No:

Date of admission:

Address

Complaints:

History of present illness:

Mode of onset:

Activity at the time of onset:

Time of onset:

Associated symptoms:

Head ache, vomiting, loss of consciousness, seizures

Past

Family history

General examination

Pulse:

BP:

CNS Examination:

Hemiparesis

Speech

Power

Conjugate gaze deviation

Barthel index

Risk factors

Obesity

Diabetes mellitus

Hypertension

Ischaemic heart disease

Smoker

Alcoholism

Hypercholesterolemia

INVESTIGATIONS

Blood sugar

Urea

Creatinine

Lipid profile

CT scan Brain

VDRL

HS CRP

Troponin T

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MASTER CHART

MASTER CHART

Sl.No:	NAME	AGE	SEX	APHASIA	CONJUGATE GAZE DEVIATION	HSCRP	TROP T	BARTHEL INDEX
1	RAMANI	72	M	+	+	+	+	<41
2	DURAISAMY	65	M	+	+	+	-	<41
3	ANGAMMAL	62	F	+	+	+	-	<41
4	SELVIN	65	M	+	+	+	-	<41
5	SELVARAJ	62	M	-	-	-	-	41-60
6	THANUMALAYAN	62	M	-	-	-	-	41-60
7	VENKATESH	73	M	-	-	-	+	41-60
8	AMEENA BEEVI	55	F	-	-	-	-	41-60
9	MANIKANDAN	59	M	+	+	+	-	<41
10	ANNAMAL	58	F	-	-	-	-	41-60
11	RANI	77	F	-	-	-	+	41-60
12	MUTHUKRISHNAN	56	M	+	+	-	-	41-60
13	GOPI	52	M	+	+	+	-	<41
14	VENKATESH	52	M	-	-	+	-	41-60
15	PUSHPAM	53	F	+	+	+	-	<41
16	SAROJA	65	F	-	-	-	-	41-60
17	KALIAPPAN	66	M	-	-	-	-	41-60
18	KADARKARAI	58	M	+	+	+	-	<41
19	MANGAMMAL	63	F	-	-	-	-	41-60
20	SELVAMMAL	75	F	-	-	-	+	41-60
21	SUDALAI	50	M	-	-	+	-	41-60
22	RAVI	65	M	-	-	-	-	41-60
23	SHANTAMMAL	56	F	+	+	+	-	<41
24	MAHESWARI	55	F	-	-	-	-	41-60
25	LAKSHMIAMMAL	49	F	-	-	-	-	>60
26	ANTHONY	62	M	-	-	-	-	41-60
27	SAMUEL	61	M	-	-	-	-	41-60
28	JEYARANAI	57	F	-	-	+	-	41-60

29	KASTHURI	74	F	-	-	-	+	41-60
30	SANKARI	58	F	+	+	+	-	<41
31	GURUVAMMAL	52	F	+	+	+	-	41-60
32	KASTHURIRENGAN	63	M	-	-	-	-	<41
33	SHENBAGARAJAN	79	M	-	-	-	-	41-60
34	PERUMAL	35	M	+	+	+	-	<41
35	PERUMAL	60	M	+	+	+	+	41-60
36	POOVAMMAL	45	F	-	-	-	-	<41
37	SHENBAGARAJAN	58	M	-	-	-	-	>60
38	ALAGARSAMY	70	M	+	+	+	-	<41
39	MURUGAN	44	M	-	-	-	-	>60
40	THANGAM	70	M	+	+	+	+	41-60
41	RAJASEKAR	45	M	-	-	-	-	<41
42	TIRUVAIMOZHI	53	M	-	-	-	-	<41
43	ESAKITHEVAR	60	M	+	+	+	-	<41
44	JANAKI	55	F	+	+	+	-	<41
45	RAMRAJ	40	M	-	-	-	-	>60
46	PAULRAJ	55	M	-	-	-	-	<41
47	ARUMUGAM	57	M	-	-	-	-	<41
48	SANKARAN	46	M	-	-	-	-	<41
49	RAMASAMY	85	M	+	+	+	+	<41
50	ALWAR	50	M	-	-	+	-	41-60
51	MUTHUSAMY	65	M	+	+	+	-	<41
52	SUCHINDRAN	65	M	+	+	+	-	<41
53	THANGAMUTHU	67	F	+	+	+	+	<41
54	BAGAVATHY	74	E	+	+	+	+	<41
55	LOURDUMARY	58	F	-	-	-	-	41-60
56	CHARLES THANGAM	69	M	-	-	-	-	41-60
57	JEBA SINGH	55	M	+	+	-	-	41-60
58	KANNIMARIAL	72	F	+	+	+	+	<41
59	SUDHAGARAN	65	M	-	-	+	-	41-60
60	KANCHANA	59	F	+	+	+	-	<41
61	NAGARAJAN	70	M	-	-	-	+	41-60
62	GEETHA	72	F	-	-	-	-	41-60

63	ANTHONY MUTHU	54	M	-	-	-	-	41-60
64	SRIDHARAN	64	M	+	+	+	-	<41
65	ESAKKIMUTHU	58	M	-	-	-	-	41-60
66	DAVID RAJA	65	F	-	-	-	-	41-60
67	CHARLES	56	M	-	-	-	-	41-60
68	CHANDRASEKAR	85	M	+	+	+	+	<41
69	KEERTHANA	60	F	-	-	-	-	41-60
70	SAVERIYAR	53	M	-	-	-	-	41-60
71	BENEDICT	79	M	-	-	-	+	41-60
72	MOSES	60	M	-	-	-	-	41-60
73	BENJITHSON	52	M	-	-	+	-	41-60
74	CHRISTY	66	F	-	-	-	-	41-60
75	ANANDA NADAR	58	M	+	+	+	-	<41
76	MURALIDARAN	65	M	-	-	+	+	41-60
77	PRADEEPAN	59	M	-	-	-	-	41-60
78	THANUPERUMAL	72	M	+	+	+	-	<41
79	THABASI	62	M	-	-	-	-	41-60
80	MARGARET	56	F	-	-	-	-	>60
81	LAKSHMIAMMAL	65	F	-	-	-	-	<41
82	SURESH	58	M	-	-	-	-	>60
83	DHANALAKSHMI	63	F	+	+	+	-	<41
84	RADHIKA	65	F	-	-	-	-	>60
85	SIVARAMAN	78	M	+	+	+	+	41-60
86	ANADAGIRIVASAN	58	M	+	+	+	-	41-60
87	EUGIN	75	F	-	-	-	-	<41
88	GURUVAMMAL	58	F	-	-	-	-	41-60
89	ROBINSON	73	M	+	+	+	+	<41
90	SINGAPERUMAL	56	M	+	+	+	-	41-60
91	SENTHIL KUMAR	64	M	-	-	-	-	<41
92	THOMSUN	55	M	-	-	-	-	<41

93	BAGAHAVTHY	74	F	+	+	+	+	<41
94	AROCKIAMARY	82	F	+	+	+	-	<41
95	SUSEELA	49	F	-	-	-	-	>60
96	THANGAPPAN	63	M	-	-	-	-	<41
97	SORNAM	73	M	-	-	-	-	<41
98	RAMANI	66	M	-	-	-	-	<41
99	SIVAGAMI	72	F	+	+	+	+	<41
100	SRIDARAN	67	M	-	-	+	-	41-60

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Office of the Dean,
Kanyakumari Govt. Medical College,
Asaripallam 629 201.

Dated 09.04.2015

Sub: Medical Education – Kanyakumari Govt. Medical College, Asaripallam – Ethical Committee approval - permission granted to II Year PG Students – Regarding.

Ref: 1. G.O. (D) No. 648 H&FW (MCA) Dept. dated 20.06.2009.
2. Individual application dated 30.01.2015
3. G.O. (D) No. 1258 dated 20.11.2014

In accordance with the powers delegated in the Govt. order cited, permission is granted to the following PG Candidates of MD General Medicine of Kanyakumari Govt. Medical College, Asaripallam to do the Project work regarding their dissertation on the following subjects.

1. ROLE OF HIGH SPECIFIC CRP AND TROPONIN T IN ACUTE ISCHAEMIC STROKE – BY Dr. U. Nagarajan, MD (General Medicine)
2. PULMONARY FUNCTION TESTS IN TYPE -2 DIABETICS AND NON-DIABETICS – A COMPARATIVE STUDY – with specification of Exclusive criteria Investigation of Echo/FB/PPBS- By Dr. M. Ilamaran (MD General Medicine)
3. PROGNOSTIC SIGNIFICANCE OF MEAN PLATELET VOLUME IN PATIENTS WITH ST ELEVATION MYOCARDIAL INFARCTION – with inclusion of comparative study between diabetic and Non-diabetic patients – By Dr. M. V. Indhuja (MD General Medicine) in the department of Thoracic Medicine, Biochemistry, Neurology, Microbiology and Pathology of Kanyakumari Govt. Medical College, Asaripallam with effect from...13:....04.2015 during their study period.

DEAN

To
The II Year MD (General Medicine) PG Students –
1. Dr. U. Nagarajan,
2. Dr. M. V. Indhuja
3. Dr. M. Ilamaran

through HOD of Medicine, KGMC, Asaripallam

Copy to
1. The HOD of Medicine, Thoracic Medicine, Neurology, Biochemistry, Microbiology and Pathology.
2. RMO/ARMO/MS/DS-KGMCH, Asaripallam

Professor and HOD, Department of MEDICINE

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7.	One legal expert	:	Mrs. Shahila Pravin, Advocate, 9442112719. E-mail Id :shahilapravin@gmail.com
8.	One Social Scientist / Representation of Govt. Voluntary Agency	:	Dr. A. Burlington IMA Secretary / Rotarian, 43A5/06, North Street, Ranithottam, Nagercoil – 629001. 9443204537.
9.	One Business man	:	Thiru. S. Rajamoni, Sujha Surgicals Nagercoil E.mail Id : sujhasur@rediffmail.com
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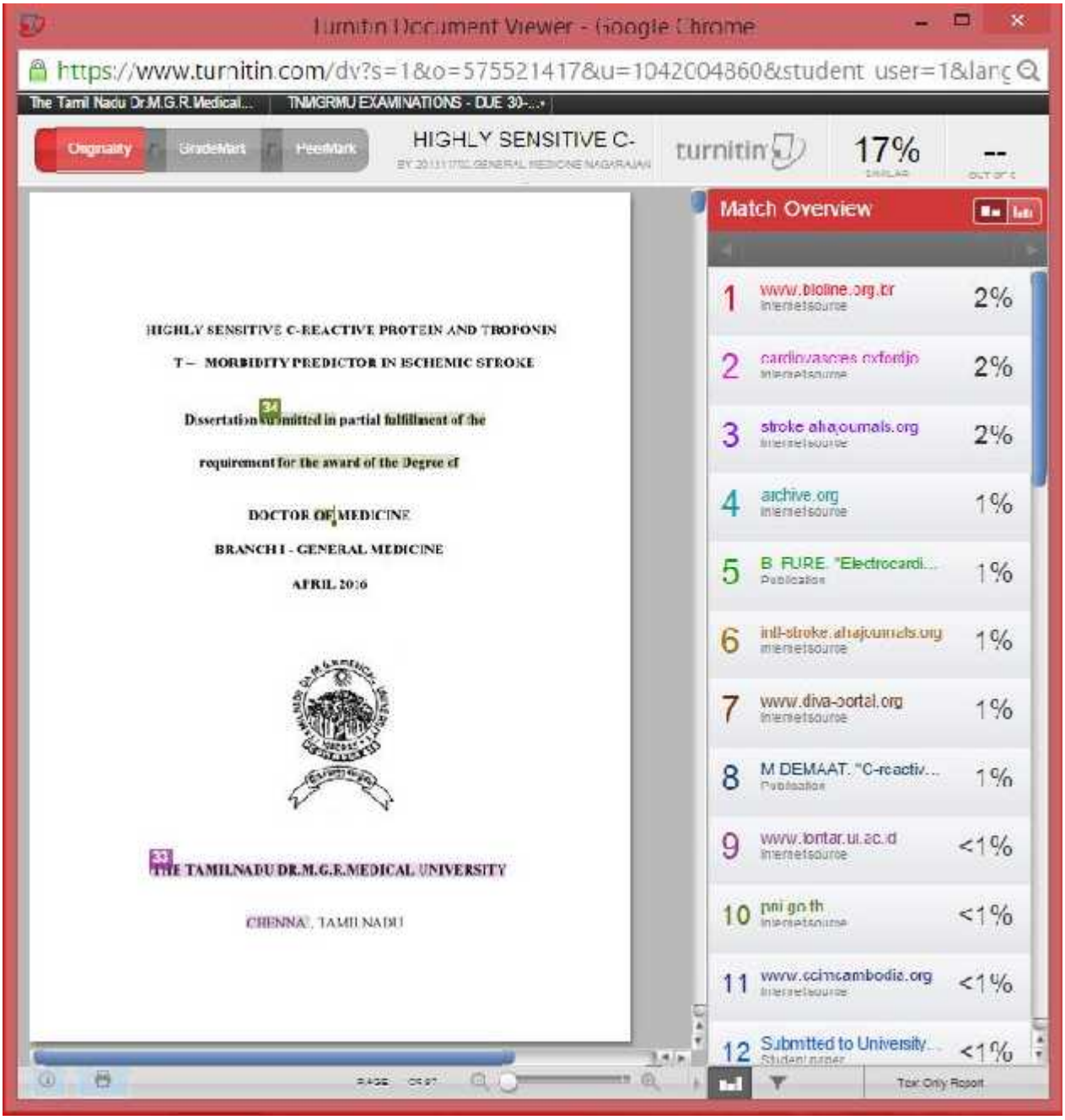
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