"SILENT BRAIN INFARCTS IN PATIENTS WITH NON SPECIFIC NEUROLOGICAL SYMPTOMS - A ONE YEAR CROSS SECTIONAL STUDY AT KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE"

By

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Dissertation

Submitted to the
KLE University, Belgaum, Karnataka

In Partial Fulfillment
of the requirements for the degree of

M. D.

in

GENERAL MEDICINE

Under the Guidance of

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MAY - 2012

KLE UNIVERSITY, BELGAUM,

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LIST OF ABBREVIATIONS USED

BP	-	Blood pressure
CBF	-	Cerebral blood flow
$CMRO_2$	-	Cerebral metabolic rate for oxygen
DBP	-	Diastolic blood pressure
ESR	-	Erythrocyte sedimentation rate
HDL	-	High density lipoprotein
hsCRP	-	High sensitivity C reactive protein
IFG	-	Impaired fasting glucose
LADIS	-	Leukoariaiosis and disability study
LDL	-	Low density lipoprotein
LVD	-	Large vessel disease
MMSE	-	Mini mental scale examination
NSCL	-	Non specific neurological complaints
OEF	-	Oxygen extraction fraction
SBI	-	Silent brain infarcts
SBP	-	Systolic blood pressure
SIVD	-	Subcortical ischemic vascular disease
SVD	-	Small vessel disease
TGL	-	Triglycerides
TNF α	-	Tumor necrosis factor alpha
WMH	-	White matter hyperintensities
WML	-	White matter lesion

ABSTRACT

Background and objectives

Silent brain infarction is considered a preclinical warning of symptomatic strokes and brain damage related to multiple deep infarcts. Present study was done to find the relation between silent brain infarcts (SBI) and non specific neurological complaints (NSCL), association of risk factors with SBI and association of high sensitivity C-reactive protein (hsCRP).

Methodology

The present one year cross sectional study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on 51 patients presenting with NSCL attending Medicine Outpatient and Inpatient Departments during the period of January 2010 to December 2010. All the relevant investigations were done and patients were evaluated with a 1.5 telsa Siemens symphony.

Results

Out of 51 patients, 26 (50.98%) were males and 25 (49.02%) were females. Patients were higher (31.37%) in the 31-45 years age group. Headache was the most common (54.90%) NSCL. 6 patients (11.76%) were obese and 4 patients (7.84%) were overweight. Most common risk factor was hypertension in 7 patients (13.78%). 13 patients (25.49%) had a mild decrease in the mini mental scale examination scores. A total of 14 patient's (27.44%) presented with SBI. Out of which 11 patients (21.57%) had subcortical infarcts and 4 patients (7.84%) had cortical infarcts and one patient among the group had both cortical and

subcortical infarct. 31 patients (60.78%) had HDL levels < 40 mg/dL, 15 patients (29.4%) presented with raised triglyceride levels and 32 patients (62.75%) had raised hsCRP levels.

Interpretation and conclusion

Patients presenting with non specific neurological complaints have to be evaluated at the earliest to detect silent brain infarcts which is a risk factor for major stroke.

Keywords

High sensitivity C reactive protein; Non specific neurological complaints; Silent brain infarcts; Stroke

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Chapter 1

Introduction

INTRODUCTION

Silent brain infarcts (SBI) are parenchymal lesions that have the MRI characteristics of previous infarcts that have not been associated in that individual with clinical signs or symptoms of stroke.[1]

A silent brain infarct is now classified as a type III cerebrovascular disorder by the National Institute of Neurological Disorders and stroke; is a specific marker of target organ damage in the brain and a powerful predictor of clinical stroke.[2]

Silent brain infarction (SBI), is considered a preclinical warning of symptomatic strokes and brain damage related to multiple deep infarcts. To prevent these further disabling diseases, it is very important to characterize and manage this preclinical stage of cerebrovascular disease.[3]

Upto half of patients with vascular risk factors are harbouring SBI's on MRI and with first ever ischemic stroke; this percentage was as high as 57% in old patients.[4]

Silent lacunar strokes occur in as many as one-third of people over the age of 65, and more than double the risk for development of dementia, particularly when present in the thalamus.[5]

Inflammatory processes are involved in all stages of the development of atherosclerosis. C-reactive protein is a sensitive marker of systemic low grade inflammation.[6]

It has been identified as an independent predictor of clinical end points such as myocardial infarction and stroke, and has been linked to an increased risk of Alzheimer disease and vascular dementia.[6]

Histopathological findings showed that CRP has direct prothrombotic and proatherosclerotic effects, suggesting it is primarily related to executive function; the cognitive function most vulnerable to vascular diseae.[7]

A study demonstrated an association of CRP with cerebral small vessel disease as measured by white matter hyper intensities (WMH) and presence of silent brain infarcts.[6]

Another study showed that hsCRP as a inflammatory marker in cardiovascular, atheroembolic events and stroke and a recent Japanese study proved its significance in silent brain infarcts.[7]

Higher plasma levels of CRP and IL-6 were associated with increased risk of silent brain infarcts in two independent cohorts of elderly Japanese.[8]

Patients with silent brain infarcts showed decreased cerebral blood flow (CBF) and metabolic rate for oxygen ($CMRO_2$) in deep grey matter. On the other hand decreased CBF with milder increased Oxygen extraction fraction (OEF) resulting in pursued $CMRO_2$ in the cerebral cortex which indicates the presence of occult misery perfusion; suggesting that patients with SBI have reduced cerebral perfusional reserves.[9]

Arteriosclerosis of small cerebral arteries is reported to the closely related to development of silent brain infarcts.[9]

Age, male sex and hypertension were independently associated with silent brain infarction. Subclinical brain infarcts are more prevalent than symptomatic infarcts and may increase the true public health burden of stroke.[10]

Hypertriglyceridaemia and large waist circumference were significant risk factors for silent brain infarction.[11]

Independent of the other components hypertriglyceridaemia should attract attention as a modifiable factor that might contribute to the vascular pathology of lacunar infarction, irrespective of elevated blood pressure (BP) and impaired fasting glucose (IFG).[11]

A study reported that, systolic blood pressure (SBP), diastolic blood pressure (DBP) and pulse pressure were associated with presence of silent brain infarcts.[12]

In view of the above, the present study was undertaken to find the relation between silent brain infarcts and non specific neurological complaints, association of risk factors with silent brain infarcts and association of high sensitivity C-reactive protein (hsCRP) with silent brain infarcts.

Chapter 2

Objectives

OBJECTIVES

The objectives of the present study were;

1. To find the relation between silent brain infarcts and non specific neurological complaints.
2. To find association of risk factors with silent brain infarcts.
3. To find association of high sensitivity C-reactive protein (hsCRP) with silent brain infarcts.

Chapter 3

Review of Literature

REVIEW OF LITERATURE

Silent Brain infarcts

Silent Brain infarcts or asymptomatic infarcts are sometimes detected incidentally by MRI or other imaging modalities in patients who demonstrate no localized neurological symptoms of stroke.[12]

Silent brain infarcts gradually increased with age from 8% in 60 to 64 year old participants to 35% in the oldest (85 to 90 years of age). Silent brain infarcts are five times as frequent as symptomatic infarcts.[12]

The majority of silent brain infarcts were lacunar, in which small vessel disease is thought to play an important role. The finding of Uehara et al that risk factors for silent infarcts in the white matter differed from those for basal ganglia also supports this.[13]

Cerebral white matter lesions and lacunar infarcts are caused by cerebral small vessel disease. Narrowing of the small vessel lumen and failure of cerebral autoregulation result in ischemic damage of the cerebral white and sub cortical gray matter.[14]

These lesions are commonly observed on MRI scans of elderly people and are associated with an included risk of stroke, dementia and depression.[14]

Cross sectional studies showed increased severity and a higher prevalence of white matter lesions and lacunar infarcts in older age. Hypertension is

considered as the main risk factor; but other cardiovascular risk factors may be related to these lesions as well.[14]

Cerebral small vessel disease (SVD) is a common cause of vascular cognitive impairment. The MRI surrogates of SVD include white matter lesions (WML) and lacunar infarcts in the deep gray and white matter.[15]

In the leukoariaiosis and disability study (LADIS) a total of 387 subjects were evaluated with repeated MRI and neuropsychological assessment at baseline and after three years. In this study out of the 387 subjects, 72 had one or more new lacunes evident in the follow up MRI, of these, 42 (58.3%) had one lacunae 16 (22.2%) two and 14 (19.4%) three to nine new lacunes. Thirty eight cases had new lacunes affecting the frontal, 15 parieto occipital, three temporal, 29 basal ganglia and 16 infratentorial region. The number of new lacunes correlated significantly with baseline number of lacunes, baseline WML volume and WML progression score. In this baseline study total number of lacunes had no individual contribution to cognitive change but in the final study that is after three years follow up they found that number of new lacunes and white matter lesion progression had a significant association with decline of speed and motor control; and executive functions compound scores.[16]

In the LADIS study[16] they found that strategic location of lacunes in basal ganglia or in subcortical white matter of the frontal lobes played no significant role in determining longitudinal cognitive change incremental to that of the overall lesion load, as the subject with new lacunars in these areas did not differ from other subjects with new lacunes. This was contrary to what was expected in

previous cross sectional studies[5] where they found that the lesions in thalamus and putamen/pallidum were associated with lower cognitive performance. The relationship of executive dysfunction with infarct affecting the frontal – sub cortical circuits has been shown in previous stroke patients.

The main finding they found in the LADIS study[16] was that longitudinal increase in lacunes parallels significantly steeper longitudinal decline in specific cognitive domains independent of the baseline white matter lesion volume. (WML), baseline number of lacunes, and progression of white matter lesions.

The LADIS study[16] has shown that subcortical ischaemic vascular disease (SIVD), as defined by extensive WML, and multiple lacunes on MRI is associated with progressive cognitive impairment and a considerable risk of dementia.

An observational cohort study[16] done between patients aged (15 – 49 years) with first severe ischaemic stroke at Helsinki University Central Hospital (1994-2007) showed an association between multiple MRI – defined SBI's and recurrent ischemic stroke which, appeared independently of the proportionally important vascular risk factors such as diabetes and stroke etiology.

Thus SBI's reflect a high risk cerebrovascular condition; not fully explained by any independent risk factor.[16]

In an observational cohort study[16] done at Helsinki Central University hospital (1994-2007) on 1800 consecutive patients aged 15 to 49 years with first

ever ischaemic stroke authors found that, 13% of the total patients had one or more silent brain infarcts and 5% of the patients presented with leukoaraiosis.

In this cohort study[16] out of the 1008 patients 86 patients had SBI out of which 46 had single and 40 multiple SBI's. They have found that cumulative risk for recurrent ischaemic stroke was significantly higher in patients with SBI's than in those without SBI's. Risk for the composite vascular end point was higher in patients with SBI's than in without SBI's.

Until recently there has been relative neglect of small vessel lacunar stroke over considered most benign ischemic stroke subtype with attention having been mainly focused on large artery cortical ischemic stroke; a trend reflected in the advances made in therapeutic options for stroke. The prognosis during the first few years for small vessel stroke is more favourable (in terms of survival and disability) than large vessel ischemic stroke; but in the long term there is a greater risk of death; stroke recurrence; cognitive dysfunction and dementia than previously realized, and a similar loss of quality adjusted life expectedly compared to large artery stroke.[17]

Silent infarcts, usually reflecting small vessel disease, are detected in 20% of healthy elderly people, and in upto 50% in selected series with patients having increase risk factors. They are associated with subtle physical and cognitive deficits and include the risk for subsequent stroke and dementia in the general population. These SBI's were surprisingly common in patients with < 45 years of age.[18]

Small vessel disease is attributed to alterations in the intima and media of cerebral arterioles, with hyaline deposition and fibrotic hardening, and is associated with leukoaraiosis, lacunar infarcts and intracerebral hemorrhages.[19]

In a study done by Mostofa K et al[19] they have studied 28 age matured subjects ten were controls, eight SVD patients and ten LVD patients. Authors defined SVD as a lacunar stroke, with exclusion of a large infarct by clinical examination, and CT or MRI, and the absence of cardio embolic cause or large vessel atherosclerosis. Cerebral LVD was defined as a large cerebral infarct in the cardio embolic disease. A hand held side stream dark field imaging microscope was used, with a 5X objective lens system connected to a video and recording unit. These image were digitalized and 4-6 sequences per subject were assessed with the microvascular flow index.

Flow was scored as absent (0); intermittent (1) sluggish (2) or continuous. The percentage of blood vessels in a video frame with a score less than three was called the abnormal flow index.[19]

They observed that non moving extravascular granular material around vessels with the same illumination properties as erythrocytes. (wave length 530 mm).[19]

In this study[19] they found that the lower number of perfused blood vessels in SVD patients is caused by temporary occlusion or obliteration of arterioles or capillaries was due to a novel abnormality. The novel abnormality found; extravascular erythrocyte material, which is strongly associated with cerebral SVD and probably consists of agglomerations of haemoglobin because it absorbs

green light (wave length 530 mm). Extravascular erythrocyte material may be a remnant of obliterated capillaries or caused by extravasation of erythrocytes. This phenomenon may be related to microbleeds found with MRI in cerebral small vessel disease.

A study[12] conducted at Netherlands between 1995 – 1996 proved that silent brain infarcts are five times as prevalent as symptomatic brain infarcts in the general population. Their prevalence increases with age and seems higher in women and hypertensive patients.

Silent brain infarcts were more frequent in patients who had end organ damage (heart, kidney, ocular fundi). The incidence of silent brain infarcts was 72 – 73% in patients with other organ involvement versus 33-39% in those without it. This proves that there is a relation between end organ damage and silent brain infarcts.[3]

Risk factors

In a study[3] done by Hidetaka H and Masayasu M et al. at Osaka University Hospital a total of 108 subjects were studied and SBI was found in 45 subjects (42%) patients of the silent brain infarcts were localised in the subcortical white matter or in the basal ganglia. There were no lesions in the internal capsule or cortical areas. One lesion was located in the infratentorial area (right cerebellum). The distribution of lesions was slightly higher in the right hemisphere in comparison to the left hemisphere.

The incidence of SBI tended to be higher in hypertensive patients (47%) than in normotensive subjects (33%). The incidence increased significantly with advancing age in hypertensive from 28% in the 50's age group; 44% in the 60's ; and 87% in the 70's ($p<0.1$), whereas no significant increase was noted in normotensive subjects. Authors found that the incidence of SBI was higher in patients with heart and kidney involvement (50% and 60% respectively) than in patients without such involvement. In the 60's the incidence was significantly higher in patients with heart and ocular fundi (s) damage. This was not clear in the 70's because patients without organ involvement had a high incidence of SBI lesions. The study found that SBI lesions in hypertensive patients were more frequently detected (47%) in the brain areas supplied by perforating arteries (basal ganglia, thalamus, semioval centre from in normotensive patients (24% $P < 0.05$). This showed that SBI lesions in hypertensive patiens were mainly distributed in the area of perforating arteries. SBI showed a higher incidence of cardiac disease (22% versus 4%) than those without cardiac disease.[3]

A study[2] done at Jichi medical school (Japan) showed that the prevalence of SBI and multiple silent brain infarcts increased three fold in hypertensive patients with diabetes mellitus independent of age and awake blood pressure (ABP). This was in accordance with previous reports that diabetes mellitus contributes to a two to four times greater incidence of symptomatic stroke.

A previous study[1] done at Boston medical centre proved that the prevalence of SBI varied with age. It was increasing from less than eight percent in the group aged 30 to 49 years to more than 15% at age 70 to 89 years. Single SBI occurred in 185 participants (84.1%) and were commonly located in the

basal ganglia (51.9%). SBI were subcortical in 34.8%, whereas 11% of lesions were cortical.[14]

In the Framingham study[1] Hypertension has consistently been implicated as a risk factor for SBI. Vermeer demonstrated more than two fold increase in SBI in the Rotterdam scan study. However Lee et al showed more than three fold increase in SBI prevalence in those with hypertension. At autopsy, Shinkawa et al found that SBI and non SBI brains differed significantly with regards to diastolic blood pressure measurements.[13]

In the North Manhattan study[10] a lower proportion of diabetes, hypertension and cardiac disease were associated with SBI. SBI were slightly more frequent on the right side than left and were primarily small lesions. Though the majority of SBI were located subcortical, 17% involved cortical structures. The most common brain region affected was the basal ganglia (30.61%) including the lentiform; caudate, thalamic nuclei, after common locations included frontal lobes, the internal, external capsules and parietal lobes.

The prevalence of SBI was greater among hypertensive compared to non hypertensive patients across all age groups, but especially in the youngest age group.[10]

Metabolic syndrome

In the study[11] done at Kochi Health Care Centre a total of 2076 patients aged 40 to 59 years of age a with no history of stroke or clinical symptoms

underwent MRI. Metabolic syndrome was defined according to National cholesterol education programme Adult treatment panel III report.

In this study[11] mean age of the subjects was 50.9 ± 5.5 years. There were 1093 men and 983 women. Number of subjects with Mets were 188 (9.1%). A total of 118 (5.7%) were diagnosed with SBI. Subjects with SBI were older (52.5 vs 50.9 years), male dominant (72.5 vs 51.5%) and were more likely to have Mets (37.3% vs 7.4%) in comparison with those without SBI). There was no significant difference between the two groups for prevalence of a past history of IHD (0.8% vs 0.9%) or current smokers (28.8% vs 28.7%).

A study[11] done at Kochi Health Care Centre, Japan in terms of Mets components, elevated BP, impaired fasting glucose, hypertriglyceridaemia, and large waist circumference were significantly associated with SBI independent of the inter relationship between the components. On the other hand, low HDL-C was not significantly associated with SBI when we grouped WC (waist circumference) into three categories with two cut offs cone used in the new IDF definition and other used in the NCEP ATP III definition, a large WC ≥ 102cm for men and ≥ 88 cm in women was significantly associated with SBI compared with a normal waist circumference (<90 cm in men, <80 cm in women). An intermediate waist circumference (≥ 90 cm and <102 cm for men, ≥ 80 and < 88 cm for women also increased the risk of SBI.

High sensitive C reactive protein (hsCRP)

Elevated CRP levels are not disease specific but are sensitive markers produced in response to tissue injury. Infectious agents, immunological stimuli and inflammation.[17]

Cytokines such as interleukin-1, interleukin-6 and Tumour necrosis factor (TNF-α) are highly correlated with CRP levels and their function.[17]

Elevated CRP levels may be related to cerebral white matter lesions and lacunar infarcts in different mechanisms.[17]

First, CRP levels may be a marker for arteriosclerosis or small vessel disease, as they are for other atherosclerosis.[17]

Arteriosclerosis may result in white matter lesions and lacunar infarcts through vessel occlusion, disturbed cerebral autoregualtion; or increases in vascular permeability.[17]

Although no inflammatory cells are observed in the vessel wall in case of arteriosclerosis, inflammatory endothelial activation may play a role in both small and large vessel disease.[17]

Increased levels of inflammatory endothelial markers have been reported in people with white matter lesions and lacunar infarcts.[17]

Second, inflammation may be a response to ischemic tissue damage.[17]

In a state of chronic low grade inflammation oligodendrocytes and neurons may be more susceptible to hypo perfusion and hence accelerate lesion progression.[17]

Third elevated CRP levels could reflect large vessel atherosclerosis.[17]

Cortical atherosclerosis is related to cerebral white matter lesions, probably by causing reduction of blood flow and by production of inflammatory mediators and few radicals that affect the microvascular endothelium.[17]

Furthermore, carotid atherosclerosis also reflects longstanding exposure to cardiovascular risk factors, which it shares with small vessel disease. Adjustment for carotid atherosclerosis and for cardiovascular risk factors did not change the association.[17]

Fourth, inflammatory processes are strongly related to and probably part of pathogenesis of Alzhiemers disease, in which white matter lesions and lacunar infarcts are frequently observed.[17]

In Rotterdam scan study[17,20] they found that CRP as a marker of inflammation may be involved in the pathophysiology of cerebral small vessel disease is in line with observations made in relation to stroke and dementia.

A study[18] done at Osaka university Hospital between April 2002 and December 2003 found that SBI is likely to be a manifestation of cerebral small vessel disease.

In this study[18] they found that hsCRP and IL-6 levels were higher in SBI patients than in those without SBI. The prevalence of SBI increased in a step wise fashion across the tertiles of hsCRP and IL-6 levels. Additionally, increases in such inflammatory markers are associated with higher likelihood for SBI and the association persisted when traditional cardiovascular risk factors were adjusted. These findings suggest the link between inflammation and SBI.

Chapter 4

Methodology

METHODOLOGY

The present study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on patients presenting with non specific neurological complaints attending medicine outpatient and inpatient departments during the period of January 2010 to December 2010**.**

Study design

Study design was one year cross sectional study**.**

Study period and duration

The present one year study was conducted during the period of January 2010 to December 2010**.**

Source of data

All the patients who fulfill the inclusion criteria, attending medicine Outpatient department and admitted under In patient department at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Sampling size and sampling method

A total of 51 patients who fulfill the inclusion criteria attending medicine Outpatient department and admitted under In patient department at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Selection criteria

Inclusion criteria

All patients enrolled are from Department of Medicine presenting with non specific neurological complaints like headache, vertigo, dizziness, tinnitus and syncope attending medicine Outpatient department and Inpatient department and are asymptomatic at the time of examination.

Exclusion criteria

1. Old cerebro vascular accident
2. Stroke
3. Infection
4. Patients with claustrophobia, valvular prosthesis, vascular clips, cardiac pacemakers, cochlear implants, and other implanted devices sensitive to strong magnetic fields were excluded.

Method of collection data

Ethical clearance

The study was approved by the Ethical and Research Committee of J. N. Medical College, Belgaum.

Informed consent

Based on the selection criteria, the patients were selected and written informed consent (Annexure I) was obtained.

All patients were enquired about non specific neurological complaints, previous history of major risk factors; pre-existing diseases such as diabetes mellitus, hypertension, ischaemic heart disease, smoking, alcohol, recent onset of any infections were asked.

Detailed general and neurological examination was done. Height and weight were recorded on predesigned and pretested proforma (Annexure II). Body mass index for obesity was calculated by measuring height and weight in light clothes and without shoes.

All routine investigations such as Hb%, total count, differential count and erythrocyte sedimentation rate (ESR), urine routine and microscopy fasting blood sugar, fasting lipid profile, MRI Brain (1.5 telsa), hsCRP and electrocardiogram were done.

MRI Technique

Patients were evaluated with a 1.5 telsa Siemens symphony. T-2 weighted double spine echo coronal weighted sequences were acquired in 3-5 mm contagious slices from nasion to occiput with a repetition time of 4500 milli seconds and echo time of 116 milliseconds. Only lesions larger than 3 mm were considered as silent brain infarcts. Lesions were also required to have cerebro spinal fluid density on subtraction images and to be distinctly separate from circle of Willis vessels for suspected basal ganglion infarcts. Investigators blinded to subject demographic and stroke risk factor data processed and analysed these scans.

hsCRP

hsCRP is one of the "acute phase" proteins the serum or plasma levels of which rise during a general, unspecific response to infections, and non infectious inflammatory process such as rheumatoid arthritis, cardiovascular disease, cerebro vascular disease and peripheral vascular disease. CRP is synthesized in liver and is normally present as a constituent of serum or plasma in various diseases states resulting in tissue injury, inflammation, or infection CRP values are raised.

Principle of procedure

The hsCRP was based on particle enhanced turbidometric immunoassay (PETIA) technique.

A synthetic particle coated with antibody to C - reactive protein aggregate in presence of C - reactive protein in the sample. The increase in turbidity which accompanies aggregation is proportional to the C - reactive protein concentration.

CRP + ABPR → AGGREGATE (absorbs at 340 mm)

Measurement of hsCRP

Blood was drawn with minimally traumatic venipuncture for measurement of hsCRP. Blood was centrifuged at 3000rpm at 4^0C for 15 minutes and aliquots were stored at 70^0C. Circulating hsCRP was measured by enhanced turbidometric immunoassay (PETIA) technique with a sensitivity of 0.5 mg/dL.

Expected values

Expected values for healthy individuals as noted are typically 0.3 mg/dl. Hence, patients with hsCRP > 0.3 mg/dl are said to have increased hsCRP.[7]

Evaluation of cardiovascular risk factors

Hypertension was defined by casual blood pressure ≥140/90 mm Hg or by current use of anti-hypertensive therapy. This was defined by Joint National Committee VII (JNC VII) criteria.[21]

Diabetes mellitus was defined by fasting blood glucose level ≥100 mg/dL according to International Diabetic Federation (IDF) criteria.[22,23]

Hyperlipidaemia was defined as fasting total serum cholesterol level >200 mg/dL.[24]

Hypertriglyceridemia was defined by Triglyceride levels > 150mg/dl according to international diabetic federation criteria.[24]

Obesity was defined as BMI > 30 kg/m^2 according to WHO criteria.[25]

Statistical analysis

The data was tabulated in excel spaced sheet. The data was expressed as rates, ratios and percentages. The probability value of ≤ 0.05 was considered statistically significant. The p value was calculated using Fischer exact test.

Chapter 5

Results

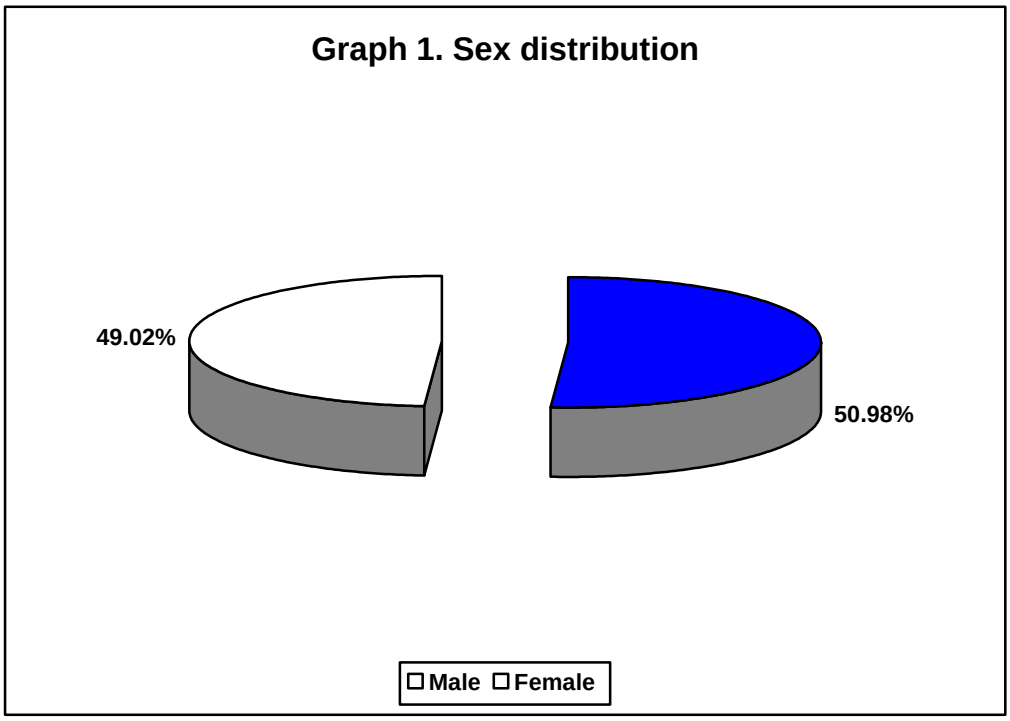
RESULTS

The present one year cross sectional study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on patients presenting with non specific neurological complaints attending medicine Outpatient and Inpatient departments during the period of January 2010 to December 2010**.**

The data was tabulated in excel spaced sheet and analysed as below.

Table 1. Sex distribution

Sex	Distribution (n=51)	
	Number	**Percentage**
Male	26	50.98
Female	25	49.02
Total	**51**	**100**

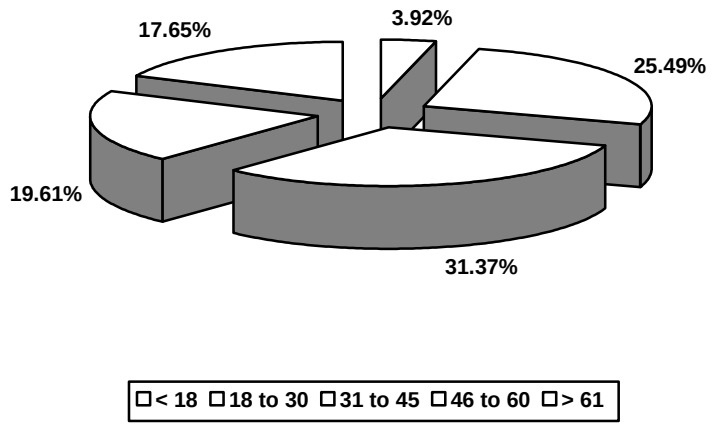


The study group included a total of 51 patients. Of which, 26 (50.98%) were males and 25 (49.02%) female patients. The male to female ratio was almost equal in the study group (1.04:1).

Table 2. Age distribution

Age group (Years)	Distribution (n = 51)	
	Number	**Percentage**
< 18	2	3.92
18 – 30	13	25.49
31 – 45	16	31.37
46 – 60	10	19.61
≥ 61	9	17.65
Total	**51**	**100**

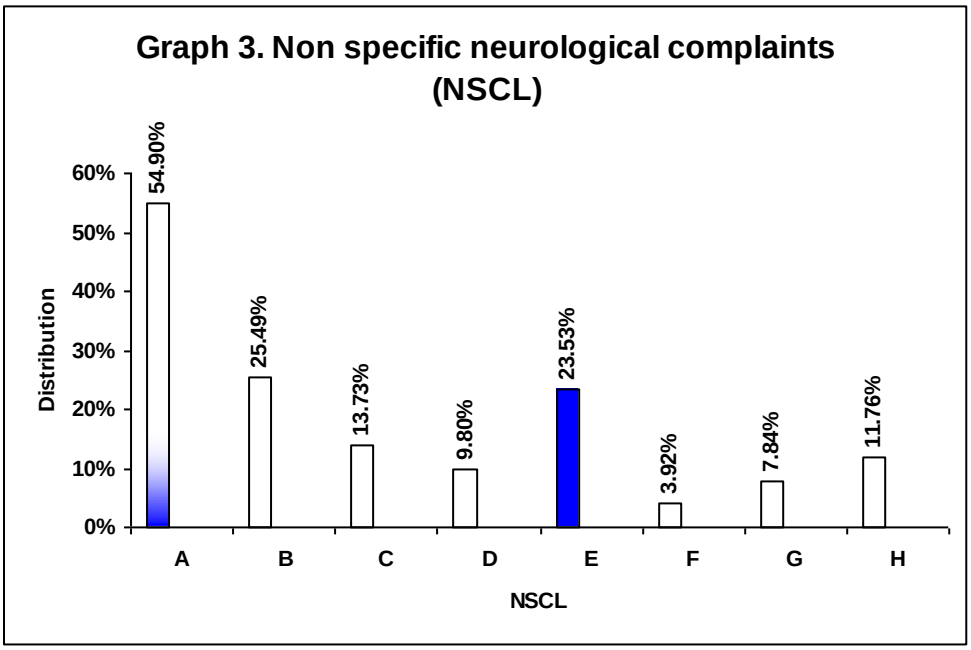
Graph 2. Age distribution



Out of the 51 patients, patients presenting with NSCL were higher in the 31-45 years age group that is 16 (31.37%) followed by 10 patients (19.6%) in the 46-60 years group and 9 patients 17.65% in the patients aged above or equal to 61 years of age. There were 35 patients above 30 years of age and 16 patients in the age group of 18-30 years presenting with non specific neurological complaints.

Table 3. Non specific neurological complaints (NSCL)

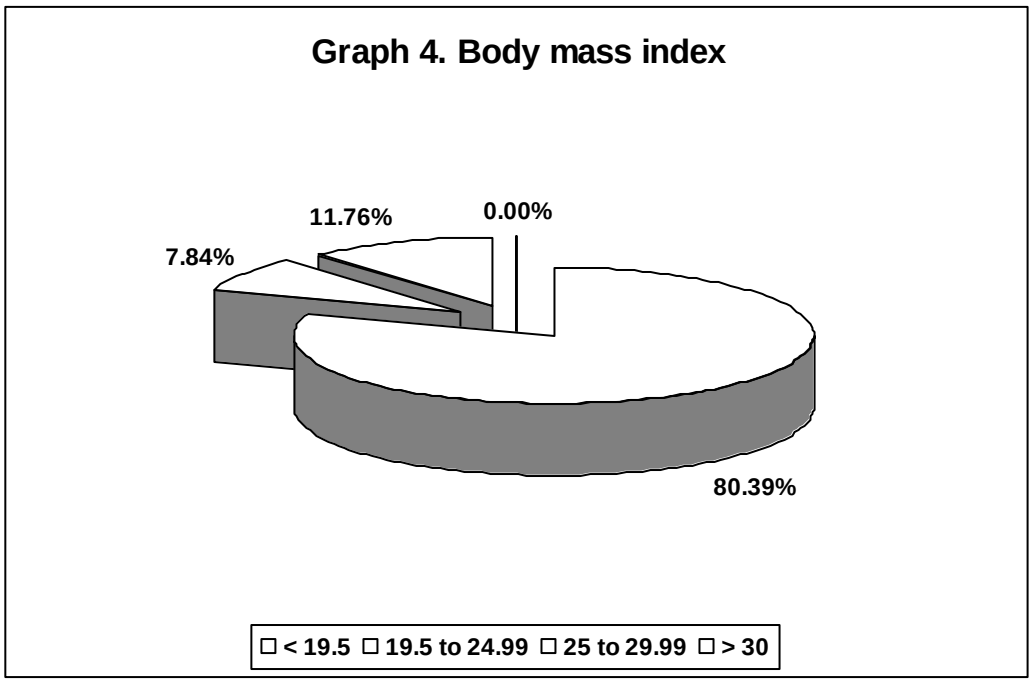
NSCL	Distribution (n = 51)	
	Number	**Percentage**
Headache (A)	28	54.90
Vertigo (B)	13	25.49
Tinnitus (C)	7	13.73
Syncope (D)	5	9.80
Giddiness (E)	12	23.53
Transient motor disturbances (F)	2	3.92
Transient sensory disturbances (G)	4	7.84
Transient loss of memory (H)	6	11.76



Out of the 51 patients, 28 (54.90%) had headache. The other NSCL symptoms included vertigo in 16 patients (25.49%), transient motor disturbances in 12 patients (23.53%), tinnitus in 5 patients (13.73%), loss of memory in 6 patients (11.76%), syncope in 5 patients (9.80%) and transient sensory disturbances in 2 patients (3.92%). Headache was the most common non specific neurological complaint.

Table 4. Body mass index

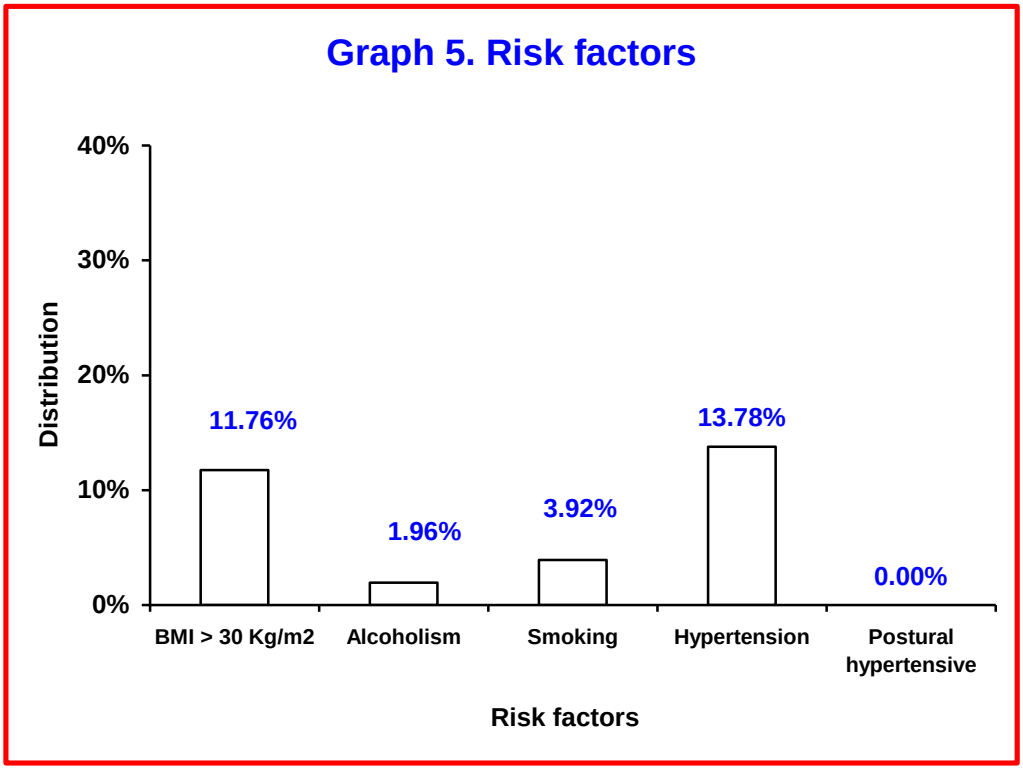
BMI (Kg/m^2)	Distribution (n=51)	
	Number	**Percentage**
< 19.5	0	0.00
19.5 – 24.99	41	80.39
25 – 29.99	4	7.84
≥ 30	6	11.76
Total	**51**	**100**



In the present study, 6 patients (11.76%) were obese and 4 patients (7.84%) were overweight. The remaining 41 (80.39%) patients had normal body mass index.

Table 5. Risk factors

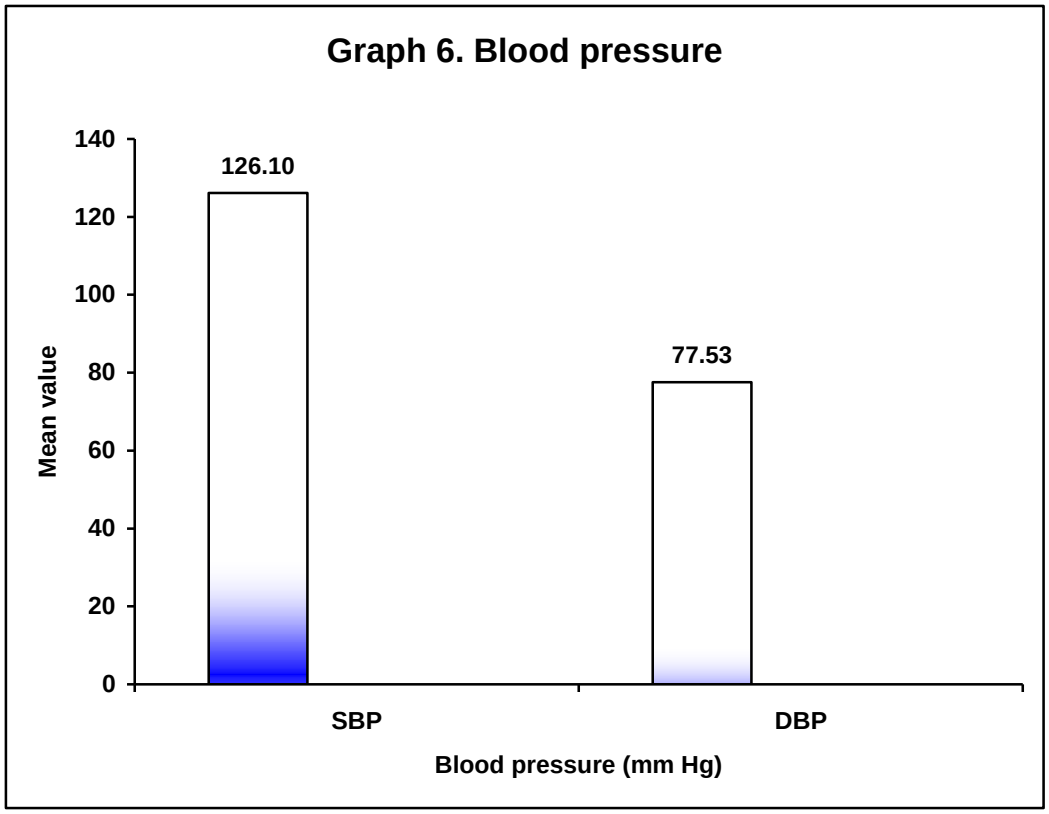
Risk factor	Distribution (n = 51)	
	Number	**Percentage**
BMI > 30 Kg/m^2	6	11.76
Alcohol	1	1.96
Smoking	2	3.92
Hypertension	7	13.78
Postural hypertension	0	0.00
Total	**3**	**5.88**



In this study, hypertension was present in seven patients (13.78%), two patients (3.92%) were smokers and one patient (3.92%) was alcoholic.

Table 6. Blood pressure

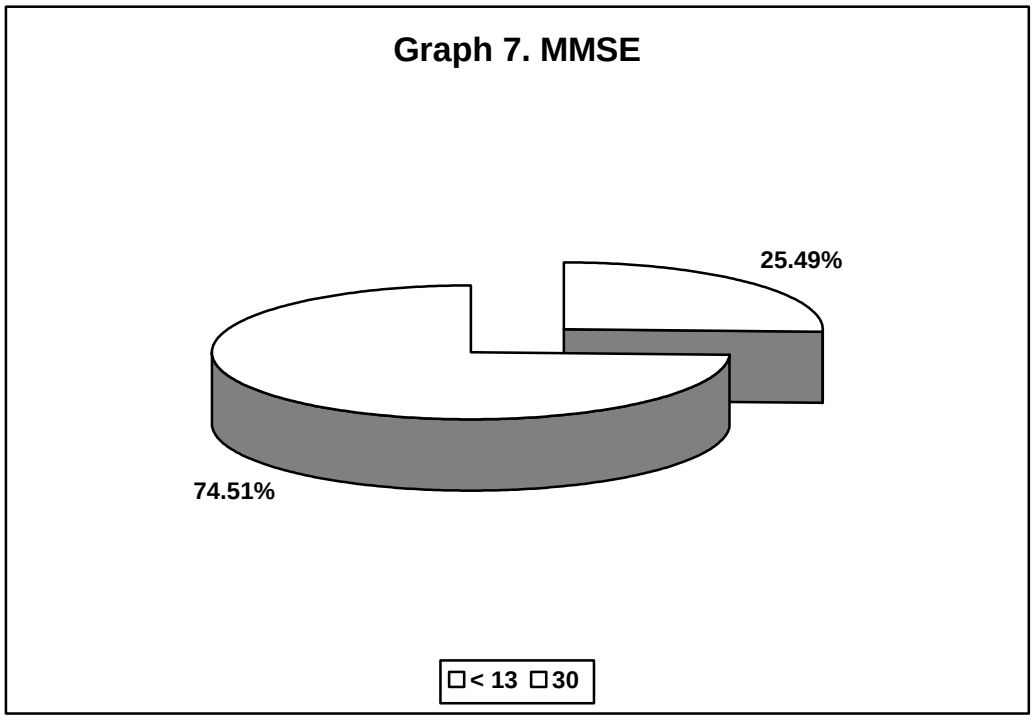
Blood Pressure (mm Hg)	Mean	SD
SBP	126.1	14.08
DBP	77.53	9.65



The mean systolic blood pressure in the study group was 126.1 mmHg and the mean diastolic blood pressure in the study group was 77.53 mmHg.

Table 7. MMSE

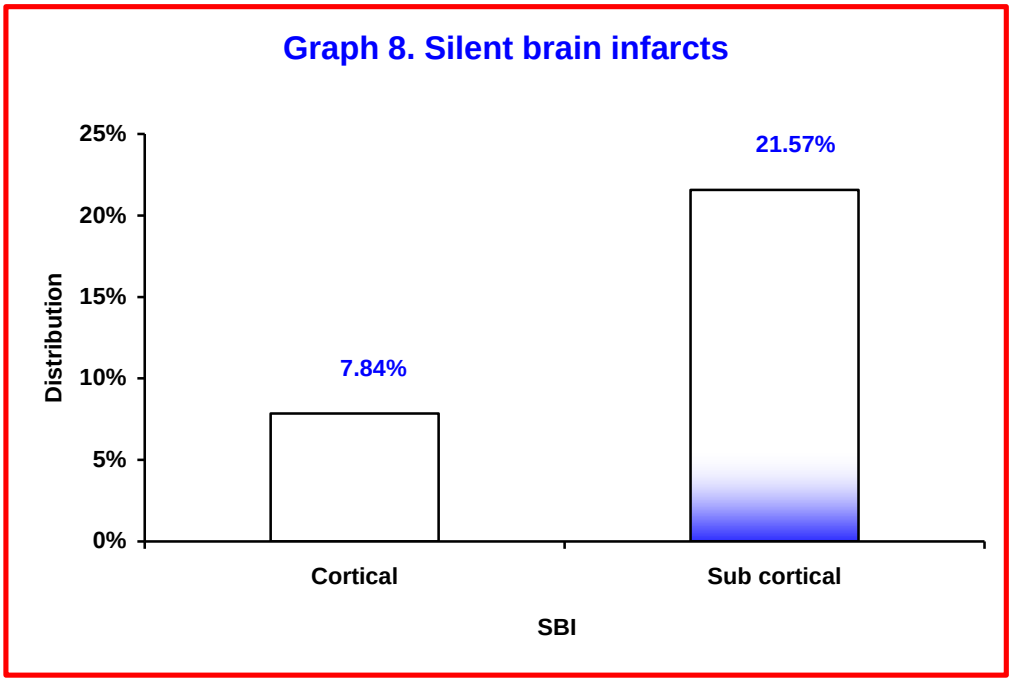
MMSE	Distribution (n = 51)	
	Number	**Percentage**
< 30	13	25.49
30	38	74.51
Total	**51**	**100**



In the present study 38 patients (74.51%) had a normal mini mental scale examination and 13 patients (25.49%) had a mild decrease in the mini mental scale examination scores.

Table 8. Silent brain infarcts

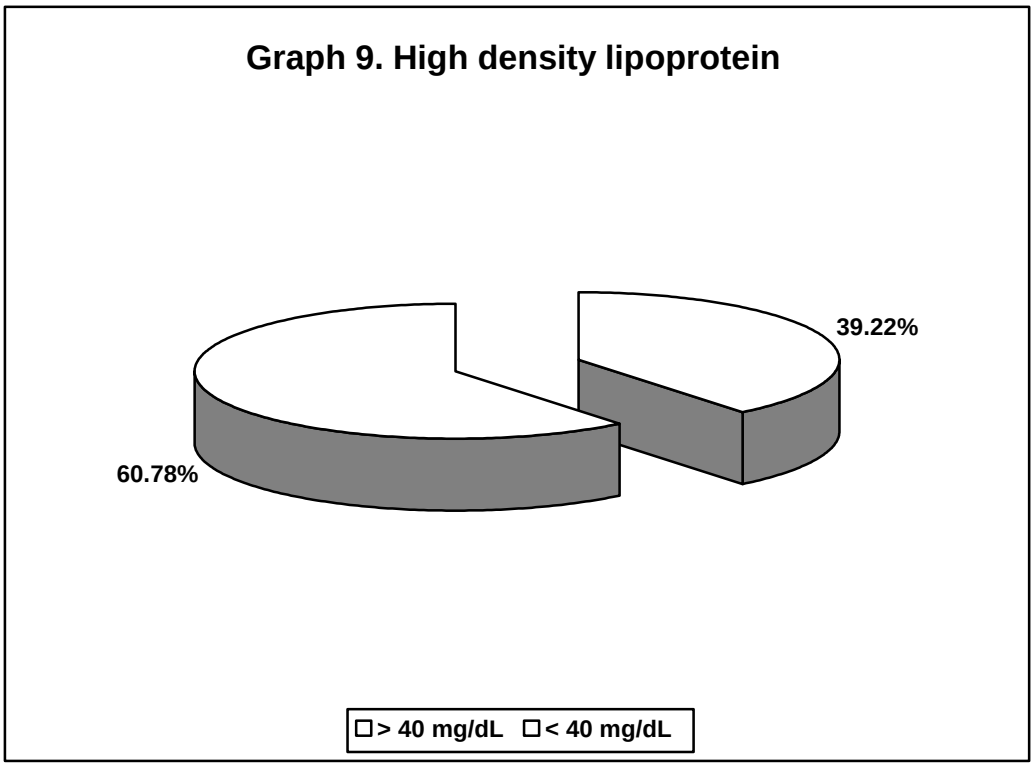
SBI	Distribution (n = 51)	
	Number	**Percentage**
Cortical	4	7.84
Sub cortical	11	21.57
Total	**15**	**29.41**



A total of 14 patients (27.44%) presented with silent brain infarct. Out of which 11 patients (21.57%) had subcortical infarcts and 4 patients (7.84%) had cortical infarcts and one patient among the group had both cortical and subcortical infarct.

Table 9. High density lipoprotein

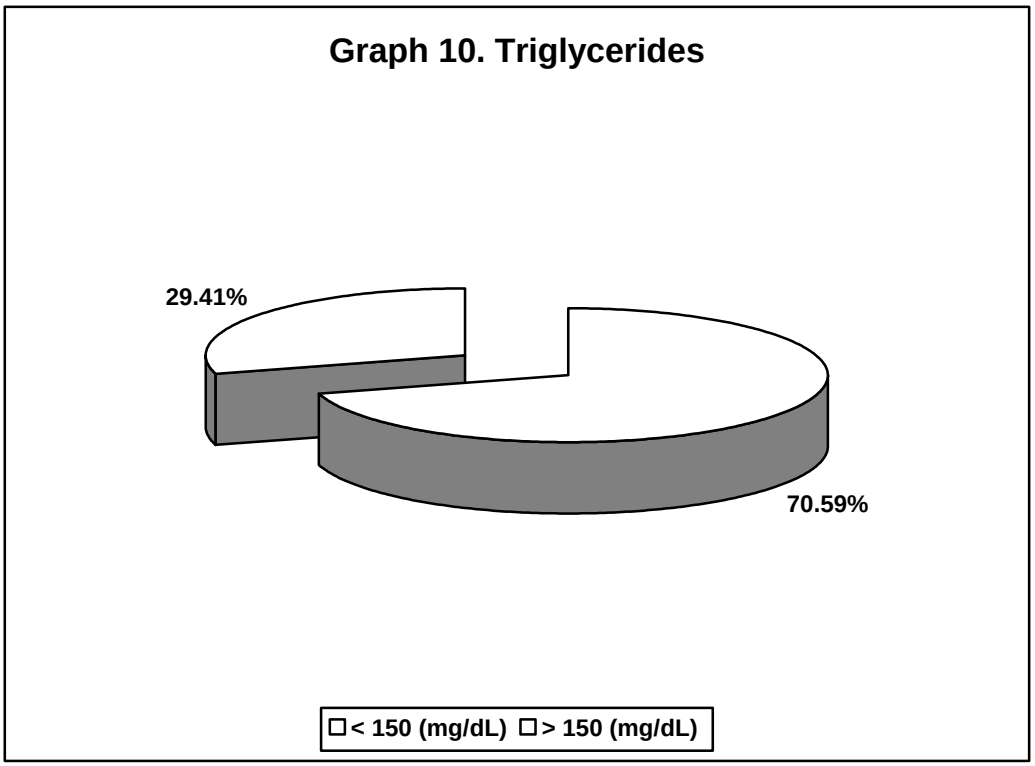
HDL Levels	Distribution (n = 100)	
	Number	**Percentage**
> 40 mg/dL	20	39.22
< 40 mg/dL	31	60.78
Total	**51**	**100**



In this study 31 patients (60.78%) had HDL level < 40 mg/dL and rest 20 patients (39.22%) had HDL levels > 40 mg/dL.

Table 10. Triglycerides

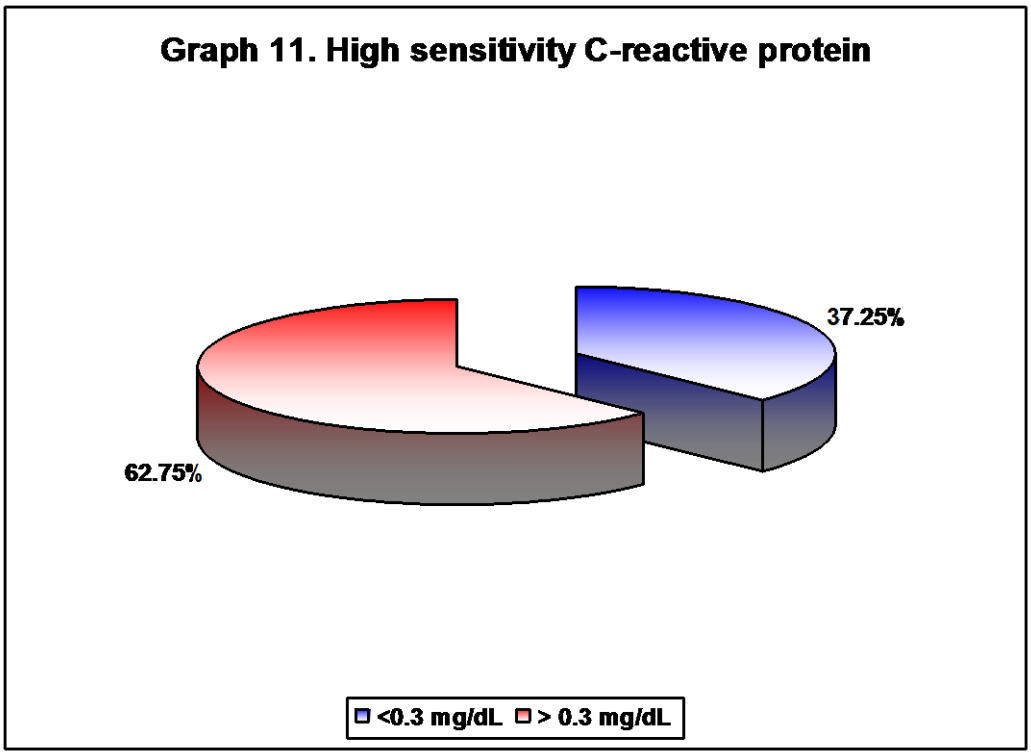
Triglycerides (mg/dL)	Distribution (n = 100)	
	Number	**Percentage**
< 150	36	70.59
> 150	15	29.41
Total	**51**	**100**



In the study group a total of 15 patients (29.4%) presented with raised triglyceride levels and rest 36 patients (70.59%) had normal triglyceride levels.

Table 11. High sensitivity C-reactive protein

hsCRP (mg/dL)	Distribution (n = 100)	
	Number	**Percentage**
< 0.3	19	37.25
> 0.3	32	62.75
Total	**51**	**100**

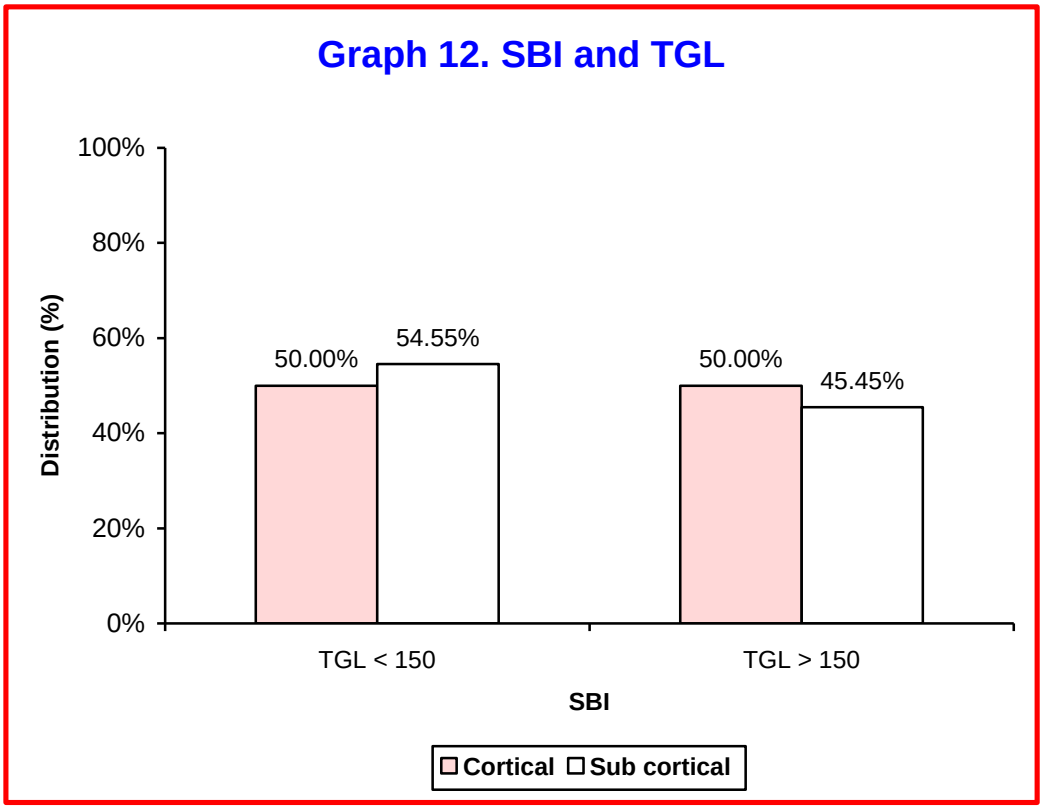


A total of 32 patients (62.75%) had raised hsCRP levels and 19 patients (37.25%) had normal hsCRP levels.

Table 12. SBI and TGL

SBI	Cortical (n = 4)		Sub cortical (n = 11)	
	Number	**Percentage**	**Number**	**Percentage**
TGL < 150	2	50.00	6	54.55
TGL > 150	2	50.00	5	45.45
Total	**4**	**100**	**11**	**100**

Fisher exact test p = 0.662

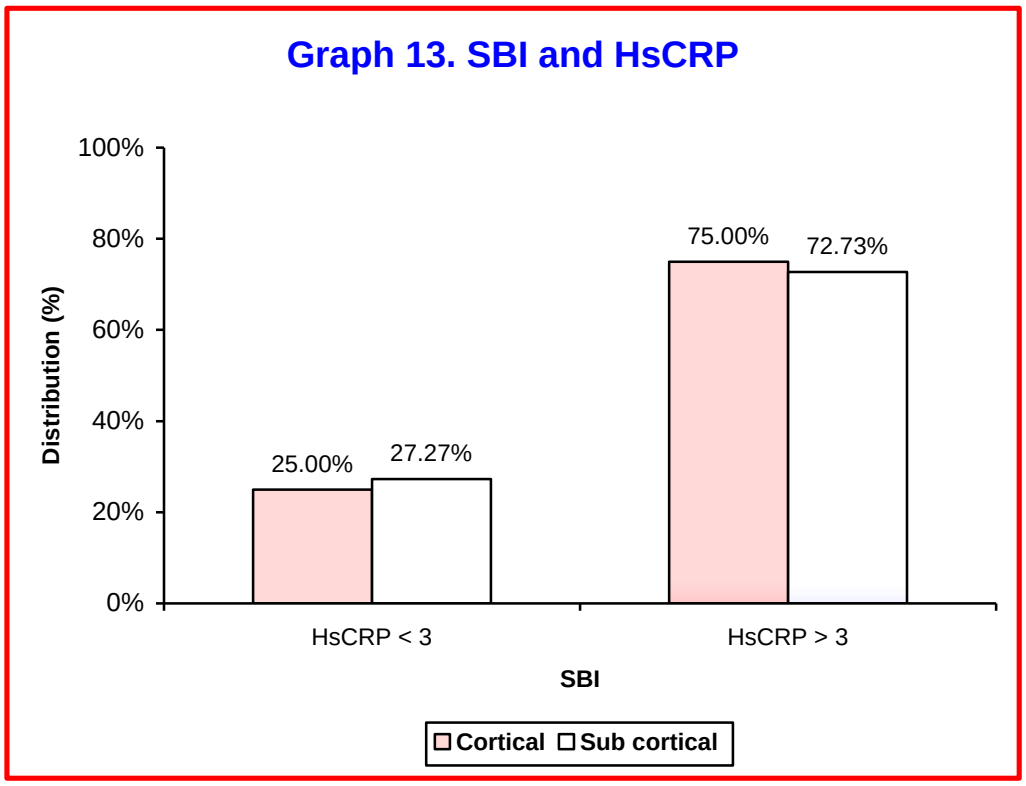


In this study cortical SBI were detected in 2 patients (50%) with raised triglyceride levels when compared to 5 patients (45.4%) who had raised triglyceride levels in the subcortical group.

Table 13. SBI and hsCRP

SBI	Cortical (n = 4)		Sub cortical (n = 11)	
	Number	**Percentage**	**Number**	**Percentage**
hsCRP < 3	1	25.00	3	27.27
hsCRP > 3	3	75.00	8	72.73
Total	**4**	**100**	**11**	**100**

Fisher exact test p = 0.725



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In the cortical SBI group 3 patients (75%) had raised hsCRP levels and in the sub cortical SBI group 8 patients (72.73%) had raised hsCRP.

Table 14. SBI with TGL and hsCRP

SBI	Cortical				Sub cortical			
	hsCRP <3 (n = 1)		hsCRP > 3 (n = 3)		hsCRP <3 (n = 3)		hsCRP > 3 (n = 8)	
	No.	%	No.	%	No.	%	No.	%
TGL < 150	0	0.00	2	66.67	2	66.67	4	50.00
TGL > 150	1	6.25	1	33.33	1	33.33	4	50.00
Total	1	6.25	3	100	3	100	8	100

Fisher exact test p = 0.500 Fisher exact test p = 0.576

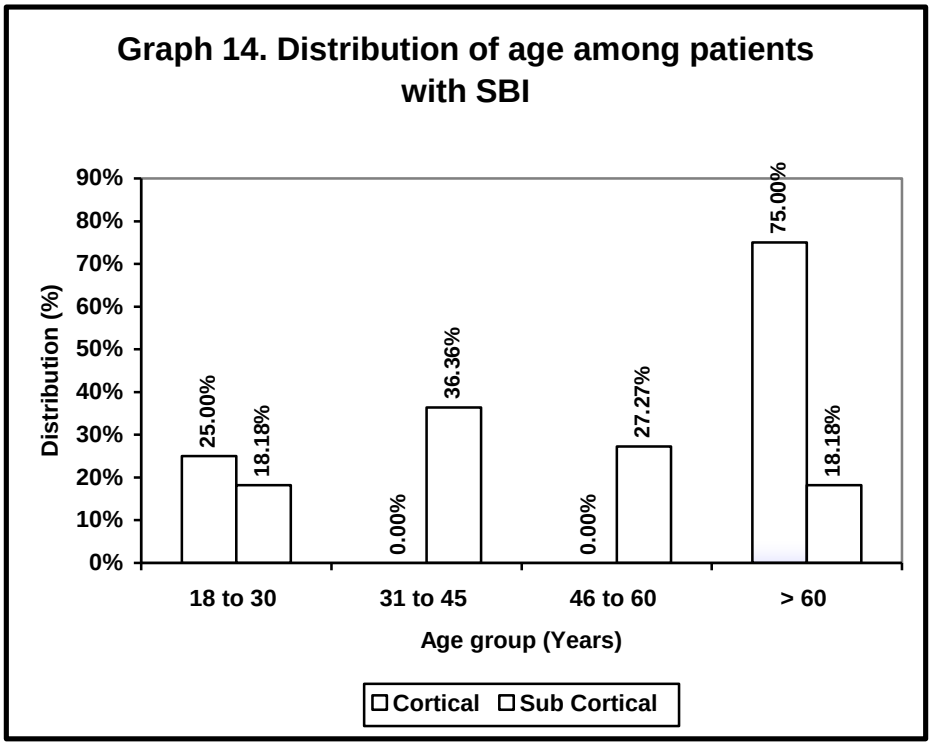
In the cortical SBI group 1 patients (33.33%) had both TGL and raised hsCRP.

In the sub cortical SBI group 8 patients (50%) had both raised triglycerides and hsCRP.

However, there was no statistically significant association was noted with SBI in the raised TGL and hsCRP group and with normal triglycerides and hsCRP group.

Table 15. Distribution of age among patients with SBI

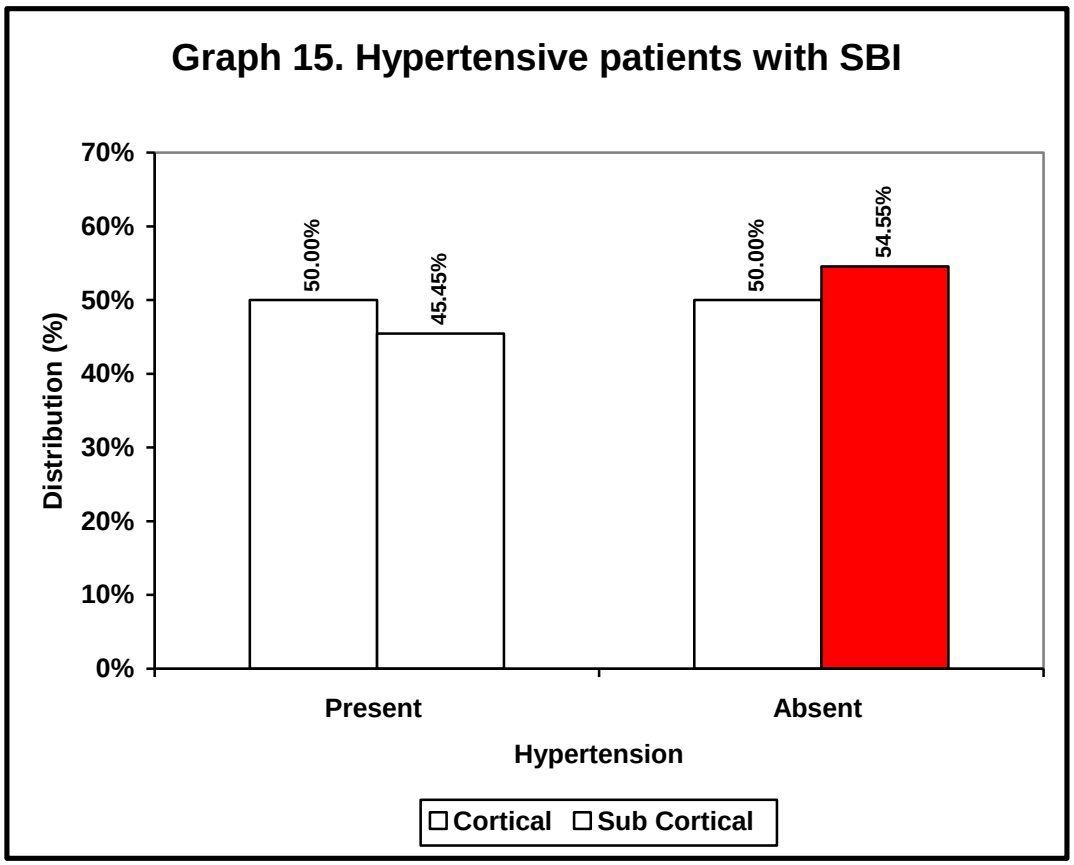
Age group (Years)	Cortical (n=4)		Sub Cortical (n=11)	
	No	**%**	**No**	**%**
18 to 30	1	25.00	2	18.18
31 to 45	0	0.00	4	36.36
46 to 60	0	0.00	3	27.27
≥ 61	3	75.00	2	18.18
Total	**4**	**100.00**	**11**	**100.00**



In the study group cortical SBI was present in 3 patients (75%) aged >61 years of age. Subcotical SBI was present in 4 (36.6%) patients aged between 31-45 years. There was higher incidence of cortical SBI in the older age group when compared to subcortical SBI group.

Table 16. Hypertensive patients with SBI

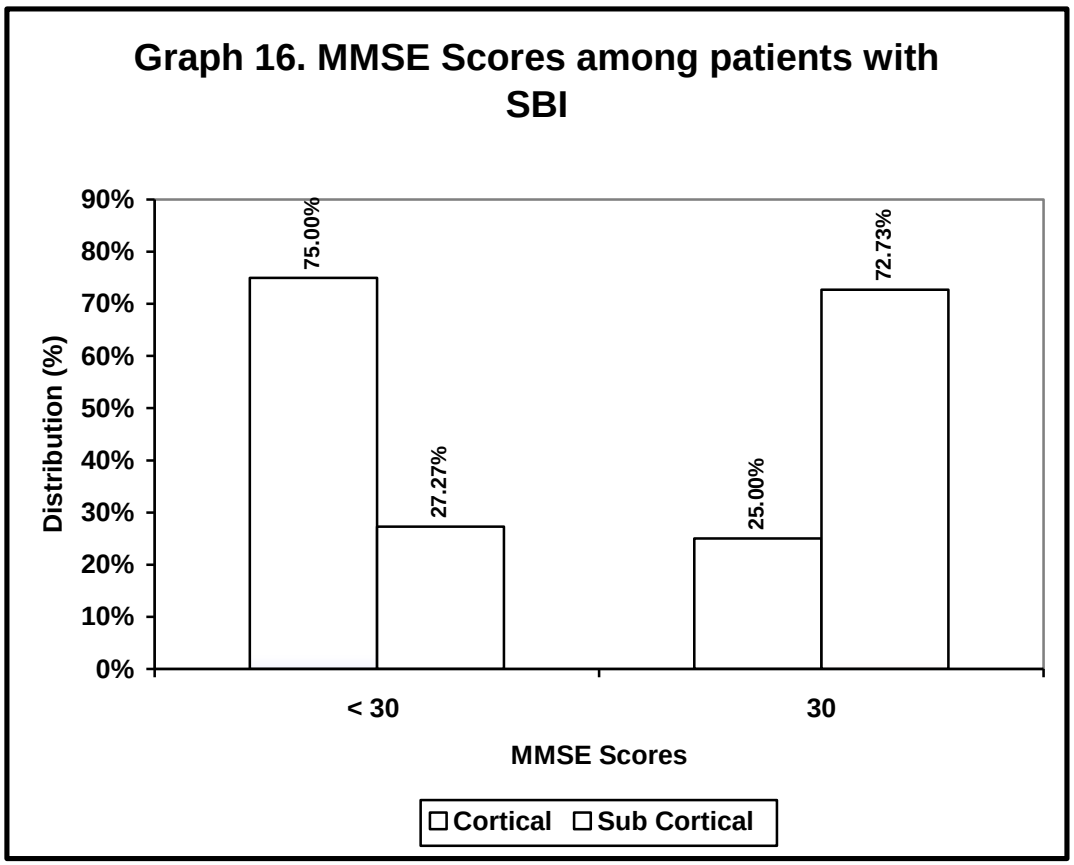
Hypertension	Cortical (n=4)		Sub Cortical (n=11)	
	No	**%**	**No**	**%**
Present	2	50.00	5	45.45
Absent	2	50.00	6	54.55
Total	**4**	**100.00**	**11**	**100.00**



In the present study 2 patients (50%) with cortical SBI had hypertension and 5 patients (45.45%) had hypertension in the patients with subcortical SBI. There was higher incidence of cortical SBI in the hypertensive patients when compared to the patients with hypertension in subcortical SBI group.

Table 17. MMSE Scores among patients with SBI

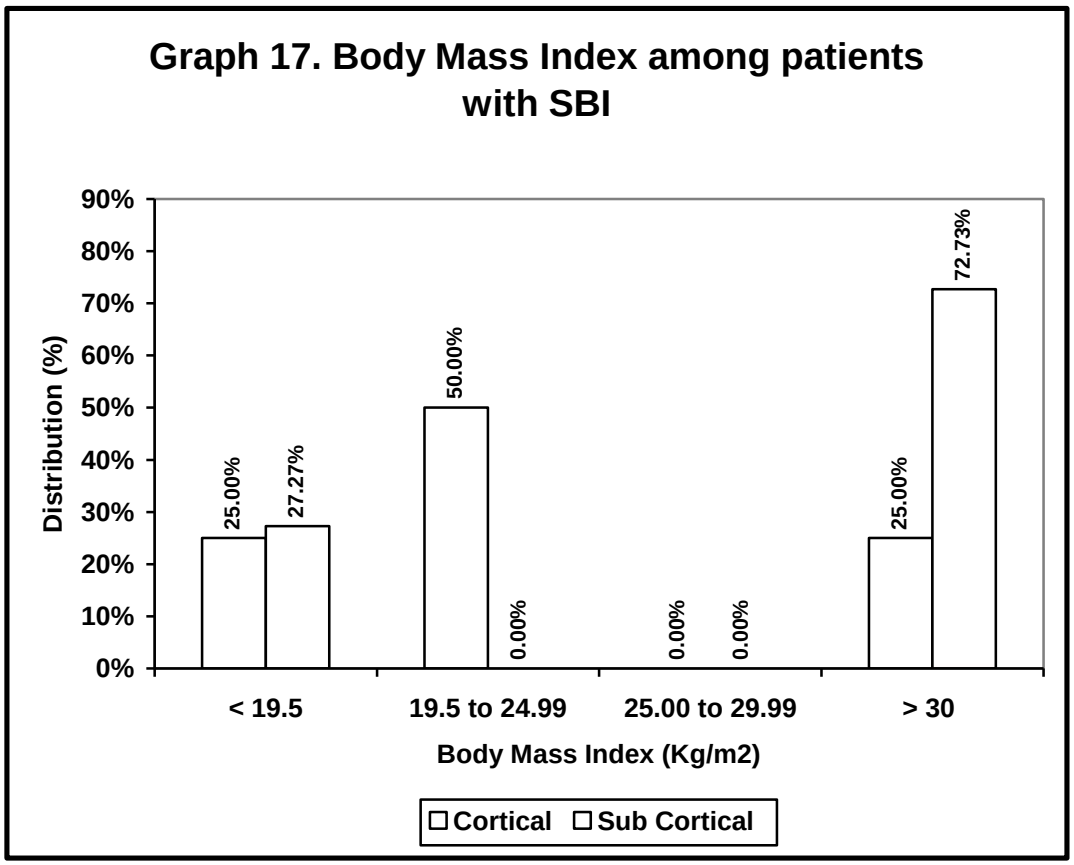
MMSE Score	Cortical (n=4)		Sub Cortical (n=11)	
	No	**%**	**No**	**%**
<30	3	75.00	3	27.27
30	1	25.00	8	72.73
Total	**4**	**100.00**	**11**	**100.00**



In this study, 3 patients (75%) with cortical SBI had MMSE < 30 and in 6 patients (42.86%) it was < 30 in sub cortical SBI group. Percentage of patients in the cortical SBI group had decreased MMSE compared to subcortical SBI group.

Table 18. Body Mass Index among patients with SBI

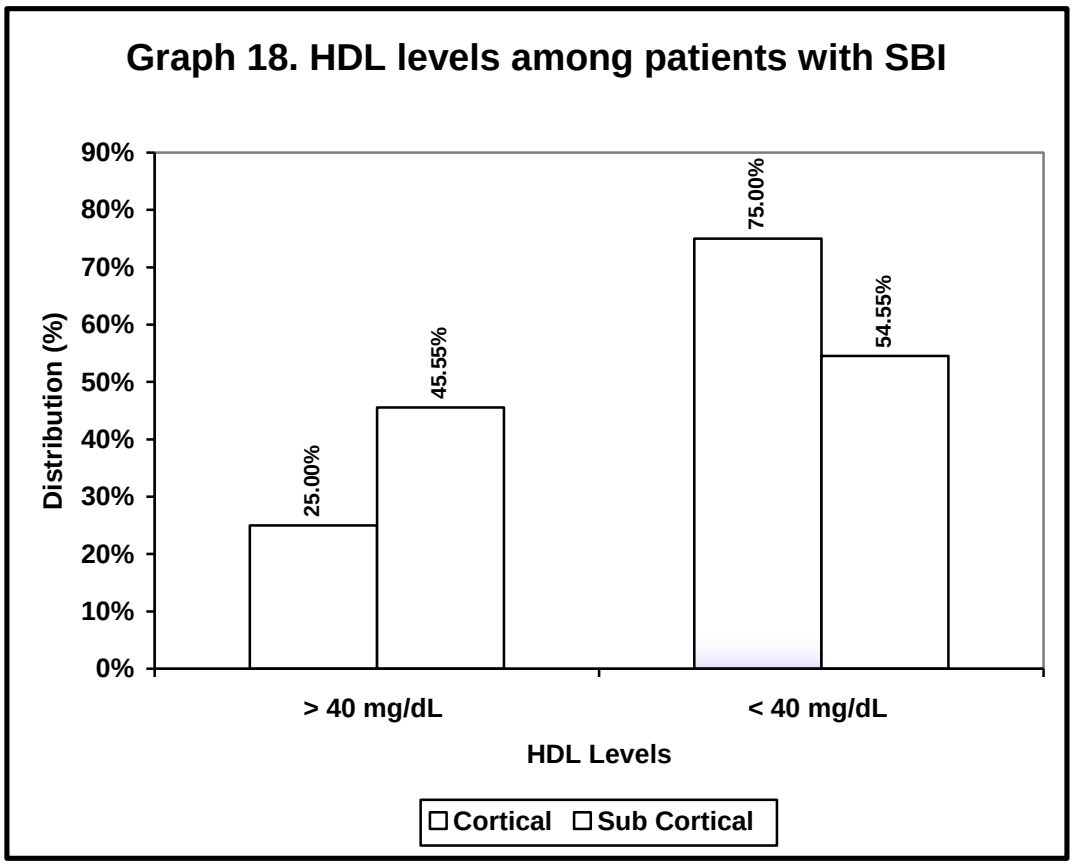
BMI (Kg/m2)	Cortical (n=4)		Sub Cortical (n=11)	
	No	**%**	**No**	**%**
< 19.5	0	0.00	0	0.00
19.5 to 24.99	3	75.00	9	81.82
25 to 29.99	0	0.00	1	9.09
≥ 30	1	25.00	1	9.09
Total	**4**	**100.00**	**11**	**100.00**



In this study 3 patients (75%) had normal BMI in the cortical SBI group and 9 patients (81.2%) had normal BMI in subcortical group. One patient each was obese in both cortical and sub cortical group.

Table 19. HDL levels among patients with SBI

HDL levels	Cortical (n=4)		Sub Cortical (n=11)	
	No	**%**	**No**	**%**
> 40 mg/dL	1	25.00	5	45.45
< 40 mg/dL	3	75.00	6	54.55
Total	**4**	**100.00**	**11**	**100.00**



In the cortical SBI group 3 patients (78%) had abnormal HDL levels and 9 patient's (64.29%) had abnormal HDL in the sub cortical SBI group suggesting abnormal HDL was higher in the sub cortical group compared to cortical group.

Chapter 6

Discussion

DISCUSSION

Asymptomatic Or silent brain infarcts are sometimes detected incidentally by MRI in patients who demonstrate no localized neurological symptoms1 of stroke. These lesions were first described by Fisher.[26] These lesions are seen as areas of focal hyper intensity on T-2 weighted range $\geq$ 3mm.[1] They have been associated with an increased risk of incident stroke and cognitive impairment.[1]

Recent imaging studies have reported the prevalence of 5.84% to 28%. Recent data from the Framingham off spring study[1] shows a prevalence of 10.7% among more than 2000 mid life (mean age 16 years) community dwelling people who were clinically stroke free. Risk factors associated with clinical stroke such as age, sex, diabetes mellitus, atrial fibrillation, hypertension, carotid artery disease and cigarette smoking have been associated with silent brain infarcts.[28]

The non modifiable risk factors are age, gender, race and family history. The modifiable risk factors are hypertension, heart disease, atrial fibrillation, diabetes, hypercholestraemia, carotid stenosis. Risk factors that are modified by behavioral changes include smoking, alcohol, diet and exercise for reducing obesity and waist hip ratio and stress reduction.[29]

Most of the patients who presented with non specific neurological complaints presented with history of neurological symptoms such as headache, vertigo, tinnitus, giddiness, transient motor disturbances, transient sensory disturbances, syncope and transient loss of memory.

In the Rotterdam scan study[20] they found that raised hsCRP which is a systemic marker of inflammation is associated with more prevalent and incident lacunar infarcts.

So in this study we studied the clinical profile, risk factors and association of hsCRP; TGL with silent brain infarcts.

The study group included a total of 51 patients. There were 26 males (50.98%) and 25 females (49.02%).

In a study done by Van Dijk et al[20] they found that women had a higher risk of marked sub cortical WHL incident SBI's than men. In the North Manhattan study[30] SBI's were 26.1% among men vs 15.2% in women. There was a higher prevalence of SBI's in the men when compared to females. In our study the male to female ratio was almost equal.

Out of the 51 patients, patients presenting with NSCL were higher in the 31-45 years age group that is 16 (31.37%) followed by 10 patients (19.6%) in the 46-60 years group and 9 patients 17.65% in the patients aged above or equal to 61 years of age. There were 35 patients above 30 years of age and 16 patients in the age group of 18-30 years presenting with non specific neurological complaints.

Among the patients presenting with non specific neurological complaints were majority of the patients were above 30 years. There were 35 patients above 30 years of age and 16 patients in the age group 18 to 30 years of age.

Out of the 51 patients, 28 (54.90%) had headache. The other NSCL symptoms included vertigo in 16 patients (25.49%), transient motor disturbances in 12 patients (23.53%), tinnitus in 5 patients (13.73%), loss of memory in 6 patients (11.76%), syncope in 5 patients (9.80%) and transient sensory disturbances in 2 patients (3.92%). Headache was the most common non specific neurological complaint.

In this study, majority of patients complained headache as their primary non specific neurological complaint.

In the study group 6 patients (11.7%) were obese and 4 patients were overweight. The rest of the subjects (41) (80.39%) had normal body mass index.

There was no relation with abnormal body mass index and non specific neurological complaints.

In this study, hypertension was present in seven patients (13.78%), two patients (3.92%) were smokers and one patient (3.92%) was alcoholic.

Among the non modifiable risk factors most of the patients were aged more than 45 years. Among the modifiable risk factors hypertension was present in majority of the patients.

The mean systolic blood pressure in the study group was 126.1mm Hg and the mean diastolic blood pressure in the study group was 77.5 mmHg.

A total of only 7 patients out of 51 patients were hypertensive and remaining patients were normotensive.

In the study group of patients presenting with non specific neurological complaints majority of patients 38 (74.5%) had a normal mini mental scale examination. 13 patients (25.49%) had a mild decrease in the mini mental scale examination (MMSE).

In the study group; total of (n=14) patients presented with silent brain infarcts. Out of which (21.57%) 11 patients had sub cortical infarcts and 7.84% (4) patients had cortical infarcts. One patient among the group had both cortical and subcortical infarcts.

The overall prevalence of silent brain infarcts in the study group was 27.45%. In the North Manhattan study[30] the overall prevalence was 16%.

In a study[18] done at Helsinki University Central Hospital a total of 1008 consecutive patients aged 15 to 49 with first ever ischaemic stroke were screened; they found that silent infarcts usually reflecting small vessel disease were detected in 20% of healthy elderly people and in upto 50% in suspected series with patients having stroke risk factors.

They also found that silent brain infarcts are common in patients less than 45 years of age.[18]

The overall prevalence rates were similar when compared to other studies.

In the study group of patients presenting with non specific neurological complaints a total of 31 patients (60.78%) had abnormal HDL and rest (39.22%) 20 patients had normal HDL level.

In a study done by Kato T et al.[26] they found that there is no significant association with normal HDL levels and silent brain infarcts. This finding was consistent with our finding in the study.

In the study group of patients presenting with non specific neurological complaints (NSCL) a total of 29.4% (15) patients presented with raised TGL levels and rest (36) 70.59% had normal triglyceride levels.

In the study group of patients presenting with non specific neurological complaints a total of 32 patients (62.75%) had raised hsCRP levels and rest 19 patients (37.25%) had normal hsCRP levels.

In the study group cortical SBI were detected in 50% of patients (2) with raised triglyceride (TGL) levels and 45.45% (5) had raised TGL in the sub cortical SBI group.

In the study done by Park K et al[11] they found that independent of risk factors such as elevated blood pressure, impaired fasting glucose; hpertryglyceridaemia (Hyper-TG); and waist circumference were signficiant risk factors for silent brain infarcts.

In a study done by Kato T; Inove T et al.[26] out of 100 asymptomatic patient they screened they found that only raised LDL-3 is associated with silent brain infarcts. There was no association between raised TGL and low HDL with silent brain infarcts. This finding was consistent with findings of our study.

Though higher percentage of patients with SBI's in our study had raised hsCRP values; we did not find a statistically significant association between them.

In the study group of patients presenting with non specific neurological complaints (75%) (3) patients had raised hsCRP in the cortical SBI group and 8 patients (72.73%) had raised hsCRP in the subcortical group.

In the study done by Hoshi T; Kitogawa K et al[7] they found that hsCRP and Il-6 were higher in SBI patients than in those without SBI, prevalence of SBI increased in a stepwise fashion across the tertiles of hsCRP and IL-6. This increases in such inflammatory markers were associated with higher likelihood of SBI and the associations persisted even when traditional cardiovascular risk factors were adjusted.

In the Rotterdam scan study[20] they noted that patients with higher hsCRP levels tended to have more prevalent and incident lacunar infarcts.

In the study group there was no statistical significance associated with raised Hscrp and silent brain infarct's.

In the cortical SBI group 33.33% (n=1) (4) had both raised TGL and raised hsCRP.

In the sub cortical SBI group (n=8) 50% had raised TGL and hsCRP. There was no statistically significance associated with SBI in the raised TGL and hsCRP group when compared to patients with normal TGL and hsCRP group.

In the study group cortical SBI was present in 75% of patients (3) aged > 61 years of age. In the study group subcortical SBI was present in 36.6% of patients (4) aged between 31 – 45 years of age.

There was higher incidence of cortical SBI in the older group when compared to the subcortical SBI group.

In the Framingham study[1] they found that SBI were found in patients with a mean age 61 years had higher incidence of silent brain infarcts.

This finding was consistent with cortical SBI occurring in the older age group (mean age > 61 years) in our study. Subcortical occurred in the younger age group of patients.

In the patients presenting with cortical SBI 50% of patients (2) had hypertension and 45.48% had hypertension in the patients with subcortical SBI group.

There was higher incidence of cortical SBI in the hypertensive patients when compared to hypertensive patients in the subcortical group.

In the Framingham study[1] out of 10.7% of patiens presenting with SBI 50% of patients had hypertension.

This was similar to the finding in our study; additionally we found that cortical SBI were common in hypertensive patients of older age group.

In the study group 75% (3) of patients with cortical SBI had MMSE <30 and only 42.86% (6) patients had MMSE < 30 in the subcortical group. Majority

of the patients in the cortical SBI group had decreased MMSE scores when compared to subcortical group.

In the LADIS[4] study they found that lacunes and white matter lesion were associated with a risk of progressive cognitive impairment.

The finding in our study was consistent with the LADIS study.[4]

75% of patients had normal BMI in the cortical SBI group and 81.2% (9) patient had normal BMI in the subcortical group.

Majority of patient in the study group had a normal BMI.

Overall in this study, 27.45% patients presenting with non specific neurological complaints had silent brain infarcts. Study also showed that, these patients with non specific neurological complaints have to be evaluated for the earlier detection of SBIs which is a risk factor for stroke.

The limitations of the study were smaller sample size and no follow up was done. Hence the findings of this study need to be strengthened further to find out if there is any association between patients presenting with NSCL and SBIs with traditional risk factors of stroke.

Chapter 7

Conclusion

CONCLUSION

Overall **i**n this study out of the 51 patients presenting with NSCL 14 patients (27.45%) had silent brain infarcts.

The study group revealed that the patients presenting with non specific neurological complaints have to be evaluated at the earliest to detect silent brain infarcts which is a risk factor for major stroke.

The traditional risk factors associated with stroke were present in the patients having SBI. hsCRP was raised in patients having NSCL and having SBIs. However there was no statistically significant association between them which could be attributed to the smaller sample size of the study.

Further, the findings of this study have to be confirmed involving large sample size and follow up in patients presenting with non specific neurological complaints and silent brain infarcts with traditional risk factors for stroke.

Chapter 8

Summary

SUMMARY

Silent brain infarction, is considered a preclinical warning of symptomatic strokes and brain damage related to multiple deep infarcts. To prevent these further disabling diseases, it is very important to characterize and manage this preclinical stage of cerebrovascular disease. The present study was an attempt to find the relation between silent brain infarcts and non specific neurological complaints, association of risk factors with silent brain infarcts and association of high sensitivity C-reactive protein (Hs-CRP) with silent brain infarcts.

The present one year cross sectional study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on 51 patients presenting with non specific neurological complaints attending medicine outpatient and inpatient departments during the period of January 2010 to December 2010**.** Investigations such as Complete blood count (CBC) with platelets, fasting lipid profile, FBS, Hs-CRP, ECG and urine routine and microscopy were done. Patients were evaluated with a 1.5 telsa Siemens symphony. T-2 weighted double spine echo coronal weighted sequences were acquired in 3-5 mm contagious slices from nasion to occiput with a repetition time of 4500 milli seconds and echo time of 116 milliseconds.

In the present study, 26 (50.98%) were males and 25 were (49.02%) female patients, suggesting equal sex distribution in the study group (1.04:1). Patients presenting with NSCL were higher (31.37%) in the 31-45 years age group. Headache was the most common (54.90%) non specific neurological complaint. 6 patients (11.76%) patients were obese and 4 patients (7.84%) were

overweight. Most common risk factor was hypertension in 7 patients (13.78%) and 13 patients (25.49%) had a mild decrease in the mini mental scale examination scores. A total of 14 patient's (27.44%) presented with silent brain infarct. Out of which 11 patients (21.57%) had subcortical infarcts and 4 patients (7.84%) had cortical infarcts and one patient among the group had both cortical and subcortical infarct. 31 patients (60.78%) had abnormal HDL, 15 patients (29.4%) presented with raised triglyceride levels and 32 patients (62.75%) had raised hsCRP levels.

In conclusion, out of the 51 patients presenting with NSCL 14 patients (27.45%) had silent brain infarcts. Further these patients presenting with non specific neurological complaints have to be evaluated at the earliest to detect silent brain infarcts which is a risk factor for major stroke.

Chapter 9

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Annexures

Annexure I

ANNEXURE I – CONSENT FORM

TITLE: "SILENT BRAIN INFARCTS IN PATIENTS WITH NON SPECIFIC NEUROLOGICAL SYMPTOMS – A ONE YEAR CROSS SECTIONAL STUDY AT KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE"

Objective and purpose of the study

This research is intended to study silent brain infarcts and risk factors in correlation with HsCRP Type 2 diabetes mellitus, obesity, hypertension and previous ischaemic heart disease. The principal investigator of the study is Dr. P. Sasanka under the guidance of Dr. Prakash Babaliche.

Procedure

If you agree to be part of the research study you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You will also have to give blood samples and undergo other necessary investigations

Risk and Benefits

The only risk and possible discomfort you might get is while taking blood from your arm for the investigations which may cause swelling, pain, redness, bruising or infection (rarely happens) at the site from where the blood is drawn and other complications during MRI.

Alternatives

Taking part in this study is voluntary. You may choose not to take part in this study, or if you decide to take part you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may stop your participation in this study any time. If you choose not to take part in the study you will receive the standard treatment available in the hospital.

Privacy and Confidentiality

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution / Sponsor's policy

Does not apply to this research

Financial incentives for participation

You will not be paid / offered any gifts /incentives for participating in the study.

Authorization to publish the results

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing.

If you have any questions about your rights as a participant you may call Dr. V. D. Patil, Principal and Chairman, J.N.M.C Ethical Committee for Human Research phone number 0831-2471350.

In case of the queries during study or in future you may contact following person

Principal investigator : Dr. Sasanka Pakalapati Mob No: 9164009565

Guide : Dr. Prakash Babaliche Ph. No: 0831 2473777

Consent Statement

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read, or it has been read to me, this entire consent form, and have had all my questions answered.

Name of the Participant: _____ Signature _____ / Thumb print

Name of the Witness; _____ Signature_____

Investigator Name _____ Signature_____

Date: Place:

Annexures

Annexure II

ANNEXURE II – PROFORMA

TITLE: "SILENT BRAIN INFARCTS IN PATIENTS WITH NON SPECIFIC NEUROLOGICAL SYMPTOMS – A ONE YEAR CROSS SECTIONAL STUDY AT KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE"

Name:	IP No.:
Age:	Sex:
Address:	Religion:
D.O.A:	D.O.D:
Occupation:	

HISTORY OF PRESENT COMPLAINTS AND DURATION

Headache	:
Vertigo	:
Dizziness	:
Tinnitus	:
Syncope	:
Altered sensorium	:
Weakness of limbs	:
Sensory dysfunction	:
Speech disturbance	:
Fever	:
Cough with expectoration	:
Loose stools	:
Vomiting	:

Past History

Any other neurological illness :

HTN :

Diabetes :

Cardiac illness :

Metabolic syndrome :

Dyslipidemia :

Family history

HTN :

DM :

Metabolic syndrome :

Dyslipidemia :

Obesity :

IHD :

Personal history

Diet :

Smoking :

Alcohol :

Tobacco :

General Examination

BP : Weight :

Pulse rate : regular / irregular Temperature :

Peripheral pulses :

RR/rhythm :

Carotid :

Skin :

Icterus : Pallor :

Clubbing : Cyanosis :

LN : Pedal edema :

Deformities : Bleeding Diathesis:

Subcutaneous nodules: Neurocutaneous markers:

CVS

Heart Sounds :

Murmurs :

RS

Breath Sounds:

Added Sounds:

P/A

Organomegaly:

Tenderness :

Distension :

CNS

Higher functions

Consciousness :

Memory :

Intelligence :

Halucinations & delusions:

Orientation in space and person:

Speech

Spontaneous speech

Comprehension

Fluency

Word output

Neologisms

Reading

Writing

Repetition

Naming objects

Conclusion

Cranial Nerves

1. Olfactory
    a. Sense of smell
2. Optic nerve :
    a. Visual acuity (by finger counting):
    b. Field of vision :
    c. Colour vision :
    d. Optic fundi :
3. Oculomotor, Trochlear and Abducent nerve

	Right	Left
Pupils		
Size		
Shape		

Reaction

Direct

Indirect

Eye movements

Primary position

Range of movements

Accommodation

Saccades

Pursuit

Optokinetic nystagmus

Nystagmus

4. Trigeminal nerve

Sensation

Mastigatory muscles

5. Facial nerve

6. Vestibulocochlear nerve

Hearing

Air

Bone

Caloric test

Vestibulo ocular reflex

7. Glossopharyngeal nerve

8. Vagus nerve

9. Accessory nerve

10. Hypoglossal nerve

Motor system	**Right**	**Left**
Nutrition		
Small muscle of hand		
Forearm		
Upper arm		
Leg		
Thigh		
Tone		
Power		
Shoulder joint		
Flexion		
Extension		
Adduction		
Abduction		
Elbow joint		
Flexion		
Extension		
Wrist joint		
Flexion		
Extension		
Hand grip		

Hip joint

Abduction

Adduction

Flexion

Extension

Knee joint

Flexion

Extension

Ankle joint

Flexion

Extension

Coordination

Upper limb

Finger nose test

Finger nose finger test

Lower limb

Heel knee test

Tandem walking

Conclusion

Abnormal movements

Fasciculation's

Tremors

Athetosis

Chorea

Reflexes

Superficial

Plantar

Cremastric

Abdominal

Upper

Middle

Lower

Deep

Biceps

Triceps

Supinator

Knee

Ankle

Patellar clonus

Ankle clonus

Sensory system

Pain

Touch

Temperature

Vibration

Joint and position

Romberg's sign

Cortical sensation

Tactile localization

Tactile discrimination

Stereognosis

Graphesthesia

Cerebellar signs

Nystagmus

Speech

Hypotonia

Dysmetria

Rebound phenomenon

Intentional tremor

Pendular knee jerk

Attitude

Gait

Signs of meningeal irritation

Neck rigidity

Kernig’s sign

Brudznski’s sign

INVESTIGATIONS

Hb: TLC: DC: N - L - M - E - B –

ESR:

Platelets:

Urine routine & microscopy:

Fasting Blood sugar

Fasting lipid profile

Total cholesterol : HDL cholesterol :

LDL cholesterol : Triglycerides :

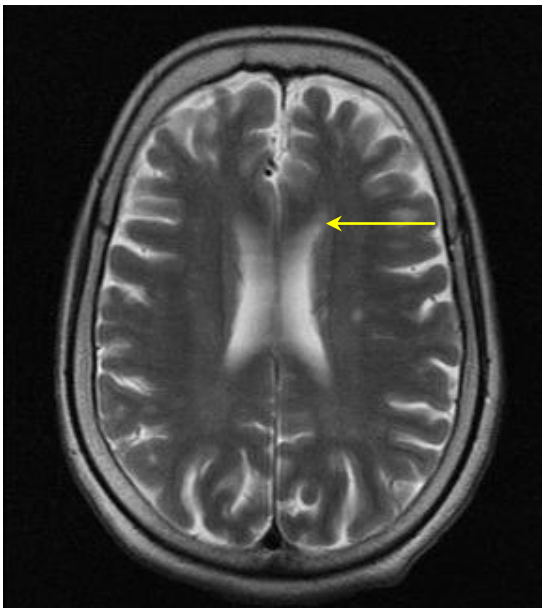
HsCRP

MRI Scan (1.5 Tesla) T1W1, T2W1 Images

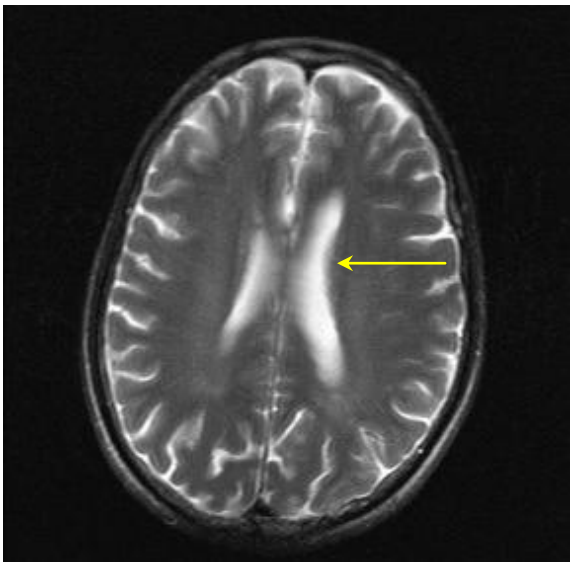
Annexures

Annexure III

ANNEXURE III – PHOTOGRAPHS



Photograph 1. T2 Hyperintensity In Corona Radiata (Subcortical SBI)



Photograph 2. T2 Hyperintensity In The Occipital Region (Cortical SBI)

ANEXURE IV - MASTER CHART

Serial Number	In Patient / Out patient number	Age (Years)	Sex	NSCL	Body mass index (Kg/m2)	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg	Alcoholism	Smoking	Postural hypotension	MMSE	Cortical SBI	Sub Cortical SBI	Total Cholesterol (mg/dL)	Low density lipoprotein (mg/dL)	High density lipoprotein (mg/dL)	Triglycerides (mg/dL)	hsCRP (mg/dL)
1	2E+06	36	F	A,D	23.00	120	80	-	-	-	30	-	-	130	80.0	40	145	3.9
2	2E+06	65	M	A	22.00	120	80	-	S	-	28	-	-	130	87.6	38	130	4.3
3	422224	18	F	A,G	24.00	126	84	-	-	-	30	-	-	163	84.8	58	101	4.4
4	424353	71	M	D	22.00	148	94	-	-	-	28	-	+	134	24.2	53	284	14.2
5	2E+06	70	M	A,C,D	24.00	160	90	Al	-	-	28	-	+	200	138.1	50	71	5.5
6	422915	22	F	E	22.00	118	70	-	-	-	30	+	+	146	84.0	33	145	4.8
7	2E+06	35	M	B	24.00	120	70	-	-	-	30	-	-	120	45.4	57	88	3.7
8	2E+06	25	M	A	25.00	117	60	-	-	-	29	-	-	123	50.2	57	79	2.5
9	2E+06	50	M	A,G	23.00	144	90	-	-	-	30	-	-	200	82.2	69	244	3.3
10	2E+06	51	M	B,C	22.00	120	70	-	-	-	30	-	-	105	30.2	50	124	3.2
11	2E+06	36	F	A	24.00	110	78	-	-	-	30	-	-	137	60.8	56	101	2.9
12	2E+06	42	M	H	24.00	120	80	-	-	-	30	-	-	130	90.0	50	120	2.2
13	2E+06	40	M	A	23.00	144	88	-	-	-	30	-	-	120	100.0	44	110	2.4
14	2E+06	32	M	A	24.00	120	78	-	-	-	30	-	-	130	90.0	50	120	2.2
15	2E+06	18	F	E	23.00	110	70	-	-	-	30	-	-	120	70.0	44	100	3.0
16	2E+06	15	M	E	21.00	120	70	-	-	-	30	-	-	100	80.0	55	106	2.3
17	2E+06	65	F	A,F,H	34.00	150	94	-	-	-	27	+	-	222	140.0	50	200	6.2
18	2E+06	19	F	C	20.00	118	60	-	-	-	30	-	-	110	64.0	45	90	3.0
19	419361	65	F	A	32.00	162	100	-	-	-	30	-	-	188	110.0	34	180	4.6
20	420040	64	M	F	22.20	130	84	-	S	-	28	+	-	120	90.0	45	170	2.3
21	420055	55	F	A,E,B	23.40	160	90	-	-	-	30	-	+	142	87.6	34	102	3.9
22	2E+06	31	F	A	26.40	120	80	-	-	-	30	-	-	190	120.6	57	62	4.3
23	2E+06	25	F	A,B	19.60	114	74	-	-	-	30	-	-	181	101.2	53	134	2.0
24	2E+06	50	M	B,C	22.30	117	60	-	-	-	30	-	-	151	76.2	57	89	4.4
25	2E+06	48	F	A,H	24.00	128	80	-	-	-	30	-	+	173	76.8	29	186	4.5
26	2E+06	50	F	A	23.00	124	72	-	-	-	30	-	-	173	67.0	50	280	3.6
27	421388	24	F	E,B	24.00	120	80	-	-	-	30	-	+	223	150.2	52	104	2.4
28	2E+06	65	M	A	22.00	116	70	-	-	-	30	-	-	130	80.0	44	130	4.3
29	2E+06	45	F	H	23.00	110	70	-	-	-	30	-	+	127	49.4	40	188	5.0
30	2E+06	55	F	A,E,H	24.00	155	90	-	-	-	30	-	+	142	87.6	34	102	2.9
31	2E+06	40	M	A,D	20.00	120	68	-	-	-	30	-	-	120	80.0	40	100	2.0
32	2E+06	26	F	A,D	20.00	118	74	-	-	-	30	-	-	159	85.2	55	94	3.1
33	2E+06	41	F	B	32.00	114	68	-	-	-	30	-	-	151	40.2	60.2	241	3.4
34	2E+06	42	F	B,G	30.00	124	84	-	-	-	30	-	-	140	85.2	34	99	5.1
35	2E+06	31	F	A,C	24.00	110	70	-	-	-	29	-	-	190	110.0	69	78	2.4
36	2E+06	65	M	A,H	20.00	128	68	-	-	-	28	-	-	210	54.0	124.2	159	3.2
37	2E+06	74	M	F	23.00	110	70	-	-	-	28	-	-	112	59.2	36	84	15.2
38	2E+06	27	F	B	20.00	128	68	-	-	-	27	-	-	136	61.0	64	54	2.6
39	2E+06	43	M	G,A	24.00	118	80	-	-	-	30	-	+	137	61.0	37	192	2.4
40	2E+06	52	M	A	27.00	144	88	-	-	-	30	-	-	218	119.0	28	353	2.4
41	2E+06	58	M	H,D	22.00	120	80	-	-	-	30	-	-	85	88.0	35.4	88	2.7

ANEXURE IV - MASTER CHART

Serial Number	In Patient / Out patient number	Age (Years)	Sex	NSCL	Body mass index (Kg/m2)	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg	Alcoholism	Smoking	Postural hypotension	MMSE	Cortical SBI	Sub Cortical SBI	Total Cholesterol (mg/dL)	Low density lipoprotein (mg/dL)	High density lipoprotein (mg/dL)	Triglycerides (mg/dL)	hsCRP (mg/dL)
42	2E+06	23	M	A	20.00	118	60	-	-	-	30	-	-	163	94.0	53	77	3.0
43	2E+06	45	F	A,B	22.00	120	82	-	-	-	30	-	-	119	79.0	28	58	3.0
44	2E+06	17	F	A	21.00	120	80	-	-	-	30	-	-	112	34.0	55	114	2.5
45	2E+06	26	M	A	30.00	130	76	-	-	-	30	-	-	114	90.0	38	223	13.1
46	421607	44	M	E,H	30.00	130	80	-	-	-	28	-	+	129	73.6	45	302	7.6
47	2E+06	18	F	C,D	24.00	118	68	-	-	-	30	-	-	184	120.0	39	121	2.5
48	2E+06	53	M	B,C	24.00	120	78	-	-	-	30	-	-	130	70.0	58	78	2.6
49	2E+06	23	M	E,F	28.00	116	76	-	-	-	29	-	-	208	79.8	70	291	3.9
50	338563	70	F	E,B	21.00	140	90	-	-	-	28	+	-	142	87.6	34	102	5.6
51	426078	45	M	B,E,G	28.00	144	90	-	-	-	30	-	+	121	31.0	66	118	3.8

Annexures

Annexure IV

ANNEXURE IV – KEY TO MASTER CHART

A	-	Headache
Al	-	Alcoholic
B	-	Vertigo
C	-	Tinnitus
D	-	Syncope
E	-	Giddiness
F	-	Transient motor disturbances
G	-	Transient sensory disturbances
H	-	Transient loss of memory
hsCRP	-	Highly sensitive C reactive protein
Kg	-	Kilogram
m	-	Meter
mm Hg	-	Millimeters of mercury
MMSE	-	Minimental scale examination
NSCL	-	Non specific neurological complaints
S	-	Smoker
SBI	-	Silent brain infarcts