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Original Research Article

STUDY OF CORRELATION OF SERUM CALCIUM WITH THE SEVERITY OF INFARCT IN ACUTE ISCHEMIC STROKE IN TERTIARY CARE CENTER IN SOUTH GUJARAT

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Abstract

Objective: To assess the correlation of serum calcium levels with severity of infarct based on infarct size and clinical status based on NIHSS (NATIONAL INSTITUTE OF HEALTH STROKE SCALE) score in acute ischemic stroke.

Methods: The study was conducted on 100 patients presenting with acute ischemic stroke, admitted in Medicine ward and MICU of medicine department at Tertiary health care center in South Gujarat.

Result- There was a negative correlation found between serum calcium levels and infarct size. There was a negative correlation between serum calcium levels and NIHSS score, that is higher the NIHSS score, they had lower serum calcium levels.

Conclusion: This study, the conclusion drawn is that patients with lower serum calcium levels on admission had a much severe stroke with respect to infarct size and NIHSS score. So a low serum calcium levels on admission can be considered to be poor prognostic marker in acute ischemic stroke.

Keywords: National Institute Of Health Stroke Scale, Serum Calcium,Diabetes Mellitus, Hypertension, Coronary Artery Disease

Introduction

Cerebrovascular diseases include some of the most common and distressing disorders:ischemic stroke and hemorrhagic stroke1. It is the second leading cause of death all over the world, causing 6.2 million deaths in 2011. Strokes cause ~200,000 deaths every year in the United States and are a major cause of disability and morbidity. A stroke, or cerebrovascular accident is defined as an abrupt onset of a neurologic deficit which can be attributed to a focal vascular aetiology(1).

Calcium is well known to be an important mediator in the death of neurons due to ischemia. Accumulation of intracellular calcium causes neuronal death which is the basic patho-mechanism of ischemic stroke(2). As a result of ischemia, the cells are starved of oxygen and glucose, there will be necrosis of cells due to the decrease in ATP levels (3). Due to depletion of ATP, membrane ion pumps stops acting and neurons depolarize, allowing rise in intracellular calcium. Cellular depolarization also causes glutamate release from synaptic

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terminal (4); excess extracellular glutamate produces neurotoxicity by activating postsynaptic glutamate receptors that increase neuronal calcium influx. Influx of calcium causes potassium channels to open and there by closing calcium channels (5).Also the influx of calcium activates a calcium sensitive protein phosphorylase calcineurin which dephosphorylates the channel , thereby inactivating it. A rise in extracellular calcium is seen due to a decrease in the extracellular space causing cytotoxic oedema (6).

Depolarization of nerve terminals cause a calcium influx along an electrochemical gradient and the consequent rise in intra-cellular calcium triggers neurotransmitter release. Much of the calcium that enters must be re-distributed within the nerve- terminals i.e. Calcium is transiently sequestered so that the calcium concentration inside declines to a normal level. Later when the calcium is pumped out, it is released from the sequestered areas (7). Many studies have shown that serum calcium levels correlate with the size as well as the severity of acute ischemic stroke. This study was done with the aim of determining the correlation of serum calcium levels with the size of infarct and severity of infarct in acute ischemic stroke based on NIHSS score (8).

Material and Methods

Setting: The study was conducted on 100 patients presenting with acute ischemic stroke, admitted in Government Rajaji Hospital & Madurai Medical College during the study period from June 2018 – June 2019

Design of the Study : Prospective observational study

Period of Study : 1 year

Inclusion Criteria: Only patients aged more than 40yrs presenting within 48-72 hours of onset of stroke and diagnosed as acute ischemic cerebrovascular stroke with clinical examination & confirmed by a computed tomography scan

Exclusion Criteria: Age < 40yrs, haemorrhagic stroke, sub-arachnoid haemorrhage, cerebral venous sinus thrombosis, posterior circulation stroke, patients with hepatic or renal disease, known malignancy, pancreatitis, patients on calcium supplements, recurrent stroke.

Observation

The results of this study which included 100 patients were as follows:-

In the present study conducted, 48% of the patients were males and 52% of the patients were females.

Table 1:

Parameters	Male		Female	
	Mean	Std. Deviation	Mean	Std. Deviation
Age (yrs)	62.07	10.19	62.91	7.93

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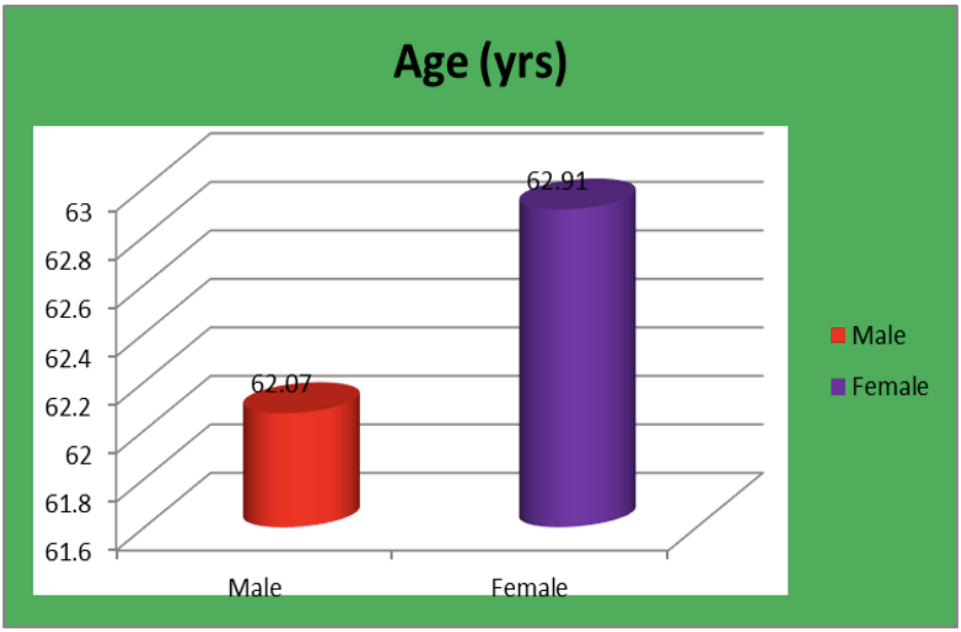

Figure 1:

There were 35 females and 65 males in the study, a total of 100 study population. The mean age of the sample was 62.37+/-9.43 with mean age of fe males being 62.07.

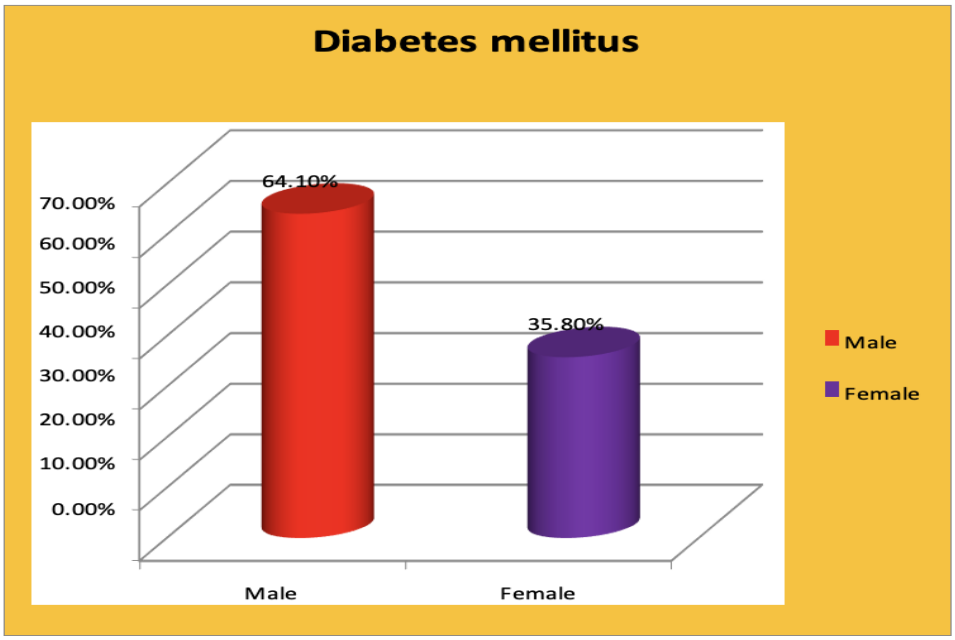

Figure 2:

Of the 100 people 34(64.1%) males and 19(35.4%) females had diabetes mellitus.

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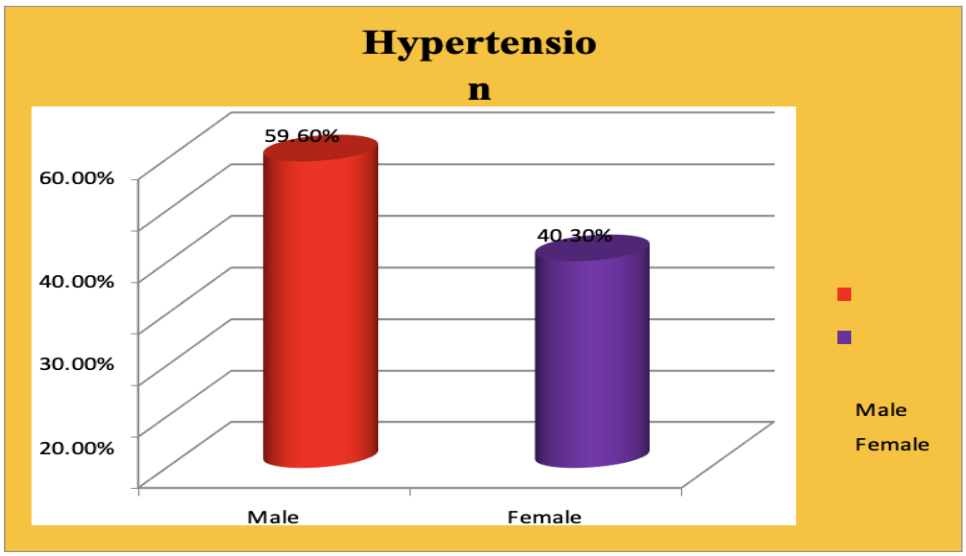

Figure 3:

31 (59.6%) males and 21 (40.3%) females had hypertension.

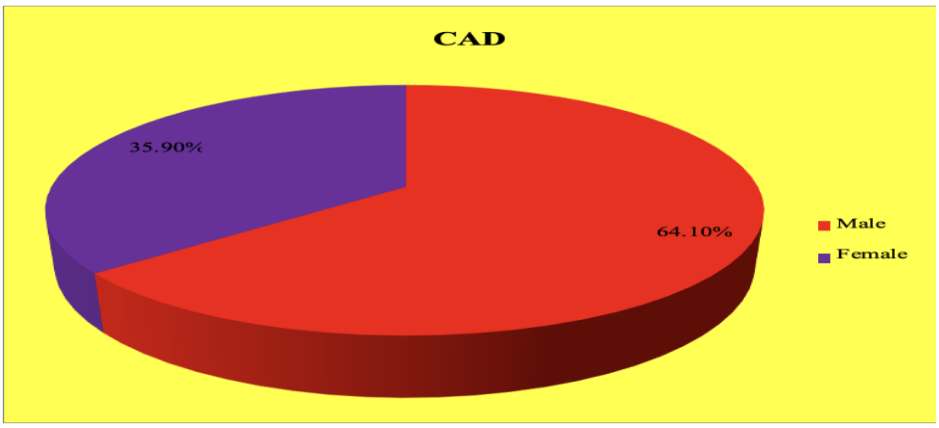

Figure 3:

25(64.1%) males and 14 (35.9%) females had CAD.

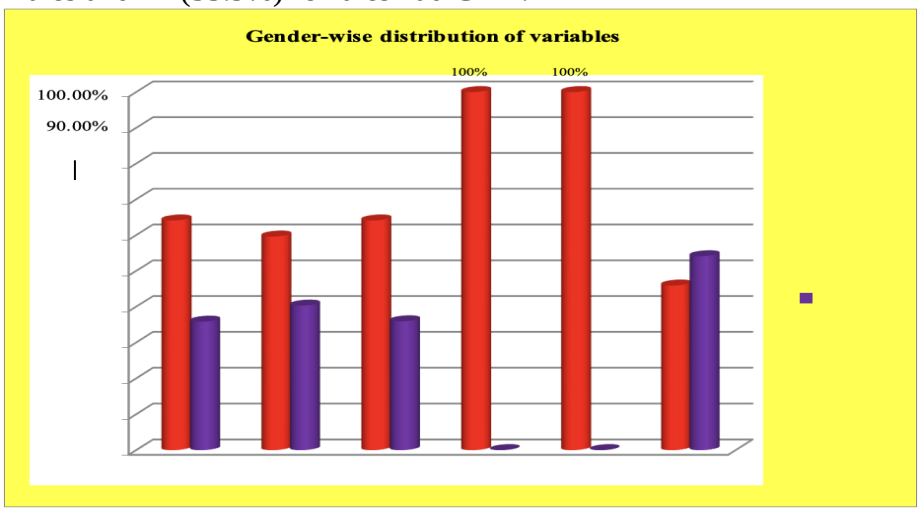

Figure 5:

Among the males 37 were smokers and 39 were alcoholics. Females in the study denied any addictions.

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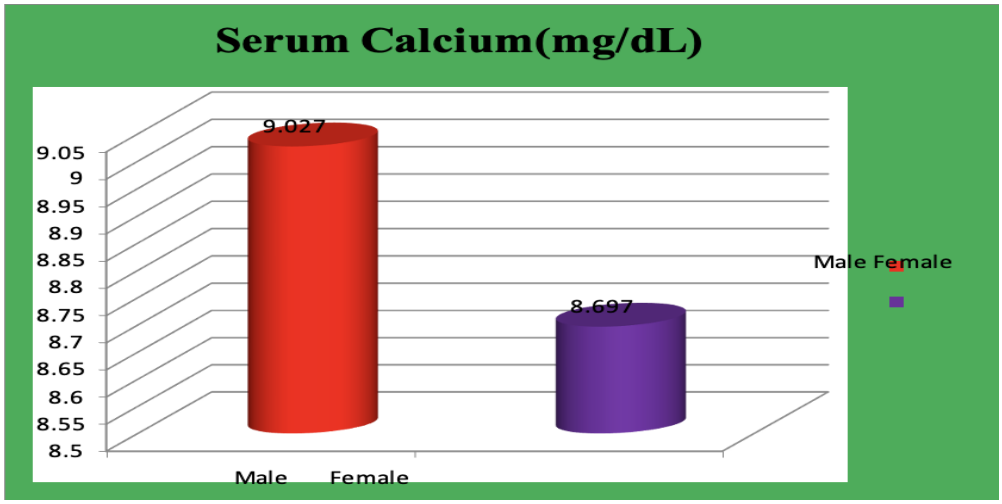

Figure 6:

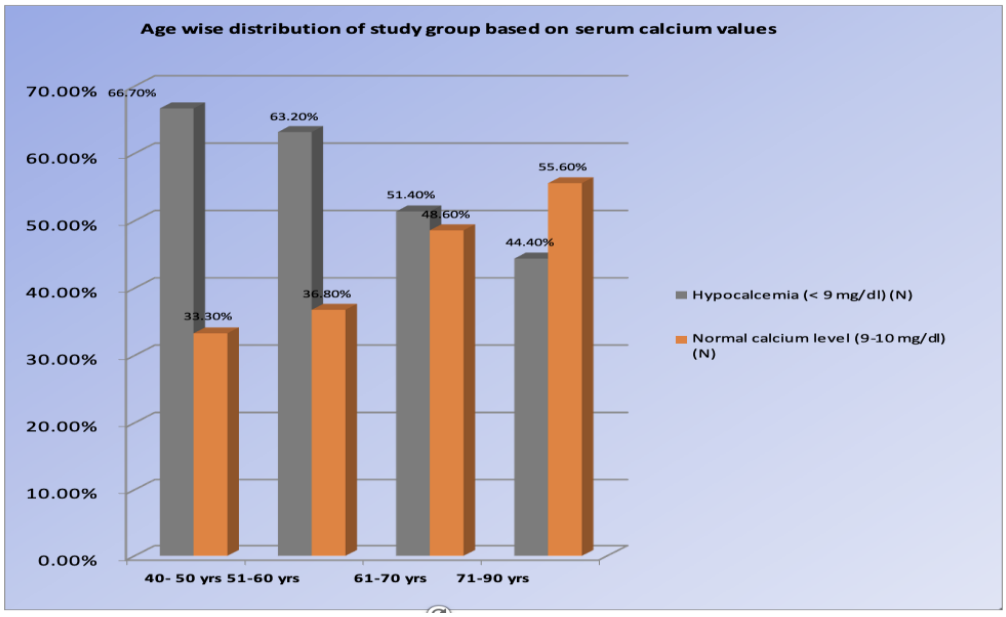

Figure 7:

56 of the population had hypocalcemia(<9) and 44 had normal calcium levels (9-11).

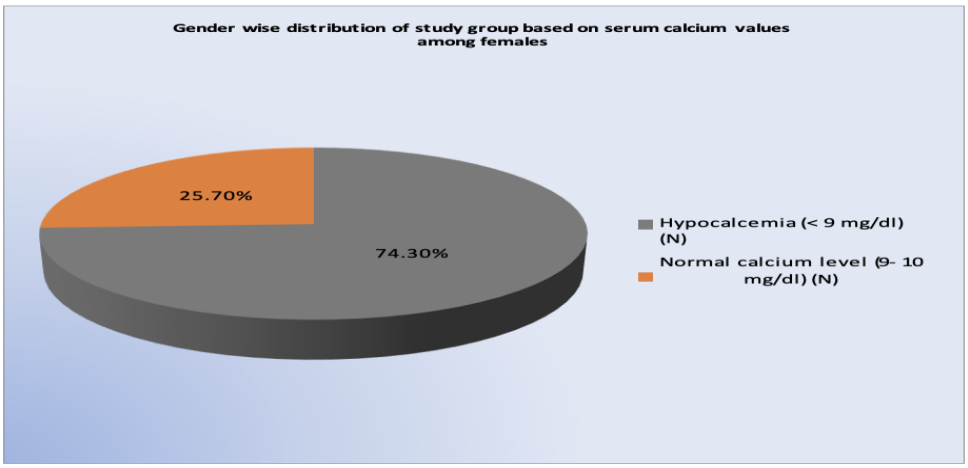

Figure 8:

74.3% of females had hypocalcemia whereas only 46.20% males had hypocalcemia

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Table 2:

Variables	Hypo-calcemia (< 9 mg/dl)		Normal calcium level (9-10 mg/dl)	
	(N)	(%)	(N)	(%)
Age 40- 50 yrs	6	66.70%	3	33.30%
51-60 yrs	24	63.20%	14	36.80%
61-70 yrs	18	51.40%	17	48.60%
71-90 yrs	8	44.40%	10	55.60%

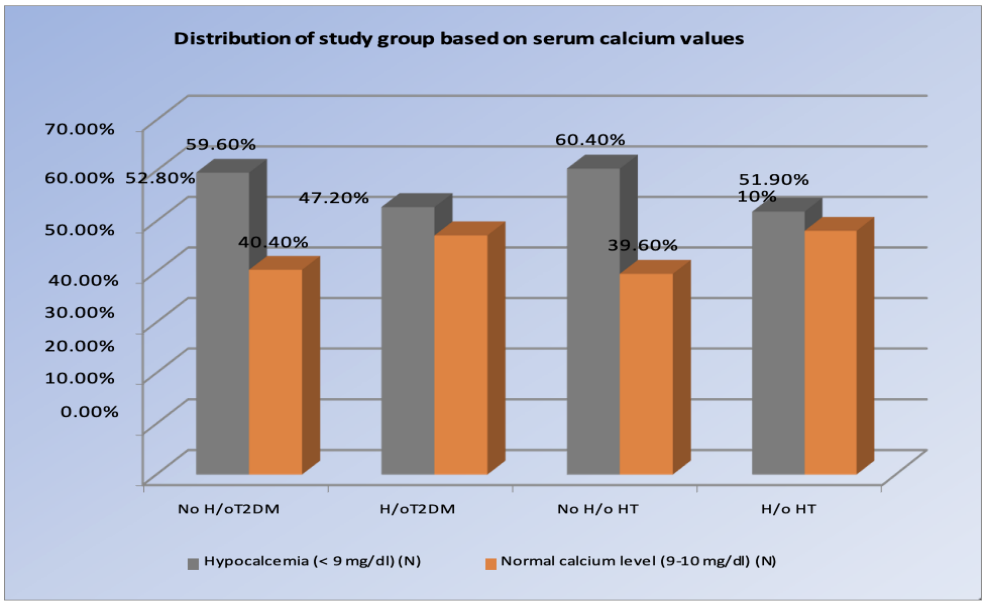

Figure 9:

52.8% of the people with diabetes had hypocalcemia whereas 51.90% of individuals with hypertension had hypocalcemia.

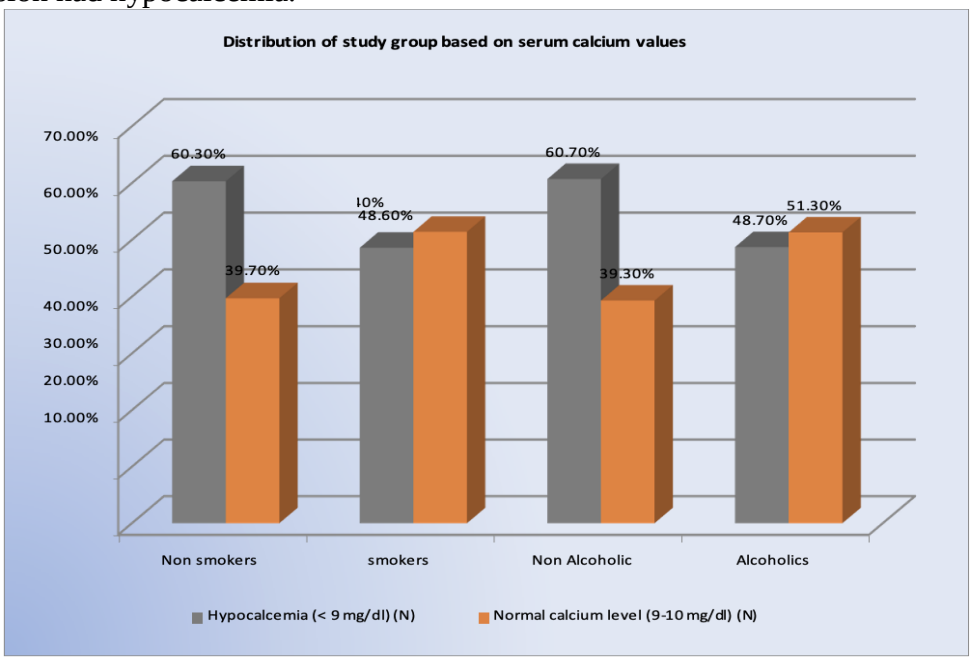

Figure 10:

48.6% of smokers had hypocalcemia whereas 48.70% alcoholics had hypocalcemia.

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Table 3:

	MALES	FEMALES
Aphasia	17(45.9%)	20 (54.1%)

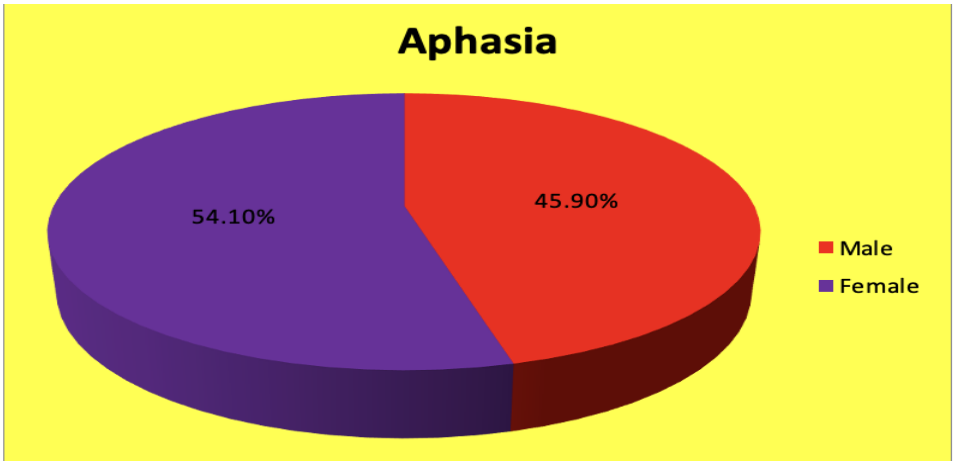

Figure 11:

54.10%(20) of those who had aphasia were females whereas 45.90% (17) were males.

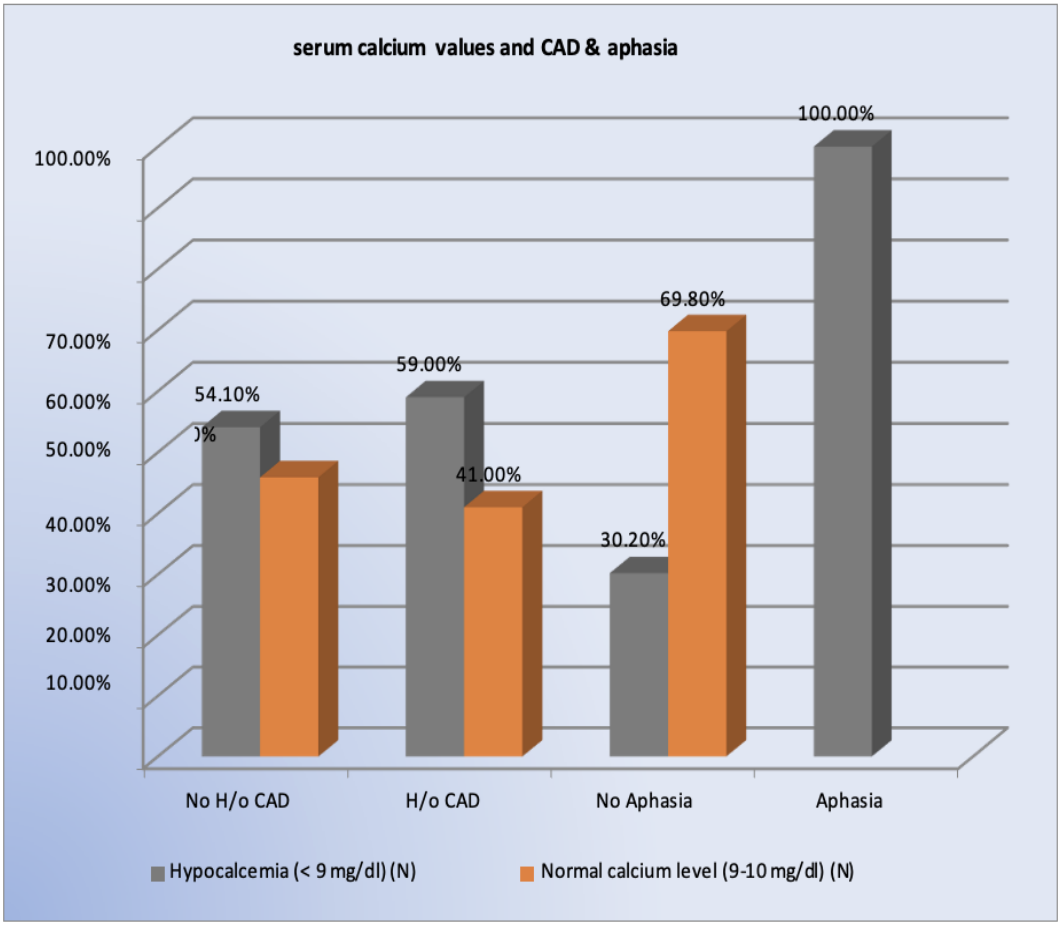

Figure 12:

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59% of those with CAD had hypocalcemia while all those who had aphasia had hypocalcemia.

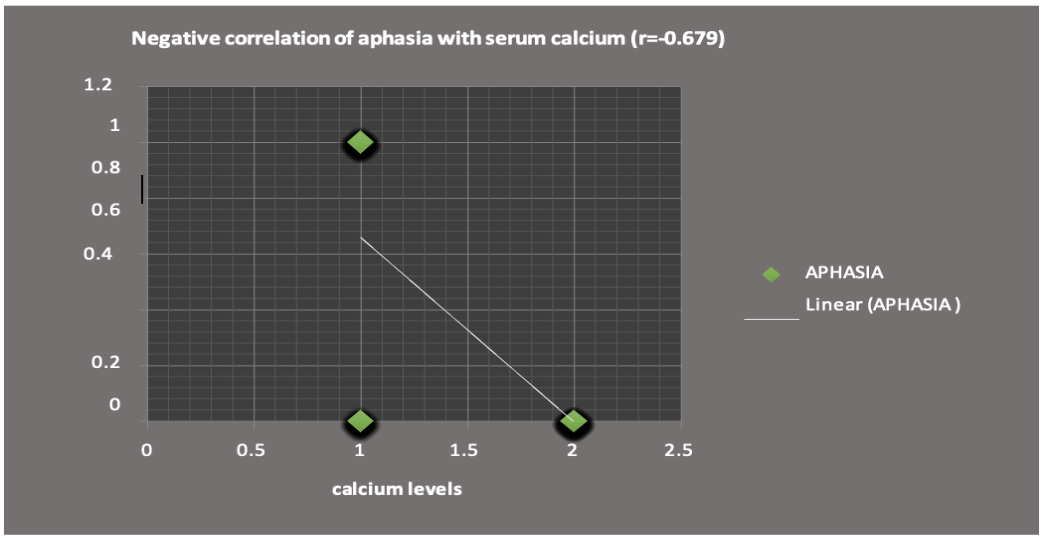

Figure 13:

Aphasia showed negative correlation with calcium levels.

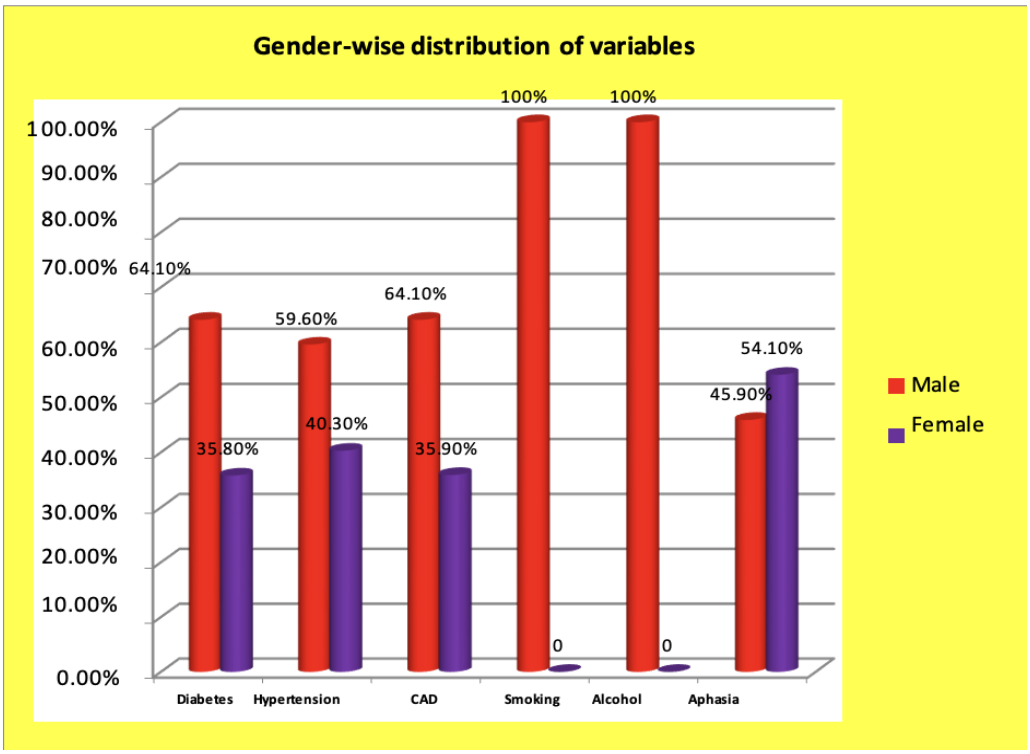

Figure 14:

T2DM, systemic hypertension, CAD did not show any correlation with serum calcium levels.

Table 4:

	MALES		FEMALES	
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION
Infarct size (cm^3)	26.21	17.68	36.52	17.84

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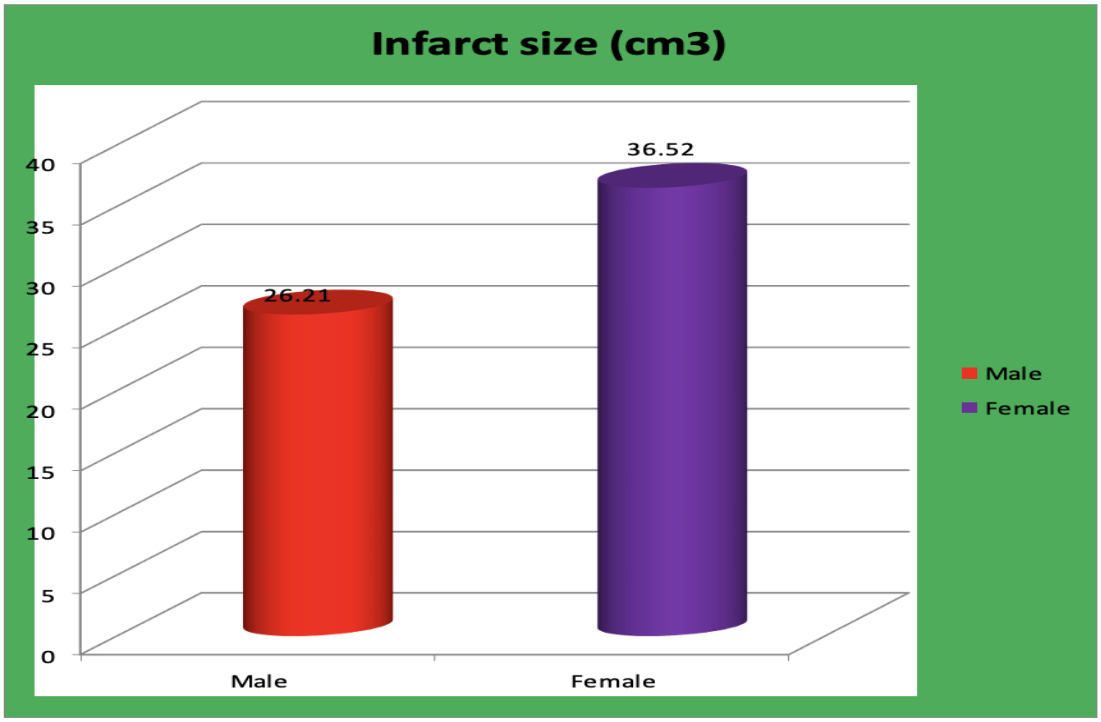

Figure 15:

The mean size of infarct in males was 26.71+/-17.68 and 36.52+/- 17.84cm3 in females.

Table 5:

	MALES		FEMALES	
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION
NIHSS score	16.01	10.18	22.68	9.69

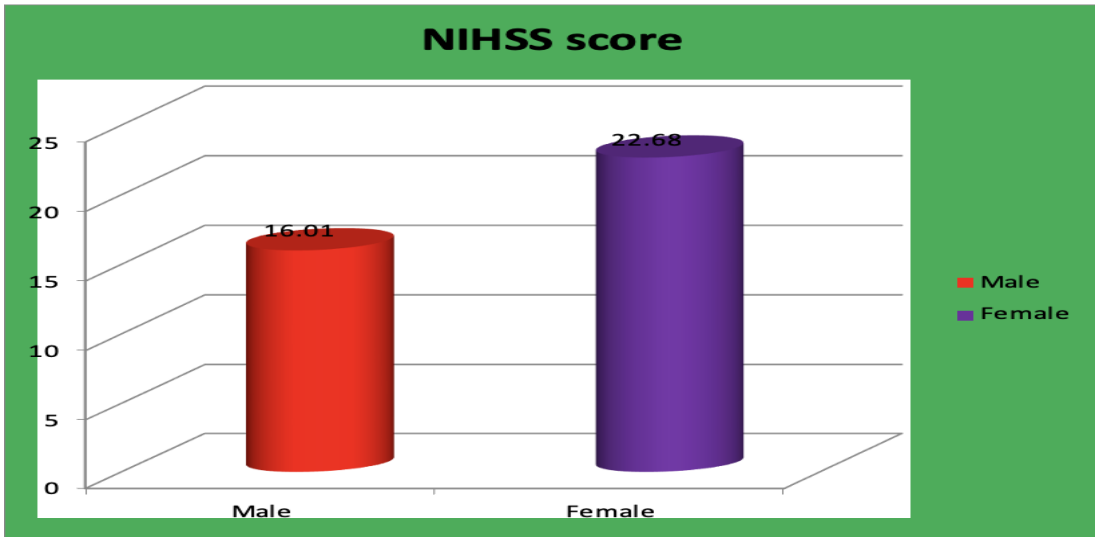

Figure 16:

The mean NIHSS score was 16.01 with a standard deviation of 10.18 and 22.68 with standard deviation of 9.69 in females.

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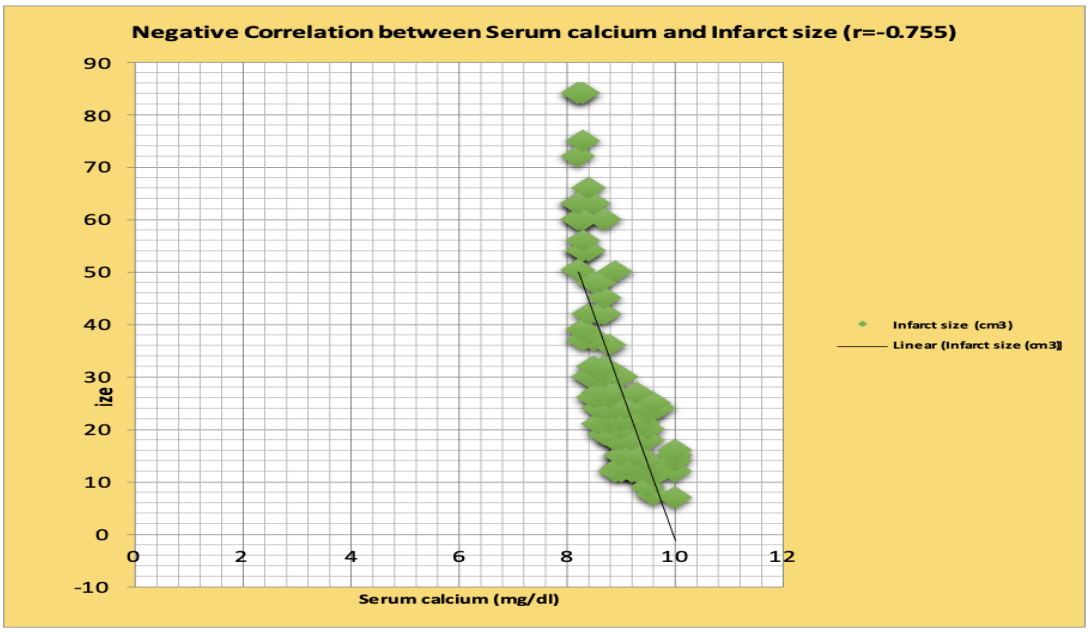

Figure 17:

Correlation between serum calcium levels with infarct size and NIHSS score:

There was a negative correlation of serum calcium with infarct size. That is lower calcium levels were associated with a larger infarct volume and vice versa. It was found to be statistically significant with p value <0.05.

Table 6:

	Serum Calcium(mg/dL)	
	r value	**p value**
Infarct size (cm^3)	-0.755	0.001*
NIHSS score	-0.823	0.001*

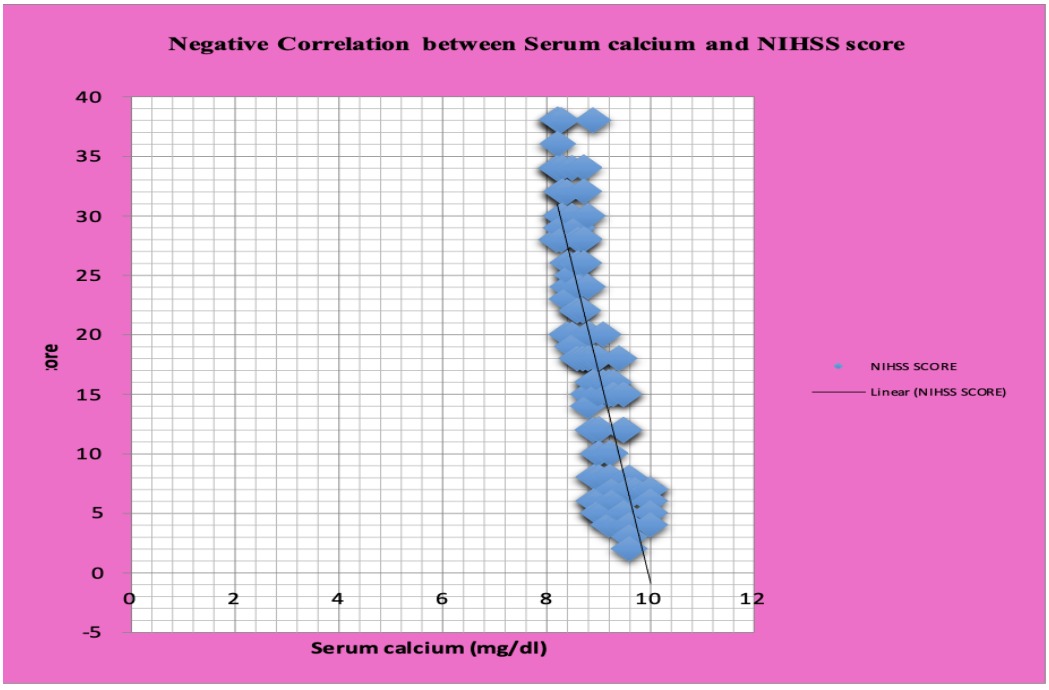

Figure 18:

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There was a negative correlation of serum calcium levels with NIHSS scores. Higher scores were associated with hypocalcemia at presentation. It was found to be statistically significant with a p value of <0.05.

Discussion

Stroke is one of the leading cause of mortality and morbidity. The severity of stroke can be assessed by thorough clinical examination, imaging studies and by certain biochemical markers. We had 100 individuals who participated in this study with 35 of them females and 65 of them males. So we had more males than females with stroke in our study. The mean age was 62, same in each gender. Individuals aged from 45years to 90 years in our study.

Our mean serum calcium was 8.9mg/dL. It was slighltly lower than the normal range. When it came to gender distribution, females had lower mean serum calcium 8.6mg/dL when compared to males 9.0mg/dL. We had more females with hypocalcemia compared to males. In a study conducted by **Meghnah Borah et al** , they found no significant difference in calcium levels between men and women.We divided the sample into those with hypocalcemia as those having below 9mg/dL and those above 9mg/dL. These groups were compared with demographic factors such as age, gender, risk factors like diabetes, hypertension, CAD and addictive behaviour like alcohol and smoking. Also we compared serum calcium levels with the size of infarct and NIHSS score and aphasia on admission. We could not find any association between factors like age, diabetes, hypertension, CAD, alcohol and smoking with serum calcium levels.

We could find significant negative correlation of serum calcium levels on admission with infarct size, NIHSS score and presence of aphasia in our patients. When serum calcium was compared with infarct size we found a negative correlation with Pearson coefficient r of -0.755 with a p value <0.05 which was statistically significant. When we compared serum calcium levels with NIHSS score on admission, we found a negative correlation with r value -0.823 with p value <0.05 which was statistically significant. Similar association was found between serum calcium levels and the presence of aphasia.

Similar to our study **Meghnah Borah et al** in their study had found a negative correlation between serum calcium levels and infarct size. They suggested that those with large infarct size would have lesser serum calcium levels. The exact mechanism behind this is still not clear. Another study by **Muhammed Ishfaq et al** found a negative correlation between serum calcium levels and NIHSS score.they measured the calcium levels within 48-72hrs of presentation. In contrast we measured the calcium levels when the patient presented to the hospital. Some people had delay coming to hospital. Hence we could not really group people as within any time period. But all the patients were having acute ischemic stroke. The serum calcium levels in our study had similar distribution as in this study. The probable reason they had given was that majority were from lower to middle socio economic group with poor nutritional status.

This can be the reason in our study population also. Similarly two other studies one by **Guven et al** and another by **Ovbiagele et al** had found that lower serum calcium levels were associated with more severity of stroke.In the study conducted by **Abha Gupta et al** found that patients with high calcium had significantly less severity of the stroke and during follow up after 7 days had better prognosis when compared to the people with lower levels of calcium, which was statistically significant(p-value 0.01). The level of calcium is found to be

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less in transient ischaemic attack and more lower in ischemic cerebral infarction than TIA.
It is probably due to intracellular influx during acute stroke. Influx of calcium causes potassium channels to open and there by closing calcium channels. Also the influx of calcium causes activation of a calcium sensitive protein phosphorylase calcineurin which dephosphorylates the channel, thereby inactivating it. A rise in extracellular calcium is due to a decrease in the extracellular space resulting in cytotoxic oedema. Depolarization of nerve terminals will cause a calcium influx along an electrochemical gradient and the consequent rise in intra-cellular calcium leads to neurotransmitter release. Much of the calcium that enters must have to be re-distributed within the nerve-terminals i.e. Calcium is transiently sequestered so that the calcium concentration inside declines to a normal level. Later when the calcium is pumped out, it is released from these sequestered areas.

Conclusion

In this study, there were patients within the age group 45 -90 yrs which is similar to the general population having maximum burden of stroke. It was found that females had a lower serum calcium levels when compared to males. The sample group as a whole had serum calcium levels in the lower range, probably it can be attributed to the socioeconomic factors also.
There was no statistically significant association between serum calcium levels and age, diabetes, hypertension, CAD, alcohol intake and smoking.

The major findings in this study were with respect to serum calcium and infarct size, serum calcium and NIHSS score. It was found that statistically significant negative correlation between serum calcium levels and infarct size. There was a statistically significant negative correlation between serum calcium and NIHSS scores on admission and also a negative correlation between serum calcium levels on admission and presence of aphasia.

From this study, the conclusion drawn is that patients with lower serum calcium levels on admission had a much severe stroke with respect to infarct size and NIHSS score. So a low serum calcium levels on admission can be considered to be poor prognostic marker in acute ischemic stroke

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