



RESEARCH ARTICLE

A STUDY ON THE LEVELS OF C-REACTIVE PROTEIN IN SUBJECTS WITH ACUTE ISCHEMIC STROKE

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ABSTRACT

Objectives: Cerebrovascular accident, which has considerable mortality and morbidity, deserves attention towards its prevention. The first lines of defense in stroke prevention are detecting and adequately treating manageable risk factors, C-Reactive protein, an acute phase reactant is an indicator of underlying systemic inflammation and a novel marker for atherothrombotic disease. Present study is an attempt to study the levels of C-Reactive protein in acute ischemic stroke and to correlate between serum C-Reactive protein levels in acute ischemic stroke.

Materials and Methods: Hundred patients with diagnosis of first ever acute ischemic stroke and hundred healthy age and sex matched controls were randomly selected for this case-control cross sectional study conducted from June 2016 to January 2017. Patients were examined, investigated as per proforma. In both cases and controls CRP levels were estimated.

Results: There were 66 (66%) cases and 15 (15%) controls who had positive C-Reactive protein levels (0.6 mg/dL). Mean CRP levels among cases was 3.7 mg/dL and controls was 0.5 mg/dL, which was statistically significant ($p < 0.05$).

Conclusion: C-Reactive protein appears to be an important risk factor for acute thromboembolic stroke at levels of > 0.6 mg/dl. measures to reduce CRP levels by using statins probably helps in a significant way for primary and secondary prevention of stroke.

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INTRODUCTION

World Health Organisation (WHO) defined stroke as "rapidly developing clinical signs of focal or global disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than vascular origin". (WHO, 1976) Stroke manifests by various neurological signs and symptoms depending on extent, area of involvement and the underlying cause. These include coma, hemiplegia, paraplegia, monoplegia, cranial nerve palsy, speech disturbance and sensory impairment, etc. Of these, hemiplegia is the most common presentation, seen in about 90% of patients. (WHO, 1976) A WHO collaborative study (Aho et al., 1980) in 12 countries showed that the incidence rates of stroke ranged from 0.2 to 2.5 per 1000 population per year. In most European countries the incidence was 4-8 per 1000 and in Japan it was 15 per 1000. In females ratios were 30 percent lower than males. In India, analysis of data from major urban, university hospitals suggests that nearly 2 percent of all hospital cases, 4.5 percent of medical cases and 20 percent of neurological admissions are

from stroke (Park, 2002; Ahuja, 1983). Cerebrovascular disease is the third leading cause of death after heart disease and cancer in many countries in the West. The WHO collaborative study showed that both in developed and developing countries nearly one-third of patients died within three weeks and 48 percent died within one year. Thus stroke, which is associated with considerable morbidity and mortality, deserves attention towards its prevention. The first lines of defense in stroke prevention are detecting and adequately treating manageable risk factors. The role of C-Reactive Protein as risk factors remains inconclusive. So, studies in this regard are necessary. Ridker et al. (1997) first reported that C-Reactive Protein level predicts future myocardial infarction and stroke. C-Reactive Protein, an acute-phase reactant, is an indicator of underlying systemic inflammation and a novel marker for atherothrombotic disease. (Natalia S Rost et al., 2001) C-Reactive Protein was discovered by Tillett and Francis in 1930, who were investigating serological reactions in pneumonia with various extracts of pneumococci. Ridker et al. concluded from a prospective study of 27,939 apparently healthy women, comparing serum levels of C-Reactive Protein and LDL-cholesterol, that the C-reactive protein level is a stronger predictor of cardiovascular events than the LDL cholesterol

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level, and that C-reactive protein and LDL-cholesterol were minimally correlated. In the present study, an attempt is made to study the levels of C-Reactive Protein levels in acute thromboembolic stroke, and an attempt has been made to correlate serum C-Reactive Protein levels in acute ischemic stroke.

MATERIALS AND METHODS

Source of data or the case is defined with diagnosis of first ever ischemic stroke and hundred healthy, age and sex matched controls attending department of medicine, Chengalpattu medical college, chengalpattu during the period of June 2016 to January 2017. The study is a case-control study in which cases and controls are selected taking into consideration inclusion and exclusion criteria. The sampling method is simple random. Detailed history was taken, clinical examination was done as per proforma and investigations were done in both cases and controls. Controls are selected with age and sex matched with cases and causes which affect the CRP levels are excluded from the study.

Inclusion Criteria

1. All patients of first ever CT proven ischemic stroke admitted within 72 hours of symptom onset.
2. 100 Age and sex matched controls.

Exclusion Criteria

1. For cases Patients with following conditions, identified by history, clinical examination and investigations are excluded from the study.
 - a. Valvular heart disease.
 - b. Congenital heart disease.
 - c. Ischemic heart disease.
 - d. Atrial fibrillation.
 - e. Acute infectious disease.
 - f. Osteoarthritis, costochondritis, rheumatoid arthritis, ankylosing spondylitis and other disorders.
 - g. Known or suspected neoplastic disorders.
 - h. Recent (less than 3 months) major trauma, burns, surgery.
 - i. Patients with ischemic stroke after 72 hours of symptom onset.
 - j. Patients taking hypolipidemic drugs and steroids (including OCPs).

2. For Controls

- Healthy persons with following conditions liable to affect serum C-Reactive
- Protein and lipid levels were taken as controls.
 - a. Acute infections.
 - b. Ischemic heart disease.
 - c. Osteoarthritis, costochondritis, rheumatoid arthritis, ankylosing spondylitis and other disorders.
 - d. Patients taking hypolipidemic drugs and steroids (including OCPs).

For every case and control selected, clinical data and results of routine investigations were prospectively recorded. In both cases and controls, blood sample was taken for C-reactive protein by performing venepuncture, and estimation was done

at BiochemLab, Chengalpattu medical college and hospital. The C-Reactive Protein test is a rapid slide agglutination procedure for the direct detection and semi quantitation of C-reactive protein. The reagent, a latex particle suspension coated with specific antihuman C-reactive protein antibodies, agglutinates in the presence of C-Reactive Protein in patients serum. The presence of agglutination indicates content of C-Reactive Protein in the sample equal to or greater than 0.6 mg/dL. Comparison of various parameters among male and female subjects with or without stroke were performed by t-test. Correlation between two variables are done by Pearson's Correlation Coefficient.

RESULTS

Total Cases: 100

Controls: 100

Age Distribution

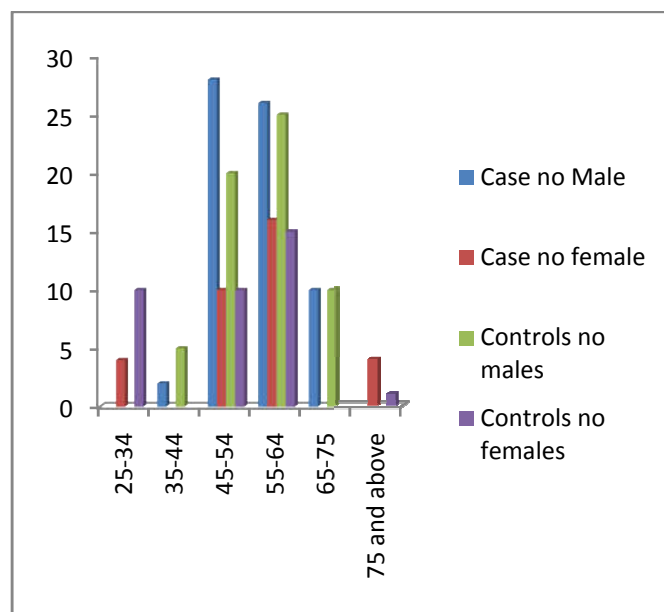
Age In Years	Case Number (%)			Control Number (%)		
	Male	Female	Total	Male	Female	Total
25-34	-	4(11.8%)	4	-	10(25%)	10
35-44	2(3%)	-	2	5(8.3%)	-	5
45-54	28(42.4%)	10(29.4%)	38	20(33.3%)	10(25%)	30
55-64	26(39.4%)	16(47.1%)	42	25(41.7%)	15(37.5%)	40
65-75	10(15.2%)	-	10	10(16.7%)	-	10
75 and above	-	4(11.8%)	4	-	5(12.5%)	5

Table 1. Showing age distribution

In this study majority of cases were in the age group of 55-64 years (42) constituting 44% of cases. In the control group majority were in the age group of 55-64 years (40), constituting 40%. The mean age of cases and controls were 55.8 years and 54.9 years respectively.

Table 2: Showing mean age and SD (years)

Parameters	Cases	Controls
Mean age	55.8	54.9
SD	± 10.34	± 8.91



Sex Distribution

Sex	Case Number (%)	Control Number (%)
Male	66 (66%)	60(60%)
Female	34(34%)	40(40%)
Total	100 (100%)	100(100%)

Table 3. Sex distribution

Symptoms	Male	Female	Total
Hemiplegia	64(97.1%)	30(88.2%)	94(94%)
Aphasia	20(10.3%)	10(29.4%)	30(30%)
Cranial nerve palsy	52(78.%)	26(76.5%)	78(78%)
Altered sensorium	0	0	0
Headache	2(3%)	0	2(2%)
Vomiting	2(3%)	6(17.6%)	8(8%)
Seizures	0	0	0

Table 4. Symptom analysis

In the present study the commonest presentation of cerebrovascular accident is hemiplegia (94%), followed by cranial nerve palsy (78%), aphasia (30%), vomiting (8%), and headache (2%). Altered sensorium and seizure were not found in any case.

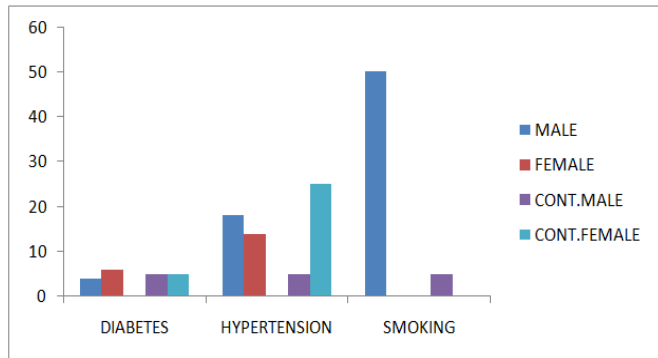


Figure 2. Risk factors in cases and controls

C-Reactive Protein Level.

C- reactive Protein	Cases			Controls		
	Male	Female	Total	Male	Female	Total
>0.6mg/dl	44(66.7%)	22(64.7%)	66(66%)	10(16.6%)	5 (12.5%)	15(15%)
<0.6 mg/dl	22(33.3%)	12(35.3%)	34(34%)	50(83.3%)	35(87.5%)	85(85%)

Table 5. Showing C-Reactive Protein distribution among cases and controls

In the present study, 66 cases and 15 controls had C-reactive protein greater than 0.6mg/dl while 34 cases and 85 controls had C-reactive protein less than 0.6. This is highly significant (P<0.05). The mean reactive protein among cases and controls were 3.7 and 0.5mg/dl respectively which is also significant (p<0.05)

Table 6. Showing mean and Standard Deviation of C-Reactive Protein mg/dL

C-Reactive Protein (mg/dL)	Cases	Controls
Mean	3.7	0.5
Standard deviation	± 3.2	± 0.12

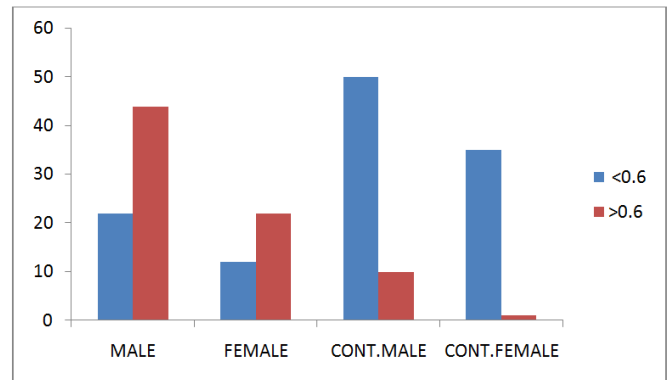


Figure 3. C-Reactive protein distribution among cases and controls

DISCUSSION AND CONCLUSION

The present study is a hospital based, cross sectional case-control study with 100 cases and 100 age and sex matched controls.

The present study was compared with the following parameters of different studies.

1. Mean age, smoking, diabetes mellitus, hypertension, mean CRP levels, mean total cholesterol in J. David Curb *et al.* (2003) study.
2. Mean age and mean CRP levels in Agarwal *et al.* (2003) study.
3. Mean age, smoking, diabetes mellitus, mean CRP levels, in Natalia S. Rost *et al.* (2001) study.
4. Mean age, positive CRP levels (> 0.6 mg/dl) in Dhamija *et al.* (2003)
5. Positive CRP levels (> 0.6 mg/dl) in Mahapatra *et al.* (2002) study.

In the present study, the mean age for cases and controls were 55.8 years and 54.9 years respectively, which is comparable to the study by Curb *et al.* (2003) 58.1 years and 55.8 years, Agarwal *et al.* (2003) 65.33 years and 65.25 years, Natalia S. Rost *et al.* (2001) 69.7 years in cases, and Dhamija R.K. *et al.* (2003) 56.48 years and 54.20 years in cases and controls respectively.

Smokers in the present study were, 50% and 25% among cases and controls respectively, which is comparable to the studies by Curb *et al.* (2003) 54.4% and 37.6% cases and controls respectively and Natalia S. Rost *et al.* (2001), 22.7% in cases.

Diabetics in the present study were 10% and 10% among cases and controls respectively which were comparable to the studies by Curb *et al.* (2003) 27% and 13.3% cases and controls respectively and Natalia S. Rost *et al.* (Natalia S Rost *et al.*, 2001) 9.5% of cases.

Hypertensives in the present study, were 32% and 30% among cases and controls respectively, which were comparable to the study by Curb *et al.* (2003), 27% and 10.6% among cases and controls respectively.

The mean CRP level in the present study was 3.7 mg/dl and 0.5 mg/dl among cases and controls respectively, which was statistically significant p < 0.05, which was comparable to studies done by Agarwal *et al.* (2003) 25 mg/dl and 4.00 mg/dl. J. David Curb *et al.* (2003) 14.3 mg/dl and 11.6 mg/dl in cases and controls respectively,

and the study by Natalia S. Rost *et al.* (2001) 5.8 mg/dl in cases.

Positive CRP levels in the present study were 66% and 15% among cases and controls respectively, which is comparable to studies done by Dhamija R.K. *et al.* (2003), 77.7% of cases and 12.54% of controls and S.C. Mahapatra *et al.* (2002) 80% of cases and 10% of controls.

We conclude that C-Reactive protein appears to be an important risk factor for acute thrombo embolic stroke at levels of > 0.6 mg/dl. Measures to reduce CRP levels by using statins probably helps in a significant way for primary and secondary prevention of stroke.

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