# Study of Serum Cystatin C, Lipid Profile and Electrolytes in Acute Stroke Patients

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## ABSTRACT

**Background:** *The effectiveness of cystatin C as a biomarker in acute hemorrhagic/ischemic stroke is being studied recently. It is due to accumulating evidence indicating a link between vascular disease of the kidney and brain. In this study we have investigated the association of serum cystatin C with first onset acute stroke.*

**Methods:** *A total of 45 patients with first onset stroke, aged more than 30 years, were selected for the study based on history, detailed clinical examinations, neuro-imaging and other related investigations. The patients were presenting within 72 hours after onset of symptoms.*

**Results:** *Serum cystatin C levels were significantly elevated ($p<0.0001$) in cases (1.60±0.88 mg/l) when compared with controls (0.82±0.11 mg/l). Serum creatinine levels were also significantly elevated ($p<0.001$) in cases (1.77±1.23 mg/dl) when compared with controls (1.05±0.18 mg/dl). Among lipid profile parameters, total cholesterol, triglycerides, LDL and VLDL cholesterol were all significantly increased in cases when compared with controls.*

**Key words:** *Acute stroke, Cystatin C, Dyslipidemia, Electrolytes.*

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## INTRODUCTION

Cystatin C (Cys-C) was first described as 'gamma-trace' in 1961 as a trace protein together with other ones (such as beta-trace) in the cerebrospinal fluid and in the urine of patients with renal failure[1]. Two years later, cys-C was identified as an inhibitor of cysteine proteases. Over the last two decades, 11 further human cysteine protease inhibitors have been identified. It was first proposed as a measure of glomerular filtration rate by Grubb and coworkers in 1985[2,3]. Since this time, there has been a growing interest in Cystatin C as a marker of GFR[4-17].Cys-C has a molecular mass of 13,343 Da, as determined both by mass spectrometry and by calculation from the amino acid sequence of its single polypeptide chain[18,19]. About 50% of cys-C carries a hydroxylated proline residue at position three, and the molecular mass of hydroxylated cys-C is thus 13,359 Da. Cys-C is unique among cystatins as it seems to be constantly produced by all human nucleated cells. It is freely filtered by the glomerulus and it is largely reabsorbed and catabolized in the proximal tubules. Cystatin C is a better predictor of renal function, particularly when the renal function is only mildly or moderately impaired. The attractiveness of cystatin C is due to the fact that there are a lot of similarities in the vascular supply to kidney and brain. Both these organs are low resistance end organs and are exposed to high volume blood flow throughout cardiac cycle. It therefore seems that micro vascular disease in kidney and brain might co-exist together.

In this current study we have tried to find the levels of serum creatinine, serum cystatin C in acute hemorrhagic/ ischemic stroke patients. Also the level of serum electrolytes and lipid profile to find the implications of cystatin C as a potential biomarker in acute stroke.

## MATERIALS AND METHODS

The study was conducted in the Department of Biochemistry, S.C.B. Medical College and Hospital, Cuttack from September 2013 to December 2014. 45 patients of age group 30-70 years, attending OPD and indoor in the Department of Medicine, S.C.B. Medical College and Hospital, Cuttack were included in the study. Patients with acute stroke were selected and diagnosed on the basis of their history, detailed clinical examinations, neuro-imaging and other related investigations. 45 age and sex matched controls were selected from department staffs with normal serum lipid profile, no symptoms and signs suggestive of stroke and no family history of the disease.

3 ml of blood was collected after overnight fasting of 8 hours from all enrolled patients and healthy controls for the assessment of lipid profile, electrolytes, creatinine, cystatin-C levels. Demographic characteristics (name, age, sex), history of risk factors (smoking, family history, medications, alcohol intake etc.), systolic and diastolic blood pressures, were recorded in detail.

The exclusion criteria included diabetes mellitus, chronic kidney disease, liver disease, hypothyroidism and malignancies.

Cystatin C was measured by turbidimetric immunoassay method[20,21].

The study was approved by '**Institutional Ethics Committee**' dated 09.10.2013.

Statistical analysis was done using SPSS and Microsoft Excel 10.

## RESULTS

The maximum number of the patients of this study was from age group 41-50 years followed by 51-60 years. The mean age was 53.44±8.97 years in study group. There was a slight female preponderance, with the male: female ratio being 0.95:1. Among all the cases, 77% were hypertensive, rest were normotensive. Among male cases 50% were smokers, 33% were alchoholic. 22% of the cases had positive family history.

Of the lipid parameters in cases and control, a significantly higher level of total cholesterol, triglycerides LDL & VLDL cholesterol was found in stroke patients when compared to healthy controls. Whereas HDL cholesterol was not significantly raised in cases when compared to controls.

Among the renal function test parameters, serum cystatin C levels were significantly increased ($p<0.0001$) in acute stroke patients when compared with controls. Creatinine levels were also significantly elevated ($p<0.001$) in cases in comparison with controls.

Serum electrolytes (Na+ and K+) though did not show any significant changes (increase or decrease) in stroke patients as compared with controls.

**Table 1: Age and Sex Distribution of Study Group**

| | Study Group (n =45) | | |
|---|---|---|---|
| | **M** | **F** | **Total** |
| 30-40 yrs | 2 | 2 | 4 |
| 41-50 yrs | 6 | 12 | 18 |
| 51-60 yrs | 9 | 6 | 15 |
| >60 yrs | 5 | 3 | 8 |
| **Total** | **22** | **23** | **45** |

**Table I**: Shows the age, sex distribution of acute stroke patients. The maximum number of the cases from the study group was in the age group 41-50 years. Out of 45 cases, 22 were male and 23 females.

**Table 2: Biochemical Parameters in Control Group and Study Group**

| S. No. | Parameter | Control group (n=45) | Study group (n= 45) |
|---|---|---|---|
| | | **Mean ± SD** | **Mean ± SD** |
| **1.** | **Cystatin C (mg/l)** | 0.82±0.11 | 1.60±0.88** |
| **2.** | **Creatinine (mg/dl)** | 1.05±0.18 | 1.77±1.23* |
| **4.** | **Serum Na+** | 137.6±4.23 | 136.7±4.33 |
| **5.** | **Serum K+** | 4.29±0.78 | 4.08±0.89 |

Statistically significant ****p**< 0.0001, as compared to control.

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**Table II**: shows the renal function test parameters. Cystatin C and creatinine levels were significantly elevated in cases as compared with controls. Serum electrolytes levels didn't show any significant changes in cases compared to controls.

**Table 3: Lipid Profile of Control Group and Study Group**

| Sl. No. | Parameter (mg/dl) | Control group (n=45) | Study group (n=45) |
|---|---|---|---|
| | | **Mean ± SD** | **Mean ± SD** |
| **1.** | **Total Cholesterol** | 153.33±28.04 | 178.33±42.7$^{\Omega}$ |
| **2.** | **Triglycerides** | 99.99±24.36 | 137.9±35.12* |
| **3.** | **HDLc** | 47.13±6.80 | 48.6±9.79 |
| **4.** | **LDLc** | 86.00±23.62 | 104.2±37.2 $^{\Omega}$ |
| **5.** | **VLDLc** | 20.13±4.86 | 27.7±14.3* |

Statistically significant Ω $p< 0.01$, as compared to control.

Statistically significant *$p < 0.001$, as compared to control.

**Table III**: shows the lipid profile parameters. Total cholesterol, triglycrides LDL, and VLDL cholesterol levels were increased significantly in study group when compared with control group.

## DISCUSSION

The association between impaired renal function and stroke has been noticed in several studies. This indicates that it may be due to similar vascular supply in both kidney and brain[22]. The study here proves that coexisting impaired renal function may lead to stroke. Renal function here is assessed by creatinine, electrolytes and cystatin Existing hypertension and dyslipidemia also are two main independent risk factors of stroke which are often associated. The co-existence of these two risk factors has more than an additive adverse impact on the vascular endothelium, which results in enhanced atherosclerosis, leading to target organ damage.

Among renal function test parameters creatinine and creatinine clearance has been established markers for assessing impaired renal function. But serum creatinine and urea are dependent upon variables like age, muscle mass and hence estimated GFR (eGFR) is used for assessing the renal function. Estimated GFR can't be used as gold standard as it is only a calculated parameter based on variables especially serum creatinine which shows a blind area even when the GFR falls up to 50% of normal.

In recent years the role of cystatin C in predicting early decline in GFR in comparison to serum creatinine and creatinine based GFR equations has been much debated. As serum cystatin C is a more precise test for kidney function, a finding in several cross sectional studies [23,24.]. It suggests that cystatin C might predict the risk of developing chronic kidney disease, thereby signaling a state of ''preclinical'' kidney dysfunction[25-32]. The present study has tried to explore the usefulness of cystatin Cover serum creatinine for identification of a better marker of early renal involvement in acute stroke patients which in turn can help in their timely intervention and management.

Cystatin C levels may thereby reflect the duration and severity of other established risk factors like hypertension[33]. It also plays an important role in the development of atherosclerosis. Being a protease inhibitor, high levels of cystatin C affects the process of vascular wall remodeling by regulating the balance of proteolytic and anti- proteolytic activities[34].

## CONCLUSION

In conclusion our findings indicate that cystatin C can serve as a very good marker of acute stroke and a better marker in predicting renal impairment in such patients.

The limitation in this study was the inaccuracy of serum creatinine as a marker of renal impairment. To overcome it cystatin C was used as a marker of impaired renal function. As ours is a unicentric study, we cannot determine causality. The results can be further established by increasing the sample size and by follow up of all the cases by measuring all the biochemical parameters after certain time period to assess the degree of progressive renal impairment in such cases.

The authors declare that they have no competing interests.

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