MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.59218/makrjms.2024.3.18.465.468

Determination of Association and Prognostic Value of Cystatin C in Ischaemic and Hemorrhagic Stroke

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OPEN ACCESS

Key Words
Prognostic value, cystatin C, ischaemic stroke, hemorrhagic stroke

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Received: 24 May 2024
Accepted: 18 June 2024
Published: 23 June 2024

Citation: Monoj Sharma, Ramprasad Atta, Kanika Jana, Srabani Ghosh, Debkumar Ray, Saumik Datta and Md Alamgir Perwana, 2024. Determination of Association and Prognostic Value of Cystatin C in Ischaemic and Hemorrhagic Stroke. Res. J. Med. Sci., 18: 465-468, doi: 10.59218/makrjms.2024.3.18.465.468

ABSTRACT

Cystatin C (Cys C) is also known as Cystatin 3. It is a protein inhibitor of cysteine protease. Cystatin C is encoded by the CST3 gene by all nucleated cells (DNA containing cells) at a constant rate. Cystatin C is a protein consists of 120 Amino Acids and contained by all tissues and body fluids (normal blood serum cystatin C value is between 0.6 and 1 mg L^{-1}). To determine serum Cystatin C levels in patients with ischaemic and hemorrhagic stroke. The present study was a Hospital based Longitudinal Comparative study. This Study was conducted for one and half year at Department of Medicine and Department of Biochemistry of Burdwan Medical College and Hospital. Total 120 patients were included in this study. In Hemorrhagic stroke , the mean Cystatin-C value within 24 hrs of stroke (mg L^{-1}) (Mean±S.D.) of patients was 1.1665±0.3495. In Ischaemic stroke, the mean Cystatin-C value within 24 hrs of stroke (mg L^{-1}) (Mean±S.D.) of patients was 1.5987±0.4432. Distribution of mean Cystatin-C value within 24 hrs of stroke (mg L^{-1}) with Group was statistically significant ($p<0.0001$). In Hemorrhagic stroke, the mean Cystatin-C value at end of 1st week of stroke (mg L^{-1}) (Mean±S.D.) of patients was 1.1728±0.3539. In Ischaemic stroke, the mean Cystatin-C value at end of 1st week of stroke (mg L^{-1}) (Mean±S.D.) of patients was 1.5087±0.4187. Distribution of mean Cystatin-C value at end of 1st week of stroke (mg L^{-1}) with Group was statistically significant ($p<0.0001$). In Hemorrhagic stroke, the mean Cystatin-C value at end of 2nd week of stroke (mg L^{-1}) (Mean±S.D.) of patients was 1.1810 ± 0.3040. In Ischaemic stroke, the mean Cystatin-C value at end of 2nd week of stroke (mg L^{-1}) (Mean±S.D.) of patients was 1.3792±0.4214. Distribution of mean Cystatin-C value at end of 2nd week of stroke (mg L^{-1}) with Group was statistically significant ($p<0.0001$). In conclusion, this study on the association and prognostic value of cystatin C in ischemic and hemorrhagic stroke reveals significant findings that could enhance stroke prognosis and management. Elevated cystatin C levels were found to be associated with the severity and outcomes of both types of stroke, suggesting that cystatin C could serve as a valuable biomarker for assessing stroke prognosis.

INTRODUCTION

Cystatin C (Cys C) is also known as Cystatin 3. It is a protein inhibitor of cysteine protease. Cystatin C is encoded by the CST3 gene by all nucleated cells (DNA containing cells) at a constant rate. Cystatin C is a protein consists of 120 Amino Acids and contained by all tissues and body fluids (normal blood serum cystatin C value is between 0.6 and 1 mg L^{-1}). It belongs to the type-II Cysteine family. It has been suggested as a sensitive bio marker of kidney function than the creatinine-based equation because serum concentration is independent of muscle mass and do not seem to be affected by age. It might also be associated with deteriorating kidney function and deteriorating cardio vascular disease. A high level of Cystatin C is also associated with cerebral artery stenosis, systemic inflammation and metabolic syndrome. High level Cystatin C has also been related to ischaemic stroke in elderly patients with increased chances of morbidity and mortality. Whether Hemorrhagic stroke is associated with Cystatin C level changes is not clearly known.

Cerebrovascular accident is a condition to the brain from interruption of blood supply due to ischaemia or hemorrhage leading to trouble speaking, walking and understanding, weakness or paralysis and other clinical signs and symptoms and association of increased level of Cystatin C with ischaemic stroke is obvious according to some studies and evidences but it has to find out or establish whether hemorrhagic stroke is associated with change in serum level of Cystatin C or not. Hospital staying stroke patients are to be evaluated by serial detecting of Cystatin C level that there is any relation in serum level of Cystatin C with prognosis with subsequent treatment and improved clinical outcome.

We undertook the study to determine the association of increased level of serum Cystatin C in ischaemic stroke (as studies show ischaemic stroke has correlation with increased serum cystatin c level) and increased or decreased level of serum Cystatin C in hemorrhagic strokes and level of Cystatin C on prognosis with treatment within stay in hospital.

The WHO-SAGE survey conducted in India in 2017-2018 found an approximate 3.823% stroke in elderly population in West Bengal. Other few studies also show quite similar proportion of stroke prevalence in West Bengal.

Aims and objective:

- To determine serum Cystatin C levels in patients with ischaemic and hemorrhagic stroke
- To evaluate serum Cystatin C level change in ischaemic and hemorrhagic stroke on prognosis with treatment
- To find out a comparative result of change in level of Cystatin C in both Ischaemic and hemorrhagic strokes

MATERIALS AND METHODS

Study design: Hospital based Longitudinal Comparative study. Study setting: Hospital based study.

Place of study: This study was conducted in the Department of Medicine and Department of Biochemistry of Burdwan Medical College and Hospital.

Study population: Patients admitted with stroke through emergency and OPD to Medicine ward (Male and Female)

Sample size: 120 (60 cases of ischaemic stroke and 60 cases of hemorrhagic stroke admitted in the hospital based on inclusion and exclusion criteria) throughout the study duration.

Sampling technique: Random serial sampling technique.

Study period: One and half year. (December, 2022 to May, 2024).

Inclusion criteria:

- Male or female aged 60 years and above
- Hypertension
- No previous history of stroke (new cases)
- No previous history of Myocardial infarction/Angina or heart failure
- With or without history of Smoking

Exclusion criteria:

- Male or Female aged below 60 years
- Previous history of Stroke/TIA
- Kidney disease (AKD, CKD, RCC)
- Previous Angina or Heart Failure or MI
- Presence of Mental disorder
- Diabetes mellitus
- Cases were taken as per above guidelines

Parameters to be studied:

- Age, Gender, Blood pressure
- Clinical presentation of patient, details previous history
- Blood sample for investigation: Serum Cystatin C, blood sugar, Kidney function test
- Radiological imaging (CT and or MRI): To exclude Ischaemic and Hemorrhagic stroke
- Urine for routine and microscopic examinations

Study tools:

- Pre designed, pre tested schedule
- Instrument to check plantar reflex,
- Centrifuge machine REMI R-8C
- Routine laboratory glass wares
- Oxalo-fluride vials, Plain vials without any coagulant

- Distilled water, Normal saline (0.9%)
- Rubber tourniquet, Disposable syringes
- Spirit, Cotton swab
- Sphygmomanometer, Stethoscope
- Nephelometer for estimation of Cystatin C
- Torch light

In Hemorrhagic stroke, the mean Cystatin-C value within 24 hrs of stroke (mg L^{-1}) (Mean±S.D.) of patients was 1.1665±0.3495 (Table 1).

In Ischaemic stroke, the mean Cystatin-C value within 24 hrs of stroke (mg L^{-1}) (Mean±S.D.) of patients was 1.5987±0.4432.

Distribution of mean Cystatin-C value within 24 hrs of stroke (mg L^{-1}) with Group was statistically significant (p<0.0001).

In Hemorrhagic stroke, the mean Cystatin-C value at end of 1st week of stroke (mg L^{-1}) (Mean±S.D.) of patients was 1.1728±0.3539.

In Ischaemic stroke, the mean Cystatin-C value at end of 1st week of stroke (mg L^{-1}) (Mean±S.D.) of patients was 1.5087±0.4187.

Distribution of mean Cystatin-C value at end of 1st week of stroke (mg L^{-1}) with Group was statistically significant (p<0.0001).

In Hemorrhagic stroke, the mean Cystatin-C value at end of 2nd week of stroke (mg L^{-1}) (Mean±S.D.) of patients was 1.1810±0.3040.

In Ischaemic stroke, the mean Cystatin-C value at end of 2nd week of stroke (mg L^{-1}) (Mean±S.D.) of patients was 1.3792±0.4214.

Distribution of mean Cystatin-C value at end of 2st week of stroke (mg L^{-1}) with Group was statistically significant (p<0.0001).

In Hemorrhagic stroke, 4 (6.7%) patients were <60 years of age, 33 (55.0%) patients were 61-70 years of age, 18 (30.0%) patient were 71-80 years of age and 5 (8.3%) patients were >81 years of age.

In Ischaemic stroke, 42 (70.0%) patients were 61-70 years of age, 14 (23.3%) patient were 71-80 years of age and 4 (6.7%) patients were >81 years of age (Fig. 1).

Association of age in group with group was not statistically significant (p = 0.1276).

DISCUSSION

The present study was a Hospital based Longitudinal Comparative study. This Study was conducted for one and half year at Department of Medicine and Department of Biochemistry of Burdwan Medical College and Hospital. Total 120 patients were included in this study.

Group -I- 60 patients with Hemorrhagic stroke.

Group -II- 60 patients with Ischaemic stroke.

Avan *et al*.[1] examined that the effect of age and sex on associations of risk factors with stroke mortality

Table1: Distribution of mean Cystatin-C value within 24 hour of stroke, 1st week of stroke and 2nd week of stroke (mg L^{-1}): Group

	Number	Mean	SD	Minimum	Maximum	Median	p-value
Cystatin-C value within 24 hrs of stroke (mg L^{-1})							
Hemorrhagic stroke	60	1.1665	0.3495	0.6300	2.0900	1.1950	<0.0001
Ischaemic stroke	60	1.5987	0.4432	0.6700	2.6100	1.6300	
Cystatin-C value at end of 1st week of stroke (mg L^{-1})							
Hemorrhagic stroke	60	1.1728	0.3539	0.6300	2.0800	1.2000	<0.0001
Ischaemic stroke	60	1.5087	0.4187	0.7000	2.4900	1.4850	
Cystatin-C value at end of 2nd week of stroke (mg L^{-1})							
Hemorrhagic stroke	60	1.1810	0.3040	0.7100	1.9800	1.2100	<0.0001
Ischaemic stroke	60	1.3792	0.4214	0.6100	2.4000	1.4000	

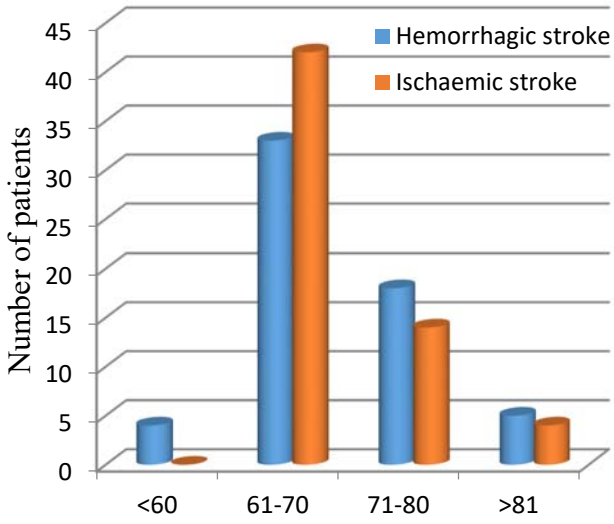

Fig. 1: Association between age in group: Group

from 1990 to 2017. Despite a growth in crude number of stroke events from 1990 to 2017, there has been an 11.3% decrease in age-standardised stroke incidence rate worldwide (150.5, 95% uncertainty interval [UI] 140.3-161.8 per 100,000 in 2017) also Zaki found that Case-control study was conducted on 66 subjects, 33 patients within the first week of stroke onset with age range from 40-75 years and 33 control healthy subjects with matched age and sex but In our study, out of 120 patients most of the patients were 61-70 years old [75 (62.5%)] but this was not statistically significant (p = 0.1276).

Ismail *et al*.[2] found that we included 174 adult patients with first-ever acute cerebrovascular ischemic stroke of not more than 48 hrs duration with normal kidney functions (78 males and 96 females with age ranged from 33-90 years) but We found that, male population was higher [67(55.8%)] than the female population [53 (44.2%)]. Male: Female ratio was 4.3:1 but this was not statistically significant (p = 0.3580).

In our study, Age was higher in Hemorrhagic stroke [69.3833±7.5422] compared to Ischaemic stroke [69.0833±6.2931] but this was not statistically significant (p = 0.8134).

Akoudad *et al*.[3] found that Persons with higher albumin-to-creatinine ratio or lower cystatin C-based estimated glomerular filtration rate levels had a higher prevalence of lacunes (odds ratio per standard deviation increase in albumin-to-creatinine ratio: 1·24, 95% confidence interval 1·07; 1·43) but We found that, Cystatin-C value within 24 hrs of stroke (mg L^{-1}) was more in Ischaemic stroke [1.5987±0.4432] compared to Hemorrhagic stroke [1.1665±0.3495] but this was statistically significant (p<0.0001).

Kim *et al*.[4] showed that the relationship between serum cystatin C levels and the incidence of major adverse events, defined as a composite of all-cause death, myocardial infarction, stroke, amputation and target vessel revascularization, was investigated but In our study, Cystatin-C value at end of 1st week of stroke (mg L^{-}1) was higher in Ischaemic stroke [1.5087±0.4187] compared to Hemorrhagic stroke [1.1728±0.3539] but this was statistically significant (p<0.0001).

Cystatin-C value in Ischaemic stroke at end of 1st week was lower in comparison to the value found within 24 hrs of stroke in Ischaemic cases but in Hemorrhagic cases Cystatin-C value was slightly higher. We found that, Cystatin-C value at end of 2nd week of stroke (mg L^{-1}) was more in Ischaemic stroke [1.3792±0.4214] compared to Hemorrhagic stroke [1.1810±0.3040] but this was statistically significant (p<0.0001).

Cystatin-C value was lesser as compare to 1st week value in Ischaemic cases but Cystain-C value was slightly greater in comparison to 1st week value in Hemorrhagic cases.

CONCLUSION

In conclusion, this study on the association and prognostic value of cystatin C in ischemic and hemorrhagic stroke reveals significant findings that could enhance stroke prognosis and management. Elevated cystatin C levels were found to be associated with the severity and outcomes of both types of stroke, suggesting that cystatin C could serve as a valuable biomarker for assessing stroke prognosis. The study indicates that measuring cystatin C levels in stroke patients may provide critical information for early intervention strategies and individualized treatment plans. By incorporating cystatin C assessment into clinical practice, healthcare providers could improve the accuracy of prognosis, tailor treatments more effectively and ultimately enhance patient outcomes. Further research is recommended to validate these findings and explore the mechanisms underlying the relationship between cystatin C and stroke pathology.

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