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# Procalcitonin – A new prognostic marker in acute ischemic stroke.

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## Abstract

**Background:** Acute ischemic stroke is an important health problem and is associated with high mortality. An assessment of early risk with an estimation of the severity and prognosis is necessary for ideal cure. The information on mortality after on acute stroke patient is still limited, but inflammation place a pathogenic role. Procalcitonin as a biomarker may help in diagnosis and prediction of prognosis of patients with acute ischemic stroke.

**AIM:** The aim of this study was to investigate the prognostic potential of procalcitonin (PCT) serum levels in acute ischemic stroke.

**Material and methods:** A prospective study was undertaken among 78 patients with acute ischemic stroke in a tertiary care hospital Bagalkot in North Karnataka. All the patients were subjected to detailed clinical examination and laboratory investigations. Patient's clinical profile, progression of disease and outcome were recorded. Procalcitonin and various other relevant factors were determined in all studies subjects. Statistical analysis was done using SPSS20.0.

**Results:** The mean age of the patients succumbed to death was 45.0 years and survived patients was 54.0 years. The mean procalcitonin levels, neutrophil granulocyte percent and serum bilirubin levels were significantly different between patients who succumbed to death and survivors of acute ischemic stroke. The survival curves also shown that the level of mortality was higher in patients with high procalcitonin levels.

**Conclusion:** The levels of procalcitonin was significantly higher in patients who died due to acute

ischemic stroke and mortality was higher in patients with high levels of procalcitonin.

**Keywords:** Procalcitonin, Acute ischemic stroke, bio marker, survival analysis.

**Introduction**

Ischemic stroke is often considered as a dreadful disease leading to mortality and long-term disability.[1] Basic and clinical research provides evidence that inflammatory mechanism plays a central role in the pathogenesis and progression of stroke. The age adjusted prevalence rate of stroke ranges from 84 to 262/100,000 in rural and 334 to 424/ 100,000 in urban areas. Some studies have shown that the incidence is 119 – 145/ 100,000.[2] But studies have shown that, there is decline in subsequent mortality.[2]At least 1 in 6 patients suffer from stroke in subsequent 5 years. Increasing age, cardiovascular co morbidities, atrial fibrillation, hypertension, diabetes mellitus and stroke are often associated with new death or new vascular events. The prevention and treatment strategies of the stroke requires a biomarker for assessing subsequent mortality.[3]

A number of systemic inflammatory processes have shown to play an important role in pathogenesis of stroke and also lead to secondary injury.

The development of stroke is also due to vascular inflammation of longer duration, rupture of plaque, thrombosis and subsequent brain ischemia or infarction.[4, 5]The literature have also established the role of procalcitonin (PCT) and C - Reactive protein (CRP) as biomarkers of acute ischemic stroke.[6, 7]

Procalcitonin (PCT) a protein comprising 116 amino acids, with a molecular weight of 13 KDs was discovered 25 years ago as a prohormone of calcitonin produced by C-cells of the thyroid gland and intra cellularly cleaved by proctolytic to enzymes to form the active hormone.

The studies also established that, the procalcitonin can be the better marker to predict the prognosis in acute stroke better than CRP. The levels of procalcitonin are in proportion to the tissue injury and hypovolemia.[8]But the association between the PCT levels and short-term outcome is not researched so far. It has been found that serum PCT level is a useful diagnostic and prognostic marker for bacterial infections. The infection markers and inflammatory molecules such as CRP, WBC, and IL-6 were suggested to be biomarkers for outcome of ischemic stroke. But PCT was suggested to be on independent risk factor for ischemic stroke. Hence, this study was undertaken in order to study the procalcitonin as a biomarker in the prognosis of acute ischemic stroke.

**Material and methods**

A prospective study was undertaken in the department of General Medicine of S. Nijalingappa Medical College & Hanagal Shri Kumareshwar Hospital & Research Centre, Bagalkot, Karnataka between June 2021 to November 2022. Patients were eligible for inclusion if they were admitted to General Medicine department with the onset of symptoms less than 48 hours of onset with acute ischemic stroke.

Acute ischemic stroke defined according to the World Health Organization criteria was adopted in this study. Clearance from institution ethics committee was obtained before the study was started. The study subjects with recent history of acute ischemic stroke were included and patients with malignant tumour, intracerebral haemorrhage, systemic infections, sub arachnoid haemorrhage, transient ischemic attack, inflammation were excluded from the study. An informed consent was obtained from all the patient/

patient attenders before including them in to the study. Procalcitonin was measured by obtaining the blood sample from each patient within 48 hours after hospitalization. The blood sample was centrifuged for 10 minutes. Procalcitonin was measured in serum sample. The clinical and laboratory details were recorded by using a pre designed proforma. The data thus obtained was entered in to an excel sheet and analysed using SPSS 20.0.

The control participants (N=100) were of similar age and sex as the acute ischemic stroke. They had no known disease and were not using any medication. The present study was approved by the ethics committee of the institute. All participants or their relatives were informed of the study protocol and their written consent was obtained.

Demographic and clinical data, including sex, age, and history of conventional vascular risk factors (hyper tension, diabetes mellitus, atrial fibrillation, hyper lipoproteinemia, habitual smoking, and alcohol abuse), were obtained. Alcohol abuse was defined as failure to fulfill responsibilities, drinking in dangerous situations, legal concerns associated with alcohol use, and continued drinking despite problems that are caused or worsened by drinking, whereas habitual smoking was defined as daily consumption of more than 10 cigarettes.

A neurologist assessed the stroke severity on admission on the basis of the National Institutes of Health Stroke Scale (NIHSS). The stroke subtype was classified according to the Trial of Org 10172 in Acute Stroke Treatment criteria, which distinguished large-artery arteriosclerosis, small-artery occlusion, cardio embolism, other causative factors, and undetermined causative factors. The clinical stroke syndrome was determined by applying the criteria of the Oxford shire Community Stroke Project: total anterior circulation syndrome, partial anterior circulation syndrome, lacunar syndrome, and posterior circulation syndrome. The Trial of Org 10172 in Acute Stroke Treatment and Oxford shire Community Stroke Project classifications were verified by brain imaging. Brain imaging (either computed Tomography or MRI) was performed routinely within 24 h after admission.

The results were expressed as percentages for categorical variables and as medians [interquartile ranges (IQRs)] for continuous variables. The Mann–Whitney U-test and the $\chi 2$ -test were used to compare the two groups. Correlations among laboratory parameters were analyzed using Spearman's rank correlation test. Associations between the severity of stroke evaluated in terms of the NIHSS scores and the serum levels of PCT were assessed using ordered logistic regression models.

**Results**

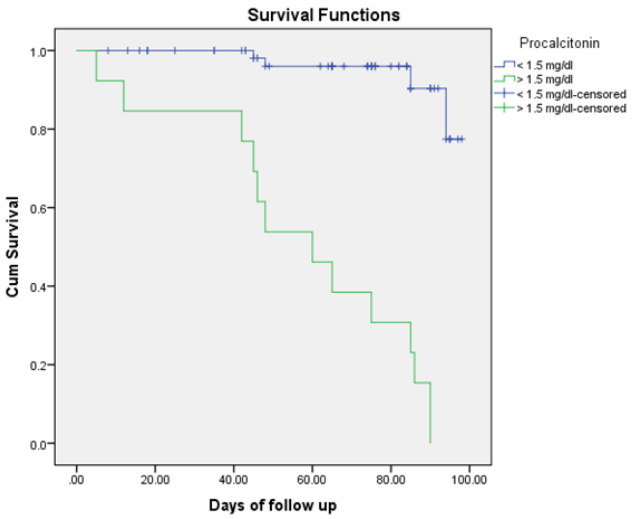
Table 1: Baseline characteristics of ischemic stroke patients

| Characteristic | Survivors | Succumbed to death | P value, Sig |
|---|---|---|---|
| Median age in years (± SD) | 54.0 (± 8.89) | 45.0 (± 9.49) | 0.055, NS |
| Male sex in numbers (%) | 34 (55.7) | 7 (41.2) | 0.288, NS |
| Comorbidities Coronary heart disease | 19 (31.1) | 3 (17.6) | 0.488, NS |
| Hypertension | 18 (29.5) | 7 (41.2) | 0.488, NS |
| PCT ng/ml | 0.14 (±0.15) | 2.36 (± 0.76) | 0.000, Sig |
| C Reactive protein mg/L | 28.8 (± 5.2) | 31.1 (± 8.4) | 0.168, NS |

| | | | |
|---|---|---|---|
| White blood cells | 6870.49 (± 2674.65) | 7388.23 (± 2202.52) | 0.467, NS |
| Neutrophil granulocyte % | 58.2 (± 11.75) | 84.76 (± 9.26) | 0.000, Sig |
| Total bilirubin mg/dl | 1.36 (± 0.35) | 2.25 (± 3.3) | 0.039, Sig |
| Triglycerides mg/dl | 214.3 (± 165.1) | 156.0 (± 69.55) | 0.161, NS |
| Urea mg/dl | 33.4 (± 19.29) | 29.86 (± 9.3) | 0.468, NS |

Table 1 above shows that the baseline characteristics of the patients enrolled in this study and the mean age of patients alive after acute ischemic stroke was 54.0 years and died was 45.0 years which was not statistically significant. The inflammatory biomarkers including PCT, CRP and neutrophils percentage in patients who died in short term were significantly higher than those who survived. Hypertension and coronary heart disease were the important comorbidities of patients in this study. Mean procalcitonin levels of alive patients was 0.14 ng/ml and 2.36 ng/ml in succumbed to death patients which was statistically significant. The CRP levels, White blood cells, triglycerides and urea was not significant between the alive and succumbed patients. There was statistically significant difference in the neutrophil granulocyte percent and total bilirubin levels.

Chart 1: Survival analysis according to procalcitonin levels.




The survival analysis shows that the survival curve had shown dip with increase in number of days of follow up in patients who had procalcitonin levels of more than 1.5 ng/ml. The curve of patients who were alive was flat over the days of follow up.

**Discussion**

This study was mainly undertaken to study the usefulness of procalcitonin in the prognosis of the patients with acute ischemic stroke. This study showed that, the patients who died due to acute ischemic stroke were younger and females.

The patients with acute ischemic stroke also demonstrated comorbidities including hypertension and cardiovascular diseases. A similar study by Yan et al also showed that, PCT was an independent prognostic marker of short-term mortality after the one set of ischemic stroke[1].

The mean procalcitonin levels were significantly lower in the patients who were alive and higher in patients who died due to acute ischemic stroke. A study by Yan et al had shown that, the mean PCT levels were significantly higher in the patients with death due to stroke than the survivors.[1]

The levels of C reactive protein, white blood cells, triglyceride levels and urea were not significantly different between the patients who were alive and succumbed.

The neutrophil granulocytes percentage and total bilirubin levels was statistically significant. But Yan et al had shown a significant difference in the CRP levels

and urea levels. White blood cells and triglyceride level were not significantly different between the survivors and died patients.[1]

The literature available had shown that the inflammatory biomarkers including CRP, WBC and IL-6 were suggested as prognostic markers in patients with acute ischemic stroke.[9, 10] Interestingly, Simon etal. found that the diagnostic accuracy of PCT markers was higher than that of CRP markers among patients hospitalized for suspected bacterial infection[11].

The survival analysis had shown that the higher levels of procalcitonin indicate death of the patients due to acute ischemic stroke.

Yan et al also shown a trend for higher mortality of patients with procalcitonin levels of > 1.5 ng/mL.[1]Procalcitonin which is a specific inflammatory biomarker and plays an important role in systemic inflammation. The increased levels of procalcitonin in blood indicates the inflammation due to acute ischemic stroke.[8] A study by Tian et al had noted significantly higher levels of acute ischemic stroke when compared with normal patients. The odds ratio of acute ischemic stroke patients was higher for the patients with increased levels of procalcitonin. Interestingly, PCT is an independent predictor of short-term functional outcome after ischemic stroke.

The procalcitonin was also proven as sensitive indicator for the acute ischemic stroke.[6] Procalcitonin is a specific inflammatory biomarker and systemic in inflammation plays a crucial role in the pathogenesis of ischemic stroke. Thus the increased PCT level of serum may due to the inflammatory process in acute ischemic stroke.

**Conclusion**

This study showed significantly higher levels of procalcitonin in patients who died due to acute ischemic stroke than the alive patients. The higher levels of procalcitonin was also associated with increased mortality in patients with acute ischemic stroke.

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