CARCINOEMBRYONIC ANTIGEN LEVELS AMONG STROKE PATIENTS

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ABSTRACT

BACKGROUND
CEA (carcinoembryonic antigen) is mainly associated with malignant conditions, but there is a modest increase in non-malignant conditions such as aging and atherosclerosis and this study is to find correlation of CEA levels in stroke patients.

MATERIALS AND METHODS
A case control study conducted from March 2016 to August 2016 in Stanley Medical College, General Medicine Department.

RESULTS
The mean CEA levels were significantly elevated in infarct group compared to control group by a mean difference of 5.09 ng/mL (73% higher), which is significant with p value of 0.0001, likewise the mean CEA levels were significantly elevated in haemorrhage group compared to control group by a mean difference of 3.26 ng/mL (64% higher). The CEA levels were significantly elevated in infarct group compared to haemorrhage group by a mean difference of 1.83 ng/mL (26% higher). This difference is significant with a p-value of 0.0071.

CONCLUSION
The CEA levels are higher among stroke patients than normal population. The elevation is more among ischaemic stroke patients than haemorrhagic stroke patients. Infarct stroke patients had 3.73 times carcinoembryonic antigen levels compared to healthy subjects, haemorrhage stroke patients had 2.75 times carcinoembryonic antigen levels compared to healthy subjects and infarct stroke patients had 1.36 times carcinoembryonic antigen levels compared to haemorrhage stroke patients.

KEYWORDS
Stroke, CEA Levels, CRP Levels.


BACKGROUND
Stroke is a medical emergency.(1) It is the abrupt interruption of cerebral blood flow to a specific brain region resulting in neurological deficits. There are two main types of stroke- (2)

1. Ischaemic.
2. Haemorrhagic.

Ischaemic Stroke can be Sub-Classified as: (2)
1. Thrombosis.
2. Embolism.
3. Systemic hypoperfusion.

Major significant risk factors for ischaemic stroke are hypertension, TIA, prior stroke, carotid artery stenosis, alcohol consumption, obesity, genetics type 2 diabetes mellitus, dyslipidiaemia, cigarette smoking, OCP use and age.(1)

CEA (carcinoembryonic antigen) is mainly associated with malignant conditions, but there is a modest increase in non-malignant conditions such as aging and atherosclerosis.(4)

CEA stimulates monocytes and macrophages to trigger the production of pro-inflammatory cytokines such as tumour necrosis factor-α, nitric oxide, interleukin-1b and -6, reactive oxygen species, eicosanoids and carbon monoxide and up-regulation of endothelial adhesion molecules and indirectly leading to atherosclerosis.(6) Further atherosclerosis increases CEA levels.

CEA has also been implicated as a marker in ischaemic stroke in various studies.

Aims and Objectives
1. To compare the levels of human carcinoembryonic antigen (CEA) in patients of acute stroke (ischaemic and Haemorrhagic) with normal population.
To compare CEA with hsCRP, which is a proven marker for atherosclerosis.

**MATERIALS AND METHODS**

**Study Design**
Case control study.

**Study Period**
March 2016 to August 2016.

**Clinically**
Focal neurological deficit persisting > 24 hours.

**Inclusion Criteria**
Patients of ischaemic and haemorrhagic stroke > 40 years.

**Exclusion Criteria**
K/C/O any cancer; history suggestive of carcinoma; valvular heart disease, arrhythmias, chronic inflammatory conditions (IBD, CTD), hypothyroidism, TIA, hsCRP > 10 mg/L, CEA > 20 ng/mL.

**Sample Size**
Sample size is 50 in each group. Sample size was taken conveniently.

**Methodology**

**Case Definition**
Patients who presented with c/o acute onset of weakness of limbs are selected clinically and they are confirmed as either ischaemic or haemorrhagic stroke radiologically.

**Control Definition**
Controls are selected in medical ward who are admitted for other atherosclerotic diseases and without any weakness of limbs clinically and radiologically.

The stroke patients are subjected to a detailed history, clinical examination and with the help of imaging, classified into ischaemic or haemorrhagic stroke.

The stroke patients are divided into 2 groups (ischaemic and haemorrhagic) of 50 subjects in each group with healthy controls as 3rd group-

- Group A- Ischaemic Stroke.
- Group B- Haemorrhagic Stroke.
- Group C- Healthy Controls.

The subjects of each group are appropriately matched for age and sex.

Basic investigations with serum CEA and hsCRP are taken within 24 hours onset of symptoms in sample A and B.

The CEA levels of the three groups are then compared.

The CEA levels are compared with hsCRP among the stroke patients.

**Reference Values**

**HSCRP Levels**
- < 1 mg/L: low risk;
- 1 - 3 mg/L: moderate risk;
- 3 mg/L: high risk;

<table>
<thead>
<tr>
<th>Groups</th>
<th>Definition of Subjects</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infarct Group</td>
<td>Ischaemic stroke patients</td>
<td>50</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>Haemorrhagic stroke patients</td>
<td>50</td>
</tr>
<tr>
<td>Control Group</td>
<td>Healthy subjects</td>
<td>50</td>
</tr>
</tbody>
</table>

**Data Analysis**

Descriptive statistics was done for all data and were reported in terms of mean values and percentages. Suitable statistical tests of comparison were done. Continuous variables were analysed with the unpaired ’t’ test. Categorical variables were analysed with the Chi-square test and Fisher Exact test. The accuracy analysis was reported as sensitivity, specificity, PPV, NPV and accuracy. Statistical significance was taken as p < 0.05. The data was analysed using SPSS version 16 and Microsoft Excel 2007.

**RESULTS**

Majority of the infarct group patients belonged to 61 - 70 years age class interval (n= 14, 28.00%) with a mean age of 65.84 years. In the haemorrhage group patients, majority belonged to 61 - 70 years age class interval (n= 16, 32.00%) with a mean age of 68.36 years. In the control group patients, majority belonged to 71 - 80 years class interval (n= 16, 32.00%) with a mean age of 65.16 years. The association between the study groups and age distribution is considered to be not statistically significant, since p > 0.05 as per unpaired ’Y’ test.
Table 2

<table>
<thead>
<tr>
<th>High Sensitivity C-Reactive Protein Groups</th>
<th>Infarct Group</th>
<th></th>
<th>Haemorrhage Group</th>
<th></th>
<th>Normal Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1.0 mg/L</td>
<td>0</td>
<td>0.00</td>
<td>2</td>
<td>4.00</td>
<td>10</td>
</tr>
<tr>
<td>1.0 to 3.0 mg/L</td>
<td>11</td>
<td>22.00</td>
<td>11</td>
<td>22.00</td>
<td>20</td>
</tr>
<tr>
<td>≥ 3.0 mg/L</td>
<td>39</td>
<td>78.00</td>
<td>37</td>
<td>74.00</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100</td>
<td>50</td>
<td>100</td>
<td>50</td>
</tr>
</tbody>
</table>

DISCUSSION

High Sensitivity C-Reactive Protein among Stroke Patients-

Majority of the infarct group patients belonged to ≥ 3.0 mg/L high sensitivity C-reactive protein class interval (n= 39, 78.00%) with a mean value of 5.32 mg/L. In the haemorrhage group patients, majority belonged to ≥ 3.0 mg/L high sensitivity C-reactive protein class interval (n= 37, 74.00%) with a mean value of 4.94 mg/L. In the control group patients, majority belonged to ≥ 3.0 mg/L high sensitivity C-reactive protein class interval (n= 20, 40.00%) with a mean value of 3.16 mg/L. By conventional criteria, the association between the study groups (infarct group vs. control group and haemorrhage group vs. control group) and high sensitivity C-reactive protein levels are considered to be statistically significant, since p < 0.05 as per unpaired 't' test. The association between the intervention groups (infarct group vs. haemorrhage group) and high sensitivity C-reactive protein levels is considered to be not statistically significant, since p > 0.05 as per unpaired 't' test.

Infarct Group vs. Control Group

The mean high sensitivity C-reactive protein levels were significantly elevated in infarct group compared to control group by a mean difference of 2.36 mg/L (43% higher). This difference is significant with a p-value of < 0.0001 as per unpaired 't' test.
**Carcinoembryonic Antigen among Stroke Patients**

Majority of the infarct group patients belonged to 5.1 - 10 ng/mL carcinoembryonic antigen class interval (n= 26, 52.00%) with a mean value of 6.96 ng/mL. In the haemorrhage group patients, majority belonged to 2.5 - 5 ng/mL carcinoembryonic antigen class interval (n= 26, 52.00%) with a mean value of 5.13 ng/mL. In the control group patients, majority belonged to < 2.5 ng/mL carcinoembryonic antigen class interval (n= 37, 74.00%) with a mean value of 5.13 ng/mL. By conventional criteria, the association between the study groups (infarct group vs control group, haemorrhage group vs control group and infarct group vs haemorrhage group) and carcinoembryonic antigen levels is considered to be statistically significant since p < 0.05 as per unpaired 't' test.

**Infarct Group vs. Control Group**

The mean carcinoembryonic antigen levels were significantly elevated in infarct group compared to control group by a mean difference of 5.09 ng/mL (73% higher). This difference is significant with a p-value of < 0.0001 as per unpaired 't' test.

**Haemorrhage Group vs. Control Group**

The mean carcinoembryonic antigen levels were significantly elevated in haemorrhage group compared to control group by a mean difference of 3.26 ng/mL (64% higher). This difference is significant with a p-value of < 0.0001 as per unpaired 't' test.

**Infarct Group vs. Haemorrhage Group**

The mean carcinoembryonic antigen levels were significantly elevated in infarct group compared to haemorrhage group by a mean difference of 1.83 ng/mL (26% higher). This difference is significant with a p-value of 0.0071 as per unpaired 't' test.

<table>
<thead>
<tr>
<th>Accuracy Analysis</th>
<th>High Sensitivity C-reactive Protein</th>
<th>Carcinoembryonic Antigen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>79.17%</td>
<td>50.00%</td>
</tr>
<tr>
<td>Specificity</td>
<td>55.56%</td>
<td>98.00%</td>
</tr>
<tr>
<td>Positive Predictive Value</td>
<td>76.00%</td>
<td>98.04%</td>
</tr>
<tr>
<td>Negative Predictive Value</td>
<td>60.00%</td>
<td>49.50%</td>
</tr>
</tbody>
</table>

**Table 6. Accuracy Analysis**

**Sensitivity**

- Sensitivity of high sensitivity C-reactive protein is high, meaning that 79% of those with hs-CRP > 3 mg/L will have stroke as diagnosis.
- Sensitivity of carcinoembryonic antigen is moderate, meaning that 50% of those with CEA > 3 ng/mL will have stroke as diagnosis.

**Specificity**

- Specificity of high sensitivity C-reactive protein is moderate, meaning that 60% of individuals diagnosed with stroke will actually have stroke.
- Specificity of carcinoembryonic antigen is very high, meaning that 98% of those diagnosed with stroke will actually have stroke.

**Positive Predictive Value**

- Positive predictive value of high sensitivity C-reactive protein is high, meaning 76% of individuals diagnosed with stroke will actually have stroke.
- Positive predictive value of carcinoembryonic antigen is very high, meaning 98% of those diagnosed with stroke will actually have stroke.

**Negative Predictive Value**

- Negative predictive value is moderate, meaning 60% of individuals with/without stroke will have hs-CRP > 3 mg/L.
- Negative predictive value is moderate, meaning 60% of individuals with/without stroke will have CEA > 3 ng/mL.

**Inference**

The diagnostic effectiveness or diagnostic accuracy in relation to stroke is very high with Carcinoembryonic Antigen compared to high sensitivity C-reactive protein.

**CONCLUSION**

The association between the study groups and age distribution is considered to be not statistically significant. The mean serum hsCRP levels in ischaemic stroke and Haemorrhagic stroke and healthy controls were 5.52 ± 2.49 mg/L, 4.94 ± 2.46 and 3.16 ± 2.41.

The hsCRP levels were higher among infarct and haemorrhagic stroke patients than control population.

The mean serum CEA levels in ischaemic stroke and Haemorrhagic stroke and healthy control were 6.96 ± 3.95 ng/mL, 5.13 ± 3.2 ng/mL and 1.87 ± 1.23 ng/mL respectively.

The CEA levels are higher among stroke patients than normal population. The elevation is more among ischaemic stroke patients than haemorrhagic stroke patients.

Infarct stroke patients had 3.73 times carcinoembryonic antigen levels compared to healthy subjects. Haemorrhage stroke patients had 2.75 times carcinoembryonic antigen levels compared to healthy subjects and infarct stroke patients had 1.36 times carcinoembryonic antigen levels compared to haemorrhage stroke patients.

Elevation of both CEA and hsCRP proves that CEA is associated with a chronic inflammatory state of atherosclerosis.
The elevation could be because of,[10]
1. Elevation of CEA in acute stroke as CEA and its family molecules act to minimise the damage to Blood-Brain Barrier.
2. Atherosclerosis, which stimulates the production of CEA.

Although further research is needed, with this result we can say that CEA[11] can be used as-
1. Marker of stroke.
2. Surrogate marker for atherosclerosis.

REFERENCES