ABSTRACT

Background: Objective of this study was to find co-relation between microalbuminuria and stroke severity based on NIH stroke scale and Modified Rankin Scale. Methods: The present study comprises 46 patients, with history and clinical features suggestive of acute ischemic stroke, and age and sex matched 46 controls, admitted in Shree Sayaji General Hospital, Baroda during January 1, 2014 to November 30, 2014. The severity of stroke was assessed using The National Institute of Health Stroke Scale (NIHSS) on admission. The Modified Rankin Scale was used to assess the outcome. Data collected was analyzed using Odd’s ratio and Chi-square test. Results: The patients with recent ischemic stroke were 5.31 times more likely to have microalbuminuria when compared to the controls (p value = 0.0001649). Presence of microalbuminuria was associated with loss of consciousness (p value= 0.025). Patients with microalbuminuria had higher NIHSS score on admission; p-value <0.05 (highly significant), and thus correlating with increased severity and poor prognosis. Patients with microalbuminuria had higher MRS score; p-value <0.05 (highly significant), and thus correlating with poor prognosis. Conclusions: Our results
Indicate that presence of microalbuminuria is associated with an increased severity and poorer short term prognosis. Thus, they may act as indicators of severity and short term prognosis in patients with acute ischemic cerebrovascular stroke.

**KEYWORDS**: Microalbuminuria, Ischemic stroke, cerebrovascular event.

**ABBREVIATIONS**

NIHSS: NIH stroke scale
MRS: Modified Rankin scale

**INTRODUCTION**

**Background**: Stroke is one of the leading causes of mortality and morbidity in adults’ worldwide, posing serious medical, socio-economic and rehabilitation problems. WHO defines stroke as rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting for more than 24 hours with no apparent cause other than vascular origin. Stroke, also called ‘Brain Attack’ because it involves an acute insult to the brain, is a major disabling disease. But, throughout the world, unfavourable trends in stroke risk factor profile, lack of prevention programs, lack of awareness of stroke risk factors and warning signals by the public and lack of emphasis on preventive training in medical schools, lead to high stroke rates and serve to widen the stroke prevention gap. This is unfortunate because stroke is well suited for prevention since it has high prevalence, high burden of illness and economic cost, well defined modifiable risk factors and effective prevention measures. Hence, there is growing interest in unifying mechanisms in ischemic stroke pathogenesis. Overtime, numerous risk factors have been found to be associated with increased occurrence of stroke. But, only one half of the cerebrovascular disease risk could be explained by conventional risk factors. The realization that atherosclerosis is an inflammatory disease has led to a search for new stroke risk factors and treatment. The markers of inflammation like C-reactive protein, intercellular adhesion molecule-1, lipoprotein associated phospholipase A2, elevated white blood cell count, interleukins, endothelial nitric oxide synthase; infectious agents like Chlamydia pneumonia, Helicobacter pylori and Cytomegalovirus; Homocysteine, Renin angiotensin system, Tissue factor, Fibrinogen, Lipoprotein (a), Cytokine transforming growth factor, etc., have been proposed as new risk factors for stroke. One more addition to the growing list is ‘Microalbuminuria’.
Micro-albuminuria is defined as an increase in urinary albumin excretion ranging from 30 to 300 mg per 24 hours or 30 to 300 ug/mg of creatinine on spot urine sample. It reflects glomerular component of systemic capillary leak which is fundamental to the pathogenesis of any acute stress condition. Microalbuminuria has been associated with many disease entities like diabetic nephropathy, hypertension with left ventricular hypertrophy and renal insufficiency, etc. Microalbuminuria has been associated with clinical risk factors for stroke like diabetes, hypertension, ageing, history of myocardial infarction, obesity, smoking and left ventricular hypertrophy. But, there was little information regarding microalbuminuria as an independent risk factor for stroke or as a predictor of stroke outcome. With the availability of sensitive and relatively inexpensive methods for detection of microalbuminuria, many studies were conducted in different parts of the world to determine the potential use of microalbuminuria, as a marker of stroke risk and outcome in non-diabetic population.

**Aims:** The aim of this case control study is to present 46 cases of acute ischemic cerebrovascular stroke and 46 controls; and to detect presence of microalbuminuria in each of them. The clinical examination findings have been studied and presented in details. Also, the NIHSS score and Modified Rankin Scale score were calculated.

**Objectives and Goals**
- To study the presence of microalbuminuria in non diabetic acute ischemic stroke patients compared to non diabetic healthy individuals.
- To correlate the degree of microalbuminuria with the severity of stroke.
- To evaluate the prognostic significance of microalbuminuria in these recent ischemic stroke patients.

**MATERIALS AND METHODS**
The present study comprises 46 patients, with history and clinical features suggestive of acute ischemic stroke, and age and sex matched 46 controls, admitted in Shree Sayaji General Hospital, Baroda during January 1, 2014 to November 30, 2014. All cases and controls were non-diabetic. WHO defines stroke as rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting for more than 24 hours with no apparent cause other than vascular origin. Micro-albuminuria is defined as an increase in urinary albumin excretion ranging from 30 to 300 mg per 24 hours or 30 to 300 ug/mg of creatinine on spot urine sample. Inclusion criteria for cases was patients of any age and both sexes with first time
ischemic stroke within 72 hours of onset of symptoms, the diagnosis of stroke being
established by WHO definition of stroke and Ischemic lesion was confirmed by CT Scan
brain/MRI brain. Informed consent obtained from all patients. Inclusion criteria for controls
was age and sex matched normal healthy individuals, without any past or present history of
hypertension, diabetes, cerebrovascular stroke, hepatic or renal insufficiency. Patients with
hemorrhagic stroke, subarachnoid hemorrhage or cerebral venous thrombosis, patients with
diabetes, patients with hypertension, systemic infection including bacterial meningitis,
nephropathy and abnormal urinalysis, neoplastic disease, recent history of surgery or severe
trauma were excluded. Detailed history of the patient included in the study was taken. They
were asked in details about their symptoms, the onset, duration and progress of the same, as
also associated other symptoms. They were specifically asked for symptoms of headache/
vomiting/ vertigo/ gait imbalance/ speech disturbances/ sensory symptoms/ visual complaints
among the other symptoms. Past history regarding any illness was elicited, especially history
for risk factors for stroke, i.e. hypertension, diabetes, ischemic heart disease and previous
TIA/stroke was asked as also about treatment of the same. Family history of stroke, diabetes,
hypertension, and ischemic heart disease was taken. Personal history regarding diet, sleep,
appetite, substance abuse, bladder and bowel habits was taken. Detailed menstrual and
obstetric history of female patient was elicited. Vital data (temperature, pulse, respiration and
blood pressure) of the patients were meticulously measured. General examination for pallor,
icterus, cyanosis, clubbing, koilonychia, neck veins, lymphadenopathy and back and spine
abnormality. Complete CNS examination was done systematically along with examination of
the other systems like respiratory, cardiovascular, gastrointestinal and musculoskeletal
systems. After that, clinical diagnosis was made. The NIHSS score for all the patients at
admission were calculated. The severity of stroke was assessed using The National Institute
of Health Stroke Scale (NIHSS) on admission. The Modified Rankin Scale was used to assess
the outcome. Data collected was analyzed using Odd’s ratio and Chi-square test.

Chi-square test was used to test the significance of proportions of predisposing factors and
presence of microalbuminuria between cases and controls. Similar tests were used to find the
significance of proportion of presenting factors and mean pattern of parameters between
cases and controls, as well as between the microalbuminuria positive and negative patients.
Modified Rankin Score (MRS) was obtained as follows:

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No symptoms at all</td>
</tr>
<tr>
<td>1</td>
<td>No significant disability despite symptoms; able to carry out all usual duties and activities</td>
</tr>
<tr>
<td>2</td>
<td>Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance</td>
</tr>
<tr>
<td>3</td>
<td>Moderate disability; requiring some help, but able to walk without assistance</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance</td>
</tr>
<tr>
<td>5</td>
<td>Severe disability; bedridden, incontinent and requiring constant nursing care and attention</td>
</tr>
<tr>
<td>6</td>
<td>Dead</td>
</tr>
</tbody>
</table>

RESULTS AND DATA ANALYSIS

Microalbuminuria was found in 34 (73.9%) patients with recent ischemic stroke and in 16 (34.7%) controls. Thus patients with recent ischemic stroke were 5.31 times more likely to have microalbuminuria when compared to the controls (p value = 0.0001649).

As per table 1, among all the presenting symptoms of stroke, loss of consciousness was the only symptom that reached statistically significant levels (p value = 0.025). Other presenting symptoms did not gain statistical significant levels (p value >0.05). Thus as loss of consciousness is a sign of severe stroke, microalbuminuria can be used as marker of severity of myocardial infarction. The study of Microalbuminuria in ischemic stroke by Beamer NB\(^1\) also showed that microalbuminuria is associated with increased risk of stroke.

As per table 2, 21 patients with NIHSS score more than or equal to 10 had microalbuminuria, while only 2 patients did not have microalbuminuria. p-value was less than 0.05, thus there is a significant correlation between microalbuminuria and higher NIHSS score on admission. High NIHSS scores are related with more severity. The presence of microalbuminuria is associated with higher NIHSS score, representing a more severe infarct, as compared to absence of microalbuminuria. The study by Turaj et al\(^2\) also showed a strong co relation of urine albumin excretion and NIHSS score.

As per table 3, 20 patients with MRS score more than 3 had microalbuminuria, while only 2 patients did not have microalbuminuria. p-value was less than 0.05, thus there is a significant correlation between microalbuminuria and higher MRS score. MRS score >3 are associated with poor prognosis and outcome.\(^3\) The presence of microalbuminuria is associated with
higher MRS score, representing a poor prognosis as compared to absence of microalbuminuria.

**Table 1: Microalbuminuria and presenting symptoms.**

<table>
<thead>
<tr>
<th>Presenting symptoms</th>
<th>Microalbuminuria</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present (n=34)</td>
<td>Absent (n=12)</td>
</tr>
<tr>
<td>Headache</td>
<td>3 (8.8%)</td>
<td>2 (16.6%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4 (11.7%)</td>
<td>2 (16.6%)</td>
</tr>
<tr>
<td>Motor weakness</td>
<td>31 (91.1%)</td>
<td>9 (75%)</td>
</tr>
<tr>
<td>Loss of consciousness</td>
<td>15 (47%)</td>
<td>1 (8.3%)</td>
</tr>
<tr>
<td>Speech disturbance</td>
<td>14 (41.1%)</td>
<td>5 (41.6%)</td>
</tr>
<tr>
<td>Vertigo</td>
<td>4 (11.7%)</td>
<td>0</td>
</tr>
<tr>
<td>Tingling</td>
<td>0</td>
<td>1 (8.3%)</td>
</tr>
<tr>
<td>Convulsion</td>
<td>4 (11.7%)</td>
<td>3 (25%)</td>
</tr>
</tbody>
</table>

**Table 2: Microalbuminuria and NIHSS score.**

<table>
<thead>
<tr>
<th>Microalbuminuria</th>
<th>Present (n=34)</th>
<th>Absent (n=12)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIHSS &lt; 10</td>
<td>13</td>
<td>10</td>
<td><strong>0.0072</strong></td>
</tr>
<tr>
<td>NIHSS &gt; 10</td>
<td>21</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3: Microalbuminuria and MRS score.**

<table>
<thead>
<tr>
<th>Microalbuminuria</th>
<th>Present (n=34)</th>
<th>Absent (n=12)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRS &lt; 3</td>
<td>14</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>MRS &gt; 3</td>
<td>20</td>
<td>2</td>
<td><strong>0.0119</strong></td>
</tr>
</tbody>
</table>

**DISCUSSION**

This is a case control study of 92 indoor patients; 46 cases and 46 controls. All cases and controls were non-diabetic. Both cases and controls were selected after meeting the including criteria and excluding the exclusion criteria. The average age of the patients was 55.5 years. 52% of the patients were males and 48% were females. The male to female ratio was 1.1:1.

The most common presenting complaint was motor weakness, followed by speech disturbance. Microalbuminuria was found in 34 (73.9%) patients with recent ischemic stroke and in 16 (34.7%) controls. Thus patients with recent ischemic stroke were 5.31 times more likely to have microalbuminuria when compared to the controls (p value = 0.0001649).

Presence of microalbuminuria was associated with loss of consciousness (p value= 0.025). Patients with microalbuminuria had higher NIHSS score on admission; p-value <0.05 (highly significant), and thus correlating with increased severity and poor prognosis. Patients with
microalbuminuria had higher MRS score; p-value <0.05 (highly significant), and thus correlating with poor prognosis. Hence Microalbuminuria can be used as a marker of severity of ischemic stroke.

CONCLUSION

Our results indicate that presence of microalbuminuria is associated with an increased severity and poorer short term prognosis. Thus, they may act as indicators of severity and short term prognosis in patients with acute ischemic cerebrovascular stroke. These results reinforce the available evidence, and point towards a potential use of microalbuminuria, as a marker of stroke risk and outcome in non-diabetic population.

REFERENCES