Section: Biochemistry

Original Research Article

ESTIMATION OF ISCHEMIA MODIFIED ALBUMIN IN ACUTE STROKE WITH AND WITHOUT DIABETES MELLITUS

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ABSTRACT

Background: Acute stroke is a major cause of mortality and morbidity worldwide. Early diagnosis remains a challenge, particularly during the initial hours when radiological findings may be inconclusive. Ischemia-Modified Albumin (IMA), an established marker of ischemia, has been evaluated in various ischemic conditions. Diabetes mellitus may influence serum IMA levels because of increased oxidative stress. The present study was undertaken to estimate serum IMA levels in acute stroke patients with and without Diabetes mellitus. **Materials and Methods:** A hospital-based case-control study was conducted on 150 subjects. The study included 50 patients with acute stroke and Diabetes mellitus, 50 patients with acute stroke and without Diabetes mellitus, and 50 apparently healthy controls. Patients presenting within 12 hours of symptom onset with radiologically confirmed stroke were included. Serum IMA was estimated by the Albumin Cobalt Binding (ACB) method using a Beckman Coulter AU480 autoanalyzer. Serum albumin and random blood glucose were also estimated. Receiver operating characteristic (ROC) curve analysis was done to evaluate the diagnostic utility of IMA. **Result:** mean serum IMA levels were significantly higher in patients with acute stroke with Diabetes mellitus (108.1±5.36 U/mL) and without Diabetes mellitus (96.37±4.41 U/mL) than in healthy controls (66.32±5.18 U/mL) ($p<0.001$). Although IMA levels were higher in Diabetic than non-Diabetic stroke patients, the difference was not statistically significant. ROC curve analysis yielded an area under the curve of 0.953 with an optimal cut-off value of 105.17 U/mL, providing a sensitivity of 72%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 78%. **Conclusion:** Serum IMA levels are significantly elevated in acute stroke patients irrespective of diabetic status. Estimation of IMA may serve as a useful adjunctive biomarker in the diagnosis of acute stroke. Larger studies warranted to establish clinically applicable cut-off values and validate its routine clinical use.

INTRODUCTION

Stroke is defined as the rapid development of clinical signs of focal or global disturbance of cerebral function lasting for more than 24 hours or leading to death, with no apparent cause other than that of vascular origin. More recently, the American Heart Association/American Stroke Association defined stroke as an episode of neurological dysfunction caused by cerebral infarction or intracerebral haemorrhage. Ischemic stroke accounts for nearly 85% of all strokes and remains a major cause of mortality and long-term disability worldwide.[1-4]

The diagnosis of acute stroke is primarily based on clinical evaluation and neuroimaging. However, radiological evidence may be absent during the early stages of cerebral ischemia, making early diagnosis difficult in some patients. Therefore, there is a need for reliable biochemical markers that can support the diagnosis of acute stroke during the initial hours of presentation. Ischemia-Modified Albumin (IMA) is one such marker that has gained considerable attention. It is the only ischemic biomarker approved by the United States Food and Drug Administration for the early diagnosis of myocardial ischemia and has subsequently been evaluated in several ischemic conditions, including acute stroke.[5-7]

IMA is produced when the N-terminal region of human serum albumin undergoes structural modification during ischemia, resulting in reduced binding affinity for transition metals such as cobalt. The Albumin Cobalt Binding (ACB) assay indirectly

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estimates IMA by measuring the amount of unbound cobalt in serum. Although serum albumin concentration may influence IMA estimation, previous studies have demonstrated the potential usefulness of IMA as a marker of tissue ischemia.[5-8] Diabetes mellitus is associated with increased oxidative stress, endothelial dysfunction and accelerated atherosclerosis, all of which contribute to an increased risk of ischemic stroke. Previous studies have reported significantly higher IMA levels in diabetic patients and have suggested that poor glycaemic control is associated with elevated IMA concentrations.[9,10] Although IMA has been evaluated in diabetic patients with symptomatic lacunar infarction and in coronary artery disease with and without diabetes mellitus, studies evaluating its role in acute stroke patients with and without diabetes mellitus are scarce.[11,12]

In view of the limited literature addressing the influence of diabetes mellitus on serum IMA levels in acute stroke, the present study was undertaken to estimate and compare serum IMA levels in acute stroke patients with and without Diabetes mellitus and to evaluate its diagnostic utility in a tertiary care institute, Guntur Medical College, Guntur.

Objectives

1. To estimate and compare serum Ischemia-Modified Albumin (IMA) levels in acute stroke patients with and without Diabetes mellitus and healthy controls.
2. To evaluate the diagnostic utility of serum Ischemia-Modified Albumin in acute stroke patients with and without Diabetes mellitus.

MATERIALS AND METHODS

Study design and setting: A hospital-based case-control study was conducted in the Department of Biochemistry, Guntur Medical College, Guntur. The study population comprised confirmed cases of acute stroke with and without diabetes mellitus attending the Emergency and Intensive Care Unit of the Department of Neurology, Government General Hospital, Guntur. Apparently healthy volunteers attending the Blood Bank, Government General Hospital, Guntur, served as controls.

Study population

A total of 150 subjects were recruited and divided into three groups:

- **Group I:** Fifty patients with acute stroke and diabetes mellitus.
- **Group II:** Fifty patients with acute stroke without diabetes mellitus.
- **Group III:** Fifty apparently healthy volunteers as controls.

Inclusion criteria

- Patients aged >18 years.
- Patients presenting within 12 hours of onset of symptoms.
- Clinically suspected acute stroke with diagnosis confirmed by computed tomography (CT) and/or magnetic resonance imaging (MRI).

Exclusion criteria

- Patients presenting after 12 hours of onset of symptoms.
- Patients with liver disease, renal failure, malignancy or pregnancy.

Sample collection: Under strict aseptic precautions, 3.5 mL of venous blood was collected into two vacutainer tubes containing serum separator gel with clot activator. The samples were allowed to clot at room temperature for 30 minutes and centrifuged at 5000 rpm for 10 minutes to separate the serum. Serum samples were analysed immediately whenever possible. When immediate analysis was not feasible, the samples were stored at −20°C and analysed within 72 hours of collection.

Biochemical analysis: Serum Ischemia-Modified Albumin (IMA) was estimated by the Albumin Cobalt Binding (ACB) end-assay method using a Beckman Coulter AU480 automated chemistry analyser. Serum albumin was estimated by the bromocresol green (BCG) method, and random blood glucose was estimated by the glucose oxidase–peroxidase (GOD–POD) method.

Statistical analysis: Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Data were expressed as mean ± standard deviation (SD). Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic utility of serum Ischemia-Modified Albumin and determine the optimal cut-off value. A p-value <0.05 was considered statistically significant.

RESULTS

Serum Ischemia-Modified Albumin (IMA) levels were highest in acute stroke patients with diabetes mellitus (108.10 ± 5.36 U/mL), followed by acute stroke patients without diabetes mellitus (96.37 ± 4.41 U/mL), and healthy controls (66.32 ± 5.18 U/mL) [Table 1]. Pairwise comparison revealed significantly higher serum IMA levels in both acute stroke groups compared with healthy controls ($p<0.001$). However, there was no statistically significant difference in serum IMA levels between acute stroke patients with and without diabetes mellitus ($p=0.116$) [Table 2].

Table 1: Serum Ischemia-Modified Albumin (IMA) levels among the study groups

Group	Minimum	Maximum	Mean ± SD (U/mL)
Acute stroke with diabetes mellitus (n=50)	99.34	116.39	108.10 ± 5.36
Acute stroke without diabetes mellitus (n=50)	88.55	104.81	96.37 ± 4.41
Healthy controls (n=50)	57.65	74.68	66.32 ± 5.18

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Table 2: Pairwise comparison of serum Ischemia-Modified Albumin (IMA) levels among the study groups

Comparison	p-value
Acute stroke with diabetes mellitus vs Healthy controls	<0.001
Acute stroke without diabetes mellitus vs Healthy controls	<0.001
Acute stroke with diabetes mellitus vs Acute stroke without diabetes mellitus	0.116

* A p-value <0.05 was considered statistically significant.

Table 3: Random Blood Glucose (RBS) levels among the study groups

Group	RBS			
	Minimum	Maximum	Mean	SD
Acute stroke with Diabetes mellitus (n=50)	176.00	483.00	247.54	70.39
Acute stroke without Diabetes mellitus (n=50)	63.00	144.00	103.92	19.31
Healthy controls (n=50)	86.00	149.00	110.96	15.75

The mean random blood glucose level was highest in acute stroke patients with diabetes mellitus (247.54 ± 70.39 mg/dL), followed by healthy controls (110.96 ± 15.75 mg/dL) and acute stroke patients without diabetes mellitus (103.92 ± 19.31 mg/dL) [Table 3].

Table 4: Serum Albumin levels among the study groups

Group	ALBUMIN				P-value
	Minimum	Maximum	Mean	SD	
Acute stroke with Diabetes mellitus (n=50)	3.31	4.32	3.62	0.27	< 0.001*
Acute stroke without Diabetes mellitus (n=50)	2.94	4.56	3.81	0.34	
Healthy controls (n=50)	3.64	4.62	4.02	0.25	

* A p-value <0.05 was considered statistically significant

The mean serum albumin level was lowest in acute stroke patients with diabetes mellitus (3.62 ± 0.27 g/dL), followed by acute stroke patients without diabetes mellitus (3.81 ± 0.34 g/dL), and highest in healthy controls (4.02 ± 0.25 g/dL) [Table 4]. The difference in mean serum albumin levels among the study groups was statistically significant (p<0.001).

Table 5: Correlation between serum Ischemia-Modified Albumin (IMA) and serum albumin among the study groups

Study Group	Correlation coefficient (r)
Acute stroke with Diabetes mellitus (n=50)	-0.824
Acute stroke without Diabetes mellitus (n=50)	-0.876
Healthy controls (n=50)	-0.618

A negative correlation was observed between serum Ischemia-Modified Albumin (IMA) and serum albumin levels in all the study groups (Table 5). The strongest negative correlation was observed in acute stroke patients without diabetes mellitus (r = −0.876), followed by acute stroke patients with diabetes mellitus (r = −0.824), while healthy controls showed a relatively weaker negative correlation (r = −0.618).

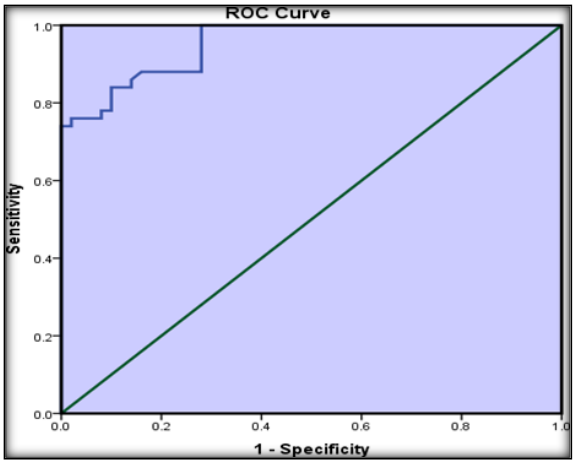

Figure 1: Receiver Operating Characteristic (ROC) curve of serum Ischemia-Modified Albumin (IMA) for the diagnosis of acute stroke

The receiver operating characteristic (ROC) curve demonstrated good diagnostic performance of serum Ischemia-Modified Albumin (IMA) for the diagnosis of acute stroke [Figure 1]. The area under the curve (AUC) was 0.953. At the optimal cut-off value of 105.17 U/mL, the sensitivity and specificity were 72% and 100%, respectively. The positive predictive value and negative predictive value were 100% and 78%, respectively.

DISCUSSION

The present study demonstrated significantly higher serum Ischemia-Modified Albumin (IMA) levels in acute stroke patients with and without diabetes mellitus than in healthy controls. This finding is consistent with the study by Abboud et al,[13] who reported significantly elevated serum IMA levels in patients with acute stroke. Gunduz et al,[14] also observed significantly higher serum IMA levels in patients with cerebrovascular accidents than in healthy controls and suggested that IMA could serve as a diagnostic marker in the emergency setting. Nayak et al,[15] further demonstrated elevated serum IMA levels in acute ischemic stroke patients and highlighted its prognostic significance. In the present study, serum IMA levels were higher in acute stroke

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patients with diabetes mellitus than in those without diabetes mellitus; however, the difference was not statistically significant. Piwowar et al,[16] reported higher IMA levels in patients with diabetes mellitus than in non-diabetic individuals and attributed this to hyperglycaemia-associated oxidative stress. Similar observations were made by Kaefer et al,[17] and Ukinc et al,[18] who also demonstrated increased IMA levels in patients with diabetes mellitus. Mishra et al,[19] reported significantly higher IMA levels in coronary artery disease patients with diabetes mellitus than in non-diabetic patients. The absence of a statistically significant difference between the two stroke groups in the present study may be explained by differences in antidiabetic treatment, as some patients were receiving oral hypoglycaemic agents while others were on insulin therapy.

The mean serum albumin level was significantly lower in acute stroke patients than in healthy controls. Gillum et al,[20] in the NHANES I Epidemiologic Follow-up Study, reported that lower serum albumin concentrations were associated with an increased incidence of stroke and higher stroke-related mortality. Xu et al,[21] also observed lower serum albumin levels in patients with different subtypes of ischemic stroke. Folsom et al,[22] reported lower serum albumin levels in diabetic individuals than in non-diabetic individuals, a finding that was also observed in the present study. A negative correlation was observed between serum albumin and serum IMA levels in all the study groups, indicating that lower serum albumin levels were associated with higher serum IMA concentrations. Receiver operating characteristic (ROC) curve analysis demonstrated excellent diagnostic performance of serum IMA, with an area under the curve of 0.953, an optimal cut-off value of 105.17 U/mL, sensitivity of 72%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 78%. These findings suggest that serum IMA may serve as a useful adjunctive biomarker in the diagnosis of acute stroke. However, further large-scale studies are required to establish clinically applicable cut-off values and to standardize and validate IMA estimation methods.

CONCLUSION

Serum Ischemia-Modified Albumin (IMA) levels were significantly elevated in acute stroke patients with and without diabetes mellitus compared with healthy controls. Although serum IMA levels were higher in acute stroke patients with diabetes mellitus than in those without diabetes mellitus, the difference was not statistically significant. Serum IMA demonstrated excellent diagnostic performance, suggesting that it may serve as a useful adjunctive biomarker in the diagnosis of acute stroke. Further large-scale studies are required to establish clinically applicable cut-off values and validate its routine clinical use.

Limitations

1. The study was conducted at a single tertiary care centre with a relatively small sample size, which may limit the generalizability of the findings.
2. The history of antidiabetic medication was not considered while interpreting serum Ischemia-Modified Albumin (IMA) levels, which might have influenced the observed differences between acute stroke patients with and without diabetes mellitus.

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