

Relationship Between the Atherogenic Index of Plasma and Glycated HbA1C, Serum Uric Acid, and Homocysteine in Type 2 Diabetes and Acute Stroke

Jingxuan Ma¹, Yinong Cui² and Xi Yang¹

¹Department of Endocrinology, First Central Hospital of Baoding, Hebei, China

²Department of Neurology, First Central Hospital of Baoding, Hebei, China

ABSTRACT

Objective: To examine the association between the atherogenic index of plasma (AIP) and glycated haemoglobin A1c (HbA1c), serum uric acid (SUA), and homocysteine (Hcy) in individuals with type II diabetes mellitus (T2DM) and acute stroke.

Study Design: A descriptive study.

Place and Duration of the Study: Department of Endocrinology, First Central Hospital of Baoding, Hebei, China, from January 2023 to January 2024.

Methodology: Ninety patients were categorised based on NIHSS score: mild (n = 30), intermediate (n = 30), and severe (n = 30). Forty healthy participants were selected as the comparison cohort. Variations in lipid profiles, blood glucose, SUA, and Hcy concentrations were compared. Logistic regression analysis was conducted to determine the risk factors for T2DM and acute stroke. Spearman's rank correlation assessment was used to evaluate the relationship between AIP and HbA1c, SUA, and Hcy.

Results: The comparison cohort demonstrated a lower frequency of hypertension compared to the mild ($\chi^2 = 4.667$; $p = 0.031$), moderate ($\chi^2 = 8.750$; $p = 0.003$), and severe cohorts ($\chi^2 = 12.153$; $p < 0.001$). Moreover, the comparison cohort exhibited markedly lower concentrations of TG, TC, LDL-C, FPG, HbA1c, SUA, Hcy, and AIP, whereas maximum concentrations were observed in the severe cohort (all $p < 0.05$). HDL-C concentrations were significantly decreased in the severe cohort, whereas maximum HDL-C concentrations were noted in the comparison cohort ($p = 0.002$). Logistic regression determined that HDL-C functioned as an independent protective factor against T2DM and acute stroke ($p < 0.05$), whereas HbA1c, SUA, Hcy, and AIP were distinct risk elements of these diseases ($p < 0.05$). Spearman's rank correlation assessment revealed positive correlations between AIP and HbA1c, SUA, and Hcy.

Conclusion: HbA1c, SUA, Hcy and AIP are potential risk factors for acute stroke in patients with T2DM. AIP is positively correlated with HbA1c, SUA, and Hcy.

Key Words: Type II diabetes mellitus, Acute stroke, Atherogenic index of plasma, Glycated haemoglobin A1c, Serum uric acid, Homocysteine.

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INTRODUCTION

Type II diabetes mellitus (T2DM) accounts for approximately 90% of all cases of diabetes.¹ Cardio-cerebrovascular disease is the primary contributor to mortality in patients with T2DM, with nearly 50% of cases attributed to cerebrovascular diseases. Among people aged ≥ 25 years, someone dies from a stroke every six seconds.² Studies have demonstrated that individuals with T2DM have a two- to four-fold increased risk of stroke compared to the general population.³ Glycated haemoglobin A1c (HbA1c) has been internationally recognised as the gold standard for long-term blood glucose monitoring.

Dyslipidaemia, homocysteine (Hcy), and hyperuricemia are distinct risk elements for cardio-cerebrovascular diseases. AIP is a simple and convenient biomarker for assessing the degree of atherosclerosis. To date, studies on the connection between AIP and HbA1c, SUA, and Hcy in patients with T2DM and acute stroke are scarce.

The current study aimed to examine the association between the AIP, HbA1c, SUA, and Hcy in individuals with T2DM and acute stroke and provide clinical reference for the diagnosis and treatment of acute stroke in patients with type II diabetes.

METHODOLOGY

This retrospective study of 90 participants with T2DM and comorbid ischaemic stroke was conducted at the First Central Hospital of Baoding, Hebei, China, from January 2023 to January 2024. All patients were evaluated for neurological impairments using the NIHSS and categorised into three sub-cohorts based on NIHSS score: mild, moderate, and severe, with 30 patients in each cohort. Forty healthy individuals receiving physical examinations during the same timeframe were selected as the comparison cohort. The ethical committee of the hospital approved the study.

Correspondence to: Dr. Jingxuan Ma, Department of Endocrinology, First Central Hospital of Baoding, Baoding, Hebei, China

E-mail: majingxuan1022@126.com

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The inclusion criteria were patients who met the diagnostic criteria for T2DM and whose imaging study results indicated ischaemic stroke, those aged <75 years, and those with complete clinical data. Patients with significant liver or kidney impairment, cardiac dysfunction, acute gastrointestinal bleeding, autoimmune diseases, or haematological disorders; those with a history of ischaemic stroke with significant residual neurological symptoms and signs; those with malignant tumours; and those with incomplete clinical data were excluded.

Baseline data, including age, gender, smoking history, alcohol consumption, BMI, and history of hypertension, were collected. Venous blood was drawn from the patients' elbows. Furthermore, 2–3 mL of fasting venous blood was extracted from all the patients. The blood sample was allowed to clot for 30 minutes and was centrifuged at 3500 rpm for 10 minutes at 4°C to collect the upper serum. A fully automated biochemical analyser (Beckman Coulter, model AU5800, USA) was employed to detect TG and TC using the oxidase method, HDL-C using the direct method, LDL-C using the surfactant washing method, FPG using the hexokinase method, HbA1c using high-performance liquid chromatography, SUA using the uricase method, and Hcy using the enzyme circulation method. AIP was calculated using the following equation: $\log(\text{TG}/\text{HDL-C})$.

Statistical analyses were performed using SPSS 27.0. Measurement data with a normal distribution were presented as mean \pm standard deviation. Levene's test was utilised to assess the homogeneity of variances, and ANOVA was used for comparisons across multiple cohorts. Categorical data were presented by frequency (percentage) and compared

using the χ^2 test. Multivariable logistic regression was employed to evaluate factors correlated with acute stroke in patients with T2DM, such as hypertension, TG, TC, HDL-C, LDL-C, FPG, HbA1c, SUA, Hcy, and AIP. Spearman's rank correlation analysis was used to assess the associations between AIP and HbA1c, SUA, and Hcy. Results were considered statistically significant at $p < 0.05$.

RESULTS

Significant differences were found in hypertension incidence among the four cohorts. The prevalence of hypertension was notably decreased in the comparison cohort compared with those in the mild ($\chi^2 = 4.667$; $p = 0.031$), moderate ($\chi^2 = 8.750$; $p = 0.003$), and severe cohorts ($\chi^2 = 12.153$; $p < 0.001$; Table I).

The concentrations of TG, TC, LDL-C, FPG, HbA1c, SUA, Hcy, and AIP in the comparison cohort were significantly lower than those in the mild, moderate and severe cohorts, with the highest concentrations were found in the severe cohort ($p < 0.05$). Conversely, the HDL-C concentration in the severe cohort was considerably lower compared with those in the moderate, mild, and comparison cohorts, and the highest HDL-C concentration was observed in the comparison cohort ($p = 0.002$; Table II).

Multivariable logistic regression showed that HDL-C was an independent protective factor against acute stroke in patients with T2DM ($p < 0.05$), whereas HbA1c, SUA, Hcy, and AIP were risk factors ($p < 0.05$; Table III). Spearman's rank correlation showed a positive correlation between AIP and HbA1c, SUA, and Hcy concentrations (Table IV).

Table I: Baseline data of the four cohorts.

Category	Cohort				F/ χ^2	p-values*
	Comparison (n = 40)	Mild (n = 30)	Moderate (n = 30)	Severe (n = 30)		
Age (years) ($\bar{x} \pm s$)	64.75 \pm 2.87	64.73 \pm 1.91	65.37 \pm 2.80	65.73 \pm 2.75	1.108	0.348
BMI (kg/m ²) ($\bar{x} \pm s$)	27.70 \pm 2.59	28.29 \pm 2.60	28.75 \pm 2.32	28.53 \pm 1.90	1.272	0.287
Gender (M/F)	21/19	16/14	17/13	15/15	0.275	0.965
Alcohol consumption [n (%)]	15 (37.50)	12 (40.00)	11 (36.67)	13 (43.33)	0.352	0.950
Smoking [n (%)]	14 (35.00)	13 (43.33)	15 (30.00)	12 (40.00)	1.658	0.646
Hypertension [n (%)]	10 (25.00)	15 (50.00)	18 (60.00)	20 (66.67)	14.424	0.002

*One-Way ANOVA; Pearson's Chi-square test; A p-value of <0.05 was considered statistically significant.

Table II: Comparison of biochemical parameters among the four cohorts ($\bar{x} \pm s$).

Category	Cohort				F	p-values*
	Comparison (n = 40)	Mild (n = 30)	Moderate (n = 30)	Severe (n = 30)		
TG (mmol/L)	1.52 \pm 0.23	2.39 \pm 0.45	2.89 \pm 0.50	3.15 \pm 0.57	93.899	<0.001
TC (mmol/L)	2.88 \pm 1.08	5.97 \pm 0.88	6.63 \pm 0.73	7.08 \pm 0.88	156.395	<0.001
HDL-C (mmol/L)	1.44 \pm 0.46	1.36 \pm 0.19	1.26 \pm 0.17	1.16 \pm 0.20	5.382	0.002
LDL-C (mmol/L)	2.63 \pm 0.26	2.67 \pm 0.25	2.78 \pm 0.30	2.91 \pm 0.44	5.091	0.001
FPG (mmol/L)	5.49 \pm 1.53	5.90 \pm 1.144	6.30 \pm 1.73	6.88 \pm 1.27	5.681	0.001
HbA1c (%)	5.33 \pm 0.72	7.42 \pm 1.27	7.86 \pm 1.52	8.42 \pm 1.47	42.509	<0.001
SUA ($\mu\text{mol/L}$)	242.66 \pm 7.68	251.35 \pm 7.89	265.41 \pm 4.60	276.42 \pm 6.89	155.408	<0.001
Hcy ($\mu\text{mol/L}$)	8.45 \pm 1.81	12.95 \pm 2.74	16.62 \pm 3.81	21.32 \pm 6.34	66.657	<0.001
AIP	0.05 \pm 0.18	0.24 \pm 0.10	0.36 \pm 0.09	0.43 \pm 0.11	57.883	<0.001

*One-Way ANOVA; A p-value of <0.05 was considered statistically significant.

Table III: Multivariable logistic regression assessment of potential risk elements for acute stroke in individuals with T2DM.

Variables	β	SE	Wald χ^2 value	OR (95% CI)	p-values*
Hypertension	0.353	0.881	0.160	1.423 (0.253-7.998)	0.689
TG	0.582	1.026	0.322	1.790 (0.240-13.372)	0.570
TC	0.104	0.808	0.017	1.110 (0.228-5.407)	0.897
HDL-C	-4.929	1.441	11.693	0.007 (0.000-0.122)	0.001
LDL-C	0.336	1.200	0.078	1.399 (0.133-14.706)	0.780
FPG	0.511	1.107	0.213	1.666 (0.190-14.583)	0.645
HbA1c	2.414	1.195	4.085	11.181 (1.076-116.226)	0.043
SUA	2.322	1.162	3.993	10.195 (1.046-99.4080)	0.046
Hcy	2.257	0.921	6.000	9.555 (1.570-58.150)	0.014
AIP	2.347	0.994	5.576	10.450 (1.490-73.291)	0.018

*Multivariable logistic regression; A p-value of <0.05 was considered statistically significant.

Table IV: Correlations between AIP and HbA1c, SUA, and Hcy concentrations.

Items	r	p-values*
HbA1c	0.526	<0.001
SUA	0.702	<0.001
Hcy	0.636	<0.001

*Spearman's rank correlation; A p-value of <0.05 was considered statistically significant.

DISCUSSION

Abnormal lipid metabolism is a major cause of atherosclerosis.⁴ In patients with T2DM, dyslipidaemia is mainly manifested by increased TG and decreased HDL-C concentrations. Early detection of dyslipidaemia in patients with T2DM, along with timely implementation of effective interventions, is crucial for preventing atherosclerosis, reducing cardio-cerebrovascular events, and decreasing mortality.^{5,6} AIP is a sensitive predictor of lipid metabolism disorders.⁷ Moreover, previous studies have shown that AIP is a distinct risk element for arterial disease in individuals with T2DM.^{8,9} The findings of the current study exhibited that the concentrations of TG, TC, LDL-C, and AIP in patients with T2DM with acute stroke were markedly increased, and the HDL-C concentrations notably decreased compared with those in the comparison cohort. Some studies have shown that individuals with acute cerebrovascular disease often suffer from concomitant glucose metabolism disorders.¹⁰ The results of the current study also demonstrated that the FPG and HbA1c concentrations in T2DM patients with acute stroke were markedly decreased. Furthermore, multifactorial logistic regression revealed that HDL-C was an independent protective factor against acute stroke in individuals with T2DM ($p < 0.05$), whereas HbA1c and AIP were distinct risk factors ($p < 0.05$).

SUA is a distinct risk factor for the development and progression of atherosclerosis, T2DM, and cardiovascular diseases.¹¹ In this study, the SUA concentrations in T2DM patients with acute stroke were notably increased ($p < 0.05$). Multifactorial logistic regression also indicated that SUA was a distinct risk factor for acute stroke among individuals with T2DM. This emphasises the value of SUA in assessing the progression of acute stroke among individuals with T2DM, consistent with the findings of previous studies.^{12,13} Additionally, the study results showed that Hcy concentrations in T2DM patients with acute stroke were markedly decreased ($p < 0.05$), consistent with other research findings.¹⁴ The results of multifactorial logistic regression indicated that Hcy is a distinct risk element

for acute stroke among individuals with T2DM. The mechanism is associated with increased Hcy concentrations that damage the vascular endothelium, stimulate platelet adhesion to the vascular intima, and induce an inflammatory response in the arteries, thereby promoting atherosclerosis.¹⁵ Additionally, high Hcy concentrations can cause thickening and fibrosis of the vessel walls, increase the activity of coagulation factors VI and VII, and promote thrombosis.¹⁶ Evidence has revealed that AIP is a standalone predictor for overall mortality and cardiovascular incidents.¹⁶ AIP can be easily calculated from standard lipid profiles.¹⁷ In the present study, Spearman's rank correlation exhibited a positive association between AIP and HbA1c, SUA, and Hcy concentrations.

The study had several limitations. First, the present study adopted a retrospective design, which limited control over certain variables patient selection, such as the impact of recent dietary habits on lipid, glucose, and SUA concentrations. Second, because patients were enrolled at different times, there may be some discrepancies in blood sample results due to periodic calibration of testing equipment. Lastly, the modest sample size may have limited study outcomes.

CONCLUSION

HDL-C, HbA1c, SUA, Hcy, and AIP concentrations are associated with the incidence of acute stroke among patients with T2DM. HbA1c, SUA, Hcy, and AIP are distinct risk factors for acute stroke in the population, whereas AIP is positively correlated with HbA1c, SUA, and Hcy concentrations.

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ETHICAL APPROVAL:

Ethical approval of this study was obtained from First Central Hospital of Baoding, prior to initiation of the research work.

PATIENTS' CONSENT:

Informed consent was obtained from patients to publish the data concerning this study.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

JM: Designed this study and prepared this manuscript.

YC: Collected and analysed clinical data.

XY: Participated in the acquisition, analysis, data interpretation, and manuscript, writing.

All authors approved the final version of the manuscript to be published.

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