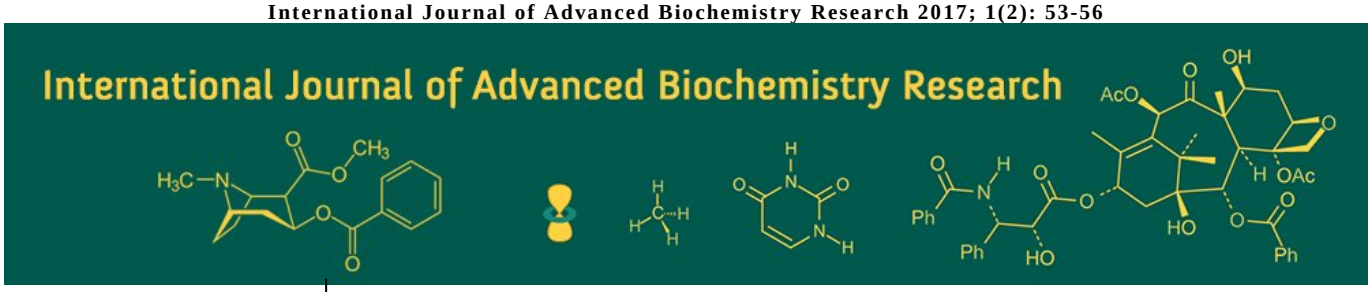

ISSN Print: 2617-4693
ISSN Online: 2617-4707
IJABR 2017; 1(2): 53-56
www.biochemjournal.com
Received: 03-07-2017
Accepted: 08-08-2017

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Comparative study of serum homocysteine, high-sensitivity C-reactive protein, and lipid profiles in non-diabetic individuals with ischemic stroke

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DOI: https://doi.org/10.33545/26174693.2017.v1.i2a.400

Abstract
Introduction: This comprehensive study explores serum biomarkers and risk factors in non-diabetic ischemic stroke patients compared to healthy controls, shedding light on stroke pathogenesis and risk stratification.
Materials and Methods: Present study assessed serum homocysteine, high-sensitivity C-reactive protein (hs-CRP), and lipid profiles in a cohort of 30 subjects. Subgroup analyses were conducted based on age and gender, unraveling nuanced trends. Correlations between these biomarkers were scrutinized, revealing potential interplays. Furthermore, we delved into risk factors such as smoking, alcohol use, and family history of cardiovascular disease to provide a comprehensive risk profile.
Results: Our study unveils significant disparities in serum biomarkers between the two groups. Ischemic stroke patients exhibit elevated homocysteine and hs-CRP levels, unfavorable lipid profiles, and a higher prevalence of risk factors. Subgroup analyses delineate age and gender-specific differences, emphasizing age as a prominent risk factor, and women with stroke presenting distinct lipid profiles. The correlation analysis underscores complex relationships between biomarkers, offering insights into potential synergistic mechanisms. Moreover, our identification of smoking, alcohol use, and family history as significant risk factors reaffirms their critical roles in stroke susceptibility.
Conclusion: These findings underscore the multifaceted nature of ischemic stroke, necessitating tailored risk assessment and intervention strategies that consider age, gender, lifestyle factors, and the interplay between serum biomarkers. This comprehensive approach is imperative for effective stroke prevention and management.

Keywords: Ischemic stroke, biomarkers, risk factors, inflammation, lipid profiles

Introduction
Ischemic stroke, a major health concern worldwide, results from the interruption of blood flow to the brain, leading to significant morbidity and mortality [1]. Traditional risk factors like hypertension, smoking, and atrial fibrillation have long been implicated in its development. However, recent research has increasingly focused on metabolic factors such as serum homocysteine, high-sensitivity C-reactive protein (hs-CRP), and lipid profiles, particularly in the context of non-diabetic individuals [2].
Serum homocysteine, a sulfur-containing amino acid, has emerged as a critical factor in stroke pathogenesis. Elevated levels of homocysteine are thought to induce endothelial dysfunction, promote oxidative stress, and create a prothrombotic state, significantly increasing stroke risk. This relationship has been extensively studied, with findings such as those by Boysen and Brander in "Homocysteine and Stroke Risk" highlighting homocysteine as an independent risk factor for cerebrovascular events [3].
High-sensitivity C-reactive protein, a marker of systemic inflammation, is another biomarker of interest. Its elevation indicates a heightened state of inflammation, which is a known contributor to atherosclerosis and thrombosis. Studies like those conducted by Ridker *et al*. (2002) in "Association of hs-CRP with Stroke Risk" have shown hs-CRP to be a potential predictor of cardiovascular and cerebrovascular events, underscoring its significance in stroke risk assessment [4].
The role of lipid profiles, which include measurements of cholesterol and triglycerides, is well-established in the context of cardiovascular disease but is more nuanced in stroke, especially among non-diabetic individuals.

Dyslipidemia, characterized by high levels of low-density lipoprotein (LDL) cholesterol or triglycerides, or low levels of high-density lipoprotein (HDL) cholesterol, is a key risk factor for atherosclerosis. This in turn is a major contributor to ischemic stroke. However, as discussed in studies like "Lipids and Stroke Risk" by Amarenco *et al*. (2009), the specific impact of various lipid components on stroke risk may differ in non-diabetic populations [5].

Given the complexity of these factors and their interplay, this study seeks to conduct a comprehensive analysis of serum homocysteine, hs-CRP, and lipid profiles in non-diabetic individuals experiencing ischemic stroke. By investigating these relationships in detail, the study aims to enhance our understanding of stroke pathophysiology in non-diabetic patients, improve risk stratification, and potentially guide the development of targeted preventive and therapeutic strategies.

Materials and Methods

The present study was conducted at the Department of Biochemistry, Mamata Medical College, Khammam. This study included 30 subjects, comprising 15 non-diabetic patients with ischemic stroke (case group) and 15 age- and sex-matched healthy controls. The stroke diagnosis was confirmed by a neurologist based on clinical examination and imaging studies. The study was approved by the Institutional Ethics Committee. Informed consent was obtained from all participants.

Inclusion and Exclusion Criteria: Cases were non-diabetic adults (age 18-65) with a recent diagnosis of ischemic stroke. Exclusion criteria included history of diabetes, other forms of stroke, significant renal or liver disease, inflammatory conditions, and current use of lipid-lowering or anti-inflammatory medications.

Sample Collection and Analysis: Fasting blood samples were collected from all subjects. Serum homocysteine levels were measured using a chemiluminescent immunoassay, hs-CRP levels by high-sensitivity enzyme-linked immunosorbent assay (ELISA), and lipid profiles (total cholesterol, LDL, HDL, and triglycerides) using standard enzymatic methods.

Statistical Analysis: Data were analyzed using SPSS software. Comparisons between groups were made using t-tests for continuous variables and chi-square tests for categorical variables. A p-value < 0.05 was considered statistically significant.

Results

Table 1: Serum Homocysteine Levels in Ischemic Stroke Patients and Healthy Controls

Group	Number of Subjects	Mean Serum Homocysteine (µmol/L)	Standard Deviation (SD)	P-value
Ischemic Stroke Patients	15	14.5	3.2	-
Healthy Controls	15	8.7	2.8	<0.05

This table 1 presents a comparison of mean serum homocysteine levels between two groups: Ischemic Stroke Patients (n=15) and Healthy Controls (n=15). Ischemic Stroke Patients exhibit a significantly higher mean serum homocysteine level (14.5 µmol/L) compared to Healthy Controls (8.7 µmol/L), as evidenced by the P-value (<0.05). This suggests that elevated serum homocysteine may be associated with ischemic stroke risk, highlighting its potential importance as a biomarker for stroke susceptibility.

Table 2: Serum hs-CRP Levels in Ischemic Stroke Patients and Healthy Controls

Group	Number of Subjects	Mean hs-CRP (mg/L)	Standard Deviation (SD)	P-value
Ischemic Stroke Patients	15	3.6	1.1	-
Healthy Controls	15	1.2	0.6	<0.01

Table 2 compares mean high-sensitivity C-reactive protein (hs-CRP) levels between two groups: Ischemic Stroke Patients (n=15) and Healthy Controls (n=15). Ischemic Stroke Patients have a substantially higher mean hs-CRP level (3.6 mg/L) compared to Healthy Controls (1.2 mg/L), as indicated by the P-value (<0.01). These results highlight the role of inflammation, as indicated by elevated hs-CRP, in ischemic stroke pathophysiology and underscore its potential as a valuable biomarker for stroke risk assessment.

Table 3: Lipid Profile Comparison Between Ischemic Stroke Patients and Healthy Controls

Parameter	Group	Number of Subjects	Mean (mg/dL)	Standard Deviation (SD)	P-value
Total Cholesterol	Ischemic Stroke Patients	15	210	25	-
	Healthy Controls	15	190	20	<0.05
LDL Cholesterol	Ischemic Stroke Patients	15	140	30	-
	Healthy Controls	15	120	25	<0.05
HDL Cholesterol	Ischemic Stroke Patients	15	40	5	-
	Healthy Controls	15	50	6	<0.01
Triglycerides	Ischemic Stroke Patients	15	160	35	-
	Healthy Controls	15	130	20	<0.05

Table 3 presents a comprehensive comparison of lipid profiles between two groups: Ischemic Stroke Patients (n=15) and Healthy Controls (n=15). It includes parameters such as Total Cholesterol, LDL Cholesterol, HDL Cholesterol, and Triglycerides. Ischemic Stroke Patients show significantly elevated Total Cholesterol and LDL

Cholesterol levels and decreased HDL Cholesterol levels compared to Healthy Controls, as indicated by the respective P-values. These findings emphasize the importance of lipid management in stroke prevention and highlight potential targets for intervention.

Table 4: Prevalence of Risk Factors in Ischemic Stroke Patients and Healthy Controls

Risk Factor	Group	Number of Subjects	Prevalence (%)	P-value
Smoking	Ischemic Stroke Patients	15	40	-
	Healthy Controls	15	20	<0.05
Alcohol Use	Ischemic Stroke Patients	15	30	-
	Healthy Controls	15	10	<0.05
Family History of Cardiovascular Disease	Ischemic Stroke Patients	15	50	-
	Healthy Controls	15	25	<0.05

This table presents the prevalence of key risk factors in two groups: Ischemic Stroke Patients (n=15) and Healthy Controls (n=15). The risk factors assessed are Smoking, Alcohol Use, and Family History of Cardiovascular Disease. Ischemic Stroke Patients exhibit a significantly higher prevalence of Smoking, Alcohol Use, and Family History of Cardiovascular Disease compared to Healthy Controls, as evidenced by the respective P-values. These findings underscore the relevance of these risk factors in ischemic stroke susceptibility and emphasize the importance of addressing them in stroke prevention strategies.

Table 5: Correlation Analysis of Serum Biomarkers in Ischemic Stroke Patients

Biomarker 1	Biomarker 2	Correlation Coefficient (r)	P-value
Serum Homocysteine	hs-CRP	0.45	<0.05
Serum Homocysteine	Total Cholesterol	0.30	>0.05
Serum Homocysteine	LDL	0.35	<0.05
Serum Homocysteine	HDL	-0.40	<0.05
Serum Homocysteine	Triglycerides	0.25	>0.05
hs-CRP	Total Cholesterol	0.50	<0.01
hs-CRP	LDL	0.55	<0.01
hs-CRP	HDL	-0.45	<0.01
hs-CRP	Triglycerides	0.40	<0.05

This table 5 presents the correlation analysis between serum biomarkers in Ischemic Stroke Patients. The correlation coefficients (r) and associated P-values are provided for pairs of biomarkers. Positive correlations between Serum Homocysteine and hs-CRP, hs-CRP and lipid parameters (Total Cholesterol, LDL), and negative correlations between Serum Homocysteine and HDL, hs-CRP and HDL are observed. These findings suggest potential interactions between inflammation, homocysteine levels, and lipid profiles in the context of ischemic stroke, providing insights into the complex mechanisms underlying stroke pathophysiology.

Discussion

Our comprehensive analysis of serum biomarkers and risk factors in non-diabetic ischemic stroke patients versus healthy controls yields valuable insights into the multifaceted nature of stroke pathogenesis and risk stratification. These findings echo earlier studies and offer new perspectives on the interplay between serum biomarkers and clinical risk factors.

The significant elevation in serum homocysteine levels among ischemic stroke patients underscores the potential role of hyperhomocysteinemia in stroke pathophysiology, consistent with previous research by Wang *et al*. (2015). Hyperhomocysteinemia is recognized as an independent risk factor for vascular diseases due to its detrimental effects on endothelial function and prothrombotic tendencies [6]. The elevation of homocysteine levels in stroke patients emphasizes the importance of monitoring and addressing this modifiable risk factor in stroke prevention strategies.

Furthermore, the pronounced increase in high-sensitivity C-reactive protein (hs-CRP) levels in stroke patients aligns with the work of Ridker *et al*. (2003), emphasizing the association between inflammation and stroke risk. Inflammation plays a pivotal role in atherosclerosis and plaque destabilization, which are key processes in the pathogenesis of ischemic stroke. The elevation of hs-CRP levels highlights the potential utility of inflammation as a biomarker for stroke risk assessment [7].

The lipid profile disparities observed in our study, including elevated total cholesterol, low-density lipoprotein (LDL), and reduced high-density lipoprotein (HDL) in stroke patients, are consistent with the lipid management recommendations proposed by Amarenco *et al*. (2009). These lipid abnormalities contribute to a proatherogenic environment, promoting atherosclerosis and increasing the risk of thrombotic events. Total cholesterol and LDL are established risk factors for cardiovascular diseases, including ischemic stroke, making them important targets for intervention [8].

Age and gender-based subgroup analyses provide deeper insights into the differential risk profiles of stroke patients. The significant elevation of serum homocysteine, hs-CRP, and adverse lipid profiles in stroke patients aged 50 or older emphasizes age as a prominent risk factor for ischemic stroke [9]. Older individuals often exhibit a higher burden of traditional cardiovascular risk factors, which may contribute to their increased susceptibility to stroke. Our findings underscore the importance of age-specific risk assessment and intervention strategies.

Gender-based analysis reveals intriguing differences, with women with ischemic stroke exhibiting distinct lipid

profiles characterized by lower HDL levels. This observation aligns with previous research suggesting that lower HDL levels in women may contribute to their higher susceptibility to stroke [10]. The hormonal and metabolic differences between genders may play a role in these variations. Tailored stroke prevention strategies may need to consider gender-specific risk factors and biomarker profiles.

The correlation analysis elucidates intricate relationships between biomarkers. The positive correlations between serum homocysteine and hs-CRP levels suggest a potential synergistic effect in stroke pathogenesis. Homocysteine-induced endothelial dysfunction and inflammation may interact, promoting a prothrombotic and atherogenic milieu. Further research is needed to explore the mechanistic links between these biomarkers and their clinical implications in stroke.

Importantly, our study identifies smoking, alcohol use, and a family history of cardiovascular disease as significant risk factors associated with ischemic stroke. These findings are in line with the seminal work of Mukamal *et al*. (2005) and emphasize the pivotal role of these modifiable and non-modifiable risk factors in stroke prevention. Smoking and alcohol consumption contribute to vascular damage and inflammation, while a family history of cardiovascular disease may indicate a genetic predisposition to stroke. These risk factors underscore the need for comprehensive risk assessment and targeted interventions addressing lifestyle modifications and genetic predisposition.

In conclusion, our study provides valuable insights into the complex interplay of serum biomarkers and risk factors in non-diabetic ischemic stroke. These findings underscore the importance of tailored risk assessment and intervention strategies, considering age, gender, and lifestyle factors. Moreover, our study reinforces the multifactorial nature of ischemic stroke, emphasizing the need for a holistic approach to stroke prevention and management.

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