BRIEF RESEARCH COMMUNICATION

Atherogenic Index of Plasma in Acute Coronary Syndrome: An Observational Study in a Tertiary Care Hospital

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Received on: 30 September 2023; *Accepted on:* 04 November 2023; *Published on:* 05 December 2023

Abstract

Atherogenic index of plasma (AIP) is a log of triglyceride (TG) to high-density lipoprotein (HDL) ratio in mmoL/L is a surrogate marker of lipoprotein size of low-density lipoprotein and HDL, smaller the size, greater the atherogenicity.

Materials and methods: A total of 102 participants with acute coronary syndrome (ACS) and 90 non-coronary artery disease (CAD) asymptomatic participants, not on lipid reduction, were consequently observed and the traditional risk factors and lipidogram were noted and AIP was calculated from the lipidograms.

Results: Atherogenic index of plasma values was considerably higher in patients with ACS than in Non-CAD patients $p < 0.00001$ and was raised in the male gender $p < 0.01$.

Discussion: Atherogenic index of plasma used as a predictive and prognostic marker in CAD, ischemic stroke, metabolic syndrome it's been studied that higher the AIP, higher the angiographically proven lesions according to the Gensen score.

Conclusion: Atherogenic index of plasma is an economical and novel biomarker of atherogenicity.

Keywords: Acute coronary syndrome, Atherogenic index of plasma, Coronary artery disease, High-density lipoprotein, Low-density lipoprotein, Triglycerides.

Indian Journal of Medical Biochemistry (2023): 10.5005/jp-journals-10054-0214

Introduction

Cardiovascular disease stands as a prominent global threat among non-communicable diseases, claiming a significant number of lives. Its prevalence continues to rise, fuelled in part by rapid urbanization and lifestyle changes that promote sedentary habits. Acute coronary syndrome (ACS), a manifestation of coronary artery disease (CAD), encompasses ST-elevation myocardial infarction (MI), non-ST-elevation MI, and unstable angina, affecting individuals across various age groups, including the young. This study aims to assess the potential of the atherogenic index of plasma (AIP) as a biomarker in patients, comparing its relevance between individuals with ACS and those without any signs of CAD, denoted as the non-CAD group.

In addition to traditional risk factors such as hypertension, diabetes mellitus, cigarette smoking, male gender, family history, and low-density lipoprotein (LDL) concentrations, the AIP is increasingly recognized as a biomarker, not just in ACS, but also in ischemic stroke. Liu et al. highlighted the close association of AIP with the risk of both cardiovascular and cerebrovascular diseases, surpassing the predictive capability of individual lipoprotein cholesterol concentrations alone.[1]

It was Frohlich and Dobiásová in 2001 who first introduced the concept of $\log_{10}$ (TG/HDL-C) (mmoL) as the AIP, providing a valuable metric to assess the atherogenic potential of lipoprotein profiles.[2,3] The AIP ratio, derived from this formula, serves as an indicator of LDL particle size and ranges from negative to positive values. A negative value corresponds to an LDL particle with a diameter smaller than 25.5 nm. This measurement is crucial for differentiating between LDL pattern A, denoting normal LDL particles, and LDL pattern B, indicating highly atherogenic small dense cholesterol-depleted LDL particles.[4] It was observed that normolipidemic CAD patients exhibited higher positive values of the AIP compared to healthy subjects.[5,6] This insight holds significant importance in understanding and diagnosing atherosclerosis-related risks.

Elevated AIP, has been angiographically associated with CAD along with high TG levels and low HDL cholesterol, which is found to correlate with smaller lipoprotein particles and increased atherogenicity.[2,3] Research indicates that individuals with smaller and denser LDL and HDL lipoprotein particles face a heightened risk of CAD, whereas larger HDL particles are linked to reduced CAD risk.[7] These small dense LDL particles are particularly prone to oxidation due to their lower antioxidant content, leading to endothelial dysfunction. The oxidized LDL particles are recognized by scavenger receptors, triggering foam cell formation, a hallmark of atherosclerosis.[2] Moreover, AIP is not solely a diagnostic tool but also holds prognostic value. Studies have demonstrated that AIP

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How to cite this article: Bugge SK. Atherogenic Index of Plasma in Acute Coronary Syndrome: An Observational Study in a Tertiary Care Hospital. Indian J Med Biochem 2023;27(1):14–17.

Source of support: Nil

Conflict of interest: None

Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.

levels are higher in patients with ACS and reduce during treatment, as confirmed angiographically.[2,8]

In our current study conducted at a tertiary hospital in Hyderabad, India, we aimed to explore the significance of the AIP in assessing cardiovascular risk and predicting prognosis. To achieve this, we compared AIP values between individuals with active ACS and those without ACS to assess the risk within the control population, providing valuable insights into the relevance of AIP in assessing and anticipating cardiovascular risks, and offering a substantial contribution to the field of cardiovascular research and patient care.

Materials and Methods

Study Design and Participant Selection

This observational study, conducted at Malla Reddy Narayana Multispecialty Hospital in Hyderabad, Telangana, India, focused on patients admitted to the Coronary Care Unit and Emergency Departments between August 2018 and July 2019. The study was carried out following ethical approval from the Ethics Committee of Malla Reddy Medical College for Women, Hyderabad, Telangana, India, the affiliated institution of the hospital.

Patients diagnosed with ACS were included, comprising individuals with both ST-elevation MI and non-ST-elevation MI, who were not on lipid reduction medications. The diagnosis of acute MI was made by cardiologists based on a comprehensive assessment involving clinical, electrophysiological, and biochemical markers. Control participants were selected from individuals without CAD. Detailed histories of risk factors, such as smoking habits, diabetes history, hypertension, and family background of CAD, were collected and recorded. Participants younger than 18 years and those with severe renal insufficiency, nephrotic syndrome, myocarditis, infectious endocarditis, multiple arteritis, pericarditis, dissecting aortic aneurysm, or mitral valve prolapse were excluded from the study.

Demographic data including gender, age, and systolic and diastolic blood pressure were recorded. Hypertension was defined as systolic blood pressure (SBP) ≥140 mm Hg, diastolic blood pressure (DBP) ≥90 mm Hg, a previous doctor-diagnosed history of hypertension, or current use of antihypertensive medication.[4] Diabetes was defined as fasting glucose levels >126 mg/dL. Additionally, participants who had been smoking for at least six months daily and those consuming alcohol at least 5 days a week for 6 months were included in the study.[9]

Blood Sample Collection and Processing

Blood samples were obtained from participants after an overnight fast and collected in red top-containing vacutainer tubes. The samples were processed on the same day, with centrifugation carried out within 4 hours after clot formation.

The participant's serum triglycerides and high-density lipoprotein (HDL) were processed on Siemens Dimensions RXL autoanalyzer, according to the machine operating instructions.

To facilitate AIP calculations, triglyceride, and HDL values were converted from mg/dL to mmoL/L, following the methodology established in the original article by Dobiásová.[4] The lipogram information then was utilized for AIP calculation, using this formula:

$$\log_{10} (TG/HDL\text{-}C) (mmoL)$$

Atherogenic index of plasma values falling within the range from –0.3 to 0.1 were classified as low risk, from 0.1 to 0.24 as medium risk, and above 0.24 as high cardiovascular risk. Additionally, AIP values were categorized into quartiles to assess risk stratification. Quartile 1 (Q1) (< –0.1); Quartile 2 (Q2) (–0.1–0.08); Quartile 3 (Q3) (0.08–0.26); Quartile 4 (Q4) (>0.26). This quartile division provided a nuanced understanding of AIP's association with cardiovascular risk.[10–12]

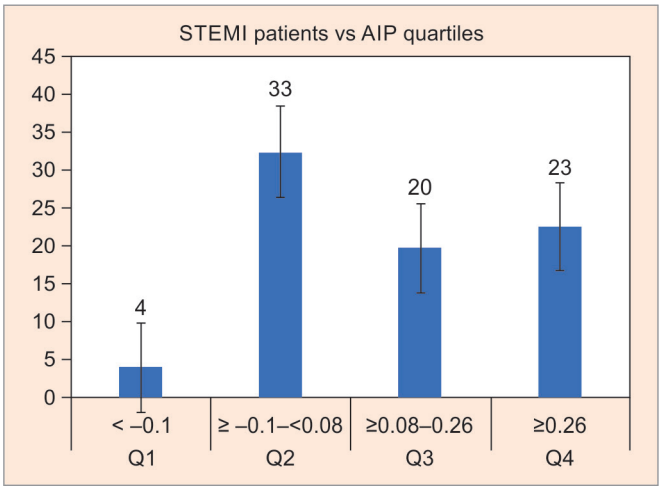

Fig. 1: Characteristics of the study population

Statistical Methods

The demographic information of the participants, as well as the risk factors for CAD and lipid profile data necessary for AIP calculation, were organized in Microsoft Excel. The data were summarized as means (SD) for the entire group and separately for men and women. Comparative analyses were conducted using independent sample *t*-tests, with statistical significance set at a *p*-value less than 0.05. The analyses were performed using SPSS version 22.

Results

Characteristics of the Study Population

The study cohort comprised 102 participants diagnosed with ACS, ranging in age from 22 to 84 years. Among them, 76% were males, and 24% were females. 80 of 102 (78%) participants with ACS had ST-elevation MI as seen in Figure 1, and 22% were sufferers of non-ST-elevation MI. The non-CAD group, consisting of asymptomatic individuals without CAD, included 90 participants aged between 18 and 76 years, with 69% being male and 31% female. The mean ages for the ACS and non-CAD groups were 49.8 (±14.81) years and 45.8 (±13.49) years, respectively (Table 1) 002E.

AIP Analysis

The highest recorded AIP was 1.129, observed in a 36-year-old participant who was a smoker and alcoholic, with no family history of CAD. In the ACS group, 18.6% of participants fell into the 4th quartile (AIP >0.54), with a mean AIP value of 0.74. Significant differences in AIP quartiles were observed based on gender ($p < 0.01$), hypertension status in both genders ($p < 0.01$), and presence of ACS ($p < 0.00001$).

Among participants without CAD but with hypertension, higher levels of triglycerides ($p < 0.006$) and AIP values ($p < 0.012$) were noted when compared to their non-hypertensive counterparts without CAD. Additionally, diabetics in the non-CAD group exhibited a statistically significant increase or decrease? in triglyceride values ($p < 0.024$) compared to non-diabetic participants in the same

Table 1: Characteristics of the study population

	Total (192)	*Non-CAD (n = 90)*	*ACS (n = 102)*	*p-value*
Males [*n* (%)]	140 (72.9)	62 (68.8)	78 (76.5)	0.015
Age	48.13 ± 18.22	45.8 ± 13.497 (22–76 years)	49.8 ± 14.81 (22–84 years)	
Hypertensive [*n* (%)]	66 (34.47)	32 (35.5)	34 (33.3)	
Diabetic [*n* (%)]	49 (25.5)	27 (30)	22 (21.5)	
Smokers [*n* (%)]	67 (34.8)	17 (18.8)	50 (49.01)	
Alcohol consumers [*n* (%)]	92 (47.9)	37 (41.1)	55 (53.92)	
Family history [*n* (%)]	35 (19)	16 (17.7)	19 (18.62)	
Triglyceride	1.51 ± 1.25	1.51 ± 0.79 (0.23–3.77 mmol/L)	1.94 ± 0.459 (0.3–10.1 mmol/L)	<0.00001
HDL	1.25 ± 0.64	1.02 ± 0.23 (0.49–1.70 mmol/L)	1.02 ± 0.314 (0.36–2.37 mmol/L)	
AIP – study range	0.16 ± 0.31	0.12 ± 0.27 (–0.857–0.69)	0.19 ± 0.35 (–0.818–1.129)	<0.00001

group. However, there was no statistically significant difference in AIP ratios concerning alcoholism and family history among participants with ACS in this study.

Discussion

The findings of our study underscore a significant association between AIP levels and ACS among participants when compared to those in the non-CAD (asymptomatic) group ($p < 0.00001$). This result aligns with a study conducted by Cai et al.,[13] where the AIP was analyzed to assess the severity of ACS in males aged 35 years or younger. Additionally, our study revealed a notable gender-based difference, consistent with traditional ACS risk factors, with males displaying significantly elevated AIP values compared to females ($p < 0.01$).[13]

Furthermore, our study mirrored previous research conducted by Li et al., indicating a substantial correlation between AIP and Type 2 diabetes as well as hypertension among participants in the non-CAD group. These correlations were observed both in identifying metabolic syndrome and for early risk stratification of ACS in diabetic and hypertensive patients.[7,11,14]

Atherogenic index of plasma has been demonstrated by Huang et al. to be closely correlated with the fractional esterification rate of HDL-C, particularly about small-dense LDL (sdLDL). A higher proportion of sdLDL within AIP indicates intricate interactions within lipoprotein metabolism and aids in forecasting plasma atherogenicity. These small dense LDL particles, being smaller and less efficiently cleared from the bloodstream, face increased oxidative stress, transforming into oxidized LDL in the body. This process triggers inflammatory responses in the sub-endothelium of blood vessels, leading to enhanced binding to the subendothelial matrix and the formation of foam cells. These foam cells, formed as macrophages and smooth muscle cells engulf oxidized LDL, initiating the development of atherosclerosis. Additionally, AIP regulates the reverse cholesterol transport process, managing the recycling or disposal of excess cholesterol.

Elevated AIP levels may lead to adipocytes storing surplus triglycerides as fat and increasing the accumulation of cholesterol crystals in the various layers of atherosclerotic arteries. This accumulation causes narrowing and blockage of the arterial lumen, ultimately resulting in atherosclerosis.[14] AIP has also been shown to denote the angiographical progression of atherogenicity.[2,8,15] Atherogenic index of plasma serves as an independent predictor for major cardiovascular and cerebrovascular events, such as cardiac death, myocardial infarction, and stroke, irrespective of clinical condition.[15]

Notably, interventions like glucose-lowering medications, such as pioglitazone, have proven effective in reducing AIP values, thereby decreasing cardiovascular risk. Additionally, research suggests that adopting a healthier lifestyle, including engaging in moderate-to-vigorous physical activities, increasing aerobic exercise duration, reducing sedentary behavior, and enhancing cardiorespiratory fitness, can inversely correlate with AIP levels. This implies that a healthy lifestyle contributes to mitigating cardiovascular disease risk through improvements in AIP.[9]

Finally, AIP can be used to assess the small dense LDL particles at no cost, especially in developing countries like India.[13] This present study is first of its kind AIP study in the Telangana region of India among ACS patients to show the AIP that ranged from –0.8 to 1.29 (mmoL/mmoL).

Limitations

This study was done in a single center and the sample size is small. Hence results were interpreted with caution.

Conclusion

Atherogenic index of plasma is an economical and safe predictive biomarker of ACS in patients, as small dense LDL with their oxidation is atherogenic and AIP reflects their presence and thereby the risk.

Acknowledgment

Authors would like to thank Late Dr J Rama Rao for the encouragement and Tabitha Grace Royal for proofreading.

Declarations

Ethical Approval

Ethical approval from the Ethics Committee of Malla Reddy Medical College for Women, Hyderabad, was taken.

Authors' Contribution

Dr Surya Kantha Bugge is the sole author of this article.

Availability of Data and Materials

Ethical committee approvals and other data if required are available.

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