Original Article

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Internal Medicine Section

A Cross-sectional Study of Atherogenic Index of Plasma and Angiographic Profile by Gensini Score in Patients of Acute Coronary Syndrome

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ABSTRACT

Introduction: Coronary Artery Disease (CAD) is the leading cause of death worldwide. India has the highest burden of Acute Coronary Syndrome (ACS). Atherogenesis is a multifactorial process, abnormalities in lipoprotein metabolism especially elevated Low Density Lipoprotein Cholesterol (LDLc) remains one of most attributing key factor. Atherogenic Index of Plasma (AIP), can be calculated easily from the formula AIP=Log 10 Triglyceride (TG)/High Density Lipoprotein Cholesterol (HDLc). The AIP is inversely proportional to the diameter of LDLc particles, which indirectly reflects Small Dense LDLc levels. AIP has been proposed as a marker for Cardiovascular (CV) risk.

Aim: The study aimed to assess the correlation between AIP and the Angiographic Profile by Gensini Score (GS) in ACS patients and also to evaluate the relationship between AIP and in-hospital mortality of ACS patients.

Materials and Methods: This study was a hospital based cross-sectional study. This study was done from November 2019 to October 2020 in the Department of Cardiology, Sriram Chandra Bhanja Medical College, Odisha, India. A total of 240 patients of ACS were included in the study. AIP was calculated from the lipid profile of all the ACS patients. Coronary Angiography was done in all of these patients. Correlation of the AIP was done with the severity of CAD according to Gensini scoring system. Chi-square test was used to compare continuous variables $p<0.05$ was considered significant. Spearman's rho correlation was also used to compare AIP with GS. Statistical analysis was performed using Statistical Package for the Social Sciences, (SPSS) 26 (IBM).

Results: Majority of the cases were males 194 (80.8%) and females were 46 (19.2%). The Spearmans rho coefficient between AIP and GS was 0.663. It was statistically significant ($p<0.001$). AIP had positive correlation (value) with severity of CAD by GS. In-hospital mortality was 5%. It was more in high risk AIP group with a p-value of 0.006 which was statistically significant.

Conclusion: AIP shows positive correlation with the severity of CAD in terms of GS. High AIP is also associated with increased in-hospital mortality. AIP can be used in the treatment of ACS patients and is a suitable alternative to various costly biomarkers of CAD. Therefore, AIP can be advocated for routine measurement in clinical practice.

Keywords: Coronary artery disease, High density lipoprotein, Triglyceride

INTRODUCTION

The CAD is the leading cause of death worldwide. The 2019 heart disease and stroke statistics update of the American Heart Association (AHA) reported that 48 percent of persons ≥20 years of age in the United States have CVD [1]. India has the highest burden of Acute Coronary Syndrome (ACS) [2]. The adult treatment panel III has recognised importance of high TG and low HDLc in CVD calling this combination an atherogenic dyslipidemia along with raised LDLc [2].

ACS encompasses the diagnosis of unstable angina, Non-ST Elevation Myocardial Infarction (NSTEMI), ST Elevation Myocardial Infarction (STEMI) [3]. Abnormalities in lipoprotein metabolism especially elevated LDLc remains one of most attributing key factor in the pathogenesis of ACS.

LDL is an independent risk factor and a major intervention target for CAD [4,5]. A number of studies have confirmed that dyslipidemia and inflammation play an important role in the pathogenesis of atherosclerosis [6]. In clinical practice even after lowering LDLc levels to the recommended level, 50% of the CV risk still remain [6].

Small, dense Low-Density Lipoprotein (sdLDL) is more atherogenic than buoyant LDL [7]. Therefore, sdLDL is considered as a risk factor for atherosclerosis and a predictor of CV disease [7]. The 2002 National Cholesterol Education Program listed sdLDLc as a new risk factor for CAD and recommended the measurement of sdLDLc [8]. However, due to the complexity and high cost of testing, the use of this measurement is limited in clinical practice.

In 1998, Dobiasova M et al., introduced a term called AIP, that can be calculated easily from estimated serum or plasma TG and serum or plasma HDLc value using the formula [8]: AIP=Log10 (TG/HDLC) [9,10] expressed in mmol/L or mg/dL. The Atherogenic Index of Plasma, defined as logarithm of ratio of concentration of TG to HDL cholesterol [9] correlates well with size of HDL and LDL particles and with fractional esterification rate of HDL cholesterol. AIP has been proposed as a marker for CV risk and it can be easily calculated from standard lipid profile [10].

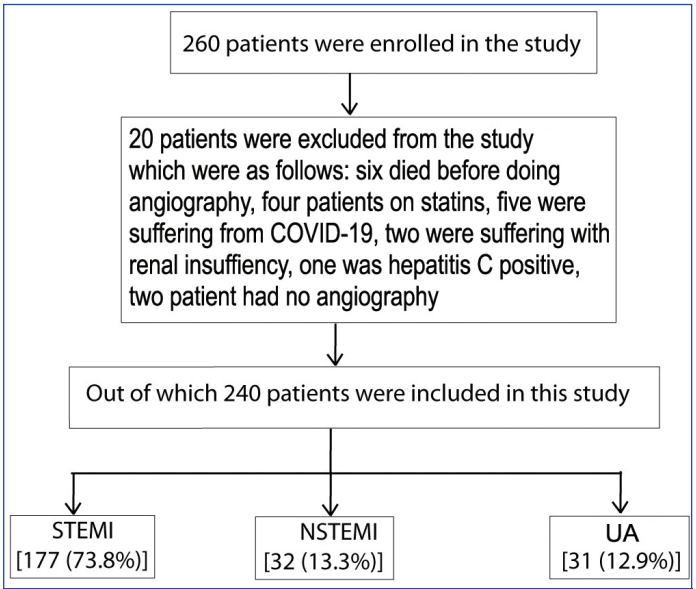
AIP is a new indicator involved in dyslipidemia. The AIP is closely related and inversely proportional to the diameter of LDLc particles, which indirectly reflects small dense LDLc levels [10]. This value has been established as an index for predicting plasma atherosclerosis and CAD [10].

It adds predictive value beyond that of individual lipid especially in conditions like clinical manifestations of atherogenesis with normal lipid profile. As a surrogate of the smalll low-density lipoprotein particle size and needing no extra cost, AIP was proposed to be an economic and reliable indicator for CAD clinically. AIP as a biomarker may assist in the prevention of CAD [10].To date, a few studies

have detected an association between AIP and atherosclerosis related conditions [11]. Further, in India there were very few studies on association between AIP and ACS. So, this study was done to know the association between AIP and GS and also to find the relationship between AIP and in-hospital mortality of ACS patients.

MATERIALS AND METHODS

This study was a hospital based cross-sectional study done during November 2019 to October 2020 in the Department of Cardiology, Sri Ram Chandra Bhanja Medical College and Hospital, Tertiary Referral Center in Cuttack, Odisha. Patients of ACS [Unstable angina (UA), NSTEMI and STEMI] admitted to the Department of Cardiology, meeting both inclusion and exclusion criteria were enrolled. The study received approval from the Institutional Ethical committee with IEC No. 537 in 2019. Out of 260 patients of ACS, 240 patients were selected as shown in the [Table/Fig-1]. Twenty patients were excluded from the study. Informed consent was taken from all the selected patients.



[Table/Fig-1]: Flow chart depicting selection of participants.

Inclusion criteria: Patients diagnosed with ACS {STEMI, NSTEMI, UA} with age >18 years were included in this study.

Exclusion criteria: Age <18 years, Viral infections like Human Immuno Deficiency Virus (HIV), Hepatitis C Virus (HCV), Hepatitis B Virus (HBV), COVID-19, Renal Insuffiency, Chronic liver diseases, History of taking statins and/or anti-lipidemic drugs, Post Percutaneous Coronary Intervention (PCI)/Post Coronary Artery Bypass Grafting.

Study Procedure

Lipid profile was done within 24 hours of admission. AIP was calculated from the lipid profile of all the patients by using the following formula AIP=Log 10(TG/HDLc) [9,10]. Coronary Angiography was done in all of these patients by using Siemens Artis Zee Cath Lab. AIP was divided into three groups low risk, intermediate risk and high risk [11]. Correlation of the AIP was done with the severity of CAD according to Gensini Scoring (GS) sytem by applying Spearman's rho coefficient [12]. GS is an angiographic scoring system for quantification of the severity of CAD in which GS <20 means less severe and GS ≥20 means more severe CAD [12]. In-hospital mortality was noted by clinical monitoring and observation of the patients. It was compared with the AIP groups by applying the Chi-square test.

STATISTICAL ANALYSIS

Statistical analysis used were One- way ANOVA test for continuous variables, Pearson Chi-square (χ^2) test for categorical variables. Continuous variables with normal distribution were expressed as mean±Standard Deviation (SD). Chi-square test was used to compare continuous variables. $p<0.05$ was considered significant. Spearman's rho correlation was also used to compare AIP with GS. Statistical analysis was performed using SPSS 26 (IBM).

RESULTS

Age distribution: The maximum number of patients were found in 41 to 70 years of age group followed by less than 40 years of age group with a share of 87.5% and 7.9% respectively as shown in the [Table/Fig-2].

Age group (years)	Number	Percent
≤40	19	7.9
41-70	210	87.5
>70	11	4.6
Total	240	100.0

[Table/Fig-2]: Distribution of ACS cases by Age.

Base line characteristics of study population: The mean age was 55.7±9.7 years. Majority of the cases were males 194 (80.8%) and females were 46 (19.2%) in number as shown in the [Table/Fig-3]. There was no significant association between gender and AIP (p-value=0.45).

Parameters	Minimum	Maximum	Mean	SD
Age	19.0	90.0	55.721	9.7878
Body mass index	18.60	35.08	24.6473	2.60495
Waist hip ratio	0.80	1.23	0.9420	0.07161
Atherogenic Index of plasma	-0.5900	0.8300	0.133	0.224
Total cholesterol	81.0	437.0	187.563	51.5218
Triglyceride	39.0	807.0	154.312	93.9615
High-density lipoprotein	23.0	139.0	45.067	10.5306
Low-density lipoprotein	25.0	342.0	109.896	44.4774

[Table/Fig-3]: Base line characteristics of study population.
SD: Standard deviation

Distribution of risk factors: Diyslipidemia is the most common conventional risk factor seen in 41.3% of cases, followed by Type 2 Diabetes Mellitus (T2DM) seen in 35.4% of cases. Third common risk factor was smoking seen in 34.2% of cases. BMI was normal in 57.9% of cases, 36.3% of cases were overweight and obesity was found in 5.8% of cases. Hypertension was seen in 32.1% of cases as shown in the [Table/Fig-4].

Risk factors	Number	Percentage
Hypertension	77	32.1
T2DM	85	35.4
Smoker	82	34.2
Dyslipidemia	99	41.3
Family history	17	7.1
Obesity	14	5.8

[Table/Fig-4]: Distribution of Risk Factor samong the ACS patients.

Distribution of atherogenic index of plasma: In this study AIP- was divided in to three groups- low risk, intermediate risk and high risk. It was found that 46.3% of patients belong to low CV risk AIP group, followed by 34.2% of high risk group. Least number of patients belonged to intermediate risk group 19.6% as shown in [Table/Fig-5].

AIP	Number	Percent
Low risk (≤0.10)	111	46.3
Intermediate risk (0.11-0.21)	47	19.6
High risk (>0.21)	82	34.2
Total	240	100.0

[Table/Fig-5]: Distribution of Atherogenic Index of Plasma (AIP) among ACS patients.

Comparison of the number of coronary arteries involved with AIP: An elevated trend of AIP was observed with the increase in number of coronary arteries involved on applying Chi-square test, p-value was significant 0.001 (<0.05) as shown in the [Table/Fig-6]. In this study Left Main Coronary Artery (LMCA) was involved in 4.6% of cases, LMCA+Double Vessel Disease (DVD) in 0.8% of cases, LMCA+Triple Vessel Disease (TVD) in 0.4% of cases.

Coronary artery involved	AIP			Total
	Low	Intermediate	High	
SVD	71 (64.0%)	21 (44.7%)	23 (28.0%)	115 (47.9%)
DVD	5 (4.5%)	14 (29.8%)	33 (40.2%)	52 (21.7%)
TVD	4 (3.6%)	8 (17.0%)	24 (29.3%)	36 (15.0%)
Normal	31 (27.9%)	4 (8.5%)	2 (2.4%)	37 (15.4%)
Total	111 (100%)	47 (100%)	82 (100%)	240

[Table/Fig-6]: Comparison of the number of coronary arteries involved with AIP. Chi-square test; p-value=0.001; SVD: Single vessel disease; DVD: Double vessel disease; TVD: Triple vessel disease

Comparison of Gensini score with AIP: In this study majority of the patients with GS less than 20 belong to low AIP group (89.2%),with least number of patients belong to high AIP group (4.9%). In GS ≥20 group, more number of patients were presented with high AIP (95.1%), followed by intermediate group (42.6%). Less number of patients presented with GS ≥20 and with low AIP with significant p-value of 0.001(Chi-square test) as shown in the [Table/Fig-7].

Gensini score	AIP			Total
	Low risk	Intermediate risk	High risk	
<20	99 (89.2%)	27 (57.4%)	4 (4.9%)	130 (54.2%)
≥20	12 (10.8%)	20 (42.6%)	78 (95.1%)	110 (45.8%)
Total	111 (100%)	47 (100%)	82 (100%)	240 (100%)
Chi-square test (p-value=0.001)				

[Table/Fig-7]: Comparison of Gensini Score (GS) with AIP.

Distribution of data for AIP and Gensini score was checked using Shapiro-wilk Test and appropriate Spearman's rho correlation was computed. The mean AIP was 0.133±0.2 and mean GS was 22.08±18.02. The spearman's rho coefficient between AIP and GS was 0.663 and it was statistically significant (p<0.001) as shown in the [Table/Fig-8].

Spearman's rho		AIP	Gensini score
AIP	Correlation coefficient	1.000	0.663
	Sig.(2 tailed)	-	0.000
	Number	240	240
Gensini Score	Correlation coefficient	0.663	1.000
	Sig.(2 tailed)	0	-
	Number	240	240
(p-value <0.001)			

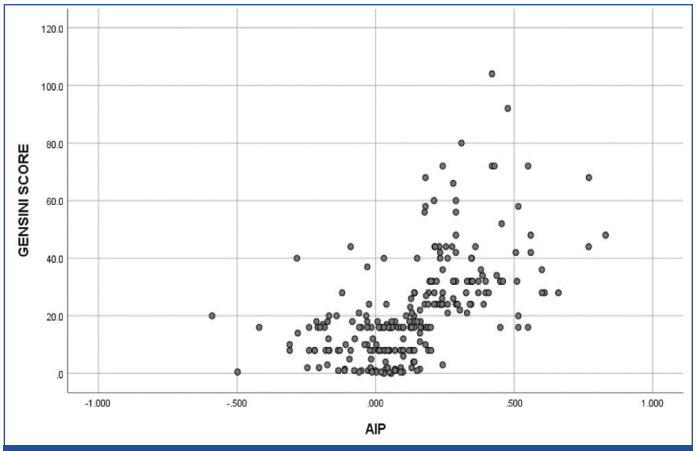
[Table/Fig-8]: Correlation between AIP and Gensini score.

The correlation between AIP and Gensini score by scatter plot is shown in the [Table/Fig-9].

Comparison of In-hospital mortality with AIP: In our study in hospital mortality was 5%. It was highest in high AIP group that is 11% followed by intermediate AIP group (4.3%) with the application of Chi-square test as shown in the [Table/Fig-10] p-value was significant (p=0.006).

DISCUSSION

The mean age of this study was 55.7±9.7 (Mean±SD) which was comparable to the International Registry of ACS Registry study in Transitional countries (ISACSTC) Registry [13] with mean age of 62.6±11.9 years. Minimum age was 19 years and maximum age was 90 years. Of the 240 patients, majority were males 194 (80.8%)



[Table/Fig-9]: Scatterplot of correlation between AIP with Gensini score.

Parameters	Low risk AIP	Intermediate risk AIP	High risk AIP	Total
Mortality	1 (0.9%)	2 (4.3%)	9 (11.0%)	12 (5.0%)
Survive	110 (99.1%)	45 (95.7%)	73 (89.0%)	228 (95.0%)
Total	111 (100.00%)	47 (100.0%)	82 (100.0%)	240 (100.0%)
Chi-square test (p=0.006)				

[Table/Fig-10]: Comparison of In hospital mortality with AIP.

and females were 46 (19.2%) in number, which was comparable to the study of Sidhu NS et al., [14]. In their study, 75.8% were males and 24.2% were females. In present study, there was no significant association between gender and AIP (p-value=0.45). This was in accordance with Ni W et al., [15].

In our study, dyslipidaemia was the most common risk factor found in 41.3% of patients. The prevalence of dyslipidemia in India varies from 10-73% depending on area of residence (rural vs urban), socioeconomic status (high vs middle or low), diet and physical activity [16].

Second most common risk factor of ACS in this study was T2DM seen in 35.4% of patients which was comparable to that of CREATE Registry [17] (30.4%) and more than that of Inter Heart Study [18] (16.2%). Hypertension was seen in 32.1% of patients in this study. It was close to that of CREATE registry [17] (37.7%) and Inter heart study [18](34.6%). Family history was noted in 7.1% of patients in this study. It was low when compared to study of Anil Kumar E et al., (30%) [19]. Comparison of risk factors between present study and Inter Heart study [18] as shown in [Table/Fig-11].

Risk factor	Present study %	Interheart study [18]
Type 2 diabetes mellitus	35.4	16.2
Smoking	34.2	53
Hypertension	32.1	34.6
Obesity	5.8	46.5

[Table/Fig-11]: Comparison of risk factors.

In this study BMI was normal in 57.9% of cases, 36.3% of cases were overweight and obesity was found in 5.8% of cases.

In our study, obesity (5.8%) was less when compared with that of Interheart study (46.5%) [18]. In this study mean BMI was 24.64±2.6 which is in accordance with the Third Joint task force of European Society of Cardiology Committee for practice Guidelines [20] where mean BMI was 27±1.8.

Majority of the patients in our study presented with STEMI (73.8%) followed by NSTEMI (13.3%) and UA (12.9%). It was comparable to study by Anil Kumar E et al., where 72% presented with STEMI, 18% with NSTEMI and 10% with Unstable angina [19].

In this study, majority of patients belonged to low risk category of AIP (46.3%), followed by high risk AIP category (34.2%) and only 19.6% of patients belonged to intermediate risk of AIP. This was

in contrast to the study of Ilhamifithri I et al., where 8.3% of cases were in low risk, 37.5% in intermediate risk and 54.2% belonged to high riskgroup; the variation could have occurred because this study was done in a small group of 24 patients only [21].

Coronary angiography in this study population revealed Single Vessel Disease (SVD) in 47.9% cases, Double Vessel Disease (DVD) in 21.7% of cases, Triple Vessel Disease (TVD) in 15% of cases and normal coronary arteries in 15.4% of cases. In the study, conducted by Ilhamifithri I et al., SVD was observed in 31.2% of cases, DVD in 34.3% of cases and TVD in 21.8% [21]. Normal coronary artery was seen in 12.5% of cases. In our study, LMCA was involved in 4.6% of cases, which was in accordance with the study conducted by Ilhamifithri I et al., in which LMCA was involved in 3.1% of cases [21].

Comparing the number of coronary arteries involved with that of AIP an upward trend of AIP was observed with an increase in number of coronary arteries involved. Among the cases with high AIP, 29.3% of patients had TVD, 40.2% of patients had DVD and 28% of patients had SVD. This was similar to the study of Cai G et al., [22]. In this study, 35.12% of patients had TVD, 16.51% of patients had DVD and 12.99% of patients had SVD. Among high AIP individuals more number of patients presented with TVD and DVD, less number of patients presented with SVD.

The number of cases with high Gensini Score (≥20) were 45.8% and low Gensini score were 54.1% of cases. Cases with highrisk AIP had high GS score when compared to that of patients with low risk AIP group. This was in accordance with the study of Cai G et al., which postulated that with the elevated GS score and number of lesion vessels, the AIP level increased gradually ($p_{for\ trend}$ all< 0.05) [22]. Moreover, the prevalence of ACS, acute myocardial infarction, unstable angina pectoris and the value of GS were also elevated as AIP quartiles increased in this study ($p_{for\ trend}$ < 0.001) [22].

A large-sample case-control study in China also indicated that AIP was significantly associated with CAD with an adjusted OR 95% CI of 1.66 (1.367–2.016) [23]. To date, a few studies have detected an association between AIP and atherosclerosis related conditions [23]. Distribution of data for AIP and Gensini score was checked using shapiro-wilk test and appropriate Spearman's rho correlation was computed. The Spearman's rho coefficient between AIP and GS was 0.663, it was statistically significant (p<0.001). It implies that AIP had highly significant positive correlation with severity of CAD in terms of Gensini score. It was in accordance with Elyamani AS et al., study (p<0.001) with Spearman's rho coefficient of 0.692 [24]. Present study was also in accordance with Liu T et al., [25]. This study involved 1131 in patients who were divided in to Chronic Total Occlusion (CTO) group (398) and control group (733). In this study, Gensini score (r=0.325, p<0.001) showed significant positive correlations with the AIP [25].

In-hospital mortality found to be 5% in our study which was in accordance with that of Sharma R et al., study (7.9%) [26]. The p-value was significant (p=0.006). Our study was in accordance with Qin Z et al., study [27]. In this study, the incidence of Major CV and Cerebrovascular Adverse events (MACCEs) considered to be a combination of cardiogenic death, Myocardial Infarction, repeated revascularization and stroke was 20.5% in high AIP group with T2DM patients undergoing PCI. The AIP is positively associated with the risk of all-cause death in elderly women with arterial hypertension according to the Bendzala M et al study [28]. So there was a statistically significant positive association between high AIP and in hospital mortality.

Limitation(s)

This study was carried out in a single center with a small sample size. So conclusion should be done with caution. Further confirmation by conducting a multi center study with large sample volume should be done.

CONCLUSION(S)

AIP shows positive correlation with the severity of CAD in terms of Gensini score. High AIP is also associated with increased in-hospital mortality. AIP is considered as a good predictor of the severity of CAD and multi vessel involvement in Indian population. Classification of patients according to AIP may direct needful therapy. AIP can be used in the treatment of ACS patients and is a suitable alternative to various costly biomarkers of CAD. Therefore, AIP can be advocated for routine measurement in clinical practice.

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