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Original Research Article

Fibirogen to Albumin Ratio Severity of Coronary Artery Disease in Diabetes Mellitus Patient

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Abstract:

Introduction: Coronary artery disease (CAD) is one of the commonest causes of mortality and morbidity. The Fibrinogen/Albumin Ratio (FAR) is a newer marker of inflammation that has been shown to be a predictor of short-term prognosis in patients with acute myocardial infarction. Utility of FAR in predicting angiographic severity of CAD and clinical outcomes is not yet clear in Indian patients.

Objective: To study the role of fibrinogen-to-albumin ratio (FAR) as predictor of the angiographic severity of the coronary artery disease, and the short-term prognosis in the patients undergoing coronary angiography.

Material and Methods: The present study was conducted in the Dept. of Cardiology, Sri Jayadeva Institution of Cardiovascular Sciences. A detailed history, physical examination and all routine investigations along with serum albumin, fibrinogen, ECG & 2-D Echo were done for all the patients. Samples were drawn at admission, before angiography. All the patients underwent clinically indicated invasive coronary angiography. SYNTAX SCORE was calculated using an online SYNTAX SCORE calculator.

Results: Out of the 237 patients for final analysis, the majority (81.4%) were male. The mean age of the patients was 57 years. The mean fibrinogen level was 397.97 mg/dl, the mean serum albumin level was 4.05 g/dl and the mean FAR was 101.07 mg/g. with FAR below it was considered as low FAR and above it was considered as high FAR. The mean CAG Syntax score was 22.02. Majority of patients (58.6%) had acute coronary syndrome (ACS), while remaining had stable coronary artery disease. Two FAR groups were found to have comparable proportions of patients across the two Syntax score groups (low SS < 23, high SS > 23). The p-value for the correlation between FAR and Syntax Score was not significant (p=0.941).

Conclusion: FAR was not found to be associated with CAD severity among Indian patients with stable CAD and ACS in the present study. This study didn't find any correlation between the FAR and short-term prognosis.

Keywords: Fibrinogen, Albumin, CAD.

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Introduction

Coronary artery disease (CAD) is one of the most common causes of mortality and morbidity across the globe. It's the leading cause of demise in India, and the contribution to mortality is rising. Number of deaths because of CAD in the year 1985 doubled by 2015.[1] Conventional risk factors for CAD can be divided into non-modifiable and modifiable risk factors. The former includes age, gender and family history, while the latter includes diabetes mellitus (DM), smoking, dyslipidaemia, hypertension and obesity. Recently, a number of newer cardio-vascular biomarkers have been identified, that are of great interest as more than 60.0% CAD in the Indians remains unexplained by the conventional risk factors.[2 ,3] Recently, an attempt has been made to incorporate these biomarkers into traditional scoring systems to add to their prognostic value, however, risk stratification of CAD remains far from perfect.[4] The goal of risk stratification is not only to predict outcomes but also to guide management, triaging and more importantly urgency of treatment needed. This is even more relevant in a resource-constrained setting.[5]

Fibrinogen is a short half-life protein and an indicator of the state of coagulation and a biomarker of inflammation.[6] It's reported that the level of plasma fibrinogen in the patients having ACS was much higher than healthy controls and a higher level of plasma fibrinogen may be an independent predictor of the major adverse cardiac events during the short- term, and long-term follow-up.[7] On the

contrary, albumin is inversely related to the degree of the inflammatory response and it's an important inhibitor of platelet activation and aggregation.[8] Studies indicate that low albumin is associated with atherosclerotic cardio-vascular diseases (ASCVD), and is related to major adverse cardio-vascular events (MACE).[9] Hypoalbuminemia has been identified as a risk factor for incident myocardial infarction (MI) in cases with CAD.[10] Several studies reported the association between low serum albumin and the increased risk of cardio-vascular mortality and morbidity.[11]

The Fibrinogen/Albumin Ratio (FAR) has performed better than individual fibrinogen and albumin level in determining the severity of the acute myocardial infarction (AMI) and predicting short-term prognosis of these patients. [12,13] A prospective cohort investigation conducted in China revealed that CVD patients with high FAR levels and diabetes had a poorer 5-year prognosis.[14]

Therefore, both fibrinogen and albumin are important factors of systemic inflammatory and hemorheological alterations. The fibrinogen–albumin ratio (FAR), comprising both of these indicators, has been reported as a new inflammatory marker closely related to CAD progression and severity of CAD.[13] However, the prognostic value of the FAR for patients with CAD among the Indian population is unclear. Purpose of this study is to explore the relationship between the FAR and angiographic severity of CAD and short-term prognosis in Indian patients with CAD who are undergoing coronary angiography and revascularization

Material and Methods: The study conducted in the Dept. of Cardiology, Sri Jayadeva Institution of Cardiovascular Sciences. A detailed history, physical examination and all routine investigations along with serum albumin, fibrinogen, ECG & 2-D Echo were done for all the patients. Samples were drawn at admission, before angiography. All the patients underwent clinically indicated invasive coronary angiography. SYNTAX SCORE was calculated using an online SYNTAX SCORE calculator. A detailed history, physical examination and routine investigations including CBC, renal function test, liver function test, lipid profile, serum albumin, fibrinogen, and ECG were done for all the patients. Samples were drawn at admission, before angiography. A 2-D echocardiogram for assessment of LV function was performed on each patient before the procedure.

Statistical Analysis: All continuous values were summarized as Mean ± SD. Clinical and demographic characteristics of study groups were compared by means of the Student's t-test for continuous variables. Categorical variables were presented in percentages and compared using the $\chi 2$ statistics or Fisher exact test. A p-value < 0.05 was considered significant. All statistical tests were two-sided. Statistical analysis was performed using SPSS 23.0 version (IBM Corporation, USA)

Results

Overall, 237 patients were recruited into the study. Mean age of the patients was 57 years ranging from 31 to 80 years. Mean BMI was 24.47 kg/m2 (Table 1). Mean fibrinogen level was 397.97 mg/dl, the mean serum albumin level was 4.05 g/dl and the mean FAR was 101.07 mg/g. The mean value of FAR was taken as the reference value for the analysis below which it was considered as low FAR and above it was considered as high FAR. The mean CAG Syntax score was 22.02, suggesting an overall low complexity of coronary artery disease in study cohort.

Table 1: Distribution of studied patients based on baseline characteristics

	Mean	Median (IQR)	Minimum	Maximum
Age (Years)	57.00±10.44	57.00 (50.0-65.0)	31	80
Height (cm)	161.17±7.05	162.00 (157.0-165.0)	140	178
Weight (kg)	63.85±10.90	63.00 (56.0-70.0)	37.1	97.0
Body Mass Index (kg/m^2)	24.47±3.64	24.00 (21.9-26.6)	14.80	38.90
Pulse Rate (bpm)	85.41±48.05	80.0 (74.0-88.0)	60	146
Serum Albumin (g/dl)	4.05±0.47	4.05 (3.78-4.34)	1.430	6.444
Fibrinogen (mg/dl)	397.97±122.00	382.0 (314.0-480.0)	168	781
Ratio Fibrinogen/ Albumin (mg/g)	101.07±38.10	92.93 (74.12-121.53)	26.072	234.265
Total Cholesterol (mg/dl)	143.95±41.26	139.7 (113.95-170.0)	69.0	294.0
LDL Cholesterol (mg/dl)	87.39±32.55	81.0 (62.0-110.5)	33.20	206.00
HDL Cholesterol (mg/dl)	39.47±11.45	38.0 (32.0-45.5)	12.8	89.2
CAG -SYNTAX SCORE(SS)	22.02±8.80	23.0 (16.0-28.0)	3.0	38.5

Majority of study patients (81.4%) were male (Table 2). In terms of age, the highest percentage of patients (36.7%) were in the age group of 51-60 years followed by 22.4% in the age group of 41-50 years. Regarding the diagnosis, the majority of patients (41.4%) had stable coronary artery disease (CSA), while (35.4%) were diagnosed with ST-elevation myocardial infarction (STEMI). The remaining

patients were diagnosed with non-ST elevation myocardial infarction (NSTEMI) and unstable angina.

Table 2: Distribution of studied patients based on the demographic profile

Demographic Profile		Frequency (n-237)	Percentage
Sex	**Male**	193	81.4%
	Female	44	18.6%
Diagnosis	**Stable CAD**	98	41.4%
	Unstable Angina	5	2.1%
	Non-STEMI	50	21.1%
	STEMI	84	35.4%

Admitting diagnosis was ACS in 58.6% and stable CAD in remaining 41.4 percent (Table 3). Regarding the duration of symptoms in stable CAD, most patients (49.4%) had symptoms for 1 month to 1 year, followed by 33.8% who had symptoms for less than 1 month and 16.8% who had symptoms for more than 1 year. Among patients with ACS, the majority of patients (40.5%) presented within for 2 to 7 days of symptom onset, followed by 32.9% who had symptoms onset 7 days to 1 month back and 17.3% who had symptoms more than 1 month back. Only 9.3% presented within 48 hours from onset of symptoms.

Table 3: Distribution of studied patients based on ACS vs CSA, duration of stable CAD and ACS

		Frequency (n-237)	Percentage
ACS vs CSA	**ACS**	139	58.6%
	Stable CAD	98	41.4%
Duration of Stable CAD	**< 1 month**	80	33.8%
	1 month to 1 year	117	49.4%
	More than 1 year	40	16.8%
Duration of ACS	**Within 48 hrs**	22	9.3%
	48 hrs to 7 days	96	40.5%
	7 days to 1 month	78	32.9%
	More than 1 month	41	17.3%

ACS patients who presented within 7 days of onset of ACS were found to have a statistically significant higher proportion of elevated FAR values as compared to those presenting beyond 7 days.

Table 4: Correlation between FAR and CAG Syntax Score

FAR	CAG Syntax Score		p-value
	<23 (n=119)	**≥23 (n=118)**	
Low (n=136)	68 (57.1%)	68 (57.6%)	0.941
High (n=101)	51 (42.9%)	50 (42.45)	

No significant correlation was seen between the CAG Syntax score and serum albumin or fibrinogen levels (Table 5).

Table 5: Correlation of albumin and fibrinogen with Syntax Score

		CAG SYNTAX Score
Serum Albumin	**Pearson Correlation (r)**	-0.031
	P value	0.636
Fibrinogen	**Pearson Correlation (r)**	-0.017
	P value	0.797

Very few secondary outcome events were reported during the follow-up period of 6 months. Three suspected CV deaths (unwitnessed) occurred, 2 were having high FAR values. Test for statistical significance could not be applied as the events were too less in number. All the other events including no-reflow/slow flow, major bleeding, heart failure, rehospitalization and MACE (excluding CV deaths) were not noticed in both the FAR groups.

Discussion

Albumin is an essential protein in human plasma. It's been proposed that the serum albumin concentration is inversely related to the inflammatory and the haemostatic processes. Fibrinogen, produced by the liver, serves as an indicator of the procoagulant state and plays a role in inflammatory responses at various levels.

Therefore, both fibrinogen and the albumin are main markers of systemic inflammatory, and hemorheological alterations. The fibrinogen–albumin ratio (FAR), comprising these two entities, has been reported as a new inflammatory marker closely related to CAD progression and severity of CAD.[17]

In the present study we noted that out of the 237 patients, the majority (81.4%) were male, while the remaining 18.6% were female. Swaminathan CR & Prasath PA [15] in their study of the correlation between the Clinical Profile and Angiographic Severity of CAD in ST Elevation Myocardial Infarction and Non-ST Elevation Myocardial Infarction Patients, reported that 82.3% of patients were males and 17.7% were females. This exhibits a striking male predominance in coronary artery disease in Indian patients, which was also observed in the present study.

Karahan O et al [16] conducted a single-centre, observational study on relationship between FAR and the severity of CAD in STEMI cases and concluded that FAR was related significantly to SS in predicting the extent, and severity of CAD in STEMI cases.

Li M et al [17] conducted a single-centre, observational study on the relation of FAR to the severity of CAD and the long-term prognosis in non-ST elevation ACS cases and concluded that FAR was independently associated with the severity of CAD, and prognosis, helping to enhance risk stratification in the NSTE-ACS cases undergoing PCI.

Celebi S et al [18] conducted a single-centre, observational study on the association between FAR and CAD severity in stable CAD cases and concluded that the novel inflammatory index, FAR, was associated significantly with the severity of CAD among stable CAD cases.

Demir M et al [19] conducted a single-center, observational study of FAR predicting burden of CAD among NSTEMI patients and concluded that in the moderate-high Syntax score (SS) group FAR value is considerably higher than those with the low SS group.

Present study had representation of both ACS and stable CAD, 58.6% had ACS and 41.4 % had stable CAD. Whereas, Karahan O et al [16] studied only STEMI patients, Demir M et al [19] and Li M et al [17] studied NSTEMI-ACS patients, and Celebi S et al [18] studied only stable CAD patients.

In the present study, no statistically significant association was observed between FAR, and the Syntax Score($p>0.05$). This is unlike the studies done by Karahan O et al [16], Celebi S et al [18] and Demir M et al [19], which found that there was a significant correlation between FAR, and Syntax score ($p< 0.05$). Study by Li M et al [17] also found that FAR was related significantly to Gensini Score in predicting CAD severity ($p< 0.05$).

Present study is the only study done among Indian CAD patients. The observed difference from previously published studies could have arisen due to racial variation, demographic variations and heterogenous study population (comprising of both stable CAD and ACS patients) recruited in the present study.

Li M et al [17] conducted a single-centre, observational study on the relation of FAR to the severity of CAD and the long-term prognosis with non-ST elevation ACS cases. Their study showed that FAR was an independent predictor for the MACE at 30 days, 6 months, and 1 year after the DES implantation.

Present study did not find a correlation between FAR, and the short-term prognosis of CAD among the Indian population. Low event rates observed during the study duration in the present study as well as racial and demographic differences could have resulted in the lack of correlation between FAR and MACE in the present study.

Conclusion

In conclusion, FAR was not found to be associated with CAD severity among Indian patients with stable CAD and ACS in the present study. FAR was not found to be a predictor of short-term MACE in the study population

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