

Association of Fasting Blood Sugar to High-density Lipoprotein Ratio with Short Term Outcome in Patients of Acute Coronary Syndrome: A Cohort Study

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ABSTRACT

Introduction: Acute Coronary Syndrome (ACS), which includes Unstable Angina (UA) and Myocardial Infarction (MI) both ST-elevated and non-ST-elevated (STEMI and NSTEMI), is a critical condition with high morbidity and mortality, emphasising the need for early identification of prognostic markers. Although biomarkers like Fasting Blood Sugar (FBS) and High-Density Lipoprotein cholesterol (HDL-c) have been individually linked to Cardiovascular (CV) health, the combined FBS/HDL-c ratio's (F:H) potential as a prognostic marker for short-term outcomes in ACS patients is not well understood.

Aim: To investigate the association of F:H ratio Major Adverse Cardiovascular Events (MACE) and CV mortality within 30 days of discharge in ACS patients.

Materials and Methods: The present hospital-based analytical cohort study was conducted from June 2023 to May 2025 at the tertiary care teaching hospital, in Pondicherry, India. The study included 95 patients, of age >18 years and both genders, newly diagnosed with ACS. On admission, FBS and HDL-c levels were measured, and outcomes were evaluated 30-day post-

discharge. Analysis was done in Statistical Package for Social Sciences (SPSS) software (ver_24.0) and inferential statistics was done based on the normality of the variables and p-value <0.05 was considered statistically significant.

Results: Among 95 ACS patients, majority were males (70.5%), with the mean age of 59.89±13.31 years. About 64.2% had diabetes and the ACS types included NSTEMI (36.8%), UA (30.5%), and STEMI (32.6%). Mean FBS and HDL-c was 141.67±57.80 mg/dL and 38.69±12.96 mg/dL, and the F:H was 4.075±2.42. Within 30-day post-discharge, 24.2% experienced MACE, and 10.5% suffered CV death, with F:H significantly associated with MACE (p<0.001) and CV death (p 0.030). The diagnostic level was found to be at ≥3.26 by Receiver Operating Characteristics (ROC) curve and the sensitivity and negative predictive value was 73.91% and 83.78%, respectively. At ≥3.26 found to be statistically significant with MACE (p 0.019).

Conclusion: Elevated F:H strongly associate with adverse outcomes in ACS, suggesting their usefulness as a prognostic marker for targeted therapies, requiring further studies with larger populations.

Keywords: Blood glucose, Cholesterol, Major adverse cardiovascular events

INTRODUCTION

The ACS an umbrella term for disorders caused by abrupt, reduced blood flow to the heart, encompassing UA, NSTEMI, and STEMI [1]. It is a foremost global cause of morbidity and mortality, requiring prompt detection and appropriate treatment to improve patient outcomes [2,3]. Its pathogenesis often involves atherosclerotic plaques rupture and thrombus formation, blocking coronary arteries partially or completely [1,4]. Understanding its mechanisms and identifying prognostic markers are vital in early and accurate identification of high-risk patients is crucial for improving outcomes [4].

Biomarkers play a crucial role in diagnosing, risk stratification, and ACS treatment [5-7]. They support physicians in assessing the severity of the condition, forecasting outcomes, and tailoring treatment strategies [5,6,8]. In recent practice interest has been seen focused on metabolic and lipid biomarkers, including Fasting Blood Glucose (FBG) and HDL-c, due to their relationship to CV risk and its outcomes [9-11]. Incorporating these markers into clinical practice can enhance prognostic accuracy and enable tailored therapies [7].

FBG reflects the glycaemic status, with elevated levels linked to endothelial dysfunction, oxidative stress and inflammation, all contributing to the atherosclerosis progression [11-13]. Consequently, monitoring FBG levels in ACS patients is essential for comprehending individuals at heightened risk of adverse outcomes

and notifying effective glycaemic management strategies [11,12]. Similarly, HDL-c known for its protective CV effects complements FBG in assessing the risk [14-18]. Given the individual prognostic significance of both FBG and HDL-c in CV outcomes, combining these markers as ratio offers a more comprehensive evaluation of CV risk in ACS patients [9,10]. The F:H integrates the detrimental effects of hyperglycaemia with the protective benefits of HDL-c, potentially identifying high-risk patients even when individual markers appear normal [19].

Various studies suggest this ratio provides a valuable tool for identifying high-risk patients and predicting adverse outcomes in ACS patients [9,10,20]. Yet, there is insufficient evidence regarding the prognostic value of this ratio in predicting short-term adverse CV outcomes among these patients. Previous research [9,19,20] predominately focused on individual biomarkers in isolation, and there is lack of robust studies in evaluating the combined ratio as a comprehensive prognostic marker in ACS patients [10]. With this background, the objective of the study was to investigate the F:H with risk of developing MACE in patients with ACS and to find the association of the F:H with MACE and CV mortality in patients with ACS at 30-day post-discharge after admission.

MATERIALS AND METHODS

The present present hospital-based cohort study was conducted in the Department of General Medicine, at Mahatma Gandhi Medical College and Research Institute, a tertiary care teaching hospital in

Pondicherry, India for the period of two years (June 2023 to May 2025) after obtaining Institutional Human Ethics Committee (IHEC) approval (MGMCR/Res/01/2021/31/IHEC/81).

Sample size calculation Considering the prevalence of diabetes among ACS patients were 37.6% [21], with absolute precision of 10% and 5% as the nonresponse rate, the sample size was calculated as 95 (calculated using OpenEpi software ver. 3.01; Open-Source Epidemiologic Statistics for Public Health). Consecutive sampling technique was used to include the patients for the study until the desired sample size was achieved.

Inclusion criteria The included study participants were the newly diagnosed ACS patients (STEMI, NSTEMI, and UA) confirmed by Electrocardiography (ECG) and 2D Electrocardiogram (ECHO) over 18 years of both genders.

Exclusion criteria Patients with known history of CV disorders, dyslipidaemia patients who were on medication, liver disorders, cerebrovascular accident, pregnant and lactating mothers were excluded from the study.

Study Procedure

After obtaining the informed consent, data were collected using a preformed performa. The questionnaire included demographic details, lifestyle factors (e.g., alcohol and smoking), and prior medical history. Patients diagnosed with dyslipidaemia were taken when (Total Cholesterol (TC) >200 mg/dL; Low-Density Lipoprotein cholesterol (LDL-C) >130 mg/dL; HDL-c <40 mg/dL (men) and <50 mg/dL (women); Triglycerides (TGL) >150 mg/dL). Followed by laboratory investigations such as FBS and HDL-c levels were measured upon admission and assessed F:H. MACE was also assessed. The outcome of the study were the MACE and mortality at the end of 30-days.

STATISTICAL ANALYSIS

The data was entered in MS Excel (Ver_2007) software and analysis was carried out using SPSS (Version 24.0, developed by IBM Corp, Armonk, New York) software. Categorical variables were measured in terms of frequencies and percentages. Continuous variables were expressed as mean and Standard Deviation (SD) or median with Interquartile Range (IQR). Data were analysed based on the type of variables and the normal distribution between two groups. Independent t-test is done for parametric and Pearson's Chi-square test is done for non-parametric variables. The p-value <0.05 was considered as statistically significant.

RESULTS

The mean age of the study participants were 59.89±13.31 years. [Table/Fig-1] shows the sociodemographic, Co-morbidity and risk factors among the study participants. The outcomes of the study were projected in [Table/Fig-2], where 35 (36.8%) presented with NSTEMI and about 23 patients (24.2%) had MACE. A significant majority of 85 patients (89.5%) survived, whereas 10 patients (10.5%) succumbed to the condition at the end of 30-days follow-up. [Table/Fig-3] shows the clinical and laboratory investigations among the study participants.

Variables		Results
Age (in years) (mean±SD)		59.89±13.31
Gender	Male	67 (70.5)
	Female	28 (29.5)
Type 2 diabetes mellitus	Yes	61 (64.2)
	No	34 (35.8)
Systemic hypertension	Yes	53 (55.8)
	No	42 (44.2)

Dyslipidaemia	Yes	7 (7.4)
	No	88 (92.6)
Smoking	Yes	13 (13.7)
	No	82 (86.3)
Alcohol	Yes	19 (20.0)
	No	76 (80.0)

[Table/Fig-1]: Demographic details of the study participants (N=95). Numbers in brackets represents percentages. SD: Standard deviation

Outcome		n (%)
ACS diagnosis	NSTEMI	35 (36.8)
	STEMI	31 (32.6)
	UA	29 (30.5)
Death	Yes	10 (10.5)
	No	85 (89.5)
Outcome	MACE	23 (24.2)
	No MACE	72 (75.8)

[Table/Fig-2]: Outcome of the study among the participants (N=95). ACS: Acute coronary syndrome; NSTEMI: Non-ST segment elevation of Myocardial infarction; STEMI: ST segment elevation of myocardial infarction; UA: unstable angina; MACE: Major adverse cardiovascular events

Variables	Mean±SD
Vitals	
Systolic Blood Pressure (SBP) (mmHg)	123.68±22.26
Diastolic Blood Pressure (DBP) (mmHg)	75.68±12.60
Laboratory investigations	
Fasting Blood Sugar (FBS) (mg/dL)	141.67±57.80
High Density Lipoprotein Cholesterol (HDL-c) (mg/dL)	38.69±12.96
FBS: HDL-c	4.071±2.42
Haemoglobin (Hb) (mg/dL)	12.12±2.46

[Table/Fig-3]: Clinical and laboratory variables among the patients with ACS (N=95). SD: Standard deviation

[Table/Fig-4] shows the association of co-morbidity, risk factors and laboratory findings with the outcomes of the study. Considering the MACE events, patients with Type 2 Diabetes Mellitus (T2DM) had 82.6% of MACE during the follow-up period and were statistically significant (χ^2 4.470; 95% Confidence Interval (CI) 0.091, 0.955; p-value 0.034). While for the other Co-morbidity and risk factors were not statistically significant with the MACE events. As for the mortality at 30-day follow-up, none of the risk factors and Co-morbidity were not statistically significant. The F:H were strongly associated with both MACE and 30-day mortality and statistically significant (p<0.001 and 0.030, respectively) when compared to the patients without MACE and no death.

The ROC curve [Table/Fig-5] illustrates that the F:H has a certain level of effectiveness in discriminating between patients with and without MACE at the level of 3.26 value, where its sensitivity and specificity was 73.91% (95% CI: 51.59-89.77%) and 43.06% (95% CI: 31.43-55.27%), respectively. The negative predictive value was 83.78% with 95% CI was 71.19 to 91.53% in predicting the false results [Table/Fig-6].

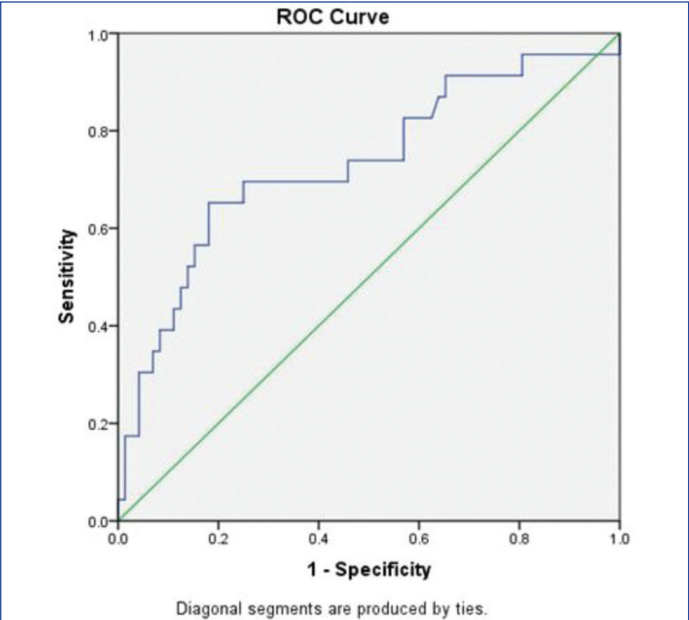
The association of F:H with the outcomes among the study participants shown that patients with ≥ 3.26 F:H had higher incidence of MACE (34%) compared to patients with ≤ 3.26 (66%), and statistically significant (p 0.019). As for the mortality at 30-day follow-up, were not statistically significant [Table/Fig-7].

DISCUSSION

The present cohort study, we assessed the association of F:H with risk of developing MACE in patients with ACS and to correlate it with CV mortality at 30-day post-discharge after admission. It was found that patients with T2DM had higher incidence of MACE when

Variables	MACE			Mortality at 30-day-follow-up		
	No	Yes	p-value	No	Yes	p-value
Co-morbidity and risk factors						
Type 2 diabetes mellitus						
Yes	42 (58.3)	19 (82.6)	0.034 ^a	54 (63.5)	7 (70.0)	0.686 ^a
No	30 (41.7)	4 (17.4)		31 (36.5)	3 (30.0)	
Systemic hypertension						
Yes	40 (55.6)	13 (56.5)	0.935 ^a	46 (54.1)	7 (70.0)	0.339 ^a
No	32 (44.4)	10 (43.5)		39 (45.9)	3 (30.0)	
Smoking						
Yes	11 (15.3)	2 (8.7)	0.424 ^a	12 (14.1)	1 (10.0)	0.720 ^a
No	61 (84.7)	21 (91.3)		73 (85.9)	9 (90.0)	
Alcohol						
Yes	14 (19.4)	5 (21.7)	0.811 ^a	18 (21.2)	1 (10.0)	0.403 ^a
No	58 (80.6)	18 (78.3)		67 (78.8)	9 (90.0)	
Dyslipidaemia						
Yes	5 (6.9)	2 (8.7)	0.780 ^a	7 (8.2)	0 (0)	0.346 ^a
No	67 (93.1)	21 (91.3)		78 (91.8)	10 (100.0)	
ACS types						
STEMI	10 (22.2)	21 (42.0)	0.103 ^a	29 (34.1)	2 (20.0)	0.275 ^a
NSTEMI	18 (40.0)	17 (34.0)		29 (34.1)	6 (60.0)	
UA	17 (37.8)	12 (24.0)		27 (31.8)	2 (20.0)	
Laboratory findings						
FBS (mg/dL)	131.31±48.77	174.13±71.74	0.002 ^b	138.65±53.12	167.40±87.94	0.138 ^b
HDL (mg/dL)	39.44±11.32	36.35±17.21	0.321 ^b	38.42±11.39	41.00±23.15	0.555 ^b
FBS:HDL-c	3.54±1.71	5.73±3.44	<0.001 ^b	3.88±1.99	5.64±4.60	0.030 ^b
Hb (mg/dL)	12.00±2.27	12.48±3.02	0.416 ^b	12.01±2.48	13.05±2.18	0.209 ^b

[Table/Fig-4]: Association of Co-morbidity, risk factors and laboratory findings with the outcomes among the study participants (N=95).
*Pearson Chi-square test; †Independent t-test was used. p-value <0.05 were statistically significant and indicated in boldface. Numbers indicated in brackets were percentages. SD: Standard deviation; ACS: Acute coronary syndrome; STEMI: ST elevated myocardial infarction; NSTEMI: Non-ST elevated myocardial infarction; UA: Unstable angina; FBS: Fasting blood sugar; HDL-c: high-density lipoprotein cholesterol; Hb: Haemoglobin; MACE: Major adverse cardiovascular events



[Table/Fig-5]: ROC Curve analysis for F:H in predicting MACE.

Diagnostic characteristics	Value	95% CI
Sensitivity	73.91%	51.59 to 89.77%
Specificity	43.06%	31.43 to 55.27%
Positive predictive value	29.31%	23.23 to 36.23%
Negative predictive value	83.78%	71.19 to 91.53%
Accuracy	50.53%	40.07 to 60.95%

[Table/Fig-6]: Diagnostic characteristics of Fasting Blood Sugar (FBS) to High-Density Lipoprotein (FBS/HDL) Ratio at 3.26.

Variables	FBS/HDL category		Total n (%)	p-value
	≤3.25	≥3.26		
MACE				
MACE	6 (13.3)	17 (34.0)	23 (24.2)	0.019 ^a
No MACE	39 (86.7)	33 (66.0)	72 (75.8)	
Mortality at 30 days				
Yes	5 (11.1)	5 (10.0)	10 (10.5)	0.860
No	40 (88.9)	45 (90.0)	85 (89.5)	

[Table/Fig-7]: Association of Fasting Blood Sugar (FBS) to High-Density Lipoprotein (FBS/HDL-c) Ratio and outcomes among the study participants (N=95).
*Pearson Chi-square test was used. p-value <0.05 were statistically significant and indicated in boldface

compared to other co-morbidities and risk factors, and statistically significant (p 0.03). The F:H were strongly associated with both MACE and 30-day mortality and statistically significant (p<0.001 and 0.030, respectively). ROC curve showed that F:H has a certain level of effectiveness in discriminating between patients with and without MACE at the level of 3.26 value, where its sensitivity and specificity was 73.91% and 43.06%, respectively. The negative predictive value was 83.78%. The association of F:H with the outcomes among the study participants shown that patients with ≥3.26 F:H had higher incidence of MACE compared to patients with ≤3.26 and were statistically significant p=0.019.

Studies indicates that elevated FBG are associated with worse outcomes in patients with ACS. Study done by Cid-Álvarez B et al., indicated that FBG were the significant predictor of mortality in non-diabetic ACS patients [12]. Similarly, another study done by Buturlin K et al., resulted that improving plasma glucose levels are associated with the increased one-year mortality in non-diabetic ACS patients

[22]. Similarly, study done by Ma L et al., showed that a positive linear association with glucose level and 30-day MACE especially in STEMI patients ($p < 0.03$) was similar to our study findings [23]. Thus, elevated glucose levels impair the CV system and increases the MACE among the ACS patients. Though HDL-c which is cardioprotective factor plays a major role in ACS patients, which had anti-inflammatory, antioxidant, and anti-thrombotic properties [24,25]. Framingham study by Castelli WP et al., showed that higher HDL-c level is associated with reduced coronary events in both genders aged 49 years and older, where the HDL-c present $\geq 80^{\text{th}}$ percentile had half the risk when compared to patients in $< 20^{\text{th}}$ percentile, that underscores its protective role [26]. Moreover, reduced HDL-c was associated with worse outcomes, with increased mortality rates, which was studied by Ishida M et al., [18].

Combining FBG and HDL-c markers which had individual prognostic significance into a single ratio could offer a more accurate assessment of CV risk in ACS patients, integrating the negative effects of hyperglycaemia with the protective benefits of HDL-c [9,10]. The major advantages of F:H includes, at first, it provides a more sophisticated risk assessment by consideration both excessive glucose levels and low HDL-c levels, both of which are independently associated with poor CV outcomes, where it helps to identify people at higher risk of adverse outcomes despite having generally normal levels of FBG or HDL-c when viewed separately. Second, the F:H may improve risk categorisation and allow for more personalised treatment options. Finally, F:H is relatively easy to obtain from routine blood test, making it a practical and cost-effective tool for clinical settings [14,24].

The FBS to HDL-c cholesterol (F:H) ratio has been identified as a major predictor of CV events in a variety of investigations. In our study, both MACE and CV mortality at 30-day follow-up showed statistically significant ($p < 0.001$ and 0.030 , respectively) implying that F:H emerged as a critical marker for the adverse outcomes, emphasising its potential utility in risk stratification and prognosis in ACS patients. This is in consistent with prior research, done by Deng S et al., where greater F:H ratio was associated with an increased risk of MACE and CV death in ACS patients when the ratio at the lower quartiles [10]. Another study by Guo QQ et al., done among 6645 non-diabetic patients shown that all-cause and CV mortality increased in patients with higher F:H group (Hazard Ratio (HR) 1.284), which indicates that F:H as an independent prognostic factor for MACE in ACS patients [27].

In the current study it was found that a greater F:H (≥ 3.26) was significantly related with an elevated risk of MACE and were statistically significant, yet for the CV mortality within 30-day after discharge were not significant statistically in patients with ACS. The current study findings were similar to the study done by Deng S et al., where at the threshold values of > 3 and more had an increased risk for MACE and CV death in patients with ACS [10]. This is in also consistent with the study done by Guo QQ et al., where the survival analysis suggested that F:H tend to have the increased accumulated risk for ACS patients [27]. All these indicates that F:H might be a novel biomarker for the risk stratification for the clinical outcomes in patients with ACS.

There are a few strengths and limitations of the study to be worth mentioning. The strength of the study includes that this is first study in Pondicherry to assess the F:H as the predictive factor for ACS diagnosis. The consistency of our findings with existing literature reinforces the importance of comprehensive metabolic control in ACS patients. Current clinical guidelines, such as those from the American Heart Association (AHA) and the European Society of Cardiology (ESC), emphasise the management of blood glucose levels and lipid profiles in patients with CV diseases. The current study also supports these guidelines by highlighting the predictive value of the F:H, suggesting that it could be used as an additional marker for risk stratification in ACS patients.

The clinical implications of our findings suggest that: (i) The F:H should be incorporated into risk stratification tools for ACS patients to identify those at higher risk of adverse outcomes; (ii) Patients with a high F:H might benefit from personalised treatment plans that include intensive lifestyle interventions, pharmacotherapy aimed at improving both glucose and lipid profiles, and possibly newer therapeutic agents targeting both metabolic pathways; (iii) Enhanced monitoring during hospitalisation and closer follow-up post-discharge for patients with elevated F:H can help mitigate the risk of MACE and mortality.

Limitation(s)

One of the major limitations was that it was a hospital-based study where the generalisability of the result was not possible. Finally, the duration of the follow-up was shorter (30-day) to assess the MACE, where the longer-term outcomes were unable to assess.

CONCLUSION(S)

The current study demonstrated that an elevated F:H is significantly predictive of short-term adverse CV outcomes in patients with ACS. Specifically, an F:H ratio ≥ 3.26 effectively identifies individuals at higher risk of MACE within 30 days post-discharge. Furthermore, the presence of T2DM notably increases the risk of these adverse events, underscoring the importance of rigorous metabolic control in ACS management. Compared to assessing FBS and HDL-c individually, the combined ratio provides superior prognostic value, allowing for improved patient risk stratification. Hence, the study advocates incorporating the F:H ratio into clinical practice to facilitate targeted therapeutic interventions and enhance personalised patient care.

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Authors' contribution: VR, SS- Conceptualisation; VR, SS, KSC- Methodology; VR, DM- Software; SS, KSC- Validation; DM- Formal Analysis; DM- Investigation; VR, DM- Resources; VR- Data Curation; DM- Writing – Original Draft Preparation; VR, SS- Writing – Review and Editing; KSC- Visualisation, Supervision; VR, SS- Project Administration.

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