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Study of clinical profile of patients with acute coronary syndrome and the correlation of serum fibrinogen and grace score as a prognostic marker for predicting 3 month mortality in those patients

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ABSTRACT

Introduction. Acute coronary syndrome (ACS), encompassing unstable angina, non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI), is a major global health concern due to its high morbidity and mortality. Research highlights a link between ACS and elevated acute phase reactants like C-reactive protein, emphasizing the role of inflammation and atherosclerosis. Serum Fibrinogen, crucial in thrombus formation and an inflammatory marker, is significant in the coagulation process. This study investigates the predictive value of serum fibrinogen levels and the GRACE score for 3-month mortality in ACS patients.

Aim. To examine the clinical profile of ACS patients and evaluate serum fibrinogen and GRACE score as prognostic markers for 3-month mortality.

Methodology. A prospective observational study was conducted on 50 patients diagnosed with ACS at Saveetha Medical College Hospital. The study included adults over 18 with ACS, excluding those with severe comorbid conditions like end-stage liver disease or malignancy. Serum fibrinogen levels were measured at presentation and at 3 months using an automated coagulation analyzer. GRACE scores were calculated, and clinical assessments including ECG, cardiac markers, and ECHO were conducted. Data analysis involved IBM SPSS Statistics, utilizing descriptive statistics, t-tests, ANOVA, and Pearson's Correlation.

Results. The study group had diverse demographics and a high prevalence of cardiovascular symptoms and comorbidities. The clinical profile of ACS showed a higher incidence of STEMI. Serum fibrinogen levels varied significantly across different Killip classes at presentation and at 3 months, with the highest levels in the more severe classes. Higher serum fibrinogen was linked to recurrent heart failure admissions and higher KILIPS class. However, there was no significant difference in fibrinogen levels between patients with and without interventions. The GRACE

score was higher in STEMI patients, those with LV dysfunction, and correlated with higher serum fibrinogen. Lower FACIT F scores, indicating higher fatigue, were associated with higher fibrinogen levels and readmissions for heart failure.

Conclusion. Higher serum fibrinogen levels and GRACE scores at presentation and at three months are indicators of severe myocardial infarction, increased heart failure readmission rates, and greater fatigue in ACS patients. These markers are valuable for evaluating morbidity in ACS and can aid in enhancing patient management strategies.

Keywords: Acute Coronary Syndrome, Serum Fibrinogen , GRACE score, TIMI score

INTRODUCTION:

Acute coronary syndrome is the collection of clinical indicators such as unstable angina, non-ST-segment elevation myocardial infarction, and ST-segment elevation myocardial infarction which stands as a leading cause of global morbidity and mortality [1]. The severity and prevalence of cardiovascular disease vary significantly due to a multitude of risk factors. Research suggests that acute coronary syndrome is associated with elevated levels of acute phase reactants like C-reactive protein, underscoring the established connection between inflammation and atherosclerosis [2]. Serum Fibrinogen, a pivotal component in thrombus formation and a recognized inflammatory marker, contributes significantly to the coagulation process [3].

Inflammation triggered by myocardial infarction serves a dual role, both promoting healing and inducing scarring. Reperfusion-induced myocardial infarcts provoke an intensified inflammatory response, which has shown correlations with favorable cardiac outcomes [4]. Mechanisms such as complement activation, free radical generation, and cytokine cascades contribute to myocardial cell necrosis. Ischemic myocardium releases IL-8 and C5a, attracting neutrophils that, while causing cytotoxicity through proteolytic enzyme release, also aid in healing. Monocyte chemoattractant protein (MCP-1) induction at the infarction site regulates mononuclear cell recruitment, fostering angiogenesis and fibroblast accumulation crucial for tissue repair. Cytokine production, including interleukin-10, serves to modulate the inflammatory response, potentially reducing myocardial injury. Ventricular remodeling, a pivotal aspect of post-infarction healing, involves the regulation of extracellular matrix deposition by matrix metalloproteinases (MMPs) and their inhibitors. Inflammatory mediators can also induce the recruitment of primitive stem cells, contributing to limited myocardial regeneration [5].

Understanding the intricate molecular and cellular processes involved in myocardial infarct healing is paramount for developing targeted therapies to enhance cardiac repair. Several studies have noted elevated fibrinogen levels in acute coronary syndrome, prompting further investigation into its potential as a prognostic marker [6]. Various risk indicators identified through randomized controlled trials have been integrated into scoring systems like the TIMI, [7] PURSUIT, [8] and GRACE scores, aiding clinicians in risk stratification and patient management. The GRACE score, incorporating clinical parameters from the Global Registry of Acute Coronary Events study, offers

robust prediction capabilities for in-hospital and 6-month mortality in acute coronary syndrome patients, with particular emphasis on the critical first three months post-event. This study aims to assess whether Serum Fibrinogen levels and the GRACE score can effectively predict 3-month mortality in individuals presenting with acute coronary syndrome [9].

AIM:

To study the clinical profile of patients with acute coronary syndrome and to correlate serum fibrinogen and GRACE score as a prognostic marker for predicting 3-month mortality in those patients.

OBJECTIVES:

- To determine the levels of serum fibrinogen in patients with Acute Coronary Syndrome.
- To determine the Clinical profile of patients with Acute Coronary syndrome
- To calculate the predictive value of elevated serum fibrinogen levels in predicting 3-month mortality in patients with acute coronary syndrome
- To use the GRACE score for assessing mortality in patients with acute coronary syndrome
- To use the FACIT F scale to assess morbidity in patients with acute coronary syndrome

METHODOLOGY:

Study Design: This study adopts a Prospective Observational design with a sample size of 50 patients. The study population comprises individuals diagnosed with Acute Coronary Syndrome, encompassing ST-elevation myocardial infarction, non-ST elevation myocardial infarction, and unstable angina. The sampling technique employed is a non-probability convenience method. The study duration spans 12 months.

Inclusion Criteria:

All patients aged above 18 years of either sex admitted with a diagnosis of acute coronary syndrome, including acute ST elevation myocardial infarction, non-ST elevation myocardial infarction, and unstable angina, at Saveetha Medical College Hospital.

Exclusion Criteria:

- Patients with end-stage liver disease
- Patients with severe malnutrition
- Patients with other chronic infections
- Patients with malignancy
- Patients undergoing large-volume blood transfusion
- Patients with clotting disorders

Study Procedure:

Prospective observational study was carried out on 50 patients aged above 18 years diagnosed with Acute Coronary Syndrome, including acute ST-elevation myocardial infarction, non-ST elevation myocardial infarction, and unstable angina. Patients were recruited from the General Medicine OPD, Cardiology OPD, and Emergency Medicine OPD at Saveetha Medical College & Hospitals over a period of 12 months, commencing from the date of ethical clearance. Serum Fibrinogen levels were assessed upon presentation using an automated coagulation analyzer, and GRACE scores were calculated. Additionally, ECG, cardiac marker testing (including Troponin I and CKMB), and ECHO were conducted for all patients. Coronary angiography was performed, and the necessity for intervention via PTCI/CABG was noted. Patients were followed up for 3 months to monitor hospitalization for heart failure, with a repeat test for Fibrinogen conducted at this time.

Data Analysis:

The acquired data were analyzed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp, Armonk, NY). Descriptive statistics including frequency analysis, percentage analysis, mean, and standard deviation were utilized for categorical and continuous variables, respectively. The Independent sample t-test was employed to ascertain significant differences between bivariate samples in Independent groups. Multivariate analysis was conducted using one-way ANOVA with Tukey's post-hoc test. Pearson's Correlation was used to explore the correlation between variables. A significance level of <0.05 was considered in all statistical analyses.

Results:

The table presents baseline characteristics of 50 study participants. The average age is 55.05 years with a standard deviation of 10.85 years, showcasing a diverse age range: 8% are between 31-40 years, 28% between 41-50 years, 34% between 51-60 years, 20% between 61-70 years, and 10% are over 70 years old. In terms of gender, 62% are male and 38% are female. The majority of participants, 96%, report chest pain, followed by palpitation (58%), sweating (48%), giddiness (12%), dyspnea (40%), and other symptoms (16%). Co-morbidities are also notable, with 64% having Type 2 Diabetes Mellitus and 38% suffering from Hypertension. Lifestyle factors show that 20% of the participants are smokers, 16% consume alcohol, and the majority do not engage in these habits. Clinically, 54% exhibit raised Jugular Venous Pressure, 22% have pulmonary edema, 12% experience cardiogenic shock, and 80% show elevated cardiac biomarkers (Trop-I, CK-MB). This profile suggests a group significantly affected by symptoms and signs related to cardiovascular issues, possibly acute coronary syndrome.

Table 1: Baseline characteristics of study participants

Parameter	Total no of participants n=50 (%)
Age in years (mean ± SD)	55.05 ± 10.85

Age in years	
31-40	4 (8)
41-50	14 (28)
51-60	17 (34)
61-70	10 (20)
>70	5 (10)
Gender	
Male	31 (62)
Female	19 (38)
Symptoms	
Chest pain	48 (96)
Palpitation	29 (58)
Sweating	24 (48)
Giddiness	6 (12)
Dyspnea	20 (40)
Others	8 (16)
Co-morbidities	
Type 2 DM	32 (64)
HTN	19 (38)
Smoking	
Present	10 (20)
Absent	40 (80)
Alcohol	
Present	8 (16)
Absent	42 (84)
Signs	
Raised JVP	27 (52)
Pulmonary edema	11 (22)
Cardiogenic shock	6 (12)
Elevated Trop-I, CK-MB	40 (80)

Table 2 outlines the clinical profile of acute coronary syndrome (ACS) among 50 participants. The types of ACS observed include 26% with Non-ST-segment Elevation Myocardial Infarction (NSTEMI), 56% with ST-segment Elevation Myocardial Infarction (STEMI), and 18% presenting with unstable angina. When assessing left ventricular function via ECHO, 38% had normal function, 44% exhibited mild dysfunction, 16% moderate, and 2% severe. In terms of treatment, thrombolytic agents were used in 34% of cases, with Streptokinase administered to 32% and Tenecteplase to 2%. Various interventions were employed, including Coronary Artery Bypass Grafting (CABG) in 16% and Percutaneous Transluminal Coronary Intervention (PTCI) to various

arteries, most commonly to the Right Coronary Artery (RCA) in 26%. Notably, 28% did not receive any of these interventions. Finally, a significant proportion, 52%, were hospitalized for heart failure, indicating the severity of the conditions within this group. This profile reflects a diverse range of ACS types and severities, alongside varied treatment approaches.

Table 2: Clinical profile of ACS in the study participants

Parameter	**Total no of participants n=50 (%)**
Type of ACS	
NSTEMI	13 (26)
STEMI	28 (56)
Unstable angina	9 (18)
ECHO LV function	
Normal	19 (38)
Mild	22 (44)
Moderate	8 (16)
Severe	1 (2)
Thrombolytic agent used	
Streptokinase	16 (32)
Tenecteplase	1 (2)
Intervention	
CABG	8 (16)
PTCI to LAD	10 (20)
PTCI to LAD, OMA	1 (2)
PTCI to LAD, RCA	1 (2)
PTCI to LCX	2 (4)
PTCI to RCA	13 (26)
PTCI to RCX and LCX	1 (2)
None	14 (28)
Hospitalisation for Heart failure	
Yes	26 (52)
No	24 (48)

Figures 1 and 2 show the comparison between serum fibrinogen levels at presentation and at 3 months post-presentation across four Killip classes (I, II, III, IV).

At presentation:

Killip class I (20 participants) had an average serum fibrinogen level of 287.9 mg/dL with a standard deviation (SD) of 82.8. Killip class II (16 participants) showed a mean level of 382.3

mg/dL (SD 77.5). Killip class III (9 participants) had a higher average of 457.9 mg/dL (SD 32.6). Killip class IV (5 participants) had the highest average fibrinogen level of 479.8 mg/dL (SD 47.4).

At 3 months:

Killip class I's level decreased to an average of 261.2 mg/dL (SD 66.7). Killip class II's level decreased to 325.1 mg/dL (SD 71.1). Killip class III had an average level of 400.8 mg/dL (SD 44.1). Killip class IV had a slight decrease to an average of 430.6 mg/dL (SD 32.2). The F-values (7.194 for presentation and 16.069 for 3 months) with a p-value of 0.0005 in both cases indicate a statistically significant difference in serum fibrinogen levels between the groups at both time points. The double asterisks (**) suggest a high level of statistical significance. This data implies that there are notable differences in serum fibrinogen levels among the groups, both at the time of presentation and after 3 months, with the levels generally being higher in Groups III and IV compared to Groups I and II.

Figure 1: Comparison of baseline Serum fibrinogen using Killip Class

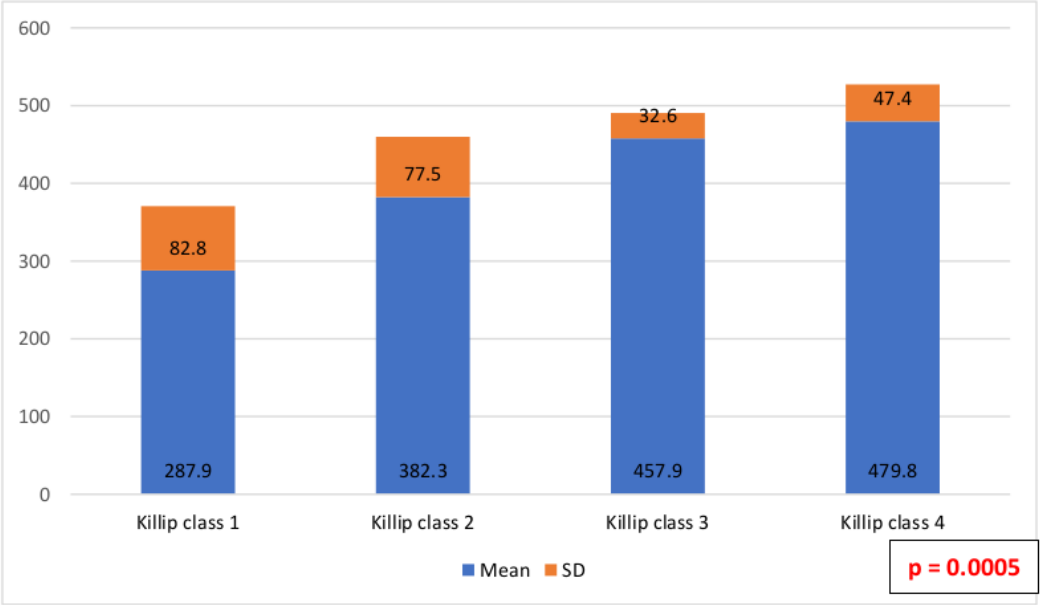


Figure 2: Comparison of 3-month Serum fibrinogen using Killip Class

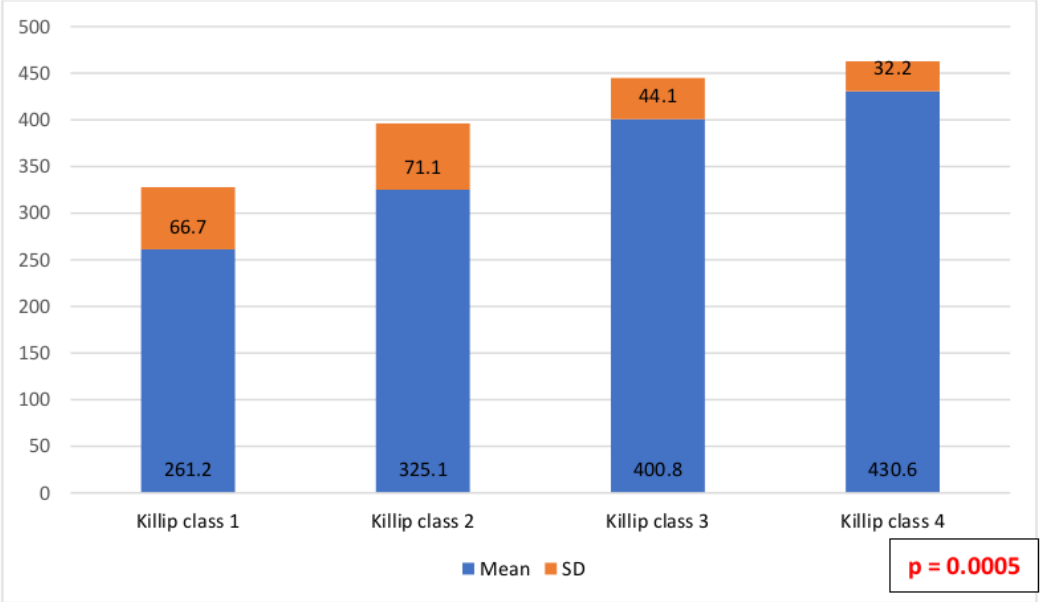


Figure 3 shows a comparison of Serum fibrinogen at presentation and 3 Months with hospitalization for heart failure within 3 months by Independent sample t-test. It was found that patients who had high serum fibrinogen levels had recurrent admissions for heart failure and correlation of which was of high statistical significance (at presentation t-value=8.944, p-value=0.0005<0.01 at 3 months t-value=9.205, p-value=0.0005<0.01)

Figure 3: Comparison of Serum fibrinogen in patients with heart failure hospitalization

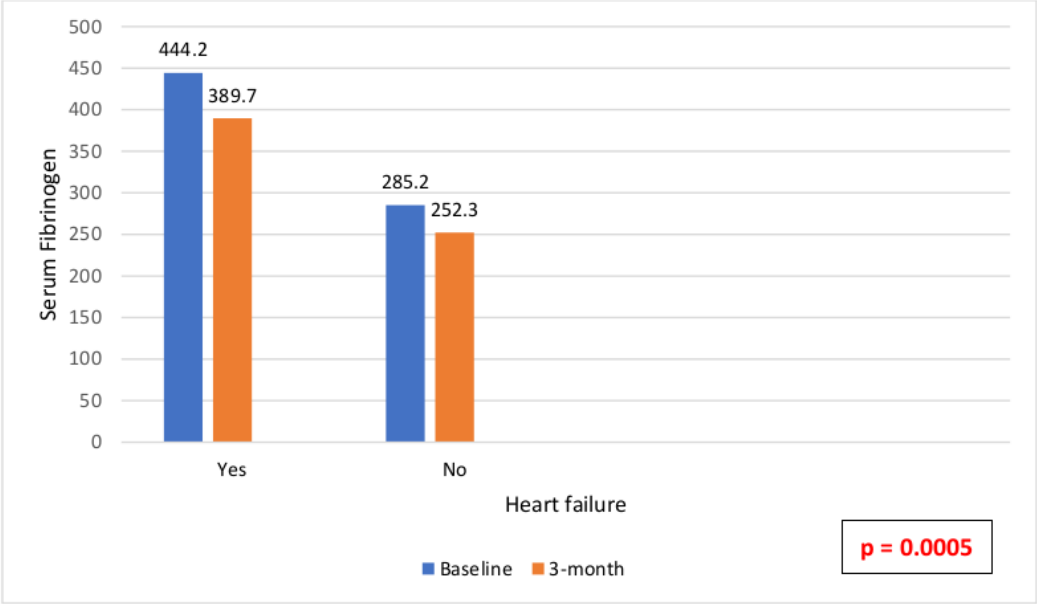


Figure 4 shows a comparison of Serum fibrinogen at presentation and 3 Months in patients with intervention by PTCI/CABG and patients with no intervention by PTCI/CABG by Independent sample t-test and it was found that patients who underwent i[illegible]rmation with PTCI/CABG had increased fibrinogen levels at presentation and 3 months but there is no statistically significant difference (p value>0.05)

Figure 4: Comparison of Serum fibrinogen in patients with intervention by PTCI/CABG

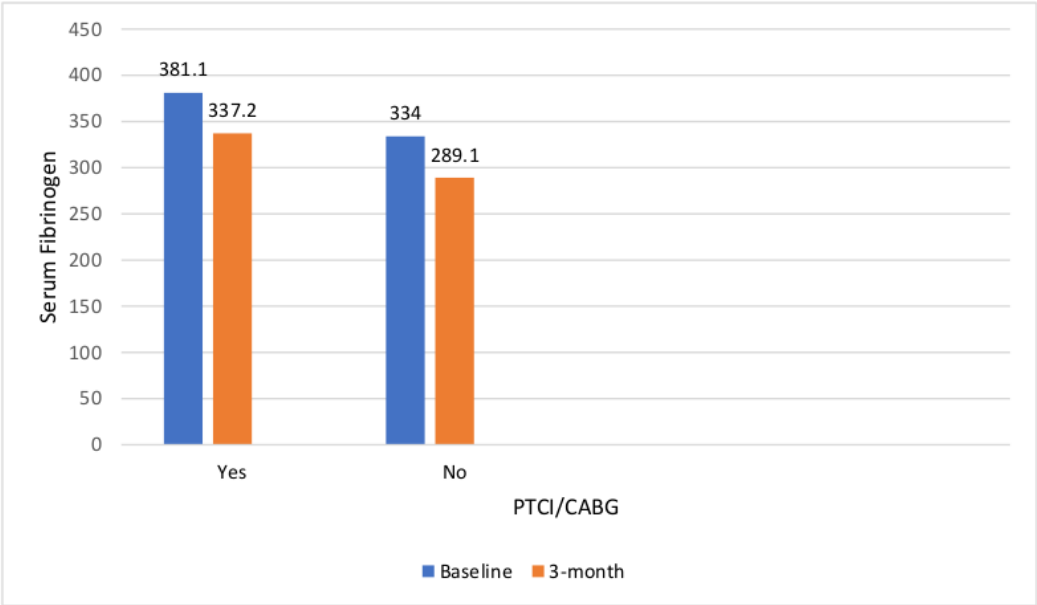


Figure 5 shows the comparison of GRACE score at presentation with hospitalization for heart failure within 3 months (t-value=8.312, p-value=0.0005). It was found that the patients with higher GRACE scores at admission were associated with an increased incidence of admissions for heart failure within 3 months.

Figure 5: Grace score at presentation with hospitalization for heart failure within 3 months

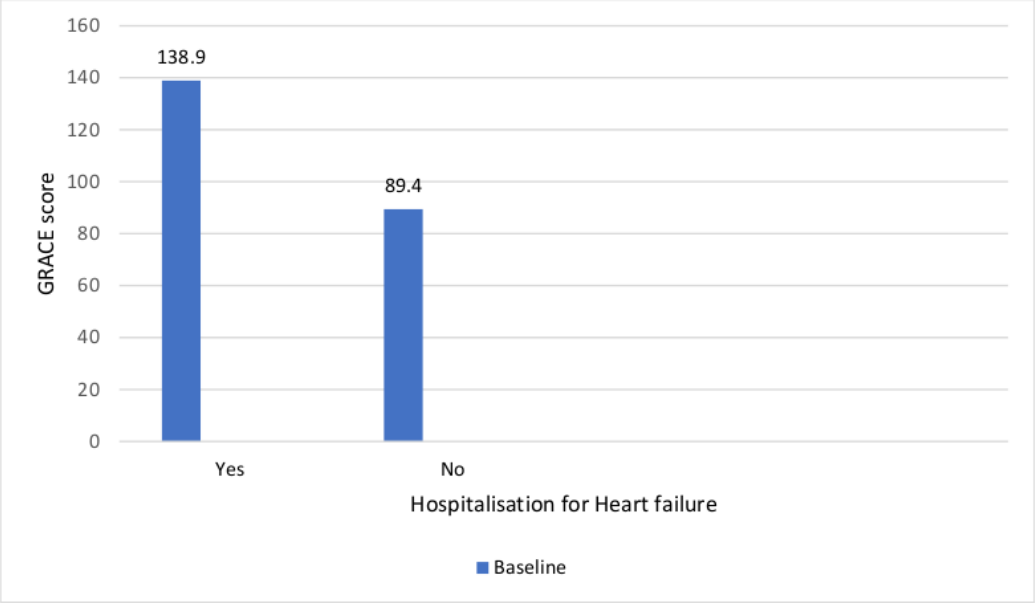
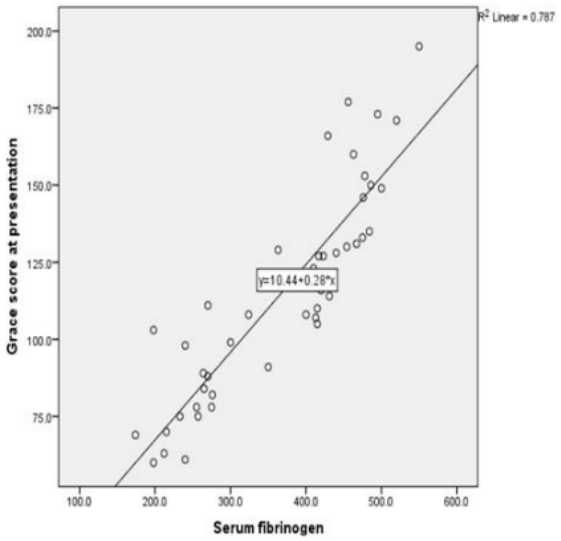
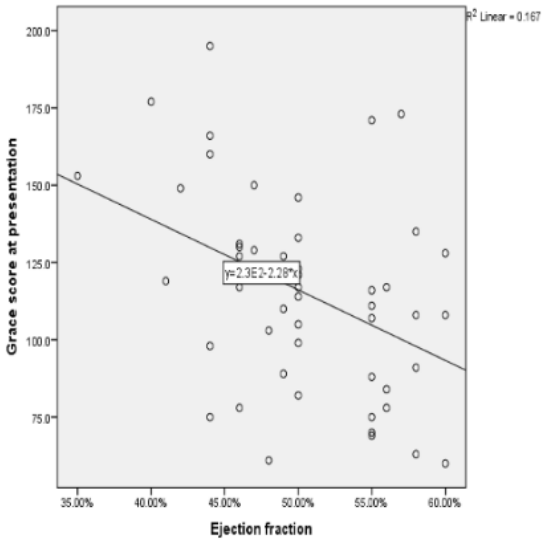


Figure 6 (a,b,c) shows a scatter plot of GRACE score Serum fibrinogen correlation at presentation (r-value=0.887, p-value=0.0005) which shows a higher statistically positive correlation, Ejection fraction correlation with GRACE score at presentation (r-value=-0.408, p value=0.003) which shows a higher statistically negative correlation and Facit F Scale score correlation with GRACE score at presentation (r-value=−0.957, p-value=0.0005) which shows a higher statistically negative correlation.

Figure 6: Correlation of GRACE score with (a) serum fibrinogen, (b) Ejection fraction, (c) Facit F scale score


R² Linear = 0.787
Grace score at presentation
Serum fibrinogen
y=10.44+0.28*x

(a)


R² Linear = 0.167
Grace score at presentation
Ejection fraction
y=2.3E2-2.28*x

(b)

(c)

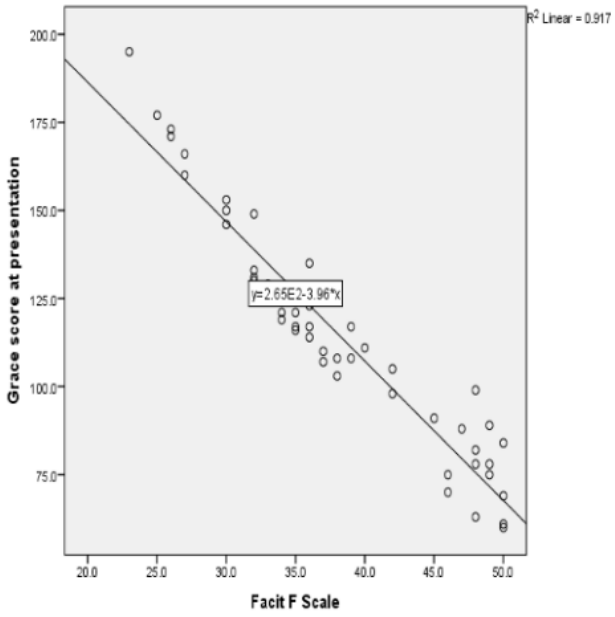
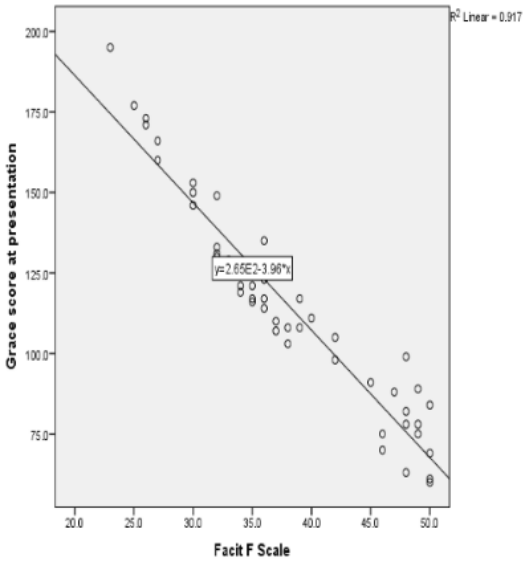
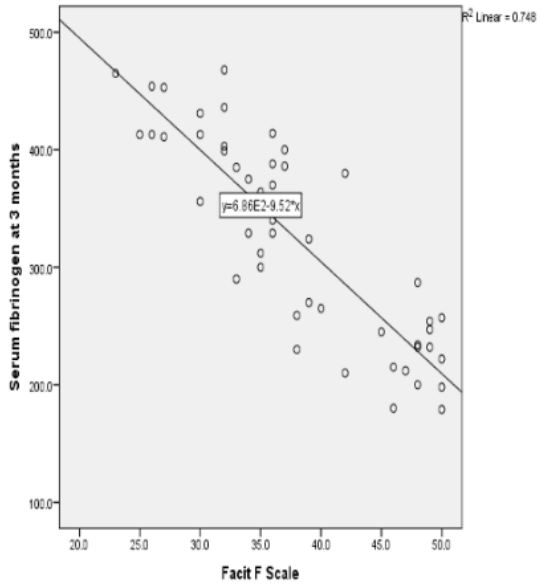

R² Linear = 0.917
Grace score at presentation
Facit F Scale
y=2.65E2-3.96*x

Figure 7 (a) and (b) shows the Facit F Scale score correlation with Serum fibrinogen at presentation (r-value=−0.875, p value=0.0005 and at 3 months (r-value=-0.865, p-value=0.0005). The study showed a high statistically negative correlation between Facit F Scale score and serum fibrinogen.

Figure 7: Correlation of Facit F scale score with (a) serum fibrinogen at baseline, (b) serum fibrinogen at 3-month



(a)



(b)

DISCUSSION:

The study's results encompass various aspects of acute coronary syndrome (ACS) among 50 participants. The baseline characteristics reveal a mean age of 55.05 years with a standard

deviation of 10.85 years, a male predominance (62%), and a high prevalence of chest pain (96%). Notably, a significant percentage of participants have Type 2 Diabetes Mellitus (64%) and Hypertension (38%), alongside lifestyle factors such as smoking (20%) and alcohol consumption (16%). Clinically, 54% exhibit raised Jugular Venous Pressure, and 80% show elevated cardiac biomarkers, highlighting the severity of cardiovascular issues in the cohort. The clinical profile of ACS varied, with 56% presenting with STEMI and 26% with NSTEMI. The majority had either normal or mildly dysfunctional left ventricular function, but a significant proportion (52%) were hospitalized for heart failure. Various interventions, including Coronary Artery Bypass Grafting and Percutaneous Transluminal Coronary Intervention, were used, but 28% received no such interventions.

The study's crucial findings pertain to serum fibrinogen levels. Notably, fibrinogen levels at presentation and after 3 months significantly differed across the four Killip classes, with the highest levels observed in classes III and IV. This finding suggests a potential link between higher fibrinogen levels and more severe cardiac conditions. Additionally, a significant correlation was found between high serum fibrinogen levels and recurrent admissions for heart failure. However, no statistically significant difference in fibrinogen levels was noted between patients who underwent interventions and those who did not. The GRACE score's association with heart failure hospitalization is another critical finding. Higher GRACE scores at admission correlated with increased heart failure admissions within 3 months, emphasizing the score's prognostic value. The study also observed correlations between GRACE score, serum fibrinogen, ejection fraction, and the Facit F Scale score, suggesting these factors are interconnected in the context of ACS severity and outcomes.

In this study, females exhibited a higher mean serum fibrinogen level at presentation (387.36 mg/dl) compared to males (358.16 mg/dl), paralleling findings from M. Eliasson et al.,[10] who observed higher serum fibrinogen and lower tissue plasminogen activator activity in women than men among 1,288 patients. Similarly, MC Stone et al. found a significant positive correlation between plasma fibrinogen levels and the incidence of myocardial infarction (MI) in a study of 297 men, with a notably higher MI incidence in patients with elevated fibrinogen and either high cholesterol or high systolic blood pressure.[11]

In our study, male participants with serum fibrinogen levels above 400 mg/dl mostly had diabetes (50%) or hypertension (37%). A notable observation was the lower diabetes prevalence among males with higher fibrinogen levels (>400 mg/dl), possibly due to undiagnosed diabetes, as indicated by high random blood glucose levels in 53.8% of these individuals without a prior diabetes diagnosis. Similar to findings by Karlson J et al.,[12] chest pain was the most common symptom in our study (96%), also with other symptoms like palpitations, sweating, and dyspnea. Culic V et al. found that women were more likely to experience non-specific chest pain, especially those with diabetes – a trend also noted in our study [13]. Ryan et al.'s research identified various symptom clusters in MI, underscoring the variability of clinical presentations [14].

David D McManus et al. [15] highlighted the relationship between the number of comorbidities and increased mortality post-MI, aligning with our findings of prevalent comorbidities like diabetes and hypertension. Ciril Baechli et al.'s study also indicated increased risks associated with

comorbidities in younger patients with acute MI [16]. Regarding lifestyle factors, our study observed no significant differences in serum fibrinogen levels between alcohol consumers and non-consumers, contrasting with Arthur L Klatsky et al.'s findings of a negative association between alcohol consumption and first myocardial infarction [17].

Diann E Gaalema et al. reported a high prevalence of smoking among MI patients, which was also observed in our study. However, smokers in our cohort had lower serum fibrinogen levels and GRACE scores, suggesting a different risk profile than non-smokers [18]. Sven Meyer et al. and Marc V Samsky et al. provided insights into the clinical profiles of acute heart failure and cardiogenic shock post-MI, respectively, which were relevant to our study's findings of elevated JVP, pulmonary edema, and cardiogenic shock [19,20].

Our study's cardiac marker analysis revealed higher fibrinogen levels and GRACE scores in patients with elevated markers, aligning with Landes Berg et al.'s findings on the prognostic value of these markers [21]. Udaya Rala panawa et al. also highlighted the association of smoking and alcohol abuse with STEMI, reflecting the patterns observed in our study's ACS type distribution and serum fibrinogen levels [22]. Lastly, our study utilized the FACIT F scale to measure fatigue, revealing significant correlations with GRACE scores and serum fibrinogen levels, both at presentation and at 3-month follow-ups. This underscores the multifaceted nature of MI presentations and the importance of considering various physiological and lifestyle factors in patient assessment and management.

CONCLUSION:

Acute coronary syndrome (ACS) carries a high mortality risk, making the use of predictive markers and scoring systems crucial for mortality assessment. Our findings indicate that serum fibrinogen levels are significantly elevated in STEMI patients compared to those with NSTEMI and unstable angina, both at initial presentation and three months later. A notable trend is observed in patients with left ventricular (LV) dysfunction, where those with severe LV dysfunction exhibit higher fibrinogen levels than those with mild or moderate dysfunction. Furthermore, patients readmitted for heart failure within three months post-ACS had higher initial fibrinogen levels compared to those not readmitted. Similarly, increased serum fibrinogen was associated with higher KILIPS class at the onset of symptoms. Although patients undergoing interventions like PTCI/CABG displayed elevated fibrinogen levels initially and at three-month follow-up, this did not translate to a statistically significant correlation. The study also showed that the GRACE score was higher in STEMI patients than in those with NSTEMI and unstable angina, and was further elevated in patients with LV dysfunction, especially severe cases. Those requiring repeated hospitalizations for heart failure within the first three months had a higher GRACE score at presentation. Additionally, a higher GRACE score was correlated with increased serum fibrinogen levels both at presentation and after three months. Moreover, lower FACIT F scores, indicating greater fatigue, were linked to higher fibrinogen levels at both time points. These scores were notably lower in patients who needed recurrent hospital admissions for heart failure and in those

with higher GRACE scores initially. In conclusion, our study determines that higher serum fibrinogen levels and GRACE scores at presentation and at three-month follow-up are indicative of more severe myocardial infarction, increased rates of heart failure readmission, and greater fatigue levels. Thus, serum fibrinogen and GRACE score serve as valuable predictive markers for evaluating morbidity in ACS patients.

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