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Original Article

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Role of Serum D-Dimer Level in Acute Coronary Syndrome Patients

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Abstract

Background: Chest pain is a frequent symptom in emergency and cardiology department and often presents a diagnostic challenge. Because coronary thrombosis is a hallmark of acute coronary syndromes (ACS), the substrates of the coagulation and fibrinolysis cascades may be considered as a marker of coronary thrombosis. Objectives: The aim of the study was to determine the role of D-dimer value in patients of acute coronary syndrome. **Subjects and Methods:** A total of 100 ACS patients who admitted in Comilla Medical College Hospital during July 2014 and December 2014 were enrolled in this study. Demographic characteristics were assessed by a standardized questionnaire. Conditions that increased plasma D-dimer other than ACS were excluded. Plasma D-dimer was measured. 2.5 milliliter (ml) of blood was collected from each patient in 3.2% trisodium citrate. D-dimer test was measured immunometrically for all patients regardless of troponin I results. **Results**: Total of 100 ACS patients were enrolled. Mean age of these patients were 40.9±12 years. Out of which 59% is male and 41% is female. Plasma D-dimer levels correlated with complication of ACS, creatinine clearance, troponin-I level and Death. D-dimer levels were raised among patients with troponin I positive results and normal in those with negative troponin I results. A significant correlation was found between high D-dimer level and positive troponin I results. **Conclusion:** D -Dimer, an expression of ongoing thrombus formation and lysis, is a marker of substantial incremental value for the early diagnosis of acute coronary syndromes presenting with chest pain. It adds independent information to the traditional assessment for myocardial infarction. D -Dimer can be incorporated into clinical decision models in the Emergency and Cardiology Department. D-dimer is useful coagulation marker use to evaluate extent of coronary thrombosis and may predict in-hospital cardiovascular complication.

Keywords: Chest pain, Coronary thrombosis, Acute coronary syndromes (ACS), D -Dimer

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Introduction

Chest pain is a very common presentation to the emergency department and the early diagnosis and prognostic evaluation of acute chest pain must be carried out in this department: chest pain might be the first and only symptom of acute coronary syndrome (ACS). The diagnosis of ischaemic chest pain in the emergency department is currently based on clinical history, serum enzyme levels and electrocardiogram (ECG) findings.[1] Serial ECG and serum enzyme measurements are very useful for the recognition of myocardial infarction (MI) and unstable angina pectoris (UA), but have limited diagnostic value in the early stages of these syndromes. Cardiac enzyme levels may take several hours to rise after pain onset and the ECG has suboptimal sensitivity for the early diagnosis of MI.[2] ACS occurs when an unstable plaque ruptures. ACS is a term that encompasses both unstable angina and myocardial infarction (MI). Unstable angina is characterized by new onset or rapidly worsening angina (crescendo angina), angina on minimal exertion or angina at rest in the absence of myocardial damage. In contrast, MI occurs when symptoms occur at rest and there is evidence of myocardial necrosis, as demonstrated by an elevation in cardiac Troponin or creatine kinase-MB isoenzyme.[3] In general ACS caused by an imbalance between myocardial oxygen supply and demand. It represents a dynamic state in which patient frequently shift from one category to another, as new ST elevation can develop after presentation and cardiac biomarkers can become abnormal with recurrent ischemic episodes.[4] ACS may present as a new phenomenon or against a background of chronic stable angina. The pathophysiology is thought to be related to a ruptured or eroded atherosclerotic plaque in a major coronary artery that then leads to thrombosis at the ite and thrombo-embolism and ischemia to the downstream myocardium.[5] Acute coronary syndrome commonly known as a heart attack, results from the interruption of blood supply to a part of the heart, causing heart cells to die. This is most commonly due to occlusion (blockage) of a coronary artery following the rupture of a vulnerable atherosclerotic plaque, which is an unstable collection of lipids and macrophages in the wall of an artery. The resulting ischemia and ensuing

oxygen shortage, if left untreated for a sufficient period of time, can cause damage or death of heart muscle tissue (myocardium).[6] Acute coronary syndrome commonly known as a heart attack, results from the interruption of blood supply to a part of the heart, causing heart cells to die. This is most commonly due to occlusion (blockage) of a coronary artery following the rupture of a vulnerable atherosclerotic plaque, which is an unstable collection of lipids and macrophages in the wall of an artery. The resulting ischemia and ensuing oxygen shortage, if left untreated for a sufficient period of time, can cause damage or death of heart muscle tissue (myocardium).[7]

These syndromes are related but do have different clinical behavior, outcomes and therapeutic management. ACS sometimes fatal and are difficult to diagnose promptly. Therefore, in this study we examined the utility of rapid D-dimer measurement in serum for the screening of ACS. We also investigated the utility of rapid D-dimer measurement for the diagnosis of ACS. Several decades of clinic and laboratory research have pointed out the association between hemostatic system constituents and coronary artery disease (CAD) investigating the possible predictive value of these constituents in the progression of the disease.[8] Both coagulation and fibrinolytic systems play an important role in the clinically silent evolution and progression of atheroma and in events that follow the rupture of the plaque resulting in clinical symptoms. Thrombus formation in a disrupted atherosclerotic plaque trigger most of the cardiovascular ischemic events. As the thrombus is dissolved by the fibrinolytic system researchers hypothesized that a decrease in fibrinolytic activity could be a risk factor for ischemic events.[9] D-Dimer fragments are produced when plasmin, an enzyme that activates fibrinolytic system degrades fibrin to remove it from blood vessels, ducts and organic fluids. When the conversion of fibrinogen in fibrin takes place, the mechanism that keeps the hemostatic balance is activated, with the conversion of plasminogen to plasmin, for fast removal of fibrin, preventing thrombotic complications.[10] D-Dimer plasma levels evaluate not only the activation of the fibrinolytic system, but also the severity of a hypercoagulability condition.

Subjects and Methods

Study Design

This observational cross-sectional study was conducted over a 12-month period, from November 2014 to April 2015, at Comilla Medical Hospital, Comilla, Bangladesh.

Place of Study

The study was conducted at Comilla Medical Hospital, Comilla, Bangladesh.

Study Population and Sampling Technique

The study population consisted of 100 patients, selected based on predefined inclusion and exclusion criteria. Purposive sampling was used to select participants. Inclusion criteria included patients presenting with polyps who were willing to participate in the study. Exclusion criteria included patients with other types of malignancies or systemic diseases affecting the gastrointestinal tract.

Study Procedure

Data collection was conducted through clinical examinations and laboratory investigations. All participants on randomly selected ACS patient in Comilla Medical Hospital a detailed medical history review, clinical examination, and relevant diagnostic tests, including imaging studies where necessary.

Statistical Analysis

Data were analyzed using SPSS version 27 (SPSS Inc., Chicago, IL, USA). Descriptive statistics, including frequency and percentage for categorical variables, were used to summarize the data. Results were presented in tabular and graphical formats for clarity.

Results

Table 1: The coronary risk factors of the study population

Characteristics (n = 100)	Value
Age (years) (mean ± SD)	40.9 ± 12
Male	59 (59)
BMI	26± 06
Diabetes mellitus	52 (52)
Current smoker	57(57)
Total cholesterol (mg/dL) (mean ± SD)	196 ± 42
HDL cholesterol (mg/dL) (mean ± SD)	48 ± 15
LDL cholesterol (mg/dl) (mean ± SD)	150 ± 40
Triglyceride (TG)	220±30
Positive family history	58 (58)
Hypertension	72(72)
Known ischemic heart disease	48 (48)

Values are mean±SD. All other values are n (%).

Table 1 show the coronary risk factors of the study population. It observed that, HDL cholesterol mean ± SD 48±15, LDL cholesterol mean ± SD 150± 40, Total cholesterol mean ±SD 196±42, Triglyceride mean ± SD 220 ± 30, Forty-eight (48%) had a history of ischemic heart disease, 58% had positive family history, 72% had hypertension, 35 patients had gone recent hospitalization.

Table 2: Clinical, Laboratory, and Electrocardiographic findings at current hospitalization

Characteristics (n = 100)	Value
LOS (days)	5.5 ± 4.5
Recurrent chest pain	60 (60)
Fibrinogen (mg)	444 ± 111
Random Blood sugar	120 ±15
C-reactive protein	0.9 ± 1.7
CPK (mg/dL)	83 ± 52
AST (IU/L)	42 ± 82
LDH (IU/L)	555 ± 213

Values are mean±SD. All other values are n (%).

Clinical, Laboratory, and Electrocardiography findings showed that Mean length of hospital stay was 5.5 ± 4.5 days. Mean fibrinogen level was higher than normal (444 ± 111 mg). Median CRP level was 0.9 ± 1.7 (range, 0.12–10), LDH level was higher 555±213 than normal.

Table 3: Bivariate correlation between ELISA D-Dimer levels and other variables

	D-Dimer ELISA	
Variable	r	P
Sex (male)	0.25	0.02
Older age	0.43	0.0001
Systolic Hypertension	0.35	0.002
Smoking	0.26	0.03
Fibrinogen	0.40	0.0002
CRP	0.35	0.003
LOS	0.47	0.04

Table 3 show the correlation between D-Dimer Levels and Other Variables showed that mean D-dimer level was 466 ± 283 ng/mL (normal <250 ng/mL). Statistical analysis yielded a significant correlation of ELISA D-dimer level with cardiac risk factors of male sex (r = 0.25, P = 0.02), older age (r = 0.43, P = 0.0001), smoking (r = 0.26, P = 0.03), and hypertension (r = 0.35, P = 0.002), level of acute phase reactants fibrinogen(r = 0.40, p = 0.0002) and CRP(r = 0.35, p = 0.003) and LOS (r = 0.47, p = 0.04).

Table 4: Level of cardiac markers and D-dimer in patients diagnosed with cardiac chest pain, stratified by ACS subgroup and compared with D-dimer.

Group OR Subgroup	No of patient	Creatine kinase MB u/l	Statistical significance	Troponin I ng/ml	Statistical significance	D-Dimer ng/ml	Statistical significance
UA	10	31.73±25.74	NS	0.29	NS	365± 149	p<0.001
NSTEMI	45	76.92±61.89	p<0.001	9.93	p<0.001	465±240	p<0.001
STEMI	40	68.10±59.04	p<0.001	9.06	p<0.001	899±355	p<0.001

Table 4 show the Data presented as mean±SD. Mann-Whitney U-test as comparison method were used. In between group comparison, P<0.01 was considered to be statistically significant (NS-not significant p>0.01).

Table 5: Distribution of the patients by outcome associated with the level of D-dimer (n=100).

Characteristics	D-Dimer	
	r	P
Arrhythmia	0.40	0.007
Heart rate	0.24	0.029
Heart Failure	0.43	0.0001
Cardiogenic shock	0.43	0.0001
Death	0.44	0.009

Table 5 show the Plasma D-dimer levels correlated with complication of ACS (Heart failure; p < 0.0001, arrhythmia; p < 0.007 and death; p < 0.009, Heart rate; p<0.029, Cardiogenic.

Figure 1 show that the study included 100 patients (59 men, 41 female) of mean age 40.9 ± 12 years.

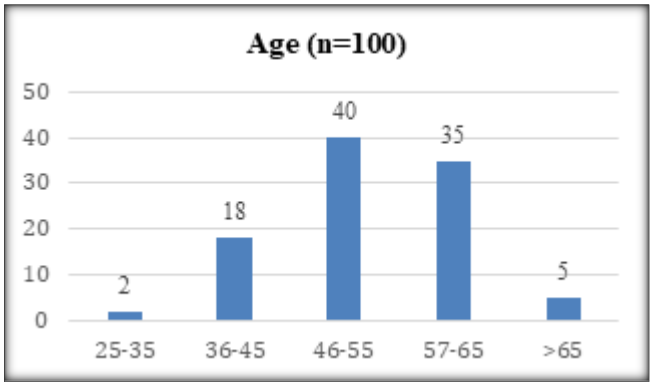

Figure 1: Age distribution of the patients (n=100)

Figure 2 show the sex distribution of the patients. Here, out of 100 patients most of them were male 59 (59%).

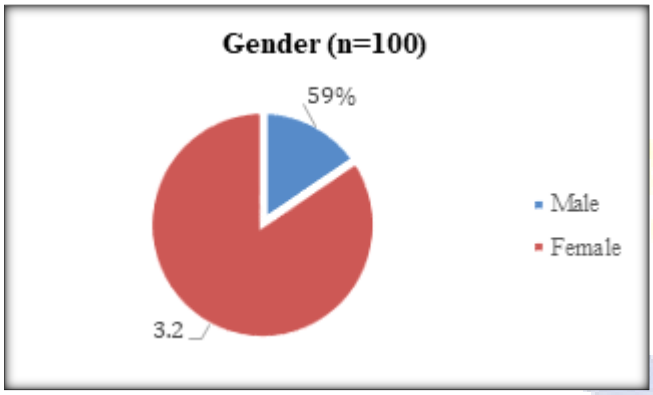

Figure 2: Sex distribution of the patients (n=100)

Figure 3 show the distribution of acute coronary syndrome patients. Here, out of 100 patients of ACS 40 cases were STEMI, 45 cases were NSTEMI and rest of them Unstable angina.

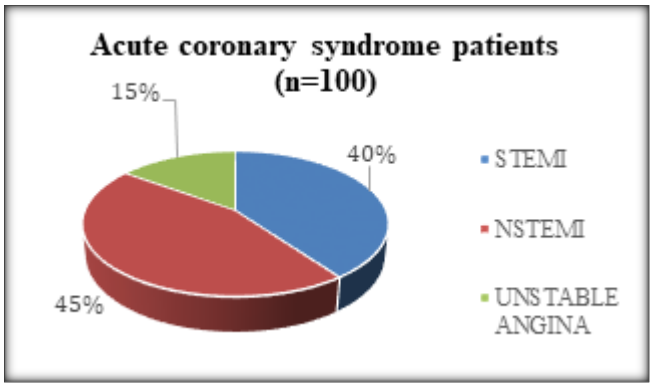

Figure 3: Distribution of acute coronary syndrome patients

Discussion

This prospective study demonstrates that high D-dimer ELISA levels at admission add information about the magnitude of the Acute coronary syndrome patients. D-dimer levels were associated with cardiac risk factors, and disease severity (as measured by CRP and fibrinogen levels and LOS). The correlation with the coronary risk factors suggests that patients with high-risk ischemic heart disease have elevated D-dimer levels. Previous studies have shown a link between unstable angina and hemostatic abnormalities. Elevated levels of fibrinogen, von Willebrand factor, factor VII and plasminogen activator inhibitor have all been associated with coronary events.[11] High levels of D-dimer were also noted in patients with unstable angina. Specifically, D-dimer was increased in the peripheral blood of patients with UA, without overlap with levels in patients with stable angina.[12] Elevated levels of D-dimer may reflect a systemic prothrombotic state and, possibly, focal vessel wall related fibrin formation and degradation associated with unstable atherosclerotic plaque activity. Another study assessed the diagnostic value of hemostatic markers in patients presenting to the emergency department with chest pain syndromes.[13] They found that D-dimer levels were significantly higher in patients with acute myocardial infarction and UAP than in non-ischemic patients. A level of >500 μg/L had an independent diagnostic value for myocardial infarction and increased the diagnostic sensitivity of the electrocardiogram and history from 73% to 92%. The relationship between serum D-dimer levels and ACS is unclear and published data are contradictory. For example, small studies show that D-dimer levels are higher in patients with MI than in patients with other forms of ACS.[14] In contrast; Gurfinkel et al. found normal D-dimer concentrations in patients with MI compared with healthy volunteers.[15] In a study of 300 patients admitted to the emergency department with acute chest pain, Bayes-Genis et al. showed that D-dimer levels in acute MI and USA were considerably elevated secondary to MI.[6] Creatine kinase-MB, myoglobulin and TPI are generally used as markers of ACS, but these markers directly reflect the damage to myocardial muscle and do not reflect coronary thrombosis. Markers that reflect the obstructive events in the coronary arteries would be more useful than those reflecting the damage to myocardial muscles.[16] Elevated D-dimer concentrations may reflect a systemic prothrombotic state and, possibly, focal vessel-wall related fibrin formation and degradation associated with unstable atherosclerotic plaque activity. Another study of Ieko et al. showed that D-dimer and plasmin–plasmin inhibitor complex levels in the acute phase of ACS were significantly higher than those in the recovery phase, suggesting intracoronary thrombosis.[16] Specifically, D-dimer concentrations were increased in the peripheral blood of patients, with USAP, without overlap with levels in patients with stable angina. Shitrit et al. demonstrated that serum D-dimer levels were higher in patients admitted to the emergency department with normal ECG and USAP.[6] Similarly, in the present study, only the D-dimer level was significantly higher in patients with STEMI and NSTEMI when compared with USAP, whereas there were significant differences in the CK-MB and TPI levels. Like Bayes-Genis et.al we suggest that the D-dimer level is useful for diagnosing STEMI and NSTEMI in patients admitted to the emergency department with acute

chest pain.[6] For this reason, Bayes- Genis et al. suggested that serum D-dimer levels should be studied, in addition to other cardiac markers, in patients presenting to the emergency department with acute chest pain and normal ECG findings. Similarly, in the present study, serum D-dimer levels were significantly higher in patients admitted to the cardiology department with chest pain with a diagnosis of ACS. Hoffmeister investigated the coagulation profile in acute coronary syndrome patients and demonstrated a persistently strong trend of elevated D-dimer levels during the first 10 days after admission.[17] Accordingly, Oldgren et al. showed that on long term follow-up (median 29 months) of patients with ACS, higher baseline levels of D-dimer were correlated with increased mortality.[8] Although our study found that performance of the D-dimer ELISA at admission adds information on disease severity in this patient population, we did not assess the diagnostic value of the test for ACS. Another study showed that marked increases in circulating D-dimer were indicative of thrombotic complications in patients with MI, suggesting that D-dimer, besides being a useful marker for early diagnosis, is also a risk factor for the development of MI complications.[11]

Of the ten patients in the present study who died, two had STEMI, four had NSTEMI and none had USAP. Serum D-dimer levels were significantly higher in patients who died compared with those who lived. We believe the diagnosis of ACS at admission to the ED should be based on clinical factors such as history, physical examination, and electrocardiography, and not on blood markers. Moreover, the generally low specificity of the available D-dimer assays (ELISA, latex agglutination assay, turbidometric immunoassays) and their wide variations in sensitivity preclude their use as a diagnostic tool.[16]

Because of the low interassay correlation and the lack of a D-dimer reference standard, we used the ELISA, which is currently considered the gold standard methodology. However, the ELISA also requires more complex laboratory equipment and is more expensive and time-consuming than the other assays. Therefore, we suggest that in addition to cardiac enzymes, use of the D-dimer test to selected patients with ACS and normal ECG who have an atypical presentation. It is also indicated in patients in whom information on the magnitude of the coronary disease is important in the emergency room setting, as the D-dimer level was found to correlate well with the degree of coronary artery disease noted during catheterization.

Limitations of the study

The present study was conducted in a very short period due to time constraints and funding limitations. The small sample size was also a limitation of the present study.

Conclusion

This observational study provides important insights into the epidemiological and clinical features of colorectal polyps in a Bangladeshi population. The findings indicate that colorectal polyps are most prevalent in individuals aged 51-65 years, with a slightly higher incidence in males. Adenomatous polyps were the most common type, highlighting the need for early detection due to their potential to progress to colorectal cancer. The study also identified significant associations between colorectal polyps and conditions such as Peutz-Jeghers syndrome and inflammatory bowel diseases. Additionally, smaller, single polyps were more frequently observed, with pedunculated polyps being the most common morphological type. These findings emphasize the importance of regular screening, especially in older individuals, to facilitate early intervention and reduce the risk of colorectal cancer.

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