Original Research Article

Cystatin-C as a potential risk factor for acute myocardial infarction with normal renal function

Bharat Lochan[1], K. Babu Raj[2*]

[1]First Year Post Graduate, [2]Reader
Department of Medicine, Rajah Muthiah Medical College, Annamalai University, Chidambaram, Tamil Nadu, India
[*]Corresponding author email: **drkbrp19@gmail.com**

International Archives of Integrated Medicine, Vol. 6, Issue 1, January, 2019.

Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 15-12-2018 **Accepted on:** 20-12-2018
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: Bharat Lochan, K. Babu Raj. Cystatin-C as a potential risk factor for acute myocardial infarction with normal renal function. IAIM, 2019; 6(1): 1-7.

Abstract

Background: Myocardial Infarction accounts for 20% of all medical emergency admissions and has the highest risk for adverse effects and deaths. Risk of CAD could be prevented by various strategies and most of the developed countries could reduce the incidence and mortality related to CAD especially Myocardial Infarction by various preventive methods. Cystatin-C thus acts as an independent risk factor for Myocardial Infarction and heart failure.

Aim and objective: To estimate the Serum level of Cystatin-C in Acute Myocardial Infarction with normal renal function

Materials and methods: The study included 40 patients admitted in the medicine ward of RMMCH. The study period was from February 2018- July 2018. Patients with acute coronary syndromes were identified over a period according to the criteria and were included in the study. Primary complaints like angina, dyspnea, symptoms of cardiac failure were recorded. Risk factors for coronary artery disease like diabetes mellitus, systemic hypertension, smoking, hyperlipidemia, renal failure, and other complaints if any were noted. Clinical examination included a detailed general examination including vital signs and systemic examination of cardiac, respiratory, gastrointestinal, and nervous systems. 2 ml of blood was withdrawn from all patients within 12 hours of onset of symptoms for measuring Cystatin-C.

Results: The common age was 52 to 59 years (47.5%) and 45 to 51 years (45.0%). The mean age of the study patients was 51.10 ±5.47 years. The majority of the patients had ST-elevated MI (N=27, 67.5%). Among STEMI, 14 patients were AWMI (N=14, 51.9%) IWMI- STEMI was identified in 18.5% patients. Likewise, posterior wall MI-STEMI was the diagnosis for 18.5% and Inferior-lateral-

STEMI was the feature for 11.1%. The mean Cystatin-C for STEMI was 1.24 ± 0.26 whereas it was 1.38 ± 28 for NSTEMI. The difference was statistically insignificant (t=1.46, p=151). The overall Cystatin-C Mean was 1.29 ± .27, which was higher than the normal level. The correlation of Cystatin-C with LV function is poor (r = .181, p=26). The relationship was weakly positive and insignificant. That was when Cystatin 'C' was more, LV function was less and vice-versa. The correlation of Cystatin-C with TIMI was negative i.e. when Cystatin was more, TIMI was less and vice-versa but the relationship was poor (r=.126, p = .44) and insignificant.

Conclusion: Cystatin-C plays an important role in the pathogenesis of Acute Myocardial Infarction, and one of the mechanisms is thought to be that Cystatin-C facilitates the progress of atherosclerosis by regulating inflammation. Cystatin-C is less influenced by age, gender, and muscle mass and thus may be a better indicator of cardiovascular risk especially Myocardial Infarction.

Key words

Myocardial Infarction, Cystatin-C, LV function, STEMI score.

Introduction

Myocardial Infarction accounts for 20% of all medical emergency admissions and has the highest risk for adverse effects and deaths. Risk of CAD could be prevented by various strategies and most of the developed countries could reduce the incidence and mortality related to CAD especially Myocardial Infarction by various preventive methods [1]. Some of the risk factors of coronary heart disease are non-modifiable like age, male sex and family history of atherosclerosis. Modifiable risk factors include hypertension, hyperlipidemia, diabetes mellitus and a smoking cigarette which are commutable risk factors of myocardial infarction [2]. Clinical evaluation of suspected acute myocardial infarction depends on patient history, electrocardiographic findings, and cardiac enzymes and other biomarkers. Cystatin-C is a cysteine protease inhibitor, secreted by all nucleated cells. This protein is less influenced by age, gender, and muscle mass [3]. Cystatin-C regulates inflammation and thereby facilitates the progression of atherosclerosis and hence involves in the pathogenesis of Myocardial Infarction [4]. Cystatin-C is expressed in all of the nucleated cells, regulates the activity of cysteine protease, and plays a role in the dynamic balance of production and degradation of ECM. Cystatin-C and its fragments may also affect the phagocytic and chemotactic ability of neutrophil, participates in the inflammatory process and regulates inflammatory responses [5]. Inflammation plays an important role in the development of atherosclerosis. Moreover, ECM degradation and positive arterial remodeling relate closely to plaque destabilization, suggesting that cystatin-C may facilitate plaque resulting in Myocardial Infarction. Cystatin-C thus acts as an independent risk factor for Myocardial Infarction and heart failure [6]. The current study demonstrated that serum levels of Cystatin-C were independently associated as a risk factor for the development of Myocardial Infarction in patients with normal renal function. Renal impairment patients were excluded in order to avoid the well-known effects of renal insufficiency over atherosclerosis and Cystatin-C [7].

Materials and methods

The study included 40 patients admitted in the medicine ward of RMMCH. The study period was from February 2018- July 2018. Patients with acute coronary syndromes were identified over a period according to the criteria and were included in the study. Primary complaints like angina, dyspnea, symptoms of cardiac failure were recorded. Risk factors for coronary artery disease like diabetes mellitus, systemic hypertension, smoking, hyperlipidemia, renal failure, and other complaints if any were noted. Clinical examination included a detailed general examination including vital signs and systemic

examination of cardiac, respiratory, gastrointestinal, and nervous systems.

Inclusion criteria

- Those attended the OPD/casualty of Rajah Muthiah Medical College having Acute Myocardial Infarction.
- Admitted within 12 hours after the onset of symptoms.
- ECG changes showing STEMI / NSTEMI with elevated cardiac enzymes.

Exclusion criteria

- Patients with abnormal renal function.
- Patients with thyroid dysfunction.
- Patients with any malignancies.
- Patients underwent any recent surgeries.

Laboratory Investigations

Blood urea and serum creatinine were used to rule out frank renal failure. Electrocardiogram was taken to look for ST elevation or new onset left bundle branch block identified by comparison with previous ECG if available. In all cases, an Echocardiography was obtained to assess the left ventricular function and ejection fraction. Within 12 hours of the onset of symptoms, Cystatin-C levels were measured in blood. Cystatin-C can be measured in a random sample of serum (the fluid in blood from which the red blood cells and clotting factors have been removed) using immunoassays such as nephelometry or particle-enhanced turbidimetry. 2 ml of blood was withdrawn from all patients within 12 hours of onset of symptoms for measuring Cystatin C.

Statistical analysis

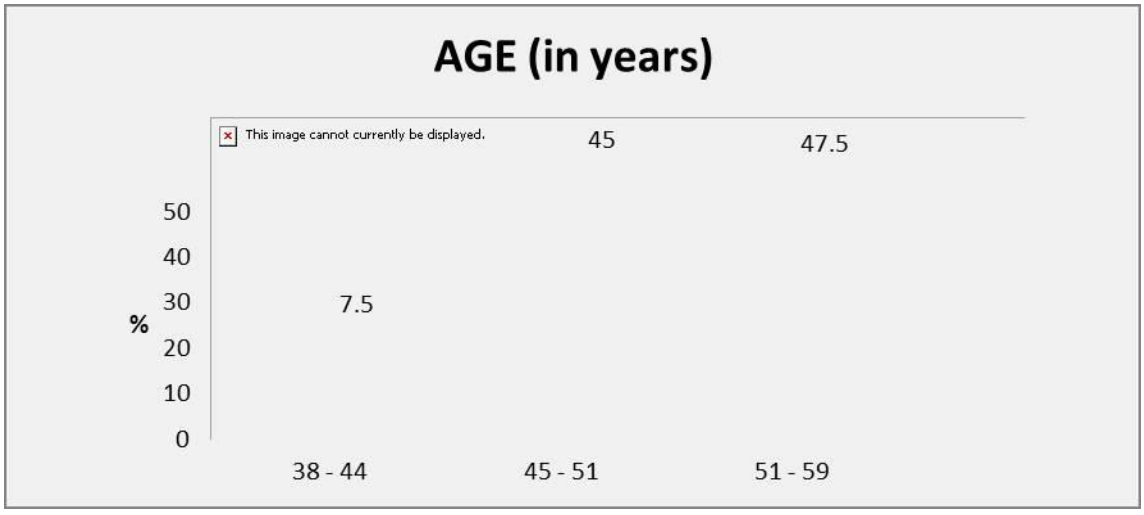
The data collected were analyzed and expressed as Mean ± SD. One way Analysis of variance (one way ANOVA), Pearson's correlation test was used in the present study. Statistical software namely SPSS 20 was used for the analysis of the data and Microsoft Word and Excel to generate graphs and tables. Level of Significance: $P < 0.05$ was considered as significant while analyzing the data.

Results

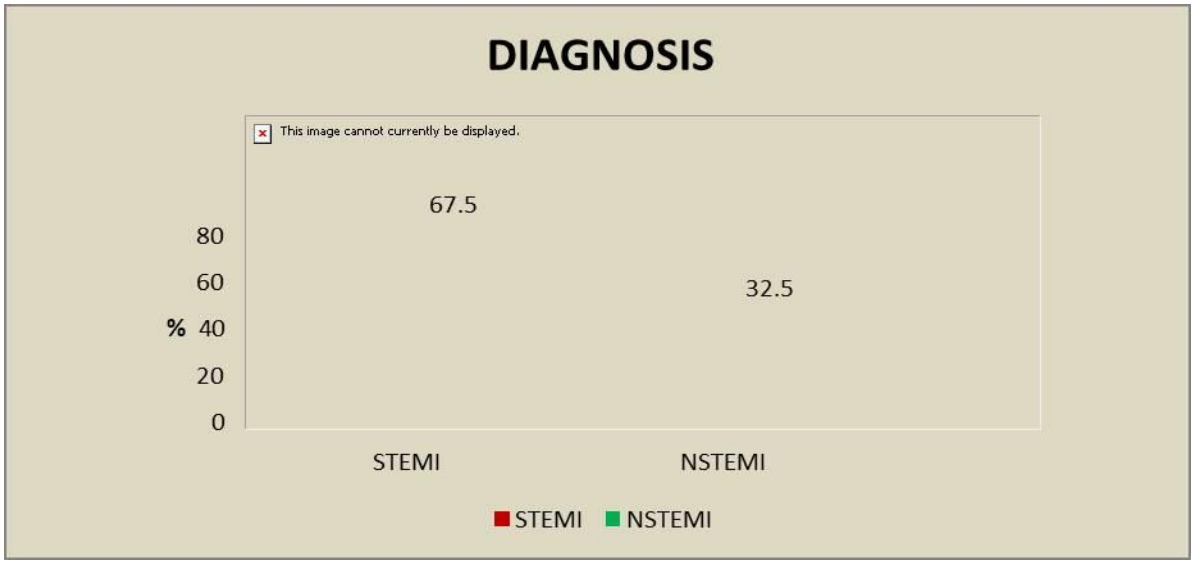
The common age was 52 to 59 years (47.5%) and 45 to 51 years (45.0%). The mean age of the study patients was 51.10 ± 5.47 years (**Graph – 1**). STEMI was the common findings in the present work (N=27, 67.5%) as per **Graph – 2**. The cardiac enzyme was elevated in most of the patients (N=34, 85%) as per **Graph - 3**.

The mean Cystatin-C for STEMI was 1.24 ± 0.26 whereas it was 1.38 ± 0.28 for NSTEMI. The difference was statistically insignificant (t=1.46, p=151). The overall Cystatin-C Mean was 1.29 ± 0.27, which was higher than the normal level (**Graph – 4**).

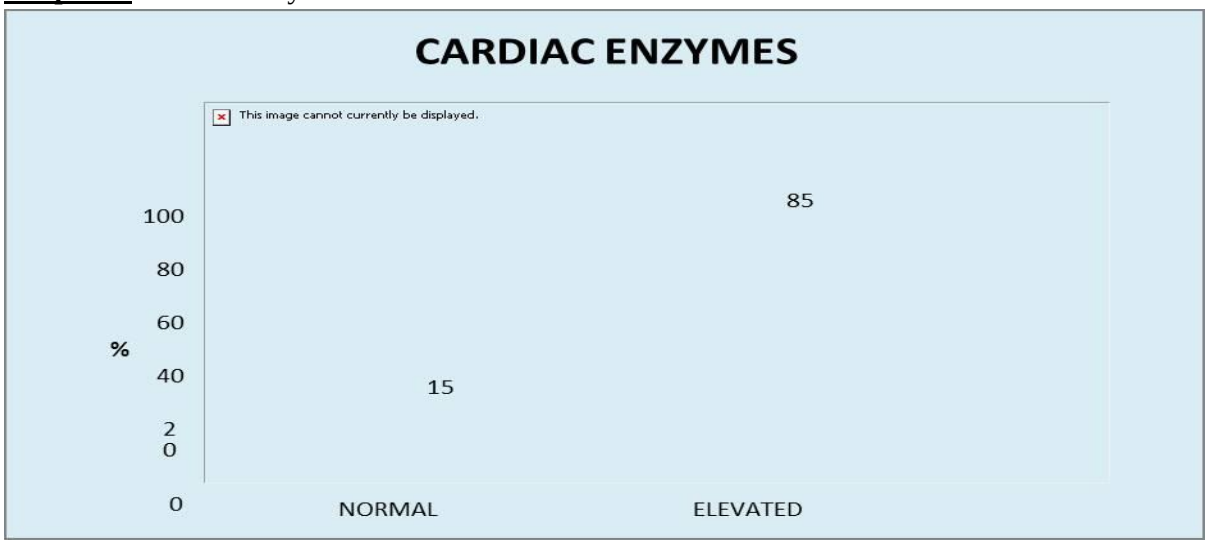
Graph – 1: Age distribution.



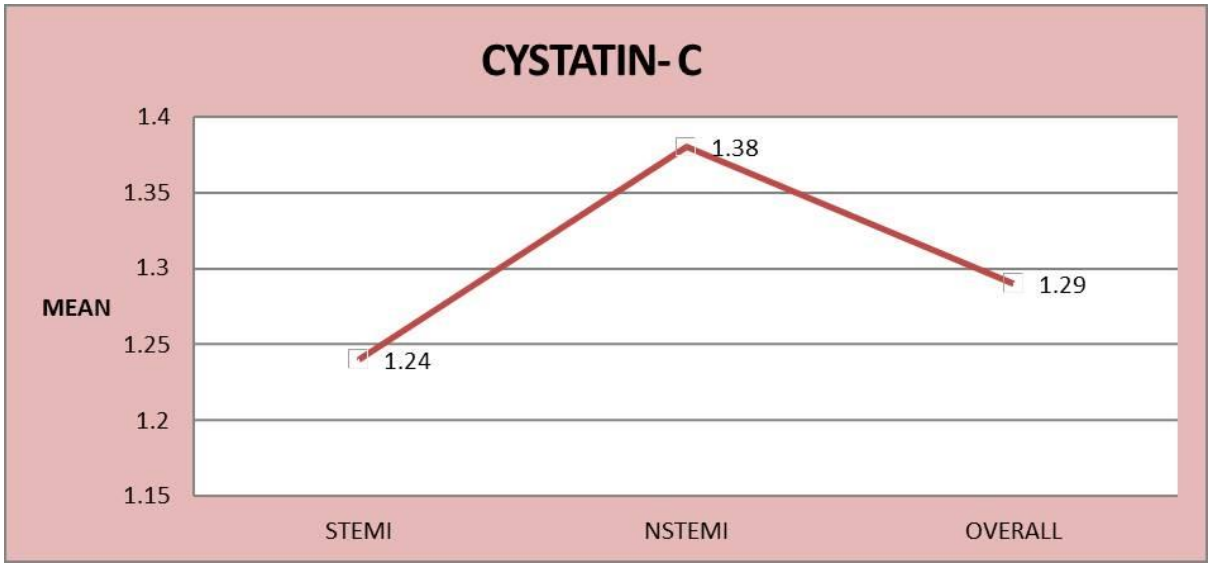
Graph – 2: Diagnosis.



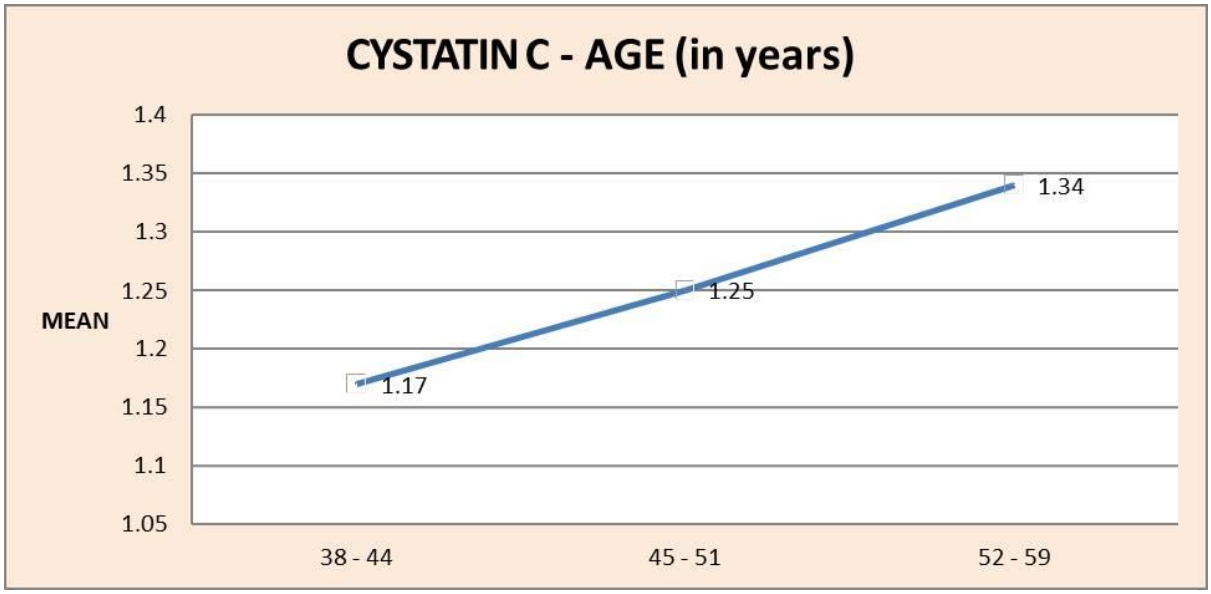
Graph – 3: Cardiac enzymes.



Graph – 4: Diagnosis VS Cystatin-C STEMI VS NSTEMI.



Graph – 5: Cystatin with Age.



The difference in Cystatin in relation to age was studied by ANOVA. The mean cystatin was higher for 52-59 years (1.34 ± 0.29) followed by 45-51 years (M = 1.25 ± 0.24) but the difference was insignificant (F=.770, P=.47) as per **Graph - 5**.

Discussion

Cystatin-C is expressed in all of the nucleated cells, regulates the activity of cysteine protease, and plays a role in the dynamic balance of production and degradation of ECM [8]. Cystatin-C and its fragments may also affect the phagocytic and chemotactic ability of neutrophil, participates in the inflammatory process and regulates inflammatory responses [9]. Inflammation plays an important role in the development of atherosclerosis. Moreover, ECM degradation and positive arterial remodeling relate closely to plaque destabilization, suggesting that Cystatin-C may facilitate plaque vulnerability as a result of Myocardial Infarction [10]. The pathophysiology of myocardial infarction is basically the breakdown of vulnerable plaque based on platelet aggregation, different levels, and different characteristics of thrombosis. The intercellular networking that occurs among smooth muscle cells, macrophages, T lymphocytes, and endothelial cells leads to a fibroproliferative response, in which the extracellular matrix (ECM) plays an important role [11]. Each component of the ECM possesses unique structural properties that determine its own role during the development of atherosclerotic plaques. Not only does the ECM provide the structural integrity of the plaques, but it also participates in several key events such as cell migration and proliferation, lipoprotein retention, and thrombosis Cysteine proteinase, the major enzyme in ECM degradation, and its inhibitor as Cystatin-C is expressed in the plaque. An excess of cysteine proteinase over Cystatin-C may contribute significantly to ECM destruction rendering the plaque more prone to rupture. The study population consists of 40 Acute Myocardial Infarction patients among which 27 patients were STEMI and 13 patients were NSTEMI. All patients had a normal renal function [12]. All the patients had normal thyroid function and no recent surgeries. The age group of all patients was between 30 to 60 years of age. Patients with renal impairment, prior history of recent surgeries, malignancies, thyroid dysfunction were excluded from the study as they would have elevated levels of Cystatin-C. A single sample of blood was collected from all the patients within 12 hours of onset of symptoms. Cystatin C was elevated among 33 patients which constitute 82.5% of the total patients included in the study. The mean Cystatin C was 1.29±0.27 which was

higher than the normal value according to various studies. In Prospective Epidemiological Study of Myocardial Infarction (PRIME), Cystatin- C predicted the occurrence of the first coronary events in men aged 50 to 59 years old and displayed a strong relation with CAD independent of eGFR [13]. The mean values of Cystatin C for STEMI were 1.24±0.26 whereas it was 1.38±0.28 for NSTEMI. The difference is statistically insignificant but it was higher among NSTEMI patients. The overall Cystatin C mean was 1.29±0.27 which was higher than normal level [14]. Correlation of Cystatin-C among age and gender was also statistically insignificant which concludes that Cystatin-C was less influenced by age and gender [15]. Cardiac enzyme was elevated and there was Left Ventricular dysfunction in most of the study patients but the correlation of Cystatin C values with Left Ventricular function, cardiac enzymes, and TIMI scoring was statistically insignificant [16, 17].

Conclusion

Cystatin-C is to be considered as an independent risk factor for Acute Myocardial Infarction in patients with normal renal function. The mean Cystatin-C was 1.29 $\pm$ 0.27, which was higher than the normal value. The difference in Cystatin-C between STEMI vs NSTEMI was statistically insignificant even though the value is higher for NSTEMI. Correlation of Cystatin 'C' with LV function and TIMI scoring is insignificant. The relationship between Cystatin-C with gender was insignificant. Cystatin-C plays an important role in the pathogenesis of Acute Myocardial Infarction, and one of the mechanisms is thought to be that Cystatin-C facilitates the progress of atherosclerosis by regulating inflammation. Cystatin-C is less influenced by age, gender, and muscle mass and thus may be a better indicator of cardiovascular risk especially Myocardial Infarction.

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