www.jmscr.igmpublication.org
Impact Factor (SJIF): 6.379
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossrefDOI: https://dx.doi.org/10.18535/jmscr/v6i10.166

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Study of Cystatin C as a Risk Factor for Myocardial Infarction in Patients with Normal Renal Function

Authors
Dr G. Arul Venkadesh[1*], Prof. Dr M.Senthilvelan[2], Dr K. Baburaj[3], Dr A. Elaiyaraja[4], Dr Jayaram Kosalram[5], Dr G.Sivachandran[6]
[1,6]Post Graduate, Department of General Medicine, Rajah Muthiah Medical College, Annamalai University, Chidambaram,Tamilnadu
[2]Professor & HOD, Department of General Medicine, Rajah Muthiah Medical College, Annamalai University, Chidambaram,Tamilnadu
[3]Reader, Department of General Medicine, Rajah Muthiah Medical College, Annamalai University, Chidambaram,Tamilnadu
[4,5]Senior Resident, Department of General Medicine, Rajah Muthiah Medical College, Annamalai University, Chidambaram, Tamilnadu
*Corresponding Author
Prof Dr M. Senthilvelan
Professor & HOD, Department of General Medicine, Rajah Muthiah Medical College, Annamalai University, Chidambaram, Tamilnadu, India
Email: *profmsv@hotmail.com*

Abstract
Objective and Design: *Cystatin C facilitates the progression of atherosclerosis by regulating inflammation and thereby it has a significant impact on pathogenesis of Myocardial Infarction. In this study we assessed the association between cystatin C and Myocardial Infarction in a consecutive series of patients with normal kidney function.*
Materials and Methods: *40 Patients of age 30 to 60 years of both sexes, attending casualty within 12hours after the onset of symptoms in Rajah Muthiah Medical college and hospital, Annamalai University during the period of November 2016 till August 2018, diagnosed as Acute Myocardial Infarction with normal renal function, normal thyroid function without any malignancies / recent surgeries were taken for present study.*
Results: *Cystatin C was elevated among 82.5% of the total patients participated in the study. Cystatin C being less influenced by age, gender, and muscle mass and can be considered as a better indicator of cardiovascular risk especially Myocardial Infarction. CYSTATIN C to be considered as an independent risk factor for Acute Myocardial Infarction in patients with normal renal function.*
Keywords: *Acute Myocardial infarction, STEMI, NSTEMI, CYSTATIN C.*

Introduction

Myocardial Infarction accounts for 20% of all medical emergency admissions and has the highest risk for adverse effects and deaths.[1] 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. Some of the risk factors of coronary heart disease are non modifiable like age, male sex and family history of atherosclerosis. Modifiable risk factors includes hypertension, hyperlipidemia, diabetes mellitus and smoking cigarette which are commutable risk

factors of myocardial infarction. 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. Cystatin C regulates inflammation and thereby facilitates the progression of atherosclerosis and hence involves in the pathogenesis of Myocardial Infarction. Cystatin C acts as an independent risk factor for Myocardial Infarction [2] and heart failure [3].

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.

Aims and Objectives

To estimate the Serum level of Cystatin - C in Acute Myocardial Infarction with normal renal function and to compare the levels of Cystatin - C in predicting the severity and prognosis of STEMI and NSTEMI patients.

Materials and Methods

40 Patients belonging to age 30 to 60 years of both sexes, attending casualty within 12 hours after the onset of symptoms in Rajah Muthiah Medical college and hospital, Annamalai University during the period of November 2016 till August 2018, diagnosed as Acute Myocardial Infarction with normal renal function, normal thyroid function without any malignancies / recent surgeries were taken for present study.

Observation and Results

The present work aims to analyse cystatin 'C' in Myocardial Infarction. A total of 40 patients with Myocardial Infarction was selected and analysed. Overall cystatin 'C' was studied by descriptive statistics such as mean and standard deviation (sd). Cystatin 'C' in relation to types of Myocardial Infarction is analysed by independent sample 't' test. Cystatin C with respect to subtypes of STEMI is analysed by Analysis of variance (ANOVA) as its subtypes consists of more than 2 variables. Cystatin 'C' in relation to Left Ventricular function and TIMI score is studied by reason correlation coefficients. The entire statistical procedure is carried out by statistical packages of social sciences (Spss-21).

Table: 1 Age Distribution

AGE (in year)	Number	Percentage	Mean	S.D
38-44	3	7.5	51.10	5.47
45-51	18	45.0		
52-59	19	47.5		
Total	40	100		

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.

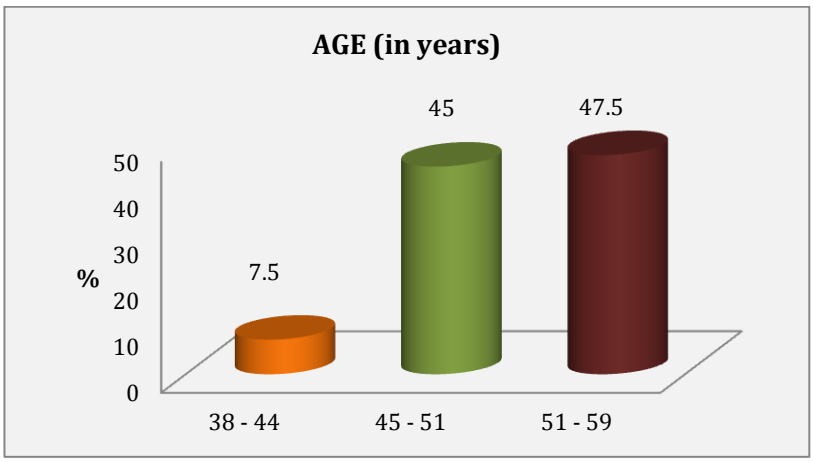

Table: 2 Gender Distributions

Gender	Number	Percentage
Male	24	60
Female	16	40
Total	40	100

The majority of the study patients were male (N=24, 60%).

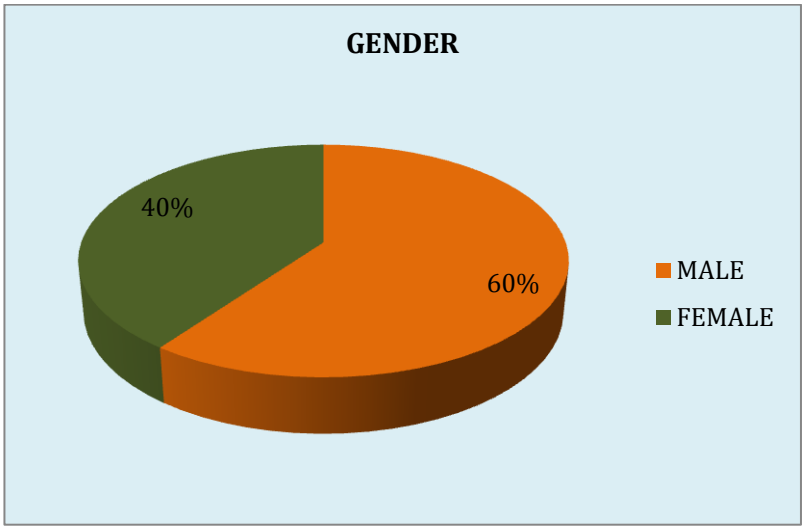

Table 3 Diagnosis

Cardiac Enzymes	Number	Percentage
STEMI	27	67.5
NSTEMI	13	32.5
Total	40	

Table 3(a) STEMI frequency is cystatin 'C' in relation subtypes of STEMI

	N	Mean	S.D	ANOVA	
				'F'	'P'
STEMI AWMI	14	1.24	.25	1.16	.35
STEMI IWMI	5	1.31	.22		
STEMI PWMI	5	1.08	.36		
STEMI INFOR LATERAL	3	1.41	.01		

The mean cystatin 'C' was comparatively higher for inferlateral –STEMI (M=1.41±.01) and IWMI-STEMI (M=1.31±22). The differences in cystatin 'C' among subtypes of STEMI is statistically insignificant (F=1.16, p = 35).

Table: 4 Cardiac enzymes

Cardiac Enzymes	Number	Percentage
Normal	6	15
Elevated	34	85
Total	40	100

The cardiac enzyme was elevated in most of the patients (N=34, 85%).

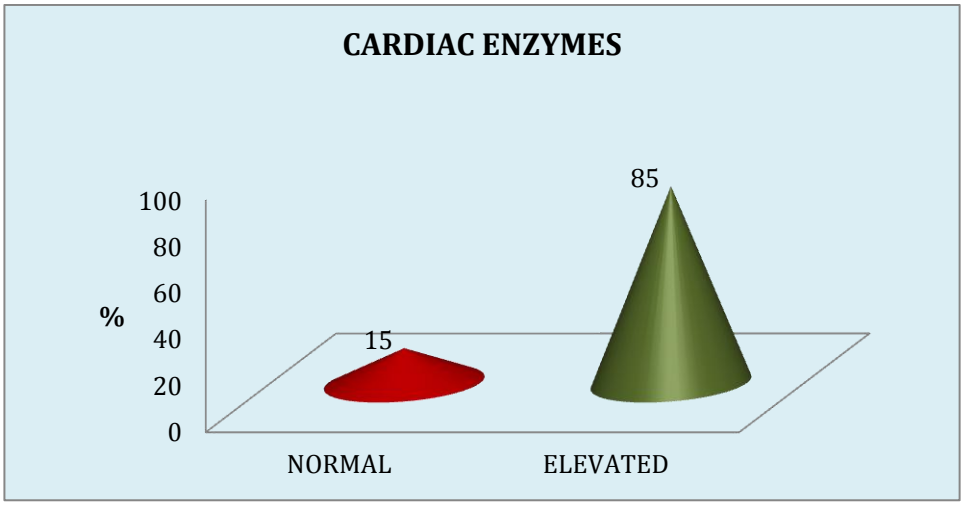

Table: 5 LV Function

LU FUNCTION	Number	Percentage
Normal	9	22.5
Mild	14	35.0
Moderate	9	22.5
Severe	8	20.00
Total	40	100

LV function was normal for only 22.5%, in MI. Mild LV dysfunction was observed in 35% of the patients. Moderate and severe dysfunctions were 22.5% and 20% respectively.

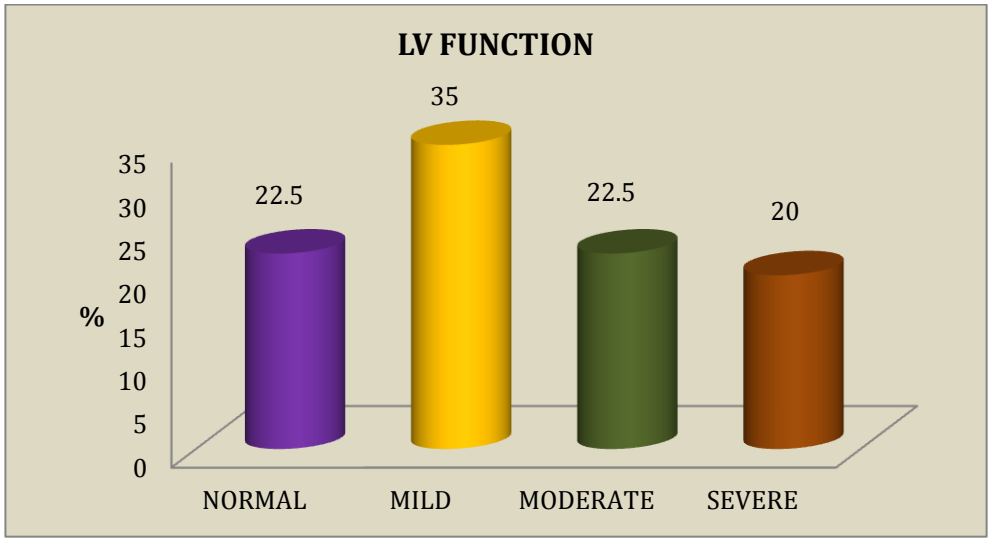

Table: 6 Diagnosis Vs cystatin 'C' STEMI VS NSTEMI

Diagnosis	N	Mean	S.D	Independent Sample Test	
STEMI	27	1.24	.26	1.46	.151
NSTEMI	13	1.38	.28		
Overall	40	1.29	.27		

The mean cystatin 'C' for STEMI was 1.24 ± .26 whereas it was 1.38 ± 28 for NSTEMI. The difference is statistically insignificant (t=1.46, p=151). The overall cystatin 'C' Mean was 1.29±.27, which was higher than normal level.

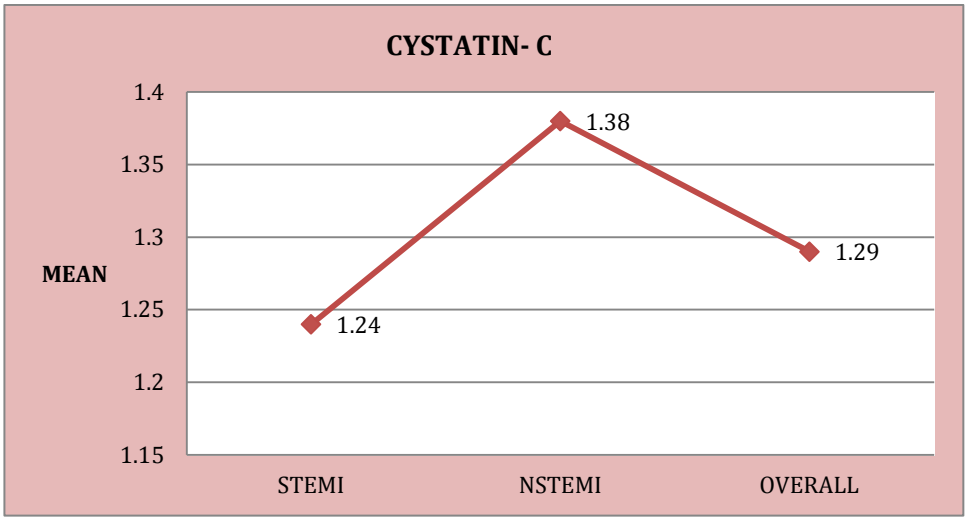

Table: 7 Relationship of cystatic 'C' in relation to gender

Gender	N	Mean	S.D	Independent Sample TGT	
				't'	'P'
Male	24	1.27	.28	.36	.72
Female	16	1.30	.27		

The Mean cystatin 'C' was comparatively higher for females (M=1.30±.27) than males (m=1.27±.28), but the difference is statistically insignificant.

Table: 8 Cystatin in relation to age

Age (in yrs)	N	Mean	S.D	ANOVA	
38-44	3	1.17	.39	.770	.47
45-51	18	1.25	.24		
52-59	19	1.34	.29		

The difference in cystatin in relation to age is studied by ANOVA. The mean cystain was higher for 52-59 years (1.34 ± .29) followed by 45-51 years (M = 1.25 ± .24). But the difference is insignificant (F=.770, P=.47).

Table: 9 The correlation of cystatin 'C' with TIMI

	'r'	'p'
Pearson's correlation	.126	.44

The correlation of cystatin 'c' with TIMI is negative ie when cystatin is more, TIMI is less and vice-versa but the relationship is poor (r=.126, p=.44) and insignificant.

Table: 10 TIMI Score

TIMI SCORE	Number	Percentage	Mean	S.D
1	12	30	2.20	.99
2	12	30		
3	12	30		
4	4	10		
Total	40	100		

In TIMI scores 1, 2 and 3 each of 30% were observed. Only 10% had TIMI score of 4. The Mean TIMI score was 2.20 ± .99.

Discussion

Cystatin C is produced by all the nucleated cells, which regulates the activity of cysteine protease, and plays a major role in maintaining the balance

of production and degradation of Extracellular matrix. Cystatin C also affects the phagocytic and chemotactic ability of neutrophil and thereby regulates the inflammatory responses and hence plays a major role in the development of atherosclerosis. Also Extracellular matrix degradation by means of Cystatin C activity and arterial remodeling closely relate to plaque stabilization[8].

The pathophysiology of myocardial infarction is basically the rupture of vulnerable plaque leading to platelet aggregation resulting in coronary thrombosis. Extracellular matrix provides the structural integrity of the plaques, and also participates in several events such as cell migration, proliferation, lipoprotein retention, and thrombosis. An excess of cysteine proteinase over cystatin C results in destruction of Extracellular matrix resulting in plaque more prone to rupture which results in Myocardial Infarction.

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. All the patients had normal thyroid function and no recent surgeries. The age group of all patients were 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 constitutes 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 of age 50 to 59 years old, and suggested a strong relation with CAD independent of renal impairment[4].

Reference ranges of Cystatin C quoted by Kyhse – Anderson et al[5] was 0.61-1.21 mg/L, by Norund et al[6] 0.7-1.21 mg/L[7]. This difference in the range of Cystatin C may be probably due to difference in the calibrated material.

The mean values of Cystatin C for STEMI was 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.

Correlation of Cystatin C among age and gender was also statistically insignificant which concludes that CYSTATIN C was less influenced by age and gender.

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.

Conclusion

CYSTATIN C to be considered as a risk factor for Acute Myocardial Infarction in patients with normal renal function.

Cystatin C influences the pathogenesis of Myocardial Infarction by regulating inflammation thereby promoting atherosclerosis.

Cystatin C being less influenced by age, gender, and muscle mass and thus a better indicator of risk of various cardiovascular events especially Myocardial Infarction.

Bibliography

1. Capewell S, McMurray J. Chest pains-please admit: is there an alternative? A rapid Cardiological assessment service may prevent unnecessary admissions.Br Med.J.2000; 320:951-52.
2. Nagesh CM, Roy A. Role of biomarkers in risk stratification of acute coronary syndrome .Indian J Med Res. 2010; 132(5): 627–633.
3. Sarnak MJ, Katz R, Stehman-Breen CO, Fried LF, Jenny NS, Psaty BM,et al.

Cystatin C Concentration as a Risk Factor for Heart Failure in Older Adults. Ann Intern Med. 2005; 142: 497-505.

4. Luc G, Bard JM, Lesueur C, Arveiler D, Evans A, Amouyel P, Ferrieres J, Juhan-Vague I, Fruchart JC, Ducimetiere P: Plasma cystatin-C and development of coronary heart disease: The PRIME Study. Atherosclerosis. 2006, 185:375–380.
5. Kyhse–Andersen J, Schmidt C, Nordin G, Anderson B, Nilsson Ehle, et al. Serum Cystatin C, determined by a rapid, automated, particle – enhanced turbidometric method is a better marker than serum creatinine for glomerular filtration rate. Clin. Chem. 1994; 40:1921-1926. [PubMed]
6. Norfund L, Fex G., Lande J, Von Schenck H, Nilsson JE, et al. Reference intervals for the glomerular filtration rate and cell – proliferation markers; Serum /cystatin C and serum b2 microglobulin I cystatin C ratio. Scand. J. Clin.Lab Invest 1997; 57: 463-470. [PubMed]
7. Pergande M, Jung K. Sandwich enzyme immuno assay of cystatin C in serum with commercially available antibodies. Clin chem 1993; 39: 1885-1890.
8. Moushumi Lodh, Ashok Parida, et al Cystatin C in ACS, EJIFCC 2013 Jul; 24(2): 61–67. Published online 2013 Jul 16.