ORIGINAL ARTICLE

Prevalence, Determinants and Clinical Significance of Cardiac Troponin-I Elevation among Individuals with Hypertensive Emergency: A Prospective Observational Study

Kapil Gupta[1], Madhu Kiran[2], Sushant Chhabra[3], Mahish Mehta[4], Nitesh Kumar[5]

Abstract

Introduction: Cardiac troponin-I (cTnI) elevation release during hypertensive emergencies (HEs) is a frequent epiphenomenon that may tangle management of individuals being treated for HEs. The primary objective of this study was to determine the prevalence, determinants, and clinical significance of cTnI elevation and secondary objective was to find out the prognostic significance of cTnI elevation in patients admitted for HE in the emergency department (ED) of a tertiary care hospital.

Methodology: The investigator has employed the quantitative research approach with a prospective observational descriptive design. The population of this study comprised of 205 adults, which included both males and females, who were more than or 18 years of age. The subjects were selected by non-probability purposive sampling technique. The study was conducted from August 2015 to December 2016 (16 months). Ethical permission was obtained from the Institutional Ethics Committee (IEC), Max Super Speciality Hospital, Saket, New Delhi and well-informed written consents were taken from the subjects. The analysis of data was done with the help of SPSS, version 17.0.

Results: Out of 205 patients in the study, cTnI elevation was found in 102 patients (49.8%). Moreover, there was increased duration of stay in the hospital in patient with elevated cTnI level with mean duration stay 1.55 $\pm$ 0.82 (p <0.001). In addition, cTnI elevation was associated with increased mortality, 11 out of 102 in an elevated cTnI group (10.8%) with p <0.002.

Conclusion: It was found that cTnI elevation in individuals affected by various clinical factors. The authors highlighted a high frequency of mortality among the individuals presented with HE with elevated cTnI level, whereas the presence of cTnI was associated with greater odds of death.

Keywords: Cardiac troponin-I, Emergency department, Hypertensive emergency, Patients.

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Introduction

Hypertensive emergencies are characterized by severe elevations in blood pressure (BP) (>180/120 mm Hg), complicated by new or worsening target organ dysfunction and requiring immediate reduction in BP to limit end-organ damage.[1] As per the report of World Health Organization (WHO), 1.13 billion people have hypertension, and among them, two-third are living in low- and middle-income nations. The WHO has stated that hypertension is a major reason of premature deaths at global level.[2] By the end of 2025, the prevalence of hypertension in Indian males and females will be 22.9 and 23.6%, respectively.[3] Acute HEs are found most commonly in patients with known hypertension who fail to adhere with antihypertensive therapy regimen. Although HEs were reported to represent as many as 3% of ED visits in one study, more recent study ranks HEs as accounting for between 0.5 and 0.6% of ED visits.[4] The essential hypertension accounts for 20–30% of malignant hypertension. However, essential hypertension is the predominant cause of malignant hypertension, accounting for approximately 82% of all cases.[5] As per American and European guidelines, troponin assay is the preferred biomarker for the diagnosis of acute myocardial infarction. Troponin levels are measured in patients presenting to the ED, not only for chest pain but also for a wide variation of presentations often.[6] Cardiac troponins are considered as the key biomarkers for the diagnosis of acute myocardial infarction in the ED. Moreover, cardiac troponins are also important in stratum of other cardiac disorders, that is, ischemic heart disease, coronary syndrome. The biomarker has a significant role in the diagnosis of cardiac disorder such as acute myocardial infarction when the clinical presentation and electrocardiogram (ECG) results do not indicate a comprehensive diagnosis.[7] In patients without suspected acute coronary syndrome, an increased cTn concentration is common in the ED. The majority of an increased cTn was prevalent in myocardial injuries compared to myocardial infarction.[8] In the ED, lots of people have elevated troponin concentrations, without cardiac disorders. While troponin is cardiac specific, it may be elevated due to acute non-cardiac clinical conditions and significant impact on outcome and prognosis. Cardiac troponin levels can be increased in various conditions such as

[1,3,4]Department of Emergency Medicine, HCMCT Manipal Hospitals, Dwarka, New Delhi, India

[2]Department of Emergency Medicine, Shanti Ram Medical College and General Hospital, Kurnool, Andhra Pradesh, India

[5]Department of Emergency Medicine, Jodhpur, Rajasthan, India

Corresponding Author: Kapil Gupta, Department of Emergency Medicine, HCMCT Manipal Hospitals, Dwarka, New Delhi, India, Phone: +91 9716875562, e-mail: kapilg51@gmail.com

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infection, sepsis, kidney, pulmonary, neurological, and critically ill patients without evidence of myocardial ischemia.[9–11] For the accurate interpretation of clinical findings, an adequate level of troponin depends on the patient's characteristics.[12] cTnI elevation during HEs is a frequent epiphenomenon that may tangle the management of individuals being treated for HEs. It is reported that cTnI elevation in individuals with a HE is affected by a variety of clinical factors. The mortality in patients with HE has a high incidence rate.[6,13] In myocardial injuries, cardiac troponins are recommended for prompt and accurate diagnosis. In clinical practices, the use of high-sensitivity troponin assays has been increased in recent time. Various studies have highlighted that there should be a specific cut-offs for troponin assay according to age, gender, and comorbid diseases conditions.[14] In suspected acute coronary syndrome patients, cTn is a crucial indicator of hospitalization. Cardiac troponin is strongly associated with increased risk of heart failure.[15,16]

Several direct and indirect retrospective studies are done on cTnI, mostly including older age-group people with small sample size. The clinical utility of cTnI in HE is currently lacking and the clinical variables which has got direct relationship with cTnI elevation in HE has not established yet.

This study was sought to determine the prevalence, determinants, and clinical significance of cTnI elevation and to find out the prognostic significance of cTnI elevation in patients admitted for HE in the ED of tertiary care hospital.

Objectives of the Study

The primary objective of this study was to determine the prevalence, determinants, and clinical significance of cTnI elevation and secondary objective was to find out the prognostic significance of cTnI elevation in patients admitted for HE in the ED of a tertiary care hospital.

Methodology

The investigators have employed the quantitative research approach with prospective observational descriptive design. The population of the current study consisted of 205 adults that included both male and females, who were more than or 18 years of age. The subjects were selected by non-probability purposive sampling technique, which decided the subjects who met the inclusion criteria. The study was conducted from August 2015 to December 2016 (16 months). The patients with acute coronary syndrome or ST elevation myocardial infraction (STEMI), non ST elevation myocardial infraction (NSTEMI), obstructive coronary artery disease, cocaine abuse, severe aortic stenosis, pericarditis, pulmonary embolism, pregnancy, supraventricular tachycardia, and chronic kidney disease were excluded from this study. The criteria for admission, every HE presenting to the ED required an admission. The admission diagnosis of the subjects was hypertensive crisis. cTnI evaluation are usually done as a part of routine evaluation in patients attending HE. No extra cost was bore by the patient for the study purposes. The investigations, that is, echocardiography (ECHO), left ventricular ejection fraction (LVEF) and ECG were done as a part of routine investigations in the ED. The ECHO and LVEF were done bedside by the on-call cardiologist and the calculation was done by eyeballing method. The subjects were stratified into the following two groups: Elevated cTnI and normal cTnI levels. Ethical permission was taken from the ethical committee and well-informed written consents were taken from the subjects. Anonymity and confidentiality of the subjects were maintained while carrying out the study.

Statistical Analysis

The subjects were stratified into two groups: Elevated cTnI and normal cTnI levels and comparison of two groups was done using Student's *t*-test. As other factors such as diabetes mellitus, hypercholesterolemia, elevated blood urea nitrogen (BUN), and tachycardia may also be associated with an elevation of cTnI in HE patients, based on the previous hypothesis and research, various quantitative and qualitative variables were analyzed using Chi-squared test or Fisher's exact test to calculate the determinants of cTnI elevation in HEs. The statistical testing was conducted with the statistical package for the social science system version SPSS 17.0. Continuous variables are presented as mean ± SD, and the categorical variables are presented as absolute numbers and percentage. The comparison of normally distributed continuous variables between the groups was performed using Student's *t*-test. Nominal categorical data between the groups were compared using Chi-squared test or Fisher's exact test as appropriate; $p < 0.05$ was considered statistically significant.

Results

Out of 205 patients in the study, cTnI elevation was found in 102 patients (49.8%). As listed in Table 1, the majority of the population belonged to the age above 50 years with the mean age of 56.10 ± 13.84 in normal cTnI level and 57.02 ± 15.22 in elevated cTnI level ($p = 0.650$). There was an increased frequency of cTnI level in males as compared to females. In males, 55% in patients with normal and 63% in elevated cTnI patients whereas the frequency in females was 48% in normal and 39% in elevated cTnI patients. In addition, Table 2 showed that there was an increased duration of stay in the hospital in patient with elevated cTnI level with mean duration stay 1.55 days ± 0.82 ($p < 0.001$). There was an increased mean value of BUN 64.62 ± 21.92 mg in patients with elevated cTnI as compared with normal cTnI 31.16 ± 12.10 mg. Similarly, the serum creatinine level in elevated cTnI 2.07 ± 0.86 mg as compared to the normal cTnI 0.89 ± 0.42 mg (Table 3). Analysis showed in Table 4 that cTnI elevation was associated with an increased mortality; 11 out of 102 in elevated cTnI group (10.8%) with $p < 0.002$.

Discussion

Our study sought to determine the prevalence of cTnI elevation in the patient admitted with HE and determine the factors associated with elevation of cTnI and the clinical significance of elevation of cTnI on subsequent outcomes. In our study, we found that out of 205 study populations, the prevalence of elevated cTnI was 102 (49.8%). In this context, Afonso et al.[13] also revealed that an elevation of cTnI was common in one-third of the studied population. We demonstrated in our study that there is an increased frequency of cTnI elevation in increasing age-group mostly above 50 years of age with the mean age of 57.02 ± 15.22 years. Despite the increasing frequency of cTnI in the increased age-group, there is statistical significance seen between cTnI elevation and different age-groups. Although the study conducted by Afonso et al.[13] showed statistical significance of cTnI elevation in patients admitted for HE. AlQassas et al.[10] and Lee et al.[8] stated that an elevated level of cTnI was not associated with age. cTnI was found to have an independent prognostic factor and its elevation was

Table 1: Demographic and clinical profile of the subjects ($n = 205$)

Sl. No.	*Variables*		*Frequency*	*%*
1	Age (years)	21–30	07	3.41
		31–40	26	12.68
		41–50	38	18.54
		51–60	53	25.85
		61–70	46	22.44
		>70	35	17.07
2	Gender	Female	87	42.43
		Male	118	57.56
3	Duration of stay (days)	1	165	80.49
		2	17	08.29
		3	22	10.73
		4	01	0.49
4	Diabetes	No	40	19.51
		Yes	165	80.49
5	Hypertension	No	01	0.49
		Yes	204	99.51
6	Elevated cholesterol	No	134	65.37
		Yes	71	34.63
7	Thyroid disease	No	168	81.95
		Yes	37	18.05
8	Smoking	No	155	75.60
		Yes	50	24.40
9	Alcohol	No	143	69.75
		Yes	62	30.25
10	Pulmonary edema	No	123	60
		Yes	82	40
11	LVEF (<55%)	No	119	58.05
		Yes	86	41.95
12	LVH	No	126	61.46
		Yes	79	38.54
13	Need for intubation	No	157	76.59
		Yes	48	23.41
14	Mortality	No	194	94.63
		Yes	11	05.37

Table 2: Clinical characteristics and its correlation with cardiac troponin-I ($n = 205$)

	Troponin-I		
	Normal	*Elevated*	
Variables	*Mean ± SD*	*Mean ± SD*	*p*
Age (years)	56.10 ± 13.84	57.02 ± 15.22	0.650
DOS (days)	1.08 ± 0.39	1.55 ± 0.82	<0.001
Heart rate	132.46 ± 10.86	142.76 ± 11.08	<0.001
SBP	212.83 ± 21.57	229.41± 22.14	<0.001
DBP	137.80 ± 10.63	143.95 ± 12.55	<0.001
MAP	162.40 ± 8.93	171.64 ± 12.27	<0.001

associated with poor prognosis.[17] In our study, there is a statistical increased duration of stay at hospital among the study population with the elevated cTnI as compared to the normal cTnI with mean duration of stay in elevated cTnI 1.55 ± 0.82 days with p <0.001. The duration of hospital stay is varying in the study population with the maximum frequency in 1 day to minimum 4 days. Various clinical comorbidities such as DM, HTN, COPD, hypercholesterolemia, thyroid disease, smoking, and alcohol intake were analyzed among the study population during the study period. It was found that comorbidities such as diabetes mellitus, hypertension, chronic obstructive pulmonary disease, and hypercholesterolemia has no statistical correlation with cTnI elevation in setting of HE. Although the study by Mahajan et al.[18] reported a significant association with elevated cTnI in the study population, other comorbidities such as thyroid disease, smoking, and alcohol were significant with elevation of cTnI.

Table 3: Correlation of laboratory characteristics between normal and elevated troponin-I amongst study population ($n = 205$)

	Troponin-I		
	Normal	*Elevated*	
Laboratory characteristics	*Mean ± SD*	*Mean ± SD*	*p*
BUN	31.16 ± 12.10	64.62 ± 21.92	<0.001
Serum creatinine	0.89 ± 0.42	2.07 ± 0.86	<0.001
Total protein	6.88 ± 0.16	6.76 ± 0.24	<0.001
Direct bilirubin	0.19 ± 0.06	0.196 ± 0.09	0.555
Indirect bilirubin	0.78 ± 0.12	0.82 ± 0.11	0.013
SGPT	38.50 ± 6.39	39.80 ± 9.57	0.254
SGOT	41.51 ± 6.99	45.76 ± 11.65	0.002
ALP	68.34 ± 15.27	73.60 ± 18.80	0.029
Albumin	4.16 ± 0.33	4.06 ± 0.24	0.012
HbA_1c	6.74 ± 0.23	6.96 ± 0.38	<0.001
Serum uric acid	2.77 ± 1.54	3.76 ± 1.78	<0.001
C-reactive protein	0.67 ± 2.89	1.89 ± 071	<0.001

Clinical characteristics such as heart rate, BP, and mean arterial pressure were also analyzed in the study population to search out the correlation between the normal cTnI and the elevated cTnI group. It was found that the significant correlation exists between these clinical characteristics and elevated cTnI. The mean values of the following characteristics among the population with normal and elevation cTnI levels are heart rate (132.46 ± 10.86, 142.76 ± 11.08), systolic BP (212.83 ± 21.57, 229.41 ± 22.14), diastolic BP (137.80 ± 10.63, 143.95 ± 12.55), mean arterial pressure (162.40 ± 8.93, 171.64 ± 12.27) with p <0.001. These findings have been found to be consistent with the findings reported in some of the previous studies done by Alcalai et al.[19] and Korff et al.[20] An elevation of BUN levels in the setting of HE is likely the result of vasomotor alterations in renal blood flow and activation of renin angiotensin–aldosterone system (RAAS). So, the worsening in BUN profile could reflect hemodynamic and neurohormonal alterations while serum creatinine only reflects the renal status.[21–23] Likewise laboratory variables such as BUN, serum creatinine observed in our study found to be statistically significant with elevation of cTnI. The mean value for BUN 64.62 ± 21.92 and serum creatinine 2.07 ± 0.86 with p <0.001 found in the study population with an elevated cTnI level. So, our analysis demonstrated a significant correlation between cTnI elevation and BUN and serum creatinine. Lee et al. also highlighted that an increased TnI is significantly associated with an increased serum creatinine.[8] Marie et al. concluded that an elevated levels of cTnI were common in patients with non-cardiogenic shock.[24] Decreased renal function, higher body mass index, elevated leukocyte count, reduced left ventricular systolic ejection fraction, higher lactate level, and ST-segment depression were significantly

Table 4: Correlation between selected variables and normal and elevated troponin-I level ($n = 205$)

			Troponin-I Level				
			Normal		*Elevated*		
Sl. No.	*Variables*		*Frequency*	*%*	*Frequency*	*%*	*p*
1	Age (years)	21–30	1	1.0	6	5.9	0.242
		31–40	16	15.5	10	9.8	
		41–50	22	21.4	16	15.7	
		51–60	26	25.2	27	26.5	
		61–70	20	19.4	26	25.5	
		>70	18	17.5	17	16.7	
2	Gender	Female	48	46.6	39	38.2	0.226
		Male	55	53.4	63	61.8	
3	Duration of stay (days)	1	99	96.1	66	`64.7	<0.001
		2	0	0.0	17	16.7	
		3	4	3.9	18	17.6	
		4	0	0.0	1	1.0	
4	Diabetes	No	17	16.5	23	22.5	0.275
		Yes	86	83.5	79	77.5	
5	Hypertension	No	1	1.0	0	0.0	1.000
		Yes	102	99.0	102	100.0	
6	Elevated cholesterol	No	71	68.9	63	61.8	0.281
		Yes	32	31.1	39	38.2	
7	Thyroid disease	No	92	89.3	76	74.5	0.006
		Yes	11	10.7	26	25.5	
8	Smoking	No	86	83.5	69	67.6	0.008
		Yes	17	16.5	33	32.4	
9	Alcohol	No	81	78.6	62	60.8	0.005
		Yes	22	21.4	40	39.2	
10	Pulmonary edema	No	102	99.0	21	20.6	<0.001
		Yes	1	1.0	81	79.4	
11	LVEF (<55%)	No	101	98.1	18	17.6	<0.001
		Yes	2	1.9	84	82.4	
12	LVH	No	102	99.0	24	23.5	<0.001
		Yes	1	1.0	78	76.5	
13	Need for intubation	No	103	100.0	54	52.9	<0.001
		Yes	0	0.0	48	47.1	
14	Mortality	No	103	100.0	91	89.2	<0.001
		Yes	0	0.0	11	10.8	

associated with elevated level of cTn. Our data are consistent with the study. Some other laboratory variables such as total protein, indirect bilirubin, serum glutamic-oxaloacetic transaminase (SGOT), alkaline phosphatase (ALP), and albumin have also been associated with an elevation of cTnI level in the study population is found to be significantly correlated with $p < 0.05$.

In our study, analysis showed a mean value for HbA_1c (6.96 ± 0.38), fasting blood sugar [FBS (117.20 ± 25.17)], post-prandial blood sugar [PPBS (219.43 ± 62.83)], high-sensitivity C-reactive protein [hsCRP (1.89 ± 071)] was found to be clinically significant with an elevation cTnI. Khan et al. highlighted that the findings of ECHO showed that patients with high TnI level had low LVEF (<35%).[25] This finding is consistent with this study. Pulmonary edema may accompany with severe hypertensive states and has been attributed to ventricular dysfunction.[26] Our analysis showed any precipitating factors leading to increase in left ventricular filling pressure, subendocardial ischemia, and hypoxia could be responsible for high prevalence of cTnI elevation in HE and pulmonary edema or need for mechanical intubation.[27] Therefore, these patients frequently develop left ventricular hypertrophy and transient left ventricular dysfunction. So, these may explain the current observation and it has been observed in several previous studies also.[21] The present study revealed that TnI has a significant correlation with LVEF while Khan et al.[25] showed that the LVEF levels had a negative correlation with the levels of TnI ($r = -0.5394$, $p = 0.001$). In addition, the normal cTnI group has no death and the elevated cTnI group has 10.8% mortality with $p < 0.002$. So, the increased frequency of death was associated with cTnI elevation in HE. In this context, Amit et al. reported that a positive troponin result was associated with a clinically important increased mortality.[6] So, overall, this study also characterized previously undocumented determinants of cTnI elevation in HE.

Conclusion

An elevation of cTnI in individuals with HE is a common phenomenon that might frequently complicate the management of HE. It was found that the cTnI elevation in individuals presenting with HE in the ED is affected by various clinical factors apart from those previously believed to be responsible for the release of cTnI in HE. We observed a high frequency of mortality among the individuals presented with HE with elevated cTnI level, so the presence of elevated cTnI was associated with greater odds of death.

Limitations of the Study

- The present study was conducted in a single ED.
- The sampling technique was non-probability purposive sampling.

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Orcid

Kapil Gupta https://orcid.org/0000-0001-9150-1019
Madhu Kiran https://orcid.org/0000-0001-8068-7137
Sushant Chhabra https://orcid.org/0000-0001-5781-138X
Mahish Mehta https://orcid.org/0000-0001-6897-7369
Nitesh Kumar https://orcid.org/0000-0001-6075-534X

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