Original Article

Diagnostic Accuracy of Cardiac Biomarkers in Chronic Kidney Disease Patients for Detecting Occurrence of Acute Coronary Syndrome: A Comparative Study

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Abstract

Introduction: The diagnosis of coronary artery disease or acute coronary syndrome (ACS) is difficult in patients of chronic kidney disease (CKD). This study was planned to evaluate the role of cardiac biomarkers in diagnosis of ACS in such patients. To evaluate the role of biochemical cardiac markers in the diagnosis of ACS in patients with CKD and to study the relation of stage of kidney disease and biochemical cardiac biomarkers. **Materials and Methods:** Atotal of 350 patients in different stages of CKD were enrolled and subjected to measurement of blood levels of creatine kinase (CK) MB and Troponin I (Trop I). The data were analyzed by dividing subjects into groups based on positivity of biomarkers, presence of electrocardiogram (ECG) changes, and stage of CKD. **Results: S**ensitivity of CK MB and Trop I was 60.81% and 56.76% and specificity was 72.1% and 83.33%, respectively. Although both showed low positive predictive values, the negative predictive value of both CK MB and Trop I was good. Stage of CKD did not significantly affect the level or positivity of the biomarker in patients with ECG changes. **Conclusions:** CK MB and Trop I potentially rule out the probability of ACS in patients showing negative test results, which should always be interpreted in light of ECG changes in CKD patients.

Keywords: Acute coronary syndrome, cardiac enzymes, chronic kidney disease, creatine kinase MB, Troponin I

Introduction

Patients with chronic kidney disease (CKD) often have cardiac comorbidities and acute or chronic symptoms that may represent heart failure or an acute myocardial infarction (AMI).[1] The prevalence of coronary artery disease (CAD) in CKD patients has been estimated to vary from 15% to 73%.[2] Patients with CKD are at high risk for acute coronary syndrome (ACS) and cardiovascular death, since they are predisposed to accelerated atherosclerosis compared to general population.[3]

Acute coronary events have been noted to occur during hemodialysis. High prevalence of left ventricular hypertrophy (LVH), reduced coronary vasodilator reserve, underlying CAD, anemia, and hemodialysis can simultaneously reduce myocardial oxygen delivery at a time when the increased heart rate is producing a greater myocardial oxygen requirement. This mismatch between oxygen supply and demand may account not only for the many clinically apparent cardiac events occurring during dialysis but also for episodes of silent ischemia.[4]

The diagnosis of myocardial infarction is quite difficult in these patients as they exhibit baseline changes in electrocardiogram (ECG), echocardiogram, and atypical cardiac symptoms and are not fit for exercise tolerance test. Hence, the diagnosis is made by biochemical markers.[5] Cardiac biomarkers of necrosis such as creatine kinase (CK)-MB, myoglobin, and cardiac troponins are difficult to interpret

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in patients with CKD because they may be elevated in the absence of AMI.[6]

It has been clearly established that troponin levels are increased in patients with renal failure, even in the absence of clinically suspected myocardial ischemia.[7]

It is important to recognize that despite the several theories of why troponin levels are elevated in patients with CKD, the significance of this finding should not be easily dismissed. Numerous studies have shown that there is a strong prognostic implication of elevated troponin levels in cardiology patients and in patients with CKD. Elevated cTnT and cTnI have both been shown to be predictive of increased risk of mortality and cardiovascular disease events.[8,9]

Early identification of patients who have end-stage renal disease (ESRD) and are at a heightened cardiovascular risk may facilitate timely action and more aggressive management.[10] Cardiac biomarkers are often required to help clinical assessment and to increase the ability to early identify "vulnerable" patients of ESRD with cardiovascular risk.

Objectives

1. To evaluate the role of biochemical cardiac markers in the diagnosis of ACS in patients with CKD
2. To study the relation of stage of kidney disease and biochemical cardiac biomarkers.

Materials and Methods

The study was carried out after approval from the Institutional Ethics Committee, G.G.S. Medical College and Hospital, Faridkot, and Faculty of Medical Sciences, BFUHS, vide letter no. BFUHS/2K18p-TH/14434. Three hundred fifty patients with CKD, in the age group of 20–70 years, presenting to the Medicine Department of G.G.S Medical Hospital, were enrolled in this cross-sectional study by consecutive sampling after obtaining their written informed consent. The study was conducted from April 2018 to September 2019. These included patients in all stages of CKD, both on hemodialysis or not on hemodialysis. Patients with trauma and muscular diseases (muscular dystrophies and dermatomyositis) were excluded from the study. Demographic details of the patient, symptoms, relevant history such as diabetes and hypertension and findings of physical examination were recorded.

Investigations carried out on every patient included hemoglobin, serum creatinine, blood urea, serum electrolytes, and ECG. Estimated glomerular filtration rate (eGFR) was calculated for each patient using both epidemiology (EPI) and MDRD equation. No significant difference was found in staging of CKD by applying both formulas. However, we have used EPI formula for calculation of results.

Cardiac biomarkers such as CPK-MB and Troponin I (Trop I) were tested. Trop I was measured with ichromax Tn-I using fluorescence immunoassay. CK-MB was measured using CK (NAC act.) KIT using MOD. IFCC method. A cutoff value of 25 IU/L for CK-MB and <0.10 ng/ml for Trop-I was considered for declaring the result as positive for elevated CK-MB and Trop I, respectively.

Statistical analysis

Categorical variables were presented as number and percentage (%) and continuous variables were presented as mean ± standard deviation and median. Normality of data was tested by Kolmogorov–Smirnov test. If the normality was rejected, nonparametric test was used. Quantitative variables were compared using Mann–Whitney test (as the datasets were not normally distributed) between the two groups and Kruskal–Wallis test between more than two groups. Association for qualitative variables was assessed using Chi-square test. Spearman's rank correlation coefficient was used to assess the correlation of various parameters with CK-MB and Trop I. Diagnostic accuracy was analyzed by calculating sensitivity, specificity, predictive values, and area under the receiver operating characteristic (ROC) curve. $P < 0.05$ was considered statistically significant. The data were entered into an MS Excel spreadsheet and analysis was done using IBM SPSS statistics for windows, version 21.0. Armonk,NY: IBM Corp.

Results

In the present study, majority (27.43%) of the patients belonged to 61–70 years followed by 41–50 years (26%). Around 17% of the patients belonged to 51–60 years of age group and 14.29% of the patients belonged to 31–40 years. Very few patients were ≤20 years. The mean value of age of study subjects was 48.91 ± 15.13 years. Majority of the patients (211, 60.29%) were male and only 139 out of 350 patients were female. The mean value of diastolic blood pressure and systolic blood pressure was 89.04 ± 11.98 mmHg and 141.7 ± 22.59 mmHg, respectively, and the median (interquartile range) was 90 (80–100) mmHg and 140 (130–150) mmHg, respectively. A total 173 (49.43%) patients are hypertensive [Table 1].

The mean value of hemoglobin was 7.74 ± 1.52 mg% and the median (interquartile range) was 7.8 (6.9–8.5) mg%. The mean value of blood urea was 153.73 ± 57.61 mg% and the median (interquartile range) was 145 (120–179) mg%. The

Table 1: Descriptive statistics for study population

	Mean±SD	Median (IQR)
Age (years)	48.91±15.13	50 (40-63)
Gender (female %/male %)	39.7/60.3	-
Hemoglobin (g %)	7.74±1.52	7.8 (6.900-8.500)
Diastolic blood pressure (mmHg)	89.04±11.98	90 (80-100)
Systolic blood pressure (mmHg)	141.7±22.59	140 (130-150)
Blood urea (mg %)	153.73±57.61	145 (120-179)
Serum creatinine (mg %)	5.57±3	4.8 (3.400-6.800)
ECG findings (number of negative/positive)	276/74	-
Stage of CKD (3/4/5): Number of subjects	18/105/227	-

SD: Standard deviation, ECG: Electrocardiogram, CKD: Chronic kidney disease, IQR: Interquartile range

mean value of serum creatinine was 5.57 ± 3 mg% and the median (interquartile range) was 4.8 (3.4–6.8) mg%.

Majority (64.86%) of our patients were in Stage-5, 30% of the patients were in Stage-4, and 18 (5.14%) out of 350 had Stage-3 CKD. None was found to be in Stages 1 or 2.

ECG findings of 78.86% of the patients were negative for any changes suggestive of ACS. Only 74 (21.14%) patients had positive ECG findings. Out of 74 patients, 25 patients had ST depression followed by 17 patients each with T wave inversion and Tall T waves. Few patients had other findings, which included atrial fibrillation, atrial premature contraction, ventricular extrasystole, and bundle branch blocks.

In the present study, majority, 228 (65.14%), of the patients had normal CK-MB and 122 (34.85%) out of 350 patients had elevated CK-MB. The mean value of CK-MB of study subjects was 29.12 ± 24.08 IU/L.

The association of positivity of CK-MB test with stages of CKD was not found to be significant ($P > 0.05$). Furthermore, the distribution of positive CK-MB was comparable between the various stages; 16.67% in Stage 3, 29.52% in Stage 4, and 38.77% in Stage 5 [Table 2]. The mean value of CK MB in Stage 3 was 19.28 ± 5.78 IU/L, in Stage 4 was 27.33 ± 23.16 IU/L, and in Stage 5 was 30.72 ± 25.18 IU/L. It was evident that the mean value of CK-MB was lower in Stage 3, but the difference was not statistically significant.

The association of CK-MB with study subjects of CKD with positive ECG findings was not found to be significant ($P > .05$). The mean value of CK MB in Stage 3 was 23 ± 0 IU/L, in Stage 4 was 52.53 ± 48.38 IU/L, and in Stage 5 was 39.71 ± 24.99 IU/L. It was evident that the mean value of CK-MB was lower in Stage 3, but the difference was not statistically significant. The association of CK-MB with stage in study subjects without suggestive ECG findings was also not found significant ($P > 0.05$). The mean value of CK MB in Stage 3 was 19.06 ± 5.88 IU/L, in Stage 4 was 23.13 ± 11.57 IU/L, and in Stage 5 was 27.64 ± 24.58 IU/L. It was evident that the mean value of CK-MB was lower in Stage 3, but the difference was not statistically significant [Table 3].

Around 75% of the patients had negative Trop I and 88 patients out of 350 had positive Trop I. The mean value of Trop I of study subjects was 0.97 ± 2.2. Significant association was seen between Trop I and stages ($P < .05$). 11.11% of the patients with Stage 3 had positive trop I as compared to 16.19% of the patients in Stage 4 and 30.40% of the patients in Stage 5. It can be concluded that proportion of the patients with positive Trop I finding increases significantly with the increase in the stage of CKD [Table 2]. The mean value of trop I in patients with Stage 3 was 0.14 ± 0.16 ng/ml, Stage 4 was 0.69 ± 1.65 ng/ml, and Stage 5 was 1.16 ± 2.47 ng/ml. Hence, the mean value of Trop I was significantly higher in advanced stages as compared to the lower stage [Table 3].

The association of Trop I and stage in study subjects with positive ECG findings was not found ($P > 0.05$). The mean value of trop I in Stage 3 was 0.1 ± 0 ng/ml, in Stage 4 was 2.86 ± 3.23 ng/ml, and in Stage 5 was 2.21 ± 3.09 ng/ml. It was evident that the mean value of Trop I was lower in Stage 3, but the difference was not statistically significant. No significant association was seen between Trop I and stage in study subjects without suggestive ECG findings ($P > 0.05$). The mean value of Trop I in Stage 3 was 0.14 ± 0.17 ng/ml, in Stage 4 was 0.32 ± 0.78 ng/ml, and in Stage 5 was 0.81 ± 2.11 ng/ml. It was evident that the mean value of Trop I was lower in Stage 3, but the difference was not statistically significant [Table 3].

Significant association was seen between stages of CKD and ECG findings ($P < 0.05$). 78.38% of patients with positive ECG findings were in Stage 5 as compared to 61.23% of the patients with negative ECG findings. Hence, it can be concluded that patients with positive ECG finding have significantly higher chances of being in advanced stage CKD as compared to the patients without ECG findings [Figure 1].

Significant association was seen between CK MB and ECG findings ($P < 0.05$). 60.81% of the patients with positive ECG findings had positive CK-MB as compared to 27.90% of the patients with negative ECG findings. It can be concluded that the patients with positive ECG findings has significantly higher chances of positive CK MB. The mean value of CK-MB in negative ECG findings was 25.64 ± 20.53 IU/L, which was significantly lower as compared to the patients with positive ECG findings (42.08 ± 31.12 IU/L) [Table 4].

Significant association was seen between Trop I and ECG findings ($P < 0.05$). 56.76% of the patients with positive ECG findings had positive Trop I as compared to 16.67% of

Table 2: Association of creatine kinase-MB and Troponin-I with stages of chronic kidney disease irrespective of electrocardiogram changes

Biomarker status	Stage of CKD			Total, *n* (%)	*P*
	3 (*n*=18), *n* (%)	4 (*n*=105), *n* (%)	5 (*n*=227), *n* (%)		
Creatine kinase-MB					
Negative	15 (83.33)	74 (70.48)	139 (61.23)	228 (65.14)	0.065
Positive	3 (16.67)	31 (29.52)	88 (38.77)	122 (34.86)	
Troponin-I					
Negative	16 (88.89)	88 (83.81)	158 (69.60)	262 (74.86)	0.008
Positive	2 (11.11)	17 (16.19)	69 (30.40)	88 (25.14)	

CKD: Chronic kidney disease

Table 3: Comparison of mean values of creatine kinase-MB and Troponin-I in different stages of chronic kidney disease with and without positive electrocardiogram changes

Stage of CKD	Creatine kinase-MB		Troponin-I	
	Mean±SD	Median (IQR)	Mean±SD	Median (IQR)
Irrespective of ECG changes				
3 (*n*=18)	19.28±5.78	18 (16-23)	0.14±0.16	0.1 (0.100-0.100)
4 (*n*=105)	27.33±23.16	20 (17-30)	0.69±1.65	0.1 (0.100-0.100)
5 (*n*=227)	30.72±25.18	22 (15-40)	1.16±2.47	0.1 (0.100-1.155)
P	0.201		0.009	
Positive ECG findings				
3 (*n*=1)	23±0	23 (23-23)	0.1±0	0.1 (0.100-0.100)
4 (*n*=15)	52.53±48.38	34 (23-59)	2.86±3.23	2.3 (0.100-5.565)
5 (*n*=58)	39.71±24.99	34 (20-53)	2.21±3.09	0.9 (0.100-3.400)
P	0.621		0.519	
Nonsuggestive ECG findings				
3 (*n*=17)	19.06±5.88	18 (15-21)	0.14±0.17	0.1 (0.100-0.100)
4 (*n*=19)	23.13±11.57	20 (16-24)	0.32±0.78	0.1 (0.100-0.100)
5 (*n*=169)	27.64±24.58	20 (14-28)	0.81±2.11	0.1 (0.100-0.100)
P	0.539		0.064	

SD: Standard deviation, ECG: Electrocardiogram, CKD: Chronic kidney disease, IQR: Interquartile range

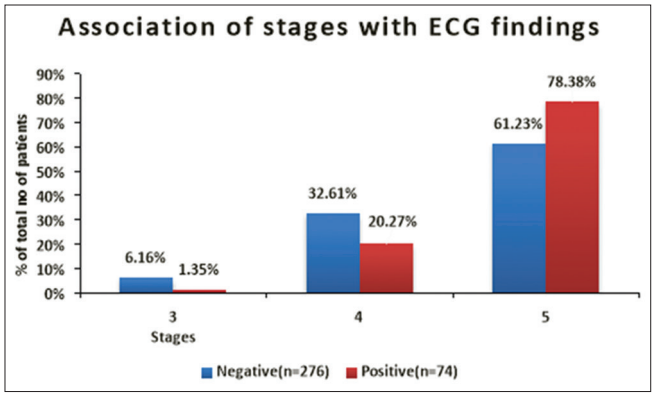

Figure 1: Association of stages of chronic kidney disease with presence of electrocardiogram findings

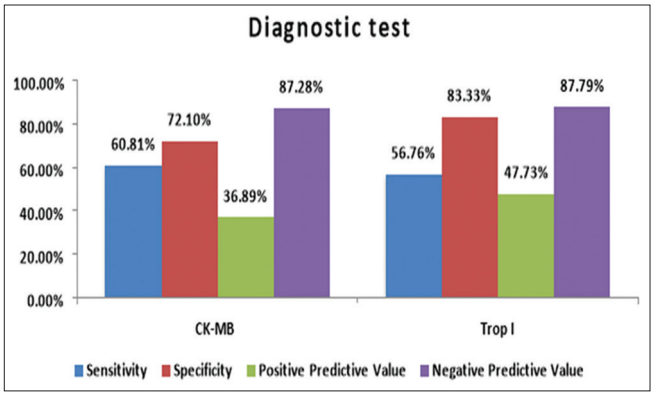

Figure 2: Comparison of diagnostic accuracy of creatine kinase-MB and Troponin I

the patients with negative ECG findings. It can be concluded that the patients with positive ECG findings have significantly higher chances of positive Trop I. The mean value of Trop I in negative ECG findings was 0.61 ± 1.73 ng/ml, which was significantly lower as compared to the patients with positive ECG findings (2.31 ± 3.1 ng/ml).

Sensitivity of CK-MB was 60.81% as compared to 56.76% of Trop I, and on the other hand, specificity of Trop I was more as compared to CK-MB (83.33% vs. 72.1%). This suggests that among patients with positive ECG findings, 60.81% and 56.76% were correctly diagnosed by CK-MB and Trop I, respectively, and among those with nonsuggestive ECG findings, 83.33% and 72.1% were correctly diagnosed by Trop I and CK-MB, respectively. Negative predictive value of both CK-MB and Trop I was quite good; 87.28% of CK-MB and 87.79% of Trop I, whereas positive predictive value was quite low; 36.89% of CK-MB and 47.73% of Trop I [Table 5 and Figure 2].

On ROC analysis, the area under curve (AUC) was found to be 0.665 for CK-MB and 0.7 for TROP-I [Table 5 and Figure 3].

No significant correlation was seen between blood urea and CK-MB or Trop-I. Significant but weak positive correlation was seen between serum creatinine and CK-MB and serum creatinine and Trop-I. Both CK-MB and Trop-I were found to have significant but weak negative correlation with eGFR [Figure 4a and b].

Discussion

In our study, majority of the patients (27.43%) were in the age group of 61–70 years. From this, we can infer that the prevalence of CKD rises with the advancing age. Common causes of CKD include diabetes mellitus and hypertension which are long-standing diseases and show their effects on kidney with increasing duration of the disease. In a similar

Table 4: Association of creatine kinase-MB and Troponin-I with electrocardiogram findings

Biomarker	ECG findings		Total	*P*
	Negative (*n*=276), *n* (%)	Positive (*n*=74), *n* (%)		
Creatine kinase-MB				
Negative	199 (72.10)	29 (39.19)	228 (65.14)	<0.0001
Positive	77 (27.90)	45 (60.81)	122 (34.86)	
Mean±SD	25.64±20.53	42.08±31.12	29.12±24.08	<0.0001
Median (IQR)	20 (14-25)	34 (22-54)	21 (15-34)	
Troponin I				
Negative	230 (83.33)	32 (43.24)	262 (74.86)	<0.0001
Positive	46 (16.67)	42 (56.76)	88 (25.14)	
Mean±SD	0.61±1.73	2.31±3.1	0.97±2.2	<0.0001
Median (IQR)	0.1 (0.100-0.100)	0.9 (0.100-3.700)	0.1 (0.100-0.120)	

SD: Standard deviation, ECG: Electrocardiogram, IQR: Interquartile range

Table 5: Diagnostic accuracy testing of creatine kinase-MB and Troponin I

Diagnostic test	95% CI				
	Sensitivity	Specificity	Positive predictive value	Negative predictive value	AUC
CK-MB	60.81 (48.77-71.96)	72.1 (66.41-77.31)	36.89 (28.33-46.09)	87.28 (82.25-91.31)	0.665 (0.612-0.714)
Troponin I	56.76 (44.72-68.23)	83.33 (78.40-87.53)	47.73 (36.96-58.65)	87.79 (83.20-91.49)	0.7 (0.649-0.748)

CK-MB: Creatine kinase-MB, CI: Confidence interval, AUC: Area under curve

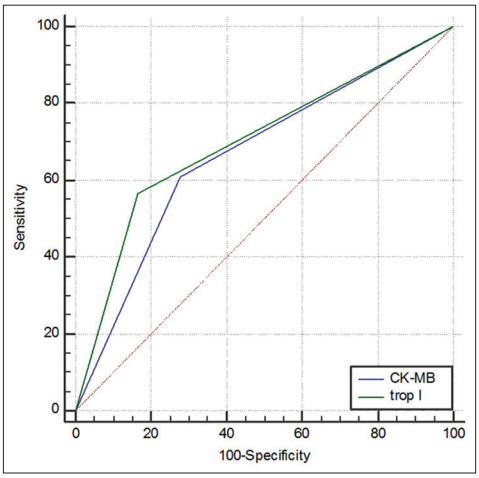

Figure 3: Receiver operating characteristic curve for creatine kinase-MB and Troponin I

study conducted by McClure *et al*., the highest number of patients were more than 80 years of age.[11]

In our study, we found that predominantly patients with CKD are male. However, in previous studies, no such relation has been found between CKD and gender. A study conducted by Bikbov *et al*. showed that prevalence of CKD is more in females.[12] The reason for the difference might be smaller sample size of our study or regional differences in the EPI of disease.

In our study, a majority (64.86%) of patients were of Stage 5 of CKD. In early stages of CKD, mostly patients are asymptomatic. Being a tertiary care hospital, most of the patients admitted in our hospital are usually referred in advanced stages, mainly being Stage 4 or 5.

In our study, most patients were found to be anemic. The mean value of hemoglobin was 7.74 ± 1.52. Ryu *et al*. also concluded in their study that the prevalence of anemia was more in CKD patients with prevalence and severity both increasing as the stage with progresses.[13] Anemia is an important risk factor for myocardial ischemia.

In our study, most of the patients are hypertensive. Ku *et al*. concluded that hypertension and CKD are interlinked. Hypertension leads on worsening of kidney functions, which ultimately again increases the blood pressure.[14] Hypertension and resulting LVH leads to specific ECG changes.

We also found association of stage of CKD with the presence of positive ECG findings, suggesting higher occurrence of cardiovascular abnormalities in advanced stages of the disease. However, ECG changes in CKD patients may present due to LVH and electrolyte imbalance which need to be ruled out using appropriate diagnostic tests.

Chartyn *et al*. conducted a study, in which they concluded that CAD in higher stages of CKD patients usually remains undiagnosed due to lower use of coronary angiography.[15]

In our study, majority of the patients, i.e., 65.14% (228), had negative values of CK-MB and 34.85% (122) of patients had positive values for CK-MB. The elevated CK-MB levels were significantly associated with presence of abnormal ECG.

However, earlier studies have suggested that CK-MB is not a specific marker for diagnosing ACS as it can be

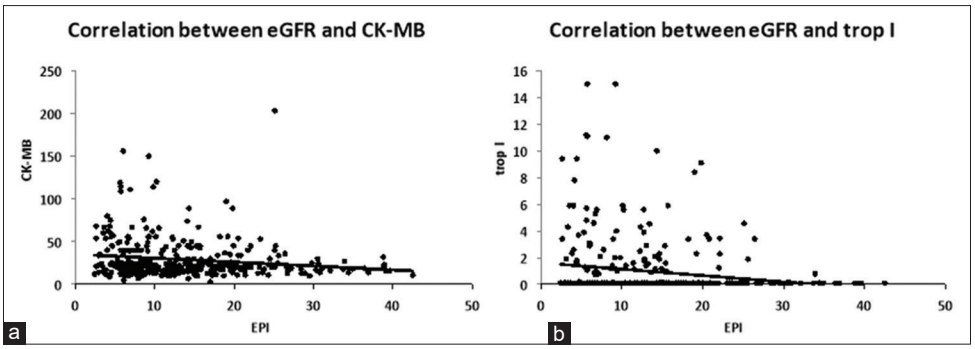

Figure 4: (a) Correlation of creatine kinase-MB with estimated glomerular filtration rate. (b) Correlation of Troponin I with estimated glomerular filtration rate

elevated in renal failure itself. Odum *et al*. conducted a study and concluded that CKD patients can have elevated CK-MB without underlying CAD.[16] DeFilippi and Herzog alsoconcluded that interpretation of cardiac markers in patients of CKD is very difficult.[1]

In our study, we found that CK-MB showed a significant but weak positive correlation with serum creatinine levels and weak negative correlation with eGFR. However, we could not find a significant association of CK-MB levels with different stages of CKD. Furthermore, difference in CK-MB levels in different stages of CKD was not significant in both patients with negative or positive ECG. This suggests that though levels of CK-MB varied in different stages, the increase was not significant enough and positivity of the test was explained by its association with positive ECG findings only.

Various other studies have also found no relation between stages of CKD and CK-MB levels. A study by Quiroga *et al*. concluded that CK MB is a very good marker for stratifying cardiovascular risk in patients on hemodialysis.[17]

In our study, 262 (75%) patients had negative Trop I and 88 (25%) patients out of 350 had positive Trop I levels. Significant association was found between Trop I and stages of CKD. Maximum number of patients who had positive Trop I were in Stage 5. The mean value of Trop I was significantly higher in higher stages as compared to lower stages when studying the total study group, irrespective of the presence or absence of ECG changes. Trop I levels also showed a significant but weak positive correlation with serum creatinine levels and weak negative correlation with eGFR.

Haller *et al*. also conducted one study, in which they concluded that cardiac troponins can be raised in patients of CKD without underlying ischemia, so its significance is low.[18] Kanderian and Francis conducted a study and concluded that troponins are markers of ischemia, but there can be other conditions which cause elevation of troponins one of them is renal failure.[19]

However, our study found a significant association between Trop I and ECG findings. This suggests that if ECG changes are present, there are higher chances of Trop I to become positive. On comparing the Trop I levels among different stages of CKD separately in the two groups, i.e., with positive and with negative ECG abnormalities, the Trop I levels or positivity of the test did not vary significantly. This suggests that the results of Trop I test need to be interpreted in light of ECG changes, and in the presence of abnormal ECG, it has definitive utility.

McCullough *et al*. conducted a study and found that Trop I is still superior to myoglobin and CK-MB in the evaluation of patients with chest and renal dysfunction.[20]

A study conducted by Hussein MM found that although Trop I is elevated in CKD patients, but the values are not significantly high to diagnose ACS. Freda *et al*. also observed that although troponins can be elevated in renal failure in absence of ischemia, its negative predictive value is still high.[21]

Flores *et al*. concluded that cardiac troponins are useful for diagnosing ACS, but their cutoff values are different from general populations.[22]

On comparing the diagnostic accuracy of CK-MB and Trop-I, sensitivity of CK-MB was more (60.81%) as compared to 56.76% of Trop I. Hence, we can infer that among patients with positive ECG findings, 60.81% and 56.76% were correctly diagnosed by CK-MB and Trop I, respectively. On the other hand, specificity of Trop I was more as compared to CK-MB (83.33% vs. 72.1%), that is among patients without any suggestive ECG findings, 83.33% and 72.1% were correctly diagnosed by Trop I and CK-MB, respectively. On ROC analysis, AUC of 0.7 for Trop I and 0.66 for CK-MB suggests optimal ability of the biomarkers to distinguish the two groups.

Negative predictive value of both CK-MB (87.28%) and Trop I (87.79%) was quite good, whereas positive predictive value was quite low for both: 36.89% of CK-MB and 47.73% of Trop I. Reason for low positive predictive values may be low prevalence of ECG abnormalities (21%) in the study group. However, the high negative predictive value indicates high probability that patients with negative tests do not have ACS.

Our study has a limitation that we only assessed ECG for diagnoses of ACS and did not include echocardiography and angiography for establishing the diagnosis of CAD in our protocol. The strength of the study could have been increased if the results were compared with coronary angiography, which is gold standard for diagnosing CAD and ACS. However,

inability to use contrast in patients with renal derangement refrained us from including angiography, both invasive as well as CT, in the study protocol.

Conclusions

The results indicating good specificity and negative predictive value suggest that the cardiac biomarkers, CK-MB and Trop-I, are still promising tools to rule out the occurrence of ACS in the patients with negative test results. Among the two, Trop-I has slightly better diagnostic accuracy.

However, since the sensitivity is low for both the markers, it can be inferred that chances of missing the diagnosis are high. To improve that, combining the different biomarkers or assessing them by sequential measurements may be done in patients. The results of these tests should always be interpreted in light of ECG changes in CKD patients.

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Conflicts of interest

There are no conflicts of interest.

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