ORIGINAL ARTICLE

FREQUENCY OF ELEVATED TROPONIN T IN PATIENTS OF CHRONIC RENAL FAILURE WITHOUT CLINICALLY SUSPECTED ACUTE MYOCARDIAL INFARCTION

Syed Affan Ali, Sumera Kazmi, Mir Jalal-ud-din*, Muhammad Iqbal Qasim, Zahid Gul Jadoon***

Department of Medicine, Abbottabad International Medical College, Abbottabad, *Women Medical College, Abbottabad, **Frontier Medical College, Abbottabad Pakistan

Background: Cardiac Troponins are established markers of myocardial injury; however, they may be elevated in chronic renal failure (CRF) patients even in absence of acute myocardial infarction. The objective of the study was to determine the frequency of elevated Troponin T in patients of chronic renal failure without clinically suspected acute myocardial infarction. **Methods**: This cross-sectional study was conducted at Medical B Unit of Ayub Teaching Hospital, Abbottabad from 16th December 2013 to 16th June 2014. A sample of 117 patients of chronic renal failure was included in the study without any gender discrimination. The patients were defined as known chronic renal failure when renal failure was reported in their past medical history and by estimation of glomerular filtration rate (GFR). Those patients who had raised Troponin T due to any other reason like acute myocardial ischemia (chest pain, electrocardiographic changes and greater than 20% elevation in Troponin T from baseline), sepsis, heart failure and those who were receiving cardiotoxic chemotherapy were excluded. The subjects were enrolled by non-probability consecutive sampling. Results were analysed by SPSS 16.0 **Results:** Out of 117 participants, 72 (61.5%) were males and 45 (38.5%) were females. The mean age of the study participants was 52.08±14.21 years. Elevated Troponin T was found in 45 (38.5%) of the patients. There is statistically significant association between the stage of CRF and elevated levels of Troponin T. Statistically significant negative correlation (r=-0.213,p=0.021) *was* found between the Glomerular Filtration Rate and serum levels of Troponin T. **Conclusion:** A high proportion of CRF patients have elevated Troponin T and the rise is significantly associated with the stage of chronic renal failure.

Keywords: Chronic renal failure, Troponin T, Acute myocardial infarction

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INTRODUCTION

Troponins are present in striated muscles but not in smooth muscles. The function of Troponin T is to attach the troponin complex to tropomyosin. Cardiac Troponin T is present in cardiac muscle and is released in blood stream due to cardiac damage like acute myocardial infarction (AMI). The World Health Organization (WHO) criteria uses the cardiac troponin T in the diagnosis of acute myocardial infarction.[1] Besides this there are variety of medical and surgical conditions in which the Troponin T is raised in blood in the absence of myocardial infarction. These conditions are renal failure, critical illness, transplant vasculopathy, use of medicines like doxorubicin and trastuzumab, snake venom, amyloidosis, post-cardiac surgery, severe burns, intense physical exertion, cardiomyopathies like hypertrophic obstructive cardiomyopathy (HOCM) and takotsubo cardiomyopathy, septicaemia, advanced congestive heart failure, cardiac dysrhythmias (bradyarrhythmias, tachyarrhythmias and heart blocks), cerebrovascular accidents, pulmonary embolism, endocarditis, myocarditis and pericarditis.

Chronic renal failure (CRF) is defined as irreversible, substantial, and long-standing loss of renal function.[2] CRF is a major cause of mortality all over the world and was globally responsible for 400,000 deaths in 1990 reaching up to 735,000 deaths in 2010.[3] CRF is divided into five stages according to the glomerular filtration rate (GFR). Stage 1 is characterized by kidney injury with adequate renal functioning (GFR>90 mL/min/1.73 meters square). In stage 2, minimal renal impairment is noticed with GFR 60–89 mL/min/1.73 meters square. Stage 3 is labeled when the renal impairment is moderate with GFR 30–59 mL/min/1.73 meters square. In stage 4, there is severe renal impairment with GFR of 15–29 mL/min/1.73 meters square. Terminal stage of renal failure is classified as stage 5 which is characterized by GFR<15 mL/min/1.73 meters square.[4]

High serum troponins may be observed in patients with renal insufficiency even in the absence of myocardial infarction.[5] The exact mechanism underlying elevation of Troponin T in CRF is still unclear. Possible explanation of raised troponin T in chronic kidney disease (CKD) is the occurrence of small infarcts in the myocardium. These are very tiny infarcts

which do not manifest clinically in the form of chest pain, sweating or dizziness. This is possible as patients with CKD are more at risk of ischemic heart disease due to hypertension and accelerated atherosclerosis. Confirmation of this fact has been made by demonstrating myocardial tissue micro-infarcts in CKD patients with elevated troponin T.[6] Also these small infarcts cannot be detected with the help of creatine kinase–muscle/brain (CK–MB) as CK–MB is not raised due to these micro–infarcts. Studies have also suggested that other than acute myocardial insult, Troponin T might also be elevated in patients with congestive cardiac failure.[7] Congestive cardiac failure is frequently found in patients with chronic renal failure. This might be the result of increased prevalence of hypertension and ischemic heart disease in chronic renal failure.

In clinical practice it is a great challenge to interpret raised troponin T in patients with chronic renal failure. The consensus till now is to serially measure troponin T if there is a suspicion of acute coronary insult in a patient with chronic renal failure. If a patient of CRF is unwell and presents with chest pain, palpitations, sweating, dizziness and on examination has a low blood pressure and chest crepitations, then troponin T should be done at the time of presentation. Within 9 hours of presentation, troponin T should be measured again to check for any variation from the baseline. If troponin T is raised from the baseline on 2nd measurement, it is in favour of myocardial damage. According to National Academy of Clinical Biochemistry (NACB), if troponin T is raised more than 20% from the baseline within 9 hours of presentation in a patient of CKD, it is suggestive of acute myocardial infarction.[8] However, if troponin T levels are the same as the baseline on 2nd measurement, acute myocardial infarction is excluded and it can be concluded that raised troponin T is due to chronic renal impairment.

It is noteworthy that harm may result from erroneously diagnosing acute coronary syndrome (ACS) when a non-ACS condition like CRF is present. This may subject patients to unnecessary coronary angiography and its potential risks and potentially unnecessary revascularization/stenting; therefore, it is pertinent to know the frequency of elevated Troponin T in patients of CRF in absence of acute myocardial infarction. The objective of our study was to determine the frequency of elevated Troponin T in CRF patients in absence of acute myocardial infarction. Findings of this study would help physicians and cardiologists in evidence-based decision making for the management of such patients.

MATERIAL AND METHODS

A total of 117 patients over a period of six months from 16th December 2013 to 16th June 2014 were included in this cross–sectional study which was conducted at Medical B Unit of Ayub Teaching Hospital, Abbottabad. The sample size was calculated with specified absolute precision using World Health Organization (WHO) software "Sample size determination in health studies.[9] The following formula was used with 18% of given value of known prevalence of elevated Troponin T in CRF patients without acute myocardial infarction[10] absolute precision of 8%, and Confidence level of 95%, the sample size was 117.

$$n = \frac{z^2_{1-\alpha}\ p(1-p)}{d^2}$$

The sampling technique was non-probability consecutive sampling. Informed consent was taken from the patients before data collection. Data was collected through a structured proforma. Approval of the Hospital Ethical Committee was obtained at the time of the study. All the patients whose history and previous medical records confirmed the presence of CRF were included. Glomerular filtration rate of the patients was calculated from serum creatinine by using Modification of Diet in Renal Disease Study Equation to re-confirm the presence of CRF. This equation is:

GFR (mL/min/1.73 m2)= 175×(Scr/88.4)-1.154×(Age)-0.203×(0.742 if female)×(1.212 if black) (SI units). Weight of the patient is not needed for estimation of GFR by this equation.[11] Baseline Troponin T of the patients was done by Troponin T sensitive assay by Roche Cobas®. Blood samples for Troponin T were drawn by venipuncture and then collected in tubes with pre-added heparin. Serum creatinine and Troponin T were carried out in laboratory of Ayub Teaching Hospital. Troponin T cut-off value that was considered as elevated was >100 ng/L. ECG was also carried out. Previous medical records were evaluated regarding presence of coronary artery disease, heart failure and administration of cardiotoxic chemotherapeutic drugs to fulfil the exclusion criteria of the study. Troponin T of patients who had clinical manifestations and ECG changes suggestive of acute myocardial infarction was repeated and they were excluded from the study if Troponin T showed greater than 20% elevation from the baseline. The data was analysed by SPSS version 16.0 for windows.

RESULTS

A total of 117 patients with CRF were inducted in this study. The mean age of the patients was 52.08±14.21 years with minimum and maximum age of 24 and 82 years respectively. There were 72 (61.5%) male patients and 45 (38.5%) female patients in the study (Table-1). Frequency of elevated Troponin T in patients of CRF is shown in figure-1. Troponin T of 45 (38.5%) patients of chronic renal failure was raised whereas Troponin T of 72 (61.5%) CRF patients was not raised. Based on stages of CRF, 7 (6%) patients were in stage 3, 45

(38.5%) patients were in stage 4 and 65 (55.5%) patients had stage 5 CRF. Troponin T was found raised in 45 (38.5%) patients whereas 72 (61.5%) patients had normal values of Troponin T (Table–2). Table-2 describes the distribution of elevated Troponin T by stage of the chronic renal failure. Frequency of elevated Troponin T showed an increase with increase in stage of chronic renal failure, and the result is statistically significant (p=0.003). Correlation between glomerular filtration rate and levels of Troponin T showed negative correlation (r = - 0.213) and the relationship was statistically significant (p=0.021).

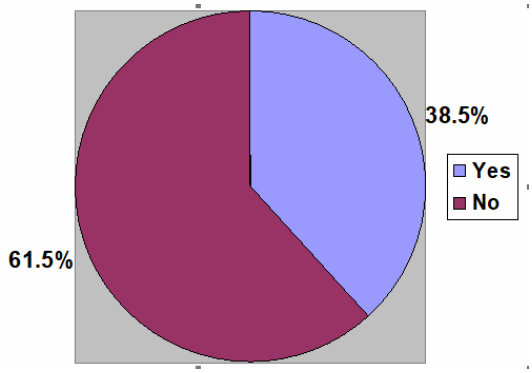

Figure-1: Frequency of elevated Troponin T in chronic renal failure patients

Table-1: Distribution of CRF patients according to gender

Gender	Number of patients	Percentage
Males	72	61.5
Females	45	38.5
Total	117	100

Table-2: Distribution of Elevated Troponin T according to CRF stages.

Stages of CRF	Elevated Troponin T		Total
	Yes	No	
Stage 3 CRF	1 (14.3%)	6 (85.7%)	7 (6%)
Stage 4 CRF	11 (24.4%)	34 (75.6%)	45 (38.5%)
Stage 5 CRF	33 (50.8%)	32 (49.2%)	65 (55.5%)
Total	45 (38.5%)	72 (61.5%)	117

DISCUSSION

Chronic renal failure is a globally prevalent condition with significant health and financial implications. Patients of chronic renal failure may have raised Troponin T without acute myocardial ischemia. According to a study the prevalence of elevated Troponin T in end-stage renal disease patients was reported as 30–85% with the Troponin T cut off value of 0.1 microgram/litre.[12] According to our study the frequency of elevated Troponin T in CRF patients was 38.5%. Results of our study are in agreement with those of Dierkes *et al*. which reported elevated Troponin T in 38% of CRF patients.[13] Our results were also closer to the study results reported by Blich *et al.* who reported elevated Troponin T in 35.2% of renal failure patients.[10] Raised Troponin T in CRF is strongly linked with reduced glomerular filtration rate. This fact was shown by a study done by Ahmadi F *et al.*[14] Results of our study are also consistent with this fact. Our study results were slightly less as compared to the study done by Choy JB *et al.* in a tertiary care teaching hospital that included 113 patients which showed that Troponin T was elevated in up to 42% CRF patients without myocardial ischemia.[15]

Analysis done by Musso P and colleagues revealed elevated Troponin T in 47% of CRF patients without myocardial ischemia.[16] These results are higher as compared to our results. This difference might be due to the difference in sample sizes which was 49 patients in the study by Musso P whereas patients in our study were 117. Study done by Ooi DS and House AA showed elevated Troponin T in 29% of haemodialysis patients.[17] This difference in results might be due to the sample size which was 174 patients in the study by Ooi DS. Other reason might be that in the study by Ooi DS, samples for troponin T measurement were repeated in 125 patients at 1-month intervals whereas in our study we did not repeat Troponin T measurements at such intervals. In our study, Troponin T was repeated after 9 hours only in those patients who had a clinical suspicion of acute coronary insult and those patients were excluded from our study that showed more than 20% elevation of troponin T from the baseline measurement [8]. A study done by Dubin *et al*. showed detectable levels of High sensitivity cardiac Troponin T (hs-TnT) in 81% of subjects with chronic renal insufficiency.[18] The discrepancy between study results is probably due to the usage of hs-TnT assay in this study whereas we did not use hs-TnT assay. hs-TnT assay is capable of detecting even slight elevations of Troponin T. The second reason which may have resulted in this difference in results might be the large sample size of the study by Dubin *et al.* which included 2464 study participants whereas sample size of our study was 117.

A study done by Abbas *et al*. showed elevated Troponin T levels in 43% of CKD patients without cardiovascular disease.[19] The slight difference in the results from our study might be due to the fact that Abbas *et al*. included all the subjects in whom dialysis was not commenced yet whereas we included CKD patients irrespective of whether they were on haemodialysis or not. The prevalence of elevated Troponin T in end-stage renal disease patients on haemodialysis has been reported in the range of 20–90%.[20] The second difference was that of the sample size which was 222 patients in the study by Abbas *et al*. whereas our sample size was 117 patients. Further large-scale studies are needed to generate more data on

frequency of elevated Troponin T in CRF patients in absence of acute myocardial infarction in Pakistan.

CONCLUSION

It is concluded from this study that a significant proportion of CRF patients had elevated Troponin T in absence of acute myocardial infarction. Moreover, frequency of elevated Troponin T increased with deterioration in renal function. Therefore, interpretation of Troponin T should be made with caution with respect to stage of CRF. Also Troponin T interpretation in CRF should be based on serial measurements as a single reading is not discriminatory. If elevated Troponin T level is unaltered on 2 measurements then it can be safely attributed to chronic renal failure and such patients should not be exposed to unnecessary coronary angiography and its associated risks like contrast nephropathy and radiation exposure. However, if there is more than 20% elevation of Troponin T from the baseline within 9 hours, it is indicative of acute myocardial ischemia in a CRF patient and such patient should be managed for acute myocardial infarction with a multi-disciplinary approach.

AUTHORS' CONTRIBUTION

SAA: Concept, data collection, data analysis, manuscript writing, manuscript review. SK: Data collection, data analysis, manuscript writing, manuscript review. MJD: Data collection, data analysis, manuscript writing, manuscript review. MIQ: Data analysis, manuscript review. ZGJ: Data analysis, manuscript review

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Address for Correspondence:

Syed Affan Ali, Department of Medicine, Abbottabad International Medical College, Abbottabad-Pakistan
Cell: +92 333 504 2702
Email: affanali.dr@gmail.com