

Research Article

## Serum Cardiac Troponin I: A Marker for Predicting Cardiac Mortality in Indian Chronic Kidney Disease Patients

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### ABSTRACT

Excess Mortality among patients with Chronic Kidney Disease (CKD) remains high because of an excessive cardiovascular risk related to a high incidence of cardiac hypertrophy, cardiomyopathy, heart failure, and coronary artery disease. Cardiac troponins are frequently elevated in patients with end-stage renal disease (ESRD) in the absence of acute myocardial infarction. Hence, we aimed to prospectively evaluate the relationship between troponin elevations and cardiac mortality. 200 CKD patients from a private nephrology Out Patient Department (OPD) were registered in this study. 180 patients were enrolled in this present study because the 20 patients were not in regular follow up, hence excluded from the study. The patients were divided into three groups based on the serum troponin I levels as follows: Group I : cTn I <0.09 ng/dl, Group II :cTn I 0.1-1 ng/dl and GroupIII I :cTn I >1 ng/dl. Routine biochemical analysis and echocardiography were done in all the patients. Cardiac troponin I and High Sensitive C-Reactive Protein (HSCRP) were also done in all the patients. When compared to the three groups, the 3rd group patients with high cTn I concentration ( $6.52 \pm 2.5$ ) had ten deaths were noted during the follow-up period presumed to be cardiac cause.

Conclusion: The troponin I may be an effective prognostic marker of cardiac mortality in patients with chronic kidney disease.

**Keywords:** cTnI, Chronic Kidney Disease, High Sensitive C-Reactive Protein, Myocardial infarction, Cardiac Mortality

### INTRODUCTION

In patients with end stage renal disease (ESRD), cardiovascular disease is more common and even leads to death<sup>1</sup>. In chronic kidney disease (CKD) patients, generally cardio vascular disease (CVD) develops earlier and it is independent of glomerular filtration rate (GFR)<sup>2</sup>. The mortality in CKD patients is predominantly due to cardiovascular disease rather than kidney failure needing dialysis support<sup>3</sup>. In hemodialysis patients, the mortality rate is approximately 50 % 4-6.

The diagnosis of myocardial infarction in this patient population is a challenging one since most of this population are asymptomatic. Currently available markers like creatinine kinase -MB isoenzyme (CK- MB), Cardiac troponin T are still in dispute regarding their reliability and specificity respectively towards the prediction of myocardial infarction<sup>7-12</sup>. Unlike Cardiac troponin T, CK-MB existing in skeletal muscle also, Cardiac troponin I existing only in cardiac muscle has been shown to be a very good reliable marker for the diagnosis and prediction of myocardial damage and infarction<sup>13-17</sup>.

Analysing the serum biomarker cTnI will indicate the progression and severity of disease which would not only help to classify the disease status but also would serve as an effective tool for choosing the treatment modality as early as possible in these patients. With this focus in our mind, we aim to evaluate the serum cardiac troponin I level

and try to establish a relationship between cardiac status and chronic kidney disease pertaining to cardiac mortality in Indian context.

### MATERIALS AND METHODS

200 CKD patients from a private nephrology OPD were registered in this study. Patients with previous history of MI, ACS and heart failure on dialysis were excluded from the study. Patients who were in regular follow-up for a period of at least 6 months were taken for the study and total follow-up period was 1 year. 180 patients were enrolled in this present study because 20 patients were not in regular follow up and hence excluded from the study. All the patients underwent stress test at the start of the study and none of them showed who stress test positive. The patients were divided into three groups based on the serum troponin I levels as follows: Group I : cTn I <0.1 ng/dl, Group II :cTn I 0.1-1 ng/dl and GroupIII I :cTn I >1 ng/dl. Routine biochemical analysis, estimation of Cardiac troponin I, high sensitive C-reactive protein (HSCRP) and echocardiography were done for all the patients. From all the study population, written informed consent had been collected before the commencement of the study. Baseline ECG was done in all patients and repeat ECG was done as and when the patients symptoms necessitated it and it was not done on a protocol basis.

Table 1: Comparison of the clinical parameters among three groups

S. No	Parameters	Group I cTnI <0.09 ng/dl (N =78)	Group II cTnI 0.1-1 ng/dl (N = 62)	Group III cTn I >1 ng/dl (N = 40)	Group I Vs Group II	Group I Vs Group III	Group II Vs Group III
1	Age years	63.5±11.14	62 ± 8.16	55.22 ± 20.38	NS	NS	NS
2	Hemoglobin gms%	8.93 ± 2.45	9.5 ± 2.02	9.84 ± 2.22	NS	NS	NS
3	Sugar mg/dl	191.78 ± 55.14	176.75 ± 79.13	159 ± 99.11	NS	NS	NS
4	Urea mg/dl	83.42 ± 53.79	116.37 ± 42.89	101.44 ± 43.21	NS	NS	NS
5	Creatinine mg/dl	3.82 ± 1.49	4.2 ± 2.78	5.72 ± 2.44	NS	<0.0001	<0.0001
6	HSCRP mcg/dl	2.14 ± 1.84	2.20 ± 1.38	2.24 ± 1.7	NS	NS	NS
7	Cardiac Troponin I ng/dl	0.024 ± 0.01	0.68 ± 0.05	6.52 ± 2.5	<0.0001	<0.0001	<0.0001
8	Ejection Fraction (%)	67.14 ± 5.68	45.68 ± 4.10	20.5 ± 5.88	<0.0001	<0.0001	<0.0001
9	GFR (MDRD) ml/min/1.73 m <sup>2</sup>	54.35 ± 10.47	36.07 ± 12.42	13.6 ± 7.65	<0.0001	<0.0001	<0.0001
10	Death (%)	Nil	Nil	10 (25)	-	-	-

Follow-up The patients were enrolled and categorised based on the serum cTnI levels. In the present study, enrolled patients had been monitored for 12 months. The final events of the study were 1) cardiac death; 2) acute myocardial infarction/damage and 3) the intervention. The confirmation of these events could be done with the support of Hospital records, outpatient clinical records and interviews with the patient or primary physician.

#### STATISTICAL ANALYSIS

The values of clinical parameters have been expressed as mean value ± SD. Statistical significance between two groups has been done by comparison of means using MedCalc 9.0 (Belgium). The P value less than 0.05 has been considered to be statistically significant.

#### RESULTS

The number of patients enrolled were 180 (Male: 144, Female: 36). Age ranged from 42 to 76 (61.3±12.9). The patients were classified in to three groups (Group I: 78, Group II: 62 and Group III: 40 patients) based on cTnI levels (Table 1). When compared to the three groups, the 3rd group patients with high cTn I (>1 ng/dl) concentration (6.52 ± 2.5) had ten deaths (25 %) during the follow-up period presumed to be due to cardiac causes. Serum creatinine was significantly higher (5.72 ± 2.44) and the ejection fraction was low (20.5 ± 5.88) % in this high cTnI group compared to the other two groups. In group II where the troponin I level were relatively low (cTnI 0.1-1 ng/dl), though the patients had low ejection fraction, there were no deaths during the follow up period. In Group I where the cTnI is very low (cTn I <0.1n/dl) and the ejection fraction is relatively high, no deaths were noticed during the follow-up period. HSCRP levels were not statistically significant in all the 3 groups studied. Blood pressure was nearly the same in all the groups.

#### DISCUSSION

The troponin complex composed of three components which are produced by different genes and have different structures and different molecular weights also. In general, troponin complex plays a key role in muscle contraction

and relaxation. The normal individual does not contain cTnI in their blood stream. In patients with skeletal muscle injury Cummins et al.18 and Larue et al.19 have reported the absence of cTnI in blood stream while Adams et al.20 have reported that there is an elevation in cTnI which is specific only for myocardial injury.

cTnI is expressed only by tissues of myocardium whereas creatine kinase, creatine kinase-MB and troponin T are expressed by other tissues also14,15& 21. This finding has created enormous interest towards using cTnI as a marker for detecting subclinical ischemia and adverse cardiac outcomes. Since Left ventricular hypertrophy (LVH) is common adverse cardiac outcomes in patients with ESRD and the increase in troponin I level may be used as predictive marker for LVH22, 23. The results obtained in the present study are in conformity with the earlier studies22, 23. Many earlier studies have not brought out any relationship between troponins and death in patients with ESRD24-26. In our study has been taken in to consideration and ten deaths were noticed in end stage renal disease patients in a group consisting of 40 patients (Group 3). This result is a highly significant one and hence any elevation in cardiac troponin I level should warrant further cardiac evaluation.

In conclusion, the present study indicates that a significant increase in cardiac troponin I is correlated to LVH. The increased serum concentration of cardiac troponin I probably originate from the heart and is a marker of LVH. The assessment of cTnI concentration should thus be the first line evaluation in the diagnosis of acute coronary disease in CKD patients27. Hence the routine measurements of cTnI may assess the cardiovascular risk factors in early stages of CKD and help the patients requiring aggressive cardiac risk reduction strategies.

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