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Correlation of Serum Cardiac Troponin-T with Chronic Kidney Disease

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Abstract
Aims and Objectives: *Correlation of serum Cardiac Troponin-T with Chronic kidney disease patients.*
Material and Methods: *The present study was undertaken at Maharana Bhupal Govt. Hospital, attached to R.N.T. Medical College Udaipur (Raj.).*

- *Patients admitted with sign and symptoms due to deranged renal functions were stratified into stages of CKD according to guidelines of the National Kidney Foundation [Kidney Dialysis Outcomes Quality Initiative (KDOQI)]*
- *Methods of measurement of GFR: Cockroft-Gault formula*
- *Clinical history was recorded including age, sex, weight, height, and primary renal diagnosis, and blood pressure, history of diabetic and smoking history.*
- *Blood samples were collected in the non fasting state.*
- *Descriptive statistical analysis was carried out in this study.*

Observation and Conclusion: *In this study population, 100 patients of various stages of CKD (II to V) were included to evaluate level of cardiac Troponin-T in CKD. They were non-diabetic, and were not on dialysis with no history suggestive of adverse cardiac event. The mean age of patients was 42.93±13.43 years of which 69% patients were male and 39% patients were female. The mean of blood urea was 163.49±85.54 mg/dl (ranged 65-377 mg/dl). The mean of serum creatinine was 3.99±2.64mg/dl (ranged 1.42-12.7 mg/dl). Mean Cardiac troponin T level was found 0.082± 0.138 ng/ml among these patients. Troponin T found positive (level >0.1ng/ml) in only 25 (25%) patients, 36 patients were having Trop-T level <0.014 ng/ml and 38% (38) patients were having Trop T level between (0.014-0.1) ng/ml. Serum cardiac Troponin T differed between chronic kidney disease stages, being more commonly increased in the presence of more advanced chronic kidney disease and the difference is significant.*
According to this study all CKD patients should undergo for cardiac Troponin T level as these patients are definitely associated with raised level of cardiac troponin T showing increased chances of adverse cardiovascular event to occur in future.

INTRODUCTION

Chronic renal failure (CRF) refers to an irreversible deterioration in renal function which classically develops over a period of years. Initially it manifests only as a biochemical abnormality eventually loss of excretory, metabolic & endocrine functions of the kidney. This leads to the development of the clinical

symptoms & signs, which are referred to as uremia when death is likely to occur without renal replacement.

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function and a progressive decline in Glomerular Filtration Rate (G.F.R).

In 2002, the NKF (National Kidney Foundation) defined CKD: (1) Kidney damage for ≥ 3 months, as confirmed by kidney biopsy or markers of kidney damage with/without a decrease in G.F.R. And/or (2) G.F.R < 60 ml/min/1.73m^2 for ≥ 3 months with/without kidney damage. (Kidney damage is ascertained by either kidney biopsy or markers of kidney damage such as proteinuria, abnormal urinary sediments or abnormalities on imaging studies).

There is a widely accepted classification, based on guidelines of the National Kidney Foundation [Kidney Dialysis Outcomes Quality Initiative (KDOQI)], in which stages of CKD are defined according to the estimated G.F.R.

Classification of Chronic Kidney Disease (CKD)

STAGE	0	I	II	III	IV	V
GFR(ml/min/1.73m^2)	>90	≥90	60-89	30-59	15-29	<15 ESRD

CVD RISK FACTORS IN CKD

Coronary artery disease (CAD) is the major cause of death in patients with chronic kidney disease (CKD), responsible for up to 45% of overall mortality. The cardiovascular mortality rate in end stage renal disease patients on hemodialysis is approximately 10 to 20 times higher than in the general population. The incidence of cardiovascular disease was increased by 40% even in early stage of CKD. Early detection of cardiovascular disease could facilitate more aggressive treatment of those at increased risk.

Risk factors Classified as either "traditional" or "non-traditional".

Table:-Traditional and non-traditional risk factors

Traditional factors	Non-traditional factors
Older age	Albuminuria
Male sex	Hyperhomocystenemia
Higher LDL cholesterol	Hyperlipoproteinemia
Lower HDL cholesterol	Anemia
Diabetes	Abnormal Ca^{++}/PO_4^- metabolism
Hypertension	
Smoking	ECF volume overload
Physical inactivity	Electrolyte imbalance
Menopause	Oxidative stress
Family history of CVD	Inflammation (C-reactive protein)
LVH	Malnutrition
	Thrombogenic factors
	Sleep disturbance
	Altered NO/endothelium balance

CKD patients develop clinically silent myocardial injury; hence silent cardiac pathology underlies these cardiac troponin-T elevations. This elevated cardiac troponin-T is a specific marker of myocardial injury in patients of CKD because of high organ specificity. The increase in cardiovascular complications like myocardial injury in CKD occurs very early in the progression of disease, hence early detection by measuring cardiac troponin -T level will help to diagnose and treat the cardiac complications.

Cardiac troponin-T (cTnT) is a component of the contractile apparatus of the cardiac muscle. Because of its high tissue specificity, cTnT is a cardio-specific, highly sensitive marker of myocardial damage. However, increase in serum cTnT concentration has been reported in patients with CKD in the absence of acute myocardial infarction .In many studies, it is shown that it is possible to use the increased level of Troponin to predict the fatality and future heart problems in those patients. Consistently elevated levels of cTnT are to be proved as an independent prognostic factor for adverse cardiovascular events in this population.

The correlation of Troponin in end stage renal disease and in patients on dialysis has been studied widely but there is few data regarding cTnT level in pre-end stage CKD patients who do not require dialysis treatment. The objectives of studying the cTnT in patients with CKD stage 2, 3, 4 and 5 to choose these patients for early diagnostic studies and cures of their heart problems.

AIMS AND OBJECTIVES

This study was conducted at Maharana Bhupal Govt. Hospital attached to R.N.T Medical College, Udaipur (Raj.) to know "Correlation of serum Cardiac Troponin-T with Chronic kidney disease."

1. To estimate Cardiac Troponin T in patients of chronic renal failure.
2. Estimation of blood urea and serum creatinine for selection of patients.

MATERIAL AND METHODS

The present study was undertaken at Maharana Bhupal Govt. Hospital, attached to R.N.T. Medical College Udaipur (Raj.).

(1) PATIENTS

1. Patients admitted with sign and symptoms due to deranged renal functions and were stratified into stage II CKD (GFR =60-89 mL/min/1.73m^2), stage III CKD (GFR = 30-59 mL/min/1.73 m^2), stage IV CKD (GFR = 15-29 mL/min/1.73 m^2) and end stage, V (GFR = <15 mL/min/1.73m^2) according to guidelines of the National Kidney Foundation [Kidney Dialysis Outcomes Quality Initiative (KDOQI)]

2. Methods of measurement of GFR:

Cockroft-Gault formula as follows:

Males: (140 - age) x weight (kg)/ 72 x serum creatinine (mg/100 mL)

Females: 0.85 (140 - age) x weight (kg)/ 72 x serum creatinine (mg/100 mL)

3. Clinical history was recorded including age, sex, weight, height, and primary renal diagnosis, and blood pressure, history of diabetic and smoking history.

(2) SAMPLE ANALYSIS

1.Blood samples were collected in the non fasting state.

2. Serum creatinine was measured by buffered kinetic Jaffe' reaction method on SIEMENS AUTOANALYSER.

3. Blood urea estimation - Urea nitrogen method employs a urease/glutamate dehydrogenase coupled enzymatic activity done on SIEMENS AUTOANALYSER.

4. Serum cTnT was measured with a third generation electro-chemiluminescent immuno-assay COBAS e411 ANALYSER (Roche Diagnostics Ltd.).

Statistical Methods

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients , Student t test (two tailed, independent) has Inter group analysis) on metric parameters, Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Significant figures

+ Suggestive significance (P value: 0.05<P<0.10)

* Moderately significant (P value: 0.01<P ≤ 0.05)

** Strongly significant (P value: P≤0.01)

Statistical software:

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

INCLUSION CRITERIA

1. Patients with chronic kidney disease stage II to stage V who were non-diabetic, non – pregnant and not on dialysis.
2. Patients who himself or his relatives given consent.

EXCLUSION CRITERIA

1. Symptoms suggestive of Acute Myocardial Infarction or unstable angina before admission.
2. Electrocardiographic changes indicative of ischemia (ST–segment elevation or depression) on admission.
3. Newly developed pathologic Q waves on admission ECG.
4. Previous coronary angioplasty or coronary bypass surgery.
5. Other heart diseases and debilitating diseases with the possibility of serum cTnT elevation, such as congestive heart failure, valvular heart disease (VHD),
6. Patients having acute renal failure.
7. Patients on dialysis.
8. Patients having GFR >90 ml/min. per 1.73 m^2.
9. Patients with diabetic nephropathy, patients on treatment with estrogen, corticosteroids, sulphonylurea, phenobarbitones & beta-blocker.
10. Patients with chronic liver diseases.
11. Patients having high billirubin level.

OBSERVATIONS

The present study constitutes 100 patients with chronic kidney failure who met inclusion criteria and exclusion criteria. They were selected from the patients admitted in medical wards, nephrology ward and OPD of M.B.G. Hospital, attached to R.N.T. Medical College, Udaipur (Rajasthan).

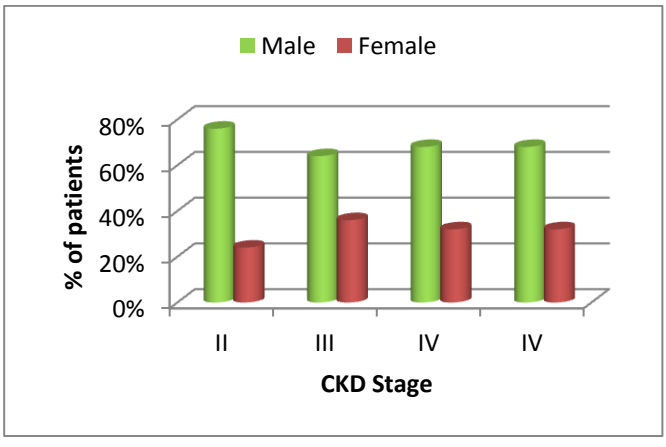
The following tables highlight the most pertinent observations:

Table 1. Distribution of patients in study

CKD stage	GFR (mL/min/1.73 m^2)	No. of patients	%
II	80-89	25	25.0
III	30-59	25	25.0
IV	15-29	25	25.0
V	<15	25	25.0
Total		100	100.0

In the present study out of 100 patients were divided into various CKD stages (stage II – V).Each stage contains 25 patients. out of 100 patients 69 (69%) were male. Out of these 69 (69%) male patients 19 belong to CKD stage II, 16 patients belong to stage III, 17 patients were in stage IV and 17 patients were in stage V.

Out of 100 patients 31(31%) were female patients and in this group 6 females were in stage II, 9 were in stage III, 8 females were in stage IV, and another 8 females were in stage V.



Patient's age ranged from 18-85 yrs. 16 (16%) patients were in age group18-29 yrs . 54 (54%) patients were in age group 30-49yrs. 30(30%) patients were in age group 50 yrs and above.

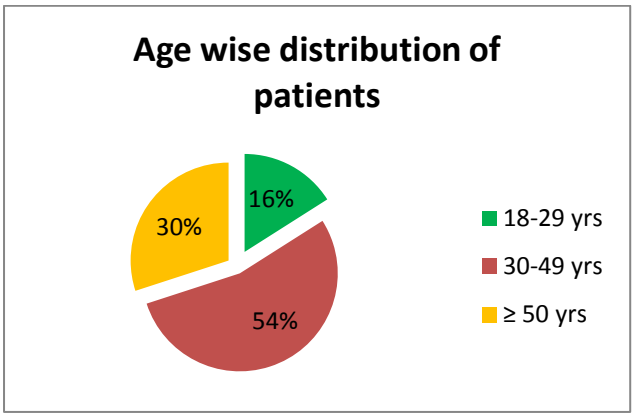


Table 2. Distribution of patients according to blood urea level in CKD

Blood Urea level (mg/dl)	No. of patients	%
<100	26	26.0
100-200	48	48.0
>200	26	26.0
Total	100	100

Patient's blood urea ranged between 65 to 377 mg/dl. 26 (26%) patient's blood urea level was <100 mg/dl, 48(48%) patient's blood urea level was in 100-200 mg/dl range, 26(26%) patient's urea level was >200 mg/dl .

Table 3. Distribution of patients according to S. creatinine level in CKD

S. creatinine level (mg/dl)	No. of patients	%
< 3.0	51	51.0
3.1-5.0	19	19.0
>5.0	30	30.0
Total	100	100

Patient's serum creatinine ranged from 1.42-12.7 mg/dl. 30 (30%) patient's s. creatinine was >5 mg/dl, 19 (19%) patient's s. creatinine level was 3.1-5.0 mg/dl range, 51 (51%) patient's s. creatinine was < 3.0 mg/dl range.

Table 4. Distribution of patients according to ECG

ECG	Stage				Total
	II	III	IV	V	
NORMAL	24 96.0%	16 64.0%	14 56.0%	11 44.0%	65 65.0%
LVH	1 4.0%	2 8.0%	3 12.0%	5 20.0%	11 11.0%
LVH, LAD	0 0.0%	1 4.0%	2 8.0%	1 4.0%	4 4.0%
LBBB	0 0.0%	0 0.0%	2 8.0%	3 12.0%	5 5.0%
RBBB	0 0.0%	2 8.0%	0 0.0%	1 4.0%	3 3.0%
Tall T wave	0 0.0%	0 0.0%	0 0.0%	1 4.0%	1 1.0%
LVH strain	0 0 .0%	3 12.0%	3 12.0%	3 12.0%	9 9.0%
CWR	0 0.0%	0 0.0%	1 4.0%	0 0.0%	1 1.0%
Sinus trachycardia	0 0.0%	1 4.0%	0 0.0%	0 0.0%	1 1.0%
Total	25 100.0%	25 100.0%	25 100.0%	25 100.0%	100 100.0%

Patients ECG was normal in 65 (65%) patients. Most common abnormal ECG finding was presence of LVH found in 11(11%) patients. Other ECG pattern found in this study were LAD, LBBB, RBBB, LVH strain, LVH+LAD, Sinus Tachycardia, Tall T WAVE.

Table 5. Distribution of patients according to serum cardiac Troponin-T level

Trop T Level (ng/ml)	Stage				Total
	II	III	IV	V	
< 0.1	25 100%	20 80%	16 64%	14 56%	75 75%
≥0.1	0 0%	5 20%	9 36%	11 44%	25 25%
Total	25 100.0%	25 100.0%	25 100.0%	25 100.0%	100 100.0%

In the present study of 100 CKD patients 25 patients of stage II, 20 patients of stage III, 16 patients of stage IV, 14 patients of stage V had serum cardiac Troponin-T level was < 0.1ng/ml. 5 patients of stage III, 9 patients of stage IV, 11 patients of stage V had serum cardiac Troponin-T level was ≥ 0.1ng/ml.

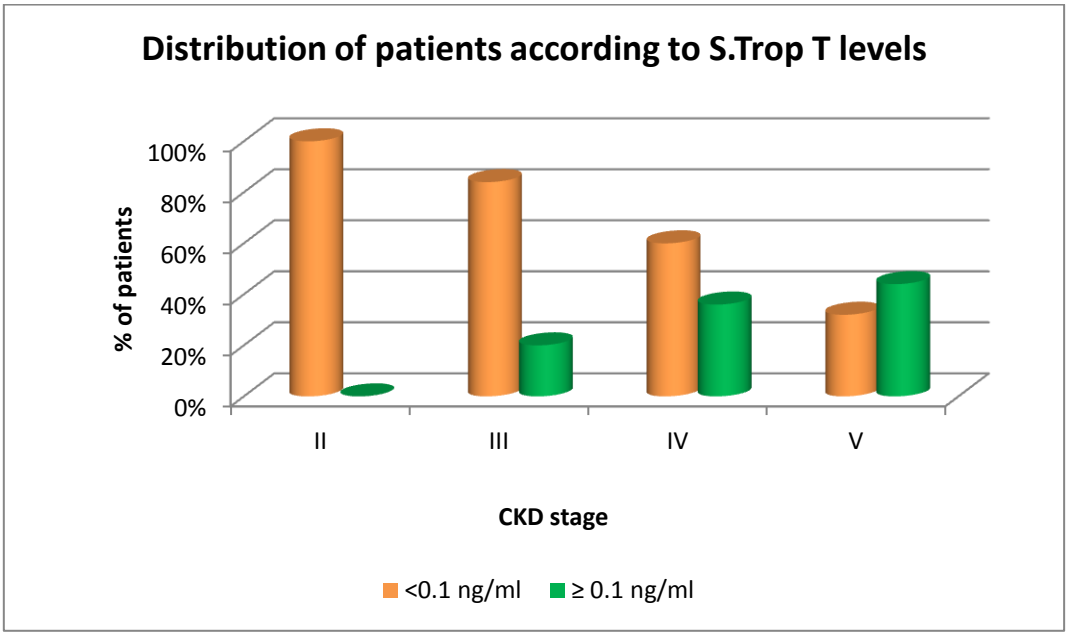


Table 6. Comparison of study variables according to the stage of chronic kidney disease

Variables	CKD stages				P value
	II	III	IV	V	
Age (years)	34.84±8.68	44.92±14.18	45.08±15.38	46.88±11.75	0.007
Male	19 (76%)	16 (64%)	17 (68%)	17 (68%)	0.828
Female	6 (24%)	9 (36%)	8 (32%)	8 (32%)	
Weight (kg)	65.00±4.78	66.04±7.97	63.40±9.58	65.84±6.88	0.591
Blood urea (mg/dl)	89.68±16.55	125.68±41.24	188.56±76.01	250.05±82.51	0.001
S. creatinine (mg/dl)	1.51±0.12	2.26±0.47	4.55±0.99	7.64±1.98	0.002
S.Trop T (ng/ml)	0.013±0.002	0.057±0.089	0.130±0.195	0.128±0.118	0.002

As above data showed, among different study variables of CKD stage II, III, IV and V patients, significant P value (< 0.05) seen in of Blood urea, serum creatinine and cardiac Troponin-T measurements.

DISCUSSION

In CKD, patients develop clinically silent myocardial injury hence silent cardiac pathology underlies these cardiac troponin T elevations. This elevated cardiac troponin T is a specific marker of myocardial injury in patients of CKD because of

high organ specificity of cardiac troponin T. The increase in Cardiovascular complications like myocardial injury in CKD occurs very early in the progression of disease hence early detection by measuring cardiac troponin T level will help to detect and treat the cardiac complications. Various studies were conducted to detect and treat the cardiac complication. Mean serum cardiac Troponin-T level was 0.082±0.130 ng/ml.

Out of 100 patients 75 patients had cTnT <0.1ng/ml and only 25 patients ≥0.1ng/ml. The increased cTnT was commonly found in more severe CKD (0-stage II, 5-stageIII, 9-stageIV, and 11-stageV).So Troponin-T was positive in 25 patients.

This study demonstrates that 36% CKD patients had cTnT <0.014ng/ml (normal), but 38% CKD patients had cTnT level between 0.014-0.1ng/ml. This intermediate Trop-T level in CKD patients does not require cardiac intervention and this finding was common in CKD stage III-V.

Kiatchoosakun S *et al* (2008) study showed 28 patients (28.2%) had cTnT > 0.01 micro/L and two patients (1.8%) had cTnT > 0.1 microg/L cTnT concentration was commonly increased in more severe CKD (9 patients in stage III and 20 patients in stage IV) which is comparable to the present study. In the study done by C. Löwbeer et al, 35 patients out of 115 patients had serum Cardiac Troponin T concentrations of more than 0.1 ng /ml.

On applying correlation statistics, there was statistically significant correlation between the value of cardiac troponin T and severity of renal failure which is similar to the studies done in the past. Musso P *et al*. (1999) studied Cardiac troponin elevations. 47% CKD patients displayed cTnT concentrations elevated above the upper reference limit. The elevated cTnT values observed were below the values detected in acute myocardial infarction i.e. below 0.1ng/ml and were not associated with adverse cardiac events during follow-up.

Hojs R *et al.* (2005) [89]did a study on cardiac troponin T in patients with Kidney Diseases showed that cTnT detected in serum from patients with end-stage renal failure is derived from myocytes and this effect could be caused by sub-clinical myocardial ischemic release of troponin, myocardial remodelling, or from uremic pericarditis or myocarditis.

Abbas NA *et al.* (2005) [90] studied correlation of Cardiac troponin and renal function in non-dialysis patients with chronic kidney disease in 222 patients: 56 had stage 3 (moderate CKD); 70 stage 4 (severe CKD); and 96 stage 5 (kidney failure) .this findings are comparable to the present study.

CONCLUSION

According to our study all CKD patients should undergo for evaluation of cardiac troponin T level as these patients are definitely associated with development of hypothyroidism and raised level of cardiac troponin T showing increased chances of adverse cardiovascular event to occur in future.

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