A Study on Elevated Level of Cardiac Troponin in Patients of Chronic Kidney Disease Stage 3 to above, on and off Haemodialysis

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\textbf{Abstract}

The Kidney Disease Outcomes Quality Initiative (KDOQI) of the National Kidney Foundation (NKF) established a definition and classification of CKD in 2002. Kidney disease is the ninth leading cause of death in the United States. 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 biochemical diagnosis of myocardial infarction in patients with CKD is always complicated by the fact that serum markers of myocardial necrosis such as creatine kinase, MB-fraction of creatine kinase. (CK-MB) are commonly increased in end stage CKD patients, even in the absence of clinically suspected myocardial infarction. Cardiac troponin (cTn) is a component of the contractile apparatus of the cardiac muscle. Because of its high tissue specificity, cTn is a cardio-specific, highly sensitive marker of myocardial damage. However, increases in serum cTn concentration have been reported in patients with CKD in the absence of acute myocardial infarction. Various study suggest that Elevations of cTnI not associated with ACS were common in patients with CKD stage 3 to 5, and there was an increase in mortality with higher concentrations of cTnI. \textbf{Objective:} To assess the elevated level of cardiac troponin in patients of Chronic kidney Disease stage 3 to above, on and off Haemodialysis. \textbf{Material and Method:} Cross sectional analytical study was carried out in our institution for duration of 1 year. Total of 100 subjects was enrolled in the study. \textbf{Result:} High cardiac Troponin level (>1ng/ml) was associated with advanced stage or increased severity of disease. \textbf{Conclusion:} We concluded that higher Troponin value is more associated with higher stage of CKD and disease severity and also associated with increased age due to decreased GFR in advancing age but not significantly affected by co-morbid condition so every CKD patient should be tested for cardiac Troponin to identify the severity of disease.

\textbf{Keywords:} (KDOQI), National Kidney Foundation (NKF), Coronary artery disease (CAD), Cardiac troponin.

\textbf{INTRODUCTION}

The Kidney Disease Outcomes Quality Initiative (KDOQI) of the National Kidney Foundation (NKF) established a definition and classification of CKD in 2002 \cite{1}. The KDOQI and the international guideline group Kidney Disease Improving Global Outcomes (KDIGO) subsequently updated these guidelines These guidelines have allowed better communication among physicians and have facilitated intervention at the different stages of the disease \cite{2}. CKD is associated with an increased risk of cardiovascular disease and end-stage renal disease (ESRD). Kidney disease is the ninth leading cause of death in the United States. 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 \cite{3, 4}. The biochemical diagnosis of myocardial infarction in patients with CKD is always complicated by the fact that serum markers of myocardial necrosis such as creatine kinase, MB-fraction of creatine kinase. (CK-MB) are commonly increased in end stage CKD patients, even in the absence of clinically suspected myocardial infarction \cite{5, 6}. Cardiac troponin (cTn) is a component of the contractile apparatus of the cardiac muscle. Because of its high tissue specificity, cTn is a cardio-specific, highly sensitive marker of myocardial damage \cite{7}.

However, increases in serum cTn concentration have been reported in patients with CKD in the absence of acute myocardial infarction. Most studies have demonstrated that increased cTnT is a powerful predictor of mortality and associated with LVH in the hemodialysis patients. Currently, there is few data regarding cTnT level in pre-end stage CKD (stage 3-4) patients who do not require dialysis treatment \cite{8, 9}. Various study suggest that Elevations
of cTnI not associated with ACS were common in patients with CKD stage 3 to 5, and there was an increase in mortality with higher concentrations of cTnI [10].

MATERIAL AND METHOD

Cross sectional analytical study was carried out in our institution for duration of 1 year. Total of 100 subjects was enrolled in the study. Informed patients consent was obtained before clinical examination. Thorough history taking and clinical examination were done. Patient’s proforma was maintained which include all demographic particulars, past medical, surgical, personal and family, drug history and clinical examination was done. For quantitative Cardiac Troponin ST AIA-PACK cTnI 2nd-Gen is used, ST AIA-PACK cTnI2nd-Gen designed for IN-VITRO DIAGNOSTIC USE for the quantitative measurement of cardiac troponin I (cTnI) in human serum. According to their eGFR CKD categorized into three stages: Stage 3, Stage 4, Stage 5 (ESRD) and their hemodialysis status was also noted.

SELECTION CRITERIA

Inclusion Criteria
- Patient with CKD stage 3 to ESRD with or without Haemodialysis.
- Male and female age > 18 yrs.

Exclusion Criteria
- Acute case of cardiovascular disease.
- Patients with myocarditis.
- AKI in seriously ill patients.
- Known case of liver disease.
- Patients with pulmonary embolism

STATISTICALLY ANALYSIS

Statistical evaluation was performed by statistical package for social sciences (SPSS) version 16 for window statistics program using the unpaired t test/single factor ANOVA and categorical variables were analysed with chi squared test and Fisher Exact Test. Correlation of CKD with disease severity and advancing age and co-morbid condition were obtained using Pearson’s formula. Arithmetic mean calculated by our data. A P value <0.05 was considered statistically significant.

RESULT

100 Patients enrolled in the study were divided into three stage of CKD by eGFR. 35 Patients were in stage 3, 21 patients in stage 4 and 44 patients in stage 5. All these patients again divided based on quantitative Troponin-I >.1 ng/ml and <.1ng/ml. Among 100 patients, 70 patients with Troponin-I >.1 ng/ml and 30 patients with Troponin-I <.1ng/ml showing statistically significance (P=.008759), most of the patients with Troponin-I >.1ng/ml were in ESRD. 70 Patients, those had Troponin>.1ng/ml among them 56 patients were aged more than 50 yrs and only 14 patients had age less than 50 yrs (p=.0126),46 were male and 24 were female (p=.7557), and 38 patients were smoker and 32 were nonsmoker (p=.3573).

| No of patients | CKD staging |
|---------------|-------------|
| 35            | Stage3      |
| 21            | Stage4      |
| 44            | Stage5      |

| Troponin value in different stages of CKD |
|-------------------------------------------|
| CKD Stages | Troponin >.1ng/ml | Troponin <.1ng/ml | P value |
|------------|--------------------|--------------------|---------|
| Stage 3 (35) | 23                | 12                 | P=.008759 |
| Stage 4 (21) | 10                | 11                 |         |
| ESRD (44)    | 37                | 07                 |         |
| Total        | 70                | 30                 |         |

| Variables in those patients had Troponin>1ng/ml |
|-----------------------------------------------|
| Variables | Stage3 | Stage4 | Stage5 | P-value |
|-----------|--------|--------|--------|---------|
| Age <50 yrs | 7      | 3      | 4      | p=.126  |
| >50 yrs | 16     | 7      | 33     |         |
| Sex Male | 17     | 8      | 21     | p=.7557 |
| Female | 11     | 4      | 9      |         |
| Smoking Smoker | 15     | 4      | 19     | p=.3573 |
| Non-smoker | 8      | 6      | 18     |         |

Out of 70 patients those had increased Troponin>.1ng/ml, 63 had some co-morbid condition and most of the patients were (28) diabetic (p=.483888) and 20 patients were Hypertensive (p=.249577), four patients with Chronic lung disease and,11 patients with altered lipid profile (p=.73148).
In present study 42 patient were on dialysis and 58 patient were not on dialysis. Troponin value is higher in patient those were not on dialysis or patient on dialysis having decreased value of Troponin, but it is not statistically significant.

### Elevated Troponin level in relation to dialysis

| Dialysis | Stage3 | Stage4 | Stage5/ESRD | p-value |
|----------|--------|--------|-------------|---------|
| On dialysis (32) | 7 | 4 | 21 | 32 | P=.1278 |
| Non dialysis(38) | 16 | 6 | 16 | 38 | |
| **Total** | **23** | **10** | **37** | **70** | |

**DISCUSSION**

We studied 100 CKD patients and their quantitative Troponin value. In present study more patients with increased Troponin were seen in more severe form of CKD similar to Songsak study [11] out of 103 patient,28 patients (28.2%) had cTn> 0.01 micro/L and concentration was commonly increased in more severe CKD cardiac troponin is high in higher stage. In Flores- Solis LM study [12] the other cardiac disease group included 140 patients (33%) and the other non-cardiac disease group included 286 patients (67%). They found elevated cTnl higher than 99th percentile in 32% of patients. The prevalence of elevated cTnl was higher in patients with CKD stage 5 or ESRD.In present study increased Troponin value were more associated with increased age of CKD patients similar to previous study of Nasir A Abbas [13] study which was done in 222 patients, increased troponin value >.001µ/L was seen in patient with increased age was significantly. In present study Increased Troponin value not significantly associated with gender in contrast to ChristoferDefilippi et al., [14] study, out of 148 patients, 89.2% patients were male had cardiac Troponin 6.3 to 14.3 ng/ml. progressive higher cardiac troponin were statistically significant associated with male.In this present study smoking not significantly affect the cardiac Troponin in CKD patients similar to previous study by Songsak kiatchoosakun [11], 30 out of the 103 patient were smoker and troponin value not significantly raised in those patient. In Songsak [11] study out of 103 patients 20, 17 patients were in stage3 associated with HTN and DM respectively and stage 4 they were 21 and 18 with increased Troponin value but it was not statistically significant similarly in present study co-morbid conditions like DM, HTN, dyslipidemia not significantly affects the Troponin value of CKD patients, this is also seen in another previous study of Christopher Defilippi et al., [14] study in 148ckd patients, 91.9%, 50.7% and 12% patients present with HTN, DM and chronic lung disease, and these patients had increased troponin value associated these with co-morbid conditions but without statistically significant. In Diana Wayand et al., [15] study 566 serum samples obtained from the 59 patients, Troponin T was above the upper reference limit in 16.6% and Troponin I in 12% the mean cardiac Troponin t increased with dialysis, but the mean cardiac Troponin I decreased markedly cardiac troponin I decreases on dialysis although statistically not significant similarly to present study.

**CONCLUSION**

We concluded that higher Troponin value is more associated with higher stage of CKD and disease severity and also associated with increased age due to decreased GFR in advancing age but not significantly affected by co-morbid condition so every CKD patient should be tested for cardiac Troponin to identify the severity of disease.

**LIMITATION**

Because of study was carried out at tertiary care hospital, it does not truly reflects the etiological spectrum of CKD prevalent throughout the country. Due to lack of long term followup prognostic value could not be determined. It is possible to check the reversibility of Troponin value in controlled disease patients those were previously in morbid condition.

**REFERENCES**

1. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, Hogg RJ, Perrone RD, Lau J, Eknoyan G. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Annals of internal medicine. 2003 Jul 15;139(2):137-47.
2. Levin A, Stevens PE, Bilous RW, Coresh J, De Francisco AL, De Jong PE, Griffith KE, Hemmelgarn BR, Iseki K, Lamb EJ, Levey AS. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney international supplements. 2013 Jan 1;3(1):1-50.
3. Herzog CA, Ma JZ, Collins AJ. Poor long-term survival after acute myocardial infarction among patients on long-term dialysis. New England Journal of Medicine. 1998 Sep 17;339(12):799-805.

4. Herzog CA. Diagnosis and treatment of ischemic heart disease in dialysis patients. Current opinion in nephrology and hypertension. 1997 Nov;6(6):558-65.

5. Robbins MJ, Epstein EM, Shah S. Creatine Kinase Subform Analysis in Hemodialysis Patients without Acute Coronary Syndromes. Nephron. 1997;76(3):296-9.

6. Jaffe AS, Ritter C, Meltzer V, Harter H, Roberts R. Unmasking artifactual increases in creatine kinase isoenzymes in patients with renal failure. Translational Research. 1984 Aug 1;104(2):193-202.

7. Antman E, Bassand JP, Klein W, Ohman M, Sendon JL, Rydén L, Simoons M, Tendera M. Myocardial infarction redefined—a consensus document of the Joint European Society of Cardiology/American College of Cardiology committee for the redefinition of myocardial infarction: the Joint European Society of Cardiology/American College of Cardiology Committee. Journal of the American College of Cardiology. 2000 Sep 1;36(3):959-69.

8. Freda BJ, Tang WW, Van Lente F, Peacock WF, Francis GS. Cardiac troponins in renal insufficiency: review and clinical implications. Journal of the American College of Cardiology. 2002 Dec 18;40(12):2065-71.

9. Wayand D, Baum H, Schätzle G, Schärf J, Neumeier D. Cardiac troponin T and I in end-stage renal failure. Clinical chemistry. 2000 Sep 1;46(9):1345-50.

10. Flores-Solis LM, Hernandez-Dominguez JL. Cardiac troponin I in patients with chronic kidney disease stage 3 to 5 in conditions other than acute coronary syndrome. Clinical laboratory. 2014;60(2):281-90.

11. Kiatchoosakun S, Sahasthas D, Wongvipaporn C, Pongskul C. Cardiac troponin-T in pre-end stage kidney disease. Medical journal of the Medical Association of Thailand. 2008 Dec 1;91(12):1806-1811.

12. Flores-Solis LM, Hernandez-Dominguez JL. Cardiac troponin I in patients with chronic kidney disease stage 3 to 5 in conditions other than acute coronary syndrome. Clinical laboratory. 2014;60(2):281-90.

13. Abbas NA, John RI, Webb MC, Kempson ME, Potter AN, Price CP, Vickery S, Lamb EJ. Cardiac troponins and renal function in nondialysis patients with chronic kidney disease. Clinical chemistry. 2005 Nov 1;51(11):2059-66.

14. DeFilippi C, Seliger SL, Kelley W, Duh SH, Hise M, Christenson RH, Wolf M, Gaggin H, Januzzi J. Interpreting cardiac troponin results from high-sensitivity assays in chronic kidney disease without acute coronary syndrome. Clinical chemistry. 2012 Sep 1;58(9):1342-51.

15. Wayand D, Baum H, Schätzle G, Schärf J, Neumeier D. Cardiac troponin T and I in end-stage renal failure. Clinical chemistry. 2000 Sep 1;46(9):1345-50.