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Prognostic Value of Elevated Cardiac Troponin I Levels in Pre-dialysis Chronic Kidney Disease Patients without Cardiac Symptoms

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Authors' contributions

This work was carried out in collaboration between all authors. Authors VCW and HIBG designed the study, wrote the protocol and wrote the first draft of the manuscript. Author EPO managed the analyses of the study and performed the statistical analysis. Authors EPO and RIOJ managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Introductory Concepts: Elevation of cardiac troponin I may be a marker of increased risk of cardiovascular outcomes such as left ventricular hypertrophy, congestive heart failure, ischemic heart disease and reduced survival in asymptomatic CKD patients.
Aim: To measure serum cardiac troponin I concentration in pre-dialysis chronic kidney disease (CKD) patients who do not have any acute symptoms of cardiac disease and determine its relationship with cardiovascular risk factors.
Methodology: Cross-sectional study conducted from January 2014 to December 2015. Blood pressure, serum cardiac troponin I, HDL-cholesterol, total cholesterol, triglyceride, fasting plasma glucose, urine and serum albumin, urine and serum creatinine concentrations were measured in 83

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diagnosed chronic kidney disease patients attending the renal clinic and 83 age- and sex-matched healthy control subjects. Body mass index (BMI), estimated glomerular filtration rate (eGFR), urinary albumin-creatinine ratio (UACR) and LDL-cholesterol were calculated.

Results: CKD patients had higher cardiac troponin I, higher blood pressure, higher serum creatinine, higher UACR, higher triglyceride, lower serum albumin, lower HDL and lower eGFR than controls. Twenty-two (26.5%) patients, but no controls, had elevated cardiac troponin I. Patients with high cardiac troponin I levels had a higher prevalence of diabetes mellitus and obesity but similar prevalence of other cardiovascular risk factors compared to patients with normal cardiac troponin I levels. Cardiac troponin I levels increased progressively with reduced renal function and the highest elevations were observed among patients in CKD stages 4 and 5.

Conclusion: Elevated cardiac troponin I was associated with higher prevalence of diabetes and obesity but reduced eGFR among pre-dialysis CKD patients. Further research is required to determine the effect of reduced GFR and uremia on the diagnostic and prognostic efficiency of cardiac troponins, particularly in end-stage renal disease patients.

Keywords: Cardiac troponin I; pre-dialysis; chronic kidney disease patients; prognostic value; cardiovascular disease.

1. INTRODUCTION

Chronic kidney disease (CKD) is an independent risk factor for coronary artery disease (CAD) and acute myocardial infarction (AMI) [1,2]. Cardiovascular disease (CVD) is the most important and most common cause of mortality in patients with CKD [1]. CKD patients have an increased risk of cardiovascular disease mortality that is about 20 times higher than that in the general population and this risk is heightened in end-stage renal disease (ESRD) [1,2]. The most common cardiac manifestation in CKD is left ventricular hypertrophy (LVH), predominantly as a result of hypertension and anemia [3]. The prevalence of LVH increases with declining glomerular filtration rate (GFR) and may be as high as 70% to 95.5% before initiation of dialysis [4]. LVH is a powerful independent predictor of cardiovascular mortality in uremic patients [3,4].

Cardiovascular disease begins early in the course of chronic kidney disease. Individuals with CKD are more likely to die of cardiovascular disease than to develop kidney failure requiring dialysis [5,6]. Traditional cardiovascular risk factors (e.g., diabetes mellitus, hypertension, dyslipidemia, obesity, and smoking), as well as those specifically or more commonly associated with renal disease (e.g., anemia, albuminuria, LVH, hyperparathyroidism, and the calcium – phosphate product) may be associated with increases in cardiac troponin levels in CKD patients [7].

Cardiac troponins (cTns) are the biomarkers of choice for detecting cardiac injury in patients with renal failure [8]. They are particularly useful in patients with ESRD because there is little difference between the predialysis and postdialysis levels [8,9]. They are used in the diagnosis and risk stratification of patients with suspected acute coronary syndrome (ACS) and myocardial infarction (MI) [9,10]. Serum troponin elevations in stable, asymptomatic CKD patients may also have prognostic implications. They may reflect subclinical microinfarctions and predict worse long-term cardiovascular outcomes and all-cause mortality [1,8,11].

However, elevations of cardiac troponins may not always be due to myocardial necrosis [12]. In patients with severe renal dysfunction cardiac troponin I (cTnI), as well as cardiac troponin T (cTnT), elevations are commonly found that cannot be linked to myocardial injury [1,11,12]. Troponin I is the only troponin isotope present in the myocardium that is not expressed during any developmental stage in skeletal muscle. The cardiac specificity of this isoform improves the accuracy of diagnosis in patients with acute or chronic skeletal muscle injury and possible concomitant myocardial injury. However, in some animal models and certain diseases of skeletal muscle (polymyositis and genetic muscular dystrophies or myopathy resulting from chronic renal failure) re-expression of some cardiac isoforms of cardiac troponin T has been noted [11]. Though re-expression of cardiac isoforms in skeletal muscles has been excluded by improved analytical methods and different investigators, current immunoassay tests still show that 18% to 75% of patients with end-stage renal failure have elevated cardiac troponin T levels compared to 4% to 17% of elevated cardiac troponin I levels [11]. The higher unbound cytosolic pool and higher molecular weight may explain why troponin T is more frequently found elevated than

troponin I [12]. Though the mechanisms of these elevations have not yet been clearly determined [2,11,12] elevated serum cardiac troponins in CKD may be caused by uremic toxins, loss of membrane integrity and constant outflow from the free cytosolic troponin pool, amplified elevation of normal low levels because of impaired protein clearance, abnormal protein metabolism, silent myocardial ischemia, left ventricular hypertrophy, and inflammation [1,12].

The level of cardiac troponins in CKD patients who are asymptomatic for acute cardiac diseases, may have a determinant role in prognosis and risk assessment of cardiovascular diseases. The ability to detect significant cardiac disease in asymptomatic CKD patients at an early stage before they get to ESRD could facilitate more aggressive and focused treatment of those at increased risk. This cross-sectional study was undertaken to measure serum cardiac troponin I concentration in pre-dialysis CKD patients who do not have any acute symptoms of cardiac disease and determine its relationship with cardiovascular risk factors.

2. METHODOLOGY

2.1 Subjects

The target population included diagnosed chronic kidney disease patients (those with symptoms and signs of renal disease and/or glomerular filtration rate (GFR) < 60 ml/min/1.73 m^2 for ≥ 3 months, with laboratory or radiological evidence) above the age of 18 years who were stable and ambulatory and attending the Renal Clinic of the University of Port Harcourt Teaching Hospital (UPTH). Patients on dialysis and those with acute renal failure or other acute illness were excluded. A corresponding number of age- and sex-matched control subjects with normal renal function and no history of cardiovascular disease, diabetes, hypertension, or other acute or chronic condition were drawn from the general population. Approval was obtained from the Ethical Committee of UPTH and informed consent was obtained from all participants. Demographic, social and medical data of participants were assessed with the use of questionnaires.

2.2 Physical Examination

Blood pressure (BP) of each participant was measured with a mercury sphygmomanometer after ten minutes of rest on two occasions and hypertension was defined as a BP equal to or greater than 140/90 mmHg or the use of antihypertensive drugs. Participants were weighed bare footed and wearing light clothing on a weighing balance placed on a flat surface. Their heights were measured on a portable collapsible stadiometer and body mass index (BMI = weight/$height^2$) was calculated.

2.3 Specimen Collection

After 10-12 hours overnight fast and observing aseptic procedure, 10ml of venous blood was drawn from the antecubital fossa of each participant into a fluoride oxalate bottle for fasting plasma glucose analysis, an EDTA bottle for analysis of lipids and a plain bottle for the estimation of serum creatinine, albumin and cardiac troponin I. Plasma/serum was separated from blood cells after centrifugation at 2500 g for 10 minutes, harvested with a clean Pasteur pipette and stored at -20°C. Freshly voided spot mid-stream urine was also collected from each participant in a plain bottle for determination of urinary albumin-creatinine ratio (UACR).

2.4 Laboratory Analysis

Urine and serum creatinine concentrations were analysed using the modified Jaffe method and the serum value obtained was used to calculate the estimated glomerular filtration rate (eGFR) of each participant using the Abbreviated Modification of Diet in Renal Disease (MDRD) formula: $32788 \times (\text{serum creatinine in } \mu mol/L)^{-1.154} \times (Age)^{-0.203} \times 1.210$ (if black) x 0.742 (if female) [13]. Estimation of fasting plasma glucose was done using the colorimetric glucose oxidase method [14], urine and serum albumin by the BCG (Bromocresol Green) method [14], HDL-cholesterol by precipitation technique, total cholesterol and triglyceride by enzymatic method [14] and LDL-cholesterol was calculated using the Friedewald's formula: (Total cholesterol) – (HDL-C) – (Triglyceride/2.2) in mmol/L [15]. Cardiac troponin I was determined using ELISA technique (Calbiotech). Reference ranges provided by the manufacturer for cardiac troponin I was ≤ 0.5 ng/ml. Cardiac troponin I was considered positive for levels higher than 0.5 ng/ml.

2.5 Statistical Analysis

Data obtained from this study was analysed using the Statistical Package for Social Sciences (SPSS) version 20.0 (SPSS Inc. Chicago, Illinois, U.S.A.). Frequencies and percentages were obtained for categorical variables. Differences in

proportions were analysed using the Chi-squared test. The means of continuous variables were compared using one way analysis of variance (ANOVA) and expressed as mean ± standard deviation (SD). Pearson correlation statistics and multiple regression analysis were used to determine associations between cardiac troponin I and clinical and biochemical parameters. P-values less than or equal to 0.05 were taken to be significant in all analyses.

2.6 Definition of Variables

CKD Stages: Stage 1: eGFR ≥ 90 ml/min/1.73 m^2 with kidney damage (persistent albuminuria), stage 2: eGFR = 60 – 89.9 ml/min/1.73 m^2 with kidney damage, stage 3: eGFR = 30 – 59.9 ml/min/1.73 m^2, stage 4: eGFR = 15 – 29.9 ml/min/1.73 m^2, stage 5: eGFR < 15 ml/min/1.73 m^2 [4].

Albuminuria: UACR of < 30 mg albumin/g creatinine (3.4 mg albumin/mmol creatinine) was regarded as normal, UACR of 30 – 300 mg/g (3.4-33.9 mg/mmol) as microalbuminuria and UACR of > 300 mg/g creatinine (> 33.9 mg/mmol) as overt albuminuria (macroalbuminuria) [16].

Type 2 diabetes: Defined as a FPG ≥ 7.0 mmol/L or the use of hypoglycemic medication [16].

Obesity: Defined as BMI ≥ 30 Kg/m^2 [16].

3. RESULTS

There were 83 CKD patients made up of 41 (49.4%) males and 42 (50.6%) females and 83 age- and sex-matched control subjects consisting of 41 (49.4%) males and 42 (50.6%) females. CKD patients were divided into three groups based on the eGFR: Group 1 (CKD stages 1 and 2), group 2 (CKD stage 3) and group 3 (CKD stages 4 and 5). Thirty-five (42.2%), 27 (32.5%) and 21 (25.3%) patients were in groups 1, 2 and 3 respectively.

CKD patients had higher systolic (*P* = .01) and diastolic blood pressure values (*P* = .02) than controls (Table 1). Fifty (60.2%) patients had hypertension. Forty-seven (94%) of these hypertensive patients were able to specify the antihypertensive drugs they were taking, which included various combinations of angiotensin-converting enzyme inhibitors (lisinopril, captopril, ramipril), angiotensin-receptor blockers (losartan, valsatan), calcium-channel blockers (amlodipine, nifedipine), diuretics (spironolactone, frusemide) and centrally-acting drugs (aldomet). Three (6%) patients did not know the names of the drugs they were taking and they were not with samples of such drugs as at the time they were interviewed. Serum cardiac troponin I (*P* < .001), triglyceride (*P* = .002), creatinine (*P* < .001) and UACR (*P* < .001) of CKD patients were higher and their serum albumin (*P* = .03), HDL (P < .001) and estimated GFR (*P* < .001) were lower than that of controls (Table 1).

Among CKD patients cardiac troponin I increased progressively along the 3 patient groups, with the highest elevations observed among patients in group 3 (CKD stages 4 and 5), but the upward trend was significant only between groups 1 and 3 (*P* = .02) but not groups 1 and 2 (*P* = .72) or groups 2 and 3 (*P* = .42) (Fig. 1).

Among CKD patients, cardiac troponin I had significant inverse correlation with estimated GFR (r = -.33, *P* = .01) but had no significant correlations with serum creatinine (r = .16, *P* = .16), serum albumin (r = - .007, *P* = .50) or UACR (r = .03, *P* = .42). Multiple linear regression was carried out to further determine the independent effect of clinical and biochemical risk factors on elevated cardiac troponin I levels but there were no significant associations observed (Table 2).

Twenty-two (26.5%) patients had elevated cardiac troponin I but none of the controls had elevated cardiac troponin I. Patients with high cardiac troponin I had higher prevalence of diabetes mellitus (*P* = .02) and obesity (*P* = .047) compared to patients with normal cardiac troponin I levels (Table 3). Prevalence of other cardiovascular risk factors was not significantly different between the two groups (Table 3).

4. DISCUSSION

Patients with chronic kidney disease in this study differed from controls in multiple baseline characteristics, including higher cardiac troponin I and cardiovascular risk factors. Twenty-two (26.5%) patients had elevated cardiac troponin I but none of the controls had elevated cardiac troponin I. In consonance with our findings, numerous studies have also documented higher prevalence of cardiovascular risk factors in patients with renal dysfunction compared to individuals with normal renal function [17,18]. Multiple regression analysis revealed that age, body mass index, blood pressure, plasma

glucose, serum cholesterol and triglyceride levels were not significant predictors of elevated cardiac troponin I among overall CKD patients. However, CKD patients with high cardiac troponin I levels had higher prevalence of diabetes and obesity. Some researchers have observed significant associations between cardiac troponin I and cardiovascular risk factors [1,7,19,20]. Abbas et al. [7] documented an elevated cardiac troponin I prevalence of 18% among pre-dialysis CKD patients, which was lower than that observed in this study. They observed that cardiac troponin I levels were more likely to be increased in patients with diabetes than in non-diabetic patients. Ahmadi et al. [1] also had a lower prevalence of elevated cardiac troponin I of 10%, which was associated with cholesterol. Chen et al. [19] reported a higher prevalence of 43.3% but did not observe any association with diabetes or obesity. Rather, increased cardiac troponin I levels were associated with age and hypertension. It is well known that traditional cardiovascular risk factors are prevalent in CKD but do not fully explain the high incidence of cardiovascular events or increased mortality rates [21].

Table 1. Comparison between characteristics of controls and CKD patient groups

GFR (ml/min/1.73 m^2)	Control ≥90	CKD1-2 ≥60	CKD3 30-59.9	CKD4-5 <30	*P*
Clinical data					
Number (n = 166)	83	35	27	21	
Age (years)	40.8 (9.3)	40.6 (14.8)	47.4 (14.0)	44.7 (11.9)	.24
BMI (Kg/m^2)	26.0 (6.5)	24.4 (3.6)	26.4 (4.6)	23.5 (3.9)	.18
SBP (mmHg)	120.0 (15.8)	127.1 (21.2)	130.0 (16.0)	141.8 (24.6)	.01*
DBP (mmHg)	74.5 (8.3)	79.5 (11.1)	80.8 (12.3)	88.6 (18.8)	.02*
Laboratory data					
Creatinine (µmol/L)	83.5 (12.3)	86.5 (9.5)	153.7 (28.2)	475.7 (185.0)	<.001*
eGFR (ml/min)	103.6 (31.3)	92.8 (22.3)	51.2 (12.0)	17.0 (7.2)	<.001*
FPG (mmol/L)	4.7 (1.3)	5.5 (1.2)	5.2 (3.0)	4.3 (0.8)	.15
TC (mmol/L)	4.6 (0.5)	4.7 (1.2)	4.8 (1.0)	4.2 (0.9)	.31
Triglyceride (mmol/L)	0.9 (0.4)	1.3 (0.8)	1.7 (1.0)	1.2 (0.6)	.002*
HDL (mmol/L)	1.0 (0.2)	0.8 (0.2)	0.7 (0.2)	0.7 (0.2)	<.001*
LDL (mmol/L)	3.0 (0.6)	3.3 (1.0)	3.3 (1.1)	2.9 (0.7)	.41
Albumin (g/L)	43.2 (2.1)	38.8 (9.3)	40.5 (6.7)	40.1 (6.9)	.03*
UACR (mg/g)	5.6 (13.5)	155.2 (194.4)	371.8 (586.7)	536.8 (984.0)	<.001*
Troponin I (ng/ml)	0.3 (0.1)	0.7 (0.2)	0.9 (0.3)	1.2 (0.8)	<.001*

** P-values ≤ .05 significant; BMI – Body Mass Index; SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure; eGFR – estimated Glomerular Filtration Rate; FPG – Fasting Plasma Glucose; TC – Total Cholesterol; HDL – High Density Lipoprotein; LDL – Low Density Lipoprotein; UACR - Urinary Albumin-Creatinine Ratio. All values are Mean (SD)*

Table 2. Factors associated with elevated cardiac troponin I levels in CKD patients

Variable	Beta coefficient	*P*	95% confidence interval
Age (years)	.18	.47	-.01 to .03
BMI (Kg/m^2)	-.07	.80	-.09 to .07
SBP (mmHg)	-.24	.39	-.02 to .009
DBP (mmHg)	.30	.21	-.008 to .03
FPG (mmol/L)	.11	.51	-.06 to .11
Total cholesterol (mmol/L)	-.03	.86	-.17 to .15
Triglyceride (mmol/L)	-.07	.73	-.39 to .28
HDL (mmol/L)	-.08	.68	-1.06 to .70
LDL (mmol/L)	-.11	.62	-.36 to .22

** P-values ≤ .05 significant; BMI – Body Mass Index; SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure; FPG – Fasting Plasma Glucose; HDL – High Density Lipoprotein; LDL – Low Density Lipoprotein*

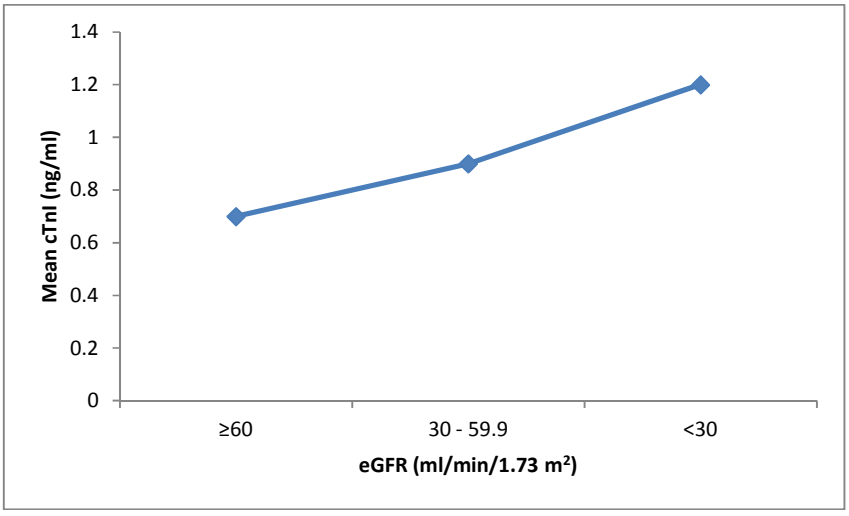

Fig. 1. Mean cTnI of CKD patients according to eGFR
eGFR – Estimated glomerular filtration rate; cTnI – Cardiac troponin I

Table 3. Prevalence of cardiovascular risk factors in patients with high and normal cardiac troponin I

Risk factor	Frequency (%)		*P*
	High cTnI (n=22)	Normal cTnI (n=61)	
Hypertension	13 (59.1)	34 (55.7)	.98
Diabetes Mellitus	8 (36.4)	6 (9.8)	.02
Obesity	22 (100.0)	12 (19.7)	.047
Dyslipidemia	11 (50.0)	30 (49.2)	1.0
Hypercholesterolemia	6 (27.3)	13 (21.3)	.83
Hypertriglyceridemia	7 (31.8)	18 (29.5)	.99
Low HDL	10 (45.5)	28 (45.9)	1.0
High LDL	7 (31.8)	9 (29.5)	.99

** P-values ≤ .05 significant*

Cardiac troponin T has been observed to have higher prevalence rates in CKD patients compared to cardiac troponin I despite the fact that the current cardiac troponin T assays do not detect cross-reacting isoforms from skeletal muscle [7,8]. The prevalence of increased troponin values among patients with chronic renal failure in the absence of clinically suspected ischemia may be as high as 53% to 100% using the new high sensitivity cardiac troponin assays [17,22,23]. However, in patients with advanced renal failure, cardiac troponin concentrations develop higher peaks and troponin remains detectable for longer periods. Patients with ESRD usually have elevated troponin values before any acute cardiac event. Repeated early measurements are needed to detect a pronounced rise indicating an acute ischemia [22].

Elevated cardiac troponin I in this study was associated with reduced eGFR. Highest elevations of cardiac troponin I were observed among patients in CKD stages 4 and 5. In support of these findings, several studies have reported an inverse correlation of cardiac troponins with eGFR in CKD patients without acute cardiac symptoms [1,2,7,17,19]. Ahmadi et al. [1] noted that elevation of cardiac troponin I concentration was associated with decreased glomerular filtration rate and occurred only among patients in CKD stage 4. Wang et al. [2] observed that elevation of cardiac troponin increased with progression of CKD stages and a statistically significant rise began in CKD stage 3. Abbas et al. and Chen et al. also published that patients with more advanced stages of CKD had higher cardiac troponin I levels compared to patients in earlier CKD stages [7,19]. Decreased GFR has been found to be an independent risk factor for CVD outcomes and all-cause mortality, and is also related to increased prevalence of left ventricular hypertrophy (LVH) [24]. Increased cardiac troponin I levels observed in ESRD may

be a true reflection of underlying myocardial injury associated with cardiovascular co-morbidities such as LVH and congestive heart failure that frequently occur in these patients [19,2]. On the other hand, impaired catabolism and reduced clearance of troponins induced by uremia in CKD patients may also result in false positive elevations of serum troponin levels [19,20]. The possibility that increased troponin levels may reflect analytical interference from uremic serum cannot also be ruled out [19]. This brings into question the clinical utility of cardiac troponins in patients with renal dysfunction and may limit the use of cardiac troponins for the diagnosis of acute coronary syndromes in ESRD [17]. In CKD patients, the use of cardiac troponins in diagnosis has not yet been clearly standardized and the ability of cardiac troponins at the usual prognostic thresholds to predict risk for subsequent adverse cardiac events is reduced in patients with renal insufficiency [25].

5. CONCLUSION

CKD patients had higher mean cardiac troponin I and higher prevalence of traditional and uremia-related cardiovascular risk factors compared to controls. Twenty-two (26.5%) patients, but no controls, had elevated cardiac troponin I. Elevated cardiac troponin I was associated with a higher prevalence of diabetes mellitus and obesity, and reduced eGFR. Use of cardiac troponin I levels in the diagnosis of myocardial injury in CKD patients should be done with caution because of the possibility of false-positive increases.

6. LIMITATION

This study was a cross-sectional study, so patients were not followed up over a period of time to ascertain cause and effect. Further research is required to determine the effect of reduced GFR on the diagnostic and prognostic efficiency of cardiac troponins, particularly in ESRD patients.

CONSENT

All authors declare that written informed consent was obtained from the patient (or other approved parties) for this study.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Ahmadi F, Dolatkhani F, Lessa-Pezeshki M, Mahdari-Mazdeh M, Abbasi M, Mohebi-Nejad A. Cardiac troponins in patients with chronic kidney disease and kidney transplant recipients without acute cardiac symptoms. Iranian Journal of Kidney Diseases. 2014;8:31-36.
2. Wang S, Qin L, Wu T, Deng B, Sun Y, Hu D, et al. Elevated cardiac markers in chronic kidney disease as a consequence of hyperphosphatemia-induced cardiac myocyte injury. Med Sci Monit. 2014;20: 2043-2053.
3. Vickery S, Webb MC, Price CP, Abbas NA, Lamb EJ. Prognostic value of cardiac biomarkers for death in a non-dialysis chronic kidney disease population. Nephrol Dial Transplant. 2008;23:3546-3553.
4. Ulasi II, Arodiwe EB, Ijoma CK. Left ventricular hypertrophy in African black patients with chronic renal failure at first evaluation. Ethn Dis. 2006;16:859-864.
5. Amaresan MS. Cardiovascular disease in chronic kidney disease. Indian J Nephrol. 2005;15:1-7.
6. Thomas R, Kanso A, Sedor JR. Chronic kidney disease and its complications. Prim Care Clin Office Pract. 2008;35:329-344.
7. Abbas NA, John RI, Webb MC, Kempson ME, Potter AN, Price CP, et al. Cardiac troponins and renal function in nondialysis patients with chronic kidney disease. Clin Chem. 2005;11:2059-2066.
8. Jaffe AS, Babuin L. Troponin: The biomarker of choice for the detection of cardiac injury. CMAJ. 2005;173:1191-1202.

9. McCullough PA, Nowak RM, Foreback C, Tokarski G, Tomlanovich MC, Khoury NE, et al. Performance of multiple cardiac biomarkers measured in the emergency department in patients with chronic kidney disease and chest pain. Acad Emerg Med. 2002;9:1389-1396.
10. Iliou MC, Fumeron C. Cardiovascular disease in chronic renal failure patients. Saudi J Kidney Dis Transpl. 2005;16:129-39.
11. Bel MS, Soldevila JG, Lianos JO. Biological markers of myocardial necrosis. Rev Esp Cardiol. 2003;56:703-720.
12. Hamm CW, Giannitsis E, Katus HA. Cardiac troponin elevations in patients without acute coronary syndrome. Circulation. 2002;106:2871-2872.
13. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: A new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999;130:461-470.
14. Randox Laboratories Ltd., Antrum, BT294QY, UK. Manual Procedures, 4th Edition. 1996;126-189.
15. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma without the use of preparative ultracentrifugation. Clin Chem. 1972;18: 499-502.
16. Afolabi MO, Abioye-Kuteyi EA, Arogundade FA, Bello IS. Prevalence of chronic kidney disease in a Nigerian family practice population. SA Fam Pract. 2009; 51:132-137.
17. Twerenbold R, Wildi K, Jaeger C, Gimenez M, Reiter M, Reichlin T, et al. Optimal cutoff levels of more sensitive cardiac troponin assays for the early diagnosis of myocardial infarction in patients with renal dysfunction. Circulation. 2015;131:2041-2050.
18. Adejumo OA, Okaka EI, Madumezia G, Okwuonu CG, Ojogwu LI. Assessment of some cardiovascular risk factors in predialysis chronic kidney disease patients in Southern Nigeria. Niger Med J. 2015;56: 394-399.
19. Chen S, Huang C, Wu B, Lian X, Mei X, Wan J. Cardiac troponin I in non-acute coronary syndrome patients with chronic kidney disease. PLoS ONE. 2013;8: e82752.
DOI: 10.1371/journal.pone.0082752.
20. Iliou MC, Fumeron C, Benoit MO, Tuppin CL, Calonge VM, Moatti N, Buisson C, Jacquot C. Factors associated with increased serum levels of cardiac troponins T and I in chronic haemodialysis patients: Chronic haemodialysic and new cardiac markers evaluation (CHANCE) study. Neprol Dial Transplant. 2001;16: 1452-1458.
21. Herzorg CA, Asinger RW, Berger AK, Charytan DM, Diez J, Hart RG et al. Cardiovascular disease in chronic kidney disease. A clinical update from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int. 2011;80:572-86.
22. Agzew Y. Elevated serum cardiac troponin in non-acute coronary syndrome. Clin Cardiol. 2009;32:15-20.
23. Agewall S, Giannitsis E, Jernberg T, Katus H. Troponin elevation in coronary vs. non-coronary disease. European Heart Journal. 2011;32:404-411.
24. Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Culleton B, Hamm LL et al. Kidney disease as a risk factor for development of cardiovascular disease: A statement from the American Heart Association Councils on kidney in cardiovascular disease, high blood pressure research, clinical cardiology, and epidemiology and prevention. Circulation. 2003;108:2154-2169.
25. Alam GK, Lieb DB. Biochemical markers of myocardial ischemia in renal failure. Hosp Physician. 2002;1:27-31.

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