

## Original Article

### Association between troponin I level and cardiovascular risk factors in asymptomatic hemodialysis patients

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#### ABSTRACT

**Objective:** Patients on hemodialysis (HD) have a high risk for cardiovascular morbidity and mortality. Cardiac troponins are biomarkers for diagnosing acute myocardial injury or infarction. There is considerable controversy that exists in the frequency and significance of cardiac troponins in predicting cardiac injury and ischemia in HD patients.

**Methods:** In this cross-sectional study, all HD patients more than 18-year-old, who were at least 3 months under HD, and had no sign and symptom of active cardiovascular disease (CVD), in two HD centers were enrolled. One hundred and one patients fulfilled the inclusion criteria. Blood sample for cardiac troponin I (cTnI) was drawn before the initiation of HD session during their routine monthly blood testing from patients' vascular access arterial line. cTnI levels were measured by a high-sensitivity assay, VIDAS troponin I Ultra kit, and correlated with patients' demographic, clinical, and laboratory results.

**Findings:** The patients' different demographic and clinical characteristics had no statistically significant correlation with troponin levels except for marginal trend for past medical history of diabetes and hyperlipidemia with corresponding *P* values of 0.072 and 0.055. Twenty-six patients had cTnI level more than 0.01 µg/L and only two patients had cTnI level more than 0.11 µg/L. For laboratory results, only fasting blood sugar had statistically significant correlation with patients' cTnI level ( $r = 0.357$ ,  $P = 0.0001$ ).

**Conclusion:** Frequency of significant elevation of cTnI level in our asymptomatic HD patients was very low and if such elevation is found in this population, it may be considered as a sign of active CVD.

**Keywords:** Cardiovascular disease; hemodialysis; troponin I

#### INTRODUCTION

Patients on hemodialysis (HD) have a high risk for cardiovascular morbidity and mortality.<sup>[1]</sup> Cardiac troponins are biomarkers usually used to diagnose acute myocardial injury and infarction.<sup>[2]</sup> There is considerable controversy that exists in the significance of cardiac troponins in predicting cardiac injury and ischemia in chronic renal failure patients, especially in

patients on HD.<sup>[3,4]</sup> In this study, we evaluated cardiac troponin I (cTnI) and its correlation to cardiovascular risk factors in our HD patients.

#### METHODS

In this cross-sectional study, from November 2013 to January 2014, all end-stage renal disease (ESRD)

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patients under HD in two Isfahan University HD centers who fulfilled the following inclusion criteria were enrolled in this study.

All patients, who were at least 18-year-old, at least 3 months on HD, had no sign and symptoms of active cardiovascular disease (CVD), gave an informed consent to participate in this study, and used anonymously the information from this study as a research publication, were enrolled.

This study was approved by the Isfahan Kidney Diseases Research Center/Isfahan University of Medical Sciences and registered as a Grant number: 292135. From all 220 HD patients in these two HD centers, 101 patients had the above-mentioned inclusion criteria to enter into this study.

Demographic characteristics of the patients, including gender, age, predialysis body mass index (BMI), education level, cause of kidney failure, duration of HD, weekly dialysis session number, history of hypertension, hyperlipidemia, diabetes, CVD, limb-amputation, previous coronary care unit or Intensive Care Unit hospitalization, were recorded from patients' recordings.

Laboratory data including serum albumin, calcium, phosphorus, triglyceride, cholesterol, high-density lipoprotein, low-density lipoprotein, white blood cell count, platelet count, fasting blood sugar (FBS), and hemoglobin level were also recorded from patients' medical charts.

Blood sample for cTnI was drawn before the initiation of HD session during blood sampling for their routine monthly blood testing from patients' vascular access arterial line, and sent immediately to the laboratory for analysis.

cTnI levels were measured by a high-sensitivity assay, VIDAS troponin I Ultra kit (Biomerieux, Marcy-l'Etoile, France) and by Vidas 12 device (Biomerieux Italia S.p.a., Ponte A Ema, Italy) in the Laboratory of Al-Zahra Hospital. The assay principle combines a one-step immunoassay sandwich method with a final fluorescent detection (ELFA).

In 2000, the Consensus Committee of the European Society for Cardiology and the American College of Cardiology recommended that the diagnosis of myocardial necrosis can be made when the level of cardiac troponin is > the 99<sup>th</sup> percentile of a reference control group with imprecision <10%. The imprecision study result with the smallest measurable concentration of cTnI, with an inter-lot coefficient of variation <10%, is 0.11 µg/L.<sup>[5]</sup>

The measurement values of the VIDAS troponin I Ultra kit range from 0.01 to 30 µg/L. The analytical

detection limit, defined as the smallest concentration of cTnI which is significantly different from the zero concentration with a probability of 95%, is <0.01 µg/L.

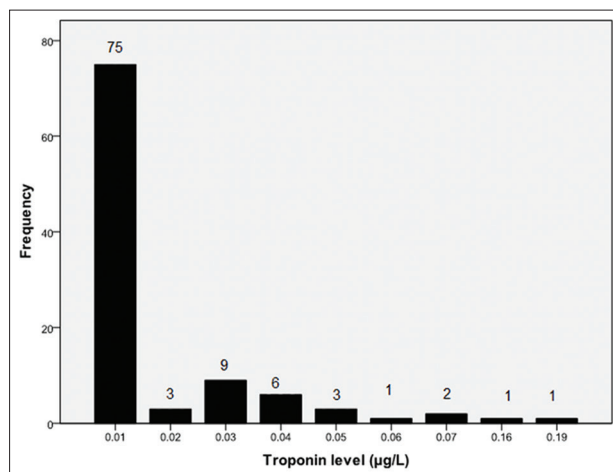
Data were reported as frequencies and means ± standard deviations (SDs) for patients' demographic and clinical variables. The statistical analysis including one-way analysis of variance (ANOVA) and unpaired sample *t*-test was used to compare the cTnI level between different clinical parameters. Pearson correlation test was performed to find any correlation between demographic and laboratory parameters with cTnI level by using SPSS software for windows (SPSS, Chicago, IL, USA) version 20.

## RESULTS

One hundred and one patients treated by HD were contributed and entered into the final analysis study. The difference of patients' different demographic and clinical characteristics with troponin levels was analyzed by unpaired sample *t*-test and ANOVA [Table 1]. None of the mentioned parameters had statistical significance except for marginal trend for past medical history of diabetes and hyperlipidemia with corresponding *P* values of 0.072 and 0.055.

Range of cTnI levels was 0.01–0.19 (mean ± SD: 0.02 ± 0.026). Frequency of the cTnI levels in our patients is shown in Figure 1. Twenty-six patients had cTnI level more than 0.01 µg/L and only two patients had cTnI level more than 0.11 µg/L.

Table 2 shows the correlation of troponin level with different patients' laboratory parameters



**Figure 1:** Distribution of cardiac troponin I level in our study population. The numbers at the top of each bar indicate absolute patients' number in each of the cardiac troponin I level measurement

**Table 1: Correlation between demographic and clinical characteristics and cardiac troponin I level**

Parameter	Mean±SD	r	P	
Age (year)	56.2±14.4	-0.058	0.567	
BMI (kg/m <sup>2</sup> )	24.5±3.91	0.088	0.380	
Duration of hemodialysis (month)	53.4±51.5	-0.004	0.967	
Parameter	n (%)	Mean cTnI	cTnI SD	P
Gender				0.532
Male	58 (57.4)	0.0195	0.0229	
Female	43 (42.6)	0.0207	0.0303	
Education level				0.998
Illiterate	41 (40.6)	0.215	0.2762	
Undergraduate	33 (32.7)	0.209	0.3225	
Graduated and higher	27 (26.7)	0.167	0.1301	
History of hypertension				0.912
Positive	67 (66.3)	0.0201	0.0301	
Negative	34 (33.7)	0.0197	0.0162	
History of diabetes				0.072
Positive	52 (51.5)	0.0215	0.0276	
Negative	49 (48.5)	0.0184	0.0247	
History of hyperlipidemia				0.055
Positive	31 (30.7)	0.0197	0.0118	
Negative	70 (69.3)	0.0219	0.0304	
CCU or ICU hospitalization				0.299
Positive	43 (42.6)	0.0165	0.0141	
Negative	58 (57.4)	0.0226	0.0322	
Amputation history				0.553
Positive	3 (3.0)	0.0100	0.0000	
Negative	98 (97.0)	0.0203	0.0265	
Cause of kidney failure				0.634
HTN	14 (13.9)	0.0271	0.0419	
DM	51 (50.5)	0.0210	0.0276	
Other	36 (35.6)	0.01582	0.0556	
CVD history				0.713
Positive	39 (38.6)	0.0169	0.0149	
Negative	62 (61.4)	0.0219	0.0312	
Weekly dialysis session number				0.348
Once a week	1 (0.99)	0.01	-	
Twice a week	25 (24.75)	0.017	0.0156	
Thrice a week	75 (74.26)	0.0209	0.0290	

SD=Standard deviation, HTN=Hypertension, DM=Diabetes mellitus, CCU=Coronary care unit, ICU=Intensive Care Unit, BMI=Body mass index, cTnI=Cardiac troponin I, CVD=Cardiovascular disease

using Pearson correlation test. Only FBS had statistically significant correlation with patients' cTnI level ( $r = 0.357, P < 0.001$ ).

## DISCUSSION

It has been shown that cardiac troponins were not only released after cardiac myocyte necrosis, but also

**Table 2: Correlation of cardiac troponin I level with laboratory parameters**

Parameter (unit)	Mean±SD	r	P
FBS (mg/dL)	131.3±57.8	0.357	<0.001
Calcium (mg/dL)	8.9±1.0	0.130	0.196
Phosphorus (mg/dL)	4.4±1.1	0.046	0.648
Albumin (g/dL)	3.8±0.4	-0.124	0.218
Total cholesterol (mg/dL)	145.5±33.3	0.000	0.996
Triglyceride (mg/dL)	137.9±71.6	0.046	0.651
High-density lipoprotein (mg/dL)	41.0±10.2	0.098	0.332
Low-density lipoprotein (mg/dL)	82.2±42.0	-0.115	0.252
White blood cell count (/mm <sup>3</sup> )	6239.8±2215.4	0.039	0.697
Hemoglobin (g/dL)	10.5±1.9	-0.070	0.489
Platelet count (/mm <sup>3</sup> )	169,990.1±53,491.6	0.057	0.570

SD=Standard deviation, FBS=Fasting blood sugar

were detected in circulation in some clinical situation without any apparent cardiac injury.<sup>[6]</sup> High level of cTnI with complementary clinical presentation and other parameters such as electrocardiogram indicate acute myocardial infarction.<sup>[7]</sup>

Some authors stated that increases in cardiac troponins in patients with renal failure have reduced the sensitivity to predict adverse outcome,<sup>[8]</sup> The main coronary artery stenosis, microvascular lesions, silent plaque, rupture or subclinical myocardial fibrosis, and necrosis may cause high levels of troponin in blood circulation.<sup>[9]</sup>

The reason for cTnI elevation in HD patients is not clear.<sup>[10,11]</sup> In addition, the precise mechanism for raised cardiac troponin concentrations in the kidney failure patients is uncertain.<sup>[7]</sup> In fact, little is known about the route of degradation of cTnI; furthermore, the kinetics of decreases and the catabolic pathways of cTnI in HD patients are not known.<sup>[9,12]</sup>

Some mechanical manifestations may create controversy, for example, the dialysis membrane may also adsorb cTnI and alter its level after each HD session.<sup>[13]</sup> ESRD patients have increased mortality and morbidity due to cardiovascular events.<sup>[14]</sup> These patients also have neuropathy,<sup>[15]</sup> so they may not experience classical chest pain, and clinical presentation during coronary events is atypical. Risk for atherosclerosis has been increased in uremic patients,<sup>[16]</sup> and silent ischemia is common among ESRD patients because of associated autonomic neuropathy.<sup>[16,17]</sup> Due to simultaneous reduction of coronary artery oxygen delivery and increasing myocardial oxygen demand, both symptomatic and silent ischemic heart disease may occur frequently during HD.<sup>[16,18]</sup>

McLaurin *et al.* showed that some patients with chronic kidney disease have high cTnI levels in

their blood and it may correlate with their poor prognosis.<sup>[19]</sup> Hence, high cTnI could be either an innocent marker and may overdiagnose myocardial infarction in renal failure patients or may be an excellent test to find out the increased risk of HD patients for future cardiovascular event.<sup>[16,18]</sup>

Our finding shows that although cTnI levels are more than 0.01 µg/L in 26% of our patients, elevated level (more than 0.11 µg/L) was seen only in two persons of our asymptomatic patients.

Hussein *et al.* in their study on 93 asymptomatic HD patients showed that cTnI has a high specificity for the diagnosis of myocardial infarction in dialysis patients and it was found to be significantly correlated with the outcome of all-cause mortality at 1 year.<sup>[20]</sup> Resic *et al.* reported that periodical hemodynamics or underlying cardiac disease with specific alterations of cardiac musculature in uremia would be some possible reasons for cTnI elevation.<sup>[9]</sup>

In our study, we determined the correlation of cTnI levels in HD patients and its association with some demographic, clinical, and laboratory parameters, which only had significant positive correlation with FBS and marginally correlated with history of diabetes.

It has been shown that in diabetic patients with multiple associated cardiovascular risk factors, troponin may be used as a CVD biomarker.<sup>[21]</sup> Lin-Tan *et al.* showed that basal fasting glucose levels play an important role in short-term mortality of diabetic maintenance HD patients.<sup>[22]</sup>

According to our study, despite a history of diabetes which did not correlate with the level of troponin, higher cTnI level was detected in patients with higher FBS; it may suggest that patients with uncontrolled diabetes are at risk for cardiovascular events, and also may conclude that with better glycemic control in patients with ESRD, future cardiovascular events can be decreased.<sup>[23,24]</sup>

Interestingly, in patients with positive history of hyperlipidemia, reduced levels of cTnI were observed even if it did not reach statistical significance. It is consistent with previous reports stating that ESRD patients with hyperlipidemia had better protection from cardio-vascular events.<sup>[25,26]</sup>

Frequency of significant elevation of cTnI level in our asymptomatic HD patients was very low and if such elevation is found in this population, it may be considered seriously and should be followed more intensely for active CVD to prevent cardiovascular events.

## AUTHORS' CONTRIBUTION

All authors contributed the idea of research, design of study, data analysis and manuscript preparation.

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### Conflicts of interest

There are no conflicts of interest.

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