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Assessment of High-Sensitive Cardiac Troponin I in Coronary Artery Disease Patients Undergoing Regular Hemodialysis

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Abstract
Objective: to examine the prevalence of elevated cardiac troponin I level in asymptomatic and symptomatic end-stage renal disease (ESRD) patients on regular hemodialysis (HD) as a strong predictor of worse cardiovascular outcomes. **Background:** ESRD on regular hemodialysis patients with elevated cardiac troponin I have a higher cardiac mortality rate, it is important to detect elevated cardiac troponin I patients as predictor of worse cardiovascular outcomes. **Methods:** The patients were divided into three groups: Group (A): ischemic heart disease patients (IHD) with normal kidney function,Group (B): ischemic heart disease patients on regular hemodialysis,Group (C): non ischemic heart disease patients on regular hemodialysis. **Results:** Our study revealed elevated serum cardiac troponin I (CTnI) in group B, with normal level CTnI in other two groups (A and C). There was significant positive correlation between elevated CTnI, ejection fraction, E/A ratio and regional wall motion abnormalities. There was inverse correlation between CTnI elevation and EF%, also there was direct correlation between CTn I elevation and E/A ratio in group B. **Conclusion:** Troponin I was elevated in symptomatic IHD patients on regular HD and normal in IHD patients with normal kidney function and in non IHD on regular HD patients. The elevated CTnI may play in past a role in cardiomyopathies in IHD on regular HD and this could be related to some acute coronary syndromes in these patients which carries worse cardiovascular outcomes.

Key words: Cardiac troponin I (CTnI) – hemodialysis – ischemic heart disease.

Introduction

Cardiovascular disease accounts for roughly 50% of deaths in patients with chronic renal failure. Patients with renal failure are at higher risk for silent ischemia (17%) and atypical clinical presentation. Electrocardiogram results are not reliable, because ST segment changes are difficult to interpret secondary to electrolyte imbalances, left ventricular hypertrophy and medications[1] .Using a second-generation assay, cardiac troponins (cTns) was found to be elevated in up to 53% of patients with renal failure with no clinical evidence of acute myocardial necrosis[2]. Any elevation of cTn levels in patients with ST elevation MI, non-ST elevation MI, unstable angina, congestive heart failure and chronic kidney insufficiency portends a worse outcome. Patients with elevated cTns have a higher cardiac mortality rate, are more likely to have coronary thrombi, showers of emboli in the coronary microvasculature, and depressed ventricular function, it has been found that elevations in cTn levels from causes other than ischemic heart disease are associated with worse prognoses[3].

There is increasing evidence that elevation in serum cTnI and cTnT levels in stable asymptomatic patients with end-stage renal disease is predictive of worse long-term and short-term cardiovascular outcomes. The reason for this correlation is unknown, although a correlation between increased troponin levels and diffuse coronary artery disease in those patients has been reported[4].

PATIENTS AND METHODS

The current study was carried out after obtaining a written consent from all patients and an approval by the Faculty of Medicine, AL-Azhar University Research Ethics Committee. The study started from June 2016 to May 2017.

Inclusion criteria: Chronic renal failure patients on regular hemodialysis of at least 1 year duration, mental competence, willingness to participate in the study

Exclusion criteria: Diabetes mellitus patients, acute kidney injury patients, new hemodialysis

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patients, irregular hemodialysis patients and recent endovascular interventions.

The study was carried out in hemodialysis unit at Tanta Health Insurance Hospital (El Mogama El Tebby). Total number of patients was 90 and they were divided into three groups:

Group (A)

This group included 30 symptomatic ischemic heart disease patients with normal kidney function. Their ages ranged between 44 and 71 years with a mean±SD of 56.76±7.65 years, 17 (57%) of them were males and 13 (43%) were females.

Group (B)

This group included 30 ESRD patients on regular hemodialysis with symptomatic ischemic heart disease. Their age ranged between 38 and 75 years with a mean of 54.4±10.04 years. 24 (80%) of them were males and 6 (20%) were females. The duration of hemodialysis ranged between 1 year and 20 years with a mean of 6.32±4.8 years.

Group (C)

This group included 30 ESRD patients on regular hemodialysis with asymptomatic ischemic heart disease. Their age ranged between 21 and 76 years with a mean of 54.33±12.3 years. 14 (47%) of them were males and 16 (53%) were females. The duration of hemodialysis ranged between 1 year and 22 years with a mean of 6.55± 5.06 years. Measurement of cardiac troponin I was done by electrochemiluminescence immunoassay (ECLIA) and cobas e immunoassay analyzer.

All patients were subjected to complete history taking included personal history, number of HD sessions/ week, duration of hemodialysis session, recurrent hypotension attacks or other complications during the session, and any causes of session interruptions.

Full clinical examination and local examination included examination of the vascular access to detect access dysfunction, accepted distance of cannulation, thrill intensity, blood flow rate, ultrafiltration volume, surface area of the dialyzer, and venous pressure.

Laboratory investigations included: Kt/V (K is dialyzer blood water urea clearance (L/h), T is dialysis session length (hours) and V is distribution volume of urea (liters)), intact parathyroid hormone (IPTH) by radio immunoassays, serum ionized calcium, serum phosphorus, serum lipid profile (Total cholesterol, LDL, VLDL , HDL), complete blood count, and cardiac troponin I.

Echocardiogram was done to all patients in the studied groups. Resting ECG was done to all patients in the study and interpreted by a well experienced cardiology consultant

Statistical Method:

The collected data were analyzed by Statistical Package of Social Science program (SPSS), version 20.0. Qualitative data were expressed as number and percentage and analyzed by using chi-square and Fsher's exact test. Quantitative data were expressed as mean ± SD and analyzed by using t- test and *ANOVA* test.

Results:

Our study revealed elevated serum CTnI in one group of patients (regular hemodialysis patients with positive history of ischemic heart disease), with normal level CTnI in other two groups (Non ischemic hemodialysis patients and ischemic patients with normal kidney function).

Table (1): The mean values of patients Trop I of the three groups (IHD Normal kidney function, IHD on hemodialysis and Non IHD on hemodialysis).

	Trop I		
	IHD Normal kidney function	*IHD Dialysis*	*Non IHD Dialysis*
Mean±SD	*0.19±0.02*	*6.67±0.93*	*0.19±0.08*
f-value	*12.74*		
p- value	*<0.0001**		

**f-value Significance at the 0.05 level*

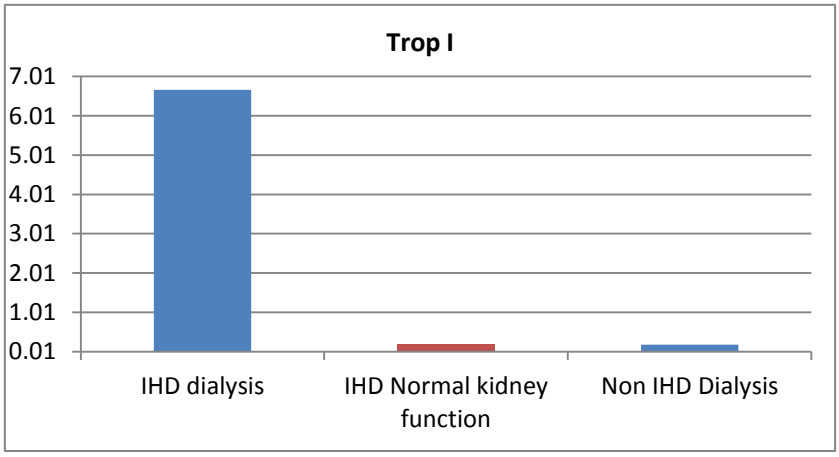

Fig (1): A mean values of Trop I of the three groups (IHD Normal kidney function, IHD on hemodialysis and Non IHD on hemodialysis).

There was significant positive direct correlation between elevated CTnI , E/A ratio and regional wall motion abnormalities. There was inverse correlation between CTnI elevation and EF%

Table (2): Correlations between Trop I and Eco , ECG findings in ischemic heart disease patients on regular hemodialysis (group B)

Variables	*Sample size*	*r-value*	*p-value*	*Significance*
Trop I ng/ml	*30*	*-0.735*	*<0.0001**	*S*
EF %				
Grading of DD	*30*	*0.0332*	*0.083*	*NS*
E/A ratio	*30*	*0.479*	*0.0074*	*S*
LVMI	*30*	*0.064*	*0.750*	*NS*
ECG changes	*30*	*0.74*	*<0.0001*	*S*

**r-value Significance at the 0.05 level (one-tail)*
r : Pearson product-moment correlation coefficient p-value: Probability value S: Significant

Table (3): Patients' Trop I values according to regional wall motion abnormalities(RWMA) in ischemic heart disease patients on regular hemodialysis (group B)

	Trop I	
RWMA	*Absent*	*present*
Mean±SD	*4.62±0.96*	*20±2.94*
t-value	*3.352*	
p- value	*0.0023**	

**t-value Significance at the 0.05 level*

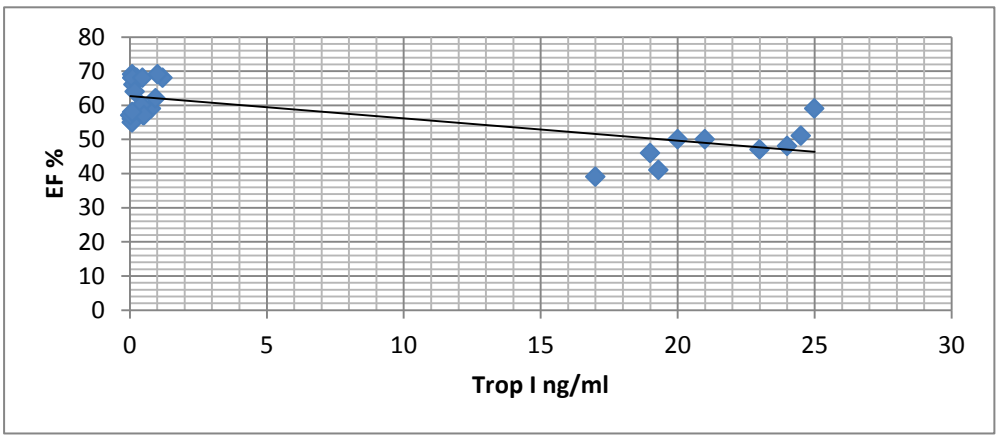

Figure (2): Correlations between Trop I and EF % in ischemic heart disease patients on regular hemodialysis (group B)

There was strong inverse correlation between troponin I and EF% as (r=-0.735 and p=<0.0001) in group (B)

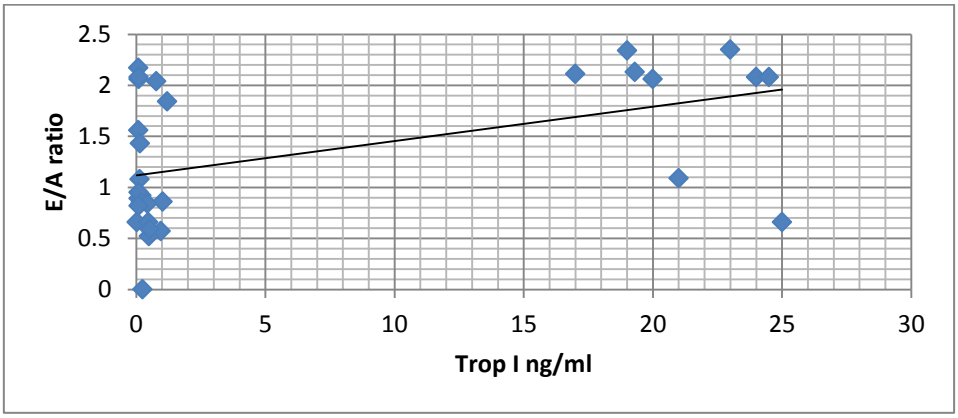

Figure (3): Correlations between Trop I and E/A ratio (ratio between E wave and A wave) in ischemic heart disease patients on regular hemodialysis (group B)

There is mid direct correlation between troponin I and E/A ratio as (r=0.479 and p=0.0074) in group (B)

In this study, there was no statistically significant correlation between CTnI level and each of Hb level, serum electrolytes (Na^+, Ca^{++}, K^+, $PO4^+$), intact parathyroid hormone level, alkaline phosphatase enzyme (ALP), changing in hemodialysis adequacy (URR and KT/V), C reactive protein, and level of lipid profile in studied groups.

Table (4): Correlations between Trop I and clinical and laboratory parameters in ischemic heart disease patients on regular hemodialysis (group B, sample size=30)

Variables	*r-value*	*p-value*	*Significance*
Trop I|(ng/ml)	*0.082*	*0.66*	*NS*
Duration of HD(Year)			
BMI	*0.059*	*0.75*	*NS*
Mean age (Year)	*0.080*	*0.68*	*NS*
Syst. Bl. pressure (mmhg)	*-0.324*	*0.080*	*NS*
Dia. Bl. Pressure (mmhg)	*0.262*	*0.161*	*NS*
Main art. pressure	*-0.325*	*0.079*	*NS*
HR(Min)	*-0.152*	*0.422*	*NS*
Hb (g/dl)	*0.165*	*0.328*	*NS*
URR	*0.220*	*0.241*	*NS*
KT/V	*-0.107*	*0.570*	*NS*
K^+ (mg/dl)	*-0.0003*	*0.998*	*NS*
$PO4^+$ (mg/dl)	*0.0052*	*0.978*	*NS*
*Ca*po4 mmol/l*	*-0.048*	*0.798*	*NS*
PTH (p/ml)	*-0.041*	*0.826*	*NS*
Serum cholesterol	*-0.231*	*0.212*	*NS*
LDL	*-0.270*	*-0.148*	*NS*

**r-value Significance at the 0.05 level (one-tail) r : Pearson product-moment correlation coefficient p-value: Probability value NS: Non Significant *There was no statistically significant correlation between CTnI and any clinical or laboratory parameters in the above table*

Discussion:

The present study was designed to evaluate prevalence of elevated cardiac troponin I in coronary artery disease patients on regular hemodialysis as a predictor of cardiovascular outcome.

In the present study, there were statistically significant difference as regard CTnI levels

between patients in three groups. The level of CTnI was elevated in symptomatic ischemic heart disease patients on regular hemodialysis (group B) than non-symptomatic ischemic heart disease patients on regular hemodialysis (Group C) and symptomatic ischemic heart disease with normal kidney function (Group A).

The explanation of these results could be due to reduced renal clearance. The healthy human heart is always prone to microloss of cardiac myocytes but, when renal failure is involved, clearance of troponin fragments due to routine myocyte loss is impaired[5].

The mechanism of elevation of CTnI in ischemic hemodialysis patients is not known. Perhaps CTnI elevations reflect microinfarctions or left ventricular hypertrophy, kidney disease-related subclinical cardiac damage may play a role[6].

Volume overload which frequently seen in anuric hemodialysis patients increases cardiac preload, this means that the heart works extra hard which may play a role in increasing process of cardiac myocyte damage in those patients[7].

The hemodynamic effects of a functioning hemodialysis arteriovenous access can cause or exacerbate heart failure. Most patients who develop heart failure from the hemodynamic demands of AV access have known cardiovascular disease and/or cardiovascular risk factors, but most hemodialysis patients have cardiovascular disease or cardiovascular risk factors[8].

Several trials have reported false-positive CTnI levels ranging from 0% to 21% in patients with ESRD. Examining the methodology of these trials may explain the divergence of results[9].

The current trial and several previous studies examined ‘‘asymptomatic’’ patients with ESRD and found false-positive elevations of CTnI levels[10].

Dialysis may differentially affect serum levels of CTnT and CTnI. Regardless of method of clearance or membrane used[11].

TnI levels decreased by up to 86% from pre to post dialysis, this also could explain that CTnI is near normal in group C[12].

In the current study, there were an inverse significant correlation between CTnI levels and EF% in ischemic heart disease patients on regular hemodialysis (group B), these results could be explained by that those patients were liable to silent acute coronary syndrome and volume overload which is frequently seen in hemodialysis patients[13].

There was direct significant correlation between CTnI levels and ischemic ECG changes in ischemic heart disease patients on regular hemodialysis (group B), these results could be explained by that those patients were liable to multivessel coronary artery disease (CAD) [14].

There was no statistically significant correlation between CTnI levels and grading of diastolic dysfunction or left ventricular mass index in ischemic heart disease patients on regular hemodialysis (group B).

There was weak correlation between CTnI and E/A ratio in ischemic heart disease patients on regular hemodialysis (group B), this could be explained by the study involved limited numbers of patients and all ECO studies had done by M-mode only.

In this study, there was no statistically significant correlation between CTnI level and each of Hb level, serum electrolytes (Na^+, Ca^{++}, K^+, $PO4^+$), intact parathyroid hormone level, alkaline phosphatase enzyme (ALP), changing in hemodialysis adequacy (URR and KT/V), C reactive protein, and level of lipid profile in studied groups.

Conclusion:

Troponin I was elevated in symptomatic IHD patients on regular HD and normal in IHD patients with normal kidney function and in non-IHD on regular HD patients.

The elevated CTnI may play in part a role in cardiomyopathies in IHD patients on regular HD and this could be related to some acute coronary syndromes in those patients which carries worse cardiovascular outcomes.

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