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Assessment of cardiac troponins status in patients on regular hemodialysis

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Abstract

Background and objectives: heart disease is a significant contributor to both fatalities and health issues among patients undergoing regular hemodialysis. Cardiac Troponins serve as sensitive indicators of heart muscle injury, playing a vital role in diagnosing acute coronary syndrome. The aim of this study is to assess cardiac troponins status in an Iraqi cohort of asymptomatic Hemodialysis patients.

Methods: One-hundred-thirty-six asymptomatic hemodialysis patients who visited the hemodialysis center at the Hawler Teaching Hospital in Erbil, Iraq, between August 2022 and May 2023 participated in this cohort. Recorded were demographic and baseline characteristics. A battery of laboratory tests was conducted, including high sensitivity cardiac troponin T, cardiac troponin T, and I. Correlations were made between different variables

Result: The occurrence rates of increased cardiac troponin T, and I, and high sensitivity cardiac troponin T among asymptomatic hemodialysis patients were 25%, 7.4%, and 76.5%, respectively. Cardiac troponin T alone showed a significant positive correlation with the duration of dialysis treatment ($p<0.05$), while cardiac troponin I was significantly associated with dyslipidemia ($P<0.05$).

Conclusion: The majority of asymptomatic hemodialysis patients have elevated cardiac troponin levels, particularly high sensitivity cardiac troponin T. Both cardiac troponins were positively associated with prior history of coronary artery disease, and low serum albumin. Cardiac troponin T was positively correlated with dialysis vintage.

Keywords: Cardiac troponin I, Cardiac troponin T, Hemodialysis, High-sensitive cardiac troponin

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Introduction

Individuals with end-stage renal disease (ESRD), who are receiving hemodialysis (HD) are at increased risk of morbidity and mortality due to cardiovascular disease (CVD).[1] Identifying and treating cardiac complications in this patient population is essential for enhancing outcomes and reducing the burden of cardiovascular events. Two cardiac troponins (cTn), cardiac troponin I (cTnI) and cardiac troponin T (cTnT), have emerged as key biomarkers for the diagnosis and prognosis of heart injury.[2] Following cardiac injury, such as myocardial infarction (MI), ischemia, or other types of cardiac stress, cTn is released into the bloodstream, and regarded as the gold standard for myocardial damage diagnosis because of its excellent sensitivity and cardiac specificity.[3] For the diagnosis of MI, the European Society of Cardiology advised detecting a rise/fall in cTn with at least a single reading above the 99th percentile and one of the following; ischemic symptoms, or new ischemic alterations characterized by electrocardiographic and/or imaging investigations.[4] Hemodialysis patients with ESRD are more likely to develop CVD as a result of a number of variables, such as fluid and electrolyte imbalances, inflammation, oxidative stress, and endothelial dysfunction.[5] Several studies have shown that even in the absence of symptoms or clinical evidence of acute coronary syndrome, increased cTn levels are frequently seen in patients receiving HD.[2, 6] These spikes are frequently linked to a chronic, mild myocardial damage brought on by conditions including myocardial stunning, left ventricular hypertrophy, and small-vessel disease.[7] According to recent studies, nearly majority of HD patients had elevated levels of high-sensitivity hs-cTnT, whereas only around one-third of patients had elevated levels of hs-cTnI.[8-11] Higher levels of cTnT and cTnI were associated with increased risk of long term mortality and major adverse cardiovascular events.[2, 12] Noppakun et al. concluded in their study that a higher risk of mortality is correlated with elevated hs-cTnT but not hs-cTnI. However, both hs-TnT and I were positively correlated with a higher risk of long term major adverse cardiovascular events.[12] This study's objective is to assess cTnT, cTnI, and hs-cTnT status in a cohort of asymptomatic hemodialysis patients in Erbil, Iraq. And to analyze the association of these enzymes to past medical history and biochemical characteristics of these patients.

Patients and methods

This cross-sectional research was carried out at the HD center at Hawler Teaching Hospital, in Erbil, Iraq, from August 2022 until May 2023. The inclusion criteria were asymptomatic patients on regular HD more than 6 months, older than 18 years of age, and with no active CVD. Exclusion criteria were patients with history of acute coronary syndrome, heart failure, pulmonary embolism, and coronary or valvular interventions within the last 6 months, as well as Patients who have had major surgeries or trauma within the last 4 weeks. The recruited subjects comprised 167 HD patients; amongst them, 31 patients were removed due to refusal (13 participants), insufficient or inadequate data (11 patients), or death (7 patients passed away within the study period). A total of 136 patients on regular HD, 3 sessions per week, each of 3-4 hours, were eligible for the current analysis. All participants went through a complete history and physical examination, and demographic variables such as gender, age, weight, height and dialysis vintage were documented. The body mass index (BMI) (kg/m2) was computed. Hypertension, dyslipidemia, diabetes mellitus, smoking, prior history of coronary artery disease, and peripheral vascular disease (PVD) were among the risk factors and comorbidities studied. Albumin, serum creatinine, total cholesterol and LDL,

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high-sensitivity C-reactive protein (hs-CRP), hemoglobin level, and cardiac troponins (cTnT, cTnI, and hs-cTnT) were all measured and studied. Blood drawn from each participant from their accesses before dialysis session, routine investigations estimated by standard methods, while cardiac troponins; cTnT and cTnI were checked by Nano-checker 710, and the hs-cTnT was measured by Electrochemiluminescence immunoassay (ECLIA) by using Cobas e411. For the analysis, the mean results of two measurements were employed. All lab studies performed in central lab of Hawler Teaching Hospital. The cutoff normal values of cTnT, cTnI, and hs-cTnT were 0 - 0.05 ng/ml, 0 - 0.04 ng/ml and 0-0.014 ng/ml respectively. The research was carried out in conformity with the ethical principles outlined in the Helsinki Declaration. According to document number (meeting code 8, Number 1995, 2/11/2022), the ethics committee of the Kurdistan High Council of Medical Specialties evaluated and approved the study protocol, subject information, and permission form. Continuous data are represented by the mean and standard deviation (SD), while categorical variables are represented by frequencies and percentages. For continuous data, the student's t-test or one-way ANOVA test was employed, and for categorical variables, the chi-squared test or Fisher's exact test was used. This data was imported into Microsoft Excel and analyzed using SPSS version 25 (Chicago, IL, USA). P 0.05 was used as the statistical significance level.

Results

This study involved the participation of 136 patients, with an average age of 52.8 ± 18.9 years, among whom 70 were male. The demographic details of the examined sample are presented in Table (1).

Table (1): Baseline characteristics of the study sample

Variables		N %, mean SD
Mean age, years		52.88 ± 18.9
Gender	Male	70 (51.5%)
	Female	66 (48.5%)
Dialysis vintage	< 1 year	24 (17.6%)
	1-2 years	40 (29.4%)
	> 2 years	72 (52.9%)
BMI, kg/m^2	Underweight	38 (27.9%)
	Normal	96 (70.6%)
	Overweight	2 (1.5%)
Coronary artery disease		50 (36.8%)
Diabetes mellitus		60 (44.1%)
Hypertension		120 (88.2%)
Peripheral vascular disease		12 (8.8%)
Dyslipidemia		18 (13.2%)
Smoking status	Non-smoker	92 (67.6%)
	Ex-smoker	38 (27.9%)
	Current smoker	6 (4.4%)

BMI: body mass index

Majority of the participants showed marked elevation in hs-cTnT level with a median (interquartile range) of 0.06 (0.002-0.08) ng/ml, whereas elevated cTnI level detected in a minority of patients. The biochemical parameters are shown in Table (2).

Table (2): Biochemical measurements of the study sample

Biochemical tests	N (%), mean ± SD, median (IQT)
Low S. Albumin	38 (27.9%)
Elevated hs-CRP level	50 (36.8%)
Elevated S. Creatinine	136 (100%)
S. Creatinine, mg/dL	6.5 ± 2.86
Hemoglobin g/dL	10.2 ± 1.45
Cholesterol mg/dL	191 ± 22.6
Elevated Cardiac Troponin T	34 (25%)
Cardiac Troponin T level, ng/ml	0.39 (0.11-0.81)
Elevated Cardiac Troponin I	10 (7.4%)
Cardiac troponin I, ng/ml	0.02 (0.002-0.09)
Elevated hs-Cardiac Troponin T	104 (76.5%)
hs-Cardiac Troponin T, ng/ml	0.06 (0.002-0.08)

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high sensitivity C-reactive protein, IQT interquartile range Cardiac troponi T and I were both positively correlated with previous history of CAD, diabetes mellitus, PVD, increased hs-CRP, and low serum albumin. Whereas cTnT was associated with longer HD vintage, and cTnI with dyslipidemia. Correlation between Patient characteristics and cardiac troponins are shown in Table (3).

Table (3): Patient characteristics vs. Cardiac Troponins

Variables		Elevated cTnT n= 34	P-value	Elevated cTnI n= 10	p-value	Elevated hs-cTnT n= 104	p-value
Gender	Male	14 (20%)	0.406	6 (8, 6%)	1.00	50 (71.4%)	0.396
	Female	20 (30%)		4 (6.1%)		54 (81.8%)	
Age	<45 years	6 (15.8%)	0.359	0 (0%)	0.312	26 (68.4%)	0.353
	≥45 years	28 (28.6%)		10 (100%)		78 (79.6%)	
BMI	Underweight	8 (21.1%)	0.340	0 (0%)	0.362	26 (68.4%)	0.51
	Normal	24 (25%)		10 (10.4%)		76 (79.2%)	
	Overweight	2 (100%)		0 (0%)		2 (100%)	
Dialysis vintage							
<1 year		4 (11.8%)	0.02	2 (20%)	1.000	12 (11.5%)	<0.001
1-2 years		2 (5.9%)		2 (20%)		24 (23.1%)	
> 2 years		28 (82.4%)		6 (60%)		68 (65.4%)	
S. creatinine mg/dL	<5	2 (14.3%)	0.67	0 (0%)	1.00	10 (71.4%)	0.664
	≥ 5	32 (26.2%)		10 (100%)		94 (77%)	
Elevated hs-CRP		26 (76.5%)	<0.01	8 (80%)	0.02	46 (44.2%)	0.02
Low serum Albumin		24 (70.6%)	<0.01	8 (80%)	0.02	36 (34.6%)	0.03
Coronary artery disease		22 (64.7%)	<0.01	10 (100%)	0.01	46 (44.2%)	0.02
Diabetes Mellitus		21 (61.8%)	0.02	10 (100%)	0.01	49 (47.1%)	0.048
Hypertension		34 (100%)	0.186	10 (100%)	1.00	92 (88.5%)	1.000
PVD		10 (29.4%)	<0.01	5 (50%)	0.046	11 (10.6%)	0.373
Dyslipidemia		8 (23.5%)	0.212	6 (60%)	0.02	18 (17.3%)	0.103
Anemia		32 (94.1%)	0.176	10 (100%)	1.00	90(86.5%)	0.98
Smoking status							
Non-smoker		20 (58.8%)	0.527	6 (60%)	0.703	68 (65.4%)	0.789
Ex-smoker		12 (35.3%)		4 (40%)		30 (28.8%)	
Smoker		2 (5.9%)		0 (0.0%)		6 (5.8%)	

BMI: body mass index, PVD: peripheral vascular disease, hs-CRP: C-reactive protein

Discussion

The current study demonstrated high prevalence of elevated cTn level in asymptomatic HD patients, particularly hs-cTnT. This is in accordance with stacy et al.,[13] Mahmood et al.,[14] Krause et al.,[15] Pfortmueller et al.'s studies, [16] in which they reported elevated cardiac troponin levels in up to 71% of patients on HD. Chen et al. concluded that undergoing hemodialysis causes a short-term decrease in hs-cTnT but the levels start to rise after a period of time post-hemodialysis.[17] Our findings substantiate the difference between elevated cTnT and cTnI reported by other studies that a greater number of asymptomatic HD patients having an increased cTnT.[8, 9, 10] The differences in cellular distribution,

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biochemical, genetic, and kinetic properties of cTnT and cTnI may be the cause of the contradictory results.[12, 18]Elevated both cTnT and cTnI were positively associated with, prior history of CAD, PVD, diabetes mellitus, hs-CRP, and low serum albumin, whereas cTnT alone was associated with longer HD vintage, and cTnI with dyslipidemia. Regarding association of cTn to potential variables, our results were in concordance to several prior studies in many points and disagree with some other. In Snaedal et al.'s study, it was shown that hs-cTn increased in patients with CAD, congestive heart failure, PVD, diabetes, and protein energy wasting.[10] Peters et al. have demonstrated in a randomized study, that the initial cTnT levels showed a direct relationship with diabetes, ultrafiltration volume, arterial stiffness, and an increased likelihood of admission and cardiovascular events. Conversely, there was an inverse correlation observed with hematocrit and residual renal function.[6] Pianta et al. reported that established IHD, PVD and diabetes were more prevalent in those in the highest quartile for hs-cTnT.[11] Artunc et al, stated that cTnT was independently associated with age, gender, systolic dysfunction, dialysis vintage, residual diuresis, and hypertension, whereas cTnI was independently associated with age, systolic dysfunction, dialysis vintage, and duration of HD session.[19]In our study, dialysis vintage was significantly associated with elevated cTnT but not cTnI. We found that a larger percentage of patients who had been undergoing dialysis for more than two years had elevated cTnT and hs-cTnT compared to patients who had been undergoing dialysis for less than 2 years. This finding is in contrast to Snaedal et al.'s study in which they reported no association between cTnT variation and dialysis vintage. [10]One of the study's weaknesses is that it is a single-center cross-sectional study with a limited sample size. Furthermore, because the test was not available in our laboratory, we were unable to assess hs-cTnI. In conclusion: The majority of asymptomatic HD patients have elevated cTn levels, particularly hs-cTnT. Both cTn were positively associated with prior history of CAD, diabetes mellitus, PVD, elevated hs-CRP, and low serum albumin. cTnT was positively correlated with dialysis vintage, and cTnI with dyslipidemia. Baseline cTn measurements for HD patients might be helpful for further identification of new cardiovascular events.

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Disclosure:

The authors assert that they have no conflicts of interest.

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