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Original Article

Measurement of the serum levels of serum troponins I and T, albumin and C-Reactive protein in chronic hemodialysis patients and their relationship with left ventricular hypertrophy and heart failure

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ABSTRACT

Background: Hemodialysis patients are at high risk for cardiovascular diseases. The prognostic value of cardiac troponins, albumin and CRP in hemodialysis patients and their association with cardiac diseases has been proven. The aim of this study was to investigate the relationship between these factors and heart failure and left ventricular hypertrophy in hemodialysis patients in Sanandaj city.
Methods: A total of 90 hemodialysis patients referred to hemodialysis ward of Tohid Medical Center of Sanandaj were enrolled in the study. After receiving the required information from patients and recording them in questionnaire, blood samples were taken from them and were sen to Lab for Measurement. Finally, the data were analyzed using SPSS software and Spearman correlation coefficient for independent variables and Chi square test and correlation coefficient of Choprovert's for independent qualitative variable.
Results: In the case of LVH, 23.3% of patients were with normal thickness, 38.9% had mild LVH, 30% had moderate LVH and 7.8% had severe LVH. The mean serum albumin level in patients was 3.8 g/dl, CRP 9.4 mg/dL, and troponins I and T were 0.4 and 685.06 ng/dL, respectively. There was a statistically significant relationship between cardiac I and T troponins levels and CRP levels in patients with chronic hemodialysis ($P < 0.05$. There was a significant relationship between serum albumin level, troponins I, T and CRP with left ventricular hypertrophy in chronic hemodialysis patients ($P < 0.05$).
Conclusion: Serum levels of I and T troponins, albumin, as well as CRP, are related to heart failure and left ventricular hypertrophy in hemodialysis patients, and this can be used by physicians to determine the patient's ability and risk of disease Cardiovascular diseases.

1. Introduction

In patients with renal failure who are candidate for renal replacement therapy, there is a close relationship between pathophysiology of cardiovascular diseases, malnutrition and inflammation [1,2]. Hemodialysis is a renal replacement therapy for patients with end stage renal disease (ESRD), and hemodialysis patients are at high risk for cardiovascular diseases [3]. Cardiovascular mortality in hemodialysis patients are much higher than in the general population. The importance of the issue is so much that even some cardiovascular diseases are the main cause of deterioration and mortality in patients with ESRD [4]. It has been accepted that inflammation is the onset of many heart diseases. Uremia that can be observed in ESRD is also a chronic inflammatory condition, therefore it can cause heart diseases [5]. Although the reduction of left ventricular ejection fraction (EF) is known to be a powerful predictor of prognosis, mortality and cardiovascular diseases, most of patients with ESRD have a preserved EF amount, but the important point is that their consequences is similar to those that have reduced EF [3,6–8]. Also, left Ventricular Hypertrophy (LVH) plays a very important role in the mortality of hemodialysis patients [9].

The prognostic value of several biomarkers in patients with

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ESRD has been proven that cardiac troponins are one of these biomarkers [3]. cardiac troponins are structural proteins in the cardiomyocytes contractile system. Following myocardial damage, these troponins enter into the bloodstream, which is the reason that they are very important in the diagnosis of myocardial infarction [10,11]. Evidences suggest that, in the general population, cardiac troponin T (cTnT) levels are a reliable biochemical indicator for assessing the prognosis of myocardial infarction and unstable angina. Researchers have suggested that cTnT levels are a metabolic predictor for the risk of cardiovascular diseases in patients with renal failure, and further studies are needed to better understand this relationship. Apart from acute or asymptomatic cardiac ischemia, serum levels of cardiac troponin I (cTnI) in hypertensive patients with LVH are higher than those with hypertension but normal left ventricular mass, so troponins in the circulation reflects the condition of the left ventricular mass and the predictive power of mortality and cardiovascular outcomes by cardiac troponins is related to this relationship [12].

Serum level of albumin is regulated by several factors including nutrition, inflammation, sex and age. Serum level of albumin in patients undergoing hemodialysis is completely different. Studies have shown that a low serum level of albumin is associated with an increase in acute phase proteins [13]. Low serum levels of albumin, as a sign of nutritional status, are a strong predictor of deterioration and mortality in patients with renal insufficiency. The importance of this issue is so far as in the United States, the standardized method for monitoring hemodialysis patients is monthly measurement of serum albumin levels. Evidences suggest that hypoalbuminemia caused by renal failure can be a consequence of acute phase response activation and may lead to a chronic inflammatory condition. Also, because serum albumin levels typically indicate the nutritional status of hemodialysis patients, malnutrition in these patients can be another cause of mortality [14,15].

Studies showed that inflammation is an important factor in the progression of atherosclerosis and subsequent cardiovascular diseases. C-reactive protein (CRP) is one of the inflammatory factors of the acute phase that its level increases in inflammatory processes. Inflammatory stimuli release various cytokines, which, in turn, increase the release of CRP as a positive acute phase reactant protein [16,17]. It has been proven that levels of CRP, as an inflammatory factor, increase in renal failure [18]. CRP is also a risk factor for the progression of cardiovascular diseases. According to the Multiple Risk Factor International Trial (MRFIT), there is a strong correlation between CRP levels and mortality due to coronary and cardiovascular diseases [19]. CRP has also been proven to predict albumin concentration in patients with hemodialysis [20].

According to the high prevalence of renal diseases and renal failure, and the use of hemodialysis as the main treatment, it is essential to pay attention to complications caused by this method. As mentioned, cardiovascular diseases is one of the most important prognostic factors in these patients. Differences in methods of hemodialysis, the difference in the treatment of underlying diseases, and the potential of patients for cardiovascular diseases, increase the need for different studies in different populations. Therefore, regarding the changes in some factors in hemodialysis patients and their relationship with cardiac disease, the aim of this study was to investigate the relationship between these factors and cardiac diseases in hemodialysis patients in Sanandaj, west of Iran.

2. Material and methods

In this cross-sectional study, after approving of the ethics committee of Kurdistan University of Medical Sciences, hemodialysis patients referring to the hemodialysis ward of Tohid Medical Center of Sanandaj, the center of Kurdistan province, west of iran, were considered as the statistical population. Exclusion criteria included acute myocardial infarction (AMI) and acute coronary syndrome (ACS), which was diagnosed using history and electrocardiogram. In suspected cases, serum cardiac troponin measurements were used to reject or detect AMI. Finally, 90 patients (42 women and 48 men) were enrolled in the study. After describing the goals and all stages of the study for patients and obtaining written consent from them, the required information such as the age and duration of hemodialysis by referring to the patient's records and asking from them, and they were recorded in the pre-prepared questionnaire. Blood samples were taken at the first day of weekly hemodialysis, before hemodialysis, to quantitatively evaluation of the serum levels of albumin, CRP, troponin I and T, and sent to Tohid Medical Center Laboratory. Information about LVH diagnosed by echocardiography were recorded if available in their records and otherwise determined by the cardiologist and then recorded in the questionnaire. The criteria for diagnosis of LVH was that in women ranging from 0.6 to 0.9 as normal, 1 to 1.2 were mild, 1.3 to 1.5 was moderate and in cases more than 1.6 was severe and in men 0.6–1 As normal, 1.1 to 1.3 was considered as mild, 1.4 to 1.6 was moderate and in more than 1.7 cases it was considered as severe. Heart failure was measured by echocardiography by determining the Ejection Fraction (EF) by the cardiologist and based on $LVEF = (SV \div LV\ end\text{-}diastolic\ volume) \times 100$, with a normal value of more than 55% And based on severity was divided into mild, moderate and severe systolic failure. The CRP was measured in the hospital laboratory using the Latex Immunoturbidimetric Assay (CRP-LIA) kit, produced by Bionik co., with considering serum CRP> 6 mg/dl as positive. Serum albumin was measured using a photometric method with the Parsazmoon co. kit. In this study, serum albumin levels below 4 mg/dl were considered as hypoalbuminemia. Cardiac troponins I and T were measured by Enzyme-Linked Immunosorbant Assay (ELISA) with Abbott co. kit.

Finally, by statistical counselor, the data were analyzed by SPSS software (version 22, Armonk, NY, USA) and Spearman correlation coefficient for ordina or ratis independent variables and Chi square test, and relationship correlation intensity of Tschuprow for independent qualitative variables.

3. Results

In this study, in the case of LVH, 21 patients (23.3%) were in the normal group, 35 (38.9%) cases were mild, 27 (30%) had moderate LVH and 7 (7.8%) had severe LVH. According to Table 1, the average duration of hemodialysis in patients was 49.8 months. The mean serum level of albumin in patients was 3.8 g/dl, CRP 9.4 mg/dL, and troponins I and T were 0.4 and 685.06 ng/dL, respectively. As shown in Table 2, there was a statistically significant relationship between cardiac troponins I and T and CRP levels with heart failure in patients with chronic hemodialysis ($P < 0.05$); it should be noted that for this relationship there was a negative correlation between the mentioned factors with heart failure. According to Table 2, there

Table 1
The mean of the measured variables in the studied patients.

Variable	Mean	Standard Deviation
Age	60.00	12.17
Duration of Hemodialysis	49.85	36.04
Albumin	3.81	0.34
Troponin I	0.40	0.26
Troponin T	685.06	281.35
CRP	9.43	5.03
EF	47.39	9.18
Left Ventricular Wall Thickness	1.17	0.34

Table 2
The relationship between the measured factors with heart failure and LVH.

Variable	LVH	Heart Failure
Albumin	$P > 0.05$	$P < 0.05$
Troponin I	$P < 0.05$	
Troponin T		
CRP		

was a significant relationship between serum levels of albumin, troponins I, T and CRP with left ventricular hypertrophy in chronic hemodialysis patients ($P < 0.05$).

4. Discussion

The evaluation of blood biomarkers including CRP and troponins is recommended for assessing the risk for heart disease in the community [21]. It has also been discussed in various studies about the role of albumin in cardiac diseases and its evaluation as a diagnostic and effective factor in prognosis [9,14]. Therefore, the aim of this study was to evaluate the plasma level of cardiac troponins I and T, albumin and CRP in patients undergoing hemodialysis and the association of these factors with LVH and heart failure in patients referred to Tohid Hospital of Sanandaj.

In this study, 42 (47%) females and 48 (53%) males were studied and their average age was 60 years. So, most of studied cases were men and most of the patients were in the old age group. The mean duration for hemodialysis was 49.8 months. For LVH, 21 (23.3%) patients were in the normal range, 35 (38.9%) were in mild hypertrophy range, 27 (30%) were in the moderate range, and 7 (7.8%) were in the severe range. Therefore, the most common group was patients with mild LVH. The mean EF of patients participating in the study was 47.3% and the mean thickness of the left ventricular wall was 1.17 mm.

The mean serum level of albumin in patients was 3.8 g/dL, CRP was 9.4 mg/dL, and troponins I and T was 0.4 and 685.06 ng/dL, respectively. So, serum levels of CRP as well as troponin levels were in the increased range, but for albumin in the decreased range. In a study by Wayand et al., serum level of troponin T in 16.6% of patients increased by 0.1 μg/l, and this result in McLaurin et al. was similar and has been increased by 0.2 μg/L [22,23]. Expression of troponin T in skeletal muscles is increased in uremic conditions, which can be a reason to increase its level in patients with renal insufficiency [12]. In the study of Wayand et al. And also in the study of Möckel et al. the researchers concluded that the levels of troponins I and T do not have a significant relationship with each other. They attributed this difference to the accuracy of the methods of measuring these two factors, so that the error in the troponin T measurement method is approximately 6%, whereas this level in troponin I is 13%. In our study, although this relationship has not been statistically analyzed, the magnitude of their increase was significantly different, so that the increase in troponin T was much higher than the normal range in comparison of troponin I. In addition to the reason for this difference, another cause, probably the main reason for this study, is the difference in the effect of hemodialysis on these two factors. The level of troponin T increases after dialysis due to concentration effects, while the level of troponin I decreases after dialysis, so it is natural that troponin T levels increased [22,24]. This difference in troponin levels indicates that troponin I is a more specific agent for the diagnosis and prognosis of cardiovascular diseases in patients with renal failure. However, in individuals without renal failure, both troponins have almost the same power in predicting events [25]. Park et al. In their study reported an increase in CRP levels after dialysis, and attributed this increase to inflammatory conditions associated with dialysis. The researchers also found that extracorporeal circulation in dialysis stimulates the production of CRP [9].

In this study, in the case of the relationship between plasma levels of cardiac troponins in patients with chronic hemodialysis with heart failure, there was a significant correlation between plasma levels of cardiac troponin I, T and CRP with heart failure ($P < 0.05$); while there was no statistically significant relationship between albumin and heart failure in patients undergoing chronic hemodialysis ($P > 0.05$). Similar to the results of this study, other studies found that the prevalence of cardiovascular diseases and heart failure in hemodialysis patients with elevated levels of troponins I and T was significantly higher and increase in both types of troponin was associated with reducing cardiac function and in particular, the left ventricular systolic function [26,27]. Contrary to these findings, Buiten et al. denied the existence of this relationship and stated that there is no relationship between troponin T level and cardiac diseases. This study has suggested that the existence of this relationship in previous studies was due to their use of measurement methods that have less sensitivity and accuracy, and also the other reason is the lack of adjustment of confounding factors in hemodialysis patients. However, this issue was not mentioned for troponin I, and even noted that troponin I could be better than troponin T in reflecting structural and functional impairment of left ventricle in hemodialysis patients [28]. In the case of the association of CRP with heart failure, previous studies have shown that elevated CRP levels are associated with a variety of classic cardiovascular events [20,29]. Another study has suggested that CRP levels are a long-term marker for cardiovascular diseases, and a single measurement of this factor will can predict the risk of cardiovascular events in the coming years [19]. In the case of the association between serum albumin with heart failure, in the study of Menon et al. Similar to the present study, this relationship has been denied. Albumin, however, can be associated with inflammation, and inflammation is also one of the main causes of cardiac diseases in hemodialysis patients, but albumin is likely to be involved in inflammation with a different mechanism from the other factors, such as CRP, and does not play a role in the progression of cardiovascular diseases due to inflammation [14].

In our study, the serum levels of cardiac troponins in patients with chronic hemodialysis and their association with LVH showed that there was a significant correlation between serum levels of troponins I and T, albumin and CRP with left ventricular wall thickening ($p < 0.05$). LVH, in hemodialysis patients, has almost 75% prevalence. The relationship between cardiac troponins and LVH is also mentioned in other studies [12,30]. LVH leads to subacute microvascular cardiovascular diseases and cardiac tissue destruction, followed by cardiac troponin excretion through the membrane of hypertrophied cardiac cells, and it has already have been reported for both the general population and the patients with chronic renal failure [28,31]. In addition to ischemia, increased mechanical stress by β-adrenergic stimulation may result in significant changes in the permeability of the plasma membrane of the cardiomyocytes, followed by the exit of macromolecules. Microvascular diseases of the heart are commonly associated with LVH in renal failure. Strong correlation between left ventricular mass and troponin T can be a justification for the prognosis of this protein in patients with dialysis [19].

Moon et al. and Foley et al. in their studies have proved that serum level of albumin is associated with the risk of LVH, so that hypoalbuminemia is associated with an increased risk of LVH. However, in these studies, there is no explanation for the mechanism of the progression of ventricular hypertrophy following hypoalbuminemia, but it is very interesting to know whether LVH can be improved by improving the hypoalbuminemia and force it into regression [32,33]. In the case of CRP, in the study of Park et al.

the association between this inflammatory factor with LVH has been pointed out. As in this study, changes in CRP levels, even after a dialysis session, are strongly associated with cardiac hypertrophy. Therefore, it can be concluded that the inflammatory condition induced by the dialysis process can involve in the deterioration of LVH in hemodialysis patients [9].

5. Conclusion

According to the results of this study, serum levels of troponins I and T, as well as CRP, are associated with heart failure and LVH in hemodialysis patients and Serum level of albumin, although is not related to heart failure, showed a significant relationship with LVH. Therefore, based on the results of this study, it can be concluded that knowing the status of these factors in patients with end-stage renal disease and hemodialysis can help clinicians to know the potential and risk of cardiac vascular diseases and provide the ability to early diagnosis, assessment of the need for other diagnostic procedures such as echocardiography, and the best time for treatment.

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