

The Cardiac Troponin-I (Tn-I) and its role in the Cardiovascular Disease Recovery of Uremic Patients Threatened With Repeated Hemodialysis

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Abstract: Cardiovascular diseases (CAD) remain the most highly as one of the most frequent causes of morbidity and mortality in patients treated with hemodialysis uremia [1]. Uremia patients threatened with hemodialysis (HD) are at high risk of left ventricular hypertrophy, and myocardial ischemia, acute myocardial infarction, unstable angina pectoris, renal anemia which favors even more cardiovascular complication, early atherosclerosis (atherosclerosis praecox), perikarditis uremica, pleuritis uremica etc. One typical biomarker of myocardial damage except kreatin kinasae (CPK), LDH, CK-MB (kreatin fraction and mioglobin kinasae) in patients with End-stage-renal-disease (ESRD) threatened with hemodialysis are also high concentrations -the heart of cardiac Troponin (Tn-I) in this group of patients who are quickly increased over normal values even though a large number of patients clinical symptoms of myocardial ischemia missing. Purpose of research is the primary of the study „cross sectional“ is to verify the impact of high concentration of cardiac Troponin-Tn-I and its role in the appearance of cardiovascular disease (CAD), acute coronary syndrome, acute myocardial infarction the myocardial ischemia, and unstable pectoris angines the patients uremic threatened with chronic HD in our hospital. A number of studies have verified and verified that there significant positive correlation between high concentrations of high of cardiac troponin (Tn-I) and cardiovascular disease in patients threatened with hemodialysis uremia.

Index Terms: Cardiovascular Diseases (CAD), Haemodialysis (HD), Cardiac Troponin-I (Tn-I), End-stage-renal-disease (ESRD).

1 INTRODUCTION

Cardiovascular diseases (CAD) remain the more you like one of the main causation and more frequent with higher prevalence of mortality in patients treated with HD uremic compared with the healthy population. Numerous studies have verified that cardiovascular complications in patients with etiology multifactor. are determined that patients with ESRD and those treated with HD suffer from a permanent [14] inflammation (MIA syndrome: Malnutritio-Inflamatio-Atherosclerosis) which promotes and helps increase the concentrations of a large number of biomarker inflammation, starting from the PCR (C-Reactive Protein), interleukin-6,) etc.

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Cardiac Tn-I, interleukin- β 1, interleukin-1 α , interleukin-6, fibrinogen, it is therefore easy to conclude that patients threatened with HD uremic chronic development potential candidate diseases with atherosclerotic coro-

nary cardiac ischemia, angine pectoral, acute coronary syndrome with the highest percentage compared with the healthy population [2,3,4]. Delegated much Studies in patients treated with HD have observed a high positive correlation between the degree of renal impairment, high concentrations of Tn-I and CAD, especially in patients who have manifested -Updated and pleurisy which uremic are frequent occurrences during treatment with HD [5,6,7, 28]. The damage myocardial biomarkers: keratin kinase (CPK), MB-kinase and keratin frac-tion in patients with ESRD myoglobin and those treated with HD presented with higher values than those clerks, but in most cases in the absence of symptoms ischemia clinical syndrome of acute infarction or heart. Troponin (Tn) is a protein which is found in muscle filament is trans-versal and actin and tropomyosin content. Isoform concentration cardiac serum can be determi-ned with precision and speed using monoclonal antibodies. Tn-I conce-ntrations in patients with ESRD are extremely sensitive and serve as a warning of changes and subsequent cardiovascular disorders, hence its early examination can significantly affect the mode of treatment and reduce the rate of mortality of this group of patients. Compound Troponin consists of three subfracti-ons: Troponin-C (TN-C), Troponin-T (Tn-T) and Troponin-I (Tn-I). TN-C-troponin part of which is related to the Ca ions and results in a changing and complex contra-ction muscle and Troponin-tropomyosin. Half-life of troponin is two hours [8]. TN-C contains 4 Ca connections and is a

component of a thin filament act together and tropomyosin [9].

located in skeletal muscles and slow isoforms located in two types of muscle: skeletal and cardiac ones. Myocardial damage as a result of excessive release of Tn initially manifested by four to six hours after necrosis with peak after 14-18 hours and remain high for at least seven days after attack. Tn-T was discovered by German physician Hugo A. Katus in university of Heidelberg [10]. Tn-T tropomyosin related to it blocked to form complex tropomyosin. Troponin-T (Tn-T) in itself contains three isoforms: isoform muscle skeletal fast, slow and cardiac muscle [11,12]. Isoform of cardiac Tn-T is mainly responsible for the contractions of myocardium and molecular weight = 37-77 kDa. Tn-T is found in muscles skeletal the fetus, although these subtypes over time in adults (unless you suffer from any disease) can disappear [13]. Patients with severe renal impairment often have higher concentrations of cardiac Tn-T which is difficult to explain the phenomenon. It is assumed that cardiac Tn-T in patients treated with HD is divided into many small molecules and kidney failure because of they can not be eliminated but collected and in reduced renal tissue and assisted by the HD, while the healthy individuals where renal function is normal

Tn-C has two isoforms rapid isoform

excretor thus eliminating particles Tn-T is very regular and is without prejudice to the cardiovascular system. Determination of the profile of high concentrations of several risk factors and favorable proinflammatory coronary disease and atherosclerosis as cardiac Tn-I, C-reactive protein, cytokines (-IL-6, Interleukin-β 1, Interleukin-1α, etc ...) and their abnormalities in patients with ESRD at the initial stages of the disease should be proposed as one of compulsory examinations in patients with ESRD and those treated with chronic HD, which can significantly help in the prevention of coronary submission of sickness and its consequences. ESRD patients and those threatened with chronic HD, with high levels of Tn-I are potential candidates for development of myocardial ischemia, weakening of cardiac function, atherosclerosis the coronary arteries, the acute coronary syndromes, hypertrophy the left ventricle, atherosclerosis early in greater numbers and more frequent compared with healthy population. High levels of Tn-I and Tn-T significantly positively correlated with high rates of morbidity and mortality in patients treated with repeated hemodialysis from myocardial infarction.

2 MATERIAL AND METHODS

Working materials for the determination of cardiac Tn-I was used blood taken from veins of 120 patients (of whom 46 were male and 34 female gender) treated with chronic hemodialysis unit with HD next to the University Clinical Hospital in Tetovo and the control group of 120 healthy individuals. The 8.60 years ± average age of patients treated with HD was = 61.00 ± 8.20, whereas the control group was the average age = 59.00 ± 6.20, old. Frequency of hemodialysis for all patients treated with HD was three times a week from 4-4.5 hours.

Table No. 1: Number of total patients and control group compared by Gender and Age

	M	F	Average age
Patients N^o=120	70	50	61.00 ± 8.20
Control group N^o=120	70	50	59.50 ± 7.80

3 EXPERIMENTAL RESULTS

Concentrations of Tn-I in we develop a disease divided by basic which has brought up ESRD. High values of Tn-I (> 1.0 µg / ml) were observed in 38% of patients with arterial hypertension (HTA) where Tn-I values were = 2.420 µg / ml, to 29% of patients with diabetes mellitus (DM) values of Tn-I = 2.064 µg / ml, to 26% of patients with chronic glomerulonephritis (GMN Chr) Tn-I values were = 1.060 µg / ml, to 15% of patients with chronic Interstitial nephritis (IPN Chr) Tn-I values were = 1.020 µg/ml, to 20% of patients with terminal renal disease

without defined values of Tn-I were = 0.098 µg / ml in 29% patients with Renal Polycystosis-Dominant Adult (RPDA) Tn-I values were = 1.240 µg / ml. From the results obtained in the patients examined (HD-treated) we can conclude that patients with essential hypertension, diabetes, and chronic glomerulonephritis chronic interstitial nephritis are higher risk of cardiovascular disease compared with the same group of patients but the disease undefined basic and adult renal dominant polycystosis. Between the values obtained for cardiac Tn-I from patients repeatedly treated with HD and group values obtained from the control group (Tn-I = 0.003-0.064 µg / ml) was noted a statistically significant difference with the *p* < 0.0001. Obtained from results of our paper are compared in many other studies on the role and

high concentrations of cardiac Tn-I in patients with ESRD and those treated with chronic hemodialysis on the cardiovascular system, compared with values obtained from control group of healthy individuals. Examination of the concentration of cardiac Tn-based method defined in enzymatic heminonimuliscence-type analyzer immunometric with Immulite 2000.

	Troponin-I Cardiac (Tn-I)	p
HTA = 38%	2.420µg / ml↑↑	0.0001
RPDA = 29%	1.240 µg / ml ↑↑	0.0001
D.M = 26%	2.064 µg / ml ↑↑	0.0001
GMN Chr = 24%	1.060 µg / ml↑↑	0.0001
Nondefined = 20%	0.098µg / ml↑	0.0001
IPN Chr = 15%	1.020µg/ml↑↑	0.0001
Control Group N ^o =120	0.004-0.070µg / ml	0.0001

Table no. 2 : Concentration of Troponin-I Cardiac (Tn-I) compared by disease

4 DISCUSSION

Insufficiency of kidney function due to weakening causes accumulation and collecting small molecules fragmentation of Tn-I in patients treated with HD which mechanism may be as a reasoning and explanation of high values of Tn-I examined in ESRD serum of patients treated with chronic HD. Filament consists of transversal muscle actin, and tropomyosin complex the Troponin: Troponin-T (Tn-T), Troponin-C (Tn-C) and Troponin-I (Tn-I). Muscle are mediated by the interaction between Ca and Ca and Troponin. Exist a small number of studies which have verified that the model of dialysis may modify and change the mono-clonal subfraction of Tn-I, but not accurately are verified. Post mortem of a considerable number of patients treated with HD were found a large number of mikroinfarcts and high concentrations of Tn-I. High concentrations of Tn-I are high positive correlation with prognosis and progress of cardiovascular diseases (CAD) and the myocardial necrosis. Tn-I relates to myofibrilleveaktin to form Troponin-tropomyosin complex. There are a number of studies that have documented and verified a high positive connection between high concentrations of cardiac Tn-I and septic conditions in patients treated with HD and a fact witness on the impact and role of inflammation and sepsis to increase Tn-I values. Correction, prevention and early treatment of risk factors: treatment of various infections, treatment of dyslipidaemia, smoking cessation and konsum, treatment of HTA, regular use of aspirin, regulation of blood glucose, laboratory examinations of CPK, CK-MB, LDH, ECG and Doppler Colorechocardiography the carotid arteries (to detect the presence atheromatosity tiles) can significantly affect the prevention of cardiovascular diseases and myocardial ischemia this group of sick people clothes [15,16,17,18,]Tn-I is mostly present in heart tissue muscle and is responsible for tightening or contraction of the myocardium during cardiac ischemia. Tn-I is the molecular weight of 23.90-

KDA and that in itself contains 209 residues. Tn-I in position 22 and 23 contains two amino acid residues of the amino acid residues Serin. Të both in vivo may phosphorilising with the aid of Protein-A-kinase and protein form four forms: a defosfokinasae, two and a bisfosfokinase, monofosfokinase. Phosphorylation of Tn-I and protein changes in the structure of his own to bring up his own modification and interaction with other forms of troponin and the Tn-I antibody. Before 15 years Tn-I is known as a marker of damage and injuries convincingly on the heart muscle, therefore Tn-I last decades as a condensed, golden marker "and more specific in the diagnosis of myocardial infarction meet with CPK, CK-MB, LDH and myoglobine. Coronary Reperfusion is closely associated with a tremendous number of changes in cardiac biomarker. Troponin initial findings are thought to be due to the release of a cytoplasmic components and prolonged presence in Tn in serum, caused by ongoing division so related to a structural component. 20-48% of patients with pain precordial but without fulfilling the normal criteria for myocardial infarction have increased values in serum troponin. This is important because it is vacant during angiography in patients with high values of Tn atheromatosity not noticed while the opposite plates of patients with low Tn values were observed during angiography in coronary arteries atheromatosity plates. American Society of Cardiology in a consensus together with the American College of Cardiology has proposed that the increased values of cardiac Tn-I serve as a marker of acute myocardial infarction. There is documented evidence that even during a uremic pericardit are high values of cardiac Tn-I in particular in patients treated with recurrent chronic HD [28]. Values are troponin increased not only during but also myocardial infarction (IM) in patients with cerebrovascular insult, insult subarachnoidal, cerebral hemorrhage, endocrine disease, polymyositis, dermatomyositis and malignomat.

Numerous studies in intensive centers in patients with septicemia and their intubed in plasma were observed increased values of Tn-T and Tn-I, which tell to a close not function between left ventricle and the presence of multiorgan injuries, but still is no clear correlation between the duration of disease, survival and level of damage to vital organs with values in excess of Tn-T and Tn-I. Even in patients with ESRD are examined, the values of Tn-T and Tn-I in the absence of active coronary disease. To close 20-75% of patients treated with HD are higher concentrations of Tn-T and close to 25-53% higher concentrations of Tn-I. Over time more than a year, concentrations of cardiac Tn-I may undergo change to 50%. The presence of coronary heart disease, diabetes, and hypertension, glomerulonephritis known as risk factors in patients treated with HD significantly exacerbate health damage, already damaged by the process of hemodialysis [9,20,21]. In Given the abnormal frequency of Tn-I in patients with ESRD by many scientists is proposing that the level of Tn-I serve as a specific marker for ischemia the heart of this group of patients. Changes, modifications, and biochemical effects of cardiac Tn-I uremic patients are still unknown. In a retrospective analysis, cross-sectional of 227 patients treated with chronic HD is verified that these patients increased concentrations dominate Tn-T and cardiac Tn-I are manifested with unstable pectoral angina symptoms (APNS), but with ST -segment not very express. Concentrations of Tn-T and cardiac Tn-I in these patients have been increased by 43-60%. Increased levels of Tn-T and cardiac Tn-I showed a high positive correlation with hypercreatinemia but documented that HD treatment had no effect on growth and induction values of Tn-T and cardiac Tn-I. Mortality in these patients was 46.3% of acute coronary syndromes consequences. In patients with IRKT and those treated with HD diagnosis of myocardial necrosis is extremely difficult because other biochemical markers of myocardial damage such as CP, CK-MB and LDH are easily grown so early therapeutic interventions in a timely can significantly affect the mortality rate within the group of patients. Over 1/3 of patients with ESRD nonsymptomatic treated with HD have cardiac Tn-I increased. Tn-I levels remain stable over a three-month period and treatment with HD does not affect the reduction or normalization of higher concentrations of cardiac Tn-I [22]. Etiology of high concentrations of Tn-I in patients with ESRD and those treated with HD is still unknown. Some studies better designed slim but have tried to find a link between high values of Tn-T and Tn-I with low values of glomerular filtration rate (GFR), but failed to find any convincing correlation. Askoy with his own associates in their analysis of 62 patients treated with HD and ESRD and heart disease observed an association and connection to positive high intermediate to high

concentrations of Tn-T and Tn-I with a low degree of the GF and the high degree of cardiac injury as defined. All contemporary studies, multicentric and statistical (regression) on the high values of Tn-T and Tn-I and low glomerular filtration in ESRD patients with and those treated with HD, have documented that there is a high positive correlation with statistically significant regardless of the basic disease. There is documented evidence that high concentrations of Tn-I in patients with low GFR, ESRD and treated with HD present a high risk of cardiovascular occurrences of sickness regardless basic renal disease, and duration of treatment with HD [23,24,25,26,27]. In patients treated with HD, ESRD recurring presence of high concentrations of oxidized cholesterol (LDLox), IDL and VLDL further increase and accelerate the secretion of inflammatory cytokines: interleukin-1 (Inl-1), Inl-6 that confuses with further increase the negative effect of Tn-I and manifestations of CAD, Inl- β , Inl- α , Inl-6. The prevalence of inflammation in patients treated with HD, ESRD is very high and is still more aggravated by the constant presence of various infections: bacterial, Viral, frequent trauma, infections and fistulas arteriovenous or femoral catheter used as interference to the performance of the HD sessions. It is to verify that the patients treated with HD, oxidized LDL-cholesterol (LDLox), IDL and VLDL secretion of cytokines accelerate proinflammatory as Inl-6, PDGF (Platelet-derived-Growth-Factor), TGF β (Transforming-Growth-Factor-Beta), TNF- α and CRP and are effects and enhancements to the development of processes and CAD atherogenicity of this group of patients. Atherosclerotic plates observed in the artery Carotis media in most cases correspond to positive values in excess of cardiac Tn-I. Lesions of the above have been verified with the help of non-invasive methods: B-mode high resolution ultrasonography used for tracing and tracking of changes atherosclerotic to CIMT (Carotid-Intima-Media). Several studies have confirmed that European for Cardiovascular disease pathologies are responsible for the death of 25-45% of the Patients treated with HD. Factors of submission of CAD (Cardiovascular Disease) in patients treated with HD are many diverse etiology. Uremic cardiomyopathy is closely related to high positive correlation with the action of uremic toxins, inflammatory mediators, hyperparathyroidism-secondary and MIA syndrome (Malnutrition-Inflammation-Atherosclerosis). It is established that in patients with uremia, infarction of infarction and CAD are 10-15 times more frequent, and mortality to 53% times more frequent compared with patients with other primary diseases.

5 CONCLUSION

In conclusion we may conclude that a significant number of patients with ESRD treated with chronic

hemodialysis(HD) regardless of underlying disease has led to ESRD (HTA, Chronic Glomerulonephritis, Intersticiopyelonefritis chronica undefined illness and Adult Dominant Renal Polycystosis) showed concentrations high cardiac Tn-I are in accordance with the results published and documented by a large number of studies on the role and effects of increased cardiac Tn-I in patients with ESRD and those treated with chronic HD. In all patients examined were present CAD symptoms, unstable pectoral angina, post myocardial infarction, the myocardial necrosis, and cardiac ischemia high levels cardiac Tn-I obtained from patients showed a statistically significant positive correlation $p < 0.0001$, compared with values obtained by the group controller of healthy individual.

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