Impact Factor: 9.2 ISSN-L: 2544-980X

COMPARATIVE ANALYSIS OF SOME LABORATORY AND FUNCTIONAL PARAMETERS IN PATIENTS WITH CHRONIC HEART FAILURE WITH AND WITHOUT DIABETES MELLITUS.

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Abstract. *This scientific article assesses the functional state of the heart using echocardiography in patients with chronic heart failure with diabetes mellitus and without diabetes mellitus. We also compared pro-inflammatory cytokines IL-6, TGF-β1, potassium, urine albuminuria and glomerular filtration rate with the use of determining cystatin-C in the blood serum of patients. In patients with chronic heart failure and diabetes mellitus, it was found that the quality of life, the level of stability to physical activity and clinical condition are significantly reduced compared with patients without diabetes mellitus.*

Key words*: Chronic heart failure, interleukin-6, cystatin-C, glomerular filtration rate, β-transforming growth factor.*

Studies in recent years have noted that high comorbidity decreases quality of life, leading to impaired social adaptation and increased mortality. The incidence of comorbidity reaches 69% at 18-44 years of age, 93% at 45-64 years of age, and 98% in those over 65 years of age [17,20,21]. In most cases, chronic heart failure (CHF) and chronic kidney disease (CKD) occur in comorbidity and have a dramatic negative impact on the quality and duration of life of patients. It is increasingly common that these conditions are accompanied by diabetes mellitus (DM) or that severe complications that have been reported develop at its base.

People with cardiovascular diseases, including CHF, are several times more likely to develop CKD when compared to general population. Even a slight decrease in the functional state of the kidneys is associated with cardiovascular risk, not dependent on the influence of other factors. The presence of any two cardiovascular risk, according to NHANES III register, leads to CKD with a clutch filtration rate (CFR) of <60 ml per minute [6,22,23,54].

Fibrosis changes in the kidneys in patients with CHF lead to a decrease in CFR and the development of one of the most observed unpleasant complications of the disease CKD [5, 13, 24, 25]. Evaluation of CFR using serum creatinine levels does not always allow timely and full-fledged detection of changes in the kidneys [928, 29]. Currently, the endogenous marker cystatin-C, whose reliability is higher than that of creatinine, is being used in determining CFR. With it, not only ball filter indicators are assessed, but also the state of the renal proximal ducts. The high blood level of this marker is an early indication that pathological processes are occurring in the kidney[3, 26, 27, 52].

The results of epidemiological and population testing testify to the fact that early, even subclinical disorders of kidney function lead to a sharp deterioration in the condition of CHF's existing

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patients. According to a number of authors, kidney dysfunction in CHF is diagnosed in 32-60% of cases using criteria such as creatinine, creatinine clearance, CFR, cystatinine C, microalbinuria [8, 30, 31, 53].

It is known from numerous studies and published literature conducted in different countries of the world that the main cause of terminal kidney failure is type 2 DM [15, 32, 33]. In diabetic nephropathy, arteries, arterioles, kidney balls and ducts are complex damage. As a result, the kidneys develop diffuse or nodular glomerulosclerosis, which leads to CKD. DM increases the risk of developing CHF 2-5 times. In cases where these two pathological processes are present, the mortality rate increases by 60-80% in emergency. From a clinical point of view, 3 stages of diabetic nephropathy are distinguished. The first of these is microalbuminuria, the second is proteinuria, where kidney function is maintained, and the third is chronic renal failure.

Advances in Molecular Medicine and experimental nephrology have provided an opportunity to study the mechanisms of development of microalbuminuria and proteinuria more perfectly. According to current research, structural and functional changes develop in the kidneys much earlier than the excretion of albumins with urine. The leading place in this is occupied by podocytes, which are considered to be the main component of the ball-bearing diaphragm.It has been shown that the changes recorded occur long before microalbuminuria occurs. Podocyte is a complex structure that performs a number of functions under physiological conditions and has adaptive properties and is considered extremely sensitive to various damaging factors at the same time. Under the influence of various pathogenic agents, a number of changes (metabolic, toxic, hemodynamic) are observed in podocytes [12,18,19,34,35].

The pathogenesis of diabetic nephropathy is complex in which a number of causes are involved. Among them, more studied and proven are metabolic (hyperglycemia, hyperlipidemia) as well as hemodynamic (intrauterine hypertension, arterial hypertension) changes [1,38,39].

Hyperglycemia is a group of important metabolic factors that damage the kidney, and stable glycosylation occurs under these conditions. In the human body, there is an interaction with the processes of autoaccination and cellular receptors. As a result of the complex chemical processes that occur next, protein structures change, which in turn leads to constant cell damage. The end products of glycosylation cause the metabolism of key proteins in the body to change. They in turn increase cell proliferation and this further exacerbates diabetic nephropathy processes [7. 16. 10, 36, 37].

In moderation, the processes of proliferation and apoptosis are in equilibrium. In DM, the equilibrium shifts towards proliferation following activation of a number of factors resulting from the development of hyperglycemia and endothelial dysfunction.

DM-induced nephropathy confirms that it is a complex process. The fact that they are accompanied by Advanced CHF or recent complications at the base of diabetes not only makes patients re-admitted to the hospital, but also dramatically increases the number of deaths. This, in turn, indicates the need to continue research on the problem.

The purpose of the study is to cross-analyze certain laboratory and functional indicators in patients with chronic heart failure diabetes and without it.

Source and methods of research in the scientific study, 80 patients were observed with chronic heart failure diabetes mellitus in comorbidity and without it, and on the basis of which there is developed chronic kidney disease C2va C3A. They were in turn divided into two groups of 40 patients. The A–group was formed by CHF+diabetes-free vab-group CHF + diabetes-free patients.There were 45 (56.25%) males and 35 (43.75%) females. In order to implement the solution of the tasks set, the work of the scientific study was carried out as follows.

In patients involved in the study, CHF's diagnosis and its functional classes were determined based on their complaints, anamnesis, objective examination, and laboratory – asbobium examinations according to the criteria of the New York Society of cardiologists (New York Heart Association, 1964).

The diagnosis of diabetes mellitus was made in all cases after confirmation with the help of appropriate laboratory tests, on the advice of an endocrinologist, and follow-up was obtained type 2 diabetes mellitus with a duration of the disease of 3 or more years. During the observation, patients were regularly monitored from the side of the endocrinologist and, on their recommendation, hypoglycemic treatment was carried out.

In all patients under observation, laboratory-asbobium tests were carried out before the start of treatment and after 3 months.Also, the calculation of CFR by the levels of cystatin-C in the blood was determined by the formula of Hoek and co-authors (2003).

All immunoferment and biochemical tests were carried out on the equipment of COBAC 6000 (Germany-Japan) in the clinical-laboratory diagnostic Department of the multidisciplinary clinic of the Tashkent Medical Academy.

In statistical processing of the data obtained in the study, MS Excel (2016) used a packaged computer program. The average arithmetic and standard deviations (m±m) of the indicators presented in all tables were calculated. The reliability of differences between groups was determined by applying the styling criteria to odd and even differences.

Research results.From this point of view, we conducted a comparative analysis of the indicators of the laboratory, cardiac remodeling and CFR, in the group of patients with identified and unspecified DM present in our observation of CHF. The following table 1 provides data on exocardiography indicators conducted in the main group A and Group B patients involved in the study.

Table 1.

Chronic heart failure II-III functional class diabetes mellitus and went without itthe indications of intra-cardiac hemodynamics detected by exocardiography in patients.

№	Pointers	Group A, CHF II - III FC diabetes mellitus is present (n=40)		Group B, CHF II-III FC diabetes-free (n=40)	
		CHF II FC (n=20)	CHF III FC ФС (n=20)	CHF II FC (n=20)	CHF III FC (n=20)
1	Left ventricular end systolic scale (26-38 мм), мм	45,3±1,8	50,35±1,6	42,6±1,2	46,9±1,5
2	Left ventricular end diastolic scale (44-54 мм), мм	64,4±1,6*	69.35±1,5*	59,9±1,2	65.3±1,2
3	Left ventricular end diastolic volume (88-145 мл), мл	178,3±7,7	203,9±7,9	174,6±4,1	192,3±6,8
4	Left ventricular end sistolic volume (45-68 мл), мл	97,3±5,2*	112,3±9,1	83,15±3,4	104,15±8,1
5	Left ventricular blood throw fraction, %	42.1±1,2*	36,5±0,9**	46.2±1,0	41,7±1,3
6	Left ventricular myocardial weight,г	233,5±4,4*	247.5±6,2	220,3±3,9	240.9±5,5
Note: * - reliability of pre-treatment indication difference: * - p<0,05., ** - p<0,01.					

As presented in the table,left ventricular end systolic size was 45.3±1.8 mm and 50.35±1.6 mm in Group A patients at CHF II and III FC, respectively, and 42.6±1.2 mm and 46.9±1.5 mm in Group B,

and no reliable differences were found when they were studied in comparison (R>0.05). The diastolic size of the left ventricle was 64.4±1.6 mm and 59.9±1.2 mm in patients with Group A as well as Group B Sue'S II FS, and 69.35±1.5 mm and 65.3±1.2 mm respectively in patients with CHF's III FC, and a reliable difference was recorded (R<0.05). The left ventricular end diastolic volume was found to be 178.3±7.7 ml and 203.9±7.9 ml respectively in CHF II and III FC in the first group of patients, and no reliable differences were observed in the second group at 174.6±4.1 ml and 192.3±6.8 ml (R>0.05). A reliable difference was noted in left ventricular end systolic volume CHF II FC present in a as well as Group B patients of 97.3±5.2 ml and 83.15±3.4 ml respectively (R<0.05).In patients with CHF's III FC, no reliable difference was observed between the two groups of pointers (112.3±9.1 ml and 104.15±8.1 ml, R>0.05, respectively).

Left ventricular blood firing fraction (LVBFF) DM was present in CHF II FC patients at 42.1±1.2%, in CHF II FC patients where DM was not present, 46.2±1.0%, and a reliable difference was found (R<0.05). In patients with CHF's III FC, however, a high reliable difference was reported in both groups of 36.5±0.9% and 41.7±1.3% respectively (R<0.01). The left ventricular myocardial weight was 233.5±4.4 g and 247.5±6.2 g in the myocardial group of patients at CHF II and III FC, respectively, and 220.3±3.9 g and 240.9±5.5 g in Group B, and a reliable difference was found in patients with II FC when they were compared (R<0.05).

Based on the goals and objectives set, patients involved in the study received serum inflammation with cytokines IL-6, TGF - β1, in addition to potassium, albuminuria in the urine and cystatin-C and with it we studied the CRF. We also evaluated the indicators of physical load resistance, quality of life and clinical conditions of the main group A and B patients who have undergone DM and without it in our observation. Below are the results obtained in Table 2 and Figure 1.

Table 2

Comparative analysis of indicators of biochemical and physical load resistance, quality of life and clinical conditions in patients with chronic heart failure functional class III diabetes mellitus and without it.

№	Pointers	Group A, CHF II - III FC diabetes mellitus is present (n=40)		Group B, CHF II-III FC diabetes-free (n=40)	
		СЮЕ ФС II (n=20)	СЮЕ III ФС (n=20)	СЮЕ ФС II (n=20)	СЮЕ ФС III (n=20)
1	Cystatin-C, mcg/ml	1.26±0,04	1.56±0,08**	1.15±0,05	1.25±0,05
2	Interleukin-6, pg/ml	15.39±1,5*	23.74±1,7***	11.59±0,8	14.7±0,55
3	TGF β_1, ng/ml	4,87±0,3**	7,4±0,3*	3,58±0,27	5,89±0,4
4	Potassium, mmol/l	4.42±0,08*	5.02±0,07***	4.2±0,07	4.5±0,08
5	Albuminuria, 30-300 mg/l	351,45±10,2***	424,05±13,2***	298,96±10,5	345,95±9,7
6	6 minute walking chest, meter	312,2±16,50*	192,4±12,2**	363,2±12,31	249,4±12,50
7	Quality of life, score	55,6 ± 1,9*	70,4 ± 2,1***	48,9 ± 2,1	58,3 ± 2,0
8	Clinical case assessment, score	6,0 ± 0,3*	7,84 ± 0,27*	5,2 ± 0,19	7,08 ± 0,3
Note: * - reliability of pre-treatment indication difference: * - p<0,05., ** - p<0,01. *** - p<0,001.					

The cystatin-C indications were 1.26±0.04 mcg/ml and 1.15±0.05 mcg/ml respectively in patients with Group A as well as Group B CHF II-FC, and no reliable difference was detected (R>0.05).

The CHF-III FC was rated at 1.56±0.08 mcg/ml in the existing first group and 1.25±0.05 mcg/ml in the second group, and the differences were reliable (R<0.01). Interleukin-6 indicators were 1.33 times higher in patients with Group B CHF II-FC at 11.59±0.8 PG/ml and 15.39±1.5 PG/ml in Group A, and a reliable difference was noted (R<0.05). CHF-III FC was rated at 23.74±1.7 PG/ml and 14.7±0.55 PG/ml in the existing Group A and B, respectively, 1.46 times higher (R<0.001). In patients with Group A and Group B CHF II-FC, the difference was reliable when TGF ß1 indicators were compared (4.87±0.3 ng/ml and 3.58±0.27 ng/ml, respectively, and 1.36 times higher, R<0.01). The first group containing CHF-III FC was rated at 5.89±0.4 ng/ml in the second group at 7.4±0.3 ng/mlham, 1.27 times higher, and a reliable (R<0.01) difference was recorded. Serum potassium levels were significantly higher in patients with DM even if they were at the norm indicators in all groups (between groups II and III FC respectively 4.42±0.08 and 4.2±0.07 mmol/l, r<0.05, 5.02±0.07 and 4.5±0.08 mmol/l, r<0.001).

A high-fidelity (R<0.001) difference was recorded in Patients A and B who were accompanied by CHF II FC present DM, with albuminuria indications in the urine of 351.45±10.2 mg and 298.96±10.5 m, respectively. In patients with III FC in either group, however, this indicator was 298.96±10.5 mg and 345.95±9.7 mg NII, and a high reliability (R<0.001) difference was observed.

Patients ' level of tolerance to physical load, which we evaluated through a 6-minute walk test. In this, patients with major group A CHF II FC had a walking average of 312.2±16.50 meters for 6 minutes, while group B patients had a distance of 363.2±12.31 meters, and the difference between them was reliable. In patients with both groups ofisyue III FC, this indicator differed from each other in high reliability (R<0.01) (192.4±12.2 meters and 249.4±12.50 meters, 1.3 times less).

The following results were recorded when patients ' quality of life indicators were studied using the Minnesota survey. A score of 55.6 ± 1.9 and 48.9 ± 2.1 was found in patients with CHF II FC in group A and B, respectively, and the difference between them was reliable. In patients with group A CHF III FC, a score of 70.4 ± 2.1 was recorded and similarly was 1.2 times higher than that of group two patients (R<0.001).

The following results were obtained when the patients involved in the study were evaluated using Clinical Case Assessment Scale. A reliable (R<0.05) difference was noted in both FC patients with CHF DM compared to those without DM (the indicators were 6.0 ± 0.3 and 7.84 ± 0.27 points, 5.2 ± 0.19 and 7.08 ± 0.3 points between the groups, respectively).

Also, CFR was calculated based on the indications of cystatin-S in patients involved in the study, as we noted above.

The CFR filtration rate was measured to be 56.75±2.2 ml/min/1.73m2, and 65.8±2.89 ml/min/1.73m2, respectively, in patients with ligia and group bningsyue II FC, and reliable differences were found when comparative study (R<0.05). In patients with CHF III FC DM, this indicator was 45.8±2.6 ml/min/1.73m2 and in those without CHF III FC DM, 57.7±2.7 ml/min/1.73m2, and a high reliable difference was found (R<0.01).

Conclusion. Analysis performed observed negative changes in CHF's comorbid state, including those that did not have DM in their intra-cardiac hemodynamic displays in line with its FC when accompanied by DM. These were evident in left ventricular end diastolic size, end systolic size, myocardial weight, and blood firing fraction.Patients with DM present in CHF II-III FC have been noted to have reliably higher blood levels of cystatin-S,il-6, TGF-β1, and urine albuminuria compared to non-DM patients. Also, low CFR detected using cystatin-C in patients with DM indicates that patients in this group experience irreversible pathological changes in the kidneys, and as a result, they develop early CKD. A comparative analysis of patients showed that CHF's resistance to physical loads, quality of humor, and clinical condition when accompanied by existing DM have a suitably reliable adverse effect on non-existent DM.

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