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Biochemical Study of Angiotensin Converting Enzyme 2 (ACE2) and Its Relation with Heart Disease

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Abstract

In this study, several biochemical parameters associated with heart diseases and ACE2 enzyme were investigated. The relationship between them was found (Troponin I, Cystatin C, C-reactive protein (CRP), potassium, and Sodium, Uric acid, Lactate Dehydrogenase (LDH) enzyme, transamination enzymes AST, and ALT) in patients with serum blood in comparison to the control group. Result proofing is an important increase in the ACE2 activity in patients(0.69 ± 0.22 ng/ml) compared to the control group (0.469 0.16 ng/ml), in this context, the result revealed an important increase in the concentration of (Troponin I, Cystatin C, CRP, sodium, uric acid, LDH enzyme, AST enzyme) and the concentration of potassium has decreased significantly., a non-significant difference in ALT enzyme compared with the healthy group. The results also showed that there was an increase in ACE2 activity in the males compared with the females. The Correlation coefficient (r^2) of ACE2 with these clinical measures in this context showed a positive significant correlation with CRP in patients whereas the data verified a non-important correlation with the other biochemical parameters.

Keywords: ACE2, Troponin I, Cystatine C , CRP,Sodium and potassium,

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1. Introduction

Heart failure is considered a case in which the heart is unable to pump adequate blood to satisfy the body's demands for nutrients and oxygen. It occurs when the heart is unable to pump enough blood to satisfy the tissues' metabolic needs as a result of ischemia arrhythmias. [1], the most important symptoms of heart diseases are ,shortness of breath ,chest pain, palpitations, acute pulmonary edema, weakness in the body, tachycardia ,fatigue ,fluid retention ,swollen neck veins ,and altered pulse[1,2], heart disease leads to several complications, the most important of which are blood clots, strokes peripheral and pulmonary embolism , malabsorption , respiratory muscle weakness ,and pulmonary hypertension[3]Angiotensin changing enzyme 2(ACE2)(Ec 3.4.17.23) was discovered in2000,it is a member of the angiotensin –renin system,it is considered a mineraloprotein and consists from 805 amino acids,it is type 1 transporter protein across the wall and its moleclular weight (110-120) KDa, it was cloned in human from X chromosome.[4],ACE2 enzyme is found in the little intestine and duodenum , glandular cells of the gallbladder , proximal tubules of the kidneys, ,in reproductive cells,and it is present in epithelial ,parasitic cells,and in blood vessels through the main tissues such as heart tissue and to alesser extent in the thyroid gland ,pancreas ,liver,and placenta.[5,6] ACE2 enzyme is converted Ang I to Ang (1-9) and it converted Ang II to Ang(1-7) while Ang I is converted Ang II by ACE1enzyme[7,8] , AngII affects the kidneys,adrenal cortex,arteries ,and the brain by binding to (AT2,AT1) receptors to vasoconstrict ,increase blood pressure ,and heart diseases ,it affects the renal system to reabsorb soduim ,inhibit renin release ,excite the sympathetic nervous system and aldosterone to enhance retention,increase inflammatory response, and oxidative stress , the renin-angiotensin –aldosterone system(RAAS) contributes to the mechanical changes of heart diseases through fluid homeostasis Na+/K+ and volume and hemodynamic stability where all the products and peptides formed within the system play an essential role in heart diseases development [9,10],Ang(1-7) is increasese the expansion of blood vessele ,reduces oxidationstress and diuresis by increasing the nitric oxide concentration regulation ,these processes contribute to the protection of the kidneys and the heart ,therefore ACE2 enzyme deficiency affects the breakdown of kidney and heart tissues [11], ACE inhibitor and AngII receptor blokers (ARBs) are a group of drugs used to treat hypertension and heart disease[12,13],captopril is considered atype of treatment used

in inhibition the renin-angiotensin-aldosterone system(RAAS) ,it dilates blood vessels,reduces aldosterone secretion ,improves cardiac output ,and lowers blood pressure [14,15].

The research aims to identify the angiotensin-converting enzyme 2 and its role in affecting the incidence of cardiovascular diseases (CVD) as a member of the system of renin-angiotensin-aldosterone (RAAS), to identify its mechanism of action within the system then, study the relation between ACE2 and some of biochemical parameters ,inaddition with age ,sex , then the linear correlation coefficient of ACE2 with the same measured biochemical was done.

2. Materials and methods

Experimental

Forty blood samples were collected from heart patients groups (20-70)years and for both genders, males (32) and females(18), Additionally, 25 blood samples were taken from healthy individuals of both sexes (15 men and 10 women), were taken from the Ibn - Sina Teaching Hospital after receiving captopril treatment. The blood serum was then removed from the samples and utilized to ascertain the following biochemical characteristics.

ACE2 enzyme -was predicted by using Fine Test kit-China by enzyme-related immunoassay of ELISA technique [16]

Troponin I– was determined by using Boditech kit(korea) [17,18].

Cystatin C - was determined by using a Boditech kit (korea) [19,20].

C-reactive protein (CRP)-was determined by using Bussero(Milano) kit(Italia) [21].

Sodium and potassium -were determined by using a Biosam kit(Dubai-UAE) [22,23].

Uric acid – was determined using BIOLABO Kit -France [24].

LDH enzyme-Was determined by using BioSystems kit(Spain) [25].

Transaminase enzymes AST and ALT were determined by using a BIOLABO kit (Farance) [26,27].

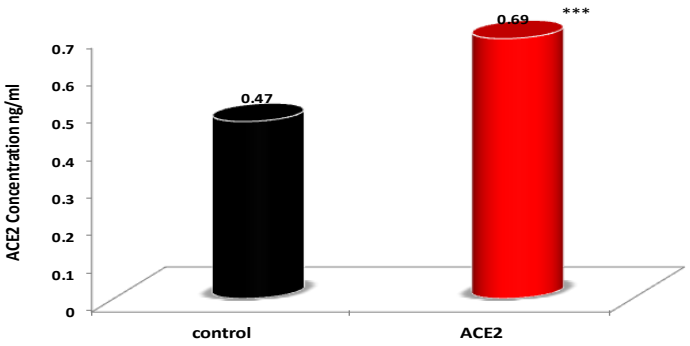
Data Analysis:

By using the statistical analysis program (SPSS 22), the cocluded data were examined using the (T- test), which was used to compare two parameters. Additionally, The mean standard deviation was calculated using conventional statistical techniques, and while using the ANOVA test for comparing more than two parameters, also correlation coefficient –r, was conducted to clarify the relationship between various clinical parameters. [28].

3. Results and Discussions

3.1. ACE2 enzyme activity before and after treatment in heart patients compared with the control group:

Table (1)is revealed that an important increase in ACE2 activity (0.69 ± 0.22 ng/ml) compared to healthy sibjects (0.47 ±0.17 ng/ml)this result is consistent with what was stated by[29]the reason may be due to the effect of Ang2 by binding to its receptors to contract blood vessel,increase cardiac output and pressure,thus increase the activity of the ACE2 enzyme[30]



*** Significant difference between heart patients before treatment and control at p<0.001

Figure (1): ACE2 activity before and after treatment in heart patients and control group

3.2. ACE2 enzyme activity in heart patients and control group according to age and sex:

Results in Table (1) showed there is an important increase in the activity of the ACE2 enzyme in the first category compared to the two categories, This result matches what was stated by both [31,32] that the activity of the ACE2 enzyme decreases in elderly individuals compared to young adults. The table also shows a non-significant increase in the activity of the ACE2 enzyme in males compared with females in both groups of patients and healthy subjects, while a significant increase of ACE2 in males, and females compared with control groups, This result is consistent with what was stated by[32,33].

Table 1: ACE2 activity in heart patients with control group according to Age and Sex.

Age groups (Year)	**The activity of ACE_2 (ng/ml) (Mean ± S.D.)**	
	Control	**Patients**
20-45	0.5 ± 0.17	* 0.81 ± 0.18 ***
46-70	0.36 ± 0.17	* 0.66 ± 0.2 ***
Sex	**The activity of ACE_2 (ng/ml) (Mean ± S.D.)**	
	Control	**Patients**
Male	0.47 ± 0.094	0.75 ± 0.21 ***
Female	0.41 ± 0.11	0.64 ± 0.18 **

3.3. ***Some of the clinical parameter concentrations of heart diseases patients compared with the control group:***

Table (2) illustrate the results that there is an important increase in the concentration rate of troponin I in heart patients compared with the control group, and this result agrees with all that the researchers reported about the increase in troponin I in heart diseases such as coronary heart disease, heart failure, and chronic kidney disease.[34] the results also showed a notable increase in Cystatine C concentration in the patients compared with the healthy subject, The reason may be that cystatin C is highly associated with biological risk factors for cardiovascular disease, such as homocystine, low HDL, and CRP. elevated cystatin C is predicted atherosclerosis in cardiovascular patients.[35], Also, cystatin C is equal to or better than creatinine in predicting chronic kidney disease, It inhibits cystine protease, increases the breakdown of collagen fibers of the heart muscle, and produces changes in the structure and function of the heart.[36] the same table also noted an increase in the concentration of CRP in the patients, as it is one of the important indicators when inflammation occurs, and it is formed in the acute protein folds in hepatocytes in response to cytokines, especially interleukin- 6, and many studies showed an increase in CRP with myocardial infarction, ischemic stroke, and sudden heart disease[37], The results also showed in Table (2) a significant increase in the concentration of uric acid compared with healthy subjects, The reason may be due to a rise in uric acid as a result of infections and an increase in interleukin-1(IL1) in gout disease, which plays an important role in heart failure, Previous studies indicated that uric acid increases with an increase in blood pressure and the renin-angiotensin system, especially with the increase of AngII.[38,39]

The results in the same table showed an increase in the activity of LDH enzyme in patients compared to healthy subjects, this increase might be due to The level of LDH in the blood is a biological indicator for predicting cardiovascular diseases, because its activity increases in the heart patients hundreds of times higher than its concentration in healthy subjects, [40] Finally, the paper revealed an important increase in liver enzyme AST and non-significant increase in ALT, which is an indicator of liver dysfunction and risk factors for cardiovascular disease, These enzymes increase in heart failure, acute myocardial infarction (AMI) as a result of damage to hepatocytes, which affects hepatic blood flow, especially in patients with metabolic syndrome.[41,42] While the results illustrate that there is a rise in the concentration of sodium and a decrease in the potassium in patients compared with healthy subjects, perhaps the reason is due to the lack of excretion of sodium in the urine leading to high blood pressure, then the incidence of cardiovascular diseases and stimulating the activation of the sympathetic nervous system - SNS, and the renin-angiotensin- aldosterone System (RAAS) to regulate sodium, while the results are showed a decrease the potassium in patients group, This is because most studies have shown that the Increasing the potassium intake in food and decreasing the sodium-to-potassium ratio reduces the risk of high blood pressure and cardiovascular disease.[43,44]

Table 2: Some clinical parameters concentration in control and heart patients

Clinical Parameters	Control Group	Patients
Troponin I ng/ml	0.53 ± 0.7	32.63 ± 7.92 ***
Cystatin C mg/L	0.77 ± 0.18	1.32 ± 0.28 ***
CRP mg/L	5.04 ± 1.24	15.3 ± 7.56 ***
Sodium meq/L	141.49 ± 14.46	149.08 ± 23.6 **
Potassium meq / L	5.2 ± 0.45	4.39 ± 0.76 ***
Uric acid mg / dl	6.69 ± 1.23	7.96 ± 1.77 **
LDH enzyme Iu/L	158.41 ± 28.9	365.75 ± 62.16 ***
ALT enzyme Iu/L	18.34 ± 4.19	21.32 ± 6.43
AST enzyme Iu/L	18.8 ± 8.7	29.67 ± 9.78 ***

*** Significant variance between patients ,and control at $p<0.001$.
** Significant difference between patients and control at $p<0.01$.

3.4. The correlation between activity enzyme (ACE2) and some of the clinical parameters in heart patients compared to the control group:

The result in Table (3) revealed ACE2 had a positive important correlation with CRP. This result is consistent with the outcomes of the study. [45] , While the other biochemical parameters and ACE2 have negligible correlations.

Table 3: Correlation procedure of (ACE2) enzyme, and some of the clinical parameters of heart patients t compared to the control group

Clinical Parameters	Control Group r-value	Patients r-value
Troponin I ng/ml	- 0.286	0.116
Cystatin C mg/L	- 0.029	0.202
CRP mg/L	0.022	0.321 *
Sodium meq/L	- 0.067	0.193
Potassium meq/ L	- 0.03	- 0.075
Uric acid mg/dl	0.041	0.131
LDH enzyme Iu/L	- 0.292	0.241
ALT enzyme Iu/L	0.04	0.126
AST enzyme Iu/L	0.121	0.003

*Correlation is Significant at $p<0.05$.

4. Conclusions

It is concluded from the present study that ACE2 activity correlated significantly with all measured biochemical parameters that related to heart dieases also the enzyme ACE2 plays an important physiological role in heart patients . It was also concluded from the research a decrease in the activity of the ACE2 enzyme with age and a rise in its effectiveness in males was higher than in females, and it was associated with a positive significant relationship with CRP..

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