SJIF Impact Factor: 5.464

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 7.
Issue: 8.
Page N. 13-20
Year: 2023

Original Article www.wjahr.com

BIOCHEMICAL ASSESSMENT OF AMINOTRANSFERASES TESTS IN PATIENTS WITH HEART FAILURE

Dr. Mohammed Riyadh Khudhur*[1], Dr. Saif Riyadh Salih[2], Dr. Khaleel Younus Khalaf[3]

[1]M.B.Ch.B.-F.I.B.M.S. (Chemical Pathology)/ Al-Salam Teaching Hospital, Mosul-Iraq.
[2]M.B.Ch.B.-F.A.B.M. /Ibn-Sena Teaching Hospital, Mosul-Iraq.
[3]M.B.Ch.B.-Higher Diploma of Family Medicine/ Nineveh Health Directorate, Mosul-Iraq.

Received date: 30 May 2023 **Revised date:** 20 June 2023 **Accepted date:** 10 July 2023

***Corresponding Author: Dr. Mohammed Riyadh Khudhur**

M.B.Ch.B.-F.I.B.M.S. (Chemical Pathology)/ Al-Salam Teaching Hospital, Mosul-Iraq.

ABSTRACT

Background: Heart failure (HF) is a leading cause of morbidity and mortality; in medical wards of hospital with more than 100,000 yearly admissions in the United Kingdom, it is expected to account for roughly 5% of hospitalizations. The prevalence of HF is generally 3-20 per 1000 people. According to broad consensus, HF causes hepatic dysfunction, which leads to an increase in enzymes suggestive of hepatocellular damage. **Aim of the study:** To determine the effect of each type of HF on ALT and AST. **Patients, Materials, and Methods:** A case-control study involving 118 person with Heart failure as cases and 30 apparently healthy people as controls. The research was conducted during the period from the 1st of November 2005 to the 15th of May 2006, in Ibn–Sena teaching hospital and Al-Salam general hospital; the cases were from the medical ward, emergency unit and cardiac care unit (CCU). The levels of Aminotransferases were tested for the entire study sample. **Results:** Among the 118 cases with HF; 66 were males and 52 were females, their mean age was 59.06 ± 10.13. BMI was 25.18 ± 3.04, current smoking found in 44.1% of them. While among the 30 controls; 16 were males and 14 were females, their mean age was 57.53 ± 5.19, the mean BMI was 25.70 ± 1.82, with 36.7% of the controls were smokers. The three types of HF showed statistically significant differences with the controls group for both ALT and AST at $p<0.001$. Moreover, there was significant association ($p\leq0.05$) of biventricular and left-sided HF in ALT in which ALT is higher in biventricular HF than left-sided HF, but for AST in biventricular HF is significantly higher than that for left and right-sided HF. Regarding the duration of HF, ALT showed significant difference between group A and group B while AST levels showed no significant difference. The sensitivity and specificity of ALT were 91.53% and 96.67% respectively while sensitivity and specificity of AST were 94.92 % and 93.33 % respectively. Multiple Logistic Regressions showed strongest association of the HF with ALT activity ($p < 0.001$) and the odd ratio was (40.65). **Conclusions:** Patients who developed heart failure frequently have abnormal hepatic function because heart failure influences the liver and causes lhepatic dysfunction. In this investigation, the three forms of cardiac failure showed increased transaminase activity. The degree of impaired liver function did not appear to be influenced by the length of heart failure. Compared to left-sided and right-sided categories of heart failure, biventricular failure exhibits a greater rise in transaminase activity.

KEYWORDS: Alanine Aminotransferase, Aspartate Aminotransferase, Heart Failure.

INTRODUCTION

HF is a significant source of morbidity and death[1], and it is estimated to account for 5% of admissions to hospital medical wards in the United Kingdom, where there are more than 100,000 admissions per year. The prevalence of HF is 3-20 per 1000 people. The yearly incidence of HF is 1–5/1000, and the relative incidence after the age of 45 will be doubled for each decade of life[1,2], despite the fact that this surpasses 100/1000 in individuals above the age of 65.

Due to the aging of the people and the higher survival rates among patients with impaired cardiac function brought on by therapeutic improvements in the management of myocardial infarction (MI), the total incidence is projected to rise in the future.[1] In general, it seems that CHF affects 1-3% of the general population and about 10% of elderly people.[2] Unlike other common cardiovascular diseases, the age-adjusted mortality attributed to HF also appears to be rising.[3] In developing nations, as they go through epidemiological transition and socioeconomic development, the

epidemiology of HF becomes rising similar to that of Western Europe and North America, with coronary artery disease being the commonest cause of HF[4], 5.17/1000 over a three-year period is the prevalence of HF in an Arab population. Ischemic heart disease (IHD) is more prevalent in men, which contributes to the higher prevalence of HF in this group. In older people, namely those over 65, IHD and hypertension (HT) are the most common causes of HF.[5]

The diagnosis of HF was made based on the patient's medical history, physical examination, and a number of laboratory tests as well as numerous invasive and noninvasive special investigations.[6]

According to widespread consensus, HF leads to hepatic dysfunction and a rise in the ALT and AST enzymes, which are signs of hepatocellular damage.[7] In general, the liver function tests were divided into:

- Tests for cell damage (amino-transferases activities).
- Tests for synthetic function (serum albumin concentration and prothrombin time).
- Tests for excretory function (direct serum bilirubin, alkaline phosphatase and Gamma-glutamyl-transpherase)[8]

Amino-transferases or Transaminases include both Alanine aminotransferase (ALT) or (Glutamate Pyruvate Tansaminase GPT) and Aspartate amino-transferase (AST) or (Glutamate Oxaloacetate Tansaminase GOT).

Plasma enzyme activity increase when only a small percentage of cells have damaged membranes, making the plasma transferases a sensitive indicator of cytoplasmic and/or mitochondrial membrane damage. Although ALT is restricted to the cytoplasm, where its concentration is higher than that of AST, liver cells nevertheless contain more ALT than AST.[8] AST has cytosolic in addition to mitochondrial forms, whereas ALT is a cytosolic enzyme.[9]

The transaminases are enzymes that interconvert pairs of amino and keto acids; for optimum activity, they require the cofactor pyridoxal phosphate. They are found throughout the body.[8]

The activities of amino-transferases are sensitive markers of liver cell damage and are useful in identifying hepatic disorders like hepatitis. The reference range for both ALT and AST is 14 U/l, although some researchers recommend adjusting amino-transferase activities for sex and body mass index (BMI), which is rarely done.[10] Both amino-transferases are typically present in the serum at low activities.

AST is present in the liver, in addition to skeletal muscle, cardiac muscle, kidney, brain, pancreas, lungs, and leukocytes in decreasing order of activity. Since the liver contains the largest concentration of ALT, these enzyme's levels serve as more accurate markers of damage to liver cells.[10]

Aim of the study: To determine the effect of each type of HF on ALT and AST.

PATIENTS, MATERIALS, AND METHODS

This study is a case–control study; patients were divided into two groups:

1. Patients: one hundred – eighteen patients with HF, age range is (20-75) years with mean ± standard deviation (SD) (59.06±10.13) years. The cases include 52 females and 66 males.

All patients were diagnosed by physician as HF and were continuing on treatment, the diagnosis was done depending on; history with physical examination, CXR, ECG abnormalities, and Echocardiography.

On admission, all of them had HF according to the Framingham criteria for the diagnosis of HF. According to the duration of HF, patients were classified into three categories; group A (1-5 years), group B (6-10 years), and group C (>10 years).

2. Control group: it includes 30 persons; 16 males and 14 females, and they were matched with the same age groups of the cases. Controls were selected from the medical staff, relatives and attendants of the out patients clinic department. HF, HT, renal, liver problems, DM, and medications were not affecting the result.

3.

The study conducted during the time from the 1st of November 2005 to the 15th of May 2006, in Ibn–Sina general teaching hospital and Al-Salam general hospital; the cases were from the medical ward, emergency unit and cardiac care unit (CCU).

Both cases and control group were interviewed and the general information was taken to fill the questionnaire.

Materials: In this study, materials were arranged into specimens, instruments, and reagents.

Specimens:

Blood samples were collected from all subjects by an antecubital venepuncture, and stressful venepuncture was avoided.

Five milliliter (ml) of venous blood have been collected from every subject then allowed to clot in plane tube, the serum was separated by centrifuge at 3000 rpm for 5 minutes, and the resultant serum was used for biochemical testing including Serum ALT activity and Serum AST activity. The samples were kept until analyzed at a weekly batches at (-20)° C.

Instruments

The instruments that were used in this study include centrifuge 3E-1 (sigma, Germany), Cecil, Ce 303,

Greating spectrophotometer (Cambridge, England), and Waterbath Gallen Kamb (England).

Reagents
All laboratory reagents used through this study which were of analar grade, obtained from the clinical chemistry laboratory of the department of biochemistry, Mosul College of Medicine, they were purchased from international suppliers and companies and all reagents will be mentioned within the related methodologies.

Methods
Serum ALT and AST activities were determined by using a kit method supplied by Syrbio Company (Syria).[11]

Determination of ALT Activity
Principle
Colorimetric determination of Alanine Aminotransferase based on the following reaction:

$$\text{L – Alanine} + \alpha\text{ oxoglutarate} \xrightarrow{\text{ALT}} \text{Pyruvate + L-Glutamate}$$

Pyruvate formed reacts with 2.4 dinitrophenyhydrazine to yield a colored hydrazone that can be measured at 546 nm (530 to 550 nm).

Reagents:
$R_{1:}$ GPT substrate

Phosphate buffer 7.4	100 mmol/l
L – Alanine	200 mmol/l
α Oxoglutarate	2.0 mmol/l

$R_{2:}$ GPT color reagent

DNPH	1.0 mmol/l
HCL	1.0 mmol/l

$R_{3:}$ NaOH 0.4 N

Procedure:
Set following tubes for each serum (one Blank tube is required for each run).

	Reagent Blank	Sample
Sample	-	0.1 ml
Solution	0.5 ml	0.5 ml
Distilled water	0.1	-

Mix and let stand exactly 30 minutes at 37C.

Solution 2	0.5 ml	0.5 ml

Mix and let stand exactly 20 minutes at 20 to 25C.

NaOH 0.4N	5 ml	5 ml

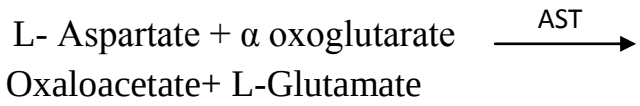
Mix by gently inversion. Read absorbance against Blank tube after 5 minutes, at wave length of 546 nm.
Obtain the activity of GPT in the serum from the table:

Absorbance	U/l	Absorbance	U/l
0.025	4.0	0.275	48.0
0.050	8.0	0.300	52.0
0.075	12.0	0.325	57.0
0.100	17.0	0.350	62.0
0.125	21.0	0.375	67.0
0.150	25.0	0.400	72.0
0.175	29.0	0.425	77.0
0.200	34.0	0.450	83.0
0.225	39.0	0.475	88.0
0.250	43.0	0.500	94.0

Determination of AST Activity

Principle

Colorimetric determination of Aspartate Aminotransferase based on the following reaction:



Oxaloacetate formed reacts with 2.4 dinitrophenyhydrazine to yield a colored hydrazone that can be measured at 546 nm (530 to 550 nm).

Reagents:

$R_{1:}$ GOT substrate

Phosphate buffer 7.4	100 mmol/l
L – Aspartate	200 mmol/l
α Oxoglutarate	2.0 mmol/l

$R_{2:}$ GPT color reagent

DNPH	1.0 mmol/l
HCL	1.0 mmol/l

$R_{3:}$ NaOH 0.4 N

Procedure:

Set following tubes for each serum (one Blank tube is required for each run).

	Reagent Blank	Sample
Sample	-	0.1 ml
Solution	0.5 ml	0.5 ml
Distilled water	0.1	-

Mix and let stand exactly 30 minutes at 37C.

Solution 2	0.5 ml	0.5 ml

Mix and let stand exactly 20 minutes at 20 to 25C.

NaOH 0.4N	5 ml	5 ml

Mix by gently inversion. Read absorbance against Blank tube after 5 minutes, at wave length of 546 nm.

Calculation For AST (GOT):

Obtain the activity of GOT in the serum from the table:

Absorbance	U/l	Absorbance	U/l
0.020	7.0	0.100	36.0
0.030	10.0	0.110	41.0
0.040	13.0	0.120	47.0
0.050	16.0	0.130	52.0
0.060	19.0	0.140	59.0
0.070	23.0	0.150	67.0
0.080	27.0	0.160	76.0
0.090	31.0	0.170	89.0

Statistical analysis

The data collected during the study were summarized in sheets of Microsoft Excel 2007. The statistical analysis performed by using IBM-SPSS 26. The normality of these data tested by Shapiro-Wilk test, and the parametric tests were decided to be chosen. Nominal data was expressed in frequencies and proportions while numerical data was expressed in means and standard deviations. The Pearson chi square test (x^2) used for the nominal data. The numerical data were comparing by the t-test performed for independent two means between the controls groups and parameters studied groups. One-Way ANOVA and Duncan Multiple Range Test. Multiple Logistic Regression test was used to examine the relation between HF and predictors that may influence it. P-value ≤ 0.05 considered as significant.

RESULTS

The results of the data that were analyzed are arranged according to the grouping of the subjects enrolled in the study.

The demographic characteristics of the studied groups were demonstrated in table (1) which showed that among the 118 cases with HF; 52 were females and 66 were males, their age ranged from (20-75) years with a mean ± SD of (59.06 ± 10.13). BMI was 25.18 ± 3.04, current smoking found in 44.1% of them. While among the 30 controls; 16 were males and 14 were females, their age ranged from (28-66) years with a mean ± SD of (57.53 ± 5.19), the mean BMI was 25.70 ± 1.82, with 36.7% of the controls were smokers.

Table (1): Demographic characteristics of the studied groups.

Demographic Characteristics		Mean ± SD			
		Control		Cases	
Age (year)		57.53 ± 5.19		59.06 ± 10.13	
BMI (kg/m^2)		25.70 ± 1.82		25.18 ± 3.04	
		No.	%	No.	%
Gender	Male	16	53.3	66	55.9
	Female	14	46.7	52	44.1
	Male: female	1.14		1.27	
Smoking	Smoker	11	36.7	52	44.1
	Non-smoker	19	63.3	66	55.9

Comparison of measured Aminotransferases between the study groups was demonstrated in table (2) and revealed that there were statistically significant differences between each subgroup of cases with the controls group for both ALT and AST at p<0.001. Moreover, there was significant difference (p≤0.05) between biventricular and left-sided HF in ALT in which ALT is higher in biventricular HF than left-sided HF, but for AST in biventricular HF is significantly higher than that for left and right-sided HF.

Table (2): Comparison of measured Aminotransferases between the study groups.

Parameters	Mean ± SD			
	Control (n=30)	Cases (n=118)		
		Biventricular HF (n=55)	Left-sided HF (n=46)	Right-sided HF (n=17)
ALT(U/l)	8.76 ± 2.6	31.93 ± 12.8 [a]	22.63 ± 11.2 [b]	26.88 ± 8.7 [ab]
AST(U/l)	8.48 ± 2.4	34.71 ± 1.7 [a]	24.38 ± 10 [b]	22.32 ± 7.7 [b]

One-Way ANOVA with post hoc Dunken test had used
Means with different letters horizontally have significant difference at p≤0.05

Comparison of measured Aminotransferases in patients according to duration of heart failure was showed in table (3) and demonstrated that there was statistically significant concerning ALT among the duration groups and the real difference found by post hoc test was found between group A and group B. AST levels showed no significant difference among the duration groups.

Table (3): Comparison of measured Aminotransferases in patients according to duration of heart failure.

Parameters	Mean ± SD		
	Duration (year)		
	Group A (n=85)	Group B (n=25)	Group C (n=8)
ALT (U/l)	25.95 ± 11.54 [a]	32.6 ± 14.5 [b]	29.13 ± 10.91 [ab]
AST (U/l)	27.89 ± 11.56 [a]	32.96 ± 13.39 [a]	26.88 ± 6.62 [a]

One-Way ANOVA with post hoc Dunken test had used
Means with different letters horizontally have significant difference at p≤0.05

Distribution of the studied groups according to ALT activity was demonstrated in table (4). This table elicited that the upper reference range as a cut-off point, 91.5% of the cases were higher than the cut-off level and 3.3 % of the control group were higher than the cut-off level with significant difference (p <0.001). The sensitivity was 91.53% and specificity is 96.67%.

Table (4): Distribution of the studied groups according to ALT activity.

ALT (U/l)	>14		≤14		Sensitivity %	Specificity %	p-value
	No.	%	No.	%			
Cases	108	91.5	10	8.5	91.53	96.67	<0.001
Controls	1	3.3	29	96.7			

Distribution of the studied groups according to AST activity was demonstrated in table (5). This elicited that the upper reference range as a cut-off point, 94.9% of the cases were higher than the cut-off level and 6.7% of the control group were higher than the cut-off level with significant difference (p <0.001). The sensitivity is 94.92 % and the specificity is 93.33 %.

Table (5): Distribution of the studied groups according to AST activity.

AST (U/l)	>14		≤14		Sensitivity %	Specificity %	p-value
	No.	%	No.	%			
Cases	112	94.9	6	5.1	94.92	93.33	<0.001
Control	2	6.7	28	93.3			

Multiple Logistic Regressions was conducted and demonstrated in table (6) and clarified the presence of strongest association of the HF with ALT activity (p < 0.001) and the odd ratio was (40.65).

Table (6): Multiple logistic regression model for predictors of HF.

Variable Xi (predictors)	Regression Coefficient (B)	p-value	OR	C.I.
ALT	3.705	<0.001	40.65	5.29-312.56

DISCUSSION

For all severe kinds of heart disease, HF is the "final common pathway".[12] HF is a serious health issue that is becoming more prevalent in the general population[13], and it is mostly the end stage of hypertensive, coronary, and VHD due to an aging population of greater size and the extension of cardiac patients' lives through contemporary medication.[14]

Through hepatic congestion and circulatory dysfunction, HF can have an impact on the liver.[15] The literatures have not gone into great detail regarding the connection between cardiac and hepatic problems.[16] A highly vascular organ, the liver receives about 20% of the cardiac output. A linear relationship between blood pressure and its flow is expressed by the fact that 70% of the hepatic blood flow originates from the portal system and 30% is delivered via the hepatic artery. By boosting oxygen extraction, the liver can maintain normal oxygen intake, with as much as 95% of the blood's oxygen being taken in a single pass through the liver.[16] Cardiogenic ischemic hepatitis, congestive liver fibroses, and cardiac cirrhosis are among the range of heart illnesses that can damage the liver.[16]

Amino-transferase tests were performed in this investigation on all HF patients (biventricular, left- and right-sided). When compared to the control group, there is a considerable rise in ALT and AST activity in the cases, which is consistent with the abnormal results that were seen.

The sensitivity of ALT was (91.53%) and the specificity was (96.67%) with (p<0.001), by multiple logistic regression model for predictors of HF, the odd ratio for ALT was high (40.65) with (p<0.001), the sensitivity of AST was (94.92%) and the specificity was (93.33%) with (p<0.001). These findings were consistent with many studies which have confirmed that HF is associated with liver dysfunction and the degree of LFTs changes is not consistent[17-21], in this study, the duration of HF did not have a direct relation to the degree of changes of LFTs and this is mimic to other studies [21-23] that did not have found clear association between the duration of HF and LFTs changes.

In the second half of the past century liver function test in HF have been the subjects of many researchers. Felder 1950 had studied the effect of chronic congestive HF on certain LFTs to evaluate hepatic dysfunction in congestive HF and had found no definite changes of liver function in HF.[22] Richman 1961 study was on the effect of HF on liver dysfunction particularly enzyme changes, and had concluded that HF is accompanied by abnormal LFTs especially alteration in ALT and AST activities in the serum.[24] Dunn 1973 had studied the liver function in CHF and had explained the structural and functional derangement and the pathogenesis of liver dysfunction in HF patients and had mentioned that all types of HF is associated with different picture of LFTs.[23] Hesse 1976 had explained the pathological mechanism of albumin changes in HF before and after treatment.[25]

Although the relationship between the heart and the hepatic dysfunction is well established[16], it is surprising that the pattern of liver dysfunction in HF has only been defined recently.[7]

Results obtained by Batin *et al*, (1995) had suggested that liver function tests are of great prognostic

importance in HF patients and can be used for follow up of HF patients to predict the prognosis because these tests are simple and generally available instead of or with difficult and expensive investigations like echocardiography, measurement of filling pressure for left ventricular, and other investigations.[18]

Deranged LFTs may be due to the result of hepatic congestion secondary to the effects of fluid overload as, well as, raised filling pressures and could be due to reduced cardiac output and hepatic blood flow causing hypoxic injury.[19]

It is not recognized which of these mechanisms is the leading but in severe and protracted HF, patients may end with cardiac cirrhosis.[18]

Passive congestion and reduced systemic perfusion are both important in the development of liver function abnormalities.[19]

It has been recommended that the extent of abnormalities of LFTs correlate with the severity of heart failure assessed by invasive hemodynamic parameters, in addition to a considerable inter-patient variability (some patients with mild HF can have abnormal LFTs results and some patients with marked hemodynamic abnormalities can have normal LFTs results).[19]

It remains possible, nonetheless that the abnormal LFTs are replacement marker of heart dysfunction and although not accurate, they may provide a collective measure of tissue oxygenation as, well as, peripheral tissue distention and edema, these are two of the chief patho-physiological changes that arise in HF.[18]

No clear association between medications including diuretics usage and the degree of abnormalities of LFTs.[17,18]

In this study, transaminases activities were significantly higher in biventricular HF compared with that of left-sided and right-sided HF, this was in agreement with the findings of other researches which stated that transaminases activities rise in HF (biventricular, left-sided and right-sided HF) by two mechanisms: hypoxia due to low blood flow and hepatic congestion, this may be associated even with centrilobular necrosis may add to the alteration in liver transaminases activities.[21,23]

CONCLUSIONS

Patients who developed heart failure frequently have abnormal hepatic function because heart failure influences the liver and causes lhepatic dysfunction. In this investigation, the three forms of cardiac failure showed increased transaminase activity. The degree of impaired liver function did not appear to be influenced by the length of heart failure. Compared to left-sided and right-sided categories of heart failure, biventricular failure exhibits a greater rise in transaminase activity.

REFERENCES

1. Davis RC, Hobbs FDR, Lip GYH. ABC of heart failure: History and epidemiology. *BMJ.* 2000; 320: 39-42.
2. McMurray JJV and Stewart S. The burden of heart failure. *Europian Heart Journal.* 2002; 4: D50-D58.
3. Remme WJ and Swedberg K. Guidelines for the diagnosis and treatment of chronic heart failure. *Europian Heart Journal.* 2001; 22: 1527-1560.
4. Mendez GF and Cowie MR. The epidemiological features of heart failure in developing countries: a review of literature. *Int J Cardiol.* 2001; 80 (2-3): 213-219.
5. Agarwal AK, Venugopalan P, De Bono D. Prevalence and etiology of heart failure in an Arab population. *Europian Journal of Heart Failure.* 2001; 3: 301-305.
6. Dickstein K. Diagnosis and assessment of the heart failure patient: the cornerstone of effective management, review. *The European Journal of Heart Failure.* 2005; 7: 303-308.
7. Cogger VC, Fraser R, LeCouteur DG. Liver dysfunction and heart failure. *The American Journal of Cardiology.* 2003; 91: 1399.
8. Mayne PD. Clinical Chemistry in Diagnosis and Treatment. 6th ed. Edward Arnold; New York, USA. 1994: 117-198.
9. Johnstone DE. Special considerations in interpreting liver function tests. *American Family Physician.* 1999; 59(8): 1-9.
10. Pratt DS and Kaplan MM. Evaluation of abnormal liver-enzyme results in asymptomatic patients, review. *The New England Journal of Medicine.* 2000; 324: 1266-1271.
11. Wootton IPD and Freeman H. Microanalysis in Medical Biochemistry, 6th ed. Churchill Livingstone; Edinburgh, England. 1982: 102-105.
12. Lenfant C. Report of the task force on research on heart failure. *Circulation*. 1994; 90(3): 1118-1123.
13. Nophria A, Lewis E, Stevenson LW. Medical management of advanced heart failure. *JAMA.* 2002; 287(5): 628-640.
14. Kannel WB. Incidence and epidemiology of heart failure. *Heart Failure Reviews.* 2000; 5(2): 167-173.
15. Gieling RG, Ruijter JM, Maas AAW, Weerman MAVB, Dingemans KP, Ten KFJW, *et al.* Hepatic response to right ventricular pressure overload. *Gastroenterology.* 2004; 127: 1210-1221.
16. Naschitz JE, slobodin G, Lewis RJ, Zuckerman E, Yeshurun D. Heart diseases affecting the liver and liver diseases affecting the heart. *American Heart Journal.* 2000; 140; 111-120.
17. Lau GT, Tan HC, Kritharides L. Type of liver dysfunction of heart failureand it's relation to the severity of tricupid regurgitation. *The American Journal of Cardiology.* 2002; 90: 1405-1409.
18. Batin P, Wickens M, McEntegart D, Fullwood L, Cowley AJ. The importance of abnormalities of liver function tests in predicting mortality in chronic heart

failure. *European Heart Journal.* 1995; 16: 1613-1618.
19. Kubo SH,Walter BA, John DHA, Clark M, Cody RJ. Liver function abnormalities in chronic heart failure influence of systemic hemodynamics. *Arch Intern Med.* 1987; 147: 1227-1230.
20. Seeto RK, Fenn B, Rockey DC. Ischemic hepatitis: Clinical presentation and pathogenesis. *The American Journal of Medicine.* 2000; 109: 109-113.
21. Reinhartz O, Farrar DJ, Hershon JH, Avery GJ, Haeusslein EA, Hill JD. Importance of preoperative liver function as a predictor of survival in patients supported with thoracic ventricular assist devices as a bridge to transplantation. *The Journal of Thoracic and Cardiovascular Surgery*. 1998; 116(4): 633-640.
22. Felder L, Mund A, Parker JG. Liver function test in chronic congestive heart failure. *Circulation.* 1950; 11: 286-297.
23. Dunn GD, Hayes P, Breen KJ, Schenker S. The liver in congestive heart failure. *The American Journal of the Medical Sciences.* 1973; 265(3): 174-189.
24. Richman SM, Delman AJ, Grob D. Alterations in indices of liver function in congestive heart failure with particular reference to serum enzymes. *Am J Med*. 1961; 30: 211-225.
25. Hesse B, Parving HH, Jacobsen HL, Noer I. Transcapillary escape rate of albumin and right atrial pressure in chronic congestive heart failure before and after treatment. *Circulation Research.* 1976; 39: 358-362.