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ORIGINAL ARTICLE

Short Term Follow-up of Clinical Outcome of Patients with Heart Failure and Associated Hepatitis C Virus Infection.

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ABSTRACT

Background: There is increased risk of cardiovascular complications in hepatitis C virus (HCV)-infected patients regardless of the severity of the liver disease or the common cardiovascular risk factors.

Aim of the Study: This study is conducted to evaluate the effect of associated hepatitis C viral infection on the short-term clinical outcome of acute decompensated heart failure (ADHF) patients during their in-hospital stay and one month after discharge.

Methods: This is a prospective observational study that was conducted on patients with ADHF, who were admitted in cardiovascular department at specialized medical hospital, Mansoura University during the period between January 2018 and January 2019. The study included 100 patients with heart failure (HF), 63 males and 37 females, and their ages ranged from 28 – 88 years.

Results: There was no significant changes between heart failure (HF) patients with and without HCV regarding all demographic data, and HF risk factors. There was statistically non-significant increase in prevalence of HF with reduced ejection fraction (HFrEF) among HF patients with HCV (70.3%) than those without HCV (57.1% P>0.05). HCV infection had no significant effect on the outcome of HF clinical course, although, there was statistically significant increase in prevalence of pulmonary hypertension in HF patients with HCV 35.1% than without HCV 11.1%.

Conclusion: HCV-Infection in patients with ADHF has no effect on all aspects of patient's clinical states. Among patients with ADHF, the main predictors of short-term post discharge clinical status are patient age and the whole duration of chronic HF disease.

Key Words: heart failure, HCV, echocardiography, pulmonary hypertension.

INTRODUCTION

Heart failure (HF) is a chronic, progressive, and debilitating epidemic illness, which affects a growing number of adults, and is the most common cause of hospitalization and re-hospitalization among adults**.** HF results from multiple causes, including coronary artery disease (CAD), hypertension, and idiopathic dilated cardiomyopathy [1] . HCV infection has moved from the traditional picture of a localized liver-focused disease to the concept of a systemic disease capable of producing extra hepatic manifestations. Among the extra-hepatic manifestations, cardiovascular involvement has probably been underestimated. The replication of the HCV may result in myocarditis, which is complicated by cardiomyopathy in persons with genetic susceptibility [2].

Both HCV infection and cardiovascular alterations are common conditions observed in a large proportion of the general population. It is difficult, therefore, to establish whether a simple association exists between the two conditions, or whether other pathogenic mechanisms directly or indirectly link chronic HCV infection to cardiovascular disorders [3]. The aim of our study is to evaluate the effect of associated HVC infection on the short-term clinical outcome of ADHF patients during their in-hospital stay and one month after discharge.

METHODS

This is a prospective observational study that was conducted on patients with ADHF, who were admitted in cardiovascular department at specialized medical hospital, Mansoura University during the period between January 2018 and January 2019. The study included 100 patients with HF, 63 males and 37 females, and their ages ranged from 28 – 88 years. Written informed consent was obtained from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Mansoura University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Diagnosis of HF was based on presence of typical symptoms (New York Heart Association "NYHA" functional class III – IV dyspnea according to European society of cardiology) and signs, ECG, laboratory data and echocardiographic evaluation.

The studied population were classified in to 2 main groups according to presence of HCV infection into group with HCV infection (37 patients) and group without HCV infection (63 patients).

Patients with any of the following were excluded from the study: rheumatic valvular heart diseases, prosthetic valves, congenital heart diseases, acute myocardial infarction, pericardial diseases, implantable cardiac devices, chronic obstructed pulmonary diseases (COPD), chronic renal impairment, and acute hepatic decompensation.

The patients were subjected to full clinical evaluation, echo/doppler evaluation, abdominal ultrasound, laboratory investigations, follow up during hospital stay until discharge, and follow up of their clinical status after discharge for one month.

After that follow up the clinical status during hospital until discharge and after discharge for one month by phone calling with either patient or his/her relative asking about, adherence to therapy, patients' symptoms, clinical status either (improved (stabilized) or deteriorated): improved or stabilized case was considered when there was improvement or non-change in NYHA functional class after discharge while, nonimproved or deterioration of case was considered when deterioration of NYHA class in spite of intensification of post discharge medication or appearance of any major adverse cardiac events (MACE) or need hospital readmission, any readmissions after this discharge, duration between readmission after present discharge, readmission cause (Atrial fibrillation (AF), chest infection, decompensated HF, or death.

Statistical analysis

SPSS version 21 was used to analyze data. One-sample Kolmogorov-Smirnov test was first used to test the data normality. Number and percent were used to illustrate qualitative data and Chi-square test was used to test the association between categorical variables. The mean ± SD (standard deviation) represents continuous variables. Student t test was used to compare the two groups while Pearson correlation was used to correlate continuous data. For all above mentioned statistical tests done, the threshold of significance is fixed at 5% level (p-value). The results were considered non-significant when the probability of error is more than 5% ($p > 0.05$), significant when the probability of error is less than 5% ($p < 0.05$) and highly significant when the probability of error is less than 0.1% ($p< 0.001$).

RESULTS

The study comprised 100 HF patients, 37 had HCV, 63 without HCV, 62 had reduced EF (EF < 40%), 25 had mid-range EF (EF 40- 50%) and 13 had preserved EF (EF > 50%). The main HF etiology was combined hypertension/ischemic heart disease (IHD) diseases (67.0%), followed by isolated hypertensive diseases (22 %), isolated IHD (4.0%%) and idiopathic dilated cardiomyopathy (DCM) (7 %) ($P < 0.05$). There was statistical nonsignificant correlation in all HF causes between both HF patients with HCV and without HCV (($P>0.05$).

Among all HF patients, the mean age was 60 ± 10.96 years. Most patients (58) were above 60 years, 23 aged from 50 to 60 years, 14 aged from 40 to 50 years and only 5 were below 40 years ($P<0.05$). The prevalence of CAD risk factors (CAD- RF) was hypertension in 90% of patients, diabetes in 86 %, IHD in 71% dyslipidemia in 71 %, smoking in 46 %, AF in 43 % and family history of IHD in 34 % ($P<0.05$). Statistical non-significant increase of all studied CAD-RF were found between HF-patients with HCV and without HCV ($P>0.05$) (**Figure 1**).

The main symptoms among HF patients were dyspnea NYHA grade III & IV100%, GIT symptoms 38%, statistically significant increase in gastrointestinal (GIT) symptoms among HF patients with HCV (72.9%) than HF patients without HCV (72.9%) ($P<0.05$) (**Table s1**).

Systemic examination showed statistically significant increase in hepatomegaly, splenomegaly, and ascites among HF patients with HCV 21.6%, 40.5%, 40.5%, 40.5% ,54.1% and 54.1% versus 7.9%, 14.3% and 19% respectively) ($P<0.05$*) (**Table s2**).

On comparing both HF-patients with and without HCV, it revealed statistically increase in dilated PA among HF-patients with HCV (35.1% versus 11.10%) ($P<0.05$) (**Table s3).**

2D /Doppler findings among HF patients revealed mitral regurge (MR) in all patients 100%, tricuspid regurge (TR) 86%, pulmonary hypertension (PH) 85%. Comparing both HF-patients with HCV and without HCV showed statistically significant increase in severe TR among HF patients with HCV (35.1% versus 11.1%) (P<0.05), statistically significant increase in severe PH among HF patients with HCV (35.10 versus 11.10%11.10%) (P<0.05) **(Figure 2).**

Comparing both HF-Patients with HCV and without HCV revealed statistically significant increase in cirrhotic liver among HF-patients with HCV (43.2% versus12.7%) (P<0.05), significant increase in ascites among HF-patients with HCV (32.4%, 13.5% and 8.1% versus12.7%, 6.3% and 0% respectively) (P<0.05) (**Table s4**).

Studying the influence of basic demographic data one month post discharge of HF-patients revealed increasing age was more among the non-improved HF patients 62.60±10.10 versus the improved group 55.56±11.07 years (P<0.002) (**Table s5**).

Studying the influence of RF on the clinical state of HF-patients one month post discharge revealed that presence of IHD and HTN duration were directly related to non-improvement (81.0% versus 54.1% P<0.005 and (12.48 ± 4.62 versus 10.21 ± 3.68 P<0.013 respectively) (**Table s6**).

Non-improvement in follow up of clinical status was related to presence of on admission chest pain (77.2% versus 45.9% P<0.042), and on admission palpitation (42.9% versus 24.3% P<0.048), but presence of on admission dyspnea and its grades, orthopnea, PND and syncope in addition to NYHA class on discharge did not influence the post discharge follow up clinical status (P> 0.05) (**Table 1**).

Non-improvement in post discharge clinical state was associated with the following M-mode measurements: increased left atrial diameter (5.11 ± 0.51 versus 4.82 ± 0.58 p <0.012), increased LVIDs (5.40± 0.81 versus 4.970± 0.72 p <0.009), and decreased EF (0.35 ± 0.09 versus 0.402 ± 0.11 p<0.037). (**Table s7).**

The Non-improvement in post discharge clinical Status was associated with presence of the following 2D ECHO finding: marked dilated LV (76.2% versus 56.8% p <0.049), moderate/ marked dilated LA (72.0% versus 448.6% p<0.026), sclerotic mitral valve (27.0% versus 5.4% p<0.017), sclerotic aortic cusps (55 versus 18.9% p <0.009) and dilated pulmonary artery (28.6% versus 5.4% p <0.001) (**Table s8**).

The non-improvement in post discharge clinical state was associated with the presence of the following Doppler finding: moderate/sever MR (77.7% versus 48.1% p <0.014), moderate/ sever TR (66.7% versus 48.6% p <0.022) and moderate/ sever PH (66.7% versus 48.6% p <0.022) (**Table 2).**

Non- improvement in post discharge clinical state was associated with the presence of: HFrEF (73% versus 43.2%), P<0.011, ischemic HF (81% versus 54.1%) P<0.012, and IHD with previous intervention (66.7% versus 40.0%), P<0.037. HCV Infection has no relation to post discharge Clinical Status (**Table s9).**

The Non-improvement in post discharge clinical state was associated with presence of increased HF duration (4.3175 ± 1.58445 versus 2.0270 ± 0.16440 p <0.000), increased recurrent previous admission (98.4% versus 2.7% p <0.000), and only one previous admission (55.6% versus 2.7% p <0.000) (**Table 3).**Non-improvement in post discharge clinical state was associated with age above 61.5 years (P < 0.001) , HTN for more than 10.0 years (P < 0.001) , admission HR more than 92 b/m P < 0.022 , LVIDs more than 5.15 cm (P < 0.008), EF less than 0.33 (P < 0.005), creatinine clearance less than 63.33 (P < 0.043) , and HF duration of more than 2.5 years (P < 0.000) (**Table s10 & Figures s1,s2,s3,s4,s5,s6,s7)**.

Table 1. Influence of on admission, in-hospital and discharge clinical findings on one month Post discharge clinical State of HF-patients

	Improved HF Patients (n = 37)		Non-Improved HF Patients (n = 63)		Significance	
	No	%	No	%	***test***	***P value***
***On Admission* Clinical Status**						
Dyspnea	37	100 %	63	100 %		
Grade III Dyspnea	18	48.6%	26	41.3%	$X^2=0.61$	$P>0.05$
Grade IV Dyspnea	19	51.4%	37	58.7%		
Orthopnea	36	97.3%	61	96.8%	$X^2=0.89$	$P>0.05$
PND	27	73.0%	51	81.0%	$X^2=0.85$	$P>0.05$
Chest Pain	17	45.9%	48	77.2%	$X^2=10.81$	$P<0.042$*
Palpitation	9	24.3%	27	42.9%	$X^2=3.58$	0.048*
Syncope	2	5.4%	3	4.8%	$X^2=2.25$	$P>0.05$
In Hospital *Clinical* Status						

	Improved HF Patients (n = 37)		Non-Improved HF Patients (n = 63)		Significance	
Improved	37	100.0%	63	100.0%	-----	--------
Discharge Clinical Status NYHA _Class						
No Dyspnea	6	16.2%	8	12.7%	$X^2=0.26$	$P>0.05$
Grad I Dyspnea	14	37.8%	24	38.1%		
Grade II Dyspnea	17	45.9%	31	49.2%		

Table 2. Influence of on admission abnormal doppler finding on one month post discharge clinical state of Heart Failure Patients

Doppler Finding	**Improvement (37 Patients)**		**Non-Improvement ((63 Patients)**		**Significance**	
	No	%	No	%	***test***	***P value***
Mild MR	19	51.4%	13	20.6%	$X^2=10.59$	$P<0.014$*
Moderate./ Sever MR	18	48.1%	49	77.7%		
Mitral E/ A Value	1.75 ± 0.38		2.01 ± 0.08		$t=-2.30$	$P<0.038$*
Mild TR	12	32.4%	14	22.2%	$X^2=9.65$	$P<0.022$*
Moderate/ Sever TR	18	48.6%	42	66.7%		
Mild PH	12	32.4%	13	20.6%	$X^2=9.60$	$P<0.022$*
Moderate/ Sever PH	18	48.6%	42	66.7%		

Supplementary file

Table s1. Analysis of on admission presenting symptoms among heart failure patients sub-groups

	Total HF-GP (n = 100)		Non HCV HF-GP (n = 63)		HCV HF-GP (n = 37)		Non HCV GP Versus HCV GP	
	No	**%**	No	%	No	%	***test***	***Signif***
Cardiac Symptoms								
Dyspnea	100	100%	63	100%	37	100%	-----	------
Grade III Dyspnea	44	44	29	46%	15	40.5%	$X^2=0.28$	$P>0.05$
Grade IV Dyspnea	66	66	34	54%	22	59.5%		
Orthopnea	97	97.0%	61	96.8%	36	97.3%	$X^2=0.02$	$P>0.05$
PND	78	78.0%	48	76.2%	30	81.1%	$X^2=0.32$	$P>0.05$
Chest Pain	65	65	43	68.3%	22	59.4%	$X^2=1.58$	$P>0.05$
Angina Pain	46	46	32	50.8%	14	37.8%		
Atypical Pain	19	19	11	17.5%	8	21.6%		
Palpitation	100	100%	63	100%	37	100%	-----	$P>0.05$
Syncope	4	4	2	3.2%	2	5.4%	$X^2=0.88$	$P>0.05$
Syncope /Aborted SCD	1	1	1	1.6%	0	0%		
GIT Symptoms	**38**	**38%**	**11**	17.6%	27	72.9%	$X^2=16.7$	$P<0.05$*
Pain	20	20 %	10	16.0%	10	27.0%		
Nausea and Vomiting	13	13 %	0	0%	13	35.1%		
Hematemesis/ Melina	5	5 %	1	1.6%	4	10.8%		
Respiratory Symptoms	**22**	**22%**	**10**	15.9%	12	32.2%	$X^2=0.96$	$P>0.05$
Cough & Expectoration	16	16 %	9	14.3%	7	18.9%		
Hemoptysis	6	6 %	1	1.6%	5	13%		
Neurologic Symptoms	**4**	**4%**	**2**	3.2%	1	2.7%	$X^2=0.30$	$P>0.05$
TIA	2	2 %	1	1.6%	1	2.7%		
Strock	2	2 %	1	1.6%	1	2.7%		
Genital/Urinary Symp. (Vaginal Bleeding)	1	1 %	1	1.6%	0	0%	$X^2=0.59$	$P>0.05$

Table s2: Analysis of on admission systemic examination findings among heart failure patients sub-groups

	Total HF-GP (n = 100)		Non HCV HF-GP (n = 63)		HCV HF-GP (n = 37)		Non-HCV GP Versus HCV GP	
	No	**%**	No	%	No	%	***test***	***Significance***
Abnormal Abdomen Examination Findings	79	79%	26	51.2%	43	96.2%	$X^2=4.16$	$P<0.02$*
Hepatomegaly	13	13%	5	7.9%	8	21.6%	$X^2=3.86$	$P<0.049$*
Splenomegaly	24	24%	9	14.3%	15	40.5%	$X^2=8.80$	$P<0.003$*
Ascites (Mild)	32	32%	12	19%	20	54.1%	$X^2=13.12$	$P<0.001$*
Abnormal Chest Examination Findings	100	100%	65	100%	37	100%	------	-----
Diminished Air Entry	38	38%	15	23.8%	23	62.2%	$X^2=14.55$	$P<0.001$*
Fine Basal Crepitation	83	83%	55	87.3%	28	75.7%	$X^2=2.27$	$P>0.05$
mid zonal Crepitation	11	11%	5	7.9%	6	16.2%		
Wheezes	31	31%	20	31.7%	11	29.7%	$X^2=0.04$	$P>0.05$
Abnormal Cardiac Examination Findings	100	100%	65	100%	37	100%	------	-----
Variable S1	43	43.0%	24	38.1%	19	51.4%	$X^2=1.67$	$P>0.05$
Accentuated P2	51	51.0%	28	44.4%	21	56.8%	$X^2=1.41$	$P>0.05$
Apical Systolic Murmur	84	84.0%	54	85.7%	30	81.1%	$X^2=0.37$	$P>0.05$
Tricuspid Systolic Murmur	35	35.4%	19	30.6%	16	43.2%	$X^2=1.61$	$P>0.05$
Basal diastolic Murmur	49	49.0%	29	46%	20	54.1%	$X^2=0.60$	$P>0.05$
Gallop	100	100 %	63	100%	37	100%	-------	-------
Abnormal Neurologic Examination (Residual Hemiparesis)	2	2%	1	2.7%	1	1.6%	$X^2=0.12$	$P>0.05$

Table s3: Analysis of on admission 2D echocardiographic findings among heart failure patients sub-groups

2D Echocardiographic Findings	Total HF-GP (n = 100)		Non HCV HF-GP (n = 63)		HCV HF-GP (n = 37)		Non HCV GP Versus HCV GP	
	No	**%**	No	%	No	%	***test***	***Signif***
Aortic Valve								
Normal	58	58 %	35	55.6%	23	62.2%	$X^2=0.54$	$P>0.05$
Sclerotic AV Cusps	42	42 %	28	44.4%	14	37.8%		
Mitral Valve								
Normal	81	81 %	52	82.50%	29	78.4%	$X^2=0.05$	$P>0.05$
Sclerosis MV	19	19 %	11	17.50%	8	21.6%		
Tricuspid Valve (Normal)	100	100 %	63	100%	37	100 %		

2D Echocardiographic Findings	Total HF-GP (n = 100)		Non HCV HF-GP (n = 63)		HCV HF-GP (n = 37)		Non HCV GP Versus HCV GP	
	No	**%**	No	%	No	%	***test***	***Signif***
Pulmonic Valve (Normal)	100	100 %	63	100%	37	100 %		
Left Ventricle Size								
Normal	4	4 %	2	3.20	2	5.4%	$X^2=0.06$	$P>0.05$
Dilated LV	96	96 %	61	96.80	35	94.6		
LV- RSWM								
Normal RSWM	32	32 %	19	30.2%	12	32.4%	$X^2=0.06$	$P>0.05$
Abnormal RSWM	68	68 %	44	69.8%	25	67.6%		
Left Atrium		%						
Normal LA	3	3 %	2	3.20%	1	2.7%	$X^2=0.14$	0.605
Dilated LA	97	97 %	61	96.80%	36	97.3%		
Right Ventricle								
Normal RV	41	41 %	29	46%	12	32.4%	$X^2=1.78$	$P>0.05$
Dilated RV	59	59 %	34	54%	25	67.6%		
Right Atrium								
Normal RA	40	40 %	29	46%	11	29.7%	$X^2=2.58$	$P>0.05$
Dilated RA	60	60 %	34	54%	26	70.3%		
Aortic Root (Normal)	100	100 %	63	100.00%	37	100%		
Pulmonary Artery								
Normal PA	80	80 %	56	88.90%	24	64.9%	$X^2=8.28$	$P<0.004$*
Dilated PA	20	20 %	7	11.10%	13	35.1%		
Pericardium (Normal)	100	100 %	63	100.00%	37	100%		

Table s4 Influence of on admission abnormal abdominal ultrasound findings on one month post discharge clinical state of heart failure patients

	Improved HF Patients (n = 37)		Non-Improved HF Patients (n = 63)		Significance	
	No	%	No	%	***test***	***P value***
Enlarged / Cirrhotic **Liver**	10	27.0%	25	39.7%	$X^2=1.67$	$P>0.05$
Dilated **Portal Vein**	0	0.0%	3	4.8%	$X^2=1.79$	$P>0.05$
Enlarged **Spleen**	7	18.9%	17	27.0%	$X^2=0.82$	$P>0.05$
Ascites	10	27.0%	22	34.9%	$X^2=0.99$	$P>0.05$
Kidney Nephropathy	11	21.6%	33	42.9%	$X^2=9.03$	$P>0.05$
Pleural. effusion	5	13.5%	10		$X^2=0.96$	$P>0.05$

Table s5: Influence of basic demographic data on the clinical state of HF-patients one month post discharge

	Improved HF Patients (n = 37)		Non-Improved HF Patients (n = 63)		Significance	
	No	%	No	%	***test***	***P value***
Age (Mean ± SD)	55.56±11.07		62.60±10.10		$t= 3.24$	$P<0.002$*
Ages up to 60 Years	23	62.2%	19	31.2%	$\chi2 = 4.35$	$P<0.045$*
Ages Above 60 Years	14	37.8%	44	69.8%		
Gender Female	11	29.7%	26	41.3%	$\chi2 = 1.35$	$P>0.05$
Male	26	70.3%	37	58.7%		
Residence Rural	16	43.2%	24	38.1%	$\chi2 = 0.26$	$P>0.05$
Urban	21	56.8%	39	61.9%		

Table s6: Influence of risk factors on the clinical state of HF-patients one month post discharge

	Improved HF Patients (n = 37)		Non-Improved HF Patients (n = 63)		Significance	
	No	%	No	%	***test***	***P value***
HTN	32	86.5%	58	92.1%	$X^2=0.781$	0.492
HTN Duration	10.21 ± 3.68		12.48 ± 4.62		$t=2.541$	0.013*
Diabetes	31	83.8%	55	87.3%	$X^2=0.24$	0.767
Diabetic Duration	9.53 ± 3.04		10.72± 4.51		$t=1.29$	0.199
IHD	20	54.1%	51	81.0%	$X^2=8.03$	0.005*
Dyslipidemia	8	21.6%	21	33.3%	$X^2=1.04$	0.154
Smoking	21	56.8%	25	39.7%	$X^2=2.74$	0.074
FH of IHD	13	35.1%	21	33.3%	$X^2=0.034$	1.000

Table s7 *Influence of on admission M-mode measurements on one month post discharge clinical state of HF patients*

	Improved HF Patients (n = 37)	Non-Improved HF Patients (n = 63)	Significance	
	MV ± SD	**MV ± SD**	***test***	***P value***
Left Atrium (cm)	4.82 ± 0.58	5.11 ± 0.51	t=-2.56	P<0.012*
IVST(cm)	0.948 ± 0.17	0.93 ± 0.13	t=0.38	$P>0.05$
PWT (cm)	0.955 ± 0.15	0.94± 0.11	t=0.52	$P>0.05$
LVIDs (cm)	4.970± 0.72	5.40± 0.81	t=-2.65	P<0.009*
LVIDd (cm)	6.245 ± 0.76	6.54 ± 0.77	t=-2.74	$P>0.05$
Ejection Fraction	0.402 ± 0.11	0.35 ± 0.09	t=2.11	P<0.037*

HF (heart failure), IVST (interventricular septum thickness), PWT (posterior wall thickness), LVIDs (left ventricular internal diameter in systole), LVIDd (left ventricular internal diameter in diastole)

Table s8 Influence of abnormal 2D echo findings on one month Post discharge clinical state of HF patients

Abnormal 2D ECHO	Improvement (37 Patients)		Non-Improvement ((63 Patients)		Significance	
	No	%	No	%	***test***	***P value***
LV Mild Dilated	14	37.8%	13	20.6%	$X^2=5.64$	$P<0.049$*
LV Marked Dilated	21	56.8%	48	76.2%		
LA Mild Dilated	17	45.9%	17	27.0%		
LA Moderate/ Marked Dilated	18	48.6%	45	72.0%	$X^2=9.28$	P<0.026*
Sclerotic Aortic Cusps	7	18.9%	35	55.6%	$X^2=11.38$	P<0.001*
Sclerosis Mitral Valve	2	5.4%	17	27.0%	$X^2=5.72$	P<0.017*
Dilated Right Ventricle	18	48.6%	41	65.1%	$X^2=2.58$	$P>0.05$
Dilated Right Atrium	18	48.6%	42	66.7%	$X^2=3.12$	$P>0.05$
Dilated Pulmonary Artery	2	5.4%	18	28.6%	$X^2=6.44$	$P>0.05$

LV (left ventricle), RSWM (resting segmental wall motion), LA (left atrium)

Table s9 Influence of HCV, HF type and etiology on one month post discharge clinical status of HF patients

	Improved HF Patients (n = 37)		Non-Improved HF Patients (n = 63)		Significance	
	No	%	No	%	***test***	***P value***
Heart Failure Types						
HF with reduced EF	16	43.2%	46	73.0%	$X^2=9.04$	P<0.011*
HF with Mid EF	13	35.1%	12	19.0%		
HF with Preserved EF	8	21.6%	5	7.9%		
HCV Infection						
HF Without HCV	24	64.9%	39	24	$X^2=0.09$	$P>0.05$
HF With HCV	13	35.1%	24	38.1%		

	Improved HF Patients (n = 37)		Non-Improved HF Patients (n = 63)		Significance	
Etiology of Heart Failure						
Idiopathic DCM	5	13.5%	2	3.2%	X^2=8.64	P<0.012*
Hypertensive HD	12	32.4%	10	15.8%		
Ischemic HD	1	2.7%	3	4.7%		
Hypertensive and IHD	19	51.4%	48	76.7%		
HD Without Intervention	12	60.0%	17	33.3%	X^2=4.19	. P<037*
IHD With PCI/ CABG	8	40.0%	34	66.7%		

HF (heart failure), EF (ejection fraction), DCM (dilated cardiomyopathy), IHD (ischemic heart disease), PCI (percutaneous coronary intervention), CABG (coronary artery bypass graft surgery)

Table s10: Roc curve analysis for prediction of post discharge clinical state

Variables	*AUC*	*Cut Off Value*	*Sensitivity*	*Specificity*	*Significance (P value)*	Figure No.
Age	*0.699*	*61.5 y*	*0.65*	*0.7*	*0.001**	*29*
Hypertension Duration	*0.647*	*11.0 y*	*0.53*	*0.69*	*0.022**	*30*
Pulse Rate	*0.638*	*92.5*	*0.54*	*0.62*	*0.022**	*31*
LVIDs	0.659	5.15	0.67	0.57	0.008*	*32*
Ejection Fraction	*0.613*	*0.33*	*0.52*	*0.32*	*0.05**	*33*
Creatinine Clearance	0.379	63.33	0.75	0.22	0.043*	*35*
Whole HF Duration	*0.984*	*2.5*	*0.98*	*0.97*	*0.000**	*36*

AUC=Area Under the curve

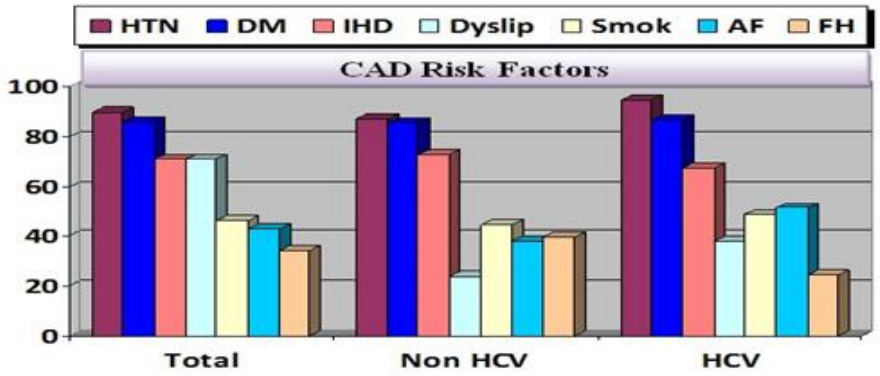

Figure (1): *Prevalence of CAD risk factors among HF groups. CAD (coronary artery disease), HTN (hypertension), DM (diabetes mellitus), Dyslip(dyslipidemia), Smok(smoking), AF(atrial fibrillation), FH(family history)*

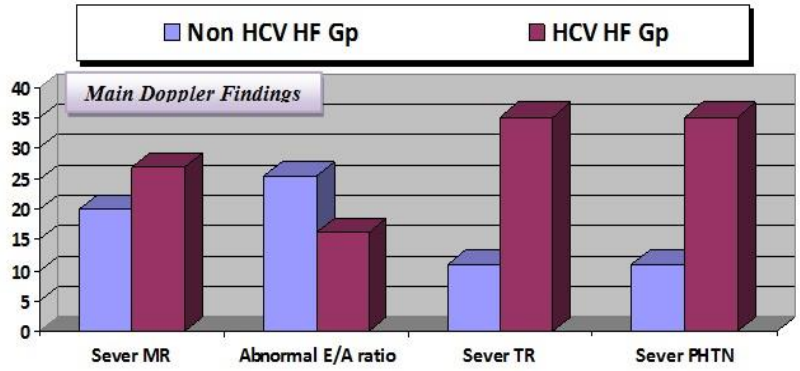

Figure (2): *Doppler findings among HF (heart failure) sub-groups.MR (mitral regurge), TR(tricuspid regurge), PHTN(pulmonary hypertension)*

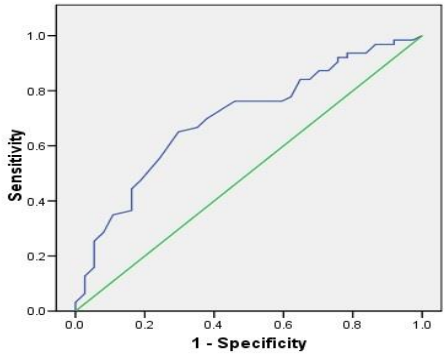

Figure (s1): Roc Curve prediction of post discharge clinical state from age

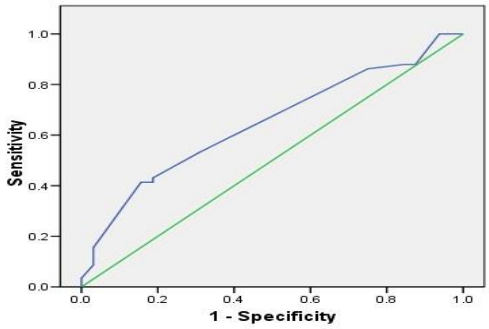

Figure (s1): Roc curve prediction of post discharge clinical state from hypertension duration

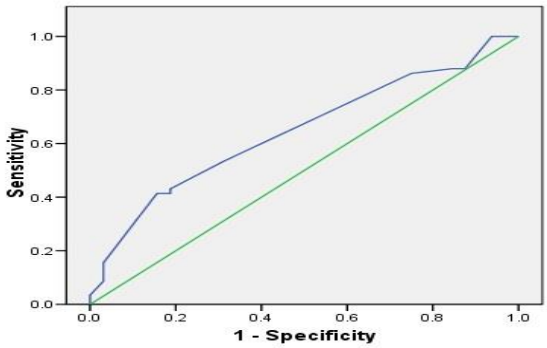

Figure (s3): Roc curve prediction of post discharge clinical status from pulse rate

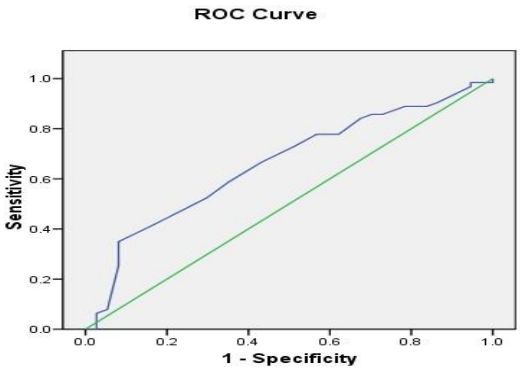

Figure (s4): Roc curve prediction of post discharge clinical state from LVIDs

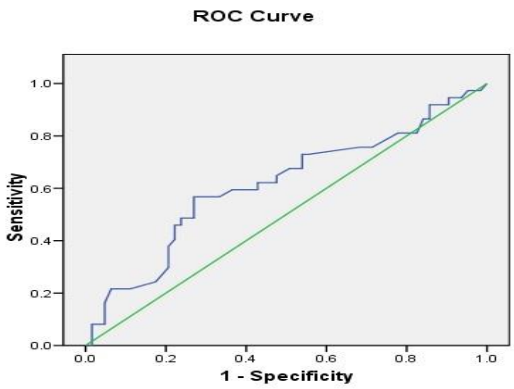

Figure (s5): Roc curve prediction of post discharge clinical state from EF

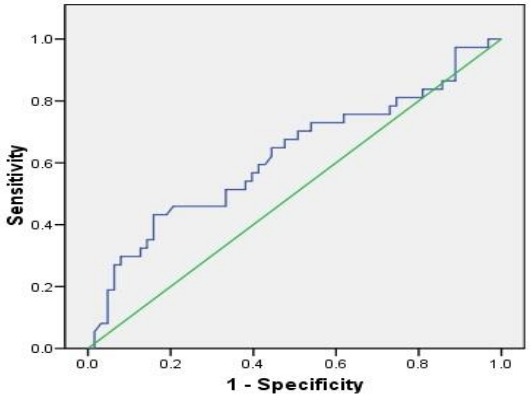

Figure (s6): Roc curve prediction of post discharge clinical state from creatinine clearance

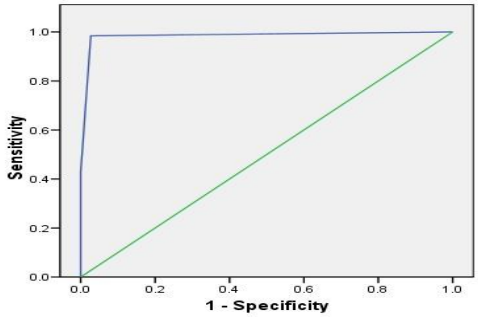

Figure (s7): Roc curve prediction of post discharge clinical state from HF duration

DISCUSSION

The prevalence of HF increases significantly with age. The prevalence increases sharply from 1% in 40-year-old individuals to 10% above the age of 75 years and doubles for each decade of life [**4**]. In our study the prevalence of HF was more among older age; (58% of patients were above 60 years, 23% aged from 50 to 60 years, 14% aged from 40 to 50 years and 5 % were below 40 years). Also, in our study the most prevalent type of HF among evaluated ADHF patients was HFrEF (62%), followed by HF with mid-range EF (HFmEF) (25%) and HF with preserved EF (HFpEF) (13%). Zamani et al showed that Patients with HFrEF respond favorably to the standard pharmacological treatment regimen and demonstrate better prognosis. In contrast, patients with HFpEF have not been shown to respond to standard pharmacological treatments, except for nitrates, and therefore, have a poor prognosis, especially during the decompensated phase of HF [**5**].

However, in our study, all HF patients (reduced-EF, mid-range -EF and preserved-EF) responded well to in-hospital anti-failure measures.

Although all patients showed in-hospital improvement,only 37% showed post discharge clinical stabilized/improved clinical state and 63% developed recurrence/deterioration of symptoms and 4% of them need readmission within one month. The non-improvement was found in 44 patients older than 60 years (69.8%), and only in 14 HF patients below 60 years (37.8%). Above 61.5 years was found to be associated with no improvement in post discharge clinical state

(P<0.001).According to CHARM (Candesartan in Heart Failure: Assessment of Reduction in Mortality and morbidity) data, older age has consistently been related to worse outcome. With the large number of deaths, age had relatively little impact on outcome until after age 60, and then the risk of death increases nearly two-fold every 10 years [**6**] .

Diabetes did not affect the post discharge clinical outcome of HF patients (P> 0.05). Although diabetes has been recognized as an important modulator of HF outcome, previous studies have not defined diabetes to be so important in multi-variable modeling, and its effect on outcome is limited only to HF patients with ischemic etiology [**7**].

In our study, the main clinical parameters on admission that would suggest the post discharge clinical outcome of HF patients include chest pain, palpitation and heart rate, the non-improved HF patients had high prevalence of on-admission chest pain and palpitation (77.2% and 42.9%) than the stabilized/improved patients (45.9% and 24.3%) (P<0.05). Also, the non-improved HF patients had increased on-admission HR (95.9± 18.1 b/m) than the stabilized/improved patients (88.1 ± 20.8 b/m) (P<o.o5). In patients with reduced LVEF, with or without signs or symptoms of HF, high heart rate (HR) has predicted adverse outcomes, irrespective of other known risk factors [**8**] **.** The CHARM investigators also found that the value of resting HR in predicting worse outcomes was independent of baseline LV EF in HF [**9**]. There was significant increase in AF among non-improved patients (55.6% and 33.2%) than the improved patients (24.3% and 18.9%) (P<0.05). In our study, echo revealed that dilated LA, dilated LV, RSWMA, reduced EF, sever MR, sever TR, sever PH and sclerotic mitral and aortic cusps are major indicators for poor outcome among HF patients, EF less than 0.33 was found to be associated with non-improvement in post discharge clinical state (P < 0.05). Reduced systolic function confers an adverse prognosis in HFrEF [**10**].

Our study showed that patients with HFrEF had poorer post discharge clinical outcome than patients with mid-range or preserved EF. Our study revealed that prolonged duration of whole HF disease and recurrent previous hospital admissions, for HF, were poor indicators of post discharge clinical outcome. HF duration of more than 2.5 years was associated with readmission (P<0.0001). ADHF is the most common form of HF that accounts for ~80% of hospitalizations. The common causes of ADHF include non-adherence to medications or diet, uncontrolled HTN; IHD, arrhythmias, COPD exacerbation, and non-steroidal anti-inflammatory drugs; all leading to HF progression [**11**] **.**

In our study only 6% of HF patients needed readmission within one month after hospital discharged. One quarter of patients admitted by acute HF suffer from early readmission during 30-90 days after discharge and more common in HFrEF than HFpEF [**12**]. In our study the most common cause of readmission was AF and chest infection, despite medications adherence. Several studies have showed that the causes for the 30-day readmission are medications non-compliance (21%–66%), smoking (60%), diet non-compliance (30%–44%), and co-morbidities (HTN, diabetes, CAD, anemia) (21%–34%) [**13**].

In the present study, there were no significant changes between HF patients with and without HCV regarding all demographic data, and HF RF. There was significant increase in PH in HF patients with HCV 35.1% than without HCV 11.1%, and significant in TR in HF patients with HCV 35.1% than HF patients without HCV 11.1%. In clinical studies, 2–10% of cirrhotic patients are at risk of developing PH. Porto pulmonary hypertension seems to be a significant prognostic factor in patients with liver cirrhosis [**14**]. The high prevalence of HCV among higher age groups and decreased incidence among younger age groups indicates a good prognostic sign about eradication of HCV in Egypt.

CONCLUSION

HCV-Infection in patients with ADHF is associated with more severe types of HF (HFrEF and HFpEF). HCV-Infection in patients with ADHF resulted in adverse morphologic and structural cardiac changes. However, HCV-Infection in patients with ADHF has no effect on all aspects of patient's clinical states. The main predictors of short-term post discharge clinical status are patient age and the whole duration of chronic HF.

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