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Cardiac manifestations in patients of hepatitis c in western Uttar Pradesh

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Abstract

Aim: To evaluate the cardiovascular manifestations in patients suffering from hepatitis C via 2D-Echocardiography.

Materials and methods: The present prospective observational study was conducted for 2 years among 100 patients in the post graduate department of Medicine at Chhatrapati Shivaji Subharti Hospital. All HCV seropositive patients were included in the present study. Blood samples were obtained from each participant using disposable needles and vacuum syringes. The serum samples were fractionated within 6 hours after collection and stored at -70°C until assay. The LA size, LVEDD size, RA Size, RV Size, LV Ejection Fraction, E/A Ratio, RA/RV Ratio, IVS Diameter, VPW Diameter and Pericardial Effusion were recorded with the help of 2D/M-mode/CD Echocardiography.

Results: Total bilirubin and SGOT was raised among 22% and 78% of the patients. Further, SGPT was raised in 88% of the patients. There was a significant difference in the left atrial size and left ventricular dimension from that of normal subjects. 26 patients included in our study group showed evidence of LV systolic dysfunction. 3 and 4 out of 100 patients in the study group were found to have RA dilatation and RV dilatation, respectively. 11 out of 100 patients of the study group were found to have dilated cardiomyopathy. The prevalence of E/A <1 was 25%.

Conclusion: The results of present study concluded that chronic hepatitis C is likely to lead to an increase in Left atrial size and left ventricular end diastolic dimension. Independent risk of dilated cardiomyopathy is possible in patients with chronic hepatitis C.

Keywords: hepatitis C, Cardiac function, Dysfunction, Echocardiography

Introduction

HCV is the leading cause of progressive liver fibrosis, resulting in cirrhosis, liver cancer, liver failure and death. It is the second most common chronic viral infection in the world with a global prevalence of about 3% (170 million people) [1]. The prevalence rate is higher in persons aged 30-49 years than in older or younger persons, and is higher in males (2.5%) than in females (1.2%) [2]. In addition to liver disease, CHC infection has been associated with many extra hepatic comorbidities, including cryoglobulinemia, lymph proliferative disease, renal disease, cardiovascular disease (CVD), diabetes mellitus (DM) and insulin resistance.

Hepatitis C virus, a major cause of chronic liver disease, frequently progresses to cirrhosis with an increased risk of hepatocellular carcinoma. Chronic hepatitis C is often silent, most of the times discovered only by routine serological, biochemical and radiological testing. Many attempts to identify the natural history and progression of hepatitis C infection have been made, but several aspects remain to be elucidated. Different lines of evidence identified a higher prevalence of fatty liver infiltration, insulin resistance (IR), and diabetes in individuals infected with HCV, with a ‘‘protective” serum lipid profile characterized by lower low-density lipoprotein levels [3].

Not only is there an association between the presence of HCV and Cardio-Vascular Disease (CVD) but there also seems to be a link between the burden of HCV infection (as demonstrated by viral load or liver disease) and CVD risk. The pro-inflammatory state resulting from HCV infection which leads to increased CVD also promotes a pro-fibrogenic environment leading to hepatic steatosis and fibrosis. It has not been established that hypertrophic cardiomyopathy may be a complication of viral myocarditis, asymmetrical septal hypertrophy has, in fact, sometimes been observed in patients with myocarditis [4].

The quantification of cardiac chamber size and function is the cornerstone of cardiac imaging with echocardiography being the most commonly used noninvasive modality. The most commonly used method for 2D echocardiographic volume calculations is the biplane method of disks summation (modified Simpson’s rule), which is the recommended 2D echocardiographic method by consensus of this committee. With various heart diseases presently being the leading cause of death worldwide, an improved understanding of disease risk may help tailor interventions and prevention efforts in patients infected with HCV. Keeping the above discussion in mind, the present study was conducted to evaluate the cardiovascular manifestations in patients suffering from hepatitis C via 2D-Echocardiography.

Materials and methods

The present prospective observational study was conducted for 2 years in the post graduate department of Medicine at Chhatrapati Shivaji Subharti Hospital. The study group consisted of 100 patients who were enrolled in the study after obtaining written informed consent from patients along with attendants and approval from Institutional Ethical Committee. The subjects were recruited according to the following inclusion and exclusion criteria:

Inclusion criteria

All HCV seropositive patients were included in the study.

Exclusion criteria

Patients with the following characteristics were excluded from the study:

1. Patients with Coronary Artery Disease, Heart failure, Valvular Heart Disease, Hypertension, Diabetes Mellitus, Congenital Heart Disease, Rheumatic Heart Disease, Tachyarrhythmias (atrial flutter, atrial fibrillation).
2. Chronic lung disease, sleep apnoea, Thyroid dysfunction, severe Anemia, Malignancy, Renal insufficiency (chronic kidney disease), chronic inflammatory disease, pregnancy and peripartum females and patients of Cerebrovascular accidents.
3. The study also excluded intravenous drug abusers, chronic alcoholics, HIV and hepatitis B virus carriers, and
4. The study did not include patients who were on drugs like antiarrhythmic, antiplatelet, antipsychotics, post carcinoma radiotherapy and/or chemotherapy.

Interview and Blood Collection

All participants were personally interviewed by the examiner using structured questionnaires to collect information on demographic characteristics (age, sex, educational levels, occupation, etc), habits of cigarette smoking and alcohol consumption, and personal history of diseases (previous diagnosis of diabetes, hypertension, heart diseases, or cerebrovascular diseases). Body weight and height were measured. Blood samples were obtained from each participant using disposable needles and vacuum syringes. The serum samples were fractionated within 6 hours after collection and stored at -70°C until assay.

Investigations

Investigations done were Anti HCV Serology, 2D/M-mode/CD Echocardiography, 12 Lead Electrocardiography (ECG), Liver Function Tests (LFT), HbsAg

HIV Serology, Complete Blood Count (CBC), Renal Function Test (RFT), TSH, fT3, fT4, Fasting Blood Sugar (FBS), Chest X-ray (PA View), Coagulation profile and ESR.

Echocardiographic Assessment

Using cross sectional images as a guide, the M mode tracing of the chambers of heart were obtained to calculate measurements according to the recommendations of American society of echocardiography. The LA size, LVEDD size, RA Size, RV Size, LV Ejection Fraction, E/A Ratio, RA/RV Ratio, IVS Diameter, VPW Diameter and Pericardial Effusion were recorded.

Function of Echocardiographic Assessment

LVEF and LVEDD (Left Ventricular End Diastolic) size were, together analysed to observe cases of dilated cardiomyopathy in patient control group. E/A ratio was taken as an index of diastolic dysfunction. RA/RV ratio was taken to assess cor pulmonale. IVS (Intraventricular Septal) diameter and VPW (Ventricular Posterior Wall) diameter were analysed for left ventricular thickness.

Statistical analysis

Data were tabulated and examined using the Statistical Package for Social Sciences Version 22.0 (IBM SPSS Statistics for Mac, Armonk, NY: IBM Corp, USA). Descriptive statistical analysis had been carried out in the present study. Results on continuous measurements are presented as Mean±SD. Categorical data has been presented as frequency distribution.

Results

Of the 100 patients, 73 were male and 23 were female with male to female ratio of 2.7:1. Mean±SD age of the patients was 34.23±9.9 years. Maximum patients belonged to 20-40 years of age (table 1).

Table 1: Demographic characteristics of the study population

Variables	Case	
	N	%
Gender		
Male	73	73
Female	27	27
Total	100	100
Age group (in years)		
<20	4	4
20-30	33	33
31-40	38	38
41-50	15	15
51-60	10	10
Total	100	100

The most common complaint found was abdominal distention (16%) followed by Vomiting and Nausea (12%), shortness of breath (11%) and fatigue (8%) as shown in table 2.

Table 2: Complaints of patients in case group

Complaints	N	%
Abdominal distension	16	16
Pain abdomen	7	7
Chest pain	5	5
Shortness of breath	4	4
Fever	11	11
Syncope	6	6
Feet swelling	8	8
Jaundice	9	9
Decrease urine output	5	5
Bleeding gums	12	12
Vomiting	8	8

The mean heart rate, systolic blood pressure and diastolic blood pressure among the study group was 81.7, 125.5 mmhg and 83.5 mmhg respectively as shown in table 3.

Table 3: Baseline findings among the study groups

Parameters	Case	
	Mean	SD
BMI	24.6	2.1
Heart rate	81.68	11.7
Systolic blood pressure	125.53	16.5
Diastolic blood pressure	83.45	14.8

Among 100 patients, the most common clinical finding was hypotension in 22% of the patients, followed by ascites (16%), hepatomegaly (15%) and splenomegaly (12%) as shown in table 4.

Table 4: Clinical findings among the study groups

Clinical findings	Case	
	N	%
Hypotension (SBP <90)	22	22
Ascites	16	16
Hepatomegaly	15	15
Splenomegaly	12	12
Pleural effusion	5	5

Total bilirubin was raised among 22% of the patients. Similarly, SGOT was raised in 78% of the patients. Further, SGPT was raised in 88% of the patients (table 5).

Table 5: Liver function tests among the study population.

Liver Function Test	N (Raised)	%
T. Bilirubin	22	22
SGOT (U/L)	78	78
SGPT (U/L)	88	88

The average QTc interval of the study group was found to be 408 milliseconds which is within the normal range. Hence, the study group was found to have no QTc prolongation. ESR has been observed to be raised in 67 out of the 100 patients in the study group with a mean of 31.8 mm/hr and standard deviation of 8.9 Further, SGPT in 88 out of the 100 patients in the study group was found to be raised with a mean of 85.4 U/L and standard deviation of 25.2. This finding indicates inflammatory myocardial injury which can further lead to systolic and/or diastolic dysfunction (table 6).

Table 6: QTc Interval and Inflammatory Markers among the study population

Parameters	Case	
	Mean	SD
QTc Interval (in ms)	408	29.5
ESR (mm/hr): N=67	31.8	8.9
SGPT (U/L) : N=88	85.4	25.2

Table 7: Observations Based on Echocardiographic parameters

Parameters	Number	Mean	SD	Normal
LA Size (in mm)	15	37.4	3.5	<40
LVEDD Size (in mm)	18	49.7	18	<55

There was a significant difference in the left atrial size from that of normal subjects ($p<0.05$). Also, there was a significant difference in the left ventricular dimension as compared to the normal subjects (table 7).

26 patients included in our study group showed evidence of LV systolic dysfunction. 3 out of 100 patients and 4 out of 100 patients in the study group were found to have RA dilatation and RV dilatation, respectively. RV dysfunction was observed in only 3 patients of the study group. 11 out of 100 patients of the study group were found to have dilated cardiomyopathy. The prevalence of E/A <1 was 25%. However, it is an oversensitive index for diagnosing Left Ventricular Diastolic Dysfunction (LVDD) because of which there is a high probability of false positive results (table 8).

Table 8: Ejection Fraction (%), Right Atrial & Ventricular Dimensions, Dilated Cardiomyopathy and Left Ventricular Diastolic Function among the subjects

Parameters	N	%
EF		
<50	26	26
50-60	9	9
60-70	65	65
Right Atrial and Ventricular Dimensions		
RA (Dilated)	3	3
RV (Dilated)	4	4
RV Dysfunction	3	3
Dilated Cardiomyopathy		
LV>= 55 mm	15	15
LVEF <= 50%	26	26
LVEF≤50% and LV≥55 mm	11	11
Left Ventricular Diastolic Function		
E/A if < 1	25	25

Discussion

Abnormalities of the cardiovascular system in chronic liver disease including chronic hepatitis C have been known now for some time, which were traditionally thought to have been due to alcoholic cardiomyopathy. Possibility of specific cardiac disorders has been recently recognized following liver transplantation in chronic hepatitis C with no previous cardiac history or risk factors. However cardiac structure and function are not well described. Echocardiography in recent studies has shown variable results and at present there are no standard diagnostic criteria in chronic hepatitis. Hence the present study was conducted with an aim to study some of these aspects.

Mean age in males and females was 34.4 years and 33.6 years respectively. Out of the 100 patients studied, 27 were females and 73 were males. This finding of male preponderance was in concurrence with the findings of Sarin *et al* [5]. The mean systolic blood pressure in the present study was 125.5 mmhg and the mean diastolic blood pressure was 83.5 mmhg signifying an increased haemodynamic status in patients of chronic hepatitis C.

There was a significant increase in the LA size and LVEDD in the study group. While most of the studies have reported normal size of cardiac chambers, Finucci *et al* [6] have reported an increased LA volume and increased LV end diastolic size, which was associated with increased stroke volume and E/A ratio. In another study, Demir *et al* [7] concluded that chronic HCV infection may be associated with left ventricular systolic and diastolic dysfunction and cardiac arrhythmias. Similarly, in this study group, 11 patients have been diagnosed with dilated cardiomyopathy. Myocarditis, an inflammation of the myocardium that can lead to dilated cardiomyopathy and heart failure, can be caused by several cardiotropic viruses including Hepatitis C. Viral, immune, and apoptotic cell death mechanisms have been postulated in the development of viral myocarditis and

its progression to cardiomyopathy attributable to necrosis and loss of myocytes.

In the present study, 26 patients in the study group showed evidence of systolic dysfunction. EF has been reported to be affected at rest in the major studies. According to Sanchez MJ *et al.* [8] and Demir M *et al,* [7] there was a significant left ventricular systolic dysfunction caused by Chronic hepatitis C. Cardiac dysfunction in patients with chronic hepatitis C is characterised by impaired contractile responsiveness to stress and/ or altered diastolic relaxation with electrophysiological abnormalities in the absence of other known cardiac disease.

Diastolic function was found to be impaired in a number of patients in the present study. 25 patients in the study group were having E/A ratio < 1 which is signifying diastolic dysfunction. The presence of diastolic dysfunction leads to abnormal left ventricular relaxation during diastole, usually owing to decreased dispensability of cardiac tissue, the result of either hypertrophy of cardiomyocytes or increased interstitial collagen deposition. Therefore, there is impedance to ventricular inflow, and the end-diastolic left ventricular pressure is elevated relative to the left ventricular end diastolic volume. Devi PV *et al.* [9] in 2014 conducted a study on cardiovascular manifestations of hepatitis C virus infection. The authors concluded that the result corroborated favorably that the more progressed is the inflammation and liver dysfunction due to HCV infection, the more likely the patient is to have cardiovascular changes of cardiac chamber enlargement and left ventricular diastolic dysfunction.

4 out of 100 patients of the study group had left ventricular hypertrophy indicated by left ventricular posterior wall thickness greater than 12 mm (benchmark thickness). In HCV patients, cardiomyopathy has been attributed to TNF alpha, intracellular sodium, NO, CO and endothelin I. Assessed by Demir *et al.* [10] there was a significant hypertrophic cardiomyopathy observed in HCV patients. However, similar results have not been produced in the present study indicating its non-significance with chronic hepatitis C.

3 out of 100 patients and 4 out of 100 patients in the study group were found to have RA dilatation and RV dilatation, respectively and RV dysfunction was observed in only 3 patients of the study group. Demir *et al*. in 2004 [11] found lower Right Ventricular Fractional Area Change (RV FAC), Tricuspid Annular Plane Systolic Excursion (TAPSE), higher Myocardial Perfusion Imaging (MPI); which indicates RV systolic dysfunction in the patient group. Similarly a significantly high E/e’ ratio also indicated diastolic dysfunction in HCV patients. In this study, a relationship between HCV infection and RV systolic and diastolic dysfunction was also found. Also PASP and PVR were found higher than the control group. It may be considered that this situation causes RV systolic dysfunction, pulmonary dysfunction and portal hypertension due to chronic hepatitis C. Furthermore, hepatic failure may lead to portopulmonary hypertension and consequent RV dysfunction without manifesting clinical symptoms. However, in the present study, there were too few patients with a tangible impact on the right atrium and ventricle. In addition, this particular area of research is in its nascent stage and only a few studies have been conducted previously presenting more scope for further research in the future.

Conclusion

Based on the results of present study, the following conclusions were drawn:

1. Systolic and diastolic functions are likely to be impaired in patients with chronic hepatitis C.
2. Chronic hepatitis C is likely to lead to an increase in Left atrial size and left ventricular end diastolic dimension.
3. Independent risk of dilated cardiomyopathy is possible in patients with chronic hepatitis C.

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