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Characterization of Respiratory Manifestations of Chronic Hepatitis C Virus Infected Patients

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ABSTRACT

Background: chronic hepatitis C virus (HCV) infection has been reported in association with several extrahepatic manifestations. Chronic HCV infection is also associated with both direct and indirect effects on pulmonary tissue.

Purpose: to evaluate phenotypes of respiratory manifestations of chronic hepatitis C virus.

Patients and Methods: 1-this study was conducted on 150 Egyptian patients with chronic hepatitis C. Patients were selected from those attending the in patients and out patients clinic of the Tropical Medicine and Chest Departments, Al-Azhar University Hospital-Damietta from September 2016 to Septamber 2018.

2-also ,50 healthy subjects matched for age and sex were included as volunteer.

3-consent was informed by all patients and volunteer shared in this study.

Results: C.O.P.D: documented in 32 patients (21.3%).

Asthma: documented in 15 patients (10%) of all patients.

Air way hyperreactivity: documented in 15patients (10%) of all patients.

Idiopathic pulmonary fibrosis (IPF): is presented in 37 patients (24.6%).

Pneumonia: documented in 10 patients (6%) of all patients.

Transudative pleural effusion: documented in 10 patients (6%) of all patients.

Adenocarcinoma: documented in 5 patients (3.3%) of all patients**.**

Pseudolymphoma: documented in 1 patient (0.006%) of all patients.

Lung abscess: documented in 10 patient (6%) of all patients.

Pulmonary embolism: documented in 5 patients (3.3%) of all patients.

Hepatopulmonary syndrom: documented in 10 patients (6%) of all patients.

Conclusion: Chronic hepatitis C virus infection is related to the development of several pulmonary abnormalities. These pulmonary manifestations of HCV infection are frequently underdiagnosed.

Recommendations: Any patient with chronic HCV infection should be evaluated with HRCT chest and pulmonary function tests for early diagnosis of pulmonary abnormalities to prevent further complications.

Keywords: Hepatitis C virus, Pulmonary manifestations of Hepatitis C virus.

Type of study design: descriptive study**.**

Introduction

Hepatitis C virus (HCV) is the most important cause of liver disease in Egypt [(1,2)], with the latest anti-HCV antibody prevalence of 14.7% [(3)]. It is a progressive disease that can lead to cirrhosis, liver failure, hepatocellular carcinoma and death [(4)].

Over the last decade, emerging clinical data suggest that chronic HCV infection can lead to multiple direct and indirect pulmonary complications [(7)]. Secondary effects of HCV infection on pulmonary disease are either related to liver cirrhosis and portal hypertension or to the autoimmune disorders that are frequently seen in association with chronic HCV infection[(8)].

Aim of the work: to evaluate phenotypes of respiratory manifestations of chronic hepatitis C virus.

Patients and Methods:

1- This study was conducted on 150 Egyptian patients with chronic hepatitis C. Patients were selected from those attending the in patients and out patients clinic of the Tropical Medicine and Chest Departments, Al-Azhar University Hospital-Damietta from Septamber 2016 to Septamber 2018.

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2- Also, 50 healthy subjects matched for age and sex were included as a control group.

Ethical review and informed consent: Consent was informed by all patients and controls shared in this study.

Inclusion criteria:

Patients with chronic viral hepatitis C proved clinically, biochemically, serologically and by ultrasonograghy.

Exclusion criteria:

(1) Patients with history of a known chest disease before diagnosis of HCV.

(2) Patients with co-morbidities as renal failure, congestive heart failure and connective tissue disorders.

(3) Patients with autoimmune liver diseases or any other causes of liver disease.

(4) Smokers.

(5) Patients positive for HBs Ag.

Enrolled subjects were divided in to :

Group I: included 50 Patients with chronic HCV infection classified as child class A eligible for treatment with sofosbuvir based regimen, according to the protocol of HCV treatment established by National Committee for control of viral hepatitis (NCCVH) [(22)].

Group II: included 50 Patients with chronic HCV infection classified as child class B eligible for treatment with sofosbuvir based regimen, according to the protocol of HCV treatment established by National Committee for control of viral hepatitis (NCCVH) [(22)].

Group III: included 50 Patients with chronic HCV infection classified as child class C in eligible for treatment with sofosbuvir based regimens.

Control group: included 50 healthy matched for age and sex as control group**.**

Methods

All studied subjects were undergone to the following before treatment:

- Full History taking.
- Full clinical assessment including general and abdominal examinations
- Laboratory investigations:
  - Complete Blood Count (CBC)
  - Liver Function tests: Serum alanine transaminase (ALT), aspartate transaminase (AST), Alkaline phosphatase (Alph), Serum bilirubin (Total and Direct), Serum albumin, Prothrombine time (PT) & concentration (pc) and international normalisation ratio (INR)
  - Renal function tests: Serum urea and creatinine.
  - Viral hepatitis markers:Hepatitis C virus antibody (HCV-Ab) and Hepatitis B surface antigen (HBs-Ag) were detected using enzyme linked immunosorbent assay (ELISA)
  - Quantitative HCV–RNA: was detected using Polymerase chain reaction (PCR) assay.
  - Fasting Blood Sugar (FBS).
  - HBA1C for diabetic patients.
  - Pregnancy test for females
- Electrocardiogram (ECG).
- Arterial blood gases (ABG).
- plain chest x-ray postero-anterior view.
- Abdominal ultrasonography
- Pulmonary function test.
- Triphsic CT abdomen when indicated.
- Liver biopsy when indicated.
- High resolution computed tomography of the chest when indicated.
- Pleural fluid analysis if there is associated pleural effusion.
- Bronchoalveolar lavage when indicated.
- chest ultrasound guided biopsy when indicated.
- Thoracoscope when indicated.

Statistical Methods

The data was collected, coded and entered into a personal computer (PC), IBM compatible 3.2 GHz. The data was analyzed with the program Statistical Package for Social Science (SPSS), under Window version 22 as follows:

-Description of the quantitative variables in the form of Mean and Standard deviation (Mean + SD).

-Description of the qualitative variables in the form of frequency and Percentage.

-Student's t-test:for two independent samples is used to compare quantitative variables.

-Correlation Coefficient (r) test: to indicate that the extent of that two variables change with one another in a linear fashion.

-One Way Analysis of Variants (ANOVA) test: for comparison between multiple groups with quantitative continuous variables.

-Chi-square test (x^2 value): was used to compare a qualitative variable between two or more independent groups.
-For calculated of cut -off values, the receiver operator curve (ROC) was calculated and the best cut off was that with best sensitivity and specificity.
-For correlation between two paramours, the Pearson's correlation coefficient (r) was calculated;
it was inverse if the sign is negative and proportional if the sign is positive; it is mild if < 0.3; moderate if more than 0.3 and less than 0.7 and powerful if more than 0.7
-For interpretation of results, Significance level (P) value was expressed as follows:
P < 0.05 = significant.
P > 0.05 = non-significant.

Results

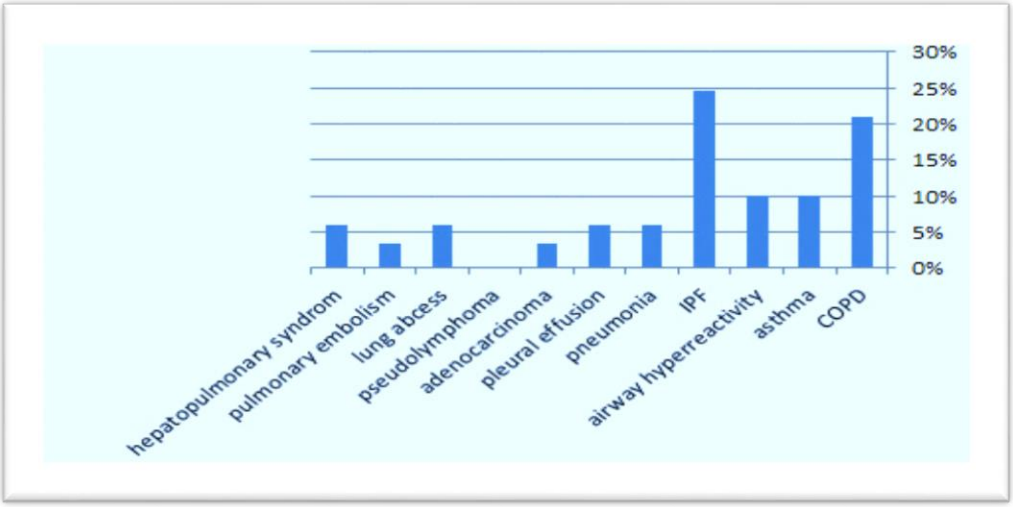

Figure1: most common pulmonary diseases in HCV related CLD patients

	Group I (50)		Group II (50)		Group III (50)		total (150)	
	N	%	N	%	N	%	N	%
COPD	20	40%	0	0%	12	24%	32	21.3%
Asthma	15	30%	0	0%	0	0%	15	1o%
Air way hyperreactivity	15	30%	0	0%	0	0%	15	10%
IPF	0	0%	25	50%	12	24%	37	24.6%
Pneumonia	0	0%	10	20%	0	0%	10	6%
Pleural effusion	0	0%	0	0%	10	20%	10	6%
Adenocarcinoma	0	0%	0	0%	5	10%	5	3.3%
Pseudolymphoma	0	0%	0	0%	1	2%	1	0.006%
Lung abscess	0	0%	10	20%	0	0%	10	6%
Pulmonary embolism	0	0%	5	10%	0	0%	5	3.3%
Hepatopulmonary syndrome	0	0%	0	0%	10	20%	10	6%

Table 1: most common pulmonary diseases in HCV related CLD patients

C.O.P.D : was documented in Group I in 20 patients(40%)and documented in Group III in 12 patients(24%)and its total percentage is 32 patients(21.3%).
Asthma: was documented in Group I in 15 patients(30%)and it represent (10%) of all patients.
Air way hyperreactivity: documented in 15patients(30%) of Group I it represent (10%) of all patients.
IPF:is presented in Group II in 25 patients(50%) and in Group III in 12 patients(24%)and its total percentage is 37 patients(24.6%).
Pneumonia:documented in Group II in 10 patients(20%) and it represent (6%) of all patients.
Trasudative pleural effusion: documented in Group III in 10 patients(20%)and its total percentage is(6%) of all patients.

Adenocarcinoma :documented in 5 patients(10%) of Group III its total percentage is (3.3%)of all patients**.**

Pseudolymphoma :documented in Group III in 1 patient(2%) its total percentage is (0.006%)of all patients.

Lung abscess :documented in 10 patient(20%) of Group II and its total percentage is(6 %)of all patients.

Pulmonary embolism : documented in 5patients(10%) of Group II and its total percentage is (3.3 %) of all patients.

Hepatopulmonarysyndrome**:** documented in 10 patients(20%) of Group III total percentage is (6 %)of all patients .

Discussion

Chronic HCV infection is associated with multiple extrahepatic manifestations including effects on the lung. These include primary effects on lung function, as well as secondary effects in the settings of progressive liver disease and drug treatment for HCV [7,8].

In our study C.O.P.D was documented in 32 patients(21.3%) and that agree with Erol ***et al.*** [9] who reported potential effect of implication of HCV infection in the development of COPD. HCV infection may play a long-term effect on pulmonary structure and may serve as a risk factor for COPD development .and the prevalence of COPD was 17.6% among patients who had the anti-HCV antibody and also agree with **Minakata *et al* .** [10] reported that prevalence of COPD of 19.3% (6/31) among patients with HCV infection.

Our results disagree with **Fischer *et al*.** [11] found no increase in the prevalence of obstructive lung diseases (OLD) in HCV and **Cesur *et al.*** [12] found that the coexistence of COPD and HCV infection was lacking.

In our study asthma was documented in 15 patients (10%) of all patients and this agree with **Erol *et al.*** [9] reported that patients with chronic HCV infection, prevalence of bronchial asthma (14.7%).

In our study air way hyperreactivity was documented in 15 patients (10%) of all patients and this disagree with **Sanaa *et al.*** [13] showed a significant difference between the studied groups as regards the presence of bronchial hyperreactivity (54% in the treated group vs. 32% in the untreated group).

In our study IPF was documented in 37 patients(24.6%)and this agree with **Raghu *et al*.** [14] reported a possible role for HCV in the etiopathogenesis of idiopathic pulmonary fibrosis. **Ueda *et al*.** [15] found that 19 of 66 (28, 8%) Japanese patients with IPF were positive for serum antibodies to HCV using the screening ELISA method (first generation).

In our study Pneumonia was reported in 10 patients(6%) of all patients and this agree with **Sanaa *et al.*** [13] who found that pneumonia is present in 8% of untreated HCV infection and in 12% in the treated group.

In our study Trasudative pleural effusion was found in 10 patients (6%) of all patients and this agree with **Albert *et al*.** [16] reported that prevalence of pleural effusion in patients with liver cirrhosis is 4% to 10% .**Sakurabayashi *et al*.** [17] reported that Fluid in the chest may be found in at least 10 percent of patients with cirrhosis, being more common on the right side influencing when in large quantities the VA/Q ratio .

In our study Adenocarcinoma :documented in 5 patients(3.3) and this agree with **Uzun *et al*.** [18] reported that anti-HCV abs were significantly higher among lung cancer patients (3/45) as compared to patients with benign lung disease (0/80) and the healthy controls (1/135) . **Malaguarnera *et al*.** [19] reported increased prevalence of anti-HCV was found in patients with lung cancer(8/22 versus 30/300) as compared to those in the control group (36% versus 10%,). **Allison *et al.*** [20] reported that HCV infection was found to be associated with a slightly increased incidence of lung cancer.

In our study we found a case of Pseudolymphoma and it is the first case to be documented in the lung in association of HCV infection.

In our study we reported 10 patients with lung abcess and 5 patients with pulmonary embolism.

In our study we found 10 patients(6%) with hepatopulmonary syndrome and this agree with **Lange and Stoller** [21] whoreported that Hepatopulmonary syndrome (HPS) had been shown to occur in 5 % to 13 % of patients with liver disease and/or portal hypertension .

Conclusion

Chronic hepatitis C virus infection is related to the development of several pulmonary abnormalities despite absence of symptoms in most patients. These pulmonary

manifestations of HCV infection are frequently underdiagnosed.

Recommendations

Any patient with chronic HCV infection should be evaluated with HRCT chest and pulmonary function tests for early diagnosis of pulmonary abnormalities to prevent further complications .

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