

Frequency of Anti-HCV antibodies in Chronic Obstructive pulmonary disease and 6-Minute walk test

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ABSTRACT

Aim: To determine the frequency of anti HCV antibody in patients of chronic obstructive pulmonary disease and its impact on 6 minute walk test.

Study design: Cross sectional study

Methodology: Total 107 patients were selected after demographic data and confirming them clinically and on spirometry as suffering from COPD, 3ml of blood was taken for anti HCV antibody test performed by third generation ELISA (Ortho HCV ELISA) kit, all those selected patients then underwent abdominal ultrasound to rule out cirrhosis and 6-minute walk tests (6MWT) as per protocol.

Results: Out of 107 cases 14(13.1%) were positive for anti HCV antibody, majority of study cases were from age group > 45 years (85%), the mean duration of COPD was significantly different for anti HCV +ve (5.28±1.48) years and anti HCV -ve cases (6.72±3.15) p-value <0.01. 6MWT shows significant decline in distance covered by anti HCV +ve cases (425 meters) than anti HCV-ve (549 meters) p-value <0.04. Post 6MWT there was significant drop in oxygen saturation in anti HCV +ve (89.6%) than anti HCV-ve (93.8%) cases p-value <0.01.

Conclusion: Chronic hepatitis C virus can affect the lungs with or without liver cirrhosis, and 6-MWT can be a useful noninvasive, free of cost test for the monitoring of lung functions and physical health in patients prior, in between and post antiviral treatment and can be helpful in evaluation of physical and lung health before liver transplantation.

Keywords: HCV, COPD, 6MWT.

INTRODUCTION

Hepatitis C virus (HCV) is a trophic virus that produces hepatic and extra hepatic manifestations, like mixed cryoglobulinemia, lichen planus, porphyria cutanea tarda, Non-Hodgkin's lymphoma (NHL), monoclonal gammopathies, sialadenitis, cardiomyopathies glomerulonephritis¹. Pulmonary involvement is one of the most important extra hepatic manifestations of chronic HCV infection².

In Pakistan prevalence of HCV infection varies between 4-7%³. Several reports have suggested an important role for latent viral infections, in particular adenovirus and human immunodeficiency virus (HIV), in the etiology and/or progression of chronic obstructive pulmonary disease (COPD)⁴. Kanazawa et al. have hypothesized that chronic HCV infection might also function as a trigger for inflammation in the lungs hence, either initiating or exacerbating the development of COPD.⁵ In a cross-sectional study to the prevalence of HCV infection in a sample of chronic obstructive pulmonary disease (COPD) patient, prevalence of HCV was 7.5% (95% CI 6.52-8.48) and showed more severity of disease⁶.

Another study shows the HCV prevalence of 8.3% in COPD patients⁷.

Chronic HCV infection is also associated with both direct and indirect effects on pulmonary tissues the direct effect of HCV on the lung may present as worsening of the lung function as initiation or exacerbation of pre-existing asthma and / or COPD, also, an interstitial pneumonitis and / or pulmonary fibrosis. Since HCV is well known to induce chronic inflammation and fibrosis of the liver, it was thought that HCV may play a similar role in the lung and be involved in the pathogenesis of pulmonary fibrosis. HCV-positive patients without clinical pulmonary symptoms have significantly increased epithelial permeability compared with controls, suggesting early interstitial lung disease⁸.

Interestingly not only HCV causes lung manifestations but its treatment with Interferon therapy is also related with certain complications like interstitial pneumonitis, pulmonary sarcoidosis, pleural effusion, exacerbation of bronchial asthma, bronchiolitis obliterans organizing pneumonia and acute respiratory distress syndrome⁹. The 6MWT is a practical simple test which doesn't require any special equipment or training and used as measure of functional status and predictor of morbidity and mortality in cardiopulmonary diseases¹⁰.

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METHODOLOGY

This cross sectional study was conducted in outpatient department of medicine at central park medical college hospital Lahore. Written and informed consent were taken from each participant. Sample size was calculated by using open-epi software anticipated proportion (P) of HCV in patients of COPD was 7.5%, taking confidence level (1-a) of 95% and absolute precision (d) of 5%⁷.

After the demographic data all those patients suspected or diagnosed as chronic obstructive pulmonary disease patient in past were selected and all those patients were excluded from the study who has history of bronchial asthma currently or in past, Interstitial lung disease ,acute lung infections decompensated liver disease, severe anemia corrected with blood transfusion in past 6 months, surgical procedure in past, hemodialysis , acute exacerbation of pulmonary disease, history of unstable angina or myocardial infarction in past one month, heart failure, morbid obesity, those who have taken 6-minute walk test earlier ,requiring oxygen supplementation, mechanical ventilation, suffering from osteoarthritis, rheumatoid arthritis or any other physical disability which curtails their physical capacity, history of impaired cognition, stroke, encephalopathy due to any cause, systolic blood pressure of >180 and diastolic blood pressure of >110mmHG, patient received antiviral therapy, radiation or chemotherapy in past and co infection with HBV, HDV and HCV. Those selected underwent the spirometry test by digital hand held spirometer (AMD-3450) under supervision of consultant pulmonologist having 10 years' experience in spirometer data interpretation, patients were given demonstration how to hold mouth piece of spirometer during sitting position and nose clip was applied, after 2-3 slow expiratory volume measurements at least three forced expiratory measurements were noted, chronic obstructive lung disease was diagnosed according to GOLD definition of Forced Expiratory Volume in 1 minute to Forced Vital Capacity in 1 minute Ratio (FEV1/FVC1) <0.70.

After clinically and spirometric assessment of COPD, 3ml of blood sample was taken for Anti HCV antibody detection by a trained phlebotomist in a vacutainer; test was done by 3rd generation ELISA (Enzyme Linked immunosorbent Assay) method. Selected participant than underwent abdominal ultrasound performed by an expert sonologist with 5 years' experience to rule out cirrhosis with following features the appearance of the liver surface, liver parenchymal texture, portal vein size, splenic size, presence of ascites and varicose veins in the portal and perisplenic area. All of these study participants

were examined by senior physician and then study participants underwent 6-minute walk test according to protocol by American Thoracic society¹⁰ on a 100 feet long flat surface, before the test a dyspnea scale in printed form was given to them to comment on the level of dyspnea they fell before the test, Blood pressure, pulse rate and oxygen saturation were noted after the rest of 10 minutes, than patients were instructed to walk not to run or jog, informed to stop the test if they are unable to complete, can take rest in between and resume the test once they fell comfortable within given 6 minutes, at the end of test again all subjects were asked about the dyspnea level ,Oxygen saturation was noted on predesigned pro-forma.

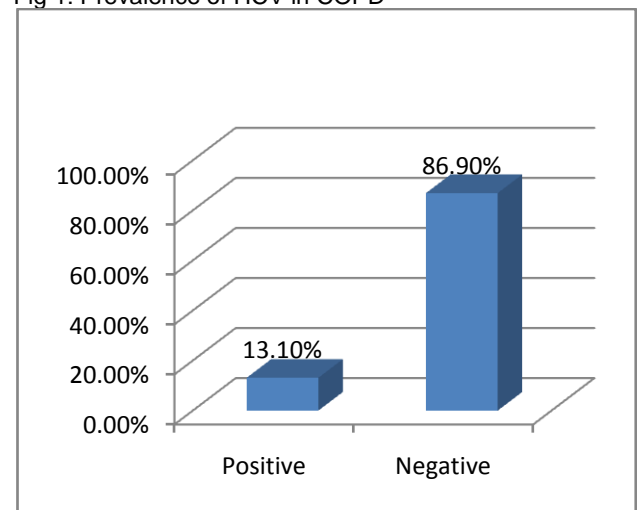
Data were stored and analyzed using SPSS version 16.0, Pearson chi square test performed to see the association of HCV with age-group, gender, smoking and other qualitative variables, independent sample t-test was used to compare the mean levels of COPD and smoking duration, and Borg and O2 test results.

Paired sample t-test used to compare the results of pre and post test results in HCV positive and negative cases, pie chart used to display the prevalence of HCV and Bar chart display the results of pair sample t-test results. P-values less than 0.05 were considered significant.

RESULTS

In this study total number of study participants was divided in to two groups according to age, with age less than 45 years and second group of COPD patients with age more than 45 years. HCV positive cases were 14(13.1%) and 93(86%) were HCV negative cases (Fig:1).

Fig 1: Prevalence of HCV in COPD



Majority of patients were from age group (>45 years) 91(84.1%), while 16(15.1%) were from age group (<45 years). Males were more in number 84(78.6%) and females were 23(22.5%), out of 107 study participants 72(67.7%) were active smokers, while 22(21%) were Ex-smoker, and 13(10%) were nonsmoker. Out of 14 HCV+ve cases 9 were currently smoking and 2 were ex-smoker and 3 had never smoked (Table1).

Table 1: Association of HCV with age, gender, smoking and COPD

Characteristics	Positive (n=14)	Negative (n=93)	P value
Age group			
<=45 Years	2(14.3%)	14(15.1%)	0.94
>45 Years	12(85.7%)	79(84.9%)	
Gender			
Male	11(78.6%)	73(78.5%)	0.99
Female	3(21.4%)	20(21.5%)	
Smoking status			
Smoker	9(64.3%)	63(67.7%)	0.47
Ex-Smoker	2(14.3%)	20(21.5%)	
Non-Smoker	3(21.4%)	10(10.8%)	
COPD stages			
Mild	3(21.4%)	20(21.5%)	0.53
Moderate	8(57.1%)	36(38.7%)	
Severe	2(14.3%)	28(30.1%)	
Very Severe	1(7.1%)	9(9.7%)	

*p<0.05 was considered significant using Pearson chi square test

The mean disease duration in HCV +ve cases was (5.28 years) and HCV -ve cases (6.72 years) with p-value (<0.05). Duration of smoking was also significantly different between HCV+ve (17 years)

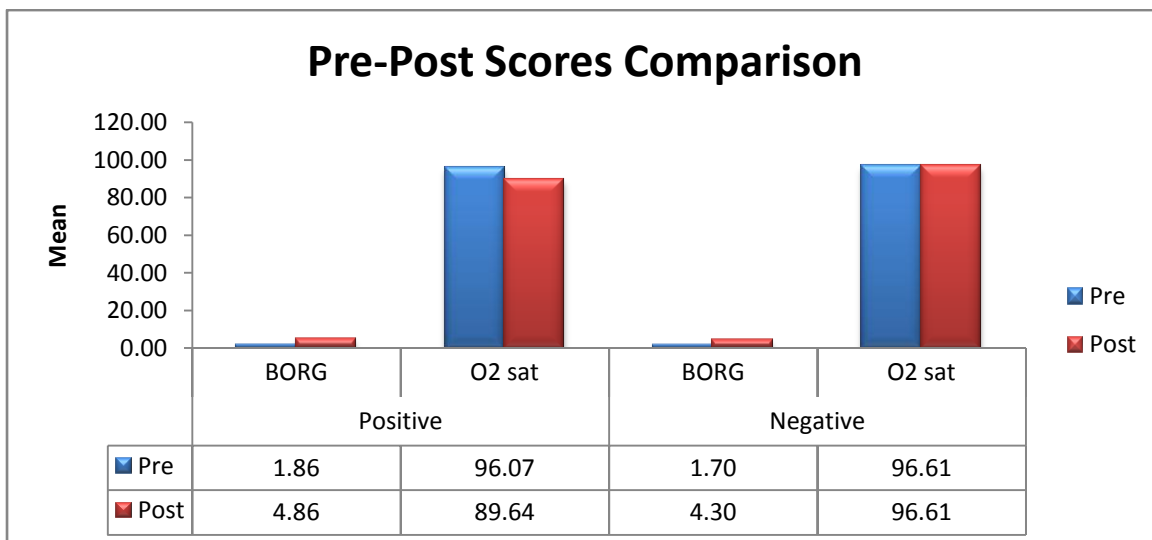
and in HCV-ve negative (23 years) with p-value (<0.08). The mean of Borg dyspnea score (post-test) in HCV+ve was (4.85) and in HCV-ve cases was (4.29) with p-value (0.43). Mean distance covered by HCV+ve cases in 6-minute walk test was (425 meters) and HCV-ve cases covered distance of (549 meters) with p-value of (<0.04). Post 6-minute walk test Oxygen saturation was also different in HCV+ve (89.6%) and in HCV-ve was (93.8%) with p-value (<0.01) table 2. The pre and post dyspnea score and oxygen saturation in HCV+ve and HCV-ve cases, paired sample t-test gives significant differences in scores with p-value<0.05 (Fig. 2).

Table 2: Mean comparison of variables between HCV Positive and Negative cases

HCV antibody	Mean	St. Deviation	P value
Duration of COPD symptoms (years)			
positive	5.28	1.48	<0.01*
Negative	6.72	3.15	
Duration of smoking (years)			
positive	17.07	11.88	0.08
Negative	23.35	12.62	
Borg scale (post test)			
positive	4.85	2.24	0.43
Negative	4.29	2.52	
Distance in meters			
positive	425.14	191.80	0.04*
Negative	549.82	216.16	
Post test O2 sat			
positive	89.64	3.79	<0.01*
Negative	93.87	4.19	

*p<0.05 was considered significant using independent sample t-test

Fig 2: Pre and Post Borg score and Oxygen saturation levels



DISCUSSION

HCV is associated with a wide spectrum of clinical and biological extra-hepatic manifestations.¹¹ Its estimated prevalence among the 15–59 years age group is about 14.7%.¹² Around 30% to 70% of patients with chronic hepatitis C have an extra-hepatic manifestation of HCV during the course of the disease¹³.

The general principle that the coexistence of multiple inflammatory stimuli produces a more severe inflammatory response might also apply to acute inflammatory stimuli. This mechanism might be particularly important in the development of exacerbations of asthma and COPD.¹⁴ Chronic liver disorder decreases glutathione synthesis in the liver, and an inadequate supply of glutathione in the lung would render the lung vulnerable to oxidative damage¹⁵.

Also Kanazawa et al⁵ reported an accelerated decline of lung function in COPD patients with concomitant hepatitis C infection. They have suggested that the airway disease may be related to the underlying chronic inflammatory disorder. It is also possible that the number and importance of different inflammatory hits may change as the airway disease evolves. Severe COPD is associated with the development of lymphoid follicles in the small airways, implying the presence of an adaptive immune response. This immune response could be due to chronic infection or the exposure of auto-antigens as a result of increasing tissue damage. The extent to which the coexistence of more than one acute or chronic inflammatory stimulus produces additive or synergistic effects¹⁶.

Mahmoud M. El-Habashy et al in their study also concluded that COPD patients associated with chronic HCV infection have significant decrease in pulmonary function compared with HCV negative COPD patients. These findings suggest that chronic HCV infection is associated with accelerated decline of lung function in patients with COPD¹⁷.

Mahmoud M El-Habashy et al in another study which was carried on chronic HCV+ve non cirrhotic patient found that, twelve patients showed pulmonary dysfunction, seven of 60 patients (11.67%) showed hypoxemia, intrapulmonary shunting was observed in three out of 12 and two patients fulfilled the diagnostic criteria of HPS¹⁸.

In our study we also found HCV+ve patients showed declined in oxygen saturation and decrease in the distance covered during the 6-minute walk test in comparison to HCV-ve chronic obstructive pulmonary disease patient and out of 14 patient who were chronic HCV positive eight had mild to

moderate COPD on spirometry. Alameri HF et al,¹⁹ in their prospective study, found that the distance walked by hepatitis C patients was less than that walked by hepatitis B patients or control subjects, which indicates there are multiple mechanisms playing their role in various lung manifestations ultimately resulting in respiratory insufficiency and those who covered less than 306 meters had increased mortality.

It's not only the HCV which itself causes the decline in lung functions but its treatment with conventional interferon and pegylated interferon's which is also related with decline in lung functions, Mahwish et al, in her study also found that treatment with conventional interferon is associated with obstructive pattern on spirometer at 6 months of therapy.²⁰

In this study we noted that five patients who are suffering from COPD were nonsmoker and had anti HCV antibodies so the reason for COPD could be HCV, yet needs to be established by large cohort study which helps in knowing the cause and effects of HCV on lungs.

Our study has little potential limitation like small sample size, no control group, 6MWT was once carried out, and further studies are required to know more about the cause and effects of HCV on respiratory system.

Conclusion:

Patients who are suffering from COPD needs screening for anti HCV antibodies and once they diagnosed as HCV+ve and selected for treatment with antiviral medicine, properly investigated about the lung involvement of HCV, so they can be prevented from further decline in respiratory capacity, and all those patients who are undergoing liver transplantation also needs to be checked for physical and respiratory capacity with 6MWT and this test can be a good tool to screen out and predicts about the morbidity and mortality.

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Conflict of interest: None

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