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Hepatitis C Virus Infection and the Risk of Chronic Obstructive Pulmonary Diseases in Azadi Teaching Hospital, Duhok, Kurdistan

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Abstract

Hepatitis C Virus (HCV) infection might act as a triggering factor for inflammation in the lungs, hence, either initiating or exacerbating the development of Chronic Obstructive Pulmonary Disease (COPD). The objective of this paper was to study the association between HCV and COPD patients. The study was conducted at Azadi teaching hospital in Duhok province between July 2016 and December 2016. All documented COPD patients were included in the study. The diagnosis of COPD was performed according to American Thoracic Society (ATS) guidelines. Information on patient's demographic characteristics was gathered by using a standardized questionnaire. Antibody to Hepatitis C Virus (anti-HCV) was evaluated by Enzyme-Linked Immunosorbent Assay (ELISA) method. All anti-HCV patients were tested for HCV-RNA by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR). The results obtained were analyzed by entering the data in a binary format as a Microsoft Excel spreadsheet. A p value of less than 0.05 was considered to be statistically significant. The study included 97 COPD patients and 220 control subjects. Considering the demographic profile between the two categories, the variables significantly associated with COPD patients were older age (p = 0.0005), male sex (p = 0.000), smoking (p = 0.000), and history of exposure to occupational and environmental pollutants (0.000). Five patients were positive for HCV (15.5%) in the COPD group, while 1 patient in the control group was positive for HCV (0.45%) (OR, 11.902; 95% CI, 1.329-273.090; p = 0.011). There were no statistically significant risk factors between the COPD/HCV positive and COPD/HCV negative patients. It can be concluded that older age, male sex, smoking, and history of exposure to occupational and environmental pollutants were independent risk factors for COPD patients. The high prevalence of HCV in COPD patients might indicate the need for HCV screening in such vulnerable group. Meanwhile, ensuring appropriate treatments for HCV positive patients is an essential measure.

Keywords

HCV, COPD, Risk factor, Duhok

Abbreviations

HCV: Hepatitis C Virus; COPD: Chronic Obstructive Pulmonary Disease; ATH: Azadi Teaching Hospital; ATS: American Thoracic Society; Anti-HCV: Antibody to Hepatitis C Virus; ELISA: Enzyme-Linked Immunosorbent Assay; RNA: Ribonucleic Acid; RT-PCR: Reverse Transcriptase Polymerase Chain Reaction; OR: Odds Ratio; CI: Confidence Interval; FEV1: Forced Expiratory Volume in One Second; FVC: Forced Vital Capacity, SD: Standard Deviation; IVD: Intravenous Drug

Introduction

The worldwide prevalence of Hepatitis C Virus (HCV) is approximately 3%, with up to 180 million people infected chronically [1]. Geographic variations exist, from 0.4% to 1.1% in North America to 9.6% to 13.6% in North Africa [1]. In Iraq, the prevalence of HCV infection is reported to be 0.4% with a very low rate in Duhok governorate [2,3]. Of concern, HCV is the primary cause of death from liver disease and is the leading indication for liver transplantation [4]. HCV is transmitted through percutaneous (e.g. blood transfu-

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sion, needle stick inoculation, high-risk behavior) and less frequently by non-percutaneous (e.g. sexual contact, perinatal exposure) routes [5]. Majority of patients with acute HCV infection are asymptomatic. In contrast, patients with chronic HCV infection generally complain of nonspecific symptoms such as anorexia, nausea, fatigue, etc. Once patient develops liver cirrhosis intractable ascites, portal hypertension and other clinical manifestations may develop [6]. Furthermore, significant extrahepatic manifestations may also develop as a result of HCV infection [7]. A growing pile of evidence supports the notion that pulmonary involvement is one of the extrahepatic manifestations of chronic HCV infection [8]. It has been hypothesized that chronic HCV infection might act as a triggering factor for inflammation in the lungs, hence, either initiating or exacerbating the development of Chronic Obstructive Pulmonary Disease (COPD) [9]. Hence, we decided to perform this study. To the best of our knowledge, there is limited data on the frequency of HCV in COPD patients. Therefore, the aim of this paper was to study the association between HCV and COPD patients.

Patients and Methods

Setting

The Azadi Teaching Hospital (ATH) is a tertiary referral hospital dealing with all patients of chronic lung diseases. Outpatient cases are interviewed and managed in the respiratory clinic, while for the inpatient cases lay another section in the hospital on the fourth floor.

Study design and patients

The study was conducted at ATH in Duhok province between July 2016 and December 2016. All documented COPD patients were included in the study. COPD was diagnosed by a spirometry according to American Thoracic Society (ATS) guidelines; a post-bronchodilator Forced Expiratory Volume in One Second (FEV1)/ Forced Vital Capacity (FVC) of ≤ 0.7 confirms the presence of airflow limitation that is not fully reversible [10]. A written informed consent was obtained from all included patients. Information on patient's demographic characteristics was gathered by using a standardized questionnaire.

Laboratory investigations

Serum samples were tested for Antibody to Hepatitis C Virus (anti-HCV) by Enzyme-Linked Immunosorbent Assay (ELISA) method (Fortress Diagnostics Limited, Unit 2C Antrim Technology Park, United Kingdom). The ELISA was performed as per manufacturer's instructions. The specificity for HCV was reported as 99.55 respectively, while the sensitivity for HCV was accounted for 99.79%. The cutoff value for positive antibody was taken as 1 U/m. Patients with anti-HCV < 1 U/mL was considered negative for HCV [11]. All patients with positive anti-HCV antibody test were tested for serum HCV-RNA by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR), and nested-PCR with primers derived from the highly conserved 5'-untranslated regions (NS 5'R) of the viral genome.

The definition of HCV positive patient was indicated by positive anti-HCV and HCV-RNA (RT-PCR).

Statistical analysis

The result obtained was analyzed by entering the data in a binary format as a Microsoft Excel spreadsheet and the analysis was performed by STATA (version 10; StataCorp, College Station, United States of America). The association between HCV and COPD outcome was expressed as Odds Ratio (OR) with corresponding 95% Confidence Interval (CI). The chi-square test was used to test statistical significance in categorical variables. A p value < 0.05 was considered to be statistically significant.

Table 1: Demographic features of COPD patients and control group.

Parameter	Patients (no = 97) no (%)	Control (no = 220) no (%)	OR* (95% CI)	P value
Age				
Mean ± SD	64.89 ± 14.65	58.31 ± 15.51	6.580 (2.922 to 10.237)	0.0005
Gender				
Male	81 (83.51)	115 (52.27)	4.622 (2.454-8.805)	0.000
Female	16 (16.49)	105 (47.73)		
Smoking habit				
Smoker	89 (91.75)	97 (44.09)	14.107 (6.245-33.100)	0.000
Non-smoker	8 (8.25)	123 (55.91)		
History of occupational and environmental pollutants exposure				
Exposed	15 (15.46)	7 (3.18)	5.566 (2.037-15.706)	0.000
Non-exposed	82 (84.54)	213 (96.82)		

*OR: Odds Ratio "the OR was calculated, with 95% Confidence Intervals (CIs)".

Results

The study included 97 COPD patients and 220 control subjects. The demographic profile in both investigated groups is demonstrated in Table 1. A significant association was found with regards to age, gender, smoking habit and history of exposure to occupational and environmental pollutants in comparison to the control people.

Five patients were positive for HCV (15.5%) in the COPD group, while 1 patient in the control group was positive for HCV (0.45%) (OR, 11.902; 95% CI, 1.329-273.090; p = 0.011) (Table 2).

A comparative analysis for some variables between HCV positive and HCV negative patients among COPD patients is shown in Table 3. There were no statistically significant risk factors between the two categories.

Discussion

Hepatitis C virus is a hepatic infection that is associat-

Table 2: Frequency of HCV infection among COPD and control group.

Variable	Patients (no = 97) no (%)	Control (no = 220) no (%)	OR (95% CI)	P value
HCV infection				
Positive	5 (5.15)	1 (0.45)	11.902 (1.329-273.090)	0.011
Mean anti-HCV titer (U/ml)	2.52	2.1		
Mean HCV-RNA viral load (IU/ml)	3,096,940	230,000		
Negative	92 (94.85)	219 (99.55)		

*OR: Odds Ratio "the OR was calculated, with 95% Confidence Intervals (CIs)".

Table 3: Comparison of COPD patients according to HCV infection positivity.

Variable	HCV -ve (no = 92)	HCV +ve (no = 5)	OR (95% CI)	P value
Age	65.38 ± 14.82	58.60 ± 10.46	-6.780 (-20.147 to 6.587)	0.3165
Sex				
Male	77	4	0.779 (0.072-19.640)	1.000
Female	15	1		
Smoking habit				
Smoker	85	4	0.329 (0.026-8.832)	0.356
Non-smoker	7	1		
Hx occupational and environmental pollutants exposure				
Exposed	21	1	0.845 (0.034-8.863)	1.000
Non-exposed	71	4		
Previous hospitalization				
Positive	34	4	6.824 (0.670-167.242)	0.075
Negative	58	1		
History of dental intervention				
Positive	31	2	1.312 (0.144-10.399)	1.000
Negative	61	3		
History of blood transfusion				
Positive	12	1	1.667 (0.065-18.626)	0.521
Negative	80	4		
History of surgical intervention				
Positive	35	3	2.443 (0.310-22.209)	0.337
Negative	57	2		
Tattoo				
Positive	17	1	0.407 (0.017-4.148)	0.648
Negative	75	4		
Hemodialysis				
Positive	0	0		
Negative	92	5		
IVD				
Positive	0	0		
Negative	92	5		

*OR: Odds Ratio "the OR was calculated, with 95% Confidence Intervals (CIs)".

ed with chronic liver inflammation and fibrosis. Similarly, HCV infection is strongly associated with extrahepatic disease including its potential nonspecific pulmonary inflammatory reactions [12]. The infection is associated with the rapid decline of lung function in patients with COPD [13]. In this study, considering the comparative analysis in Table 1, there were four risk factors associated with COPD patients. Older age (64.89 ± 14.65), male sex, smoking, and history of exposure to occupational and environmental pollutants were independent risk factors for COPD patients. The finding of the older age was in agreement with other literatures [8]. The older age of COPD patients in our study can be a positive factor for exposure of lung to potentially harmful agents throughout the patient's life with subsequent negative effects on pulmonary function. The higher prevalence of COPD in male patients was in consistent with other studies [14]. This finding can be explained by more frequent smoking habits and environmental exposure to risk factors for development of COPD in men. However, recent studies from developed countries documented equal prevalence of COPD between both genders because women are adopting the same life style as men [15]. The significant high association of COPD with cigarette smoking and exposure to occupational and environmental pollutants has clearly been stated in the literatures [16]. Air pollutants including cigarette smoking may cause inflammation, alteration of cell growth, cellular apoptosis, abnormal cell repair, extracellular matrix destruction, and oxidative stress, which all together play an important role in the pathogenesis of COPD [16]. In our study, 5 (5.15%) of the COPD patients were positive for HCV infection, while 1 (0.45%) control subject was positive for the infection. The difference in the prevalence of HCV infection between COPD cases and control individuals was statistically significant (OR, 11.902; 95% CI, 1.329 to 273.090; p = 0.011). Our finding was in agreement with other studies [9]. The high prevalence of HCV infection in COPD patients is considered important in comparison to the low frequency rate that was documented in our work, which was previously performed [3,17]. The reason behind our finding is that patients with COPD might have had frequent admission to the hospital and thus they were more susceptible to blood borne pathogens. Although, we did not find a statistically significant difference between HCV positive and negative patients, the acquisition of hospital acquired HCV in health care setting has been documented by other investigators [18]. It is well known that HCV is associated with pulmonary diseases, including idiopathic pulmonary fibrosis and COPD [19]. A prospective study by Moormann, et al. reported that the annual decline rates in FEV1 and D_{LCO} were significantly higher in HCV positive patients in comparison to HCV negative patients [20]. It is argued that HCV infection might be a potential factor for occurrence or exacerbation of COPD through quasispecies characteristics of the virus, which are supportive of its extrahepatic infection phenomenon [21]. Therefore, HCV screening in COPD patients is reasonable policy, while ensuring appropriate treatment of HCV positive patients.

In the current study, we did not find significant risk factors between the COPD/HCV positive patients and COPD/HCV negative patients for age, sex, smoking habit, history of occupational and environmental pollutants exposure, risk factors for acquisition of HCV infection. Although HCV positive patients were younger than HCV negative patients, the association was not significant (P value = 0.3165). This finding was reported by Silva, et al. who found that COPD/HCV positive patients were also younger than COPD/HCV negative patients [9]. This scene can be justified by the 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 [8]. Dental intervention was suggested in our earlier research to be a significant risk factor for Hepatitis B Virus (HBV)-tuberculosis coinfection [17]; however, we could not document a significant association between HCV and dental intervention in this study. A more likely explanation for the discrepancy between the two studies is that the seroprevalence of HCV is very low in comparison to HBV in Duhok province.

The main limitation in this study was a short term follow up of such patients that cannot determine the etiological relationship between HCV infection and COPD patients. The small sample size was another limitation in this study.

Conclusion

Older age, male sex, smoking, and history of exposure to occupational and environmental pollutants were independent risk factors for COPD patients. The high prevalence of HCV in COPD patients might indicate the need for HCV screening in such vulnerable group. Meanwhile, ensuring appropriate treatments for HCV positive patients is an essential measure.

Further prospective studies with larger sample sizes and longer durations follow ups are warranted. This should be confidently important to understand the association between the two conditions in order to improve the management of such cases.

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