Original Article

Gallstones and Hepatitis C Infection

Association Between Gallstones and Hepatitis C Virus Infection: A study of 600 Cases at Pak Red Crescent Medical & Dental Teaching Hospital

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ABSTRACT

Objective: To compare the frequency of gallstones in patients with and without hepatitis C virus infection.
Study Design: Cross-sectional study
Place and Duration of Study: This study was conducted at the department of surgery & radiology, Pak Red Crescent Teaching Hospital, affiliated with Pak Red Crescent Medical & Dental College, Lahore from July 2016 to June 2018.
Materials and Methods: A total of 600 patients irrespective of age and sex were included in this by consecutive nonprobability sampling technique. All subjects were screened for Anti-HCV antibody by immune-chromatographic strip-test method. An equal number of patients with and without HCV infection were chosen in two different groups. Group I was seronegative and Group II was seropositive patients. Ultrasound scan of abdomen was performed on all the patients to see especially for gallstones. Data was collected for age, sex, presence or absence of gallstones, on a specially designed performa. Data was analyzed using SPSS version 21. Descriptive statistics & Chi-square test was used.
Results: Out of 600 patients, 414 (69%) were females and 186 (31%) were males. Mean age of the patients was 38 ± 1.28 years. Youngest patient was 17 years old and eldest was 90 years old. Males and females with Hepatitis C antibodies were 121 (40.33%) and 179 (59.66%) respectively. In Group II patients suffering from HCV infection had a significantly high frequency of gallstones (25.66%) as compared to HCV seronegative Group I (8.66%). P-value was significant (p=0.01).
Conclusion: There is a strong association of gallstone disease in patients suffering from HCV infection.
Key Words: Gallbladder, cholelithiasis, gallstones, Hepatitis C Virus, GBD.

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INTRODUCTION

Worldwide Hepatitis C virus infection is a major healthcare problem. It is estimated that approximately 180 million patients across the globe are infected with this virus.[1] According to world health organization (WHO), Pakistan has the world's second highest prevalence of hepatitis C, second only to Egypt.[2] Current prevalence of HCV in Pakistan is 8.64%,[3] high from previously reported prevalence rate of 4.8%.[4]
Some epidemiologic studies[5,6] reported that, HCV infection could also be an independent risk factor for gallstones.

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Only two studies were conducted in our country to investigated HCV infection as a solitary risk factor for gallstones.[5, 7]
We consistently found in our institution, lots of patients with cholelithiasis who also had HCV virus infection. Fact that HCV is an endemic in this region we planned a study, to see this association. We hypothesized that persons with HCV infection have a higher incidence of gallstone disease than those without HCV infection. The objective of the study was to compare the frequency of gallstones in patients with and without hepatitis C virus infection.

MATERIALS AND METHODS

This cross-sectional study was conducted from July 2016 to June 2018 in the department of surgery & radiology, Pak Red Crescent Teaching Hospital, affiliated with Pak Red Crescent Medical & Dental College, Lahore. The study was approved by the ethical review committee of our institution. In order to reduce the bias, all the scans were performed by the same

radiologist. All cases included in this study were referred for ultrasound scan of abdomen.

A total of 600 patients irrespective of age and sex were included in this by consecutive non-probability sampling technique. Patients with abnormal LFT's due to any cause other than Hepatitis C, abnormal lipid profile, sickle cell disease, thalassemia, history of gastric/bariatric surgery and patients taking contraceptives were excluded.

All subjects were tested for Anti-HCV antibody by strip method. An equal number of patients with and without HCV infection were chosen in two different groups. Group I was seronegative and Group II was seropositive patients. Ultrasound scan of abdomen was performed on all subjects, with special focus on hepatobiliary system. Special note was made of gallstones location whether in the gallbladder or in the bile duct, and presence or absence of cirrhosis.

Data was collected for age, sex, presence or absence of gallstones, on a specially designed proforma. Data was analyzed using SPSS version 21. Descriptive statistics were applied. Frequency and percentage were calculated for categorical variables like gender whereas mean and standard deviation were calculated. Chi-square test was used to determine the association of HCV infection with gallstones by comparing the frequency of gallstones in the two groups. p-value of <0.05 was considered significant.

RESULTS

A total number of 600 patients were included in the study which were divided into two groups. In group I, 300 patients were HCV seronegative and while in Group II 300 patients were HCV seropositive. Out of 600 patients, 414 (69%) were female and 186 (31%) were male. Mean age of the patients was 38 ± 1.28 years.

Table No. 1. Gender Distribution in study groups

Study Group	Gender		Total
	Male	Female	
Group I (HCV-ve)	65	235	300
Group II (HCV+ve)	121	179	300
Total	186	414	600
%	31	69	100

Table No.2: Frequency of gallstones in relation with gender in study groups

Study Group	Gallstones				Total
	Present		Absent		
	Male (%)	Female (%)	Male (%)	Female (%)	
Group I (HCV-ve)	5 (1.66)	21 (7)	60 (20)	214 (70.33)	300
Group II (HCV+ve)	16 (5.33)	61 (20.33)	49 (16.33)	174 (58)	300
Total (%)	21 (3.5)	82 (13.66)	109 (18.16)	388 (64.66)	600 (100)

Youngest patient was 17 years old and eldest was 90 years old. Male and females with Hepatitis C antibodies were 121 (40.33%) and 179 (59.66%) respectively. Gender distribution of both groups is given in table 1 and frequency of gallstone in relation with gender of both study groups is given in Table. 2.

Total presence of gallstone in both groups was 103 (17.6%) patients. In group I gallstones were found in 26 (8.66%) patients and in group II (HCV+ve) in 77 (25.66%) patients. Comparative frequency of gallstone in both groups is shown in table 3.

Table No. 3: Presence of gallbladder stone in study groups

Study Group	Gallstones		Total	p-value
	Present	Absent		
Group I (HCV-ve)	26	274	300	0.001
%	8.66	91.33	100	
Group II (HCV+ve)	77	223	300	
%	25.66	74.33	100	
Total	103	497	600	
%	17.6	82.83	100	

DISCUSSION

Gallstones are one of the most common biliary pathology and it has a prevalence of 10-15%. Cholesterol stone is one of the most common type. In the USA and Europe 80% stones are cholesterol or mixed, whereas in Asia 80% are pigment stones.

Transabdominal ultrasonography is one of the most common, rapid, noninvasive method of imaging the gallbladder, and this technique has contributed greatly to our understanding of the epidemiology and risk factors for gallbladder disease.[8,9]

The risk of gallbladder disease (GBD) increases with age. Traditionally it is associated with middle age females. Other potential risk factors for GBD include obesity,[10] rapid weight loss,[10] lower levels of physical activity,[11] pregnancy,[12] increasing number of live births,[13] oral contraceptive, estrogen replacement therapy,[14] diabetes mellitus,[13,15] abstinence from alcohol,[13,16,] smoking,[13] low total serum cholesterol levels,[13,17] low levels of coffee consumption,[19,20] and genetic factors.[21] However, some of these variables have not been consistently associated with GBD, and these risk factors may differ considerably among men and women.[13,17]

Liver cirrhosis is believed to be another major risk factor for gallstones,[21] and it increases the risk of gallstones two times more than other patients.[22,23] Formation of gallstones in cirrhosis are mainly due to, the changes in bile composition and impaired gallbladder motility.[22] Patients with cirrhosis are more likely to undergo cholecystectomy for emergent reasons

than those who do not have liver disease.[24] Moreover if cirrhosis is due to viral hepatitis C, the risk of gallstones becoming symptomatic is further increased than in those with alcoholic cirrhosis.[25]

Acalovschi et al. reported that HCV infection was a risk factor for gallbladder stones when comparing subjects without liver diseases.[26] Stroffolini et al, reported that gallstone prevalence was significantly higher in patients with HCV-related cirrhosis than in those with HBV-related or alcoholic cirrhosis.[27] The exact mechanisms behind the development of gallstones in HCV patients is not well understood.[28] Loriot et al. demonstrated that HCV can successfully infect gallbladder epithelial cells.[29] Many other studies also reported HCV can directly infect bile duct and gallbladder epithelial cells.[30,31] It might impair gallbladder epithelium lipid absorption and gallbladder muscle contractility function, resulting in increased propensity of development of gallstones. HCV infection is also known to have interactions with glucose and cholesterol metabolisms.[32,33] This metabolic disturbance could lead to alteration of bile composition that may contribute to the gallstones formation.

Acalovschi et al, reported 19% incidence of gallstones in HCV positive patients.[26] In present study We found that the risk of gallstones was significantly higher (25.66%) among HCV-infected patients compared with subjects without HCV infection (8.66%). Which is consistent with local [5, 7] and international data. [8, 21, 28, 34]

Bini EJ and McGready J, found that chronic HCV infection is strongly associated with GBD in men but not in women in the United States.[8] Chia-Yen Dai et al, also reported, the association between HCV infection and GB stones existed in males but not in females.[35] In current study we did not find this association. We found 20.33% of HCV positive females who had gallstone disease whereas incidence in HCV positive males was only 5.33%. We recommend further studies in different areas of our country to see this difference, that might be a regional one.

The risk of gallstones becoming symptomatic is higher in patients with cirrhosis due to viral hepatitis.[25] Furthermore patients with de-compensated liver cirrhosis are more susceptible to gallstone formation than patients with compensated liver cirrhosis.[36] It has major implications because cholecystectomy for symptomatic gallstones in patients with advanced liver disease is associated with a high risk of morbidity and mortality.[24,27] Further studies are required to clarify how this risk should be addressed in clinical practice.

This study has some limitations, sample size is not representative of the general population. The case and control patients were selected from those seeking medical care at our hospital. The patients with chronic HCV infection might have more abdominal imaging, leading to a higher likelihood of gallstones detection.

CONCLUSION

There is a strong association of gallstone disease in patients suffering from HCV infection. It may be HCV infection which is responsible for higher prevalence of gallstone disease in this region. Further studies are required to clarify how this risk should be addressed in clinical practice.

Author's Contribution:

Concept & Design of Study:	Aqeel Ahmad
Drafting:	Nasir Mahmood
Data Analysis:	Abid Hussain
Revisiting Critically:	Aqeel Ahmad, Nasir Mahmood
Final Approval of version:	Aqeel Ahmad

Conflict of Interest: The study has no conflict of interest to declare by any author.

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