ORIGINAL ARTICLE

Prevalence of Gallstone Disease in Patients of Hepatitis C Virus Infection

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ABSTRACT

Aim:To determine the association of HCV with gallstone disease in patients of hepatitis C virus infection.

Methods:This case control study was planned in Bakhtawar Amin Memorial Hospital. One hundred patients of hepatitis C within a duration of one year March-2016 to March-2017 was recruited. For HCV diagnosis, we used ELIZA test, as it is more accurate than kit screening methods. While the hundred patients in control groups were that who were not having any liver disorder. Diagnosis of gallstone disease was based on ultrasonography reporting. We noted all required patients variables and entered them in SPSS v23. For comparison of groups, we used chi-square test or paired sample t-test.

Results: Patients of cases and control groups were comparable regarding age, gender and Body mass index. The mean age was 46.2±7.4 years among cases and 44.9±6.8 among controls (p-value 0.2). There were 60 males in case group and 63 males in control group (p-value 0.4). Regarding prevalence of gallstone disease (GSD), GSD was diagnosed in only 8% patients in control group and 22% patients in cases group. While 92% patients in control group were of not having any gallbladder disorder and 78% patients in cases group were free of all gallbladder disorders (p-value 0.005).

Conclusion: HCV infection even in the absence of liver cirrhosis is an independent predictor of gallstone disease.

Keywords: hepatitis C virus, gallstone disease

INTRODUCTION

Prevalence of gallstone disease (GSD) is on the rise with a current rate of 2-15% depending upon different regions^{1,2}. Prevalence is high in industrialized regions³. Studies have described various risk factors of GSD, which include raised female sex hormones, hypercholesterolemia, obesity and sickle cell disease^{4,5}. GSD has many adverse effects on health and quality of life and especially on health care cost. Pakistan has a 2nd highest prevalence of GSD with rate of 4.7% after 15% in Egypt⁶.

Studies have found that liver disorders such as hepatitis C virus infection also have a significant effect in increasing the likelihood of GSD⁷. Some authors concluded that alcohol intake also increases the risk and severity of GSD, while others found that alcohol intake have beneficial effects and it decreases the symptoms and severity of GSD. ^{8,9} Authors have also concluded that there is no effect of hepatitis B virus infection on the incidence of GSD. ^{10,11} One study found that GSD occurs in early life in patients of HCV infection and GSD mostly effects bile duct in these patients ¹².

Bakhtawar Amin Medical and Dental College Multan Correspondence to Dr. ArifaShamim Email Id: doctors.pak01 @gmail.com.Cell 0334-6032445, H No. 221, Block C, Phase 1, Wapda Town, Multan. Hepatitis C virus (HCV) infection is also highly prevalent in Pakistan with prevalence rate of 4.8%¹³.

Therefore, it may be HCV infection that is responsible for higher prevalence of GSD in Pakistan. We found only one study from Pakistan on this critical issue and these authors found a significant positive correlation of HCV with GSD, with a higher prevalence rate in men and disease onset in younger age when compared with patients having no HCV¹⁴.

Keeping in view the higher prevalence of HCV and GSD and complication of GSD and its effects on hospital burden and morbidity and mortality due to GSD.In this study, we evaluated the association of HCV with gallstone disease in patients of hepatitis C virus infection.

METHODS

This case control study was planned in Bakhtawar Amin Memorial Hospital. One hundred patients ofhepatitis C within a duration of one year March-2016 to March-2017 was recruited. For HCV diagnosis, we used ELIZA test, as it is more accurate than kit screening methods. While the hundred patients in control groups were that who were not having any liver disorder. Diagnosis of gallstone disease was based on ultrasonography reporting. All ultrasounds were done in our hospital and by two

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consultants. Patients who were having liver disorders other than HCV and those with previous diagnosis of GSD were excluded.

We noted all required patients variables such as age, gender, BMI, prevalence of GSDand entered them in SPSS v23. For comparison of groups, we used chi-square test or paired (independent) sample t-test for analysis.

RESULTS

There were equal number 100, 100 patients in each group. Patients of cases and control groups were comparable regarding age, gender and Body mass index. The mean age was 46.2±7.4 years among cases and 44.9±6.8 years in controls (p-value 0.2). There were 40 females and 60 males among case group and 37 females and 63 males in control group (p-value 0.4). Patients were also comparable

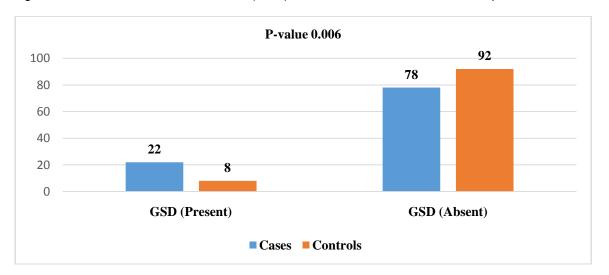
regarding body mass index (BMI). Mean BMI was 25.7±0.6 Kg/m² in case group and 26.4±0.3 Kg/m² in control group (P-value 0.12) [Table 1].

Regarding prevalence of gallstone disease (GSD), GSD was diagnosed in only 8.0% patients in control group and 22% patients in cases group. While 92% patients in control group were of not having any gallbladder disorder and 78.0% patients in cases group were free of all gallbladder disorders (p-value 0.005) [Fig. 1].

Table 1. Baseline Characteristics.

	Cases	Controls	P-value
Age (Years)	46.2±7.4	44.9±6.8	0.2
Female (%)	40	37	0.4
Male (%)	60	63	
BMI(Kg/m ²)	25.7±0.6	26.4±0.3	0.12

Fig. 1. Prevalence of Gallstone Disease (GDS) Between Cases and Control Groups.



DISCUSSION

Gallstone disease has become a common issue and has put a heavy load on hospital supplies and demands. Cholesterol stones are the commonest one. Studies have found that reduced synthesis of bile, reduced gallbladder motility and decreased production of cholesterol are the major risk factors of gallstones. In this study, we found higher prevalence of GSD in patients who presented with HCV as compared to control groups.

Many studies have concluded that liver cirrhosis is associated with higher prevalence of gallstones by we few studies have found that HCV infection in the absence of liver cirrhosis is also associated with increased risk of GSD¹⁵⁻¹⁷. This association was first time determined in 2000 in Taiwan by Chang et al.

who found a higher prevalence of GSD in HCV positive patients 11.7% versus only 6.0% in healthy subjects 18. A study conducted in Romania by Acalovschiet al. found 19% incidence of GSD in patients of HCV. 3 A study from Egypt conducted in 2014, found 15.68% incidence of GSD in HCV patients compared to only 9.9% in healthy subjects 19. A study conducted in Pakistan have found 18.65% prevalence of GSD in HCV positive patients as compared to only 6.65% in control group of patients. 14 In our study, prevalence of GSD was 22% in HCV patients and 8% among healthy subjects.

Studies have also described other risk factors of gallstone disease. Fornari et al. found that male gender is also a risk factor of GSD probably due to testosterone hormone in male patients. ²⁰ They also found that increased level of progesterone hormone

during pregnancy also have adverse effects on gallstone emptying thus increasing the risk of GSD. The exact reason of higher prevalence of GSD in HCV patients is not completely understood, it may be due to higher risk of gallbladder and other infections in these patients²¹. Loriot et al. found that HCV has direct effects on gallbladder epithelium. ²²Investigators have also found the presence of HCV or HCV antibodies in autopsy specimens of gallbladder epithelium. ^{23,24}However the reason for GSD in patients of liver cirrhosis is multifactorial e.g., the effects of liver cirrhosis on motility and bile production of gallbladder and all conducted studies have found very high prevalence of GSD in these patients as compared to the patients with HCV alone ^{25,26}.

CONCLUSION

In our study, we found that HCV infection even in the absence of liver cirrhosis is an independent predictor of gallstone disease.

REFERENCES

- Agunloye A, Adebakin A, Adeleye J, Ogunseyinde A. Ultrasound prevalence of gallstone disease in diabetic patients at Ibadan, Nigeria. NigerJClin Pract. 2013;16(1):71-5.
- Zamani F, Sohrabi M, Motamed N, Saeedian FS, Pirzad R, Abedi K, et al. Prevalence and risk factors of cholelithiasis in Amol city, northern Iran: a population based study. Arch Iranian Med. 2014;17(11):750.
- Acalovschi M, Buzas C, Radu C, Grigorescu M. Hepatitis C virus infection is a risk factor for gallstone disease: a prospective hospital- based study of patients with chronic viral C hepatitis. J Viral Hepat. 2009;16(12):860-6.
- Park SK, Andreotti G, Rashid A, Chen J, Rosenberg PS, Yu K, et al. Polymorphisms of estrogen receptors and risk of biliary tract cancers and gallstones: a population-based study in Shanghai, China. Carcinogenesis. 2010;31(5):842-6.
- Wang HH, Liu M, Clegg DJ, Portincasa P, Wang DQ-H. New insights into the molecular mechanisms underlying effects of estrogen on cholesterol gallstone formation. Biochimica et Biophysica Acta (BBA)-Mol Cell Biol Lipids. 2009;1791(11):1037-47.
- Sievert W, Altraif I, Razavi HA, Abdo A, Ahmed EA, AlOmair A, et al. A systematic review of hepatitis C virus epidemiology in Asia, Australia and Egypt. Liver Int. 2011;31(s2):61-80.
- Lai Ś-W, Ng K-C. Risk factors for gallstone disease in a hospital-based study. SouthMed J. 2002;95(12):1419-24.
- Scragg R, McMichael A, Baghurst P. Diet, alcohol, and relative weight in gall stone disease: a case-control study. Br Med J. 1984;288(6424):1113-9.
- Grodstein F, Colditz GA, Hunter DJ, Manson JE, Willett WC, Stampfer MJ. A prospective study of symptomatic gallstones

- in women: relation with oral contraceptives and other risk factors. Obstetr Gynecol. 1994;84(2):207-14.
- Lee YC, Wu JS, Yang YC, Chang CS, Lu FH, Chang CJ. Hepatitis B and hepatitis C associated with risk of gallstone disease in elderly adults. J Am Geriatr Soc. 2014;62(8):1600-2.
- Wijarnpreecha K, Thongprayoon C, Panjawatanan P, Manatsathit W, Ungprasert P. Hepatitis B virus infection and risk of gallstones: a systematic review and meta-analysis. Eur JGastroenterol Hepatol. 2016;28(12):1437-42.
- Li X, Guo X, Ji H, Yu G, Gao P. Gallstones in Patients with Chronic Liver Diseases. BioMed Res Int. 2017;2017:9749802.
- Ali SA, Donahue RM, Qureshi H, Vermund SH. Hepatitis B and hepatitis C in Pakistan: prevalence and risk factors. Int JInfect Dis. 2009;13(1):9-19.
- Shah SI, Shah S, Hannan A. Hepatitis C-a risk factor for gallstone disease. J Ayub Med Coll Abbottabad. 2014;26(1):84-7.
- Zhang F-M, Chen L-H, Chen H-T, Shan G-D, Hu F-L, Yang M, et al. Hepatitis C Virus Infection Is Positively Associated with Gallstones in Liver Cirrhosis. Digestion. 2016;93(3):221-8.
- Li X, Wang Z, Wang L, Pan M, Gao P. Liver cirrhosis: a risk factor for gallstone disease in chronic hepatitis C patients in China. Medicine. 2017;96(26):e7427.
- Acalovschi M. Gallstones in patients with liver cirrhosis: incidence, etiology, clinical and therapeutical aspects. World J Gastroenterol. 2014;20(23):72-77.
- Chang TS, Lo SK, Shyr HY, Fang JT, Lee WC, Tai DI, et al. Hepatitis C virus infection facilitates gallstone formation. Journal of gastroenterology and hepatology. 2005;20(9):1416-21.
- Mogahed M, El-Atrebi KA, Elwakeel B, Ghanem N. Prevalence of gallstone disease in egyptian patients with hepatitis c virus infection. AAMJ. 2014;12(1):257-65.
- Fornari F, Civardi G, Buscarini E, Cavanna L, Imberti D, Rossi S, et al. Cirrhosis of the liver. DigDis Sci. 1990;35(11):1403-8.
- Dai C-Y, Lin C-I, Yeh M-L, Hsieh M-H, Huang C-F, Hou N-J, et al. Association between gallbladder stones and chronic hepatitis C: ultrasonographic survey in a hepatitis C and B hyperendemic township in Taiwan. Kaohsiung JMedSci. 2013;29(8):430-5.
- Loriot MA, Bronowicki JP, Lagorce D, Lakehal F, Persico T, Barba G, et al. Permissiveness of human biliary epithelial cells to infection by hepatitis C virus. Hepatology. 1999;29(5):1587-95.
- Cacoub P, Comarmond C, Domont F, Savey L, Desbois AC, Saadoun D. Extrahepatic manifestations of chronic hepatitis C virus infection. TherapeutAdvInfect Dis. 2016;3(1):3-14.
- Cacoub P, Gragnani L, Comarmond C, Zignego AL. Extrahepatic manifestations of chronic hepatitis C virus infection. Dig Liver Dis. 2014;46:S165-S73.
- Park JH, Kim TN, Lee SH. The prevalence and risk factors of gallstones in Korean patients with liver cirrhosis. Hepatogastroenterology. 2013;60(123):461-5.
- Stroffolini T, Sagnelli E, Mele A, Cottone C, Almasio P. HCV infection is a risk factor for gallstone disease in liver cirrhosis: an Italian epidemiological survey. JViralHepat. 2007;14(9):618-23