Int. J. Curr. Res. Med. Sci. (2017). 3(3): 5-13

International Journal of Current Research in Medical Sciences

ISSN: 2454-5716

P-ISJN: A4372-3064, E -ISJN: A4372-3061

www.ijcrims.com

Original Research Article

Volume 3, Issue 3 -2017

DOI: http://dx.doi.org/10.22192/ijcrms.2017.03.03.002

Prevalence of Hepatitis C in alcoholic liver disease.

Krishan Oberoi[*] Bhupinder Singh[**], Sat Pal Aloona[**] N.S. Neki[***]

*Associate Professor **Assistant Professor ***Professor, Department of Medicine, Govt. Medical College and Guru Nanak Dev Hospital, Amritsar, 143001, India.

Corresponding author: **Dr. N.S. Neki,** Professor of Medicine, Govt. Medical College and Guru Nanak Dev Hospital, Amritsar, India

E-mail: *drneki123@gmail.com*

Abstract

Alcohol consumption and hepatitis C virus (HCV) infection have a synergic hepatotoxic effect, and the coexistence of these factors increases the risk of advanced liver disease. The main mechanisms of this effect are increased viral replication and altered immune response, although genetic predisposition may also play an important role. Traditionally, HCV prevalence has been considered to be higher (up to 50%) in alcoholic patients than in the general population. Due to the toxic combined effect of HCV and alcohol, patients with HCV infection should be screened for excessive ethanol intake. Patients starting treatment for HCV infection should be specifically advised to stop or reduce alcohol consumption because of its potential impact on treatment efficacy and adherence and may benefit from additional support during antiviral therapy. This recommendation might be extended to all currently recommended drugs for HCV treatment. In Our study on 194 patients of ALD, we found anti Hcv ab was positive in 18.6% of patients of ALD. Most of cases had developed cirrhosis and its complications. Of all Anti HCV Ab positive patients 55.6% presented with Gastrointestinal bleeding and 46.7% with Hepatic encephalopathy. The mean value of SGOT and SGPT were significantly higher in Anti HCV Ab positive patients as compared to Anti Hcv ab negative patients. The study concluded that alcoholics who are Anti HCV Ab positive are more prone to develop cirrhosis of liver with its various complication

Keywords: ALD Alcoholic Liver Disease, HCV Hepatitis C Virus, Anti Hcv Ab Anti Hepatitis C Antibodies.

Introduction

The relationship between alcohol consumption and hepatitis C virus (HCV) infection has been a high-activity focus of investigation for decades. The first studies addressing this association, published in the early 1990s, showed an increased prevalence of HCV antibodies in alcoholic patients, with up to 30%-40% prevalence of chronic HCV infection reported in this population. These high figures decreased in subsequent years, and our study has documented an estimated average weighted prevalence of HCV infection of 18.6% among alcoholics. Nevertheless, this prevalence is much higher than in the general population, reported to be about 1.5%-2%[1,2],although HCV prevalence is expected to decrease dramatically due to the availability of

new treatment[3], the association of HCV with alcohol consumption still represents a problem of great relevance. In patients with chronic HCV infection, alcohol consumption is a well-known risk factor for progression to advanced forms of liver disease and cirrhosis[4]; it also increases the

risk of developing hepatocellular carcinoma (HCC)[5]. Indeed, HCV infection and alcoholic liver disease (ALD) are the two main causes of liver transplantation in developed countries, and the coexistence of these diagnoses is linked to 10%-14% of cirrhosis cases and 8%-10% of liver transplant.

The development of in vivo models to study the pathophysiological mechanisms underlying the interaction between alcohol consumption and HCV infection represents a major challenge because of methodological and technical problems. Thus, although a synergic hepatotoxic effect appears to explain the negative consequences of the interaction between alcohol and HCV in the liver[6]. The amount of alcohol consumption necessary to increase the risk of ALD in patients with HCV infection also remains unknown. Some studies have found that 30-40 g alcohol per day increased the risk of liver disease progression[7.8], but other authors have suggested that larger amounts (approximately 80-120 g/d) are necessary to produce this effect. In any case, many studies have analyzed potential mechanisms of liver damage by the combined effects of HCV and alcohol, which may be summarized as follows.

Alterd cell – mediated immunity: Several studies have demonstrated that both alcohol and HCV can alter the differentiation and function of host dendritic cell [9-11]. Alcohol modifies the antigen-presenting function and diminishes the host response to viral peptides in hepatic cells, such as NS5 protein. Alcohol consumption may thus favor HCV evasion from immune response[11].

Incerased oxidative stress: Chronic ethanol intake increases oxidative stress through several pathways. For instance, alcohol up-regulates the expression of cyclooxygenase 2 (COX-2), which is closely related to augmented oxidative stress and free oxygen radical production [12]. HCV also increases COX-2 expression; thus, this common pathway can amplify liver damage. Furthermore, toxic effects of alcohol on mitochondrial function may inhibit cellular regeneration in the live[13,14], and HCV core proteins can also cause mitochondrial damage through free oxygen

radical generation[15].Incrased viral replication: Some in *vitro* hepatocyte studies have demonstrated an increase in HCV replication with alcohol exposure[16,17], although this effect has not been demonstrated clearly in humans. Indeed, a meta-analysis performed in 2005 reported no increase in HCV RNA levels in the blood of patients with chronic alcohol consumption[18]. Recent evidence has suggested that miR-122 facilitates the replication of HCV and that alcohol induces up-regulation of this micro-RNA, thereby promoting HCV replication[19,20]. These observations highlight the potential relevance of micro-RNA in alcohol-induced organ damage.

Liver steatosis: Most heavy drinkers develop liver steatosis and it is also known that HCV infection is associated with liver steatosis[21]. Further, non-alcoholic fatty liver disease is the main cause of chronic liver disease in developed countries[22]. The concomitant presence of ethanol, HCV infection and steatosis is associated with liver fibrosis and is able to accelerate the development of advanced liver damage[8,23].Liver iron is increased in patients with ALD and, to a lesser extent, in patients with HCV chronic infection[24,25]. Iron overload is associated with increased liver inflammatory response due to the production of reactive oxygen species and may impair immune response against HCV virus infection. Therefore, it is a key mechanism of liver injury among patients with HCV infection and excessive ethanol consumption[26].

The susceptibility to advanced liver disease due to ethanol intake or HCV infection is known to be influenced by genetic factors. The identification of genetic variants associated with the development of liver disease due to the combined effects of ethanol and HCV would thus be of interest, as it could provide insight into the pathophysiology of alcohol-HCV interaction and

help to identify high-risk patients. Many studies have separately analyzed genetic susceptibility to these two forms of liver disease, and their findings enable the identification of common genetic factors involved in liver disease progression due to alcohol or HCV.

In this regard, many allelic variants, including single nucleotide polymorphisms (SNPs), have been analyzed, but only one genetic variant has been shown to clearly influence the risk of both ALD and HCV-induced liver damage. Namely, the rs738409 SNP in the adiponutrin or patatin-like phospholipase domain containing 3 (PNPLA3) gene has been associated in several meta-analyses with ALD[27], fibrosis progression in HCV-infected patients[28], and HCC in patients with cirrhosis due to HCV infection and/or alcohol consumption.

Aims and Objectives

1. To determine the prevalence of infection with hepatitis C in patients of alcoholic liver disease by the presence of anti hcv ab
2. To know the relationship of HCV infection with the severity of alcoholic liver disease in chronic alcoholics.
3. To know the incidence of alcoholic cirrhosis in patients with HCV infection.

Materials and Methods

The present study was carried out in the Department of Medicine, Guru Nanak Dev Hospital,Government Medical college, Amritsar. This study was conducted from patients reporting to various Medicine wards of Guru Nanak Dev Hospital, Amritsar. A written informed consent was taken from all the patients or the surrogate informer of the patients prior to include them in the study. The patients were evaluated under the following clinical criteria and investigative procedure:

- History of alcohol intake 80 g per day for 10 years.
- History of pain in right hypochondrium.
- History of constitutional symptoms i.e. anorexia, nausea, vomiting, malaise.
- History suggested of alcoholic cirrhosis i.e.ascites, bruising , increasing weakness and fatigue , progressive jaundice , palmar erythema, spider naevi and features of portal hypertension .
- History of forgetfulness, tremors, fits, altered level of consciousness.
- Evidence of alcoholic liver disease on ultrasound examination which can be in the form of fatty liver, alcoholic hepatitis or cirrhosis.
- All the subjects undergone the following investigations:
- Hb , TLC , DLC
- . Serum bilirubin, SGOT, SGPT and Serum alkaline phosphatase
- Blood sugar
- Blood urea,Serum Creatinine
- Ultrasonograohy of abdomen for hepatobiliary system and evidence of portal hypertension.

Methods : Detection of Antibodies to Hepatitis C – For this Hcv antigens are immobilized on a porous immunofiltration membrane.Sample and the reagents pass through the membrane and are absorbed into the underlying absorbent pad. As the patient's sample passes through the membrane, HCV antibodies if present in serum/plasma, bind to the immobilized antigens. In the next step, the protein- conjugate is added which binds to HCV antibodies to give distinct colour.

The data from study was analysed according to standard statistical methods.

Observations

The present study was done in 194 patients of ALD who reported to various medical wards of Guru Nanak Dev Hospital, Amritsar. All the patients who were having alcoholic liver disease were males.

Table 1: showing distribution of duration of alcohol intake.

Duration of alcohol intake	No. of patients	Percentage
Upto 10 years	61	31.2
10-20 years	109	56.4
>20 years	24	12.4
Total	194	100

109(56.4%) were taking alcohol for a period 10-20 years.

Table 2: showing amount of alcohol intake in patients of alcoholic liver disease

Amount of alcohol intake	Number of patients	Number of patients
Upto 80g	67	34.5
80-100 gm	87	44.8
>100gm	40	20.6
Total	194	100

It was observed in the study that most of the patients 87(44.8%) were taking 80-100 g of alcohol daily whereas 67 (34.5%) patients were taking alcohol upto 80 g /day and 40(20.6%) patients were taking >100g/day.

Table 3: showing pattern of ultrasound findings in ALD.

Ultrasound scan abnormality	No. of subjects	Percentage%
No abnormality	2	1
Fatty liver	39	20.1
Cirrhosis	153	78.9
Total	194	100

It was observed that in total of 194 patients the most common abnormality noted on ultrasound scan of all ALD patients was cirrhosis of liver 153 (78.9%), whereas fatty liver in the remaining 39(20.1%).

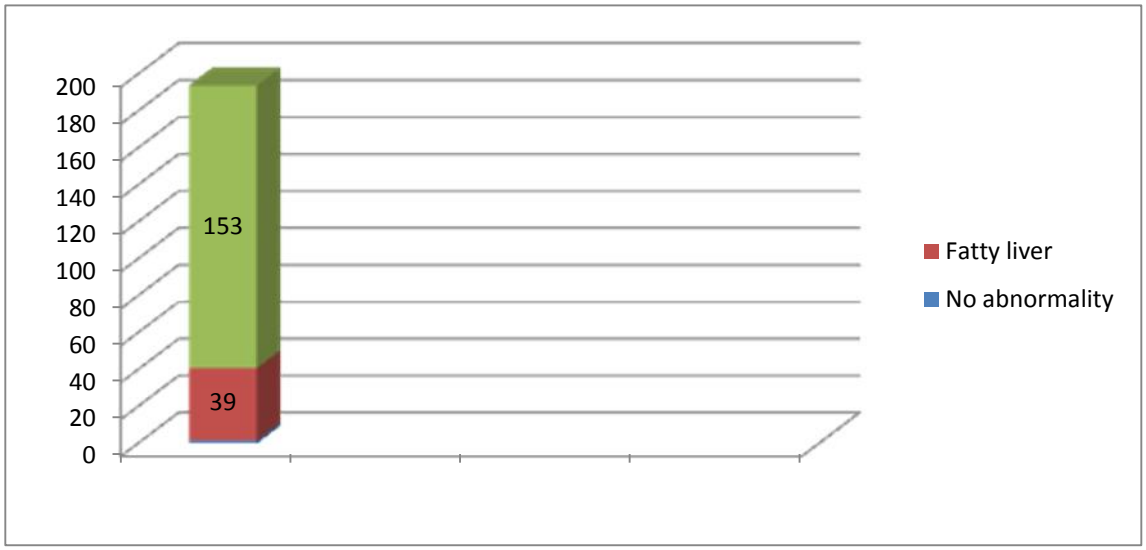

Table 4: Showing Percentage of Anti HCV Ab Positive patients among patients of ALD.

Anti HCv Ab	Number of patients	Percentage%
Positive	36	18.6%
Negative	158	81.4%
Total	194	100

It was observed that among 194 patients admitted with ALD with no previous history of viral infection, 36(18.6%]patients showed positive results for anti Hcv ab while 158(81.4%) were seronegative.

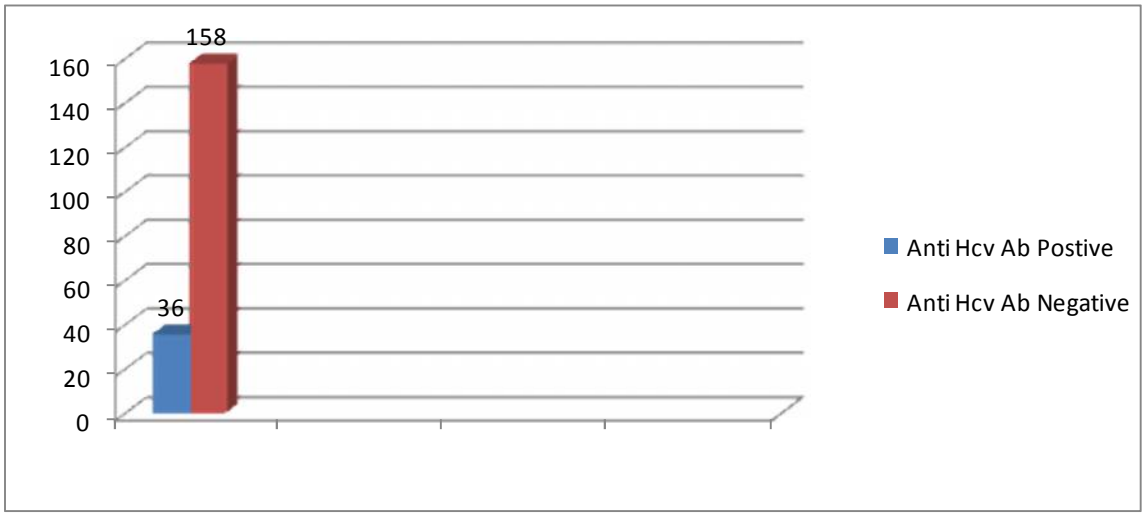

Table 5. Showing relationship of various presentations of ALD on ultrasound with anti HCV Ab

Ultrasound finding	Number of patients	Percentage
Fatty liver	3	8.3[3/36]
Cirrhosis of liver	33	91.7[33/36]
Total	36	100

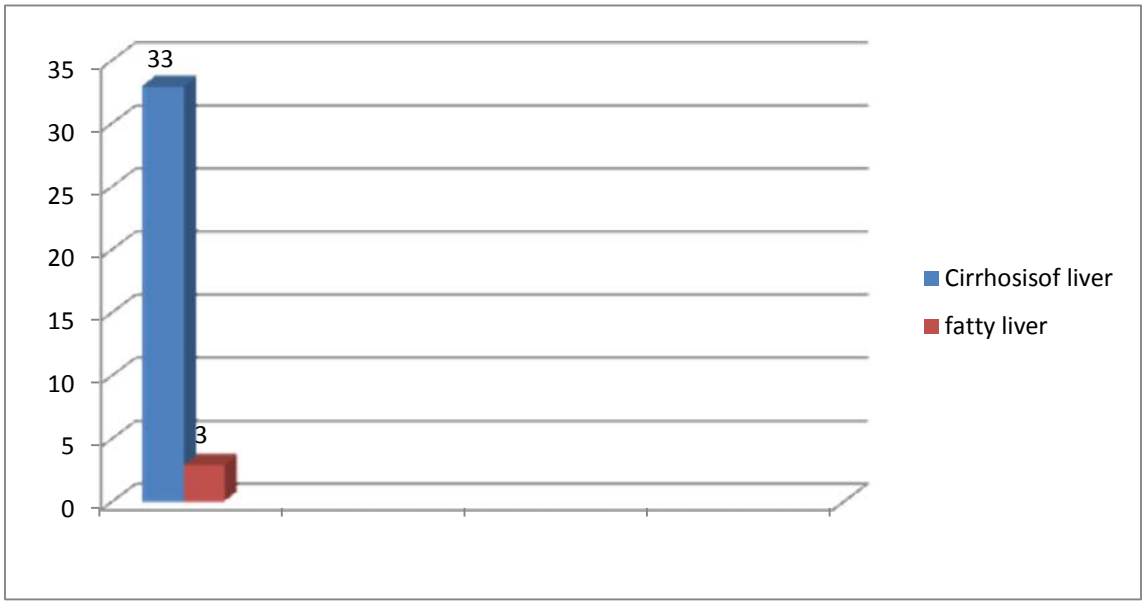

Table 6. showing clinical presentation in HCV Positive patients.

Complication	Number of patients	Percentage
GI Bleeding	20	55.6
Ascites	24	66.7
Hepatic encephalopathy	24	66.7

Ascites and encephalopathy were seen in 66.7% of HCV positive patients

Table 6. showing distribution of liver function tests in HCV positive patients.

Liver function tests	Anti -Hcv Ab positive	Seronegative patients
SGOT	144.97 IU/L	62.52 IU/L
SGPT	113.75 IU/L	54.41 IU/L
Serum bilirubin	3.08mg%	2.01 mg%
PTI	73.42%	78.86%

It was observed that the mean value of SGOT,SGPT and Serum bilirubin in patients who were HCv positive was significantly higher than those who were negative for the antibody (p value <0.005) . There was not any significant difference in the values of PTI in both groups.

Discussion

The results of the present study on prevalence of viral hepatitis C in ALD shows that serum marker for viral hepatitis c was present in 18.6% of patients with alcoholic liver disease. The results of this study more or less resemble some of earlier studies done in the patients of alcoholic liver disease are almost similar done earlier. Varga et al[29] reported the prevalence of 12.55%, Gonalez et al[30] reported 6.7%, Befritis et al[31] reported 14%, in another study by Curciarello et al [32] they reported the prevalence of 20% in alcoholic patients. A study done in Amritsar in patients of chronic liver disease showed that twenty percent of samples were positive for HBsAg and thirteen percent positive for antibodies against HCV[33]. However the prevalence of this study is not consistent with the some of the earlier studies which have reported higher prevalence of Anti Hcv Ab in subjects with alcoholic liver disease. Chang et al[34] reported prevalence of 30.9%, Coeliholitte et al [35] reported 43% prevalence . Sata et al [36] reported 55.5% and Dalekos et al [37] reported the prevalence of 27-42% in Greek population

The patients in this study who had proven cirrhosis on ultrasound scan were having Anti HCV Ab prevalence of 21.6%, it is consistent with the study by Chang et al[34] which reported the prevalence of 29.6% and Gonalez et al[30] which reported prevalence of 16.7%. .

This study also shows that the mean values of SGOT and SGPT was significantly higher ($p<0.05$) in patients who were anti-HCV Ab positive as compared to the patients who were negative for these tests, these findings are very much consistent with those of Chang et al[34] as they have also reported that SGOT levels were higher among alcoholic patients who were either HBsAg or anti-HCV Ab positive. Saigal et al[38] had also found similar results as both SGOT and SGPT were higher in HBsAg and anti-HCV Ab positive patients than those who were negative for both these markers. It was also observed in the study that the complications of hepatic encephalopathy and GI bleeding were significantly higher ($p<0.005$) who were Anti HCV Ab positive than who were negative. It is observed that ALD is more severe as judged clinically, biochemically and radiologically in those alcoholics who are Anti HCV Ab positive. So it is suggested that the persons who are Anti HCV Ab positive should refrain from consuming alcohol as the chances of development of cirrhosis and further complications are more in these patients as compared to those who are negative for Anti HCV Ab.

Conclusion

The present study included 194 patients with history of alcohol intake of more than 8 years,the following observations were made:

1. 36 (18.6%) patients showed positive results while 158 (81.4%) patients were seronegative. So the prevalence of Hepatitis c virus is 18.6% in patients with alcoholic liver disease. In case of Anti Hcv Ab positive patients , 33 (91.7%) had cirrhosis and 3 (8.3%) patient had fatty liver on ultrasound.

2. Of all the Anti Hcv Ab positive patients, 20 (55.6%) patients were having evidence of gastrointestinal bleed, however ascites was present in 24 (66.7%) patients. 24 (66.7%) patients presented with hepatic encephalopathy as the major complication. Some patients presented with more than one complication.

3. The mean value of SGOT in patients who were Anti Hcv Ab positive (144.97) was significantly higher than those who were negative for this antigen(p value<0.005), similarly the mean value of SGPT was also significantly higher in positive (113.75) patients than negative patients ($p<0.005$).

So it is clear from this study that alcoholics are more prone to have infection with Hepatitis C as compared to the non alcoholics. The alcoholics who are Anti Hcv Ab positive are more prone to develop cirrhosis of liver with its various complications.

Source of funding: Nil

Conflict of interest: None declared.

References

1.Bruguera M, Forns X. [Hepatitis C in Spain] Med Clin (Barc) 2006;127:113–117.
2.Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. Ann Intern Med. 2006;144:705–714.
3. Wandeler G, Dufour JF, Bruggmann P, Rauch A. Hepatitis C: a changing epidemic. Swiss Med Wkly. 2015; 145:w14093.
4. Hutchinson SJ, Bird SM, Goldberg DJ. Influence of alcohol on the progression of hepatitis C virus infection: a meta-analysis. Clin Gastroenterol Hepatol. 2005; 3:1150–1159.
5. Donato F, Tagger A, Chiesa R, Ribero ML, Tomasoni V, Fasola M, Gelatti U, Portera G, Boffetta P, Nardi G. Hepatitis B and C virus infection, alcohol drinking, and hepatocellular carcinoma: a case-control study in Italy. Brescia HCC Study. Hepatology. 1997;26:579–584. .
6. Hassan MM, Hwang LY, Hatten CJ, Swaim M, Li D, Abbruzzese JL, Beasley P, Patt YZ. Risk factors for hepatocellular carcinoma: synergism of alcohol with viral hepatitis and diabetes mellitus. Hepatology. 2002;36:1206–1213.
7. Wiley TE, McCarthy M, Breidi L, McCarthy M, Layden TJ. Impact of alcohol on the histological and clinical progression of hepatitis C infection. Hepatology. 1998; 28:805–809.
8. Bedogni G, Miglioli L, Masutti F, Ferri S, Castiglione A, Lenzi M, Crocè LS, Granito A, Tiribelli C, Bellentani S. Natural course of chronic HCV and HBV infection and role of alcohol in the general population: the Dionysos Study. Am J Gastroenterol. 2008;103:2248–2253.
9. Laso FJ, Vaquero JM, Almeida J, Marcos M, Orfao A. Chronic alcohol consumption is associated with changes in the distribution, immunophenotype, and the inflammatory cytokine secretion profile of circulating dendritic cells. Alcohol Clin Exp Res. 2007;31:846–854.
10. Aloman C, Gehring S, Wintermeyer P, Kuzushita N, Wands JR. Chronic ethanol consumption impairs cellular immune responses against HCV NS5 protein due to dendritic cell dysfunction. Gastroenterology. 2007;132:698–708.

11. Szabo G, Aloman C, Polyak SJ, Weinman SA, Wands J, Zakhari S. Hepatitis C infection and alcohol use: A dangerous mix for the liver and antiviral immunity. Alcohol Clin Exp Res. 2006;30:709–719.
12. Trujillo-Murillo K, Alvarez-Martínez O, Garza-Rodríguez L, Martínez-Rodríguez H, Bosques-Padilla F, Ramos-Jiménez J, Barrera-Saldaña H, Rincón-Sánchez AR, Rivas-Estilla AM. Additive effect of ethanol and HCV subgenomic replicon expression on COX-2 protein levels and activity. J Viral Hepat. 2007;14:608–617.
13. Wang T, Weinman SA. Causes and consequences of mitochondrial reactive oxygen species generation in hepatitis C. J Gastroenterol Hepatol. 2006;21 Suppl 3:S34–S37.
14. Duguay L, Coutu D, Hetu C, Joly JG. Inhibition of liver regeneration by chronic alcohol administration. Gut. 1982;23:8–13.
15. Otani K, Korenaga M, Beard MR,et al. Hepatitis C virus core protein, cytochrome P450 2E1, and alcohol produce combined mitochondrial injury and cytotoxicity in hepatoma cells. Gastroenterology. 2005;128:96–107.
16. Zhang T, Li Y, Lai JP, Douglas SD, Metzger DS, O'Brien CP, Ho WZ. Alcohol potentiates hepatitis C virus replicon expression. Hepatology. 2003;38:57–65.
17. McCartney EM, Beard MR. Impact of alcohol on hepatitis C virus replication and interferon signaling. World J Gastroenterol. 2010;16:1337–1343.
18. Anand BS, Thornby J. Alcohol has no effect on hepatitis C virus replication: a meta-analysis. Gut. 2005;54:1468–1472.
19. Bukong TN, Hou W, Kodys K, Szabo G. Ethanol facilitates hepatitis C virus replication via up-regulation of GW182 and heat shock protein 90 in human hepatoma cells. Hepatology. 2013;57:70–80.
20. Hou W, Bukong TN, Kodys K, Szabo G. Alcohol facilitates HCV RNA replication via up-regulation of miR-122 expression and inhibition of cyclin G1 in human hepatoma cells. Alcohol Clin Exp Res. 2013;37:599–608.
21. Zekry A, McHutchison JG, Diehl AM. Insulin resistance and steatosis in hepatitis C virus infection. Gut. 2005;54:903–906.
22. Blachier M, Leleu H, Peck-Radosavljevic M, Valla DC, Roudot-Thoraval F. The burden of liver disease in Europe: a review of available epidemiological data. J Hepatol. 2013;58:593–608.
23. Clouston AD, Jonsson JR, Powell EE. Steatosis as a cofactor in other liver diseases: hepatitis C virus, alcohol, hemochromatosis, and others. Clin Liver Dis. 2007;11:173–189, x.
24. Kohgo Y, Ohtake T, Ikuta K, Suzuki Y, Hosoki Y, Saito H, Kato J. Iron accumulation in alcoholic liver diseases. Alcohol Clin Exp Res. 2005;29:189S–193S.
25. Sebastiani G, Vario A, Ferrari A, Pistis R, Noventa F, Alberti A. Hepatic iron, liver steatosis and viral genotypes in patients with chronic hepatitis C. J Viral Hepat. 2006;13:199–205.
26. Purohit V, Russo D, Salin M. Role of iron in alcoholic liver disease: introduction and summary of the symposium. Alcohol. 2003;30:93–97.
27. Chamorro AJ, Torres JL, Mirón-Canelo JA, González-Sarmiento R, Laso FJ,. Systematic review with meta-analysis: the I148M variant of patatin-like phospholipase domain-containing 3 gene (PNPLA3) is significantly associated with alcoholic liver cirrhosis. Aliment Pharmacol Ther. 2014;40:571–581.
28. Singal AG, Manjunath H, et al. The effect of PNPLA3 on fibrosis progression and development of hepatocellular carcinoma: a meta-analysis. Am J Gastroenterol. 2014; 109: 325–334.
29. Varga L et al : Hepatitis B and C markers in alcoholic liver disease . J Gastroentro/Hepatol . 1994;9[4] :381-84
30. GonalezQuintela A et al ;Hepatitis C virus antibodies in alcoholic patients Eur J Ggastroentrol Hepatol . 1995 ; 7[4] :331-32
31. Befritis R, HedmanM Et al ; Chronic Hepatitis C in alcoholic patients ;prevalence , genotype and correlation to liver disease . Alcohol Clin Exp Res 1995;19[5] 1173-76

32. Curciarello J , Apraiz M et al . Hepatitis B and C virus in chronic alcoholic patients; prevalence and influence on liver injury. Alcohol Alcohol ; 1997;32 [2] :103 -11
33. Arora U, Mann A. Prevalence of Hepatitis B Virus, Hepatitis C virus and HIV in patients of chronic liver disease in Amritsar JIACM 2007;8(1):29-31.
34. Chang TT, Lin CY, Chow NH, HsuPI, Yang CC, Lin XZ. Hepatitis B and C virus infection among chronic alcoholic patients with liver disease in Taiwan. Alcohol Alcohol. 1994;29(1);75
35. Chevillotte G, Dvtbec JP, Gerolami A. Interaction between HBV and alcohol consumption in liver cirrhosis. Gastroenterology. 1983; 85(1): 141-45.
36 Sata M Fukuizumi K et al . Hepatitis B and C infection in patients with clinically diagnosed alcoholc liver disease J Virol Hepat . 1996 3[3] ;143-148
37. Dalekos GN ,Zervou E et al . Prevalence of hepatitis B and C virus infection in chronic alcohlics with and without liver disease in loannina , Greece ; low incidence of HCV infection .J Gastroentrol hepatol. 1996 11[2] 187-92
38. Saigal S,Kapoor D, Tandon N,Thakur V,Gupta RC,Aggarwal SR,Sarin SK.High sero prevalence and clinical significance of Hepatitis B and C Infection in hospitalised patients with alcoholic cirrhosis. JAPI 2002; 50:999-1000.

Access this Article in Online	
Quick Response Code	Website: www.ijcrims.com
	Subject: Epidemiology

How to cite this article:
Krishan Oberoi, Bhupinder Singh, Sat Pal Aloona N.S. Neki. (2017). Prevalence of Hepatitis C in alcoholic liver disease. Int. J. Curr. Res. Med. Sci. 3(3): 5-13.
DOI: http://dx.doi.org/10.22192/ijcrms.2017.03.03.002