Original Article

Diversity of Presentations In Decompensated Chronic Liver Disease Due To HCV

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ABSTRACT

Background: An estimated 170 million people worldwide suffer from HCV infection. Chronic hepatitis C virus (HCV) infection is often a clinically silent infection presenting many years after with complications related to decompensation, so. **Objective:** To emphasize the role of early detection and intervention in preventing complications of HCV related chronic liver disease. **Materials And Methods**: Newly diagnosed decompensated chronic liver disease (CLD) due to HCV infection presenting to respective hospitals during 2010. **Study design:** observational multicentre study. **Results:** Out of 340 new cases of decompensated chronic liver disease due to hepatitis C virus. 190 (56%) were females and 150 (54%) were male. In terms of presentation, patients were having overlapping symptoms and signs like ascites, jaundice, upper GI bleed and encephalopathy. 220 (64.7%) had clinical ascites, 70 (20.5%) had spontaneous bacterial peritonitis, 130(38.2%) had altered conscious level and150 (44.1%) had upper GI bleed. It was inferred from history that 170(50%) patients with Hepatitis C were detected while being investigated for complaints other than liver disease. Other presentations included jaundice in 10(2.9%) 50 (14.7%) with previous upper GI bleed, 80 (23.5%) with CLD, 10 (2.9%) with epigastric discomfort and 20 (5.8%) had altered conscious level. 235 (69.1%) with Child's Score B and 105(30.4%) with Child's Score C.**Conclusion:** Majority of patients become aware only when complications set in. Early detection and interventions should be stressed because the available treatment options for the complications are beyond the reach of majority of patients and don't have a permanent solution.

Key Words. HCV, CLD, decompensated

INTRODUCTION

Hepatitis C is rapidly emerging as a major health problem in developing countries including Pakistan. There is a high frequency of HCV seropositive individuals of both sexes among patients referred for chronic liver disease from different parts of Pakistan both urban and rural and among all socioeconomic classes. [1,7] An estimated 170 million people worldwide suffer from HCV infection. [8,9] Acute hepatitis C virus (HCV) infection is often a clinically silent infection, and is therefore rarely detected. A high index of clinical suspicion in addition to careful serological and virological assessment is required to identify the disease, and to determine the eventual clinical outcome after primary infection; the minority of acutely infected individuals spontaneously controls viremia in long term whilst the majority becomes chronically infected. It becomes very important to diagnose these silent and more than often ignorant victims at early stages.[10,11] We decided to evaluate the patients presenting with decompensated chronic liver disease due to HCV infection on different parameters so that some recommendations for prevention and early intervention can be inferred from this experience.

MATERIALS AND METHODS

This multicenter study was carried out at Medical Unit II Allied Hospital Faisalabad and respective hospitals of the contributors, from 1st

January 2010 to 31st December 2010, on patients presenting for routine consultancy or as emergency. Diagnosis of decompensated CLD was confirmed through clinical examination, available record and fresh relevant investigations. All the data was recorded on prescribed proforma.

INCLUSION CRITERIA

Any patient fulfilling the diagnostic criteria of decompensated CLD due to HCV

EXCLUSION CRITERIA

Decompensated CLD due to any cause other than HCV, Coinfection or superinfection with other hepatitis virus and associated alcoholism or metabolic diseases contributing to cirrhosis

STUDY DESIGN

Observational multicenter study

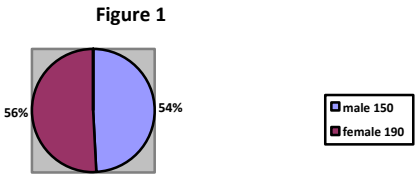
Place of Study

Medical Unit II Allied Hospital Faisalabad and respective hospitals of the contributors

RESULTS

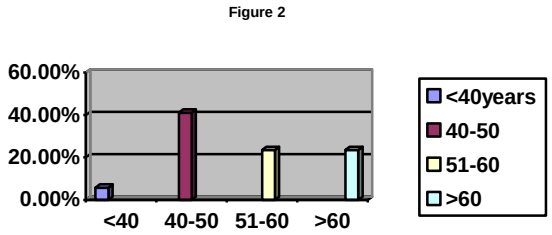
We had 340 new cases of decompensated chronic liver disease due to hepatitis C virus. 190 (56%) were females and 150 (54%) were male.

Figure-1
Percentage of Male and Female Patients presenting with Decompensated Cirrhosis of Liver due to HCV



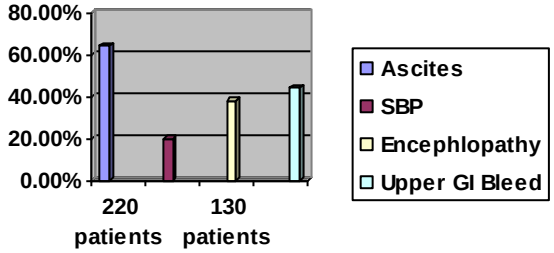
20 (5.8%) patients were below 40 years of age, 100 (29.4%) were 40-50 years, 140(41.1%) were 51-60 years and 80 (23.5%) were above 60 years.

Figure-2
Age wise presentation of Patients of decompensated cirrhosis of liver due to HCV



In terms of presentation 220 (64.7%) had clinical ascites, 70 (20.5%) had spontaneous bacterial peritonitis, 130(38.2%) presented due to altered conscious level and150 (44.1%) had evidence of upper GI bleed.

Figure-3
Various modes of presentations in Decompensated Cirrhosis of Liver due to HCV



It was inferred from history that Hepatitis C was detected on routine investigations in 170 (50%) patients, 10(2.9%) patients were detected while being investigated for clinical jaundice, 50 (14.7%) were detected while being investigated for previous upper GI bleed, 80 (23.5%) were detected while being investigated for CLD, 10 (2.9%) were detected while being investigated for epigastric discomfort and 20 (5.8%) were detected while being investigated for altered conscious level. When these patients were examined, palmer erythema 290(85.2%), ascites 220(64.7%), splenomegaly 200(58.8%), pitting ankle edema, 180(52.9%) hepatomegaly, 150 (44.1%) jaundice, 140 (41.1%) altered conscious level, were the commonest clinical findings. Breast atrophy 50(14.7%), spider angiomas,

and gynecomastia, each 40(11.7%), purpuric spots 20 (5.8%) and scratch marks 10(2.9%) were the less common signs in descending order. When Childs Score was assigned after relevant investigations, there were 235 (69.1%) with Score B and 105(30.4%) with Score C.

DISCUSSION

Hepatitis C is rapidly emerging as a major health problem in developing countries including Pakistan. There is a high frequency of HCV seropositive individuals of both sexes among patients referred for chronic liver disease from different parts of Pakistan.[1] Patients educational level has a strong influence on their awareness about the cause, organ of involvement, prevalence in society, presentation, and vaccination for Hepatitis B and treatment of these diseases. [1] Among medical and dental students of Lahore, 1.1% was positive for HBsAg and 2.1% were positive for HCV antibodies. [3] There is very high frequency of hepatitis B and C in general rural population of central Sindh and among healthy male army/naval recruits compared to other areas of Pakistan.[4,5] Similarly in India, HCV is a significant cause of chronic liver disease although HBV infection continues to account for the largest proportion of cases.[6] The global epidemiology of hepatitis B and C demonstrates a predominantly declining prevalence of the diseases. Improvement in the control of hepatitis B has been largely achieved with implementation of a more universal HBV vaccine program, although a large gap still remains in the effort toward global prevention of hepatitis B. The transmission of hepatitis C has been greatly impacted by mandatory screening of blood donors in most countries, although intravenous drug use continues to be a major source of infection. Public education regarding the risks of exposure to infected paraphernalia as well as household items such as razors is necessary in the continuing effort to curb this disease. [7] An estimated 170 million people worldwide suffer from HCV infection. According to one study from Ireland, which compares well with other European and north American figures, the predominant genotypes were 1b (33%), 3a (28%) and 1a (26%). Most patients (78%) were asymptomatic at the time of detection and only four (7%) gave a history of jaundice. [8, 9] Acute hepatitis C virus (HCV) infection is often a clinically silent infection, and is therefore rarely detected. A high index of clinical suspicion in addition to careful serological and virological assessment is required to identify the disease, and to determine the eventual clinical outcome after primary infection; the minority of acutely infected individuals spontaneously controls viremia in long term whilst the majority becomes persistently infected. Host factors including gender, age at time of infection, prior resolution of infection, symptomatic infection, host immune responses, and viral factors such as the nature of the infecting quasispecies and more speculatively viral genotype, are some features that have been correlated with disease outcome. In spite of this, on an individual patient level, it is currently not possible to predict those that will resolve infection. [10]. A significant number of patients present for the first time with decompensated liver disease and a similar proportion are not aware of the disease till late. Mortality in liver disease is related to advance Child-Pugh class. Most patients who died because of upper GI bleed were in Child class C. Upper GI bleed is the single most common cause of mortality in advanced disease. [11] The agent responsible for more than 80% of the parenterally transmitted non-A-non-B hepatitis was designated as hepatitis C virus (HCV). Diagnosis of HCV infection relies on anti-HCV and HCV-RNA detection. Using second-generation assays, diagnostic sensitivity has increased to about 95%, but detection of anti-HCV doesn't distinguish past from present infections. Only rising anti-HCV titers or HCV seroconversion confirm a recent HCV infection. In anti-HCV-negative infections and cases of early acute hepatitis, HCV-RNA detection by RT-PCR represents a valid diagnostic alternative.[12, 13, 14, 15] The HCV genotype should be systematically determined before treatment, as it determines the indication, the duration of treatment, the dose of ribavirin and the virological monitoring procedure. HCV RNA monitoring during therapy is used to tailor treatment duration in HCV genotype 1 infection, and molecular assays are used to assess the end-of-treatment and, most importantly the sustained virological response, i.e. the endpoint of therapy.[16] Only patients with detectable HCV RNA should be considered for pegylated interferon alfa and ribavirin therapy and the HCV genotype should be systematically determined before treatment, as it

determines the indication, the duration of treatment, the dose of ribavirin and the virological monitoring procedure. HCV RNA monitoring during therapy is used to tailor treatment duration in HCV genotype 1 infection, and molecular assays are used to assess the end-of-treatment and, most importantly the sustained virological response, i.e. the endpoint of therapy. [17] A patient's pretreatment HCV viral load and the rate of virus decline during therapy have been shown to correlate with the likelihood of long-term response to antiviral therapy. [18] Oxidative stress has been increasingly implicated in the pathogenesis and progression of cirrhosis. Oxidative stress is associated with the development and progression of cirrhosis. [19] Hepatic fibrosis is the main determinant of clinical outcomes of chronic hepatitis C. Liver histology is frequently considered the gold standard for assessing hepatic fibrosis. However, liver biopsy is associated with sampling error; inter observer variability, and potential complications. Clinical examination is unreliable in differentiating different stages of compensated liver disease. Among the routine laboratory tests, decreased platelet count, increase in the ratio of aspartate to alanine aminotransferase (AST/ALT), and prolonged prothrombin time are the earliest indicators of cirrhosis and portal hypertension. Initial evaluation should focus on assessment of activity and stage of liver disease for prognostication and decisions regarding treatment, and to rule out co-infections and other causes of liver disease. Subsequent follow-up should focus on detection of liver disease progression and the need for treatment. The frequency of monitoring and the tests used will depend on the patient's age, stage of liver disease, and comorbid conditions. [20] Cirrhosis develops in about one third of patients with chronic HCV infection leading to altered architecture and reduced mass along with abnormal function. Different parameters and classifications are used to classify the severity of cirrhosis. These are Fibro Meter, Fibrotest, and Hepascore and aspartate aminotransferase to platelet ratio index (APRI). Observed 100% negative predictive values for severe fibrosis and cirrhosis were, respectively, 15.4, 47.5%, 3.6, 31.9%, 0.3, 24.6%, 1.4, and 5.3% of patients. Using the most accurate original test, cirrhosis can be excluded in 47.5% of patients and is correctly diagnosed, as significant fibrosis, in 100% of patients. [21] Cirrhosis can be divided into 4 stages: stage 1, no varices, no ascites; stage 2, varices without ascites and without bleeding; stage 3, ascites+/-varices; stage 4, bleeding+/-ascites. Yearly mortality ranges from 1% in stage 1 to 57% in stage 4. According to this study, the results compares well with our experience, the yearly incidence of esophageal varices is 5-7%; their rate of enlargement is 10-12% per year. The incidence of variceal bleeding is about 25% at 2 years. Bleeding stops spontaneously in about 50% of cases but early re-bleeding occurs in 30-40% of patients. Bleeding-related mortality has declined over time and is now around 20% at 6 weeks. 2 % patients expired in Child-Pugh Class A, 30% in B and 68%, in Child-Pugh Class C. Of these 54% patients expired due to upper GI bleed, 40%, patients due to sepsis and 6%, with other causes. Most patients who died because of upper GI bleed were in Child class C. [11, 22] In another study, average duration between diagnosis and death was 8 years. Child-Pugh Class C was associated with significantly higher mortality due to upper GI bleed. [23] For assessing prognosis in patients with liver cirrhosis or HCC, there seems little reason to replace the well established Child-Turcotte-Pugh score. [11] **Error! Reference source not found.** Inclusion of serum creatinine can improve the prognostic value of Child-Pugh classification particularly class B in which the serum creatinine play a major role in properly predicting the survival as well as cirrhosis related complications. [24] Although abdominal ultrasound can detect the hepatic and extra-hepatic changes consistent with cirrhosis, its ability to distinguish chronic hepatitis from compensated cirrhosis is limited. Serum markers can rule in or rule out fibrosis in up to 35% of patients but, in individual patients, cannot differentiate the stages of fibrosis reliably. Transient elastography (Fibroscan) is of useful value for the non-invasive diagnosis of cirrhosis. At a cut-off of 21.5 kPa, transient elastography (TE, FibroScan) predicted the presence of OV with 76% sensitivity and 78% specificity and correctly classified 73% of patients. TE is currently the most accurate non-invasive method for early detection of cirrhosis in CHC (cut-off: 12.5 kPa), as compared with other available methods, but cannot replace endoscopy for OV screening. Recently, a more objective scoring classification, the model for

end-stage liver disease (MELD), has been shown to predict accurately the 3-month mortality for cirrhotic patients awaiting transplantation. [22, 25] Campbell and Pugh 5-15 scores correlated closely and can be used interachangeably. As Campbell classification does not contain the more elaborate prothrombin time determination, it probably can be used anywhere in the world. Ascites (degree) and Ascites/Nutritional State (ANS) scoring, only use history and physical examination and are, or remain, although less refined, clinically relevant. [25,26]

CONCLUSION AND RECOMMENDATIONS

HCV infection is more likely to go into chronic phase with possibility of complications. It has a very high worldwide incidence. Most of the time HCV infection remains asymptomatic and is detected very late with complications or symptoms are very vague and non-specific like fatigue, epigastric discomfort, burning hands and feet. This silent killer needs vigilance in screening at primary health care level. Every healthy person must be periodically screened for new infection and at more frequent intervals in high risk groups like medical profession, diabetics, dialysis dependant patients and intravenous drug abusers and addicts. In infected patients proper viral assessment in terms of type and viral load are essential for proper early therapeutic intervention. Once chronicity leads to cirrhosis, proper grading, regular screening for early complications and therapeutic interventions like band ligation for esophageal verices, prevention of Spontaneous Bacterial Peritonitis and dietary modifications like salt and protein restrictions are the mainstay of management.

REFERENCES

1. Khan. TS, Rizvi.F, Rashid.A. Hepatitis C seropositivity among Chronic Liver Disease patients in Hazara, Pakistan. J Ayub Med Coll Abottabad. 2003; 15:53-5.
2. Talpur.AA, Memon.NA, Solangi.RA, Ghumro.AA. Knowledge and attitude of patients towards hepatitis B and C. Pak J Surg 2007; 23:162-5.
3. Bhatti.S, Quraishi.M, Mahmood Z, Javaid K. Seroprevalence of HBsAg and HCV antibodies in healthy individuals of high socioeconomic status.Biomedica 2007; 23:131-3.
4. Altaf.C, Akhtar.S, Qadir.A, Malik.K.Z, Ahmed.P, Tariq.WZ. Frequency of Hepatitis B and C among healthy adult males from Central Sindh.Pak J Pathol 2007; 18:113-5.
5. Malik,N, Butt.T, Mansoor.N, Khan.TG, Akbar.MS, Aslam.M. Percentage of hepatitis B and C among young adult males from interior Sindh. Pak Armed Forces Med J 2008; 58:260-6.
6. Issar SK, Ramakrishna BS, Ramakrishna B, Christopher S, Samuel BU, John TJ.Prevalence and presentation of hepatitis C related chronic liver disease in southern India.J Trop Med Hyg. 1995; 98:161-5.
7. Te HS, Jensen DM. Epidemiology of hepatitis B and C viruses: a global overview. Clin Liver Dis. 2010; 14:1-21.
8. McDougall NI, McCluggage WG, Coyle PV, Sloan JM, Callender ME. Early experience with chronic hepatitis C in Northern Ireland: epidemiology and response to monotherapy. Ulster Med J. 2004; 73:25-31.
9. Matria.C, Gennaro.D, Olga.RR, Prevalence of hepatitis C virus (HCV) genotypes in Central Italy. Anticancer Research, 2003: 5129-5132
10. Fabris P, Fleming VM, Giordani MT, Barnes E. Acute hepatitis C: clinical aspects, diagnosis, and outcome of acute HCV infection. Curr Pharm Des. 2008; 14:1661-5.
11. Shah.NH, Umar.M, Anwar.F, Ishtiaq.O, Bashir.K. Association of Child-Pugh Class with Patterns of Mortality in Hepatitis C Virus Related Chronic Liver Disease. J Rawal Med Coll 2001; 5:65-7.
12. Bonino F, Brunetto MR, Negro F, et.al. Hepatitis C virus infection and disease. Diagnostic problems. J Hepatol. 1993; 17:3:78-82.
13. Pawlotsky JM. Diagnostic tests for hepatitis C. J Hepatol. 1999; 31:1:71-9.
14. Laperche S, Couroucé AM. Development of a biological diagnosis for hepatitis C. Transfus Clin Biol. 1997; 4:291-8.
15. Naz.S, Bhatti.A, Khan.MS. Emerging molecular approaches and their significance in the diagnosis and management of hepatitis C virus infection. Gomal J Med Sci 2007; 5:75-80.

16. Chevaliez S, Pawl otsky JM. Hepatitis C virus: virology, diagnosis and management of antiviral therapy. World J Gastroenterol. 2007 7; 13:2461-6
17. Chevaliez S, Pawlotsky JM. Hepatitis C virus serologic and virologic tests and clinical diagnosis of HCV-related liver disease. Int J Med Sci. 2006; 3:35-40.
18. Podzorski RP. Molecular testing in the diagnosis and management of hepatitis C virus infection.. Arch Pathol Lab Med. 2002; 126:285-90.
19. Bhandari S, Agarwal MP, Dwivedi S, Banerjee BD. Monitoring oxidative stress across worsening Child Pugh class of cirrhosis. Indian J Med Sci. 2008; 62:444-51.
20. Fontana RJ, Lok AS. Noninvasive monitoring of patients with chronic hepatitis C. Hepatology. 2002; 36:57-64.
21. Boursier J, Bacq Y, Halfon P, et.al. Improved diagnostic accuracy of blood tests for severe fibrosis and cirrhosis in chronic hepatitis C. Eur J Gastroenterol Hepatol. 2009; 21: 28-38.
22. Samiullah.S, Qasim.R, Khalid.S, Hussain.GB, Mukhtair.J, Akbar.Y. Evaluation of creatinine-modified Child Pugh score for predicting short-term prognosis of patients with decompensated cirrhosis of liver as compare to original Child Pugh score. J Ayub Med Coll Abottabad 2009; 21:64-7.
23. Choi PC, Kim HJ, Choi WH, et.al. Model for end-stage liver disease, model for end-stage liver disease-sodium and Child-Turcotte-Pugh scores over time for the prediction of complications of liver cirrhosis. Liver Int. 2009; 29:221-6.2008.
24. Lee DH, Son JH, Kim TW. New scoring systems for severity outcome of liver cirrhosis and hepatocellular carcinoma: current issues concerning the Child-Turcotte-Pugh score and the Model of End-Stage Liver Disease. Taehan Kan Hakhoe Chi. 2003; 9:167-79.
25. Farnsworth N, Fagan SP, Berger DH, Awad SS. Child-Turcotte-Pugh versus MELD scores as a predictor of outcome after elective and emergent surgery in cirrhotic patients. Am J Surg. 2004; 188:580-3.
26. Castéra L, Bernard PH, Foucher J, et.al. Early detection in routine clinical practice of cirrhosis and oesophageal varices in chronic hepatitis C: comparison of transient elastography (FibroScan) with standard laboratory tests and non-invasive scores. J Hepatol. 2009; 50:59-68.

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