

Etiological Spectrum of Liver Cirrhosis Patients Presenting to a Tertiary care Hospital in Pakistan

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ABSTRACT

Objectives: To determine the etiological spectrum in patients of Liver cirrhosis presenting to a tertiary care hospital of Pakistan. **Study:** A descriptive case series conducted from December, 2006 to December, 2007 at Services Hospital Lahore. **Patients and Methods:** One hundred patients of liver cirrhosis presenting in emergency or outpatient department of Services Hospital Lahore, were enrolled. Diagnosis of cirrhosis was made by combination of clinical and ultrasonographic findings. ELISA testing for Hepatitis B surface antigen and Hepatitis C virus antibodies was

performed. **Results:** Amongst the 100 patients 59% were male and 41% were females, majority of these had urban (82%) background. The etiology of cirrhosis was mainly viral (83%), out of which 81% had hepatitis C, 1% hepatitis B and 1% both hepatitis B and hepatitis C. The mean age (years) was 55.79 ± 13.545 (SD) and mean weight (kilograms) was 62.49 ± 8.02 ((SD). **Conclusion:** We conclude that etiology of Liver Cirrhosis is mainly Hepatitis C in our areas and males are more vulnerable to acquire.

Key Words: Liver cirrhosis, Hepatitis C

INTRODUCTION

Liver cirrhosis is the end result of hepatocellular injury that leads to both fibrosis and nodular regeneration throughout the liver.¹ Injury to hepatic endothelial cells releases chemokines and other leukocyte chemo-attractants while up regulating the expression of important inflammatory receptors leading to proliferation, loss of vitamin A and synthesis of collagens and laminin, which are key factors for fibrosis.²⁻³ Fibrosis is defined as an excess deposition of the components of extra cellular matrix within the liver. This response to liver injury is reversible. On the other hand, cirrhosis is an irreversible process. Due to fibrosis and areas of regeneration, nodular patterns develop in liver. Diagnosis of cirrhosis, especially in the advanced stage, means ultimate progression to death due to the complications occurring in due course of the disease. It is therefore important to know about the main factors responsible for this condition in order to avoid or remove them before establishment of this deadly disease.⁴ Alcoholism is the commonest cause of cirrhosis worldwide but hepatitis C and B viral

infections are leading causes in Pakistan.⁵ Among the two, Hepatitis C (HCV) has overtaken Hepatitis B (HBV) in the etiogenesis of liver cirrhosis in Pakistan.⁶⁻⁷ The primary source of HCV infection are infected blood or blood products, though sex with infected partner, multiple sexual partners and perinatal exposure are other potential sources of HCV transfusion, sexual transmission between monogamous partners is rare and transmission at the time of delivery is 1 to 5%.⁸⁻¹¹ Additional risk factors for HCV transmission are folk medicine practices such as acupuncture, body piercing, tattooing and even commercial barbering.¹¹ Spontaneous cure of HCV infection occurs in 15 to 45% of patients.¹¹ Out of remaining HCV infected patients 5 to 20% develop cirrhosis over a period of two or more decades.¹²⁻¹³ Old age, male sex, associated alcohol consumption of more than 50gm/day, obesity and HIV co-infection increases the chances of progression to cirrhosis.¹⁴⁻¹⁶ The increasing role of HCV in cirrhosis does not mean to underestimate HBV. It is estimated that 400 million

people worldwide have chronic HBV infection, causing 0.5 to 1.2 million deaths every year and being the 10th leading cause of death worldwide.¹⁷⁻¹⁸ Prevalence of HBV infection varies from 0.1% to 20% in different parts of the world, being 10% in Pakistan.¹⁹⁻²⁰ Although mode of transmission of HBV and HCV resemble each other, sexual transmission and perinatal transmission are more common in HBV infection.^{19, 21} Patients with chronic HBV infection have a 15% to 40% risk of developing cirrhosis, liver failure or hepatocellular carcinoma.²¹⁻²² Because of increased risk of hepatocellular carcinoma in cirrhotic patients with HBV and HCV, many research workers regard cirrhosis as premalignant condition.²²⁻²³ The aim of this study was to know about the recent etiological spectrum regarding causation of this disease in our area and to make comparison with similar studies carried out elsewhere.

PATIENTS AND METHODS

This descriptive case series conducted in Medical Unit III, Services Hospital Lahore from December, 2006 to December, 2007. One hundred patients of liver cirrhosis presenting in emergency or outpatient department of Services Hospital Lahore, were enrolled. Diagnosis of cirrhosis was confirmed by combination of clinical and ultrasonographic findings. Venous blood was taken and serum was tested for Hepatitis B surface antigen (HBs Ag) by and Hepatitis C virus antibodies (anti HCV Ab) by Enzyme Linked Immunosorbent Assay (ELISA). Other investigations were done according to the presentation of the patients and treatment was given accordingly. Variables were recorded, analyzed and comparison was made with other studies.

RESULTS

Amongst the 100 patients 59% were male and 41% were females and majority (82%) had urban background. The etiology of cirrhosis was mainly viral (83%), out of which 81% had hepatitis C, 1% hepatitis B and 1% both hepatitis B and hepatitis C (table 1).

The mean age of patients(years) was 55.79 ± 13.545 (SD), the mean weight (kilograms) 62.49 ± 8.02 (SD), (table 2).

Table-1
Frequency distribution of qualitative variables, n=100

	Frequency	Percentage %
Gender:		
Male	59	59
Female	41	41
Residential Area		
Urban	82	82
Rural	18	18
Etiology of cirrhosis		
Viral		
Alcoholic	83	83
Others	1	1
	16	16
Viral marker		
Hepatitis C	81	81
Hepatitis B	1	1
Hepatitis	1	1
Band C		
None	17	17

Table-2
Descriptive Statistiques of Quantitative variables, n=100

Quantitative variables	Minimum	Maximum	Mean	Std. Deviation
Age of patients(years)	21	80	55.79	13.54
Weight of patients(Kg)	45	86	62.49	8.02

DISCUSSION

According to our present case series HCV is much more common (81%) than HBV infection and alcoholic liver disease in patients with cirrhosis presenting to the tertiary care hospital here in Lahore and dual infection with HBV and HCV is least common. Our study revealed high prevalence of HCV as compared to past when HBV was the leading etiology of liver cirrhosis in central Punjab. Najam et al. in 1998 observed 44% HBsAg positivity in liver cirrhotic patients in Lahore where 19% had Hepatitis C and 7% had both.²⁴ While latter studies from same centre (Mayo Hospital) in Lahore revealed increasing trend of HCV positivity (52% and 55% respectively) in similar patients by Hussain I and Nadeem M A.²⁵⁻²⁶ This is more or less in accordance with the prevalent changing trend shown in different studies conducted at Lahore and other

centers in Pakistan. Another study from Faisalabad also showed increasing prevalence of HCV (66%).²⁷ A similar study from D. I. Khan by Mahsud and his colleagues in 2003 revealed 56.54% HCV prevalence, 30.35% of Hepatitis B virus, 4.76% of both Hepatitis B & Hepatitis C virus in 228 (67.85%) male and 108 (32.15%) female studied patients of cirrhosis.²⁸ While Farooqi J I from Swat detected 59% prevalence in 2002.²⁹ In comparison our recent study showed that HCV Ab positivity is more (81%) while HBs Ag positivity is much less (1%) as compared to all previous observational case series mentioned above from central Punjab and Khyber Pakhtoon Khawa. The reasons for this difference could be an increasing awareness and increasing vaccination against HBV and therefore decrease in the spread of HBV and its contribution to cirrhosis. However, in case of HCV no effective vaccine is yet available, and increasing HCV risk and progression of disease in these patients will definitely mean increasing cases of cirrhosis due to HCV. Males were more than female patients to acquire HCV infection in all these studies could be either because of their greater occupational exposure or other life activities; or because of underutilization of health resources by females so that they escape detection and remain unreported.

CONCLUSION

Hepatitis C virus infection is the commonest etiology of Liver cirrhosis and males are vulnerable to acquire. Therefore, early detection and treatment of HCV infection should be conducted in masses especially in all high risk individuals as no vaccine is yet developed. In order to prevent the spread of infection, HCV infected persons should be advised not to share toothbrushes and dental or shaving kits. HCV infected persons must not donate blood, body organs or other tissues. Public awareness regarding spread of the disease and avoidance of risk factors is strongly needed.

REFERENCES

1. Lawrence S, Friedman. Liver, biliary tract and pancreas. In: Lawrence M. Tierney, Stephen J, editors. Current medical diagnosis and treatment. 47th Ed. New York: Mc Graw-Hill; 2008: 584-6.
2. Saile B, Ramadori G. Inflammation, damage repair and liver fibrosis--role of cytokines and different cell types. *Z Gastroenterol.* 2007; 45: 77-86
3. Parsons CJ, Takashima M, Rippe RA. Molecular mechanisms of hepatic fibrogenesis. *J Gastroenterol Hepatol* 2007; 22:79-84.
4. Arase Y, Ikeda K, Suzuki F, Suzuki Y, Kobayashi M, Akuta N. Prolonged-interferon therapy reduces hepatocarcinogenesis in aged-patients with chronic hepatitis C. *J Med Virol.* 2007; 79:1095-102.
5. Hamid S, Ismail FW, Jafri W. Hepatitis and the health care worker- a Pakistani perspective. *J Coll Physicians Surg Pak* 2007;17: 240-5.
6. Alam I, Razaullah, Haider I, Hymayun M, Amjad M. Spectrum of precipitating factors of Hepatic Encephalopathy in liver cirrhosis. *Pakistan J.Med.Res.*2005; 44: 99.
7. Malik A, Butt SA, Tariq WZ. Hepatitis C virus in perspective, where do we stand [editorial]. *J Coll Physician Surg Pak* 1996; 6: 136.
8. Puro V, Petrosillo N, Ippolito G. Risk of hepatitis C seroconversion after occupational exposure in health care workers. *Am J Infect control* 1995; 23: 273-7.
9. Recommendations for prevention and control of hepatitis C virus (HCV) Infection and HCV related chronic diseases. Centers for Disease Control and Prevention, MNWR Recomm Rep 1998; 4: 1-39.
10. Jones MM. Children with hepatitis C. *Hepatology* 2002; 36 : S173-8.
11. Strader DB, Wright T, Thomas DL, Seeff LB. Diagnosis, Management and Treatment of Hepatitis C. *Hepatology* 2004; 39: 1147-71.
12. Strader DB, Seeff LB. The natural history of chronic hepatitis C infection. *Eur J Gastroenterol Hepatol* 1996; 8: 324-8.
13. Seeff LB, Hoofnagle JH. National Institute of Health Consensus Development Conference: management of Hepatitis C: *hepatology* 2002; 36 :1-2.
14. Benhamou Y, Bocher M, Di Martino V, Charlotte F, Azria F, Coutellier A, Vidaud M et al. Liver fibrosis progression in Human immunodeficiency virus and hepatitis C virus co-infected patients. *Hepatology* 1999; 30: 1054-8.
15. Poynard T, Bedoosa P, Opolon P. Natural History of Liver Fibrosis Progression in Patients

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- with chronic hepatitis C. *Lancet* 1997; 349: 825-32.
16. Harris DR, Gonin R, Alter HJ, Wright EC, Buskell ZJ, Hollinger FB et al. The relationship of acute transfusion-associated hepatitis to the development of cirrhosis in the presence of alcohol abuse. *Ann Intern Med*; 2001; 134: 120-4.
 17. Kowdley KV. The Cost of Managing Chronic Hepatitis B infection: A Global Perspective. *J Clin Gastroenterol* 2004; 38:132-3.
 18. Lavanchy D, Hepatitis B virus epidemiology, disease burden, treatment and current and emerging prevention and control measures. *J Viral Hepat* 2004; 11:97-107.
 19. Alexander J, Kowdley KV. Epidemiology of Hepatitis B. Clinical Implications. *Medscape Gen Med* 2006; 8 : 13-18.
 20. Malik IA, Legters LJ, Luqman M, Ahmad A, Qamar MA, Akhtar KK et al. The serological markers of hepatitis A and B in healthy populations in northern Pakistan. *J Coll physician Surg Pak* 2002; 12: 240-2.
 21. Shepard CW, Finelli L, Fiore AE, Bell BP. Epidemiology of hepatitis B and hepatitis B virus infection in United States Children. *Pediatr infect Dis J*. 2005; 24: 755-60.
 22. Lok AS, Mc Mahon B. Chronic hepatitis B. *Hepatology* 2001; 34: 1225-41.
 23. Fattovich G, Giustina G, Degos F, Diodati G, Tremolada F, Nevens F, et al. Effectiveness of interferon Alfa on incidence of hepatocellular carcinoma and decompensation in cirrhosis type C. European concerted Action on Viral Hepatitis. *J Hepatol* 1997; 27: 201-5.
 24. Nasir N, Nadeem MA, Imran M, Hussain I, Chaudhry NU. Oesophageal Varices vs Peptic Ulcer: A Study of 100 Patients Presenting in Mayo Hospital with Upper Gastrointestinal Bleeding. *Pak J Gastroenterol* 1998; 12:58-63.
 25. Hussain I, Nasrullah M, Shah AA. Prevalence of Hepatitis B and C Viral Infections in Liver Cirrhosis in Pakistan. *Pak J Gastroenterol* 1998; 12:7-11.
 26. Nadeem MA, Waseem T, Sheikh AM, Gumman MN, Irfan K, Hasnain SS. Hepatitis C Virus: An alarmingly increasing cause of Liver Cirrhosis in Pakistan. *Pak J Gastroenterol* 2002; 16:3-8.
 27. Bilal A, Qureshi FS, Omar Z, Khalid G. Frequency of Hepatitis B and C virus in patients with Decompensated cirrhosis of liver in Faisalabad. *Pak J Gastroenterol* 2006; 20:43-8.
 28. Mahsud I, Din R, Khan H. Hepatitis C: A leading cause of cirrhosis at DHQ Hospital D.I.Khan. *Biomedica* 2006; 22:122-5.
 29. Farooqi JI, Khan PM. Viral aetiology of Liver Cirrhosis patients in Swat. *Pak J Gastroenterol* 2002; 16:39-42.

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