Clinical profile of patients with cirrhosis of liver in a tertiary care hospital, Dharan, Nepal

R Maskey,[1] P Karki,[1] SV Ahmed[2] and DN Manandhar[3]

Department of Medicine, [1]B.P Koirala Institute of Health Sciences, Dharan, Nepal, [2]Nobel Medical College and Teaching Hospital, Biratnagar, [3]Nepal and Nepal Medical College Teaching Hospital, Jorpati , Kathmandu, Nepal

Corresponding author: Dr. Robin Maskey, Assistant Professor, Department of Internal Medicine, B.P Koirala Institute of Health Sciences, Dharan, Nepal; e-mail add:drmaskey@gmail.com

ABSTRACT

One hundred and five (72 males; 33 females) consecutive patients who met the inclusion criteria were studied. The mean age of the patients was 49.06 ±11.27 years (range 23-73 years). Ninety patients were adult cirrhotics (age ≥35 yrs) and the remaining 15 patients were young (age ≤35 yrs). Ninety out of 105 patients were having alcohol related cirrhosis. The commonest presenting symptoms were abdomen distension (100% in young cirrhotics vs. 84.4% in adult cirrhotics) and jaundice (93.3% in young cirrhotics vs. 84.4% in adult cirrhotics).The most common presenting signs were ascites (100% in young cirrhotics vs. 84.4% in adult cirrhotics) and icterus (93.3% in young cirrhotics vs. 84.4% in adult cirrhotics), followed by loss of body hair (73.3% vs. 71.1% in young and adult cirrhotics respectively) and spider naevi (46.7% vs. 61.1% in young and adult cirrhotics respectively). Sixty percent of young cirrhotics and 52% of adult cirrhotics were in Child's grade C at the time of presentation. Most of the deaths were seen in Child's grade C of liver disease. Alcoholic cirrhosis is common in the eastern part of Nepal. Cirrhosis is not uncommon in younger age group. Abdomen distension and jaundice were most common clinical presentations. Most patients were in Child's grade C and most deaths were due to hepatic failure.

Keywords: Cirrhosis, clinical profile, alcohol, adult cirrhotics, young cirrhotics.

INTRODUCTION

Cirrhosis named by Laennec in 1826 means orange or twany in Greek.[1] Many forms of liver injuries are marked by fibrosis. This response to liver injury is potentially reversible. In contrast, cirrhosis is not a reversible process.[2] Cirrhosis is defined by the World Health Organization (WHO) as a diffuse process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules.[3,4] The progression of liver injury to cirrhosis may occur over weeks to years. Chronic liver diseases and cirrhosis result in 26,000-35,000 deaths each year in the United States (US). Cirrhosis is the 9th leading cause of death in the US and is responsible for 1.2% of all US deaths.[5]

Cirrhosis can be classified as follows: 1) alcoholic; 2) cryptogenic or post hepatic; 3) biliary; 4) cardiac; 5) metabolic 6) inherited and 7) drug related.[6] The clinical presentation of cirrhosis is variable depending on the aetiology and whether hepatocellular or portal hypertension predominates.[6] However, severe liver injury may be present without any clinical signs. The diagnosis of cirrhosis is based on the clinical features, laboratory investigations, histology and radiologically.

The main complications of cirrhosis are gastrointestinal haemorrhage, hepatic failure, hepatocellular carcinoma, and bacterial infection. The relative frequencies of these complications in different forms of cirrhosis are difficult to determine.[7] The profile of cirrhosis may vary with different age and ethnic groups, geographical, social and etiological factors. So we undertook this study to see the clinical profiles of patients with cirrhosis of liver in B.P. Koirala Institute of Health Sciences (BPKIHS), a tertiary care hospital in eastern Nepal.

MATERIALS AND METHODS

One hundred and nine consecutive patients with the diagnosis of chronic liver disease that attended Internal Medicine OPD and medicine ward from April 2004 to March 2005 were included in the study. Patients were arbitrarily divided into two groups, young cirrhotics (age ≤ 35 years) and adult cirrhotics (age ≥ 35 years).[8] As our department looks after only adult patients, patients below the age of 15 years were not included in the study. The case of clinical cirrhosis was defined as a patient having at least one clinical sign of hepatocellular failure[9] and one of portal hypertension[10] along with at least three ultrasound (USG) findings suggestive of cirrhosis of liver[11,12] and, or liver biopsy evidence of cirrhosis in permissible cases. The diagnosis of alcoholic cirrhosis was made on the basis of history of any form of alcohol consumption >80g/dl in men and > 40g/dl in women for 10yrs.[13] Spontaneous Bacterial Peritonitis (SBP) was considered if the ascitic fluid analysis showed one of the following:

- Total leukocyte count (TLC) : >500 cells/µml.

Table-1: Characteristics of Patients with cirrhosis of liver

N=105	Mean	SD
Age	49.06	11.27
Hb (mg/dl)	9.717	2.85
TLC (mm^3)	14550.58	8720.94
Neutrophils(mm^3)	76.06	12.18
Lymphocytes(mm^3)	23.1	12.29
Platelet count	170642.86	134160.21
Urea (mg/dL)	40.95	31.62
Creatnine(mg/dL)	1.158	0.916
Sodium (mmol/l)	131.30	7.48
Potassium (mmol/l)	3.196	0.869
RBS (mg/dl)	107.04	44.44
PT (sec)	19.72	5.41
T.Bilirubin (mg/dl)	7.07	6.383
C.bilirubin (mg/dl)	4.527	4.946
T.protein (mg/dl)	5.986	1.361
Albumin (U/L)	2.326	0.508
AST (U/L)	127.08	98.37
ALT(U/L)	63.34	97.59
GGT (U/L)	153.68	282
Alkaline phosphtase	337.14	210.89
Ascitic **Fluid analysis**		
TLC (mm^3)	9180.22	2518.62
Neutrophils (mm^3)	7000.65	2325.14
Lymphocytes (mm^3)	219.46	417.18
Protein (mg/dl)	1.408	2.687
Sugar (mg/dl)	127.24	66.5

- Total polymorphonuclear (PMN) count: >250 cells µml
- Ascitic fluid culture positive

An eligible case was enrolled for the study and informed consent was taken from the patient or close relatives. Detailed history was reviewed and physical examinations were done. Blood samples were taken for investigations. Upper gastrointestinal (UGI) endoscopy was done by Olympus gastroscope and gastroesophageal varices were graded (I-IV) accordingly. Ascitic fluid was collected in an ethylene diamine tetraacetic acid (EDTA) tube for TLC and differential leucocyte count (DLC) and in a plain vial for protein and sugar. The ascitic fluid TLC and PMN counts were determined by the total and differential counting on the basis of morphologic appearance in a manual counting chamber. Another 10ml of ascitic fluid was inoculated in a blood culture bottle at the bedside. The severity of disease was assessed by using Child Turcotte Pugh criteria[14] and oesophageal varies was graded from (I-IV) according to Conn's classification.[15] USG of abdomen were done in all cases and UGI endoscopy was done as per required basis. Ethical clearance was taken from the institute's ethical review board.

Data were recorded on a predesigned proforma and managed on Microsoft excel spread sheet. Continuous variables were summarized by means and standard deviations. Due to large variation in duration and amount of alcohol consumption amongst the participants it was measured by median and range. Categorical variables were summarized by percentages. Data was divided into two parts; young cirrhotics (age ≤35years) and adult cirrhotics (age ≥ 35 years). Categorical variables between young and adult cirrhotics were compared using Pearson's Chi-square test and in case of frequencies smaller than five, fischer extract test was used. Mean values in two groups (young and adult cirrhotics) were compared using student t' test. Wilcoxson Ranxsum test was used to compare median values of amount of alcohol consumption and duration of alcohol consumption in young and adult cirrhotics. SPSS version 10 statistical software was used for data analysis. In this study, p value ≤0.05was considered as statistically significant.

RESULTS

The total number of patients enrolled for the study was 109. Out of these, 105 patients fulfilled the inclusion criteria for diagnosis of cirrhosis. Four patients were excluded: 3 patients did not fulfill the USG criteria and 1 patient left against medical advice. Seventy two were males and 33 were females with a male female ratio of 2.1: 1. Mean age of the cases was 49.06 ± 11.27 (range: 23 to 73) years. Ninety patients were adult cirrhotics and remaining 15 were young cirrhotics.

Table -2: Clinical features of study population

	Young cirrhotics (%)	Adult cirrhotics (%)
Symptoms		
Abdominal distension	100	84.4
Jaundice	93.3	84.4
Fever	60	32
Hematemesis	20	30
Melena	13.3	35.5
Signs		
Ascites	100	84.4
Jaundice	93.3	84.4
Loss of body hair	73.3	71.1
Spider naevi	46.7	61.1
Palmar erythema	13.3	35.5
Clubbing	20	16.6
Parotid swelling	20	26.6

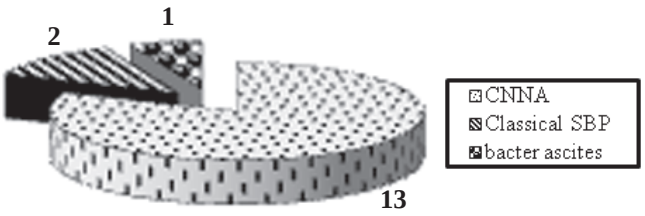

Fig.1. Variants of SBP

Baseline labaratory parameters of the study population are shown in (Table-1). The most common presenting signs were ascites and icterus, which were followed by loss of body hair and spider naevi (Table-2). Most common aetiology of the study population was alcohol related cirrhosis (86%) followed by cryptogenic cirrhosis (11%), hepatitis B (2%) and hepatitis C (1%). All young cirrhotics and 84.4% of adult cirrhotics had alcoholic cirrhosis.

The age of onset of alcohol abuse was as early as 10 years of age, with mean age of onset of alcohol abuse of 19.13±6.23 years and 23.25±16 years in young and adult cirrhotics respectively. The duration of alcohol consumption was found to be significantly longer in adult cirrhotics (p=0.001).

Out of 16 cases of SBP, 2 were young and 14 were adult cirrhotics. Among cases of SBP 13 were culture negative SBP, 2 cases were of classical SBP and one case was bacter ascites (Fig-1). Organisms were isolated from only two cases (12.5%). In both the cases monobacterial type of organisms were grown. They were *Streptococcus pneumoniae* (n=1) in young cirrhotic, and gram positive diplococci (n=1) in adult cirrhotic. There was significant difference between two groups (p=0.037).

Around 13% in both the cirrhotic groups were having esophageal varices. Most of the cases had grade 3 esophageal varices predominantly in adult (14.4%) than in young cirrhotics (6.6%) (Fig.2). Most of the patients presented in grade 1 and 2 encephalopathy (Fig.2). More than half of the patients of both groups presented in child class C (Fig. 2).

Seventy-one patients were discharged and 6 patients left against medical advice. There were 14 (11 adult and 3 young cirrhotics) deaths in our study. Almost all the deaths occurred were in Child's grade C of liver disease (Table-3). Here, the difference between the two groups was not significant.

DISCUSSION

Cirrhosis can occur at any age and often causes prolonged morbidity. It is generally believed that cirrhosis occur much less frequently in young adults than in older patients. A number of reports from the West and Japan, it was found that less than 5% of cirrhosis was under 30-35 years of age.[8] Novic DM did a study of young intravenous drug abusers and found that 43% of cirrhotics were below the age of 35 years.[16] In India, however 37% were patients of ≤35years.[17] There has not been any study in Nepal regarding the incidence of cirrhosis of liver however in 2001 a case was reported of 21 year old man having alcoholic cirrhosis with portal hypertension.[18] The results of this prospective study indicate that cirrhosis was not uncommon in young adults (around 15%).

This study showed alcohol related cirrhosis as most common etiology of cirrhosis followed by cryptogenic cirrhosis, hepatitis B infection and hepatitis C infection. In contrast to our study SK Sarin from India reported that the aetiology of cirrhosis did not differ in the young and adult cirrhotics. In Nepal alcoholic cirrhosis was more common in young cirrhotics. Social tolerance to alcohol use in Nepal is quiet high and so far alcohol consumption has not been taken seriously either by government of Nepal or by any social organistaion. Production, sale and consumption of alcohol are ever on the increase. These factors may have contributed to early onset of alcohol consumption in young cirrhotics.

AU Kakehasi did a study of clinical symptoms of patients with liver cirrhosis, and found that there were various symptoms in decompensated state, but not in compensated state. Most symptoms were due to liver cell dysfunction and portal hypertension. There were no difference in clinical symptoms between aged patients and young patients.[19] In our study also there was no difference in clinical symptoms between young and adult cirrhotics.

The mean age of alcoholic cirrhotic was 29.4±5.1 years; similar to the observations by Novic in west.[16] The duration of alcohol consumption was found to be significantly higher in adult, compared with young cirrhotic group (p=0.00) which was comparable to the study done by SK Sarin in India (p=<0.01).

Qureshi, found that adult had on presentation a higher frequency of anorexia while hematemesis was frequent in the young group (p<0.001).[20] SK Sarin, reported that

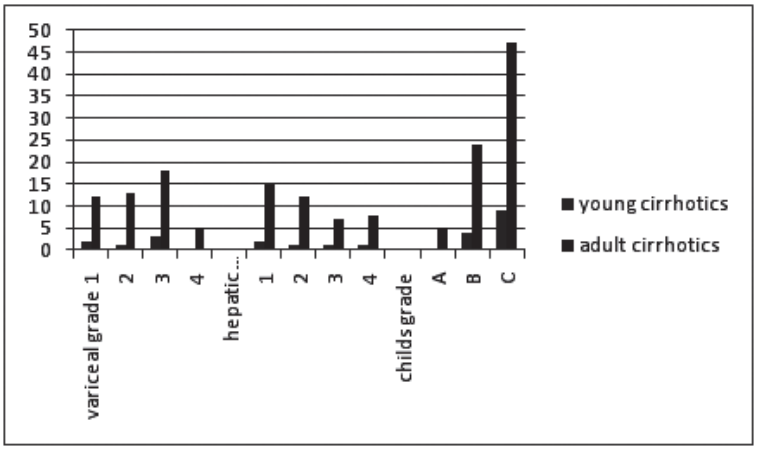

Fig.2. Grading of Oesophageal varices, Hepatic Encephalopathy and Child's Grading among young and adult cirrhotics

Table -3: Causes of death in young and adult cirrhotic patients

Parameter	Young cirrhotics (n=15)	Adult cirrhotics (n=90)
Total deaths	3(20%)	11(12.2%)
(Child's grade)		
A	0	0
B	1(6.6%)	0
C	2(13.3%)	11(12.2%)
(Mode of death)		
Hepatic coma	1(6.6%)	9(10%)
Gastrointestinal bleeding	1(6.6%)	2(2.2%)
SBP	0	1(1.1%)

the most common presenting symptom in young was hematemesis and abdominal distension in adults. In our study the most common presenting symptoms were abdomen distension and jaundice.

All cirrhotic patients with ascites can develop SBP. The prevalence of SBP in hospitalized patient ranges between 10%-30%.[21] In our study, the occurrence of SBP was 13.3% in young cirrhotics and 15.5% in adult cirrhotics. In an another study done in BPKIHS, occurrence of SBP was 24.69% in patients with cirrhotic ascites. Culture positive was 35% in previous study while in our study the rate was low (12.5%). The most frequent organisms isolated in a study done in BPKIHS were Escherichia coli and Streptococcus pneumoniae[21] which was similar to ours. This low proportion of positive ascitic fluid is probably due to the relatively low concentration of bacteria in ascitic fluid.

We had mortality of total 14 deaths (13.3%), 3 deaths (20%) in young cirrhotics and 11 deaths (12.2%) in adult cirrhotics. Among deaths there ine percent and 2.2% due to liver failure and gastrointestinal bleeding in adult cirrhotics respectively. Qureshi, reported 53.8% and 44.4 % mortality due to liver failure in both the groups and 23% and 11.1% due to variceal bleeding. SK Sarin reported 63.8% and 40.7% deaths due to liver failure; 26% and 52% due to variceal bleeding in young and adult cirrhotics respectively.

Thus we can say that alcoholic cirrhosis is more common followed by viral related cirrhosis in the eastern part of Nepal. We also found that cirrhosis is not uncommon in younger age group (age<35yrs). The age of onset of alcohol consumption is as early as 10 yrs of age. Abdomen distension and jaundice were most common clinical symptoms and signs in both the groups. Most of the patient was found to have SBP and most deaths were due to hepatic failure.

REFERENCES

1. Schiff L, Eugene R, Schiff M. Cirrhosis. In Raven, Editor. Disease of the Liver. (8th ed.). Philadelphia: Lippincott 1999: 20-725.
2. Anthony PP, Ishak K. Nayak G *et al*. The morphology of cirrhosis:definition, nomenclature and classification. *Bull World Health Organ* 1977; 55: 521-40.
3. Anthony P,P Ishak, K.G Nayak, N.C. Poulsen, H.E. Scheuer, P.J.& Sobin L.H. The morphology of cirrhosis. *J Clin Pathol* 1978; 31: 395-414.
4. Friedman SL. Hepatic fibrosis. In Schiff ER, Sorrell MF, Maddrey WC, editors. Schiff's Diseases of the Liver. (8th ed.).Philadelphia: Lippincott-Raven 1999: 371-85.
5. Centers for Disease Control and Prevention. Death rates for 72 selected causes, United States, 1993, 1994, 1995, 1996, 1997, and 1998.
6. Kasper D, Fauci A, Longo D, Braunwald E, Hauser S, Jameson J. Cirrhosis and its complications. In Raymond T. Chug, Daniel K Podolsky, editors. Harrison's Principles of Internal Medicine. (15th ed.). NY: Mc Graw Hill 2001: 1754-1756.
7. Eighth Special Report to the US Congress on alcohol and health. Washington DC: US Depart of Health and Human Services; 1993:1-35.
8. Yoshida T, Kawata H, Fukui O, Koizumi T, Asada M, Wada M. Cirrhosis of liver in Japan . *Acta Hepatolosplenol* 1965;12: 268-78.
9. Sherlock S, Dooley J. Hepatocellular failure.In Disease of liver and biliary system. (10th edition). Oxford: Blackwell Science 1997: 81-5.
10. Sherlock S, Dooley J.The portal venous system and portal hypertension. In Disease of liver and biliary system. (10th ed). Oxford: Blackwell Sciences 1997: l10-40.
11. Tehelepi H, Ralls PW, Radin R *et al*. Sonography of diffuse liver disease. *J Ultrasound Med* 2002; 9: 1033-4.
12. Richard MG. Diffuse liver disease In. Textbook of Gastrointestinal Radiology. (10th ed.). Philadelphia: WB Saunders 1994: 100-8.
13. Kasper D, Fauci A, Longo D, Braunwald E, Hauser S, Jameson J. Alcoholic liver disease In Mark E Malliard, editor. Harrison's Principle of Internal Medicine.(15th ed.). New York: Mc-Graw Hill 2001: 1752-4.
14. Child CG, Turcotte JG. Surgery in portal hypertension. In. Child CG editor. Major problems in clinical surgery: the liver and portal hypertension. Philadelphia: Saunders 1964: 1-85.
15. Conn HO. Ammonia tolerance in the diagnosis of oesophageal varices. A comparision of the endoscopic, radiological and biochemical techniques. *J Lab Clin Med* 1967; 70: 442-51.
16. Novick DM, Enlow RW, Gelb AM *et al*. Hepatic cirrhosis in young adults: association with adolescent onset of alcohol and parenteral heroin abuse. *Gut* 1985; 26: 8-13.
17. Sarin SK, Chari S, Sundaram KR, Ahuja RK, Anand BS, Broor SL. Young versus adult cirrhosis: a prospective comparative analysis of the clinical profile, natural course and survival. *Gut* 1988; 29: 101-7.
18. Biswas R, Sundarka M, De'Souza J *et al*. A case of alcoholic cirrhosis of liver at young age. *J Indian Acad Clin Med* 2001: 2: 101-2.
19. AU Kakehashi R, Watanabe S, Ikoma J, Suzuki S. Clinical symptoms of patients with liver cirrhosis. In: *Japanese J Clin Med* 1994; 52: 40-4.
20. Qureshi H, Zuberi SJ, Lodi TZ. Clinical features, course,viral markers and follow up in young versus adult non alcoholic cirrhotics- a retrospective study. *Digestion* 1989; 42: 110-15.
21. Syed VA, Ansari JA, Karki P, Regmi M, Khanal B. Spontaneous bacterial peritonitis in cirrhotic asictes: A prospective study in a tertiary care hospital, Nepal. *Kathmandu Univ Med J* 2007; 5: 48-59.