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CLINICAL SPECTRUM OF NON ALCOHOLIC CIRRHOSIS

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Cirrhosis liver is a major health problem world wide and specially in developing countries like Pakistan. It is defined as necrosis of liver followed by fibrosis and regeneration. Alcohol and viral hepatitis are the two important causes of cirrhosis. Clinical presentation of cirrhosis depends on stage of cirrhosis whether compensated or de-compensated. Most of the clinical features are common to all types but there are certain features, which are more common in one type than the other. This prospective study was conducted to find the frequency of various clinical features of non-alcoholic cirrhosis and to compare it with those reported in literature. Hundred patients of cirrhosis admitted to Medical Unit of Khyber Teaching Hospital Peshawar between March 1997 to Dec 1997 were included in the study. All the relevant details regarding history, clinical examination and investigations were recorded in specially designed proforma. The commonest presenting features were abdominal distension (61%), generalised weakness (55%), pain abdomen (52%), anorexia (45%), fatigue (38%), low grade fever (38%), nausea and vomiting (36%), swelling of feet (35%), haematemesis (33%), loss of libido (33%) and weight loss (25%). The commonest signs observed were splenomegaly (75%), anaemia (72%), ascites (65%), oedema feet (43%), jaundice (40%), leukonychia (40%), palmer erythema (35%), hepatomegaly (30%), muscle wasting (30%), bruises (27%), clubbing (24%),loss of body hair (18%), spider naevi (18%),testicular atrophy (15%) and gynaecomastia (12%). Viruses specially HBV and HCV were the main aetiological factors (76%). The data indicates that clinical features found in this study are not very different from other parts of Pakistan. Dupuytren's contractures, parotid gland enlargement and gynaecomastia are rare in our population as compared to that in western literature (alcohol in the west and viral hepatitis in our population).

Cirrhosis liver is an important health problem. It accounts for significant morbidity and mortality worldwide[1]. WHO has estimated that cirrhosis is responsible for 1.1% of all deaths. It is defined as a chronic disease of the liver characterized by diffuse destruction and regeneration of hepatic parenchymal cells and a diffuse increase in connective tissues resulting in disorganization of the lobular architecture.[2,3]

There are many causes of cirrhosis. Among them alcohol is the commonest cause in the western world[3], whereas hepatitis B and C viral infections are the most common causes of cirrhosis in our community.[4,5] In 20% of cases no cause can be found[3]. In Pakistan, every tenth person is a carrier of HBV or HCV[6]. The causes for this high prevalence include use of non sterile syringes, tattoo marks, transfusion of unscreened blood, increase in number of iv addicts, poor hygienic conditions and ignorance among masses.[7,8]

Cirrhosis can present in many ways depending upon the stage of disease process (whether compensated or decompensated cirrhosis). Hepatocellular dysfunction, portal hypertension and portosystemic shunting produce its clinical features. Most of the clinical features are common to all types but frequency of some of these may be related to underlying aetiology[9].

The aim of this study was to assess the clinical spectrum of cirrhosis in this part of the world and to compare the findings with those reported in literature. Clinical features of cirrhosis in world literature, generally means post alcoholic while this study is based on clinical findings in non-alcoholic cirrhosis.

MATERIAL AND METHODS

This prospective study was conducted on hundred (100) cirrhotic patients admitted to all of the four medical units of Khyber Teaching Hospital, Peshawer from March 1997 to Dec 1997. The patients belonging to N.W.F.P and Afghan Refugees were included. During this study, a simplified clinical approach was adopted. Printed proforma containing a comprehensive record of all aspects of the disease was completed from each patient. In every patient, the approach was methodical. Detailed

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history, clinical examination and relevant investigations were recorded. All patients were screened for HBV and HCV. One case was reported Hepatitis G virus positive. Diagnosis of cirrhosis was established on clinical grounds, deranged liver function tests (LFTs) with reversed albumin / globulin ratio, abdominal ultrasound and liver, spleen scan. Cirrhosis was histologically confirmed by liver biopsy using "tru-cut needle", performed in 78 cases. Ten patients were already diagnosed cases of cirrhosis (biopsy proven). They came with various complications. In 12 cases liver biopsy was not carried out because of contraindications. These included the patients who had one stage P.T more than 3 seconds prolonged over the control value even after replacement of vitamin K, platelet count below 80,000/cu mm and massive ascites. In such patients the diagnosis of cirrhosis was established on clinical grounds, deranged LFTs, abdominal ultrasound and liver spleen scan. The study was carried out on the following lines.

Inclusion Criteria

The following patients were included.

1. All patients aged 13 years or above.
2. No history of alcohol intake.
3. Patients with diagnosed cirrhosis liver.
4. No rise in Gamma GT (Gamma Glutamyl Transpeptidase).
5. No evidence of macrocytosis.
6. No evidence of alcohol induced liver disease on biopsy.

Exclusion Criteria

The following patients were excluded from the study.

1. Patients who were clinically suspected cirrhotic but could not be verified.
2. Patients who were suffering from other chronic systemic illness.
3. Who were suffering from malignancy.
4. When alcohol intake was suspected either on clinical or laboratory grounds. At the end of study period the proformas were analyzed for the results.

RESULTS

Among 100 cirrhotic patients, 67 (2/3) were males and 33 (1/3) were females (Table 1). All the patients were in the range of 15 to 80 years. The largest number of patients (84) fell in the age group of 20 to 60 years (Table 2). HBsAg was detected in 33 patients whereas anti HCV antibodies were positive in 42 patients. One patient was positive for HGV (detected by PCR). Seven patients were positive both for HBsAg and Anti-HCV antibodies, an evidence for co-infection. In 24 patients, no cause for cirrhosis could be found (Table 3).

Table 1: *Sex distribution of cases.*

Sex	No of patients	% age
Male	67	67%
Female	33	33%
	100	100%

Table 2: *Age distribution of 100 cases.*

Age	No of patients	%age
10 to 19 years	12	12%
20 to 29	20	20%
30 to 39	21	21%
40 to 49	26	26%
50 to 59	17	17%
60 and above	4	4%
	100	100%

Table 3: *showing viral aetiology in cirrhosis.*

Serology for Viruses	No of patients	% age
Hepatitis B Virus.	33	33%
Hepatitis C Virus	42	42%
Hepatitis G Virus	1	1%
No virus detected	24	24%
	100	100%

The common complaints of patients with cirrhosis were abdominal distension (61%), generalized weakness (55%), pain abdomen (52%), anorexia (45%), fatigue (38%), fever (38%), nausea and vomiting (36%), and swelling of the feet (35%). Loss of libido and haematemesis were found in 33%, weight loss in 25%, pruritis and melena in 12%. On admission, 15% were confused and 12% were in a state of coma. Diarrhoea and constipation/ flatulence were present in 9% and 8 % respectively. In female patients irregular menses were noted in 3% cases (Table 4).

Various signs were noted in these patients. Splenomegally (75%), anaemia (72%>), ascites (65%), peripheral oedema (43%), jaundice (40%), leukonychia (40%), palmer erythema (35%), heaptomegally (30%), muscles wasting (30%), bruises (27%) and clubbing (24%) were the most common signs. Spider naevi and loss of body hair were found in 15% of cases each. Testicular atrophy and gynaecomastia were found in 15% & 12% of male

patients respecttively. Other signs found were pigmentation (11%), umbilical hernia (7%) and inguinal hernia (2%). Five (5%) cirrhotic patients were having Koilonychia, scratch marks, flapping tremors, paper money skin and Dupuytren's contractures each. Cyanosis and caput medussae were noticed in 4% of patients each. Rarely observed signs were glossitis, purpura and fetor heapticas. Vitiligo, Kayser Fleisher ring, parotid gland enlargement, xanthomas and xanthelsma were not found in a single case in this study (table 5).

DISCUSSION

The analysis of 100 cases of non-alcoholic cirrhosis of liver showed male predominance. Hepatitis C (42%) & Hepatitis B (33%) were the leading cause of cirrhosis, which is almost similar to other studies.[1,10] Most cirrhotic patients complained of abdominal distension (61%), generalized weakness (55%), anorexia (45%), fatigue (38%), nausea and vomiting (36%), comparable to local studies.[9,11] These non-specific symptoms were more common in our study as compared to alcoholics (10%)[12]. Alcohol increases appetite and may be the reason for less number of anorexic patients in alcoholic cirrhotic. Abdominal pain was in 52% compared to 28% by Nazish et al[9] and 46% by Khan et al[13], higher to alcoholics (12.4%) by Millward et al[14]. Low grade fever was reported in 38% cases comparable to other local studies[9,11,15] but much higher than alcoholics i.e 5-10% and 9.1%.[14,16] The high frequency of pain and fever in our study could be due to continuous activity of HBV and HCV. Upper GI bleeding was reported in 33% of patients almost similar to other studies.[9,17] Loss of libido was found in 33%, low as compared to 60% in alcoholic cirrhotics[12]. This may be due to direct effect of alcohol. Weight loss was found in 25% patients while Qureshi et al[11] and Khan et al[13] reported weight loss in 38% and 18% of their patients respectively. Pruritis was less common (12%) compared to 62% of cases with primary biliary cirrhosis[18] because viruses (76%) were the main aetiological factor in our study.

Amongst the clinical signs, splenomegaly was the commonest sign (75%),

Table 4: *showing frequency of symptoms.*

Symptom	No of patients	Male	Female	% age
Abdominal distension	61	38	23	61%
Generalized weakness	55	38	17	55%
Pain abdomen	52	37	15	52%
Anorexia	35	29	16	35%
Fatigue	38	25	13	38%
Fever	38	21	17	38%
Nausea / vomiting	36	25	11	36%
Swelling feet	35	19	16	35%
Haematemesis	33	22	11	33%
Loss of libido	33	28	5	33%
Weight loss	25	16	9	25%
Confusion	15	10	5	15%
Pruritis	12	9	3	12%
Melaena	12	7	5	12%
Coma	12	7	5	12%
Diarrhea	9	5	4	9%
Constipation / flatulence	8	5	3	8%
Irregular menses	3	0	3	3%

Table 5: *showing frequency of signs.*

Signs	No of Patients	Male	Female	% age
Splenomegally	75	51	24	75%
Anemia	72	49	23	72%
Ascites	65	43	22	65%
Peripheral edema	43	29	14	43%
Jaundice	40	26	14	40%
Leukonychia	40	24	16	40%
Palmer erythema	35	21	14	35%
Hepatomegally	30	17	13	30%
Muscle wasting	30	17	13	30%
Bruises	27	15	12	27%
Clubbing	24	14	10	24%
Spider naevi	18	11	7	18%
Loss of body hair	18	16	2	18%
Testicular atrophy	15	15	0	15%
Gynaecomastia	12	12	0	12%
Pigmentation	11	6	5	11%
Umbilical hernia	7	3	4	7%
Inguinal hernia	2	2	0	2%
Koilonychia	5	2	3	5%
Scratch marks	5	2	3	5%
Flapping tremors	5	3	2	5%

almost similar to Qureshi et al (64%)[11] and Iqbal et al (70%).[15] In alcohlic cirrhosis, it was reported in 20% of the patients. The high percentage of splenomegaly in our study may be due to late presentation and portal hypertension. The second common sign was anaemia, found in 72% of cases, comparable to other studies where it was 68%[9] and 88%[11]. Occult and overt blood loss from G I tract, malnutrition, hypersplenism and thrombocytopaenia could all be contributory factors towards anemia. Ascites was found in 65% of patients, compared to 76% by Nadeem[17] and 70% by Tito et al[19] which is almost similar. The reason my be advanced stage of the disease showing features of portal hypertension. Jaundice was found in 40% cases comparable to 44%[13] and 41%[17] while in alcoholic cirrhotics, it was found in 20% cases[14]. Jaundice increases in frequency and severity during later stage of disease[20] as is in our study. Leukonychia was present in 40% while palmer erythema in 35% compared to 68% and 70% respectively by Qurashi et al[11]. The low incidence of this sign in our study could not be explained. Hepatomagly was present in 30% of patients which is less as compared to other studies, 70%[13] and 90%[14]. The reason of this low frequency may be that most of our patients were in advanced stage of disease, during which liver becomes normal or decrease in size due to extensive fibrosis[21]. Muscle wasting was found in 30% of patients, bruises in 27% and clubbing in 24% of cases. Testicular atrophy was less common (15%) in our study as compared to 20-30% in alcholic cirrhotics[14]. The reason for higher percentage in alcholics could be due to the direct effect of alcohol. Gynaecomastia was found in 12% of cases which is less as compared to 20-30% in alcoholic cirrhotics[14]. Spider naevi were found in 18% of patients. This percentage is less as compared to 50% in alcoholic cirrhotics[14]. This difference may be a direct effect of alcohol[22] or fair complexion of patients in the western world. Hair loss was observed in 18% and pigmentation in 11% of cirrhotics. Pigmentation is less as compared to 25% in alcoholic cirrhotics[14], 40% in haemochromatosis[23] and 36% in primary biliary cirrhosis[18]. As most of our patients were post infective cirrhotics (76%), therefore pigmentation was less common in our patients. The other possible cause might be dark complexion of our population in whom slight pigmentation cannot be detected easily. Umbilical hernia was found in 7% and inguinal hernia in 2% while cyanosis was found in 6% of patients. Five patients (5%) were having koilonychia, scratch marks, flapping tremours, paper money skin and Dupuytren's contracture each. Vitiligo, Kayser Fleisher ring, parotid gland enlargement, xanthelasma and xanthomas were not found in a single case. As most of patients were suffering from post infective cirrhosis, therefore these signs were absent in our study.

Less common signs in non alcoholic cirrhosis (contd. Tables)

Signs	No of Patients	Male	Female	% age
Paper money skin	5	3	2	5%
Dupuytren's contracture	5	4	1	5%
Cyanosis	6	4	2	6%
Caput medussae	4	3	1	4%
Purpura	3	2	1	3%
Fetor hepaticus	4	2	2	4%
Glossitis	3	1	2	3%
Vitiligo	0	0	0	0%
Keyser Fleisher ring	0	0	0	0%
Parotid gland enlargement	0	0	0	0%
Xanthomas / xanthelasma	0	0	0	0%

It is **Concluded** from this study that clinical features found in our cirrhotic patients are not very different from other local studies. However frequency of some of the clinical features of cirrhosis like parotid gland enlargement, gynaecomastia, Dupuytren's contracture and pigmentation are rare in post infective compared to alcoholic cirrhotics. Furthermore in this part of the country, patients with cirrhosis present with fairly advanced stage of disease.

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