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PRESENCE OF CIRRHOSIS IN NEWLY DIAGNOSED HEPATITIS C PATIENTS WITHOUT PRIOR HISTORY OF CHRONIC LIVER DISEASE.

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ABSTRACT: Cirrhosis once established has no treatment except liver transplantation. It is mostly caused by chronic hepatitis C virus which is very common in our region. As many of these hepatitis C patients are asymptomatic or have non-specific symptoms, so these patients seek medical advice late in the course of their disease. **Objectives:** To find out the presence of cirrhosis in newly diagnosed hepatitis C patients. **Study Design:** Descriptive Study. **Setting:** Hepatitis Clinic, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan. **Period:** From March to September 2018. **Material & Methods:** All newly diagnosed hepatitis C patients previously not known to have chronic liver disease were included in the study. Their demographics, symptoms, baseline CBC, LFT, PT, albumin and ultrasound findings were noted. Cirrhosis was diagnosed on the basis of clinical, laboratory and ultrasonography findings. **Results:** Three hundred and seventy three patients met inclusion criteria. Cirrhosis was present in 64 (17.2 %) patients, 52 patients had Child A and 12 has Child B cirrhosis. No patient had Child C cirrhosis. Mean age of non-cirrhotic patients was 36.74 years and of cirrhotic 47.09 years. There was no significant difference regarding gender distribution between the two groups. Seventy nine (25 %) non-cirrhotic and 11 (17 %) cirrhotic were asymptomatic at presentation and were diagnosed incidentally. **Conclusion:** About one sixth of newly diagnosed hepatitis C patients already had cirrhosis at presentation.

Key words: Cirrhosis, Chronic Liver Disease, Hepatitis C.

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INTRODUCTION

Cirrhosis is an important cause of morbidity and mortality worldwide[1] and it is amongst the commonest diseases in our medical wards. Once it is advanced, it is irreversible; nothing can be done apart from monitoring for or treating its various complications as liver transplantation is not readily available in our setup. The risk of developing complications like ascites, jaundice, variceal bleeding and encephalopathy (hepatic decompensation) is 3.9 % per year[2] which have considerable mortality rates. Once cirrhosis has developed, the risk of developing hepatocellular carcinoma is 0 to 3 percent per year in various reports.[2,3] In our region hepatitis B and C are very common, especially hepatitis C.[4,5] Most patients of acute hepatitis C and perinatally acquired hepatitis B developed chronic hepatitis.[6] So cirrhosis here is mostly caused by chronic hepatitis C and to some extent hepatitis B, other causes are rare.[7-10] Many patients of chronic hepatitis may be asymptomatic.[11] Others may have non-specific symptoms like fatigue, myalgia, arthralgia and weakness,[12] and some may have mild cognitive impairment.[13] Due to this reason many chronic hepatitis B and C patients have advanced liver disease when diagnosed.

Awareness about hepatitis B and C in our population has increased over recent years. Many people get or advised by general practitioners to get themselves tested for these viruses either routinely or on presence of non-specific symptoms. But it is thought that most of the patients still remain undiagnosed till they develop cirrhosis. The purpose of our study was to identify regional data regarding presence of advanced liver disease in chronic hepatitis C patients at presentation to health facility. This would help us to decide whether community

based screening program be instituted for early detection of hepatitis viruses. The objective of this study was to determine frequency of cirrhosis in those newly diagnosed hepatitis C patients who had no previous history of chronic liver disease.

PATIENTS AND METHODS

This descriptive study was carried out in Hepatitis Clinic, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan. All patients who attended Hepatitis Clinic for chronic hepatitis C treatment from March to September 2018 were considered for inclusion in the study. All patients who were recently (within three months) diagnosed as a case of hepatitis C were included in the study. The patients who have already been diagnosed as a case of hepatitis C for more than three months and whose serology status was not known previously but they were known to have liver disease were excluded from the study. The following features of the patients who fulfilled inclusion/exclusion criteria were noted: age and gender, symptoms, and any co-morbidities (diabetes mellitus, hypertension, alcoholism, autoimmune hepatitis, chronic kidney disease, and chronic cardiopulmonary diseases). Among investigations, complete blood count, liver function tests (total bilirubin, ALT, AST), albumin, creatinine, prothrombin time (PT) and ultrasound abdomen findings (hepatomegaly, shrunken liver, splenomegaly, and ascites) were recorded. APRI[14] and FIB 4[15] scores were also calculated.

Cirrhosis was diagnosed on the basis of:

- Clinical stigmata – clubbing, leukonychia, palmar erythema, spider nevi, peripheral edema, splenomegaly
- Lab investigations – prolonged PT, low albumin
- Ultrasound findings – shrunken liver, splenomegaly, ascites
- APRI and FIB 4 scores – APRI score 1 or more is 76 % sensitive and 72 % specific for cirrhosis;[14] FIB 4 score > 3.25 has 97 % specificity for advanced fibrosis.[15]

The data was entered and analyzed using SPSS version 25. The qualitative data was expressed as frequency and percentage. The quantitative data was expressed as mean, standard deviation and range. A p value of < 0.05 was considered to be significant. Study protocol was approved from Institutional Review Board and Ethical Committee.

RESULTS

Among 2800 patients who attended the Hepatitis Clinic for the treatment of chronic hepatitis C during study period, 373 patients were diagnosed to have hepatitis C infection within 3 months of presentation, and met inclusion/exclusion criteria. One hundred and sixty six patients (44.5%) were male and 207 (55.5%) were female. Mean age of patients was 38.51 ± 12 years with range from 8 to 82 years. Ninety patients (24.1%) were asymptomatic. Common symptoms were malaise and body aches (71.6% patients). Associated comorbidities were hypertension in 46 (12.3%) patients, diabetes mellitus in 31 (8.3%) and renal failure in one (0.3 %). Two (0.5%) patients were alcoholic.

Among these 373 patients included in study, 64 (17.2%) had cirrhosis diagnosed on the basis of one of the criteria given above; 52 had Child A and 12 had Child B cirrhosis. Comparison of demographic features and symptoms presence between non-cirrhotic and cirrhotic patients is shown in Table-I. The cirrhotic patients were significantly ($p=0.000$) older than non-cirrhotic, but gender distribution between these two groups were not significant ($p=0.675$).

Feature	Non-cirrhotic (309 Patients)	Cirrhotic (64 Patients)
Age (years) mean ± SD	36.74 ± 11.60	47.09 ± 10.15
Gender		
Male	136	30
Female	173	34
Presence of symptoms		
Symptomatic	230	53
Asymptomatic	79	11

Table-I. Demographics and presence of symptoms in cirrhotic and non-cirrhotic patients

Fifty nine (92.19%) cirrhotic patients had splenomegaly. All of these had APRI score 1 or

more, 46 had FIB-4 score more than 3.25, 18 had prolonged PT, 9 had decreased albumin and 5 had ascites. Three patients met both APRI and FIB-4 criteria having no other features. One along with APRI and FIB-4 criteria had prolonged PT. One patient had ascites and low albumin. Table-II shows serum albumin, PT, APRI and FIB-4 scores in both non-cirrhotic and cirrhotic patients.

Features	Non-cirrhotic	Cirrhotic
Serum albumin (g/dl) > 3.5 2.8 – 3.5 < 2.8	 305 4 0	 54 9 1
PT prolongation (in seconds) < 4 4 – 6 > 6	 302 7 0	 45 15 4
APRI < 0.7 0.7 - < 1 1 - < 1.5 1.5 - < 2 2 or more	 223 86 0 0 0	 1 0 14 10 39
FIB-4 < 1.45 1.45 – 3.25 > 3.25	 244 65 0	 0 14 50

Table-II. Serum albumin, PT, and APRI and FIB-4 scores in non-cirrhotic and cirrhotic patients

DISCUSSION

Hepatitis C infection is common in our region.[4,5] Most patients who acquire hepatitis C develop chronic hepatitis.[6] Worldwide, 71 million people are suffering from chronic hepatitis C[16], many of these patients are not aware of their disease. In comparison with uninfected persons, patients with chronic hepatitis C die early due to cirrhosis and hepatocellular carcinoma.[17] Chronic hepatitis C is a major cause of cirrhosis, especially in our country.[7-10, 18] Treatment of chronic hepatitis C resulting in sustained virological response (SVR) may cause regression of hepatic fibrosis and reduction of risk of complications of cirrhosis[19] but patients with advanced disease remain at risk of life threatening sequelae. The exact time when liver fibrosis becomes irreversible cannot be predicted.

Patients with chronic hepatitis C are usually asymptomatic or may have non-specific symptoms. Muhammad Umar et al showed that 25% patients of chronic hepatitis C were asymptomatic and others had vague symptoms like malaise, myalgia and fatigue.[11] Another report revealed that 60% of these patients had fatigue, myalgia, arthralgia and sleep disturbances.[12] During compensated phase of cirrhosis, patients may also be asymptomatic or have non-specific symptoms. Our study showed similar results. Due to this reason, many patients of chronic hepatitis C if not screened or incidentally found on testing for another reason remain undiagnosed until they developed features of decompensated cirrhosis. Bell BP et al found that about 20% patients had cirrhosis when first detected to be suffering from chronic hepatitis.[1] In our study, 17% patients had cirrhosis at presentation. It should be kept in mind that we included only those patients who attended Hepatitis Clinic. Many of patients who presented in medical emergency with complications of decompensated cirrhosis like variceal bleeding, hepatic encephalopathy or spontaneous bacterial peritonitis have no previous history of chronic liver disease. Such patients are also seen in medical outpatient. This means that actual percentage of these patients is higher than that we found.

Our cirrhotic patients were slightly younger (mean age 47 years) than those found in two national studies (53[20] and 54[11] years). Probably it is due to difference in study design, these two studies included patients with established cirrhosis. Similary, in other studies 58%[7], 60%[8] and 65%[9] cirrhotics were male while in our study female were slightly more than male patients, probably because overall female patients were more in our study.

CONCLUSION

About 17 % chronic hepatitis C patients had cirrhosis at the time of diagnosis. It emphasizes the need of population screening for hepatitis C so that it can be detected at an early stage of chronic liver disease before the development of advanced irreversible stage.

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Wisdom is learning what to **overlook**.

"William James"

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
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