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CLINICAL SIGNS OF CHRONIC LIVER DISEASE: IS THERE ANY DIFFERENCE IN PATIENTS WITH HEPATITIS B AND C.

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ABSTRACT

OBJECTIVE: *To observe the pattern of admission, clinical signs and their difference in patients with chronic liver disease due to Hepatitis B and C.*
PATIENTS AND METHODS: *This descriptive study was conducted in Medical wards of Civil Hospital Karachi over a period of six months from June to December 2009. One hundred and sixty four (n=164) adult patients with established diagnosis of chronic liver disease due to HBV and/or HCV infection were included in the study. SPSS 16 was used to analyze the cause of admission presence of clinical signs and to compare them in HBV and HCV patients.*
RESULTS: *A total of 164 patients were analyzed out of them 53.7% were male and 46.3% female. Mean age of patients was 51 years. The majority of patients (40.5%) were admitted in hospital with Hepatic encephalopathy, 26.8% with upper Gastro intestinal bleeding, 17.1% with ascites and its complication like spontaneous Bacterial Peritonitis and Hepatorenal Syndrome and 15.6% of patients were admitted with other causes like infections. Hepatitis C was the most common cause and present alone in 52.4% of patients followed by Hepatitis B in 40.9%, both viruses were present in 6.7% of patients. The most common signs were anemia 79.3%, ascites 78% pedal edema 73.8%, splenomegaly 72.6%, palmer erythema 48.8%, leuconychia 48.8% jaundice 35.4%, spider navei 31.1%, clubbing 26.8%. Although breast atrophy, testicular atrophy, parotid enlargement, pigmentation and ascites was more common in HCV patients while jaundice, gynecomastia, leuconychia, clubbing and palmer erythema was more common in HBV patients. However these differences were not statistically significant. Anemia, edema, splenomegaly and loss of axillary hair were equally common in both HBV and HCV patients. Interestingly spider nevi were significantly more common in HCV patients.*
CONCLUSION: *Hepatitis C virus remains the commonest cause of chronic liver disease in our country. The well known clinical signs of chronic liver disease are still valuable in the diagnosis and should be purposely looked for in these patients. The pattern of clinical signs in HBV and HCV patients although different but is not significantly different except spider nevi which were statistically more in HBV patients. Further studies might be done to validate these findings.*

KEY WORDS: Chronic Liver disease. Viral Etiology, Clinical signs, Difference

INTRODUCTION:

Cirrhosis is a serious and irreversible consequence of chronic liver disease characterized by replacement of liver tissue by fibrotic scar tissue as well as regenerative nodules, leading to progressive loss of liver function. It is a major cause of mortality and morbidity worldwide. It is also a common cause of mortality amongst Pakistani population and frequent cause of admission in our hospitals. Cirrhosis develops in about 10-20% within 5-30 years. The most common cause being viral hepatitis as compared to West where alcohol is more common. Majority of patients (90%) with chronic liver disease had evidence of HBV, HCV or co-infection[1].Cirrhosis of liver is responsible for over 10% of all hospital admissions and over 30% of all chronic illnesses in our area[2]

Alcohol is the leading cause of cirrhosis in western world, but it develops only in 10 to 15 % of alcoholics.[2] HBV and HCV infection account for a substantial proportion of liver diseases worldwide Approximately 350 million people are infected with HBV worldwide, and the World Health Organization (WHO) estimates that approximately 170 million people are infected with HCV. [1]Hepatitis B and C virus infection account for

high proportion of liver diseases in our part of world. The prevalence of hepatitis B is over 10% in the Asia- pacific region and two third of the 350 million people in the world who are chronically infected with hepatitis B infection live in this region ,The prevalence of chronic hepatitis C in the Asia-pacific region is variable between 4% to 12% [2,,3.]

Compensated Chronic liver disease is clinically latent and is diagnosed only with careful clinical examination and biochemical screening. About 30-40% of cases of compensated CLD may remain without clinical signs[4] those who become symptomatic present with general symptoms like asthenia, loss of weight and anorexia etc. The grave presentations are ascites, jaundice, hepatic encephalopathy and gastrointestinal hemorrhage.[5] The clinical signs of cirrhosis mentioned in medical literature are spider navei, clubbing, leuconychia, palmar erythema, Dupuytren's contracture, loss of axillary hair, testicular atrophy, gynaecomastia, jaundice and ascites.[6] Many of these signs even in advanced cases of cirrhosis are not regularly observed in current medical practice.

We undertook this study to document the pattern of admission in the patients with chronic liver disease due to HBV and HCV, frequency of the clinical signs and to observe any difference in these signs.

PATIENTS AND METHODS

Adult diagnosed patients of chronic liver disease admitted in medical wards of Civil Hospital Karachi from June to December 2009 were included in the study. These patients were examined carefully for the presence of clinical signs. Previous record was looked for the confirmed diagnosis and its cause; all the admitted patients with cirrhosis / chronic liver disease who had serological evidence of Hepatitis B, C or both were assessed and analyzed regarding their frequency, mode of admission and clinical signs. The patients who had cause other than HBV and HCV were excluded from this study. After a written and informed consent, data from these patients was recorded on a Performa specially designed for this purpose. The parameters included age, gender, mode of admission, etiology of disease (Hepatitis 'B' and 'C'), clinical signs at the time of presentation e.g. anemia, jaundice, spider nevi, clubbing, Terry's nail leuconychia, palmar erythema, Dupuytren's contracture, loss of axillary hair testicular atrophy, breast atrophy, gynaecomastia, parotid gland enlargement caput medusa, splenomegaly, ascites, and pedal edema. All the data was analyzed on SPSS 16.

TABLE-I:
VIRAL MARKERS IN PATIENTS N=164

Cause	Number of Patients	Percentage
HBsAg positive	67	40.9%
Anti HCV positive	86	52.4%
Both B and C positive	11	06.7%

TABLE-2:
CLINICAL SIGNS OF CHRONIC LIVER DISEASE

Total number of patients = 164

Clinical Signs	Number	Percentage
Anemia	130	79.3%
Ascites	128	78.0%
Pedal edema	121	73.8%
Splenomegaly	119	72.6%
Palmar erythema	80	48.8%
Leuconychia	80	48.8%
Loss of axillary hair	64	39%
Jaundice	58	35.4%
Breast Atrophy**	25 / 76	31.6%
Spider nevi	51	31.1%
Testicular atrophy*	30 / 88	29.5%
Clubbing	44	26.8%
Gynaecomastia*	24 / 88	13.6%
Pigmentation	22	13.4%
Caput medusi	10	6.1%
Parotidomegaly	10	6.1%
Dupuytren's contracture	01	0.6 %
Terry's Nails	00	00%

RESULT:

Total one hundred sixty four (164) patients were included in the study, eighty eight (n=88, 53.7%) were male and seventy six (n=76, 46.3%) were female. Mean age of the patients was 51 years. There was no significant difference between the ages of the two genders. The majority of patients were admitted in hospital with Hepatic encephalopathy (40.5%), upper gastrointestinal bleeding (26.8%) and ascites (17.1%). Rest of the patients (15.6%) presented with other causes like systemic infection with sepsis, stroke, pleural effusion etc. Hepatitis C was the most common cause and present alone in 52.4% of patients followed by Hepatitis B in 40.9%, both viruses were present in 6.7% of patients Table 1. The clinical signs observed in all these patients are given in Table 2. Eleven patients having evidence of both HBV as well as HCV infection were excluded from the final analysis while comparing the signs and their statistical significance in patients with HBV or HCV (Table 3).

DISCUSSION

Chronic Liver disease is a major health problem and a common cause of admission in public sector tertiary care hospitals which receive patients from all over the country. In this study we found that Hepatitis C virus infection was more common than Hepatitis B infection (52.4% vs 40.9% respectively). This pattern is now well recognized in Pakistan for last many years since availability as well as implementation of HBV vaccination program in Pakistan especially in the larger cities. In a study conducted by Khalid M [7] in NWFP province related to overall etiology of chronic liver disease patients, frequency of Hepatitis C

was 46.07%, Hepatitis B 28.21%, and both in 5.71%. Nearly similar figures were mentioned by Siddiqui SA and et al[8] and Almani A et al.[1] The relatively higher percentage of patients with HBV causing chronic liver disease in our study is partly explained by the fact that a significant proportion of our patients come from rural areas of Sindh as well as Balochistan where heath awareness as well as the HBV vaccination drives have not been very successful as compared to urban population. In other developing countries like Vietnam [9], HBV still remains more common as a cause of chronic liver disease as compared to HCV virus (47% vs 23%).

In our study encephalopathy was the commonest cause of admission (40.5%), followed by upper Gastro intestinal bleeding (26.8%), and ascites (17.1%) with its complication like spontaneous bacterial peritonitis and hepatorenal syndrome. These figures are comparable to Rohra et al [10] from Karachi and Mondal et all from Similar results were also noted by Abbas S Z [12] where the corresponding figures were 47% , 25% and 20% respectively. In another study from Lahore [13], encephalopathy was also the commonest complication of cirrhosis requiring admission to ICU in 33% of patients. Haemetemesis was reported 25.1% by Aziz MS.[2] The higher rates for the admission with encephalopathy in these patients was commonly due to potentially preventable precipitating factors, patients' lack of awareness as well as poor adherence to medical advice and treatment regarding these precipitating factors.

Another objective of this study was to document the common clinical signs that are mentioned in various medical literatures but in our setup fewer studies have been conducted to compare them with western studies. The most common clinical signs present were anemia 79.3%, pedal edema 73.80 and leuconychia in 48.8% patients. These signs are partly caused by nutritional deficiencies which are exaggerated in our patient population as compared to western because of obvious socioeconomic reasons. Jaundice was present in 35.4% of patients nearly similar to 35.9% found in another local study [2]. However ascites and splenomegaly were more common in our study (78% vs 53.8% and 72.6% vs 30.4% respectively). This difference might be due to the different patient population with different nutritional and disease status. Another local study conducted in NWFP has also shown similar results with splenomegaly, anaemia, ascites, pedal edema and jaundice in more than half of their patients.[14.]

TABLE3:
COMPARISON OF CLINICAL SIGNS IN HBV AND HCV PATIENTS
N=153

Clinical Signs	Hepatitis B n=67	Hepatitis C n=86	P value
Spider navei	29 (43.28%)	17 (19.76%)	0.002
Jaundice	32 (47.76%)	24(27.90%)	0.01
Breast Atrophy**	09/34 (26.47%)	15/36 (41.67%)	0.12
Parotidomegaly	02(2.98%)	07(8.13%)	0.17
Gynaecomatia*	09/33 (27.27%)	12/50 (24%)	0.21
Ascites	49(73.13%)	70 (81.39%)	0.22
Testicular atrophy*	10/33 (30.30%)	18/50 (36%)	0.23
Leuconychia	36 (53.73%)	39 (45.34%)	0.30
Pigmentation	05 (7.46%)	16 (18.60%)	0.47
Anemia	54 (80.59%)	69 (80.23%)	0.56
Palmar erythema	39 (58.20%)	37 (43.02%)	0.62
Caput Medusi	11(22.44%)	06 (8.57%)	0.65
Pedal edema	50 (74.62%)	63 (73.25%)	0.84
Clubbing	22 (32.83%)	18 (20.93%)	0.96
Splenomegaly	50(74.62%)	64 (74.41%)	0.97
Loss of Axillary hair	25 (37.31%)	32 (37.20%)	0.98
Dupuytren's contracture	00	00	a.
Terry's Nails	00	00	a.

* Assessed only in defined gender. *Male* - Female**
a. No statistics computed

Some of the cutaneous manifestations of cirrhosis like spider nevi, pigmentation and palmer erythema although not very specific for their diagnostic role and having no correlation to the degree of liver dysfunction or etiology of disease were also present in a significant number of our patients.

Spider nevi usually found on the trunk, face, and upper extremities. Are the central arterioles from which numerous small branching vessels radiate towards periphery, although their pathogenesis is incompletely understood, it is believed that their presence in men is associated with an increase in the estradiol to free testosterone ratio. Vascular spiders are not specific for cirrhosis as they also occur in pregnancy, in patients with severe malnutrition and in healthy persons. However the number and size of vascular spiders have been shown to correlate with the severity of chronic liver disease [15]. Patients with numerous large vascular spiders are at increased risk for variceal hemorrhage. its association with chronic liver disease is well established and proved by various studies. Nearly one third of our patients (31.1%) had spider nevi, results matching with figures of 36% as shown by Khan MM and et al [16]. Similar figures (33%) were noted in a study by Li CP [17] , however spider nevi was 50% in alcoholic cirrhotic patients as compared 27% with non- alcoholic cirrhotic patients.

Clubbing was noted in 26.8 % of patients, figures matching with 25% mentioned by Nadeem M et all [18].

Gynecomastia can result from deficiency in testosterone activity or from increased estrogen level due to impaired metabolism, additionally many cirrhotic patients take spironolactone which also inhibit testosterone metabolism [17]. It was found in 13.6% of patients most of them also having testicular atrophy.

Dupuytren's contracture and Terry's nails were not observed in any patient possibly due to the fact that these manifestations are commonly present in alcoholics and in our study there was no patient who had chronic liver disease due to alcohol.

Limitation of the study: The study was done only in admitted patients who were in decompensated stage of chronic liver disease. The pattern of clinical signs might have been different in less symptomatic outdoor patients. This study was observer based and objective bias could not be ruled

out especially in some of the cutaneous findings. The number of patients with HBV infection and HCV infection was not the same hence statistical results could have been different.

CONCLUSION AND RECOMMENDATIONS:

Hepatitis C virus remains the commonest cause of chronic liver disease in our country. The well known clinical signs of chronic liver disease are still valuable in the diagnosis and should be purposely looked for in these patients. Although breast atrophy, testicular atrophy, parotid enlargement, pigmentation and ascites was more common in HCV patients while jaundice, gynecomastia, leuconychia, clubbing and palmer erythema was more common in HBV patients. However these differences were not statistically significant. Anemia, edema, splenomegaly and loss of axillary hair were equally common in both HBV and HCV patients. Interestingly spider nevi were significantly more common in HCV patients. Further studies might be done to validate these findings.

REFERENCES:

1. Almani SA, Memon AS, Memon AI, Shah I, Rahpoto Q, Solangi R. Cirrhosis of liver: Etiological factors, complications and prognosis. J Liaquat Uni Med Health Sci 2008; 7:61-6.
2. Aziz Ms, Saed F, Farooq M. J Clinical Spectrum Of Cirrhosis Liver A Study Of 167 Case. Pak A Med F. 2009;5:
3. Chen DS. Public health measures to control hepatitis B virus infection in the developing countries of the Asia-Pacific Region. J Gastroenterol Hepatol 2000; 15: E7-10.
4. Conn HO , Atterbury CE. Cirrhosis. In: Schiff L, Schiff ER, eds. Diseases of the liver. 6th ed. Philadelphia: JB Lippincott 1987: 725-864.
5. Lawarance S, FriedmanLS. Liver, biliary tract and pancreas. In: Current medical diagnosis and treatment 41st ed. Mc Graw Hill 2002: 675-21.
6. Colinogilvie, Cristopher C, EvansCC. In: Chamberlains symptoms & signs in clinical medicine 12th Ed. Buttterworth Heisnmann 1997: 78-81.
7. Mahmood K, Muhammad N, Ziauddin, Jan A. Frequency of hepatitis B and C viral markers in patients of cirrhosis liver in the North West Frontier ProvinceJ Postgrad Med Inst . 2008; 22:140-3.
8. Siddiqui SA, Zafar J, Qazi RA. Aetiological agents of chronic liver disease (CLD) and its severity Ann Pak Inst Med Sci Apr - Jun 2005;1:88-91
9. Kakumu S, Sato K, Morishita T, Trinh K A, Nguyen HB, Banh VD et al. Prevalence of hepatitis B, hepatitis C and GB virus C/hepatitis G virus infections in liver disease patients and inhabitants in HoChi Minh , Veitnam. J Med Virol 1998; 54:243-8.
10. Rohra DK, jaipall, Khowaja AA, Mahmood A, Ahuja KL. Modes of presentation and reasons for hospitalization of patients with decompensated chronic liver disease in Civil Hospital Karachi. JDUHS 2008; 2:50-4.
11. Mondal SK, Chakrabarti S, Bhattacharya R, Bandyopadhyay D, Chakraborty PP, Nath U et all. Observations of hepatic encephalopathy profile in a tertiary care centre J Indian Med Assoc. 2006; 104:516-8, 524.
12. Abbas SZ, Batool SA, Pathan I, Muhammad SR, Abbas SQ. Liver diseases: Admissions and mortality in a medical ICU at a rural centre in Pakistan Pak J Med Sci 2007;23:713-6.
13. Shafiq F, Ijaz AU, Kashif MA, Zafar S, Shahzad SI. Chronic Liver Disease Related Admissions and Mortality Pattern in Medical ICU; Pak J Gastroenterol 2006; 20(1):72-4.
14. Iqbal S,Ruknuddin. Liver Cirrhosis In North-West Frontier Province Of . JCPSP 2002; 12: 5: 289-91.
15. Robin AC, Graham B, Sarkany I. The Hepatobiliary system and the skin. In:Freedberg IM, Eisen AZ, Wolff K et al. Fitzpatrick's Dermatology in General Medicine, 6th edn. New York: McGraw-Hill; 1998. P 1012-23.
16. Khan MM, Noor SM, Rehman S, Syed A, Khan IM, Hameed K. Cutaneous manifestation of chronic liver disease. J Pak Assoc Derma. 2005; 15:233-7.
17. Li CP, Lee FY, Hwang SJ, Chang F Y; Lin H C; Kuo B et all. Spider angioma in patients with liver cirrhosis: Role of alcoholism and impaired liver function. Scand J Gastroenterol 1999; 34:520-3.
18. Nadeem M, Yousaf MA, Zakaria M, Hussain T, Ali N. the value of clinical signs in diagnosis of cirrhosis. Pak J Med Sc 2005; 21:121-4