FREQUENCY OF HEPATOMA IN HEPATITIS B AND C POSITIVE CIRRHOTIC PATIENTS

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ABSTRACT

Objective: *To find out the frequency of hepatoma in hepatitis B and C positive patients with liver cirrhosis.*

Material and Methods: *This descriptive study was conducted at Medical 'C' unit of Postgraduate Medical Institute Lady Reading Hospital Peshawar on patients admitted from January 2004 to June 2006. Seven hundred and forty patients who had hepatitis B and C positive liver cirrhosis were included in the study. Patients were interviewed according to the proforma after fulfilling the inclusion and exclusion criteria. Blood tests including liver function tests, coagulation profile and hepatitis B, C virus profile, ultrasound, serum alpha-fetoprotein level were done. Data was analyzed at the end of study.*

Results: *Out of 740 patients with liver cirrhosis, 52 (7.03%) patients had hepatoma. Mean age was 62.3 years. Male to female ratio was 6.4:1.Thirty two percent of the patients were Hepatitis B surface antigen positive while anti HCV antibody was found positive in 68% of the patients. Alpha-fetoprotein level was elevated in all the cases. Mean alpha fetoprotein level was >653.82. Mean tumour size was 5.41cm. Tumour was unifocal in 48% of the patients while 52% of the cases had multifocal involvement. Right lobe was involved in 44%, left lobe in 6% while 50% of the patients had both lobes of the liver involved.*

Conclusion: *This study demonstrates that hepatoma is more common in HCV related cirrhosis liver. It is a tumour of advanced age.*

Key Words: *Hepatoma, Cirrhosis Liver, Hepatitis B, Hepatitis C.*

INTRODUCTION

Hepatoma is one of the most common malignant tumours of liver worldwide.[1,2] Hepatoma results in 250,000-1000,000 deaths globally per annum.[3] In 80% of cases, hepatoma develops in cirrhotic livers and among patients with cirrhosis, the annual rate of hepatoma development is in the order of 1-5% per annum.[4,5] Major risk factors for hepatoma are hepatitis B and C viruses and exposure to Aflatoxins.[6-8] Hepatitis B virus and Hepatitis C virus infections remain a major Public health problem with more than 370 and 130 million infected subjects worldwide.[9] Immigration, cheap air travel and globalization are all factors contributing to spread of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections.[10] The carrier rate of HBV in Pakistan is 7-22%.[11] Universal vaccination at birth in high prevalence areas of HBV has been shown to be highly effective in reducing carrier rates in children as well as the incidence of chronic liver disease including hepatoma.[10] Around 95% hepatomas are associated with liver cirrhosis due to Hepatitis B or C virus infection. Among them 70-80% are caused by Hepatitis C virus infection and 10 to 20% by Hepatitis B virus. High incidence of Hepatitis C virus infection is mainly due to blood transfusion or other iatrogenic causes and drug abuse carried around 30-40 years ago.[12]

Clinical presentations are weight loss, cachexia, ascites and jaundice. Its prognosis is poor and early detection is of utmost importance. The diagnostic tools are imaging, alpha-fetoprotein levels and histhology.[8] Treatment options are limited by the frequent presence of metastases[2]. Five years survival is 5-23%[13].

In order to evaluate hepatoma in our setup, we studied its frequency in hepatitis B and C positive cirrhotic patients.

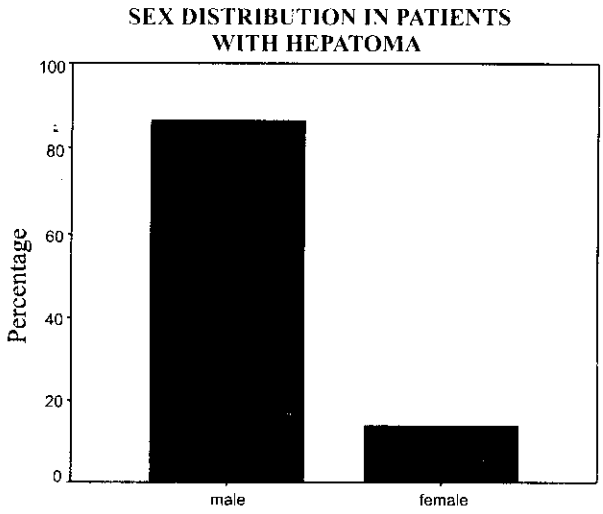

Fig.1

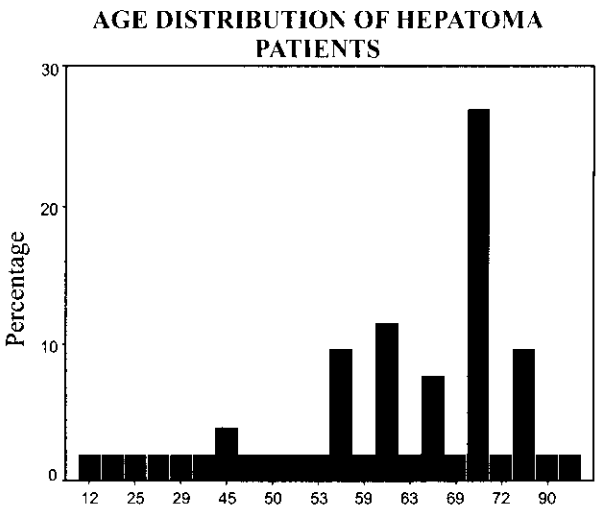

Fig.2

MATERIAL AND METHODS

It is a case series, descriptive study and was conducted in Medical C Unit of Postgraduate Medical Institute Lady Reading Hospital from January 2004 to June 2006.

All patients with liver cirrhosis who were either hepatitis B or C positive were included in the study. Patients of all age group and sex were part of study. Those who had hepatitis B or C negative liver cirrhosis were not included in the study programme. Patients who died during hospital stay were also excluded from the study.

Patients fulfilling the inclusion criteria were admitted in the unit. During hospitalization detailed clinical evaluation was performed. Blood test including liver functions, coagulation profile, hepatitis B (HBsAg) and C viruses (Anti HCV) serology (3rd generation ELISA), and alpha-fetoprotein protein levels were requested. Imaging studies including ultrasound abdomen and CT abdomen were also performed.

All the data was recorded on a proforma designed for this purpose. Positivity for serology, presence of cirrhosis, level of alpha-fetoprotein, tumour size and distribution were noted.

The data was analyzed by using SPSS windows version 10.0.

RESULTS

Total of 9260 patients were admitted in Medical C unit Lady Reading Hospital during the study period. Out of these, 740 (7.99%) patients were cirrhotic either due to hepatitis B or hepatitis C virus infection. Among these 740 patients, 536 (72.54%) were HCV positive cirrhotic while 204(27.57%) patients were found to have HBV positive liver cirrhosis.

Hepatoma was found in 52 patients (7.03%). Forty-five (86.5%) were male and seven (13.5%) were female. Male to female ratio was 6.4:1 as shown in fig.1.

The minimum age was 12 years and maximum age was 100 years. Most of the patients were in the age range of 60 to 80 years (60%) as shown in figure 2. Mean age was 62.3 years.

HBsAg was found to be positive in 18 (32%) patients with hepatoma while on the other hand 34(68%) patients with hepatoma were noted to have Anti HCV anti body positive.(Table-1)

Alpha-fetoprotein (AFP) levels were elevated in all the cases. AFP level was above 400 ng/ml in 32 (61.5%) patients, 200-400ng/ml in 13 (25.%) patients, <200ng/ml in 7(13.5%) cases (Table-2). Mean alpha-fetoprotein level was 653.82ng/ml.

Tumour size was variable. In 8 (15.4%) patients size was more than 10 cm, in 15 (28.8%) patients, size ranged from 5.1-10cm. In 29(55.8%) patients the tumour was 2-5cm (fig.3). Mean tumour size was 5.41cm.

Right lobe of the liver was involved in 23(44.2%) of the cases while 3(5.8 %) of the patients had tumour in the left lobe. Both lobes of the liver were involved in 26(50%) of the cases).

DISCUSSION

Hepatoma is the fifth most common neoplasm in the world, and the third most common cause of death.[14,15] Its incidence is highest in south east Asia and sub-Saharan African regions.[16] It has been ranked as second cancer killer in China since 1990s.[14,17] Recently in some countries like Japan, Italy, France and Switzerland incidence has increased.[18] In Pakistan incidence of hepatoma has

SIZE OF TUMOUR

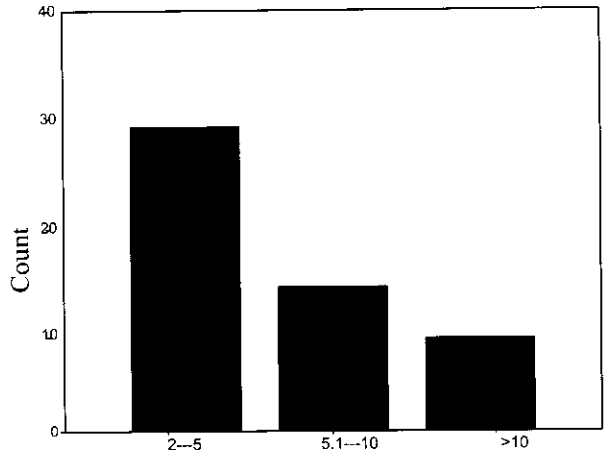

Fig.3

been reported as 8/100,000 per annum.[19]

Viral hepatitis due to Hepatitis B and Hepatitis C is a common cause of hepatoma worldwide.[20-22] Other etiological factors are Aflatoxin, Tobacco smoking, oral contraceptive and heavy alcohol intake.[23]

In our study, chronic hepatitis B and chronic hepatitis C infections accounted for 32% and 68% of hepatomas respectively. In another study from Pakistan, 67 patients were reported and had similar results. In the same study HBsAg was positive in 23% cases of hepatoma and anti HCV antibody in 67% of patients.[3]

One study from Italy reported 36% of HCV infection and 22% of HBV infection as the cause of hepatoma[24]. Our results are consistent with the more recent studies from other parts of the world, which showed an increased incidence of HCV related hepatoma.[21,22,25] This rise in HCV related hepatoma seems to be due to availability of vaccination against HBV, which is not available for HCV.

Serum alpha-fetoproteins (AFP) was raised in all of our study patients. AFP is the most commonly used marker for hepatoma.[26] Percutaneous liver biopsy was risky in our patients due to presence of cirrhosis. The risks of biopsy include bleeding due to abnormal coagulation profile and spread of tumor along the needle track. A non invasive criteria for establishing diagnosis

VIRAL STATUS IN PATIENTS WITH HEPATOMA

Viral Status	No. of patients with Hepatoma (n=52)	
	Frequency	% age
HBs Ag positive	18	34.6
Anti-HCV antibody positive	34	65.4

Table 1

ALPHA FETOPROTEIN LEVEL IN HEPATOMA PATIENTS

Alpha Fetoprotein (ng/ml)	Frequency (n=52)	%age
>50 to <200	7	13.5
200-400	13	25
>400-600	10	19.2
>600-1000	4	7.7
>1000	11	21.1
>2000	7	13.5

Table 2

of hepatoma in cirrhotic patients has been proposed.[27] The diagnosis is established when two imaging techniques (ultrasound, Computed tomography or Magnetic resonance imaging) show an incidental nodule greater than 2cm in diameter regardless of AFP or if a single positive image is associated with AFP level >400ng/ml.Therefore taking into account the above diagnostic criteria, we used AFP as our main diagnostic tool supported by imaging studies for establishing the diagnosis of hepatoma in cirrhotic patients.

Histological diagnosis is manadatory in hepatomas <2cm or in non-cirrhotic patients.[28] All of our patients were cirrhotic and the tumor size was >2cm in all the 52 patients. Hence the Liver biopsy was not mandatory to confirm the diagnosis.

Hepatoma is the 7th most common cause of cancer death in men and the 9th in women.[29,30] According to the National Cancer Registry of kingdom of Saudi Arabia, Ministry of health, collectively liver cancer was found more in males than females (Cancer Incidence Report 1994-96)[31]. There seems to be great similarity over here. In our study 80% of the males were found to have hepatoma while 20% were female patients with hepatoma.

CONCLUSION

It is concluded that hepatocellular carcinoma is one of the common complication of cirrhosis liver and the frequency is more in HCV related cirrhosis. Hence there is need for improvement in diagnosing this malignant condition at an early stage and screening programmes may be developed for its early detection.

REFERENCES

1. Peto J. Cancer epidemiology in the last century and the next decade. Nature 2001;411: 390-5.
2. Qin LX, Tang ZY. The prognostic molecular

markers in Hepatocellular carcinoma. World J Gastroenterol 2002;8:385-92.

3. Parvez T, Gumgumgi AA, Raddadi MA, Rufi AA, Sabir AA, Ibraheim MI. Hepatocellular carcinoma available diagnostic tools and their limitations. J Coll Physicians Surg Pak 2004;14: 57-60.
4. Friedman LS. Liver, Biliary tract and Pancreas. In: Tierney Jr LM, McPhee SJ, Papadakis MA. Ed. Current Medical Diagnosis & Treatment. 45th edition: USA. Mc Graw Hill. International edition.2006; 681-3.
5. Philip J. Johnson, Malignant tumours of the liver, Comprehensive Clinical Hepatology, 2nd Edition, Elsevier Mosby, Phildelphia, USA, 453-67.
6. Farooqi JI, Farooqi RJ. Hepatocellular carcinoma. J Coll Physicians Surg Pak 2001;11:776-86.
7. Yao DF, Horie C, Horie T, Shimizu I, Meng XY, Ito S. Virological features of Hepatitis C virus in patients, Liver diseases in the inshore area of the Yangtze river.Tokushima J Exp Med 1994;41:49-50.
8. Dong ZZ, Yao DF, Yao DB, Wu XH, Wu W, Qiu LW, et al. Expression and alteration of insulin like growth factor II messenger RNA in hepatoma tissues and peripheral blood of patients with hepatocellular carcinoma. World J Gastroenterol 2005;11(30):4655-60.
9. Alter MJ. Epidemiology of Viral hepatitis and HIV co-infection. J Hepatol 2006;44: S6-9.
10. Williams R. Global Challenges in Liver Diseases, J Hepatol 2006;44: 521-26.
11. Ahmed M, Tariq W. Extent of past hepatitis B virus exposure in asymptomatic Pakistani young recuits. Pakistan J Gastroenterol 1991;5: 7-9.
12. Matsui O, Detection and characterization of small hepatocellular carcinoma. J Gasroenterol and Hepatol,2004;19:S266-9.
13. American Cancer Society: Can cancer be found early? Cancer reference information, [Online] 2001[cited on January 2007], Available from;URL;//http://www.....
14. Parvez T, Anwar SM. HbsAg and hepatocellular carcinoma more common in lower socioeconomical class: Our experience. J Coll Physician Surg Pak 2001;11:669-71.
15. Parkin DM, Bray F, Ferley J, Pisani P. Estimating the world cancer burden. GLOBOCAN 2000.Int J Cancer 2001;94:153-6.
16. Hwang SJ, Tong MG Lai PP, Ko ES, Co RL, Chien D, et al. Evaluation of hepatitis B and C viral markers: Clinical significance in Asian and Caucasian patients with hepatocellular carcinoma in United States of America. J Gastroentrol Hepatol 1996;11:1949-54.
17. Jin F, Zhou SZ, Tao RF. Cancer incidence trend shanghai 1972-1994. Tumor 1999;19:255-8
18. Tominaga S, Kuroishi T, Aoki K editor. Cancer mortality statistics in 33 countries 1953-1992. Nagoya: Roppo Shupan, 1998:69.
19. Abdulmujeeb S, Jamal Q, Khanani R, Iqbal N, Kaher S. Prevalence of hepatitis B surface antigen and HCV antibodies in hepatocellular carcinoma cases in Karachi, Pakistan. Trop Doc 1997;27:45-6.
20. Badvie S, Hepatocellular carcinoma. Postgrad Med J 2000; 76:4-11.
21. Jeffers L. Hepatocellular carcinoma: An emerging problem with hepatitis C. J Natl Med Assoc 2000;92:369-71.
22. Uzunalimoglu O, Yurdaydin C, Centinkaya H, Bozkaya H, Sahin T, Colakoglu S, et al. Risk factors for hepatocellular carcinoma in Turkey. Dig Dis Sci 2001;46:1022-8.
23. Parvez T, Anwar SM. Other etiological factors besides HBV responsible for HCC in lower social class: Our experience. J Coll Physicians Surg 2002;12:268-70.
24. Donato F, Tagger A, Chiesa R.Hepatitis B and C virus infection, alcohol drinking and hepatocellular carcinoma: A case-control study in Italy. Hepatology 1997;26:579-84.
25. Ruiz J, Sangro B, Cuende JI, Beloqi O, Riezu-Boj Ji, Herreo Ji, et al Hepatitis B and C viral infections in patients with hepatocellular carcinonoma. Hepatology 1992;16:637-41.
26. Chen DS, Surg JL, Sheu JC, Lai MY, How SW, Hsu HC, et al. Serum alphafetoproteins in the early stages of hepatocellular carcinoma. Gastroenterology 1984; 86:1404-9.
27. Bruix J, Sheman M, Liovet JM, Beaugrand M, Lenicioni R, Burroughs AK et al. Clinical management of hepatocellular carcinoma. Conclusion of the Barcelona-2000.EASL Conference. J Hepatol 2001;35:421-30.
28. Gogel BM, Goiostein RM, Kuhn JA, McCarty TM, Donahoe A, Glastad A, et al. Diagnostic evaluation of hepatocellular carcinoma in cirrhotic liver. Oncology (Huntingt) 2000;14(supp-3):15-20.
29. Munoz N, Bosch X. Epidemiology of

hepatocellular carcinoma. In: Okuda K, Ishak KG. editors. Neoplasm of the Liver. Tokyo; Springer-Verlag; 1989:3.

30. Okuda K. Epidemiology of primary liver cancer. In: Tobe T, editor. Primary liver cancer in Japan.Tokyo:Spriger-verlog 1992:3.

31. Parvez T, Parvez B, Parvez K, Gumgumgi AA, Saleem Al Ahmadi, Sabir AA et al. Screening for hepatocellular carcinoma. J Coll Physicians Surg Pak 2004;14: 570-5.

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