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HEPATOMA; FREQUENCY OF HEPATOMA IN CIRRHOTIC POPULATION ATTENDING TERTIARY CARE HOSPITAL KARACHI.

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ABSTRACT... Objectives: To determine the frequency of hepatoma in patients with cirrhosis attending tertiary care hospital Karachi. **Study Period:** Six months July to December 2017. **Study Design:** Descriptive cross sectional study. **Setting:** Department of Gastroenterology, Liaquat National postgraduate Medical centre Karachi. **Patients and Methods:** The clinical history was taken from patients and ultrasound of liver was done to and mass if any and its size was noted. Noninvasive criteria for diagnosing hepatoma were utilized and all information was noted and entered in the proforma and analyzed in statistical software. **Results:** A total of 213 cases, 15.02% individual hepatitis B and 21.13% subject hepatitis C. Frequency of hepatoma in cirrhotic population detected as 10.33% (22/213). Rate of hepatoma was not significant among different age groups ($p=0.202$). Rate of hepatoma was also not significant between male and female ($p=0.59$). **Conclusion:** Persistent chronic viral hepatitis B and C infection with cirrhosis responsible for acquiring hepatoma.

Key words: Alpha fetoprotein, Cirrhosis, Hepatoma, Hepatitis-C, Hepatocellular Carcinoma.

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INTRODUCTION

Hepatoma is the common primary hepatic malignancy which is distinct from other types of primary hepatic malignancy on histological and etiological grounds.¹ Around 80%-90% of subjects with hepatoma has chronic liver disease & liver cirrhosis along with certain risk factors for acquiring liver cirrhosis includes chronic viral hepatitis B virus, hepatitis C, alcoholic hepatic disorders and non-alcoholic fatty liver disease.²⁻⁵ The risk factor for hepatoma is liver cirrhosis and the evidence reported that 50% hepatomas are associated with hepatitis B virus infection and 25% associated with hepatitis C virus.⁶ After long period of chronic liver disease the liver cirrhosis usually developed and leads to increase fibrous tissue & destruction of hepatocytes cells provides soil for generation of cancerous nodules.^{7,8} HBV infection has risk for developing hepatic malignancy 100 fold in chronic carriers.⁹ Approximately 340,000 subjects with hepatic malignancy (54% globally) are due to hepatitis B virus.¹⁰ Hepatitis C virus has risk for developing hepatic malignancy 17 folds,¹²

although it varies according to degree of liver fibrosis and around 195,000 subjects of hepatic malignancy (31% globally) are due to hepatitis C virus.¹⁰ Publications the burden of disease largely in developing countries.¹¹⁻¹³ In a local study frequency of hepatoma was found in 7.03% patients with cirrhosis of liver.¹⁴ There are multiple causes for hepatoma varies geographically, severity and duration of disease to predict the prognosis.¹⁵ Therefore the rationale of the present study was to estimate the magnitude of hepatoma in cirrhotic subjects and based on the findings of the study the appropriate health strategies can be planned to save the individuals infected with chronic viral hepatitis C and B from acquiring the complications as hepatoma.

PATIENTS AND METHODS

The six months descriptive cross sectional study was conducted in Liaquat National Hospital Karachi. The sample size calculated on the basis of the prevalence of Hepatoma = 7.03%, confidence level=95% and the bond on

error=3.5% to get the appropriate sample size (n) as 213 cirrhotic patients.

The inclusion criteria were:

- Cirrhotic patients
- Patients of age 35 to 70 years
- Either gender
- Duration > 6 months

The exclusion criteria were:

- Non consenting participants
- Non Hepatitis B and C patients
- Patients with Carcinoma Pancreas
- Metastasis from other sources like gall bladder, esophagus, spleen

Hepatoma: The serum α -fetoprotein (AFP) > 200 ng/ml along with typical enhancement pattern on ultrasound in individuals with liver cirrhosis was considered as hepatoma.

The cirrhotic patients admitted in medical wards meeting the inclusion criteria diagnosed as defined earlier was enrolled in the study by the researcher himself. Informed consent was taken from the patients for inclusion in the study after explaining the pros and cons. History was taken from patients for the duration of disease and history of hepatitis B and C. Ultrasound of liver was done to and mass if any and its size was noted. Demographics of the patients and specific information of hepatoma was noted and entered in the Proforma by the researcher. The collected data was analyzed by the SPSS software 17. Age of the patient, duration of disease and size of the tumor was presented in mean \pm standard deviation. Gender of the patient, Hepatitis B and C was presented as frequencies and percentages. Stratification of variables was done and the Chi square test was applied & the level of significance was p-value less than or equal to 0.05.

RESULTS

A total of 213 cirrhotic patients were enrolled for the study. Majority of the subjects were 41 to 50 years of age. There were 44.6% female and 55.4% male. A total of 213 cases, 15.02% patients had hepatitis B and 21.13% had hepatitis C. Frequency of hepatoma in cirrhotic population

was detected as 10.33% (22/213). Rate of hepatoma was not significant among different age groups ($p=0.202$). Rate of hepatoma was also not significant between male and female ($p=0.59$). Similarly frequency of hepatoma was also observed with respect to hepatitis B, hepatitis C, duration of disease and size of tumor but there were no significant finding after stratification. The results of the study are presented in Figure-1 to 5 and Table-I to IV.

Age Groups (Years)	Hepatoma		Total
	Yes	No	
≤ 40 Years	5(7.7%)	60(92.3%)	65
41 to 50 Years	14(14.9%)	80(85.1%)	94
51 to 60 Years	3(7.7%)	36(92.3%)	39
>60 Years	0(0%)	15(100%)	15

Table-I. Frequency of hepatoma in patients with cirrhosis with respect to age groups n= 213
Chi-Square= 4.62 $p=0.202$

Gender	Hepatoma		Total
	Yes	No	
Male	11(9.3%)	107(90.7%)	118
Female	11(11.6%)	84(88.4%)	95

Table-II. Frequency of hepatoma in patients with cirrhosis with respect to gender n= 213
Chi-Square= 0.289 $p=0.59$

Hepatitis B	Hepatoma		Total
	Yes	No	
Yes	4(12.5%)	28(87.5%)	32
No	18(9.9%)	163(90.1%)	181

Table-III. Frequency of hepatoma in patients with cirrhosis in relation to hepatitis B n= 213
Chi-Square= 0.192 $p=0.66$

Hepatitis C	Hepatoma		Total
	Yes	No	
Yes	4(8.9%)	41(91.1%)	45
No	18(10.7%)	150(89.3%)	168

Table-IV. Frequency of hepatoma in patients with cirrhosis in relation to hepatitis C n= 213
Chi-Square= 0.128 $p=0.721$

DISCUSSION

Hepatoma is a malignancy having poor prognosis with estimated prevalence approximately one million cases per year worldwide.¹⁶ The subjects with liver cirrhosis have been detected as risk for hepatoma which is the cause of mortality in cirrhotic population.^{17,18}

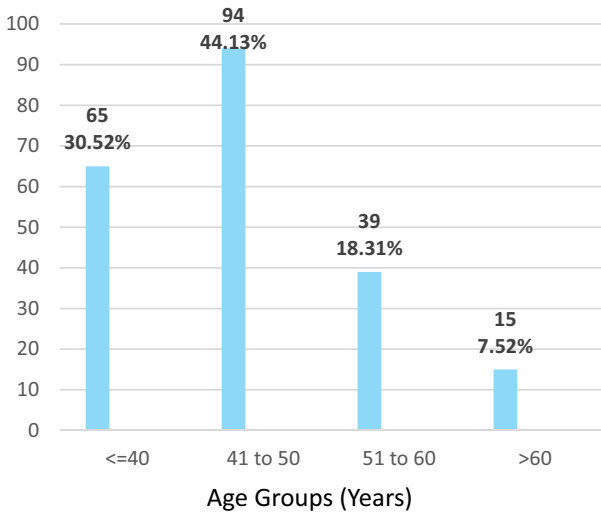


Figure-1. Age distribution of the patients n=213

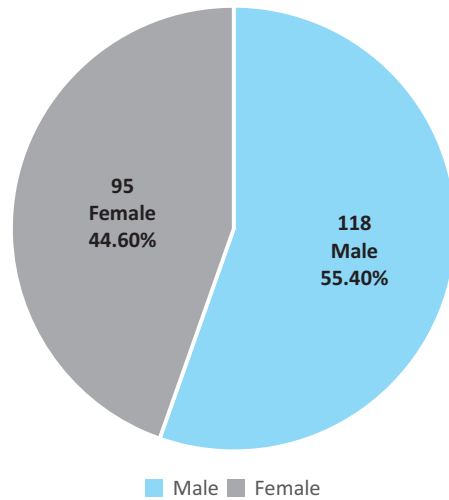


Figure-2. Gender distribution n=213

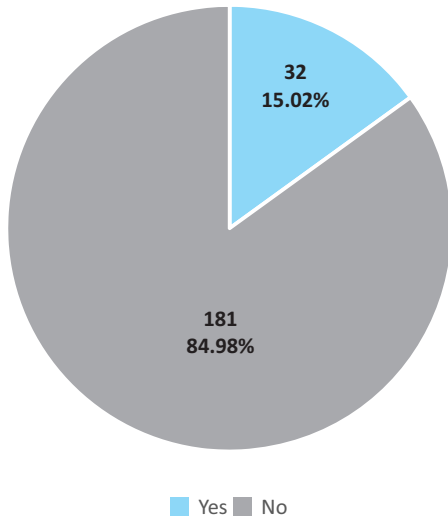


Figure-3. Hepatitis b of the patients n=213

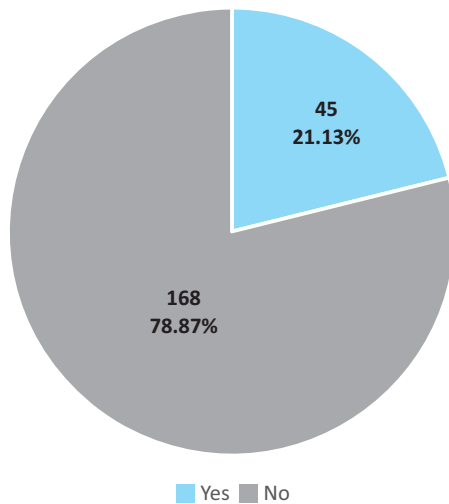


Figure-4. Hepatitis c of the patients n=213

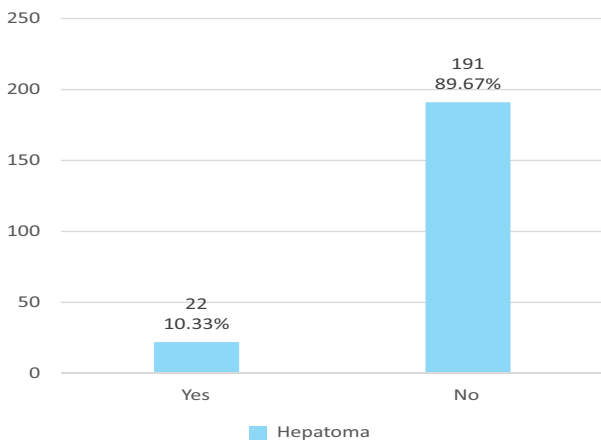


Figure-5. Frequency of hepatoma in patients with cirrhosis n= 213

It may either consequence of long standing liver disorder or independent response to hepatic insult.^{19,20} The importance of association between hepatoma and liver cirrhosis is still obscure, but the association can provide means to detect the subjects at risk of hepatoma.²¹ In our study a total of 213 cases, 15.02% patients had hepatitis B & 21.13% had hepatitis C. The burden of chronic hepatitis b virus infection reduced because of utilization of HBV vaccination whereas hepatitis C virus infection continues to rise despite of treatment especially in developing countries.²²In our study out of 213 cirrhotic patients, 44.6% were female

and 55.4% were males. This male population predominance to acquire hepatoma is also reported formerly as Stone WD, et al²³ observed 86 %, Parker RGF,²⁴ 88% & MacSween RNM,²⁵ 92% predominance of male population and our study consistent with them. The reasons is unknown but animals studies observed and castration protection against liver malignancy.²⁶ There are also the reports of hepatoma in male population taking testosterone.²⁷ The incidence of hepatoma doubled during 1983 and 2002 and is considered as 5th common cause of malignancy and third cause of mortality worldwide.²⁸⁻³⁰ Regarding its clinical impact, 80%-90% of all hepatomas occurs in individuals with chronic liver disease or cirrhosis revealed the medical importance of liver cirrhosis.^{28,29} In our study the frequency of hepatoma in patients with cirrhosis was observed in 10.33% (22/213). The prevalence for liver cirrhosis in individuals with hepatoma is approximately 80-90% in autopsied series worldwide & therefore.³¹ The former literatures observed that hepatoma usually found in histological abnormal liver and the presence of chronic liver disease is the risk factor for the development of hepatoma.^{32,33}

CONCLUSION

Liver cirrhosis predisposes to hepatoma and considered as a premalignant state and the persistent chronic hepatitis B and C viral infection account for most of the hepatoma cases. There should be some health policy at grass root level for screening of such patients for providing instant and affordable treatment.

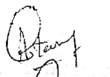

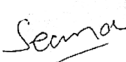
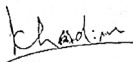
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REFERENCES

1. Yu MC, Yuan JM, Lu SC. **Alcohol, cofactors and the genetics of hepatocellular carcinoma.** J Gastroenterol Hepatol 2008; 23(suppl 1):S92-S7.
2. El-Serag HB, Rudolph KL. **Hepatocellular carcinoma: Epidemiology and molecular carcinogenesis.** Gastroenterology. 2007; 132:2557-76.
3. Poon D, Anderson BO, Chen LT, Tanaka K, Lau WY, Van Cutsem E, et al. **Management of hepatocellular carcinoma in Asia: Consensus statement from the Asian Oncology Summit 2009.** Lancet Oncol. 2009; 10:1111-8.
4. Montalto G, Cervello M, Giannitrapani L, Dantona F, Terranova A, Castagnetta LA. **Epidemiology, risk factors, and natural history of hepatocellular carcinoma.** Ann N Y Acad Sci. 2002; 963:13-20.
5. Gomaa AI, Khan SA, Toledano MB, Waked I, Taylor-Robinson SD. **Hepatocellular carcinoma: Epidemiology, risk factors and pathogenesis.** World J Gastroenterol. 2008; 14:4300-8.
6. Gurtsevitch VE. **Human oncogenic viruses: Hepatitis B and hepatitis C viruses and their role in hepatocarcinogenesis.** Biochemistry (Mosc). 2008; 73:504-13.
7. Delhaye M, Louis H, Degraef C, Le Moine O, Devière J, Gulbis B, et al. **Relationship between hepatocyte proliferative activity and liver functional reserve in human cirrhosis.** Hepatology. 1996; 23:1003-11.
8. Caillot F, Derambure C, Bioulac-Sage P, Francois A, Scotte M, Gorla O, et al. **Transient and etiology related transcription regulation in cirrhosis prior to hepatocellular carcinoma occurrence.** World J Gastroenterol. 2009; 15:300-9.
9. Szabó E, Páska C, Kaposi Novák P, Schaff Z, Kiss A. **Similarities and differences in hepatitis B and C virus induced hepatocarcinogenesis.** Pathol Oncol Res. 2004; 10:5-11.
10. Parkin DM. **The global health burden of infection-associated cancers in the year 2002.** Int J Cancer. 2006; 118:3030-44.
11. But DYK, Lai CL, Yuen MF. **Natural history of hepatitis-related hepatocellular carcinoma.** World J Gastroenterol. 2008; 14:1652-6.
12. Parkin DM, Bray F, Ferlay J, Pisani P. **Global cancer statistics, 2002.** CA Cancer J Clin. 2005; 55:74-108.
13. Parkin DM, Pisani P, Ferlay J. **Estimates of the worldwide incidence of 25 major cancers in 1990.** Int J Cancer. 1999; 80:827-841
14. Ziauddin, Muhammad R, Saeedi MI, Mahmood K. **Frequency of hepatoma in hepatitis B and C positive cirrhotic patients.** J Pak Med Inst. 2006; 20(4):395-9.
15. Venook AP, Papandreou C, Furuse J, de Guevara LL. **The incidence and epidemiology of hepatocellular carcinoma: A global and regional perspective.** Oncologist. 2010;15(suppl 4):5-13.
16. Munoz N, Bosch FX. **Epidemiology of hepatocellular carcinoma.** In: Okuda K, Ishak KG, editors. Neoplasms of liver. Tokyo, Japan: Springer-veriag; 1987. P. 3-19.
17. Ebara M, Ohto M, Shinagawa T. **Natural history of**

- minute hepatocellular carcinoma smaller than three centimeters complicating cirrhosis. *Gastroenterology*. 1986; 90:289-98.
18. Tanaka R, Itoshima T, Nagashima H. **Follow up study of 582 liver cirrhosis patients for 26 years in Japan.** *Liver*. 1987; 7:316-29.
 19. Kew MC, Popper H. **Relationship between hepatocellular carcinoma and cirrhosis.** *Semin Liver Dis*. 1984; 4:136-46.
 20. Benvegnù L, Gios M, Boccato S, Alberti A. **Natural history of compensated viral cirrhosis: a prospective study on the incidence and hierarchy of major complications.** *Gut*. 2004; 53:744-9.
 21. Fattovich G, Pantalena M, Zagni I, Realdi G, Schalm SW, Christensen E. **Effect of hepatitis B and C virus infections on the natural history of compensated cirrhosis: a cohort study of 297 patients.** *Am J Gastroenterol*. 2002; 97:2886-95.
 22. El-Serag H, Mason AC. **Rising incidence of hepatocellular carcinoma in the United States.** *N Engl J Med*. 1999; 340:745-50.
 23. Stone WD, Islam NRK, Paton A. **The natural history of cirrhosis.** *Quarterly J Med*. 1968; 37:119-32.
 24. Parker RGF. **The incidence of primary hepatic carcinoma in cirrhosis.** *Proceed Royal Soc Med*. 1957; 50:145-7.
 25. MacSween RNM. **A clinicopathological review of 100 cases of primary malignant tumours of the liver.** *J Clin Pathol*. 1974; 27:669-82.
 26. Reuber MD. **Influence of hormones on N-2-fluorenyldiacetamide-induced hyperplastic hepatic nodules in rats.** *J National Cancer Inst*. 43:445-51.
 27. Farrell GC, Uren RF, Perkins KW, Joshua DE, Baird PJ, Kronenberg H. **Androgen-induced hepatoma.** *Lancet*. 1975; 1:430-2.
 28. Velasquez RF, Rodríguez M, Navascuès CA, Linares A, Pérez R, Sotorrios NG, et al. **Prospective analysis of risk factors for hepatocellular carcinoma in patients with liver cirrhosis.** *Hepatology*. 2003; 37:520-7.
 29. Deuffic S, Poynard T, Buffat L, Valleron AJ. **Trends in primary liver cancer.** *Lancet*. 1998; 351:214-5.
 30. Corrao G, Ferrari P, Zambon A, Torchio P, Arico S, Decarli A. **Trends of liver cirrhosis mortality in Europe, 1970-1989: ageperiod- cohort analysis and changing alcohol consumption.** *Int J Epidemiol*. 1997; 26:100-9.
 31. Simonetti RS, Cammà C, Fiorello F, Politi F, D'Amico G, Pagliaro L. **Hepatocellular carcinoma. A worldwide problem and the major risk factors.** *Dig Dis Sci*. 1991; 36:962-72.
 32. Bralet MP, Règimbeau JM, Pineau P, Dubois S, Loas G, Degos F, et al. **Hepatocellular carcinoma occurring in nonfibrotic liver: Epidemiologic and histopathologic analysis of 80 French cases.** *Hepatology*. 2000; 32:200-4.
 33. Chiesa R, Donato F, Tagger A, Favret M, Ribero ML, Nardi G, et al. **Etiology of hepatocellular carcinoma in Italian patients with and without cirrhosis.** *Cancer Epidemiol Biomarkers Prev*. 2000; 9:213-6.

AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Riaz Hussain Awan	Drafting the article and shares its expert research opinion and experience in finalizing the manuscript.	
3	Seema Nayab	Contributed and conception and interpretation of data and give his expert view for manuscript designing.	
4	Khadim Hussain Awan	Collection and acquisition of data, analysis and interpretation of data and make it suitable for final revision and corresponding author	
5	Faqir Muhammad Awan	Data collection and analysis.	