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HBV Related HCC- Points to Ponder

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1. Abstract

1.1. Introduction

Hepatitis B virus (HBV) infection is a leading cause of chronic liver disease and liver cancer worldwide. Hepatocellular carcinoma (HCC) remains one of the major causes of cancer-related mortality globally. Effective prevention and management strategies for HBV infection are crucial in reducing liver-related complications, including HCC. HBV plays a distinct role in liver carcinogenesis, and there is growing knowledge about the factors contributing to its oncogenic potential. With advancements in HCC management, special attention must be given to the treatment of HBV infection in patients with HBV-induced HCC.

1.2. Material and Methods

This was a retrospective study done at Medical Gastroenterology Department, PGIMS,Rohtak conducted over a period of ten years i.e. 01.03.2016 to 28.02.2026, during which patients diagnosed to be having HCC due to HBV were enrolled in the study, after written consent for the same. The data pertaining to fifty four HBV related HCC patients was analysed.

1.3. Observations and Results

HBV related H.C.C is predominantly seen in males and older age group. Out of 54 patients, 50 (92.59%) were males and only 4 (7.41%) were females. On geographical distribution, there was clear cut predominance of rural background i.e. 51 patients (94.45%) resided in rural area and only 3 patients (5.55%) belonged to urban area. As age increased, the number of H.C.C patients increased in our study group and 51 patients (94.45%) were above 40 yrs of age. The three patients who belonged to third and fourth decade were non cirrhotic and in two there was family history of H.C.C and in both of them there was low HBV viral load and third patient was having chronic hepatitis B with high viral load and directly developed multifocal H.C.C without going into cirrhotic stage. Rest all 51 patients of HBV were cirrhotic. Out of total pool of 54 patients of H.C.C, a significant percentage of patients i.e. 25 (46.29%) had low viral load of below 40,000 I.U. or two lakhs copies/ml. The rest 29 patients (53.71%) had high HBV viral load. There was strong association with alcohol and smoking in our study group. Out of total 54 patients, 23 patients (42.59%) consumed both alcohol and smoke, 8 patients (14.81%) were only smoker and 2 patient (3.70%) were only alcoholic. Thus, in total, 33 patients (61.11%) had association with alcohol intake or smoking.

1.4. Conclusion

Good compliance on drugs is mandatory and patients should be strictly prohibited against smoking and alcohol intake which increases the risk of developing HCC. Old age male belonging to rural background are at increased risk of developing H.C.C. Majority of HBV patients develop HCC after developing cirrhosis but patients with family history of HCC can develop it even in non-cirrhotic stage. A significant percentage of patient can develop HCC with even low HBV viral load.

2. Introduction

Liver cancer which is one of the leading causes of cancer deaths worldwide has recently recorded annual death toll with700,000 around the globe [1]. Hepatocellular Carcinoma (HCC) forms the major chunk (75% -90%) of primary liver

Table1: ShowingagedistributioninHBV relatedH.C.C.

AGE (YRS)	HBV (N-54)
Oct-20	0 (0%)
21-30	1 (1.85%)
31-40	2 (3.70%)
41-50	2 (22.22%)
51-60	16 (29.62%)
61-70	20 (37.03%)
71-80	3 (5.55%)
81-90	0 (0%)

Table2: ShowingEpidemiologicalfactorDistributioninHBV relatedH.C.C.

Epidemiology	HBV (N-54)
Male	50 (92.59%)
Female	4 (7.41%)
Rural	51 (94.45%)
Urban	3 (5.55%)
Diabetes	0 (0%)
Alcohol & Smoking	23 (42.59%)
Only Smoker	8 (14.81%)
Only Alcohol	2 (3.70%)
Cirrhosis	51 (94.44%)
Non-Cirrhotic	3 (5.66%)
High HBV Viral load	29 (53.71%)
Low HBV Viral load	25 (46.29%)
Family History of HCC	8 (14.81%)
No Family History of HCC	46 (85.18 %)

Table 3: ShowingParametersDistributioninHBV Related HCC.

Parameters	HBV (N=54)
AST	53-370
ALT	48-410
S. Bilirubin	0.9- 12.5
S. Albumin	2.3-4.1
INR	0.96-1.85
Platelet Count	0.58- 2.1 L
S. Creatinine	0.7- 1,9
Fibroscan	6.3-75 Kpa
Viral Load	10^{1}-10^{11}

malignancies [2]. Most cases of HCC (75% to 90%) develop in cirrhosis resulting from chronic infection by hepatitis B virus and hepatitis C virus, alcoholic injury, Metabolic associated steatotic liver disease (MASLD) and to a lesser extent from genetically determined disorders such as hemochromatosis [3-5]. In last three decades, about 63% increase in total deaths has been reported globally because of viral hepatitis. Hepatitis B and C infections accounted for most of the morbidity and mortality since it leads to progressive hepatic damage in patients and ultimately causing cirrhosis and hepatocellular carcinoma [6]. The incidence of HCC increases with age in all populations and shows a slight decline in the elderly population. HCC shows a strong male preference. In low incidence regions, it is four times more common in males while in high prevalence areas, it is about eight times more common. It may be attributed to additional effect of other factors including higher levels of alcohol intake and smoking coupled with a higher incidence of cirrhosis in males. Animal experiments have suggested the role of sex hormones and/or hormone receptors. Orchidectomy reduces the carcinogenic effects of chemicals in male rats to the level found in females. A similar effect has been observed with stilbesterol or estradiol pellets' implantation but the effect was comparatively less. [7]. In western countries, inborn errors of metabolism and congenital abnormalities have also contributed towards HCC in some cases [8]. Our department is Model treatment center under National Viral Hepatitis Control Program where free treatment is provided to Hepatitis B and C patients (HBV & HCV), hence we have good data of the same.

3. Material And Methods

This was a retrospective study done at Medical Gastroenterology Department, PGIMS,Rohtak conducted over a period of ten years i.e. 01.03.2016 to 28.02.2026, during which patients diagnosed to be having HCC due to HBV were enrolled in the study, after written consent for the same. The total HBV patient who reported in above time period for consultation was 12,000 and out of them 54 were proven to be having HCC and data pertaining to them was analyzed. The patients who visited the Medical Gastroenterology department in last ten years and were confirmed to be having HBV infection on ELISA as well as PCR DNA and confirmed to be having HCC on Triple phase CECT scan abdomen and AFP level were investigated fully and their detailed records were collected regarding aeitiological and epidemiological factors & clinical spectrum.The detailed clinical examination and laboratory investigations were done including complete blood counts, liver function tests, kidney function tests, thyroid function test, serum electrolytes, coagulation parameters (PT, INR), blood sugar, autoimmune profile, Hbs Ag, anti HIV antibody, anti HCV antibody, Ultrasonogram abdomen, Chest x ray PA view and Fibro scan were done.

4. Observations And Results

HBV related H.C.C is predominantly seen in males and older age group. Out of 54 patients, 50 (92.59%) were males and only 4 (7.41%) were females. On geographical distribution, there was clear cut predominance of rural background i.e. 51 patients (94.45%) resided in rural area and only 3 patients (5.55%) belonged to urban area. As age increased, the number of H.C.C patients increased in our study group and 51 patients (94.45%) were above 40 yrs of age. The three patients who

belonged to third and fourth decade were non cirrhotic and in two there was family history of H.C.C and in both of them there was low HBV viral load and third patient was having chronic hepatitis B with high viral load and directly developed multifocal H.C.C without going into cirrhotic stage. Rest all 51 patients of HBV were cirrhotic. Out of total pool of 54 patients of H.C.C, a significant percentage of patients i.e. 25 (46.29%) had low viral load of below 40,000 I.U. or two lakhs copies/ ml. The rest 29 patients (53.71%) had high HBV viral load. There was strong association with alcohol and smoking in our study group. Out of total 54 patients, 23 patients (42.59%) consumed both alcohol and smoke, 8 patients (14.81%) were only smoker and 2 patient (3.70%) were only alcoholic. Thus, in total, 33 patients (61.11%) had association with alcohol intake or smoking.

In HBV group AST level varied from 53-370 IU (mean 85) whereas ALT level varied from 48-410 IU (mean 91). The serum bilirubin level varied from 0.9-12.5 (3.38) mg/dl, whereas serum albumin level varied from 2.3-4.1 (mean 3.40). The INR level varied from 0.96-1.85 (mean 1.36), whereas platelet level varied from 0.58- 2.1 lakhs/mm3 (mean 1.3). The serum creatinine level varied from 0.7-1.9 (mean 1.3) and Fibroscan score varied from 6.3-75 Kpa (mean 44). The HBV viral load ranged between 101-1011 IU/ml (mean 105). Out of total 54 patients of HBV, 50 were on monotherapy and 4 was on dual therapy.

DISCUSSION- Hepatocellular carcinoma (HCC) is a highly prevalent cancer globally, occupying the sixth place and was the third leading cause of cancer death worldwide in 2020 [9]. Viral hepatitis and alcohol consumption are the most important risk factors for the development of HCC [10]. In countries where vaccination against hepatitis B virus (HBV) is widely available, alcohol-related HCC can be more prevalent [11]. In the last decades, non-alcoholic fatty liver disease (NAFLD), now called as MAFLD has become a more prevalent risk factor for HCC due to the rise of obesity and metabolic syndrome in this country [12]. Early detection of HCC is likely beneficial, and prognosis can be calculated using tumour characteristics, clinical parameters, or both. HCC accounts for 70% of primary liver cancers and is the sixth most common cancer worldwide [9-11,13]. It is the third leading cause of cancer-related deaths in the world [10-12]. It is more common in men and the average age at diagnosis is 50 – 70 years [10-11] which is in alignment with our study group of 80 patients, in which majority of patients were males and above fifty years of age. Africa and Asia account for 80% of all HCC cases, with Asia bearing approximately 72.5%. This is thought to be due to their high rates of HBV infection, as well as high rates of aflatoxin exposure [10,11,14]. Limited access to HBV screening, vaccination, and treatment also plays a role [15]. The incidence of HCC in patients with chronic HBV infection is 44%. The rural predominance was seen because this disease occurs more commonly in rural areas due to lack of proper safe needle practices because of lack of trained health professionals in rural areas. The history of alcohol and smoking was seen in significant number of patients which is in accordance to other studies reported in literature, as smoking and alcohol are independent risk factors for causing HCC and when these factors are clubbed with HBV infection, then as expected risk of developing HCC rises. It is well known fact that majority of patients of HBV pass through cirrhotic stage for progressing into HCC and same was seen in our HBV study group and in only three young non-cirrhotic patients developed HCC and out of them two had family history of HCC and third one was in chronic hepatitis stage with high viral load and transaminases level. The HBV & HCV co-infection increases risk of H.C.C. and in our study group also, six HBV patients were co-infected with HCV. Out of 54 patients in HBV group, 50 were on monotherapy and four were on dual therapy. Out of total pool of 54 patients of H.C.C, a significant percentage of patients i.e. 25 (46.29%) had low viral load of below 40,000 I.U. or two lakhs copies/ml. The rest 29 patients (53.71%) had high HBV viral load. It highlights, that the HBV DNA which is present in blood is not alone responsible for causing HCC but cccDNA integrated in hepatocytes, has also role to play. Thus, many patients with low HBV DNA in blood developed HCC. Over the years, it has been shown that HBV infection can induce liver disease and cause disease progression, via a variety of different mechanisms, eventually leading to a malignant transformation. Chronic HBV infection can progress to advanced liver fibrosis and eventually cirrhosis as a risk factor for HCC. On the other hand, there are specific virus-related mechanisms associated with the carcinogenicity and development of HCC in chronic HBV infection even in the absence of cirrhosis. These mechanisms include HBV gene integration, causing genomic instability, and the activation of cancer-promoting signaling pathways [16]. Moreover, there is currently expanding research on the roles of epigenetics,

exosomes, autophagy, and metabolic regulation and immune suppression [17]. Jiang et al. have reviewed the literature for the mechanisms of the carcinogenicity of HBV and inducing HCC [18].

5. Conclusion

Good compliance on drugs is mandatory and patients should be strictly prohibited against smoking and alcohol intake which increases the risk of developing HCC. Old age male belonging to rural background are at increased risk of developing H.C.C. Majority of HBV patients develop HCC after developing cirrhosis but patients with family history of HCC can develop it even in non-cirrhotic stage. A significant percentage of patient can develop HCC with even low HBV viral load.

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