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Full Length Research Paper

A study of the prevalence of HCCA in patients with and without HBV in Northeast Nigeria

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Hepatitis B virus (HBV) infection has been reported as one of the aetiological factors for hepatocellular carcinoma (HCCA). This study reports the prevalence of HCCA in patients with and without HBV in Northeast Nigeria over a period of five years. A total of 114 patients consecutively diagnosed with HCCA and tested for Hepatitis B surface Antigen (HBsAg) at the University of Maiduguri Teaching Hospital (UMTH), between January 1996 and December 2000, were studied. There were 81 males and 33 females, ranging in age between 9 months and above 60 years. Of the 114 patients with HCCA, 86.8% were positive for HBsAg of which males accounted for a higher prevalence of 63.1%, while females accounted for 23.7% (2.7:1). HCCA patients from the fouth decade of life and above were observed with a higher prevalence of HBV infection. Among the HBsAg-negative patients with HCCA, no significant gender difference was observed (p > 0.05). However, 13.2% of patients with HCCA were negative for HBsAg. Viral and non-viral aetiologic factors may play a role in developing HCCA in Maiduguri.

Key words: Hepatocellular carcinoma, Hepatitis B virus.

INTRODUCTION

Hepatocellular carcinoma (HCCA) is a chronic liver disease that has been associated with chronic viral infections caused by Hepatitis B virus (HBV) and Hepatitis C virus (HCV) (Chuang et al., 1992). HBV carriage rates in Africa range from 6.5% in Tunisia in North Africa to 20% in the Gambia in West Africa (Kew, 1992). The prevalence of HBV in the sub-Saharan Africa is as high as 35% in Nigeria and 75% in Namibia (Kew, 2006). In sub-Saharan Africa, HBV is the most prevalent aetiological factor associated with HCCA (Mustapha and Pindiga, 2003; Gashau and Mohammed, 1991; Maharaj et al., 1986). Other risk factors associated with HCCA include aflatoxins, cirrhosis, ethanol abuse, haemochromatosis and alpha 1-antitrypsin deficiency (Olasode, 1998).

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The pathogenesis of HBV-associated HCCA has been studied extensively, and the molecular changes during the malignant transformation have been identified. The main carcinogenic mechanism of HBV-associated HCCA is related to the long-term inflammatory changes caused by a chronic Hepatitis B infection, which might involve integration of the HBV genome (Park et al., 2007).

HCCA has been reported to occur worldwide with an estimated 0.5 million new cases annually (Montalto et al., 2002). The link between HBV and HCCA in sub-Saharan Africa comes from studies in Senegal, the Gambia and southern Africa (Kew et al., 1979, 1987; Kirk et al., 2004). Chronic infection with HBV has been reported to have serious consequences accounting for about 75 to 80% of virus-associated hepatocellular carcinoma (Parkin et al., 2001; Magglore and Giancola, 1987; Oladeinde, 1983).

In Nigeria, there is limited information available on the association of HCCA with HBV. A recent study in Gombe, Northeast Nigeria reported a high prevalence of HBV

Table 1. Annual distribution of 114 HCCA patients diagnosed with HBsAg in Maiduguri.

Year	HCCA patients tested	HBsAg positive	HBsAg negative
1996	14	12 (85.7%)	2(14.3%)
1997	23	20 (87%)	3(13%)
1998	26	24 (92.3%)	2(7.7%)
1999	27	20 (74.1%)	7(25.9%)
2000	24	23 (95.8%)	1(4.2%)
Total	114	99(86.8%)	15(13.2%)

among patients with HCCA. A high incidence of HCCA had earlier been reported in Maiduguri, Northeast Nigeria (Gashau and Mohammed, 1991) where HBV accounts for 17.4% of apparently healthy population (Harry et al., 1994) and 38% among patients (Baba et al., 2000).

This study reports the prevalence of HCCA in patients infected with and without HBV in Maiduguri, Northeast Nigeria over a period of five years.

MATERIALS AND METHODS

Study population

This is a retrospective study of 114 patients consecutively diagnosed with HCCA and was tested for HBsAg at the Histopathology and Immunology laboratory of the UMTH between January 1996 and December 2000. Relevant clinical and histological data were extracted from laboratory records and analysed. The clinical data available for each patient included age, sex, histopathological diagnosis and HBsAg status. Patients were aged 9 months to 60 years and above, among whom 81 were males and 33 were females.

Histopathology

Liver tissues were obtained from patient by needle biopsies and fixed in a 10% formalin solution. The tissues were paraffin embedded and sectioned at 3 - 5 μm, stained with haematoxylin and eosin and examined microscopically. The histological criteria for the diagnosis of hepatocellular carcinoma ranges from well differentiated to highly anaplastic undifferentiated, and these include any of the following features: The well-differentiated to moderately differentiated malignant cells are arranged in a trab-cular, acinar or pseudoglandular pattern; the anaplastic malignant cells are pleomorphic with giant cells that may resemble spindle cell sarcoma; the variant of hepatocellular carcinoma are well -difeferentiated with polygonal cells arranged in nests or cords and separated by parallel lamellae of dense collagen bundles.

Hepatitis B surface Antigen serology

Five milliliters of blood were obtained from each subject by venopuncture and allowed to clot. The blood was centrifuged at 1 000 x g for 10 min, and the serum separated and stored at -20^{O}C until required for testing. Sera were analysed for HBsAg by enzyme immunoassay (EIA) using the MONOELISA Ag HBs PLUS kit (Bio-Rad, USA). Tests were performed according to manufacturer'sinstructions. The tests plates were read at dual wave lengths of 420 and 620 nm with a Multiskan Ex reader (Labsystems, Finland).

Data analysis

Frequency tables were formed and data were analysed with chi square test using Epi v.6.04 Info. The level of significance was assessed at p 0.05.

RESULTS

Hepatitis B surface Antigen (HBsAg) was detected in 99(86.8%) of the 114 HCCA patients tested, while 15(13.2%) of the HCCA patients were without Hepatitis B surface antigenaemia (Table 1) . There was no significant variation in the positivity rate of HBsAg among the HCCA patients between the years studied ($p > 0.05$). Among the HBsAg-positive HCCA patients, males accounted for 72(63.1%) and females for 27(23.7%), giving a ratio of 2.7:1 ($p < 0.05$). However, the prevalence of HCCA among males negative for HBsAg was not significantly different from females (7.9% vs. 5.3%) ($p > 0.05$) (Table 2). A higher prevalence of HBsAg was observed among HCCA patients aged 40 years and above (62.0%) than patients below 40 years (26.9%) ($p < 0.05$). An inverse observation was noted among HCCA patients in the same age bracket that tested negative for HBsAg.

DISCUSSION

Incidence of HCCA in sub- Saharan Africa is usually underestimated due to under diagnosis and poor documentation (Kew, 2006). High incidences have been recorded in west and southern Africa with Mozambique having the highest incidence of 112.9 per 100 000 of the population yearly among men and 31.8% in women (Prates et al., 1965).

Reports from earlier studies carried out in Maiduguri, Northeast Nigeria suggested a high incidence of hepatocellular carcinoma (HCCA) (Gashau and Mohammed, 1991; Baba et al., 2000). Both studies incriminated HBV as the most common aetiologic factor for HCCA. A recent hospital-based study in Gombe, Northeast Nigeria reported similar findings (Mustapha and Pindiga, 2003). Findings in the present study, showing a high prevalence of HBsAg among patients with HCCA (86.8%), are consistent with the above reports and further corroborate that development of HCCA is the most important consequence of HBV infection (McMahon et al., 1985).

Table 2. Age and Sex distribution of HCCA associated with and without HBsAg.

Age group (yr.)	HCCA patients	HBsAg positive		HBsAg negative	
		M	F	M	F
0-9	2	1(50%)	0	1(50%)	0
10-19	2	2(100%)	0	0	0
20-29	11	7(63.6%)	3(27.3%)	0	1(9.1%)
30-39	20	10(50%)	6(30%)	2(10%)	2(10%)
40-49	29	18(62.1%)	7(24.1%)	3(10.3%)	1(3.5%)
50-59	27	22(81.5%)	3(11.1%)	1(3.7%)	1(3.7%)
60	17	10(58.8%)	7(41.2%)	0	0
Unspecified	6	2(33.3%)	1(16.7%)	2(33.3%)	1(16.7%)
Total	114	72(63.1)	27(23.7)	9(7.9)	6(5.3)

Results obtained in this study indicated that the male to female ratio among HCCA patients infected with HBV was 2.7:1 and compares favourably with findings from similar studies carried out in Mozambique, Zimbabwe, southern Africa (Prates et al., 1965, Bosch et al., 1999), Gombe, Northeastern Nigeria (Mustapha and Pindiga, 2003) and Ile-Ife, Southwest Nigeria (Ndububa et al., 2001).

Beasley in 1988 reported that HCCA is generally associated with increasing age and significantly higher HBV prevalence was observed among persons in their forties. This and reports from earlier studies carried out in Maiduguri (Harry et al., 1994; Baba et al., 2000) is in agreement with findings obtained in this study. Studies in the developing countries have shown that HCCA tends to afflict people in their third and fourth decades of life, unlike in the developed countries where the disease is prevalent in the older population (Bojuwoye, 1995). An earlier study in Maiduguri reported a high prevalence of both HBsAg and HCCA among patients in the age group 31 - 45 years (Baba et al., 2000). The result of this study is in agreement with these previous reports.

Although, this study did not investigate other factors that might cause HCCA other than Hepatitis B virus, the presence of HCCA in 13.2% of patients without HBsAg is worrisome going by the fact that other known aetiological risk factors, particularly of non-viral origin, can be identified among the study population. Previous reports indicated that people in this locality who consume a lot of groundnuts (especially raw) and grains infested with fungus stand the risk of ingesting aflatoxins (Harry et al., 1994; Bojuwoye, 1995; Gashau, 1988). Cigarette smoking, often regarded as a status symbol among the youth in this locality, is also a risk factor to developing HCCA. There is a scarcity or no available information to link alcohol consumption and cigarette smoking to HCCA in this locality. Nonetheless, the aforementioned vices are seemingly high in this locality, especially among men in their middle-ages (Gashau, 1988). There is therefore a need to investigate both viral and non-viral aetiologic risk factors in this locality in order to have holistic epidemiological information on HCCA, and to adequately charter control and preventive strategies for the disease.

However, with available epidemiological data suggesting a significant association between HCCA and HBV infection, concerted efforts should be made toward controlling the disease burden through health education, emphasizing good environmental and personal hygiene practices. Health education messages pertaining to prevention of human immunodeficiency infection (HIV) transmission and acquired immune deficiency syndrome (AIDS) should be disseminated alongside viral hepatitis campaigns, since both viral infections share similar modes of transmission. In addition, efforts should be intensified to widen the coverage of HBV vaccination, which has recently been adopted into the national immunization scheme in Nigeria through primary health care delivery.

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