

Full Length Research paper

Hepatocellular carcinoma: Risk factors, pattern of presentation and outcome in a tertiary health facility

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Hepatocellular carcinoma is the fifth most common cancer in the world. Its incidence is increasing worldwide ranging between 3 and 9% annually. The aim of this study was to see the pattern of clinical presentation, identify the possible risk factors and the clinical outcome among HCC patients presenting at our health facility. The case records of all patients with histopathological diagnosis of HCC within the study period June 2003-May 2008 were scrutinized. Demographic, clinical presentation, investigations, risk factors and outcome data were extracted. Data analysis was done using the SPSS computer software. Logistic regression model was fitted to identify the impact of the various risk factors on HCC. A total number of 53 patients with histopathological diagnosis of HCC were registered. Their ages ranged from 35 to 73 and mean age of 50 ± 21.8 years. Thirty seven (69.8%) were males while sixteen (30.2%) were females giving M: F ratio of 2.31:1. The left lobe was affected in 15.1% (8), right lobe in 22.6% (12) and both lobes in 62.3% (33). 54.7% tested positive for HBsAg, 3.8% were HCV-Ab positive. All the patients in this study presented at an advanced stage of the disease. Aflatoxin exposure, though not proven, because no test was done to incriminate it, was highly suspected and could be a major risk factor in this study; hence efforts need to be doubled up as regards effective awareness campaigns, general health /social education and food perseveration methods.

Key words: Hepatocellular carcinoma, aflatoxin, hepatitis B and C.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the fifth most common malignancy in the world (El-Zayadi et al., 2005), complicating liver cirrhosis in most cases. It is the most common hepatic malignancy with 626,000 new cases in 2002 (Parkin et al., 2005). Its incidence is increasing worldwide ranging between 3 and 9% annually (Velazquez et al., 2003). Chronic hepatitis B viral [HBV] infection, with and without aflatoxin exposure is the predominant risk factor in Africa and Asia, and chronic hepatitis C viral (HCV) infection in the Western countries and Japan (Nagasue et al., 1985; Szilagyi and Alpert, 1995).

HCC develops in a cirrhotic liver in 80% of cases, and this pre-neoplastic condition is the strongest predisposing factor (Llovet et al., 2008). Chronic HBV carriers have a 100-fold relative risk for developing HCC, with an annual

incidence rate of 2-6% in cirrhotic patients (Bruix et al., 2001). Integration of the viral DNA into host genome was suggested to be the initiating event for HBV-induced carcinogenesis (Llovet et al., 2003).

HCC also occurs in chronic liver disease of normal aetiology, such as alcohol-related disease and haemochromatosis (Nicholas and Paul, 2003). Exposure to aflatoxin is an additional risk factor for the development of HCC (Szabo et al., 2004).

The aim of this study was to see the pattern of clinical presentation, identify the possible risk factors and the clinical outcome among HCC patients presenting at our health facility.

MATERIALS AND METHOD

This 5 year retrospective study was carried out at the Federal Medical Centre, Ido-Ekiti, Nigeria from June 2003 to May 2008. The case records of all patients with histopathological diagnosis of HCC within the study period were scrutinized and demographic; clinical presentation, investigations, risk factors and outcome data were ex-

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Table 1. Age distribution of HCC.

Age(years)	No	%
< 40	5	9.4
49-50	40	75.5
>60	8	15.1

Table 2. Signs and symptoms at presentation.

Signs/Symptoms	No	%
Weight loss	53	100
Fatigue	46	86.8
Jaundice	41	77.4
Abdominal fullness / mass	47	88.7
Body itching	3	5.7
Poor sleep	31	58.5
Anaemia	45	84.9
Ascities	46	86.8
Hepatomegaly	53	100
Hepatosplenomegaly	15	28.3

were extracted. HCC was diagnosed based on histopathological examination.

HBsAg antigen status was determined using the agglutination kits manufactured by Biotech Laboratories USA, while HCV-Ab was measured using a third generation ELISA by DIA.PRO Diagnostic, Milano, Italy. We could not estimate the Alpha foeto-protein (AFP) levels and carry out CT-scan on the patients for lack of these equipments at our centre.

Data analysis was done using the SPSS computer soft ware. Logistic regression model was fitted to identify the impact of the various risk factors on HCC. The development outcome was HCC (0 = absent, 1 = present) and the independent factors were age, sex, previous history of blood transfusion, tattoo marks, multiple sexual partners, consumption of foods stored in humid conditions, HBsAg and HCV-Ab positivity.

RESULTS

A total number of 53 patients with histopathological confirmation of HCC were registered between June 2003 and May 2008. Their ages ranged from 35 to 73 and mean age of 50 ± 21.8 years. Thirty seven (69.8%) were males while sixteen (30.2%) were females given M: F ratio of 2.31:1 and most of them reside in rural/semi-urban communities. Majority (75.5%) of the HCC patients were in the 40-59 years age range (Table 1). All the HCC patients were presented with diffuse, multinodular hepatic focal lesions on USS. The left lobe was affected in 25.1% (8), right lobe in 22.6% (12) and both lobes in 62.3% (33) of the patients. None of the patients received definitive HCC treatment safe anti-failure regimen before and during the admissions.

Pattern of presentations

The various signs and symptoms at presentation were

Table 3. Risk factors.

Risk factor	No	%
HBsAg+	31	54.7
HCV-Ab	2	3.8
Alcohol	21	39.6
Scarification/ Tattoo marks	32	60.4
Multiple sexual partners	35	66.0
Blood transfusion	5	9.4
Injection by quacks	13	24.5
Consumption of foods stored in humid conditions	27	50.9

shown in Table 2. All the patients presented with hepatomegaly and weight loss of >10% of their pre-morbid weight. 86.8% presented with fatigue, 88.7% with

Risk factors

54.7% tested positive for HBsAg, 3.8% were HCV-Ab positive, 39.6% were into heavy alcohol ingestion, 60.4% had multiple scarification marks, 66% had multiple sexual partners, 9.4% gave history of blood transfusion in the past, 24.5% confirmed having received injection from the quacks and 50.9% gave history of ingestion of foods stored in humid conditions (a likely suspected source of aflatoxin exposure) (Table 3). All patients had USS done, 71.7% had fine needle aspiration cytology (FNAC) while 28.3% had liver biopsy done.

Outcome

Forty eight (90.6%) died while on admission at the hospital while five (9.4%) discharged themselves against medical advice. The average length of stay on admission before their demise was 5 days.

DISCUSSION

HCC is the fifth most common cancer in the world and is the most common type of primary liver cancer (Nicholas and Paul, 2003). It is also the most common malignancy associated with poor prognosis (Okano et al., 2001). The incidence of HCC has increased sharply in the last 5-10 years (Bruix et al., 2001; El-Zayadi et al., 2005). It is currently the leading cause of death amongst cirrhotic patients (Sangiovanni et al., 2004).

Recent studies (Feitelson, 1992) have shown HCC occurrence predominantly in the age group 40-59 years. In this study, we found that 75.5% of our patients were in this age group. This may be attributed to the high rate of HBV infection as well as ingestion of alcohol and probably the consumption of foods stored in humid conditions (a suspected source of aflatoxin exposure).

HCC was found in this study to be more prevalent in

Table 4. Child-Pugh stage at presentation.

Child-Pugh stage	No	%
A	-	-
B	14	26.4
C	39	73.6

men (69.8%) than in women (30.2%). This was in conformity with that found by El-Zayadi et al. (2005) in their study. This may at least be explained in part by the differences in exposure to risk factors. Sex hormones and other X-linked genetic factors may play a significant role (Yu et al., 1991). It has been speculated that estrogens and androgens could modulate hepatocarcinogenesis and explain the higher incidence of HCC in men (www.cancer.gov/cancer/pdq/screening/hepatocellular/healthprofessional. Accessed Oct, 2001).

HBV and HCV infections are considered as the major risk factors that contribute to the development of HCC worldwide. Despite high frequencies of multiple scarification marks and multiple sexual partners, this study only found HBV infection a major risk factor (54.7%) compared with HCV infection (3.8%). At the moment, the national prevalence rate of HCV in Nigeria is not known, but pockets of studies tend to show a lower prevalence rate as found in this study. Olatunji et al. (2008) found HCV prevalence of 0.6% among blood donors in Ilorin.

A study in Spain by Velazquez et al. (2003), found HBV an insignificant risk factor for the development of HCC due to the considerable small number of infected patients as well as low chronicity rate in acute HBV infection (10%) compared to the high chronicity rate (50-80%) in acute HCV patients. Other studies in Egypt (El-Zayadi et al., 2005) also showed a higher incidence of HCC among HCV patients. The relative association of HBV and HCV with HCC in various geographic locations around the globe could be ascribed to the differing prevalences of these viral infections in various places. One of the factors affecting the prevalence is HBV vaccination policies adopted by each region.

In this study, viral hepatitis markers were negative in 41.5% of the HCC patients suggesting other strong aetiological factors. El-Serag (2002) equally found 14.5% of his patients remain without specific risk factors. This could be explained in part by the development of mutant or occult viral infection, or exposure to other risk factors such as aflatoxins and alcohol abuse. Exposure to alcohol abuse was particularly high in this study (39.6%). Possible exposure to "aflatoxin", though not proven as no test was conducted to incriminate it, is highly suspected in this study as 50.9% of the patients were exposed to a likely source of aflatoxin contamination (inappropriately preserved food). The duration of exposure to this could not be ascertained.

Thirty nine (73.6%) of the patients presented in Child-Pugh C while fourteen (26.4%) presented in Child-Pugh

B (Table 4). This late presentation could be due to the low level of awareness about HCC and its inherent dangers in the general population as a whole. The high poverty level in the populace is another strong factor responsible for the late presentation as most of them would have visited the herbalists or religious homes before ending up in the hospital. A valuable time would have been lost in the process. Although HB vaccination was recently included in the National programme on immunization in Nigeria, the expected reduction in the incidence of HBV and HCC will be seen 30-40 years after the launch.

It was found in this study that in the majority 62.3% (33) of the patients, the two lobes were affected, while 15.1% (8) had the lesions confined to the left lobe and 22.6% (12) in the right lobe at the time of presentation at the hospital. This was contrary to the findings in the study of El-Zayadi et al. (2005) who found 65% affecting the right lobe, 13.4% the left lobe and 21.6% affecting both lobes.

Treatment outcome showed that 90.6% (48) of the patients died while on admission in the hospital, 9.4% (5) discharged themselves against medical advice. We could not initiate any anti-tumour treatment other than that of anti-failure regimen (lactulose and metronidazole) and liver support (Livolin forte) before and during admissions as they all presented at the late stage. The averaged length of stay on admission was 5 days. This finding was not too surprising considering the nature of the disease, the poverty level and the late presentation. Complications recorded terminally included hepatic encephalopathy in the majority (88.7%) of the patients, spontaneous bacteria peritonitis (7.5%) and bleeding diathesis (3.8%).

Efforts need to be doubled up as regards effective awareness campaigns, general health/social education, food preservation methods and to down play on some of the socio-cultural beliefs among the populace militating against early presentation in Nigeria in particular and other developing countries in general. We would like to advocate aflatoxin estimation in patients' samples and in the food consumed to evaluate the contribution of aflatoxin to the development of HCC in Nigeria.

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