SERO-PREVALENCE OF HEPATITIS B AND C VIRUSES IN CIRRHOSIS OF THE LIVER IN ACCRA, GHANA

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SUMMARY

Hepatic cirrhosis is the commonest liver disease causing death in Accra, Ghana. The roles of hepatitis B (HBV) and C (HCV) virus infections in cirrhosis have not been well documented in Ghana. A nested case-control study was carried out to determine this and the role of blood transfusion in transmission of the two viruses. A total of 70 patients with cirrhosis diagnosed on combined clinical and ultrasonographic evidence and 280 controls with non-hepatic diseases were recruited for the study. HBsAg was detected in 30 out of the 70 cases, giving a prevalence rate of 42.9% compared to the rate of 7.5% (21 out of 280) among the controls. HBV infection was significantly associated with cirrhosis (χ^2 = 75.622, P = 0.000, C.I. = 28.6 – 42.156.08; OR=8.07, 95% CI=4.62 – 15.20). The risk of developing cirrhosis is 8-fold increased in patients with HBV infections than those without. The sero-prevalence of antibodies to HCV of 7.1% (5 out of 70) among cases was higher compared to the 3.6% (10 out of 280) in controls but there was no statistically significant difference between the two rates (χ^2 = 0.962, P = 0.327, C.I. = -1.42 – 5.70). Our results show that HBV infection and not HCV infection is a major risk factor for developing liver cirrhosis in Accra. There was statistically significant association between blood transfusion and HBV but not HCV infection.

Keywords: Cirrhosis, hepatitis B virus, hepatitis C virus, blood transfusion

INTRODUCTION

Liver cirrhosis is an end stage chronic liver disease which is generally irreversible. About 75% of patients with post-hepatitic cirrhosis have progressive disease despite supportive therapy and die within one to five years from serious complications[1]. Studies done in other countries have indicated an association between liver cirrhosis and chronic viral hepatitis due to hepatitis B virus (HBV) and hepatitis C virus (HCV) infections especially where these viruses are endemic[2-6]. In the natural history of HBV infection it is estimated that 10% to 33% of those who develop persistent infection end up with chronic hepatitis of which 20% to 50% may develop liver cirrhosis[7]. Longitudinal studies conducted in patients who had acquired hepatitis C by blood transfusion for 15-25 years indicated that 20% to 30% developed cirrhosis[6].

Chronic viral hepatitis is considered an important public health problem necessitating high priority strategies for prevention and control [8,9]. Estimated worldwide carriers of hepatitis B virus is 350 million[10], with an estimated 50 million chronic carriers of HBV in Africa. In sub-Saharan Africa, carrier rates range from 9% to 20%[11-14]. HBV is endemic in Ghana with sero-prevalence rates ranging from 6.7% to 10% in blood donors[15,16], 6.4% in pregnant women[17] and 15.6% in children[18] among the general population. In jaundiced patients the rate is 54.1%[19]. It is estimated that over 170 million people are infected with HCV worldwide[20] and the proportion of healthy carriers with antibodies to HCV in Africa varies from 0.5% to 10%, although it may exceed 20% in some cases[21,22]. HCV infection is the major etiologic agent of post-transfusional hepatitis worldwide and is an important cause of community acquired non-A and non-B hepatitis in certain pars of Africa[23]. Recent studies have revealed HCV sero-prevalence rates of 2.8% to 5.4% in Ghana[18, 24,25].

Edington in his study on hepatic diseases in Ghana observed that the commonest liver disease leading to death at autopsy was cirrhosis of the liver[26]. Unpublished data of causes of death over the 20-year period 1980-2000 from Department of Pathology, Korle Bu Teaching Hospital (KBTH) confirms this observation. Although liver cirrhosis is the commonest liver disease causing death at the KBTH, Accra, Ghana, there has been very little systematic investigation of the relative importance of HBV and HCV infections and other possible

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risk factors in Ghana in the causation of this disease.

The purpose of this study was to investigate the sero-prevalence of HBV and HCV infections among patients with liver cirrhosis seen at the KBTH.

SUBJECTS AND METHODS

Study site: This study was conducted at the Medical and Surgical Departments of the KBTH, Accra, Ghana, between October 2001 and September 2002. KBTH is a leading tertiary referral hospital, which serves the city of Accra (a rapidly expanding city with a population of about 2 million) and its surrounding urban population but also receives cases from all over Ghana.

Subjects: The study population included 70 patients admitted to the hospital with cirrhosis of the liver and 280 age (within 5 years) and sex matched controls who had no evidence of hepatic disease. Participation in the study was voluntary, and after extensive information was given to either the participants or their relations, informed consent was obtained from all subjects. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki, and was approved by the University of Ghana Medical School Protocol and Ethical Review Board.

Cases of cirrhosis were selected based on clinical and laboratory findings and the diagnosis confirmed using ultrasound. The following diagnostic criteria were used in patient selection:

1. Deranged liver function test results suggestive of chronic liver disease with or without jaundice
2. Diffuse liver nodularity on palpation
3. Clinical signs of portal hypertension including presence of ascites

Ultrasound finding of diffuse liver nodularity with any of the ultrasonographic features of portal hypertension and the above clinical and laboratory information was considered diagnostic of cirrhosis. These features were:

1. Splenomegaly
2. Dilated portal vein
3. Recanalisation of paraumbilical veins within ligamentum teres
4. Collateral tortuous vessels in porta hepatis
5. Dilatation of splenic vein and superior mesenteric vein
6. Ascites.

Hepatic disease was excluded in the controls based on the finding of no clinical evidence of existing liver disease combined with liver function test results within normal reference ranges. Any person with abnormal liver function test results was excluded as a control**.** Autopsies were carried out on all patients who died during the study period.

Serology and Questionnaire: Patients were interviewed using a standardized questionnaire about personal details, clinical symptoms, occupation and history of blood transfusion. Blood samples for serologic analysis were taken and the serum separated into well labelled microtubes for storage at -70^{o}C till analysed. Serologic markers for HBV (hepatitis B surface antigen [HBsAg]) and antibodies to HCV were initially screened with a particle haemagglutination test kit (Serodia, Fujirebio Inc., Tokyo, Japan) and confirmed by 3rd generation ELISA test (Abbott Laboratories, Abbott Park, IL, U.S.A.). All serologic assays were carried out according to the manufacturer's instructions. Liver function tests were performed using an auto-analyzer (ATAC 8000, ELAN Diagnostics, N.Y. U.S.A.).

Statistical analysis: All data were stored using EPI INFO 2003 Revision 2 microcomputer software. The differences in proportions of cases and controls positive for HBsAg and anti-HCV respectively were assessed by a 2-tailed McNemar's test for correlated proportions while the associations between blood transfusion and infections from hepatitis B and C viruses were evaluated using a 2-tailed Fisher's exact test. The odds ratios (ORs) and 95% confidence intervals (95% C.I.) for blood transmission as a risk factor for hepatitis B and C viral infections respectively were also calculated. All the statistical analyses were done using the SPSS 12.0 for windows microcomputer software. P values <0.05 were considered statistically significant.

RESULTS

Forty four males and 26 females with liver cirrhosis and 280 controls (176 males and 104 females) were enrolled for the study. Of the 70 patients with cirrhosis of the liver, 18 died and autopsy performed on them confirmed the diagnosis of cirrhosis thus validating the method used in diagnosing the disease in the study.

The mean age of patients with cirrhosis of the liver was 46.0 (S.D. 15.8) with a range of 15 to 90 years. The mean age of male cases of 46.1years was not different from that of female cases 46.0 years. Figure 1 shows the age distribution of all cirrhosis cases and figure 2 the age distribution of HBsAg and anti-HCV positive patients with cir-

rhosis of the liver. There was a significant difference in the proportion of cases positive for HBsAg, 42.86% (30 out of 70) compared to 7.5% (21 out of 280) of controls (McNemar's χ^2 = 75.622, P = 0.000, C.I. = 28.6 – 42.1). The anti-HCV positive rates were 5.7% (4 out of 70) and 3.6% (10 out of 280) in patients with cirrhosis of the liver and those without cirrhosis of the liver respectively. There was no significant difference between cirrhosis and controls with respect to HCV infection (McNemar's χ^2 = 0.962, P = 0.327, C.I. = -1.42 – 5.70).

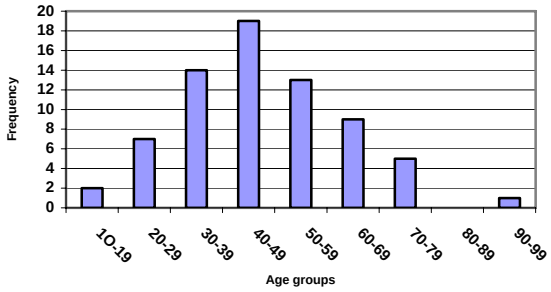

Figure 1 Age distribution of cases

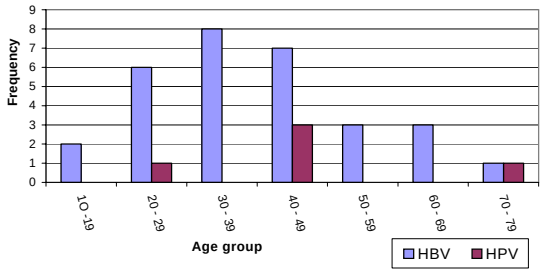

Figure 2 Age distribution of HBV-positive and HCV-positive cases

Analysis of infection with HBV and HCV as risk factors for cirrhosis showed that the risk of developing cirrhosis of the liver was strongly associated with the presence of HBV infection (OR=8.07, 95% CI=4.62 – 15.20) and that the risk of developing cirrhosis of the liver was 8-fold increased in patients with HBV infections compared to those without. The OR for HCV infection was 1.60 (95% C.I. = 0.68 – 3.95) indicating that there was a 1.6 times higher risk of developing cirrhosis compared to unexposed persons. However the risk was not statistically significant as it would be expected to lie between 0.68 (which is less than 1) and 3.95.

Out of a total of 51 cases and controls who were positive for HBsAg only 4 (7.8%) had had previous blood transfusion. Six of 299 cases and controls who were HBsAg negative had a history of previous blood transfusion. The results showed a statistically significant association between blood transfusion and HBsAg positivity (Fisher's exact test P=0.043). Those who received blood transfusion were 4 times more likely to be infected by HBV than those who did not (95% CI = 1.130 - 15.282). Only 1 of the 14 individuals who were HCV-sero-positive (7.1%) had a previous blood transfusion while 9 of the 336 who were HCV-sero-negative (2.7%) gave a history of having been transfused previously. No statistically significant association could be established between blood transfusion and HCV infection (Fisher's exact test P=0.339). Although it was estimated that there was a 2.8 times higher likelihood of an individual being infected with HCV following blood transfusion the risk was not statistically significant (95% CI = 0.329 - 23.732).

DISCUSSION

The gold standard for the diagnosis of cirrhosis is a morphologic one using either histopathological examination of liver biopsies or gross examination of the liver. However, these methodologies were not used for the initial diagnosis of cirrhosis in all cases as this would have required that the same methods be used to select controls. To overcome this weakness in the study, stringent combined clinical and radiological criteria were used. This choice was vindicated by the fact that all 18 cases of cirrhosis who died were proved by autopsy to have cirrhosis.

To our knowledge, this study is the first reported case-control study on HBV and HCV sero-prevalence among patients with cirrhosis of the liver in Ghana. The results of our study provide further evidence that HBV infection is strongly associated with the development of cirrhosis of the liver. In this study, sero-positivity for infection with HBV in patients with cirrhosis of the liver was 42.9%, suggesting that most cases of cirrhosis of the liver were virus-related chronic liver disease. Furthermore, in both sexes, the age distribution of HBsAg positive patients with cirrhosis of the liver showed that 70% were in the age range 20-49 years indicating that HBV infection was acquired in childhood through to early adulthood. How many of these cases are the result of vertical maternal-to-child transmission and how many are the result of horizontal transmission cannot be determined from this study. However, Martinson *et al* in a study of a rural population in Ghana obtained data suggesting a continuous non-uniform

acquisition of HBV infection with advancing age predominantly through horizontal transmission in childhood, with the household, rather than the domestic compound, being the primary place for transmission[27]. The age pattern observed in our study is different from that seen in patients with cirrhosis of the liver in developed countries where most cases of cirrhosis of the liver are within the age range 40 – 70 years[28,29] and are mostly alcohol-related. The observed prevalence rate (42.9%) is not different from the 39% found by Acheampong[19] and similar to that previously reported from Nigeria (56%)[30] and Indonesia (41.1%)[31], but lower than that reported from Niger (75.5%)[32] and from endemic countries in Asia such as Taiwan (74.5%)[33] and India (67.5%)[2]. It is higher than the reported rate in Japan (34%)[34]. The reason(s) for the high sero-positive rate cannot be discerned from our study. It is possible that these viral infections could be acquired per cutaneously, through mother-to-child transmission, through skin abrasions, sexual intercourse, or skin lesions. Martinson *et al* found the behaviors most strongly associated with prevalence of HBV to be sharing of bath towels (OR = 3.1, 95% CI 2.1-4.5), sharing of chewing gum or partially eaten candies (OR = 3.4, 95% CI 2.3-5.0), sharing of dental cleaning materials (OR = 2.5, 95% CI 1.3-4.6), and biting of fingernails in conjunction with scratching the backs of carriers (OR = 2.5, 95% CI 1.6-4.3)[27]. Further studies on routes of transmission are essential.

There was no significant association with HCV infection and cirrhosis of the liver among patients in our study indicating that in this setting, HCV infection does not have a significant impact on the burden of cirrhosis of the liver in Ghana.

Blood transfusion has been known as one of the major means of transmission of HBV and HCV infections[7,23]. In this study, there was significant association (OR = 4.141; CI=1.126-15.230) between transfusion history and HBV infection. Although blood transfusion was significantly associated with HBV infection compared with controls, many HBV positive cases (47 out of 51) did not admit to a past history of blood transfusion. This finding means that though transfusion is a significant means of transmitting HBV, attention must also be given to preventing HBV infections from sources other than blood transfusion. There was no significant association (OR=2.901, 95% CI= 0.339 - 2.827) between blood transfusion and HCV infections. Studies done in other places have also found that a history of blood transfusion was not always significant among HCV carriers[35,36]. Further studies are required to identify the routes of transmission of HCV in our environment.

In conclusion, our study shows that cirrhosis of the liver in Accra, Ghana is associated with HBV infection while HCV plays a less significant role in causation of cirrhosis in this locality and that while blood transfusion may be important in transmission of these viruses other modes of transmission may also be important and are in need of research attention. We suggest further studies be carried out to determine modes of transmission other than blood transfusion and to determine intervention strategy to prevent the spread of these infections. As an immediate step we suggest the testing of all pregnant women for their HBsAg status and infants born to HBsAg-positive mothers be vaccinated using the appropriate schedule to prevent perinatal transmission. We also advocate for selected vaccination of high-risk adolescents and adults.

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