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THE CENTRAL AFRICAN JOURNAL OF MEDICINE

ORIGINAL ARTICLES

Hepatitis C virus in Zimbabwe

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Background: Hepatitis B is a common cause of chronic liver disease in Zimbabwe but other viral infections are also important. The prevalence of viral hepatitis C has not been previously described in healthy rural Zimbabwean adults.

Objectives: To determine the prevalence of seropositivity to hepatitis C in rural healthy adults in Zimbabwe, and to determine if there is evidence of active liver disease in subjects who are seropositive.

Study Design: Cross sectional descriptive study.

Setting: Rural communities around different parts of Zimbabwe, as part of a larger study into the prevalence and genetic pattern of iron overload.

Subjects: An initial 150 rural Zimbabweans over the age of 12 years.

Main Outcome Measures: Presence of the following serological markers: hepatitis B surface antigen; antibodies to hepatitis C, B surface and B core antigens; hepatic enzymes and iron status determined on the basis of serum ferritin and transferrin saturation.

Results: 11 (7.7%) of the subjects were positive for antibodies to hepatitis C and they had significant elevations in hepatic enzymes and serum iron levels suggesting substantial hepatocellular damage. Twenty (14.1%) of the subjects were positive for hepatitis B surface antigen, but they did not have significant elevations in hepatic enzymes or indirect measures of iron status.

Conclusion: Seropositivity for hepatitis C is common and is approximately half the prevalence of hepatitis B chronic carrier status. Chronic hepatitis C may be more damaging to the liver than chronic hepatitis B and, therefore, may be an important cause of liver disease in rural Zimbabwe.

Introduction

Liver disease is an important cause of morbidity and mortality in Zimbabwe, accounting for more than six per cent of the deaths in three medical wards of Harare Central Hospital (IT Gangaidzo, 1994, unpublished observations). In western countries, HCV infection is the most common cause of chronic viral hepatitis and ranks a slight second below chronic alcoholism as a cause of cirrhosis, liver failure and hepatoma.¹

Infection with hepatitis B (HBV) is a major aetiological factor in many liver diseases in southern Africa,^{2,3} but the contribution of hepatitis C virus (HCV) in causing hepatic pathology is unclear.⁴ In much of sub-Saharan Africa including Zimbabwe, the mode of transmission and the seroprevalence of antibody to HCV (anti-HCV) are still to be established. Most published studies from sub-Saharan Africa give prevalence rates of anti-HCV in special groups such as blood donors or hospital patients suffering from liver disease.⁵ In

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the present study, we attempted to provide an initial approximation of the prevalence of anti-HCV in otherwise healthy Zimbabweans and to identify some consequences of seropositivity.

Materials and Methods

Selection of Subjects.

The data set for the present study was collected as part of an investigation into the prevalence and genetic pattern of iron overload among 150 Zimbabweans. Study subjects were selected in one of two patterns.

1. Sixty one subjects were predominantly husband and wife pairs from the rural Zaka District of Masvingo province, about 300 km southeast of Harare, who were studied from February to May of 1994. One of the spouse pairs was selected on the basis of an index subject showing increased hepatocellular iron on a diagnostic liver biopsy specimen. These subjects were of Shona and of Shangaan origin. The individual members of the spouse pairs were not closely related to each other because of the taboo of marrying even distant relations.
2. Eighty nine subjects were members of five families that were selected on the basis of an index subject with increased hepatocellular iron identified on diagnostic liver biopsy. These families, predominantly of Shona origin, were based in Mrewa (25 subjects), Sanyati (18), Buhera (17), Honde Valley (16) and Chegutu (13).

All subjects provided informed consent. Demographic factors included a history of injections, jaundice, blood transfusion and surgery. An estimate was made of lifetime traditional beer consumption for each individual as previously described.⁶

Laboratory Tests.

Peripheral blood samples were analysed for anti-HCV by a third generation solid phase enzyme immunoassay (EIA) consisting of recombinant antigens encoded by the HCV (ABBOTT HCV EIA 3.0*). The presence of anti-HCV was confirmed by re-testing using the same procedure. Positive sera were also tested by the Abbott HCV EIA Supplemental Assay. Hepatitis B antigen (HBsAg) was assayed using a commercial EIA kit (AUSAB EIA*). Specimens that were non-reactive by the test were considered negative for HBsAg and were not tested further. Specimens that had a positive reaction were tested again in duplicate using the same procedures. If neither of the repeat tests were reactive, the specimens were considered negative for HBsAg. If the specimen was reactive in either of the repeat tests, the sample was regarded as positive for HBsAg. The samples were also screened undiluted for anti-HBs antibody (AUSZYME MONOCLONAL®), and anti-HB core antibody (CORZYME RECOMBINANT®). The serological kits were supplied by Abbott Laboratories (Abbott Park, Illinois).

The assessment of the elevation in hepatic enzymes due to viral hepatitis is confounded by the contribution of alcohol ingestion and by the presence of iron overload. Serum ferritin and hepatic enzymes such as aspartate aminotransferase, may reflect active hepatocellular damage. Since excess dietary iron is derived from traditionally brewed beer we wished to assess the degree to which elevated serum ferritin may reflect

increased body iron stores versus viral or alcohol induced hepatocellular damage. The ratio of serum ferritin to aspartate aminotransferase (ferritin:AST) has been shown to correlate well with the hepatic iron concentration⁷ and to be constant in a given patient both in the setting of acute alcohol ingestion and after prolonged abstinence from alcohol.⁸

Serum ferritin was determined using an enzyme immunoassay and transferrin saturation was obtained by dividing the serum iron by the total iron binding capacity and multiplying by 100, as previously described.⁶ Liver function tests were measured on a Cobus Bio auto-analyser using reagents from Roche Diagnostic Systems, South Africa.

Statistical Analysis.

Index subjects who had a diagnostic liver biopsy and their spouses were excluded from the analysis for they had come to light because of clinical liver disease and might bias the results toward a higher prevalence of viral hepatitis. Rates of positivity for hepatitis markers were compared according to age category using the Fisher exact test (Table I). Rates of positivity for hepatitis markers according to five family groupings were compared using Pearson's chi square test. Estimated lifetime beer traditional consumption, gammaglutamyl transferase, alanine aminotransferase, serum ferritin and ratio of ferritin to AST had skewed distributions and were log-transformed before statistical analyses. Continuous variables were compared according to viral hepatitis status using analysis of variance models.

Age, sex and estimated beer consumption were covariates for the analyses of hepatic enzymes and indirect measures of iron status (Tables II and III). The categorical variable of sex was compared according to hepatitis status using Fisher's exact test.

Results

After exclusion of six index subjects and two spouses the data set consisted of 142 subjects, 72 males and 70 females with ages ranging from 12 to 84 years. Eleven subjects (7.7%) were positive for anti-HCV (Table I). For comparison, 20 subjects (14.1%) were positive for HBsAg, and 107 of 142 (75.3%) were positive for at least one of the following: HBsAg, HBsAb and HBcAb. Only one subject was positive for both anti-HCV and HBsAg. The prevalence of HCV antibody was significantly higher in subjects over 40 years of age while the prevalence of HBsAg was significantly lower in this age group.

Table I: Prevalence of serum markers for hepatitis C and hepatitis B according to age; p values indicate comparison between age categories.

Age category (years)	n	HCV antibody positive n (%)	HBsAg positive n (%)	positive HBsAg, HBsAb, HBcAb* n (%)
≤40	64	1 (1.6)	15 (23.4)	43 (67.2)
>40	78	10 (12.8)	5 (6.4)	64 (82.1)
(p)		(0.013)	(0.007)	(0.051)
All	142	11 (7.7)	20 (14.1)	107 (75.3)

* Positive for any one or more of hepatitis B surface antigen, anti-surface antibody and anti-core antibody (indicating previous exposure).

Discussion

The prevalence of anti-HCV ranged from 0% to 33% in five different family groupings and the difference in proportions were not statistically significantly different ($p=0.18$). The prevalence of HBsAg ranged from 0% to 75% in five family groupings and the differences in proportions were statistically significant ($p<0.0001$).

Table II shows that hepatic enzymes were significantly elevated in subjects positive for antibody to hepatitis C. Transferrin saturations and unsaturated iron binding capacities were also significantly elevated in hepatitis C antibody positive subjects while serum ferritins and the ratios of ferritin to AST were not. Table III shows that neither hepatic enzymes nor indirect measures of iron status were significantly elevated in patients positive for hepatitis B surface antigen.

Table II: Demographic and clinical features according to HCV status. Except for sex, results are given as mean \pm SE or geometric mean and SE range. Values for liver function and iron-related tests have been adjusted for age, sex and estimated beer consumption.

	Positive for antibody to HCV (n=11)	Negative for antibody to HCV (n=131)	p
Age (years)	59 \pm 6	46 \pm 2	0.03
Sex (M:F)	5:6	67:64	0.7
Estimated lifetime traditional beer consumption (L)	1 059 (282-3 981)	359 (244-506)	0.4
γ -glutamyl transferase (IU)	67 (53-85)*	20 (19-21)**	<0.0001
Aspartate aminotransferase (IU)	52 (45-60)*	26 (25-27)	<0.0001
Alanine aminotransferase (IU)	39 (33-46)*	20 (19-21)	<0.0001
Ferritin (μ g/ml)	226 (165-310)	140 (128-154)	0.15
Ferritin/AST ratio (μ g/ml)	4.1 (2.9-5.6)	4.2 (3.9-4.7)	0.9
Transferrin saturation (%)	58 \pm 5	36 \pm 2	0.0005
Unsaturated iron binding capacity (μ g/dL)	124 \pm 20	180 \pm 6	0.007

*n=10, **n=129.

Table III: Demographic and clinical features according to presence or absence of HBsAg. Except for sex, results are given as mean \pm SE or median and SE range. Values for liver function and iron related tests have been adjusted for age, sex and estimated beer consumption.

	HBsAg positive (n=20)	HBsAg negative (n=122)	p
Age (years)	38 \pm 4	49 \pm 2	0.019
Sex (M:F)	14:6	58:64	0.090
Estimated lifetime traditional beer consumption (L)	32 (12-82)	589 (400-867)	0.005
γ -glutamyl transferase (IU)	21 (18-26)	22 (20-23)*	0.9
Aspartate aminotransferase (IU)	33 (29-36)	27 (26-28)**	0.11
Alanine aminotransferase (IU)	26 (23-29)	20 (19-21)**	0.061
Ferritin (μ g/ml)	184 (145-234)	140 (128-154)	0.3
Ferritin/AST ratio (μ g/ml)	5.0 (3.9-6.3)	4.1 (3.7-4.5)	0.5
Transferrin saturation (%)	44 \pm 4	39 \pm 2	0.2
Unsaturated iron binding capacity (μ g/dL)	154 \pm 15	180 \pm 6	0.13

*n=119, **n=121.

This study is limited in that the data set was not a representative sample of the Zimbabwe population. Rather, approximately 40% of the serum samples came from a rural community near Masvingo, and the remaining samples were five family pedigrees from rural central and western Zimbabwe. None of the study subjects were from the Matabeleland province which makes up 20% of the whole Zimbabwean population. Thus we are unable to provide a precise estimate of the prevalence of antibodies to hepatitis C in this population. Nonetheless, the finding of a prevalence of almost 8% in this data set raises the possibility that hepatitis C infection is very common in the rural Zimbabwe population. Furthermore, the fact that the prevalence of hepatitis B surface antigen in the present study of 14% is similar to the large population survey of Tswana *et al*⁹ lends credence to the possibility that the true prevalence of hepatitis C is on the order of magnitude of what we found in this study.

The prevalence of anti-HCV in apparently healthy individuals varies widely within Africa and estimates range between eight and 30% of study subjects.¹⁰ However, most of these reports are in people presenting for blood donation and may not be representative of the respective populations. In this study we attempted to estimate the prevalence of anti-HCV antibodies in healthy subjects in whom the selection was random in relation to identifiable risk factors for HCV infection.

Hepatitis C positive patients in the present study had evidence of substantial hepatocellular damage. As shown in Table II, hepatic enzymes, transferrin saturations and unsaturated iron binding capacities were all elevated in hepatitis C positive patients, while serum ferritins and the ratios of ferritin to AST were not elevated. This picture is much more consistent with damage to hepatocytes than with iron loading. Interestingly, none of the hepatic enzymes or serological iron tests were significantly elevated in the hepatitis B surface antigen positive subjects. Thus, our present findings suggest that chronic hepatitis C infection more consistently causes hepatocellular dysfunction than chronic hepatitis B infection.

Furthermore, these findings indicate that hepatitis C may be a major cause of chronic liver disease in Zimbabwe, and are in keeping with other studies around the world showing that chronic hepatitis C infection is associated with a substantial risk of hepatic injury or hepatic failure necessitating liver transplant.¹¹

Several strategies have been introduced in various countries in sub-Saharan Africa to reduce the prevalence of chronic liver disease through vaccination and educational programmes.² The impact of hepatitis B vaccination in childhood may be limited by the proportion of chronic liver disease cases that is due to other viral infections such as hepatitis C since liver disease from infections other than HBV remain untreated. Determination of the prevalence of hepatitis C virus may provide essential information in deciding on public health strategies and in assessing cost effective interventions.

The mode of transmission of HCV infection differs between populations. In the West most hepatitis C occurs among

young adults with high risk behaviour or lifestyles.¹² The most efficient method of transmission of HCV is through large or repeated percutaneous inoculations with infected blood. Transmission also seems to occur through occupational exposure, sexual activity, household contact and perinatal exposure. The risk of transmission is then most dependent on the titer of virus as well as the mode of transmission.¹² The modes of transmission in Africa are not identified.

In this study we attempted to identify factors that are associated with HCV infection. The prevalences were similar in both sexes and among five family groupings. If close contact in childhood is an important mode of transmission, as occurs in hepatitis B infection¹³, then one would expect clustering of cases within family pedigrees.

Clustering of HBV infection within close relations was found in the present study. That such clustering of HCV cases is not seen in the five pedigrees that we studied raises the possibility that some other mode of transmission may be responsible in rural Zimbabweans. We also found increasing prevalence of HCV with age, and this finding is in keeping with previous reports from Cameroon.¹⁰ This finding may help in developing a hypothesis for the mode of transmission.

In case control studies, the proportion of patients with hepatocellular carcinoma who have circulating antibody to hepatitis C virus shows a pronounced geographical variation. In Japan, Spain and Italy HCV antibody is present in 47 to 83% of hepatoma patients, with relative risks of 52 (95% confidence intervals 24 to 114).¹⁴

In regions, such as Zimbabwe, where hepatitis B virus infection is endemic and is the major risk factor for hepatocellular carcinoma, antibodies to hepatitis C are present in the serum of a smaller proportion (6 to 39%) of patients, with relative risks of six (95% CI of 0.5 to 69).¹⁴ HCV infection is likely to be an important public health issue in sub-Saharan Africa. Further work is required into the modes of transmission of HCV and into possible methods of controlling infection. Our preliminary study points to the need for a larger epidemiologic survey designed to define the prevalence, consequences and risk factor for chronic hepatitis C infection in the Zimbabwean population.

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