A sero-epidemiological cross-sectional study of hepatitis B virus in Zimbabwe

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Objective. To estimate the prevalence of hepatitis B viral markers.

Design. A sero-epidemiological community-based cross-sectional study.

Setting. All nine provinces of Zimbabwe.

Participants. From April 1989 to December 1991 serum samples were collected from 1 461 males and 1 933 females in the age group 10 - 61 years, the majority in the younger age groups.

Main outcome measures. Sera were tested for hepatitis B surface antigen (HBsAg), hepatitis B e antigen (HBeAg), antibody to HBs-Ag (anti-HBs), antibody to hepatitis B core antigen (anti-HBc) and antibody to hepatitis B e antigen (anti-HBe). All sera were tested for HBsAg, anti-HBs and anti-HBc but for the detection of HBeAg and anti-HBe, only samples positive for HBsAg were examined.

Main results. The male-to-female ratio in rural and urban settings was 0.82 and 0.66 respectively. The median age for males and females in rural areas was 21 and 22 years and 28 and 26 years respectively in urban areas. The overall prevalence of HBsAg was 15.4% (males 16.8%, females 14.3%). The difference between sexes was consistent in all age groups and statistically significant ($P < 0.05$). The prevalences in urban and rural areas were almost identical (15.7% v. 15.3%).

However, the prevalence was significantly higher among males in the age group 40 - 49 years in urban areas compared with rural areas ($P < 0.0001$). Using the case-referent approach, with HbsAg-positive patients as cases and HBsAg-negative ones as referents, the crude odds ratio for rural areas compared with urban areas was 0,97. However, standardisation for year of data collection and province resulted in a relative risk of 2.0, i.e. the risk of being HBsAg-positive in rural areas is twice as high as in urban areas. Similarly, the crude odds ratio for females compared with males was 0.83, and was reduced significantly to 0.7 when standardised for year of data collection and province. The prevalences of HBeAg, anti-HBe, anti-HBs and anti-HBc were 25%, 25%, 45% and 36% respectively. The prevalences of anti-HBs and anti-HBc increased continuously with age and were about 70% higher in the age group 50 years and above compared with those under 20 years. The prevalence of any of the HBV markers — HBsAg, anti-HBs or anti-HBc — was 66% in males and 61% in females.

Conclusions. The results indicate that hepatitis B is hyperendemic in both rural and urban areas of Zimbabwe.

S Afr Med J 1996; **86:** 72-75.

Hepatitis B virus (HBV) with its acute and chronic clinical manifestations is an important public health problem, especially in developing countries. However, with the development of safe and efficacious vaccines, the need for proper vaccination strategies makes it necessary to assess the sero-epidemiological aspects of hepatitis B infection in developing nations.

Zimbabwe is in an endemic region for HBV infection (13.7%) as demonstrated in a previous study.[1] Further studies[2] showed an alarmingly high prevalence of anti-HBs in dentists (70%), indicating exposure to the virus at some stage. HBV plays an important role in the development of chronic hepatitis, liver cirrhosis and hepatocellular carcinoma.[3-6] Studies in a Taiwanese general population have shown the carrier rate to be between 15% and 20%; perinatal HBV transmission hence accounts for 40 - 50% of the carrier pool.[7] Both vertical and horizontal transmission of HBV occur relatively early in life.[4] In sub-Saharan Africa, between 70% and 95% of the adult population show evidence of past exposure to HBV infection (C. F. Kiire — personal communication).[2]

The prevalence of hepatitis B surface antigen (HBsAg) in Africa has been shown to range from about 3% in North Africa to 20% in West Africa.[8] However, recent studies in Somalia,[9-11] Cameroon,[12] eastern Nigeria[13] and South Africa[14] showed HBsAg prevalences of 16%, 20%, 9% and 10% respectively. Wide discrepancies have also been observed within countries. In Cameroon, Garrigue *et al.*[15] and Poveda *et al.*[16] reported an overall prevalence of 25% and 8% respectively. However, the main reason for such a variation may be that Garrigue *et al.*[15] studied a rural population with relatively few children, whereas the study by Poveda *et al.*[16] involved young adults aged 15 - 44 years.

The present cross-sectional study was undertaken to estimate the prevalence of clinically important HBV markers in the general population and to determine whether there had been an increase in HBsAg carriers since 1984/85.

Materials and methods

Study area

Zimbabwe consists of 9 administrative areas (provinces) and each province of approximately 10 districts. The study areas

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were randomly selected districts from each of the 9 provinces, and thus consisted of 17 districts throughout the whole country. All blood collections were done at schools, clinics, factories or rural health centres.

Study population

The aim was to select at least 200 subjects from each province, evenly distributed by rural/urban areas and sex.

Although 200 was intended to be the minimum number of volunteers from each province, only 125 individuals from Matabeleland North volunteered. Residents of the province thought that their blood would be used for HIV testing. Further, public relations were inadequate and the distance made it difficult for researchers to visit the area. As a result of another study's being carried out in Mashonaland East, the number of participants from that area was higher than planned.

We attempted to enrol both black Africans and non-black Africans; however, only 19 of the latter were enrolled. This does not correspond with their proportion of the population, but it was difficult to recruit more as they were very reluctant to give blood. Because they were so few, they were excluded from the analysis.

Specimen collection

Samples were collected between April 1989 and December 1991. Identified collection centres were first visited by research assistants and preliminary recruiting was done. Research assistants explained the objectives of the study and requested that all volunteers complete consent forms. On subsequent visits, study subjects were interviewed and questionnaire forms were completed before blood was taken. However, it was obvious that older people were reluctant to donate blood because they feared being tested for HIV antibodies.

Samples of approximately 8 ml venous blood were collected from each volunteer and test tubes containing these samples were immediately transported to the laboratory for serum separation. In the laboratory test tubes containing blood were centrifuged at 2 000 *g* for 15 minutes. All sera were separated into 3 ml sterile vials, stored at –20°C and subsequently tested.

Serological test

All sera were tested for HBsAg, anti-HBc, anti-HBs, HBeAg and anti-HBe by enzyme-linked immunosorbent assay (ELISA) (Abbott Laboratories, Chicago, Ill.). However, HBeAg and anti-HBe were tested on samples positive only for HBsAg. Results were read spectrophotometrically with the Abbott Quantum II at a wavelength of 492 nm.

Statistical analysis

To test whether a difference in prevalence between two groups was random or not, Student's *t*-test was applied. The precision in the estimates of the prevalence was calculated using 95% confidence intervals (*t* distribution). To analyse the differences in the prevalence further in respect of the characteristics studied, the cross-sectional study was analysed as a case-referent study using HBsAg-positive subjects as cases and HBsAg-negative ones as referents. An odds ratio (OR) equal to 1 should be interpreted as follows: the risk of getting the disease, i.e. of being HBsAg-positive, is the same as in respect of the variable studied, while an OR equal to 2 means that the risk is doubled (e.g. in rural areas compared with urban areas). To eliminate the effect of possible confounders Mantel-Haenzel's relative risks (RRs) were applied.

Results

The total number of volunteers participating in this study was 3 394. The distribution by year of data collection, age, sex, residence in rural/urban area and province is presented in Table I. The majority of volunteers were rural females (34.5%) and the minority urban males (14.7%), which reflects the attitude toward the giving of blood for research purposes. This is also illustrated by the age distribution — about 36% of both males and females were younger than 20 years and only 7.0% of the males and 2.4% of the females were 50 years and older. The median age for males and females in rural areas was 21 and 22 years, and 28 and 26 years respectively in urban areas. Only 32 subjects, i.e. fewer than 1%, were younger than 10 years and all were boys. Prevalence figures for this age group are therefore not provided.

Table I. Distribution of subjects by year of data collection, sex, race, urban/rural, province and age in Zimbabwe, 1989 - 1991

	Age (yrs)					
Characteristic	10 - 19	20 - 29	30 - 39	40 - 49	⩾ 50	⩾ 10
Year of data collection						
1989	606	219	215	109	85	1 234
1990	415	269	89	16	16	1 355
1991	211	597	360	139	48	1 355
Sex						
Males	529	434	274	122	102	1 461
Females	703	651	390	142	47	1 933
Urban	325	420	323	147	48	1 263
Rural	907	665	341	117	101	2 131
Province						
Harare	0	64	65	53	27	209
Midlands	119	60	45	17	12	253
Manicaland	85	144	70	43	39	381
Mashonaland C	314	60	22	10	9	415
Mashonaland E	208	417	168	35	27	855
Mashonaland W	145	155	111	30	22	463
Masvingo	150	65	128	57	12	412
Matabeleland N	119	2	3	0	1	125
Matabeleland S	92	118	52	19	0	281
Total	1 232	1 085	664	264	143	3 394

The overall prevalence of HBsAg was 15.4% (Table II). The prevalences in males and females were 16.8% and 14.3% respectively and the difference, which is statistically significant ($P < 0.05$), was consistent in all age groups. The prevalences in urban and rural areas were almost identical, 15.7% and 15.3% respectively; however, the age-specific prevalences in the urban areas was higher in the age group 40 years and above, as illustrated in Fig. 1. The difference was most pronounced among men in the age group 40 - 49 years ($P < 0.0001$).

Table II. Prevalence of HBsAg (%) by year of data collection, sex, race, urban/rural, province and age in Zimbabwe, 1989 - 1991

	Age (yrs)					
Characteristic	10 - 19	20 - 29	30 - 39	40 - 49	⩾ 50	⩾ 10
Year of data collection						
1989	11.4	9.1	7.9	10.1	7.1	10.0
1990	15.7	18.6	27.0	-	-	17.6
1991	13.7	23.8	12.5	-	23.7	19.0
Sex						
Males	15.5	19.8	16.8	17.6	11.2	16.8
Females	11.5	19.4	10.3	16.9	11.1	14.3
Urban	11.1	19.5	12.7	20.4	17.4	15.7
Rural	14.0	19.5	13.2	12.8	8.2	15.3
Province						
Harare	-	14.1	13.8	34.0	-	19.6
Midlands	24.4	15.0	-	-	-	17.8
Manicaland	8.2	14.6	4.3	-	-	9.2
Mashonaland C	10.8	6.7	-	-	-	9.4
Mashonaland E	16.3	24.5	19.6	-	-	20.8
Mashonaland W	12.4	10.3	9.0	-	-	10.8
Masvingo	13.5	23.1	10.9	17.5	-	14.9
Matabeleland N	10.1	-	-	-	-	10.4
Matabeleland S	9.8	30.5	21.2	-	-	21.7
Total	13.3	19.5	13.0	17.0	11.2	15.4

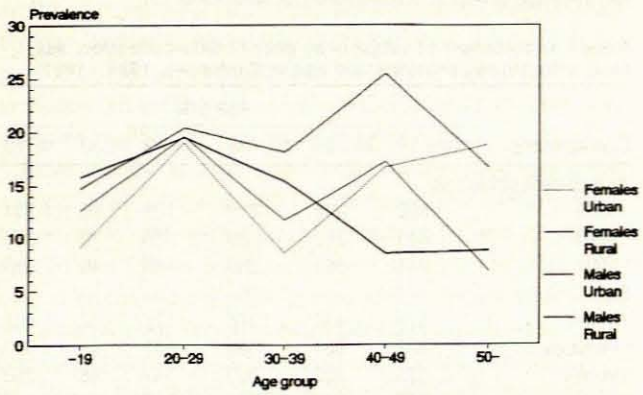

Fig. 1. Prevalence of HBsAg (%) by age for males and females in urban and rural Zimbabwe, 1989 - 1991.

There was a tendency for there to be geographical differences in the prevalence, as well as an increase by year of data collection. Table III shows the prevalence of HBsAg by year of data collection and district within provinces. Most of the increase in the prevalence by year of data collection was explained by the sampling schedule. A comparison by year was therefore possible for only a few districts — Gweru, Murewa, Mutoko and Kadoma — and not even the figures for Mutoko were statistically significant ($P = 0.099$). The geographical differences were most pronounced in Manicaland, with an extremely low figure for Chimanimani (2.8%) and a very high figure for Chipinge (36%). However, the estimate for Chipinge was only based on 33 subjects. Similar differences could also be found between Gweru and Shurugwi in Midlands (12% and 37% ($N = 57$) respectively).

The difference in the urban/rural and sex-related prevalences was analysed further by application of the case-referent approach. The crude OR for rural areas, using urban areas as a reference, was 0.97 and thus very close to 1, indicating that there was no difference (Table IV). However, when the RR standardised for both year and province was calculated, there was a statistically significant difference. The risk of a subject's being HBs-Ag positive was doubled in rural areas compared with urban areas. Similarly, when the difference in the prevalence by sex was analysed, the crude OR (0.83) indicated that the risk was lower in females. This was confirmed when standardised by year of data collection and province (RR = 0.7; $P < 0.00$).

Table III. Prevalence of HBsAg (%) by year of data collection and district in Zimbabwe, 1989 - 1991

	Year of data collection			
Province/district	1989	1990	1991	Total
Harare	-	-	18.8	19.6
Midlands				
Gweru	11.7	(12.5)	-	
Shurugwi	-	(36.8)	-	
Manicaland				
Chimanimani	2.8	-	-	
Mutare	-	-	(15.5)	
Chipinge	-	-	(36.4)	
Mashonaland C				
Chiweshe	9.7	-	-	
Guruve	-	9.0	-	
Mashonaland E				
Murewa	(16.5)	-	15.6	
Mutoko	-	22.3	29.1	
Mashonaland W				
Kadoma	9.7	(16.0)	-	
Kariba	-	-	9.2	
Masvingo				
Chiredzi	13.3	-	-	
Masvingo	-	-	16.5	
Matabeleland N	-	10.4	-	10.4
Matabeleland S	-	-	21.9	21.7
Total	10.0	17.6	19.0	15.4

Absent figures denote $N < 25$. Bracketed figures denote $N \geqslant 25$ but < 100.

Table IV. Crude OR for HBsAg for urban/rural areas and sex and RR according to Mantel-Haenzel test standardised by age, year of data collection and province (*P*-values for RR according to Mantel-Haenzel test)

	Urban	Rural	Males	Females
Crude OR	1.0	0.97	1.0	0.83
RR standardised for:				
Age		0.97		0.80*
Sex		0.96		-
Year		1.2		0.76**
Urban/rural		-		0.82*
Province		1.3		0.84
Age and sex		1.0		-
Age and year		1.2		0.8**
Age and urban/rural		-		0.8**
Sex and year		1.2		-
Sex and urban/rural		-		-
Sex and province		1.4*		-
Year and urban/rural		-		0.8*
Year and province		2.0***		0.7**
Urban/rural and province		-		0.8**

* $0.01 \leqslant P < 0.05$.
** $0.001 \leqslant P < 0.01$.
*** $P < 0.001$.

Of the other HBV markers, HBeAg and anti-HBe were only tested for in those subjects who were HbsAg positive. The prevalence was 25% for both, with a decrease by age (Table V). This decrease was most pronounced in females with prevalences of 38%, 42%, 14%, 4.5% and 1.5% in the age groups 10 - 19, 20 - 29, 30 - 39, 40 - 49, and 50 years and above. The prevalences of anti-HBs and anti-HBc were 36% and 45% respectively and these were higher in urban settings, especially for anti-HBc ($P < 0.001$) (for anti-HBs $P = 0.018$). The prevalence of anti-HBc and anti-HBs increased with age and was about 70% higher in the age group 50 years and above, compared with the under 20-year-olds (Fig. 2). The prevalence of any of the HBV markers — HBsAg, anti-HBs or anti-HBc — was 66% in males and 61% in females.

Table V. Prevalence of anti-HBs, anti-HBc, HBeAg and anti-HBe by age in HBsAg-positive cases, and whether the subject came from a rural or urban area in Zimbabwe, 1989 - 1991

HBV			Age					
markers	Rural	Urban	10 - 19	20 - 29	30 - 39	40 - 49	⩾ 50	Total
Anti-HBs	34.6	38.9	29.1	37.9	41.7	43.2	48.3	36.2
Anti-HBc	40.8	51.1	33.4	48.7	52.3	48.3	59.4	44.6
HBeAg	25.7	22.4	26.1	26.2	24.4	17.8	13.3	24.5
Anti-HBe	23.8	25.5	28.0	23.8	26.8	13.3	20.0	24.5
Any of above	75.6	76.3	68.2	82.1	79.1	71.1	62.5	75.8

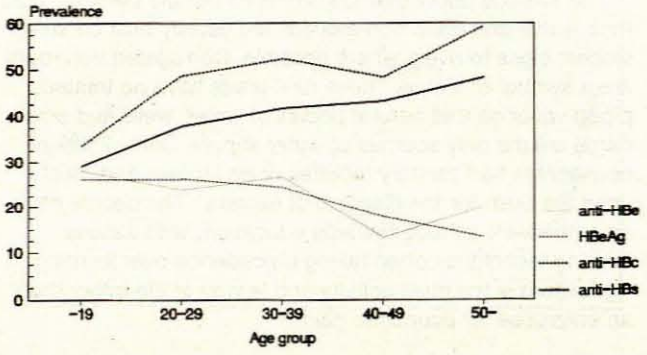

Fig. 2. Prevalence of anti-HBs, anti-HBc, HBeAg and anti-HBe by age in HBsAg-positive cases in Zimbabwe, 1989 - 1991.

Discussion

The prevalence of HBsAg marker found in this study (15.4%) indicates that Zimbabwe is a highly endemic zone. We have observed a slight increase ($P < 0.05$, one-sided test) in HBsAg carriers since the previous sero-epidemiological study (13.7%) carried out in 1984/85.[1] However, this prevalence is comparable to that observed in other studies performed in other African countries.[9-14]

Samples were collected from all nine provinces of Zimbabwe and the prevalence of hepatitis B markers varied between provinces. The highest prevalence (22%) was in Matabeleland South, close to the border with South Africa. The prevalences for Mashonaland East and Harare were also high — 21% and 20% respectively. Manicaland and Mashonaland Central, both sharing borders with Mozambique, had the lowest prevalence — 9% in both. In Manicaland the prevalences in the three districts were 2.8%, 16% and 36%, but unfortunately the last two figures are only based on 97 and 33 samples, resulting in rather unprecise estimates (95% confidence intervals (CIs) 15.5 ± 7.2 and 36.4 ± 16.7). It is none the less of interest to follow up the prevalence in all three districts as well as in the Mutoko district (95% CI 29.1 ± 6.9). It is also worth mentioning that the high prevalence in both Shurugwi and Chipinge was caused by an extremely high prevalence in the youngest age group (40% and 37% respectively).

The prevalences of HBsAg in males and females were 16.8% and 14.3% respectively and the difference was statistically significant. This finding is in agreement with studies in Cameroon[12] and Zimbabwe[1] and supports the hypothesis that males tend to become carriers more frequently than females.

There was no difference in the prevalence of HBsAg between rural and urban settings except in the age group 40 years and above. Only those who were residents of rural areas were classified as belonging to a rural setting. However, this is very difficult to control and because some of those in the 'rural group' spend some of their time in an urban setting they might therefore have the same exposure as urban dwellers.

Although our study showed a high HBeAg prevalence of 25% in HBsAg-positive individuals, a study by Spooner *et al.*[17] in Papua New Guinea indicated an HBeAg prevalence of 32% in HBsAg-positive healthy pregnant women. Unfortunately, we had no information on pregnancy; however, with such high prevalence, especially in females, it would be advisable to vaccinate infants at birth with hepatitis B vaccine.

This study was supported by the Swedish Agency for Research Cooperation with Developing Countries (SAREC).

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Accepted 15 Feb 1995.