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Prevalence of blood-borne viral hepatitis in different communities in Yemen

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SUMMARY

It is generally believed that hepatitis B (HBV) and C (HCV) viruses are highly prevalent in the Republic of Yemen. This study investigated the prevalence of HBV and HCV markers in 494 blood donors from Aden, 493 blood donors from Sana'a, 97 residents from an African ethnic minority in Sana'a and 99 residents of Soqotra Island. There were significant differences in the prevalence of HBV carriage (HBsAg: 6·7, 15, 19·6 and 26·3% respectively; $P<0·001$); past HBV infection (anti-HBc: 17·4, 18·5, 30·9 and 59·6% respectively; $P<0·001$); susceptibility to HBV (absence of HBV markers: 73·3, 61·9, 38·1 and 9·1% respectively; $P<0·001$), infectivity of HBV carriers (HBV DNA: 51·5, 33·8, 52·6 and 65·4% respectively; $P=0·028$) and HCV antibodies (RIBA confirmed or indeterminate: 0·6, 0·2, 5·2 and 5·1% respectively; $P<0·001$). A significant difference in HBV carrier rate and a borderline significant difference in the prevalence of natural infection was observed between males and females in the African community ($P=0·02$ and 0·06 respectively). In contrast, in Soqotra Island, there was no significant sex difference in HBV carrier rate but susceptibility was significantly more prevalent in males ($P=0·03$). This study illustrates that significant difference in prevalence and epidemiology exists among different communities within the same country, reflecting political, geographical and social differences. Control strategies should take these differences into account.

INTRODUCTION

Infection with hepatitis B (HBV) and C (HCV) causes major health problems. It is estimated that more than two billion individuals worldwide have evidence of previous or current HBV infection and at least 350 million are chronic carriers [1]. For HCV, it is estimated that worldwide at least 170 million are chronically infected [2].

Three levels of HBV endemicity are recognized – *high* endemicity, where the carrier rate is 8–15% and prevalence of infection is 40–90%; *intermediate*, with respective rates of between 2–7 and 16–55% and *low*, where the rates are 0·1–1 and 4–15% respectively [3]. Among the Middle Eastern countries, Bahrain, Iran and Kuwait have *low* endemicity; and Cyprus, Iraq

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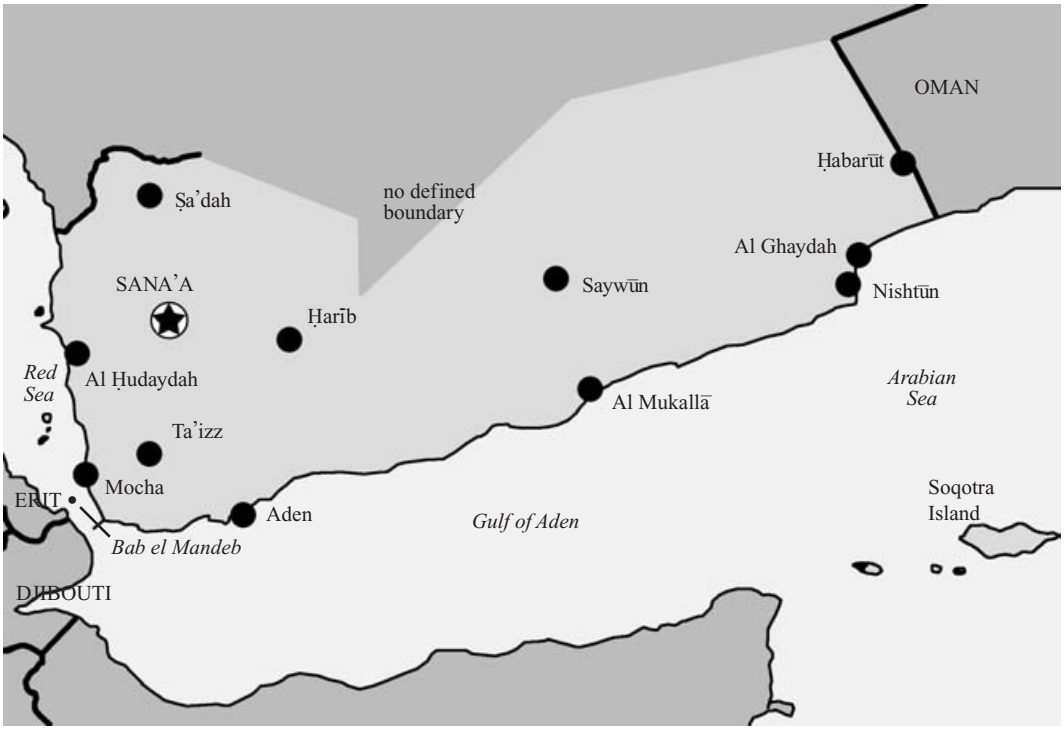

Fig. 1. Map of Yemen with the geographical area of the participants. The African community resided within the city of Sana'a.

and United Arab Emirates *intermediate* endemicity, whereas Egypt, Jordan, Oman, Palestine, Yemen and Saudi Arabia have *high* endemicity [4]. The prevalence of HCV is also variable. A prevalence of 20% has been reported from Egypt [5], whereas only 3·3% of Saudi Arabian [6] and 0·95% of Syrian blood donors are infected [7].

Few studies have examined the prevalence of HBV and HCV in Yemen. Scott reported an HBV surface antigen (HBsAg) carrier rate of 12·7% among the general population [8] and a prevalence of HCV of 2·6% [9], while Al-Robasi and Al-Harbi reported an HBsAg prevalence of 9% among blood donors [10]. These studies did not, however, consider the effect of geographical, cultural or social differences on the prevalence of these viruses across the country. Until 12 years ago, the Republic of Yemen consisted of two separate countries (currently the Northern and Southern regions). The Northern region was an Arab state and the Southern region a socialist republic. In addition, some ethnic minorities originating from Africa live in close communities and poor socio-economic conditions. This may have resulted in different transmission patterns and prevalence of hepatitis viruses. The present study examines the prevalence of HBV and HCV in blood donors attending the blood bank services of Sana'a and Aden in the Northern and Southern regions, a group of residents of Soqotra Island, in the Indian Ocean and an African ethnic minority from a shanty town of Sana'a.

METHODS

Subjects

Blood donors attending the national blood bank services of Sana'a ($n=493$) and Aden ($n=494$) were recruited consecutively. Previous and current residence was ascertained to allow adjustment for migration. Blood donation operates on a semi-voluntary basis in which relatives and friends of patients are requested to donate blood for their clinical management. For cultural reasons, only young males who consider themselves healthy donate blood. Although all blood is checked for blood-borne viruses, there is no recall system to inform donors of their possible infectious status. In addition, 99 subjects from Soqotra Island and 97 from an African ethnic community living in a shanty town of Sana'a were randomly selected after informed consent by house to house visits by outreach teams. The map in Figure 1 illustrates the location of these areas.

Serology

Sera were anonymized and screened for HBsAg (Monolisa Ag HBs Plus; Sanofi Pasteur, France) in

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Table 1. *Viral hepatitis markers in four Yemeni communities*

	Blood donors Sana'a	% positive	Blood donors Aden	% positive	African community	% positive	Soqotra Island	% positive	*P* value for trend
Number	493		494		97		99		
HBsAg	74	15·0	33	6·7	19	19·6	26	26·3	<0·001
Anti-HBc	91	18·5	86	17·4	30	30·9	59	59·6	<0·001
HBsAg and anti-HBc	165	33·5	119	24·1	59	60·8	85	85·9	<0·001
Anti-HBs only	22	4·5	13	2·6	1	1·0	5	5·1	
No HBV markers	305	61·9	362	73·3	37	38·1	9	9·1	<0·001
Anti-HCV*	1	0·2	3	0·6	5	5·2	5	5·1	<0·001
HBV DNA	25	33·8	17	51·5	10	52·6	17	65·4	0·028
Anti-HDV	0	0·0	0	0·0	0	0·0	0	0·0	

* Include RIBA positive and indeterminate.

the Faculty of Medicine and Health Sciences at the University of Sana'a. Reactive sera were further confirmed by neutralization (Murex HBsAg version 3, Abbott, USA) whereas non-reactive sera were tested for HBV core antibody (anti-HBc) (Monolisa HBc Plus; Sanofi Pasteur, France). Anti-HBc non-reactive sera were further tested for HBV surface antibody (anti-HBs) (Monolisa anti-HBs Plus; Sanofi Pasteur, France). All confirmed HBsAg positive sera were further tested for antibody against hepatitis D virus (anti-HDV) (DiaSorin ETI-AB-DELTAK-2). All sera were tested for anti-HCV (Monolisa anti-HCV Plus version 2; Sanofi Pasteur, France) and reactive sera were further confirmed by the recombinant immunoblot assay (Chiron RIBA HCV 3.0 SIA, USA). The presence of two or more specific bands on RIBA was interpreted as a positive result according to the manufacturer's recommendation. To improve the sensitivity, single band reactivity of RIBA, considered by the manufacturer as an indeterminate result, was also included in some analyses.

Molecular analysis

Viral nucleic acid was extracted using a standardized guanidinium-based method and HBV DNA was detected using an in-house polymerase chain reaction (PCR) as previously described [11].

Definition of infection status

Carriage of HBV was defined by the presence of detectable HBsAg whereas the presence of anti-HBc without HBsAg was taken to indicate past HBV infection. Overall prevalence of HBV infection was determined by the presence of HBsAg and/or anti-HBc. The absence of any HBV markers (HBsAg, anti-HBc and anti-HBs) was taken as an indicator of susceptibility. Infectivity was measured by the presence of HBV DNA among chronic carriers. The presence of HCV antibody as confirmed by RIBA was considered as an indication of HCV infection. Samples with indeterminate RIBA results were included for some, but not all, analyses. The differences in prevalence between the different groups were computed and analysed using the Epi-info 6 software (Center for Disease Control, USA). Prevalences were compared with Chi square, Chi square for trend or Fisher's exact test as appropriate.

RESULTS

All blood donors were male with a mean age of 27·4 (range 17–49) years. Fifty-one participants from the African community were male and 46 female, with a mean age of 26·9 (male 28·8, female 24; range 12–60) years. Participants from Soqotra Island consisted of 51 males and 48 females with a mean age of 31·8 (male 33·5, female 30·4; range 5–80) years.

There was a significant difference in HBV markers between Sana'a and Aden (Table 1). Seventy-four (15%) of the 493 blood donors from Sana'a and 33 of the 494 (6·7%) blood donors from Aden had HBsAg ($P<0·0001$). Similarly, evidence of natural infection was observed in 165 (33·5%) donors from Sana'a but in only 119 (24·1%) from Aden ($P=0·001$). Compared to Sana'a, significantly more donors in Aden lacked HBV markers and were susceptible to HBV infection (73·3% *vs.* 61·9%, $P<0·001$). Twenty-nine blood donors from Sana'a were originally from Aden and 8 were from abroad. Among the blood donors in Aden,

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Table 2. *Viral hepatitis markers in males and females in the African and Soqotran communities*

	African community					Soqotra Island				
	Female	% positive	Male	% positive	*P* value	Female	% positive	Male	% positive	*P* value
Number	46		51			48		51		
HBsAg	4	7·8	15	29·4	0·02	12	23·5	14	27·5	
Anti-HBc	19	37·3	21	41·2		32	62·7	27	52·9	
HBsAg and anti-HBc	23	45·1	36	70·6	0·06	44	86·3	41	80·4	
Anti-HBs only	1	2·0	0	0·0		3	5·9	2	3·9	
No HBV markers	22	43·1	15	29·4		1	2·0	8	15·7	0·03
Anti-HCV*	2	4·3	3	5·9		1	2·0	4	7·8	
HBV DNA	3	75·0	7	46·7		8	66·7	9	64·3	
Anti-HDV	0	0·0	0	0·0		0	0·0	0	0·0	

* Include RIBA positive and indeterminate.

13 had migrated from Sana'a and 5 from abroad. The differences in the prevalence of HBV markers between the North and South remained significant after adjustment for previous residence.

The HBsAg carrier rate among the African community was 19·6% (19/97) and 59 (60·8%) had evidence of natural HBV infection. Of 99 Soqotran subjects, 26 (20·2%) were HBsAg positive and 85 (85·9%) had evidence of natural HBV infection. Comparing HBV markers from these four groups, a significant difference was noted for markers of chronic carriage (HBsAg), past infection (anti-HBc), prevalence of infection (HBsAg and anti-HBc), susceptibility (absence of HBV markers) and infectivity of carriers (HBV DNA).

Within the two minority communities, further analysis was performed on sex-related differences in the markers (Table 2). In the African community, the carrier rate and prevalence of natural infection were higher in males than females ($P=0·02$ and 0·06 respectively). There were no significant carrier rate differences between males and females in Soqotra ($P=0·52$) but males were more susceptible than females ($P=0·03$). RIBA confirmed HCV infection was present in 1 (0·2%) of Sana'a and 1 (0·2%) of Aden's blood donors; 2 (2·1%) of the African and 3 (3%) Soqotrans. RIBA was indeterminate in 2 of the Aden donors (0·4%), 3 (3·1%) Africans and 2 (2%) Soqotrans. There was a trend to higher HCV prevalence in Soqotras and Africans than blood donors, but this was only statistically significant when samples with indeterminate serology are included ($P<0·001$). None of the HBsAg positive subjects had evidence of HDV infection.

DISCUSSION

This is the first report of geographical differences in the prevalence of HBV in Yemen. The overall prevalence of chronic HBV infection of 10·8% among healthy blood donors confirms that Yemen is an area with high endemicity [8, 10, 12, 13]. The higher HBV carrier rate and prevalence of natural infection in Sana'a donors may reflect different attitudes to blood donation in Aden where altruistic donations are more common. Another possible factor is the different socio-economic and health service provision before unification. The Southern Democratic Republic of Yemen had links mostly with socialist countries while the predominantly Arab North was heavily populated with a capitalist infrastructure. The Northern region also has a much larger population than the Southern region (7·5 million *vs.* 2·3 million at 1988 before unification based on UNICEF report). Consequently, the provision of health care to the larger and more densely populated Northern region may be more difficult than in the South. The number of blood donors in this study is sufficient to investigate prevalence differences between blood donors from Sana'a and Aden. However, as our blood donors were self-selected young and healthy males, our findings need to be interpreted with care, especially when extrapolating to the general population.

The African community in Sana'a represented a very deprived minority with different lifestyle and limited access to health care. Soqotra Island is also a community with many links to Africa. Similar to the African community in Sana'a, the island has a poor infrastructure and the population has limited access

to health care. It is therefore not surprising that these two communities had a significantly higher HBV carrier rate and prevalence of infection. Soqotran and African carriers were also more infectious than Sana'a blood donors (65·4, 52·6 and 33·8% respectively) although infectivity in Aden's blood donors was equally high (51·5%). In the African community, males were more likely to be infected and to be carriers than females whereas in Soqotra, males were more susceptible to HBV. The number of participants in these two latter groups however was too small to determine differences in prevalence among subgroups of these populations with enough statistical power. Further studies with larger number of participants from these two minority groups are therefore warranted.

The prevalence of HCV in the sample of Yemeni blood donors was slightly lower than the 2·6% previously reported [9, 14]. This may be due to differences in the selection of subjects. Unlike its neighbour Egypt, Yemen has not undertaken large-scale parenteral antischistosomal therapy programmes [5], which could account for the relatively low prevalence of HCV infection in Yemen. The use of RIBA for confirmation may reduce the sensitivity of detection as a drop in antibody levels may reduce the RIBA reactivity to single band [15]. When samples with indeterminate RIBA were included, the prevalence of HCV in the African and Soqotran community was significantly higher than in blood donors. This is consistent with the same mode of transmission and thus the same risk factors of HBV and HCV.

This study demonstrates that the high prevalence of HBV infection is not homogeneous across Yemen. In addition, despite sharing similar routes of transmission, HCV and HDV do not appear to be well established in this population. This study indicates that HBV prevalences can vary across communities within the same country due to political, geographical or social reasons. The recent introduction of universal vaccination of all newborns in Yemen would help to reduce the prevalence of infection in the long term. However, more effort is needed to reach the African and Soqotran minority population in order to prevent peri-natal transmission. An individual community approach would be necessary when planning control strategies.

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