

Decrease in the prevalence of hepatitis B and a low prevalence of hepatitis C virus infections in the general population of the Seychelles

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A serological survey of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections was carried out on a random sex- and age-stratified sample of 1006 individuals aged 25–64 years in the Seychelles islands. Anti-HBc and anti-HCV antibodies were detected using commercially available enzyme-linked immunosorbent assays (ELISA), followed by a Western blot assay in the case of a positive result for anti-HCV. The age-adjusted seroprevalence of anti-HBc antibodies was 8.0% (95% CI: 6.5–9.9%) and the percentage prevalence among males/females increased from 7.0/3.1 to 19.1/13.4 in the age groups 25–34 to 55–64 years, respectively. Two men and three women were positive for anti-HCV antibodies, with an age-adjusted seroprevalence of 0.34% (95% CI: 0.1–0.8%). Two out of these five subjects who were positive for anti-HCV also had anti-HBc antibodies. The seroprevalence of anti-HBc was significantly higher in unskilled workers, persons with low education, and heavy drinkers. The age-specific seroprevalence of anti-HBc in this population-based survey, which was conducted in 1994, was approximately three times lower than in a previous patient-based survey carried out in 1979. Although there are methodological differences between the two surveys, it is likely that the substantial decrease in anti-HBc prevalence during the last 15 years may be due to significant socioeconomic development and the systematic screening of blood donors since 1981. Because hepatitis C virus infections are serious and the cost of treatment is high, the fact that the prevalence of anti-HCV antibodies is at present low should not be an argument for not screening blood donors for anti-HCV and eliminating those who are positive.

Keywords: enzyme-linked immunosorbent assay; hepatitis B antibodies; hepatitis C antibodies; Seychelles.

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Introduction

Hepatitis B virus (HBV) infection is one of the major diseases of mankind, with 2000 million people infected globally and more than 350 million chronic carriers of the virus. The prevalence of chronic carriers in the general population is 8–15% in sub-Saharan Africa and the Far East, 5% in the Middle East and the Indian subcontinent, and less than 1% in Western Europe and North America. In much of the developing world (sub-Saharan Africa, most parts of Asia, and the Pacific region), the infection is acquired during childhood and is generally attributed to poor sanitary and hygienic conditions and malnutrition (1). In developed countries, the infection is often acquired

during early adulthood, mostly through sexual intercourse or intravenous injections among drug abusers. A total of 2–10% of HBV infections result in chronic infection (90% if the infection was acquired during the neonatal period). Among persons with chronic infection, 15–20% will develop liver cirrhosis and the incidence of liver cancer is 1.5–6% per year (liver cancer is the principal cause of cancer deaths in some countries with a high prevalence of HBV) (2). Interferon therapy, costing approximately US\$ 6000 per patient treated, may result in a remission rate of approximately 33% in selected cases of chronic infection (3), and may increase life expectancy — for example, by 3.1 years in 35-year-old males (4). Vaccination against HBV is highly effective at a relatively low cost (less than US\$ 2 for protecting one child); WHO has been promoting the universal use of this vaccination since 1991 through the Expanded Programme on Immunization (5).

Hepatitis C virus (HCV), which was first isolated in 1989, is responsible for the infection of more than 170 million people (6). Population-based data are available from few countries and it is estimated that the prevalence of HCV is below 2.5% in most populations in Africa, the Americas, Europe and South-East Asia, 2.5–4.9% in the Western Pacific region, and ranges from 1% to >12% in the Eastern

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Mediterranean. Individuals at risk include recipients of blood transfusions or organ transplants, immunocompromised patients, intravenous drug users, persons with unsafe sexual activity, health care users, tattooed persons, and babies of infected mothers; however, up to 40% of all HCV cases cannot be traced to any obvious source (7, 8). Acute HCV infection is often relatively mild, with only 20–30% of infected persons developing symptoms. However, as many as 70–80% of acute HCV infections result in a persistent viral infection (7, 9, 10). As with hepatitis B, the sequelae include chronic hepatitis, cirrhosis and hepatocellular carcinoma; the rates of these complications can be higher for HCV infection than for HBV infection. It is generally agreed that the clinical disease and natural history are not influenced by geographic or demographic factors. In the absence of a vaccine, pre- or post-exposure prophylaxis should be used. Interferon, particularly in combination with ribavirin, may result in a sustained virological response in up to 40% of selected patients with chronic HCV hepatitis (10, 11).

In the present study, we examined the prevalence of anti-HBc and anti-HCV antibodies in a representative sample of the general adult population of the Seychelles in order to assess the epidemiology of HCV infection because no data are available in the country; and examine whether the high endemic levels of HBV infection reported in 1979 (12) had changed as a result of rapid socio-economic development in the Seychelles over the last two decades.

Methods

The levels of anti-HBc and anti-HCV antibodies were investigated as part of a population-based health survey conducted between June and December 1994. The survey was approved by the Ministry of Health of Seychelles and the participants gave their free and informed consent. Sampling procedures and survey methods have already been described in detail (13). Briefly, the survey consisted of a random sex- and age-stratified sample of the general population aged 25–64 years; 1067 out of the 1226 (87%) eligible subjects participated in the survey. Immediately after collection, the sera were kept frozen at -20°C until analysis, which was carried out within 2 years at the Division of Immunology of the University Hospital of Lausanne, Switzerland. Anti-HBc and anti-HCV antibodies were detected using well-known commercially available enzyme-linked immunosorbent assays (ELISA). Anti-HBc was detected using an anti-HBc ELISA (Hoffmann-La Roche Diagnostics Systems, Basel, Switzerland). The test was repeated in cases with an indeterminate result. Repeat reactive samples were considered positive. Anti-HCV was detected using a second-generation anti-HCV ELISA (Hoffmann-La Roche Diagnostics Systems, Basel, Switzerland), followed, in cases of a positive or indeterminate result, by a Western blot assay (Wellcozyme WB

Murex, Temple Hill, England), testing for core, NS3, NS4 and NS5 epitopes. According to the manufacturer's instructions, the Western blot assay was considered positive if a reaction of at least two bands was observed. Blood samples were not available for 61 subjects owing to a shortage of serum so that this part of the study involved 1006 subjects.

The distribution of anti-HBc antibodies was examined across categories of selected variables. Education was categorized on the basis of reported "good", "intermediate" and "low" understanding of a second national language (either French or English, Creole being the first language). Economic situation was assessed by the ownership of a car. Alcohol intake was calculated from the reported amount and type of alcoholic beverages consumed per week on average (categories were 0 g, 1–59 g and ≥ 60 g of ethanol per day). The reported current or last job was categorized as "professional or skilled non-manual", "unskilled non-manual", "skilled manual" and "unskilled manual (or labourer)".

The distributions of anti-HBc and anti-HCV were stratified by age and sex and the 95% confidence intervals (CI) were calculated. Seroprevalences (adjusted for the actual age distribution of the population) were also calculated. The populations aged 25–34 years, 35–44 years, 45–54 years, and 55–64 years totalled 14 140, 8419, 4999 and 4390, respectively, and the probabilities that observations were sampled among these age categories were 1/57, 1/34, 1/19 and 1/17, respectively. Associations between anti-HBc and selected variables, using crude sample data, were tested using the χ^2 test. Analyses were performed using Stata for Windows, version 5.0 (Stata Corporation, College Station, TX, USA). Statistical significance was defined for $P < 0.05$.

Results

Table 1 shows that the seroprevalence of anti-HBc antibodies was higher in men than in women and increased with age ($P[\chi^2] = 0.011$). The age-adjusted prevalence of anti-HBc was 10.4% (95% CI: 7.9–13.7) and 5.8% (95% CI: 4.1–8.2), respectively, in men and women aged 25–64 years (overall age-adjusted prevalence: 8.0% (95% CI: 6.5–9.9)). The presence of anti-HBc was associated significantly with job, educational level, and alcohol intake, marginally with economic situation, and not at all with ethnic origin (Table 2).

Five sera were positive for anti-HCV antibodies and were confirmed by Western blot (overall prevalence: 0.34% (95% CI: 0.1–0.8)). Two other sera were positive by ELISA but reacted only to one epitope on the Western blot (NS4 and NS3, respectively) and were considered as indeterminate; data for these two subjects are not included in Table 1. Sera positive for anti-HCV were found in both sexes and in various age categories.

Among the five sera that were positive for anti-HCV, two were also positive for anti-HBc. The two

sera with indeterminate anti-HCV status were also positive for anti-HBc antibodies. These results indicate the presence of dual infection in the Seychelles.

Discussion

The population-based design of this serological survey permitted assessment of the prevalence of anti-HBc and anti-HCV antibodies in the general adult population of the Seychelles.

The presence of anti-HBc antibody is a lifelong marker of HBV infection, irrespective of whether a subject has recovered or has an ongoing chronic infection. Anti-HBc therefore reflects the prevalence of both recent and past HBV infections in the population. The 8.0% prevalence of anti-HBc in the Seychelles is lower than that in the general population of other tropical African countries, e.g. 90% in Zaire (now Democratic Republic of the Congo) (14), 89% in Central African Republic (15), 38% in Madagascar (16), 33% in the United Republic of Tanzania (17), and 25% in Senegal (18), but higher than that in Mauritius (4.5%) (19). In contrast, the prevalence of anti-HBc is low among general populations of most temperate climate areas in developed countries, e.g. 7.1% in Switzerland (20) and 3% in Sweden (21). The relation between anti-HBc and age found in this study is consistent with other reports (22) and expresses, in part, the fact that anti-HBc levels cumulate during a lifetime's exposure. The anti-HBc level was associated inversely with various indicators of socioeconomic status in our study, which may reflect factors involved in the transmission of HBV in endemic areas such as household contact, population density, and poor sanitary conditions (23).

Anti-HBc prevalence in the present survey was considerably lower than that found in a previous study conducted in 1979. The earlier study was carried out on 417 outpatients attending the main hospital in the Seychelles, who apparently had no hepatitis symptoms and were tested for the presence of anti-HBc antibodies using a commercial enzyme immunoassay (Organon Teknika, Boxtel, Netherlands) (12). It was found that anti-HBc population prevalence was 24.2/20.0 and 54.5/33.3 in males/females, respectively, aged 21–40 years and 41–60 years (compared with 9.1/4.3 and 15.2/10.8 in males/females, respectively, aged 25–44 years and 45–64 years in the present study).

The higher prevalence in 1979 than in 1994 may partly be because the 1979 study was patient-based, which may have favoured the selection of patients with higher risks of contracting HBV infection (hence producing an overestimate of the population prevalence of hepatitis B), while the 1994 study was truly population-based. In addition, the slightly lower specificity of the screening tests available in 1979 may have overestimated the true prevalence by 1–2%. It is, however, unlikely that the approximately two-to-threefold lower age-specific

Table 1. Distribution of anti-HBc and anti-HCV antibodies, by sex and age group, in the adult population of the Seychelles

	Age group (years)				
	25–34	35–44	45–54	55–64	25–64 ^a
Men					
<i>n</i>	115	117	125	126	–
Anti-HBc					
<i>n</i>	8 (7.0) ^b	13 (11.1)	14 (11.2)	24 (19.1)	– (10.4)
95% CI	3.5–13.3	6.5–18.2	6.3–18.1	13.1–26.9	7.9–13.7
Anti-HCV					
<i>n</i>	0 (0)	0 (0)	1 (0.8)	1 (0.8)	– (0.24)
95% CI	0–3.2	0–3.1	0.1–5.5	0–5.5	0–1.0
Women					
<i>n</i>	131	130	135	127	–
Anti-HBc					
<i>n</i>	4 (3.1)	7 (5.4)	11 (8.2)	17 (13.4)	– (5.8)
95% CI	1.1–7.9	2.6–10.9	4.6–14.2	8.5–20.5	4.1–8.2
Anti-HCV					
<i>n</i>	0 (0)	1 (0.8)	1 (0.8)	1 (0.78)	– (0.42)
95% CI	0–2.8	0.1–5.3	0–5.1	0–5.4	0–1.4
Total					
<i>n</i>	246	247	260	253	–
Anti-HBc					
<i>n</i>	12 (4.9)	20 (8.1)	25 (9.6)	41 (16.2)	– (8.0)
95% CI	2.8–8.4	5.3–12.2	6.6–13.9	12.2–21.3	6.5–9.9
Anti-HCV					
<i>n</i>	0 (0)	1 (0.4)	2 (0.8)	2 (0.8)	– (0.34)
95% CI	0–1.5	0–2.8	0.2–3.0	0.2–3.1	0.1–0.8

^a Age adjusted.

^b Figures in parentheses are percentages.

seroprevalence in 1994 than in 1979 can be accounted for only by differences in laboratories or study design. The prevalence of a condition at a given instant is related to the incidence of new cases and the duration of that condition. Since there is no reason for the duration and sequelae of HBV infection to have changed over the period considered in this study, the lower prevalence in 1994 strongly suggests that the incidence of HBV infection has truly decreased in the population. In tropical countries with high levels of endemicity (as seemed to be the case in Seychelles in 1979), HBV infection mostly results from neonatal transmission, transmission from one child to another, and through household contact (23). The reduction in HBV incidence since 1979 is compatible with fast socioeconomic development in the Seychelles (the gross national product per inhabitant increased from US\$ 600 in 1979 to US\$ 5000 in 1994), and improved sanitary and hygienic conditions. The introduction of systematic screening for HBV in blood donors since 1981 is also likely to have contributed to this reduction. Further decrease in the incidence of HBV infection in the Seychelles can be expected because hepatitis B vaccine has been given to all children at age 3 months and to many health care workers since 1995, and provided that global immunization can be sustained.

Table 2. Distribution of anti-HBc antibodies, by selected variables, in the Seychelles

Variable	No. tested	No. with anti-HBc	P (χ^2 test)
Men	483	59 (12.2) ^a	
Women	523	39 (7.4)	0.005
Ethnic group			
Black	677	70 (10.3)	
White	86	7 (8.1)	
Indian	11	4 (12.5)	
Chinese	32	1 (9.1)	
Mixed	200	16 (8.0)	0.827
Education			
With second language	681	49 (7.2)	
No second language	325	49 (15.1)	0.000
Job			
Labourer	327	77 (8.4)	
Not a labourer	679	21 (12.5)	0.038
Economic situation			
Has a car	166	10 (6.0)	
Does not have a car	840	88 (10.5)	0.077
Alcohol intake (g/day)			
0	731	62 (8.5)	
1–59	116	8 (6.9)	
≥ 60	159	28 (17.6)	0.001

^a Figures in parentheses are percentages.

At 0.34%, the prevalence of anti-HCV is relatively low in the Seychelles. In comparison, the prevalence of anti-HCV was higher in the general populations of temperate countries, e.g. 0.63% in France (24) and 1.8% in the USA (7), and tropical countries, e.g. 15% in Egypt (25), 5% in the Central African Republic (15), 1–5% in Madagascar (26, 27), 2.1% in Mauritius (but 0% in the neighbouring Rodrigues Island) (28), and 1.7% in Singapore (29). The small number of persons found to be positive for

HCV in the present study precludes meaningful analysis to identify the population groups at risk. However, the low prevalence of anti-HCV in the Seychelles is compatible with the absence of injecting drug abusers and the systematic use of disposable injection materials in health care.

With as many as 70–80% of acute infections becoming chronic (with persisting anti-HCV antibodies), the prevalence of anti-HCV antibodies would only slightly overestimate that of persons with chronic HCV infection in the population who are currently infectious. The long-term persistence of anti-HCV in the minority of subjects who recover from HCV hepatitis is less well known. The prevalence of anti-HCV antibodies could therefore slightly underestimate that of persons ever infected with HCV infection if such antibodies do not persist.

In view of the relatively small sample size used in this study and subsequent low number of identified cases, further investigations and monitoring would help to understand fully the epidemiology of hepatitis C infection in the Seychelles. Our results, however, indicate that the screening of blood donors for HCV should be seriously considered in view of the severe complications of hepatitis C and the high cost of treatment, and because one single infected regular blood donor could transmit the disease to several recipients. ■

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Résumé

Baisse de la prévalence de l'hépatite B et faible prévalence des infections par le virus de l'hépatite C dans la population générale des Seychelles

Une enquête sérologique sur les infections par les virus de l'hépatite B (VHB) et de l'hépatite C (VHC) a été réalisée aux Seychelles sur un échantillon aléatoire de 1006 personnes de 25 à 64 ans stratifié sur l'âge et sur le sexe. Les anticorps anti-HBc et anti-VHC ont été détectés à l'aide de trousse ELISA (titrage immunoenzymatique) du commerce; en cas de résultat positif pour les anti-VHC, ce test était suivi d'un Western blot. La séroprévalence des anticorps anti-HBc ajustée sur l'âge était de 8,0% (IC 95% : 6,5–9,9%) et le rapport hommes/femmes de la prévalence exprimée en pour-

centage passait de 7,0/3,1 chez les 25–34 ans à 19,1/13,4 chez les 55–64 ans. Deux hommes et trois femmes étaient positifs pour les anticorps anti-VHC, soit une séroprévalence ajustée sur l'âge de 0,34% (IC 95% : 0,1–0,8%); deux de ces sujets étaient aussi porteurs d'anticorps anti-HBc. La séroprévalence des anticorps anti-HBc était significativement plus élevée chez les travailleurs non qualifiés, les personnes ayant un faible niveau d'études et les gros buveurs. La séroprévalence par âge dans cette enquête en population réalisée en 1994 était environ trois fois plus faible que lors d'une

enquête précédente réalisée aux Seychelles en 1979 sur une population de malades. Bien que la méthodologie d'enquête soit différente, il est probable que la prévalence des anticorps anti-HBc a fortement baissé aux Seychelles depuis 15 ans. Ce résultat peut être dû à l'important développement socio-économique du pays et aussi au dépistage systématique des dons de sang

pratiqué depuis 1981. Etant donné la gravité des infections par le virus de l'hépatite C et le coût élevé de leur traitement, le fait que la prévalence des anticorps anti-VHC soit actuellement faible ne doit pas inciter à cesser de pratiquer le dépistage du VHC chez les donneurs de sang et de refuser les donneurs positifs.

Resumen

Disminución de la prevalencia de hepatitis B y baja prevalencia de las infecciones por VHC en la población general de las Seychelles

Se llevó a cabo un estudio serológico de las infecciones causadas por los virus de las hepatitis B (VHB) y C (VHC) en una muestra aleatoria estratificada por sexos y edades de 1006 individuos de 25-64 años en las Seychelles. Se emplearon pruebas comerciales de inmunosorción enzimática (ELISA) para detectar los anticuerpos anti-HBc y anti-VHC, realizándose a continuación una prueba «Western blot» cuando se detectaban anti-VHC. La seroprevalencia ajustada por edades de anticuerpos anti-HBc fue del 8,0% (IC95%: 6,5%–9,9%) y la prevalencia porcentual entre hombres/mujeres aumentó de 7,0/3,1 a 19,1/13,4 en los grupos de edad de 25–34 años y 55–64 años, respectivamente. Dos hombres y tres mujeres dieron positivo en las pruebas de anticuerpos anti-VHC, con una seroprevalencia ajustada por edades del 0,34% (IC95%: 0,1%–0,8%); dos de esas cinco personas también presentaban anticuerpos anti-HBc. La seroprevalencia de anti-HBc fue significativamente mayor entre los obreros no calificados, las personas con bajo nivel

educativo y los grandes bebedores. La seroprevalencia de anti-HBc por edades observada en este estudio poblacional, realizado en 1994, fue de aproximadamente la tercera parte de la hallada en un estudio anterior basado en pacientes realizado en 1979 en las Seychelles. Aunque existen diferencias metodológicas entre los dos estudios, probablemente la prevalencia de anti-HBc ha disminuido sustancialmente en las Seychelles durante los últimos 15 años. Ello podría deberse al importante desarrollo socioeconómico experimentado por la isla y al cribado sistemático de los donantes de sangre aplicado desde 1981. Dada la gravedad de las infecciones causadas por el virus de la hepatitis C y el elevado costo del tratamiento de la enfermedad, el hecho de que la prevalencia de anticuerpos anti-VHC sea baja en la actualidad no es razón para dejar de cribar a los donantes de sangre en busca de anti-VHC y descartar los casos positivos.

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