MARKEDLY HIGH SEROPREVALENCE OF HEPATITIS B VIRUS INFECTION IN COMPARISON TO HEPATITIS C VIRUS AND HUMAN T LYMPHOTROPIC VIRUS TYPE-1 INFECTIONS IN SELECTED SOLOMON ISLANDS POPULATIONS

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Abstract. To determine the prevalences of hepatitis B virus (HBV), hepatitis C virus (HCV), and human T lymphotropic virus type-1 (HTLV-1) infections in residents of the Solomon Islands, we surveyed 1,610 serum samples from 1,113 outpatients and 497 healthy volunteer blood donors at the Central Hospital in Honiara, the Solomon Islands. The prevalence of hepatitis B surface antigen (HBsAg) by radioimmunoassay (RIA) (n = 315, 19.6%) was significantly different from that of antibody to HBV (anti-HBV) by a second-generation enzyme immunoassay (EIA) (n = 4, 0.2%) and antibody to HTLV-1 (anti-HTLV-1) by an ELISA with Western blot analysis to verify the positivity (n = 49, 3.0%) (P < 0.0001, respectively). There were no significant differences in the prevalences of these markers between outpatients and blood donors. Hepatitis B e antigen (HBeAg) was detected by RIA in 130 (41.3%) of 315 HBsAg-positive samples. The distribution of HBsAg subtypes by EIA was 190 adr (60.3%), 111 ayw (35.2%), and 14 (0.4%) other subtypes. The HBeAg prevalence decreased with age in all groups for each subtype. There were no significant differences in the prevalence of HBeAg among HBsAg subtypes. We conclude that HBV infection is highly endemic in selected Solomon Islands populations, and that the high prevalence of HBeAg may be associated with the spread of HBV infection there.

Hepatitis B virus (HBV), hepatitis C virus (HCV), and human T lymphotropic virus type-1 (HTLV-1) are spread by infected blood, sexual intercourse, and transmission from mother to child. These viruses can either be latent or become persistent infections, and are the most significant viruses causing malignant diseases, including hepatocellular carcinoma caused by HBV and HCV and adult T cell leukemia/lymphoma associated with HTLV-1.9 The Solomon Islands are located in the southwestern Pacific Ocean (5°–12°S, 156°–170°E) in the tropical zone. There have been no recent investigations of the three viral infections among residents of the Solomon Islands. We conducted a large-scale serologic study of outpatients and blood donors at the Central Hospital in Honiara to determine the seroprevalences of HBV, HCV, and HTLV-1 in the Solomon Islands.

Infection with HBV is an especially serious problem in many countries, and it has been conservatively estimated that there are 350 million chronic HBV carriers throughout the world. The southwestern Pacific area, including the Solomon Islands, is reported to be hyperendemic for HBV infection.10 Hepatitis B e antigen (HBeAg) positivity correlates with ongoing viral synthesis and accounts for the high infectivity of HBV.8 Our laboratory previously reported that HBeAg prevalence in HBsAg-positive subjects differed depending on hepatitis B surface antigen (HBsAg) subtypes.11,12 There are no reports of the differences in prevalences of HBeAg among HBsAg-positive subjects of the Solomon Islands based on HBsAg subtypes. Thus, the possible relationship between HBeAg prevalence and HBsAg subtypes was examined.

SUBJECTS, MATERIALS, AND METHODS

Populations studied. Between April and September 1994, blood samples were collected from 1,113 outpatients (500 males and 613 females, age range = 0–85 years, mean ± SD age = 27.5 ± 13.8 years) and 497 healthy volunteer blood donors (405 males and 92 females, age range = 12–50 years, mean ± SD age = 23.8 ± 6.8 years) at Central Hospital in Honiara on Guadalcanal Island, the main island in the Solomon Islands. The total number of blood samples tested was 1,610 (905 males and 705 females, age range = 0–85 years, mean ± SD age = 26.4 ± 12.2 years; 1,495 [92.9%] Melanesians, 83 [5.2%] Polynesians, and 32 [2.0%] Micronesians). Written informed consent was obtained from all individuals who participated in the study. All procedures in this study conformed to the guidelines established by the Ethic Committee of Kyushu University Hospital. The racial percentages are only for persons from whom the samples were collected; however, they are compatible with the total island population. We excluded other nationalities such as Australians, British, Americans, Gilbertese, and Fijians from the studied subjects because we wanted to determine the seroprevalences of HBV, HCV, and HTLV-1 in native Solomon Islanders. Moreover, the acquisition of HBV and HTLV-1 infections shows not only geographic clustering but also intrafamilial aggregation.2,5,7,10 In addition, a difference in the seroprevalence of HBV infection among races has been observed.10,11 Therefore, it is important to determine the epidemiology of these infections among different races.

The Solomon Islands are part of the great islands chain that extends eastward from Southeast Asia north of Australia to New Caledonia, and are comprised of seven provinces of principal islands and islands groups (Western Province: Choiseul Island and New Georgia Islands; Isabel Province: Santa Isabel Island; Guadalcanal Province: Guadalcanal Island; Malaita Province: Malaita Island; Central Province: Rennell Island; Makira Province: Makira Island; and Temotu Province: Santa Cruz Islands) (Figure 1). The 1,610 subjects studied were from the following provinces: Western Province (n = 241), Isabel Province (n = 62), Guadalcanal Province (n = 456), Malaita Province (n = 657), Central Province (n = 88), Makira Province (n = 44), and Temotu Province (n = 62). Ethnographic and demographic data were de-
terminated by interviews conducted in their native language or in Melanesian pidgin.

After centrifugation of the samples, the sera were immediately frozen and stored at −20°C prior to analysis. All sera were tested for HBsAg, HBsAg subtype, HBeAg, antibody to HCV (anti-HCV), and antibody to HTLV-1 (anti-HTLV-1). We also selected 180 serum samples from 30 subjects in each age group to test for antibody to hepatitis B core antigen (anti-HBc).

**Assay methods.** Anti-HBc was detected by radioimmunoassay (RIA) (CORAB; Abbott Laboratories, North Chicago, IL) and HBsAg was detected by RIA (Ausria II; Abbott Laboratories). The HBsAg subtypes were determined by enzyme immunoassay (EIA) using monoclonal antibodies (HBsAg Subtype EIA; Institute of Immunology, Tokyo, Japan). These subtypes are defined by two mutually exclusive determinant pairs, d/y and w/r, and a common determinant a. With this serologic assay, HBsAg can be conventionally classified into four major subtypes: adw, ayw, adr and ayr. Hepatitis B e antigen was detected by RIA (HBeAg RIA; Abbott Laboratories). Anti-HCV was detected by a second-generation EIA (HCV EIA II; Abbott Laboratories). Screening for anti-HTLV-1 was done using the passive particle agglutination (PA) test (model FP 151; Fujirebio, Inc., Tokyo, Japan). Samples positive by the PA test were confirmed by an ELISA (Eitest-ATL; Eisai, Tokyo, Japan) and by Western blot analysis using antigens prepared from MT-2 cells. In the Western blot analysis, four proteins (p19, p24, p28, and gp68) were tested, and serum samples showing reactivity to p19 plus at least two of the three remaining proteins were considered positive. Samples positive by the three methods (PA test, ELISA, and Western blotting) were classed as positive for anti-HTLV-1. Samples positive only by the PA test were considered negative as were those positive by the PA test and ELISA but negative by Western blot analysis.

Although these serologic tests were done for all serum samples, a test for HCV RNA was conducted only for serum samples positive for anti-HCV to determine HCV viremia as a chronic HCV infection. Serum HCV RNA was detected as follows. Ribonucleic acid was extracted from 50 μl of serum by the Sepa Gene RV test (Sanko Junyaku, Tokyo, Japan), and complementary DNA was synthesized using random primers and reverse transcriptase (Super Script II; GIBCO-BRL, Gaithersburg, MD). The HCV RNA was detected by a 2-stage polymerase chain reaction using primers from the 5'-noncoding region of the HCV genome as previously described.

**Statistical analysis.** Differences in proportions were compared using the chi-square test or Fisher’s exact test. The
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Table 1
Age- and sex-specific prevalences of HBsAg, anti-HCV, and anti-HTLV-1 in the Solomon Islands, 1994*

<table>
<thead>
<tr>
<th>Age (years) group</th>
<th>No. tested</th>
<th>HBsAg positive No. (%)</th>
<th>Anti-HCV positive No. (%)</th>
<th>Anti-HTLV-1 positive No. (%)</th>
<th>No. tested</th>
<th>HBsAg positive No. (%)</th>
<th>Anti-HCV positive No. (%)</th>
<th>Anti-HTLV-1 positive No. (%)</th>
<th>No. tested</th>
<th>HBsAg positive No. (%)</th>
<th>Anti-HCV positive No. (%)</th>
<th>Anti-HTLV-1 positive No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–9</td>
<td>78</td>
<td>13 (16.7)</td>
<td>0</td>
<td>3 (3.8)</td>
<td>37</td>
<td>2 (5.4)</td>
<td>0</td>
<td>1 (2.7)</td>
<td>115</td>
<td>15 (13.0)</td>
<td>0</td>
<td>4 (3.5)</td>
</tr>
<tr>
<td>10–19</td>
<td>183</td>
<td>50 (27.3)</td>
<td>0</td>
<td>8 (4.4)</td>
<td>114</td>
<td>18 (15.8)</td>
<td>0</td>
<td>2 (1.8)</td>
<td>297</td>
<td>68 (22.9)</td>
<td>0</td>
<td>10 (3.4)</td>
</tr>
<tr>
<td>20–29</td>
<td>326</td>
<td>87 (26.7)</td>
<td>1 (0.3)</td>
<td>9 (2.8)</td>
<td>305</td>
<td>50 (16.4)</td>
<td>0</td>
<td>4 (1.3)</td>
<td>631</td>
<td>137 (21.7)</td>
<td>1 (0.2)</td>
<td>13 (2.1)</td>
</tr>
<tr>
<td>30–39</td>
<td>178</td>
<td>42 (23.6)</td>
<td>1 (0.6)</td>
<td>5 (2.8)</td>
<td>196</td>
<td>26 (13.3)</td>
<td>0</td>
<td>7 (3.6)</td>
<td>374</td>
<td>68 (18.2)</td>
<td>1 (0.3)</td>
<td>12 (3.2)</td>
</tr>
<tr>
<td>40–49</td>
<td>87</td>
<td>15 (17.2)</td>
<td>0</td>
<td>6 (6.9)</td>
<td>21</td>
<td>5 (23.8)</td>
<td>1 (4.8)</td>
<td>2 (9.5)</td>
<td>108</td>
<td>20 (18.5)</td>
<td>1 (0.9)</td>
<td>8 (7.4)</td>
</tr>
<tr>
<td>≥50</td>
<td>53</td>
<td>5 (9.4)</td>
<td>1 (1.9)</td>
<td>1 (1.9)</td>
<td>32</td>
<td>2 (6.3)</td>
<td>0</td>
<td>1 (3.1)</td>
<td>85</td>
<td>7 (8.2)</td>
<td>1 (1.2)</td>
<td>2 (2.3)</td>
</tr>
<tr>
<td>Total</td>
<td>905</td>
<td>212 (23.4)</td>
<td>3 (0.3)</td>
<td>32 (3.5)</td>
<td>705</td>
<td>103 (14.6)</td>
<td>1 (0.1)</td>
<td>17 (2.4)</td>
<td>1,610</td>
<td>315 (19.6)</td>
<td>4 (0.2)</td>
<td>49 (3.0)</td>
</tr>
</tbody>
</table>

* HBsAg = hepatitis B surface antigen; anti-HCV = antibody to hepatitis C virus; anti-HTLV-1 = antibody to human T lymphotropic virus type-1.

† P < 0.05, by chi-square test.

Mann-Whitney U test or the Kruskal-Wallis test was used to compare the mean value between or among different groups. The Mantel-Haenszel test with age-adjusted method was used to compare the difference in HBeAg prevalence between HBsAg carriers with subtype adr and those with ayw. Results are expressed as the mean ± SD. A P value < 0.05 was considered statistically significant.

RESULTS

There were no statistically significant differences in the prevalences of HBsAg, anti-HCV, and anti-HTLV-1 between the 1,113 outpatients and the 497 blood donors (HBsAg-positive = 204 (18.3%) and 111 (22.3%); anti-HCV-positive, 2 (0.2%) and 2 (0.4%); anti-HTLV-1-positive, 39 (3.5%) and 10 (2.0%), respectively). The age- and sex-specific prevalences of these viral markers are shown in Table 1. The overall prevalences of these viral markers were 19.6%, 0.2%, and 3.0%, respectively. There was a significantly high seroprevalence for HBsAg compared with those for anti-HCV and anti-HTLV-1 (P < 0.0001, respectively). The prevalence of HBsAg was very high in all age groups, ranging from 8.2% to 22.9% with the highest prevalence in the 10–19-year-old age group. The prevalences of anti-HCV and anti-HTLV-1 were lower than that of HBsAg in all age groups. Although all prevalences tended to be higher in men than in women, there was a statistically significant difference by sex only in the prevalence of HBsAg (P < 0.0001). In all age groups except the 40–49-year-old group, men had higher HBsAg positivity than women. No HCV RNA was detectable in any of the 4 anti-HCV-positive samples.

Table 2 shows the prevalence of anti-HBc in each age group in the studied population. A markedly high prevalence of anti-HBc was found in groups from 10 years old to more than 50 years old (76.7–93.3%), but this prevalence was 43.3% in children less than 9 years old.

Table 3 shows the race-specific prevalence of HBsAg and the distribution of HBsAg subtype and HBeAg positivity. The prevalences of HBsAg were 20.0% in 1,495 Melanesians, 8.4% in 83 Polynesians, and 28.1% in 32 Micronesians. The prevalence of HBsAg was significantly lower in Polynesians than in Melanesians (P = 0.0142) and in Micronesians (P = 0.0131), although the ratio between the men and women of each race was not significant. The overall HBeAg prevalence was 130 (41.3%) of 315 HBsAg-positive subjects with no significant difference between the sexes. One hundred twenty-seven (42.5%) of 299 Melanesians, 33.3% and 25.0% in Polynesians, and 100.0% and 90.0% in Micronesians (88.9%). In HBsAg-positive Polynesians, subtypes adr and ayw were present at similar frequencies. When classified by HBsAg subtypes among races, the HBeAg prevalences of subtype adr and ayw were 41.4% and 44.4% in Melanesians, 33.3% and 25.0% in Polynesians, and 100.0% and 0.0% in Micronesians, respectively. The race-specific preval-
alences of anti-HCV and anti-HTLV-1 were 3 (0.2%) and 47 (3.1%) of the 1,495 Melanesians, and 1 (1.2%) and 2 (2.4%) of the 83 Polynesians. No anti-HCV or anti-HTLV-1 positivity was found in the 32 Micronesians. There were no significant differences in anti-HCV or anti-HTLV-1 prevalence by race.

The prevalence of HBeAg in 315 HBsAg-positive subjects by age and HBsAg subtype is shown in Table 4. The prevalence of HBeAg decreased with age in all HBsAg-positive subjects. The overall prevalence of HBeAg was not significantly different between HBsAg-positive subjects with subtypes adr (41.6%) and ayw (40.5%). The prevalence of HBeAg was relatively higher in HBsAg-positive subjects with subtype adr than in those with ayw who were more than 10 years of age. The mean ± SD age was significantly younger in HBsAg-positive subjects with HBeAg than in those without HBeAg in each subtype (23.3 ± 8.3 years and 29.4 ± 8.9 years in those with adr, P < 0.0001, and 18.5 ± 9.9 years and 25.7 ± 9.3 years in those with ayw, P = 0.0001, respectively). Moreover, the mean ± SD age of HBsAg-positive subjects with HBeAg was significantly younger in those with subtype ayw (18.5 ± 9.9 years) than in those with subtype adr (23.8 ± 9.7 years) (P = 0.0068). However, the Mantel-Haenszel test with an age-adjusted method showed that there was no statistically significant difference between subtype adr and ayw (P = 0.2184, adjusted odds ratio = 1.43, compared to subtype ayw).

There were no statistically significant differences in the prevalences of HBsAg, anti-HCV, and anti-HTLV-1 or the distribution of HBsAg subtype among inhabitants in different provinces.

**Table 3**

<table>
<thead>
<tr>
<th>Race-specific prevalence of HBsAg and distribution of HBsAg subtype and HBeAg positivity among races in the Solomon Islands, 1994*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Micronesians</td>
</tr>
<tr>
<td>Polynesians</td>
</tr>
<tr>
<td>Melanesians</td>
</tr>
</tbody>
</table>

* HBsAg = hepatitis B surface antigen; HBeAg = hepatitis B e antigen; M = male; F = female; ND = not determined.
† Significant differences compared with the Melanesian group (P = 0.0142) and the Micronesian group (P = 0.0013).
‡ Ratio of each subtype or HBeAg-positive numbers to HBsAg-positive numbers of each race or total.
§ Significant differences compared with the other race groups (P < 0.0001, respectively).

**Discussion**

The prevalences of HBV markers (HBsAg = 19.6%, anti-HBe = 79.4%, anti-HCV = 0.2%), and anti-HTLV-1 (3.0%) were markedly different in the Solomon Islanders, despite similar routes of transmission of these three viruses (e.g., blood, sexual intercourse, maternal transmission). It is well documented that the prevalence of HBV infection is high in developing countries of the western Pacific and Southeast Asia. Our laboratory previously reported that HBV was the most transmissible of these three viruses in studies of hospital personnel and mentally retarded patients. This may explain the higher prevalence of HBV infection compared with HCV and HTLV-1 infections in selected Solomon Islands populations. Because the present study is a prevalence survey of a highly selected group such as blood donors and outpatients that was not selected on a population basis, the epidemiologic conclusions that we can draw from their results may be limited. Our result that Melanesians, a main race in the Solomon Islands, had a high positivity for HBsAg is consistent with previous observations among nonselected Pacific populations, despite no...
significant differences in anti-HCV or anti-HTLV-1 prevalence by race. However, the differences between the Melanesian, Micronesian, and Polynesian groups in our study may not provide reliable data because numbers in some subgroups are too small.

The prevalence of anti-HCV is considerably higher in developing countries than in developed countries, reaching 4–6% in selected populations in parts of Africa and the Middle East, in contrast to our results. There are two possible reasons for the low prevalence of HCV infection in the Solomon Islands. First, few inhabitants with chronic HCV infection originally lived in this area because none of anti-HCV-positive subjects had any HCV RNA in their serum. Second, the inhabitants had very little chance of acquiring an HCV infection through medical care because of the scarcity of medical facilities. From our surveys for HCV infection in Japan, medical interventions (especially drug treatment by injection using nonsterile syringes and needles) played a more important role in the spread of HCV infection than familial transmission.

It has been established that HTLV-1 is oncogenic and causes immune disorder diseases (myelopathy and tropical spastic paraparesis). The molecular epidemiology of HTLV-1 proviruses in the viral endemic area showed the specificity for the geographic origin of the patients. In several studies done in the southwestern Pacific, Melanesia, the ethnogeographic region that includes Papua New Guinea, the Solomon Islands, and Vanuatu, was reported to have the high prevalence of anti-HTLV-1. A previous survey of HTLV-1 infection in the Solomon Islands in the 1980s indicated that the prevalence ranged from 2% to 10% among individuals from widely separated regions. In the present study, we found a relatively high prevalence of HTLV-1 in the Solomon Islands, but no differences by island.

While the modes of HBV transmission are similar throughout the region, there is considerable variation in the importance of perinatal and household transmission and transmission by blood transfusion, secretions, and sexual intercourse. The high prevalence of HBV infection that has generally been found to more frequently occur in the tropics than in the temperate zone has been attributed to socioeconomic conditions such as poor sanitation. The inhabitants of Okinawa, the most southerly part of Japan, near Taiwan, also reported that subtype adw was the predominant subtype in Okinawa, the most southerly part of Japan, near Taiwan.

In conclusion, HBV infection is highly endemic in selected Solomon Islands populations, in contrast to HCV and HTLV-1 infections. The finding that HBeAg prevalence was high in HBsAg-positive subjects may be associated with the spread of HBV infection.

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