Japan, especially Kyushu islands, has been reported to have a very high prevalence of human T-cell leukemia virus type 1 (HTLV-1) infection in the world (1,2). Since September 2010, the serological screening for the detection of HTLV-1 antibodies in Japan can be performed for all women during pregnancy with the public funds for strategies to prevent HTLV-1 vertical transmission. Confirmation tests for screening those with positive results have been covered by insurance for all.

Vertical transmission is the most important route for HTLV-1 infection; however, horizontal (sexual) transmission is also an important route of infection in adults (3–6). Although transmission has been confirmed during infancy through breastfeeding, little is known about the epidemiological aspects of new HTLV-1 infections later in life. The transmission rate in exclusively formula-fed infants has been reported to be approximately 2–3%, indicating the possibility of alternative routes (7,8). Based on a retrospective cohort analysis in 2016, approximately 4,000 people infected with HTLV-1 experience seroconversion per year in Japan (9).

Therefore, the current study was conducted to examine how horizontal transmission affected the prevalence of HTLV-1 carriers among pregnant Japanese women in 2019.

The protocol for this study was approved by the Ethics Committee of the Japan Association of Obstetricians and Gynecologists (JAOG) (2017-5).

On December 2020, we requested 2,214 obstetrical facilities that are registered with JAOG to provide information on HTLV-1 tests for pregnant women who delivered at ≥22 weeks gestation in 2019. A total of 1,468 (66.3%) of the 2,214 obstetrical facilities responded, and information on a total of 568,626 women, accounting for approximately 66% or more of all pregnant women covered in the report by the Ministry of Health, Labour and Welfare (Japan) in 2019 (865,324 women), was provided (10). In this study, we requested the number of HTLV-1 ‘seroconverters’ whose HTLV-1 tests were negative during their previous pregnancies.

Chi-squared or Fisher’s exact test was used for the categorical variables. Differences with \( P < 0.05 \) were considered significant.

Table 1 shows the prevalence of HTLV-1 carriers and the rate of HTLV-1 seroconversion by area in Japan. In pregnant Japanese women, the prevalence of HTLV-1 carriers was 0.11%, while the rate of HTLV-1 seroconversion of the carriers was 10.7%. Considering the response rate, the number of HTLV-1 carriers among pregnant Japanese women was 952. At least 10% or more of the carriers acquired HTLV-1 through horizontal transmission.

Table 2 shows the rate of HTLV-1 seroconversion in each region of Japan. There were no significant differences in the rates in the 6 regions of Japan.

In 2019, the estimated number of HTLV-1 carriers among pregnant Japanese women was 952. In addition, at least 10% or more of the HTLV-1 carriers had horizontal transmission.

Based on the results of confirmation tests in 2011–
HTLV-1 Due to Horizontal Transmission

In 2013, the prevalence and number of HTLV-1 carriers among pregnant Japanese women were estimated to be 0.16–0.18% and 1,560–1,780, respectively (11,12). Although the number of deliveries in Kyushu islands was only 13–14% of Japanese deliveries, 51–53% of HTLV-1 carriers among pregnant Japanese women were present in Kyushu islands (11,12). The prevalence of HTLV-1 carriers in Kyushu islands and other areas were 0.60–0.66 and 0.08%, respectively (11,12). Therefore, the estimated number of HTLV-1 carriers among pregnant Japanese women in 2019 decreased to 55–60% of that estimated 6–8 years ago. However, there was no change in the distribution of HTLV-1 carriers at Kyushu islands.

During this period, the number of deliveries in Japan decreased by 10–20%; however, the prevalence and number of pregnant HTLV-1 carriers have decreased further. The migration of Japanese people from Kyushu to the metropolitan area may have contributed to the decrease in the number of HTLV-1 carriers in Kyushu islands (13); however, this has not been established. In addition, the change in the main method of confirmation for HTLV-1 infection from western blot (WB) tests followed by polymerase chain reaction (PCR, WB/PCR) to line immunoassay (LIA, LIA/PCR) during the period may have contributed to a large bias in comparing the prevalence (14). An HTLV-1 carrier is diagnosed only after confirmation tests are positive. For indeterminate cases, PCR is used as a final test to diagnose HTLV-1 infection. LIA was developed for the serological confirmation and discrimination of HTLV-1 infection (15). This assay performs well in confirming HTLV-1 seropositivity by exhibiting a low incidence of indeterminate results. In addition, the results of LIA are in good agreement with PCR results. However, the changes in the prevalence of HTLV-1 carriers may be the effect of HTLV-1 vertical transmission prevention projects since approximately 30 years ago in Japan (7,16,17).

Unfortunately, in this study, we did not request answers regarding the number of deliveries and/or the intervals from the previous pregnancies. However, at least 10% or more of the carriers acquired HTLV-1 through horizontal transmission. The rate of HTLV-1 seroconversion due to sexual contact in pregnant women in Japan may be influenced greatly by the rate of HTLV-1 infection in men in their 20–40s in the respective geographical areas of Japan. The rate of HTLV-1 infection in men has been reported to be higher in the Kyushu islands than in other regions (9). Therefore, it has been expected that the rate of HTLV-1 seroconversion due to sexual contact in pregnant women could be higher in Kyushu islands than in other regions.

### Table 1. Prevalence of human T-cell leukemia virus type 1 (HTLV-1) carrier and the rate of HTLV-1 'seroconverter' in pregnant women who delivered at ≥22 weeks' gestation in 2019 by area in Japan

<table>
<thead>
<tr>
<th>Area of Japan</th>
<th>Obstetric institute</th>
<th>Total pregnant women</th>
<th>HTLV-1 carrier</th>
<th>Total</th>
<th>LIA-positive</th>
<th>PCR-positive</th>
<th>'Seroconverters'</th>
</tr>
</thead>
<tbody>
<tr>
<td>Except Kyushu islands</td>
<td>1,221</td>
<td>485,826</td>
<td>361 (0.07)</td>
<td>342</td>
<td></td>
<td>19</td>
<td>39 (10.8)</td>
</tr>
<tr>
<td>Kyushu islands</td>
<td>247</td>
<td>82,800</td>
<td>245 (0.30)</td>
<td>239</td>
<td></td>
<td>6</td>
<td>26 (10.6)</td>
</tr>
<tr>
<td>Total</td>
<td>1,468</td>
<td>568,626</td>
<td>606 (0.11)</td>
<td>581</td>
<td></td>
<td>25</td>
<td>65 (10.7)</td>
</tr>
</tbody>
</table>

Data are presented as number (%).

'Seroconverter', subjects whose HTLV-1 tests were negative at their previous pregnancies.

HTLV-1, human T-cell leukemia virus; LIA, line immunoassay; PCR, polymerase chain reaction.

### Table 2. Rate of human T-cell leukemia virus type 1 (HTLV-1) 'seroconverter' in pregnant women who delivered at ≥22 weeks' gestation in 2019 by region in Japan

<table>
<thead>
<tr>
<th>Region of Japan</th>
<th>HTLV-1 carrier</th>
<th>Total</th>
<th>'Seroconverters'</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hokkaido-Tohoku</td>
<td>34</td>
<td>3</td>
<td>3 (8.8)</td>
</tr>
<tr>
<td>Kanto (Tokyo)</td>
<td>128</td>
<td>12</td>
<td>12 (9.4)</td>
</tr>
<tr>
<td>Hokuriku-Chubu</td>
<td>60</td>
<td>8</td>
<td>8 (13.3)</td>
</tr>
<tr>
<td>Kansai</td>
<td>81</td>
<td>10</td>
<td>10 (12.3)</td>
</tr>
<tr>
<td>Chugoku-Shikoku</td>
<td>58</td>
<td>6</td>
<td>6 (10.3)</td>
</tr>
<tr>
<td>Kyushu</td>
<td>245</td>
<td>26</td>
<td>26 (10.6)</td>
</tr>
<tr>
<td>Total</td>
<td>606</td>
<td>65</td>
<td>65 (10.7)</td>
</tr>
</tbody>
</table>

Data are presented as number (%).

'Seroconverter', subjects whose HTLV-1 tests were negative at their previous pregnancies.

HTLV-1, human T-cell leukemia virus.
women will be higher in the Kyushu islands. However, in the current study regional differences in the rate were not observed. These mothers may have been infected during the period of childcare, and vertical transmission to a former infant/child may have occurred depending on the feeding methods. Considering the total fertility rate in Japan (approximately 1.4; the number of children the couple has and those they intend to have: 1.71 and 2.07), the estimated HTLV-1 transmission risk in pregnant women, including the number of nulliparous women, may almost double to approximately 20% (18).

Based on the current results, the horizontal transmission of HTLV-1 may have increased with the decrease in the vertical transmission of HTLV-1. New HTLV-1 infections in adults may be an important public health concern in Japan, and preventive strategies are needed to reduce new transmissions.

Conflict of interest None to declare.

REFERENCES