# HTLV-1 Carrier Mothers Need Continual Support to Accomplish Their Selected Nutrition Method for Mother-to-child Transmission Prevention in Kagoshima

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# HTLV-1 Carrier Mothers Need Continual Support to Accomplish Their Selected Nutrition Method for Mother-to-child Transmission Prevention in Kagoshima

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## Abstract

INTRODUCTION: Since 2011, the nationwide mother-to-child transmission prevention program in Japan for HTLV-1 has recommended three nutritional methods: formula-feeding (FF), short-term breast-feeding (STBF) and frozen-thawed milk feeding. Here we clarify the support necessary for HTLV-1-positive mothers to accomplish their selected nutrition method in Kagoshima.

METHODS: We administered questionnaires to 93 HTLV-1-positive mothers to determine whether each baby was successfully fed by following the mother's selected nutrition method, and whether any problems were encountered. They were divided into 2 groups (FF and STBF) by chosen nutrition method and compared; the FF group comprised 23 women and the STBF group comprised 70 women.

RESULTS: We received responses from 70 of the 93 women enrolled. The success rate of accomplishing their selected nutrition method was lower in the STBF than the FF group, and the difficulty rate was higher in the STBF than the FF group. The major reasons for feeling a difficulty in accomplishing the STBF method were the lack of support for weaning, suffering from emotional stress, and inability to wean children from breast milk. In contrast, the major reason for feeling a difficulty in the FF group was not being understood by family members and/or neighbors.

CONCLUSIONS: HTLV-1-carrier mothers, especially mothers who selected the STBF method, needed continual support to accomplish their selected nutrition method for mother-to-child transmission prevention. It is necessary to improve the support environment for HTLV-1-carrier mothers in Japan without delay.

**Key words**: HTLV-1, mother-to-child transmission, breast-feeding

## Introduction

The human T-lymphotropic virus type 1 (HTLV-1) is known to be the pathogenic agent of adult T-cell leukemia-lymphoma (ATL)[1,2)]. HTLV-1 is endemic in southern Japan, the Caribbean, Latin America and western Africa[3)]. Three main routes of HTLV-1 transmission are known. The first is mother-to-child transmission[4)], mainly due to ingestion of breast milk[5)]. The second is sexual transmission, mainly from men to women[6)]. The third is transfusion of blood that includes HTLV-1-positive cellular components[7)]. Of the three, breast-feeding is the predominant route of transmission.

Lymphocytes in breast milk are responsible for transmitting HTLV-1[5]. Refrain from breast-feeding is the best and easiest way to prevent mother-to-child transmission of HTLV-1. However, the advantages of breast-feeding over formula-feeding (FF) to prevent overall child morbidity and mortality have been well established[8], especially in developing countries[9]. There are a couple of approaches to prevent mother-to-child transmission of HTLV-1 via breast milk other than refraining from breast-feeding. One is freeze-thawing of breast milk; the infectivity of HTLV-1 in breast milk was lost during the freezing and thawing processes[10]. The next possible approach to reduce the milk-borne transmission is to limit the duration of breast-feeding[11-14]. This may be related to the protective effect of maternally derived anti–HTLV-1 IgG antibodies[15].

The prognosis for ATL is extremely poor, and no vaccine is yet available. Therefore, a public health system to prevent transmission from carrier mothers to infants is important. In 1990, the Japanese government decided not to introduce a nationwide system of HTLV-1 prevention based on the Health Labour Sciences Research Grant reports[16], which recommended implementation of appropriate prevention plans only in endemic areas. One of the reasons was that introduction of a prevention system in a non-endemic area might increase the risk of confusion. Another reason was that the number of HTLV-1 carriers was expected to decrease with or without intervention because there was a trend toward a reduced rate and duration of breast-feeding at that time.

However, the Health Labour Sciences Research Grant reports in 2010 suggested that the number of HTLV-1 carriers had not decreased, contrary to expectations, and that the distribution of HTLV-1 carriers had spread into non-endemic areas[17]. The phenomenon may be explained by the flow of the population from endemic rural areas to non-endemic major urban cities during the period of high economic growth in Japan. A nationwide system of HTLV-1 prevention is needed under such circumstances, and the Ministry of Health, Labour and Welfare introduced a nationwide mother-to-child transmission prevention program. It recommended three nutritional methods: FF, short-term breast-feeding (STBF) of <3 months after birth, and frozen-thawed milk feeding. Nation-wide screening of pregnant women for HTLV-1 infection was implemented in Japan in 2011[18].

On the other hand, in 1985, Kagoshima University began a study on the prevention of HTLV-1 transmission in collaboration with the local government of Kagoshima Prefecture. Kagoshima prefecture is located in Kyushu, in the south of Japan. Many HTLV-1-positive people live in Kyushu. In the 1985 study, Takahashi et al. determined that the seroconversion rate of STBF children was nearly equal to that of bottle-fed children[11]. Therefore, the prefecture-wide "ATL Prevention Decade Plan" to promote FF or STBF for HTLV-1 carrier mothers began in 1997. Approximately two-thirds of the HTLV-1 carrier pregnant women chose STBF, which was a higher rate than in other endemic prefectures[19]. In the previous report, in Kagoshima Prefecture, there were not many obstetrics facilities that cared for HTLV-1 carrier mothers when weaning from the breast[20]. Therefore, only 75% of HTLV-1 carrier mothers accomplished their selected nutrition method. In this study, we introduced a support system performed by visiting public health nurses. But it remains unclear whether HTLV-1-positive pregnant mothers are successfully implementing their selected nutrition method, especially STBF; in addition, whether any support is necessary for success is unknown.

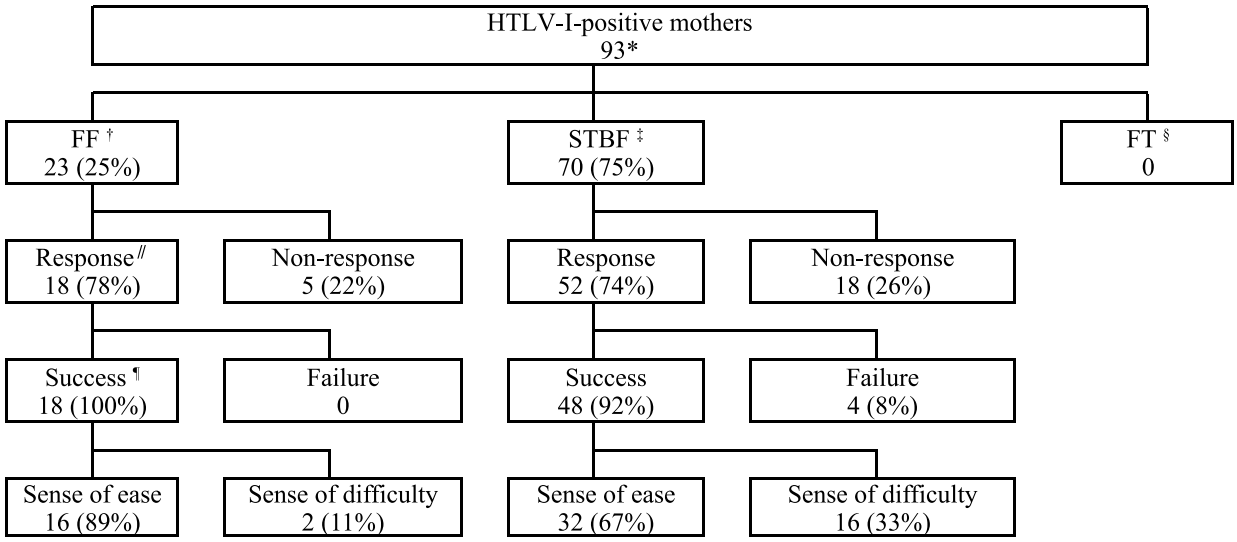
The aim of this study was to clarify the support necessary for HTLV-1-positive mothers to achieve success with their selected nutrition method in Kagoshima.

## Methods

During the nation-wide screening of pregnant women for HTLV-1 infection, informed consents were obtained before screening for the antibody. Screening for HTLV-1 antibody was performed using the passive particle agglutination method (PA) or the chemiluminescent immunoassay (CLIA). Positive results were confirmed by Western blot analysis or an immunofluorescence assay[18]. The obstetricians or midwives in the obstetrics facilities in Kagoshima Prefecture recommended HTLV-1 positive pregnant woman to use one of three nutritional methods: bottle-feeding, STBF (<3 months), or frozen-thawed milk, as outlined in the HTLV-I mother-to-child transmission (MTCT) prevention health guidance manual compiled by the Ministry of Health, Labour and Welfare[18].

We obtained the cooperation of 48 of the 50 obstetrics facilities in Kagoshima Prefecture by the end of 2013. We visited these obstetrics facilities to obtain informed consent for this study from HTLV-1-positive pregnant woman between January 2013 and December 2013. We obtained informed consent from 93 HTLV-1-positive pregnant women. We investigated the choices made for nutrition methods before the delivery. No mother selected frozen-thawed milk (FT). Accordingly, the HTLV-1-positive pregnant women

**Figure 1**. Response rate, success rate, and rate of sense of difficulty in accomplishing the selected nutrition method"




* We visited obstetrics facilities in Kagoshima prefecture to obtain informed consent for this study from HTLV-1-positive pregnant woman between January 2013 and December 2013.

† FF: formula-feeding

‡ STBF: short-term breast-feeding (<3 months)

§ FT: frozen-thawed milk

// Response: We received replies from them.

¶ Success: They accomplished their selected nutrition method.

participants were divided into 2 groups: the FF group, consisting of 23 mothers; and the STBF group, consisting of 70 mothers.

In this study, support was introduced through visiting public health nurses after childbirth. They visited upon request from the mothers, with a frequency of approximately once per month. They provided consultation to help the mothers who were anxious about the nutritional status of their baby. We administered questionnaires to all 93 enrolled participants three months after delivery to determine whether each baby was successfully fed by following the selected nutrition method, and whether any problems were encountered. Frequency analysis was performed with the Fisher's exact test.

The study protocol was reviewed and approved by the Ethics Committee of Kagoshima University Graduate School of Medical and Dental Sciences (No.196).

## Results

1. Response rate

We received replies from 52 of 70 (74%) STBF group subjects and 18 of 23 (78%) FF group subjects. Both groups had almost the same response rate (Fig.1). No significant differences were found between Kagoshima city and the urban area for the nutrition method choice.

2. Accomplishment rate

Successful use of the selected nutrition method was accomplished by 48 (92%) of the STBF group and the entire FF group. No significant difference was found between the two groups in accomplishment rate (Fig.1).

In addition, no significant differences were found in accomplishment rate between primiparas and multiparas.

3. Rate of feeling a difficulty in successful use of the selected nutrition method

In the STBF group, 16 (33%) found it difficult to achieve success with the selected nutrition method, as did 2 (11%) of the FF group. No significant difference in this rate was found

**Table 1.** The reasons for feeling a difficulty using the selected method

| Group | Case number |
|---|---|
| Formula-feeding (FF) group | 2 |
| Feeling a difficulty | 2 |
| Lack of understanding from family members and/or neighbors * | 2 |
| Medical support was insufficient † | 1 |
| Short-term breast-feeding (STBF) group | 20 |
| Feeling a difficulty | 16 |
| Difficult to wean from the breast ‡ | 4 |
| Trouble with breasts § | 4 |
| Sense of desolation after weaning from breast // | 4 |
| Medical support for how to wean was insufficient ¶ | 3 |
| Lack of understanding from family members and/or neighbors | 1 |
| Failure to wean from the breast within 3 months | 4 |
| Difficult to wean from the breast | 2 |
| Medical support for how to wean was insufficient | 1 |
| Plan to go abroad ** | 1 |

(Multiple answers allowed)

* "Lack of understanding from family members and/or neighbors" included "It was difficult to explain to friends and relatives, excluding parents, why breast feeding was impossible" and "suffered from questions about breast-feeding."

† "Medical support was insufficient" means that the mother did not receive support as expected from a medical institution (The details were unwritten).

‡ "Difficult to wean from the breast" means STBF mothers found it considerably difficult to wean from the breast.

§ "Trouble with breasts" included mastitis and pain or discomfort caused by engorged breasts with weaning.

// "Sense of desolation after weaning from breast" included feelings of "I am not required by my baby" and "Why is it just me who cannot breast-feed?"

¶ "Medical support for how to wean was insufficient" means that the mother received insufficient support to wean from the breast.

** "Plan to go abroad" means that the mother expected to provide their baby passive immunity through the transfer of IgA antibodies found in breast milk in anticipation of traveling to a developing country.

between the two groups (Fig.1).

4. Reasons for feeling a difficulty in using the selected method

The reasons for feeling a difficulty for successful use of the selected nutrition method are listed in Table 1.

The major reason in the FF group was not being understood by family members and/or neighbors. In contrast, the major reasons for feeling a difficulty in accomplishing the STBF method were lack of support for weaning, suffering from emotional stress, and inability to wean children from breast milk. The major reasons for feeling a difficulty differed between groups.

## Discussion

This study shows that HTLV-1-positive mothers found it considerably difficult to use their selected feeding method, regardless of the method chosen. Therefore, HTLV-1-positive mothers need much support to be successful with their selected method. Furthermore, the STBF group needed more support than the FF group, as evidenced by their lower accomplishment rate and the higher rate of feeling a difficulty with using the method despite the major reasons for feeling a difficulty differing between groups (Fig.1).

Because the total success rate (92%) of this study was higher than the rate (75%) of the previous report[20], the support by public health nurses might be effective. However, not all mothers could achieve their goals by using this support. Because the major reasons for feeling a difficulty with the STBF method were the lack of the support for weaning, suffering from emotional stress, and the inability to wean children from breast milk, further support is necessary (Table 1). Support by midwives may resolve these problems since they are specialists in childbirth, postpartum issues (including nursing), and women's health care. They can also help resolve the cognitive, emotional and technical problems of weaning. However, the economics of introducing such support is problematic.

On the other hand, the major reasons for feeling a difficulty

while using the selected method in the FF group was different that the STBF group in that feeling a lack of being understood by their family members and/or neighbors would make some mothers feel afraid of revealing their HTLV-1 carrier status (Table 1), which could occur if they attempted to explain why they refrained from breast feeding[19-21]. To eliminate prejudice against the HTLV-1 carriers, educational activities are required.

All 18 mothers in the FF group accomplished their selected nutrition method. According to our results, FF seemed to be the most reliable and easiest way to prevent mother-to-child transmission of HTLV-1. Additionally, in developed countries, including Japan, infectious diseases and malnutrition are not main causes of infant mortality. In light of this, the question of why the Japanese government recommends STBF as a nutrition method for these mothers is raised. Although the benefit of STBF is unclear, breast-feeding per se is beneficial to not only the health of the infants but also the health of mothers[8]. HTLV-1 causes ATL or HAM in only a minority (approximately 5%) of carriers after a long incubation period. In addition, the FF method cannot protect against all mother-to-child transmission. Approximately 3% of infants will be infected by their mothers, even if formula fed. The infection route of HTLV-1 when the FF method is used remains unknown[18]. Therefore, the optimal nutrition method for HTLV-1 carrier mothers is still controversial; more studies are needed to clarify this issue.

The limitations of this study include its small sample size and a possible selection bias. However, in 2012, the rate of pregnant carrier women was only 1.3% even in Kagoshima, which is located in a pandemic area. Theoretically, there are approximately 200 pregnant carrier women per year in Kagoshima. This study enrolled approximately half of all suspected carrier pregnant women in Kagoshima, which lends credence to the results.

In conclusion, HTLV-1-carrier mothers, especially mothers who chose the STBF method, need continual support to accomplish mother-to-child transmission prevention. Despite the fact that the Japanese government introduced a HTLV-1 mother-to-child transmission prevention health program by recommending three post-delivery nutrition methods, there exists no post-delivery system of support to achieve success in preventing transmission via those methods. In our study, 8% of STBF mothers failed in their selected method, as such, approximately 20% of those mothers' babies could become HTLV-1 carriers, of which 5% could suffer from associated diseases including ATL and HAM in future. However, if a support system were introduced, it would take time to see the effect. So even if there are unsolved problems, it is necessary to immediately improve the support environment for HTLV-1-carrier mothers in Japan. Any future trials in Japan will be important in informing optimal preventative strategies in other countries.

## Disclosure of potenial conflict of interests

The authors declare that there is no conflict of interest regarding the publication of this paper.

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# 鹿児島県の HTLV- Ⅰ母子感染予防の栄養法達成のための母親への継続的な支援が必要

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【背景】2011 年より栄養法として人工栄養、短期母乳、凍結母乳の３つが選択候補にあげられた HTLV-1 母子感染対策は全国的な取り組みが開始された。鹿児島県において HTLV-1 陽性妊婦が出生前に決定した栄養法が実施完了できるのに必要な支援について明らかにする。
【方法】同意取得した出産３か月経過後の母親 93 名に質問票を送付し回収した。決定した栄養法で人工栄養、短期母乳の２群に分け、比較検討した。
【結果】93 名のうち 70 名から回答を得た。選択した栄養法を完遂できた率は、人工栄養群にくらべ短期母乳群が低かった。また、栄養法を遂行するのに困難を感じた率は人工栄養群にくらべ短期母乳群が高かった。その困難を感じた主な原因は、短期母乳群では「断乳時の支援不足」、「感情的な苦しみ」、「子どもがお乳から離れない」であった。対照的に人工栄養群では「家族または周囲の人々の理解不足」であった。
【考案】HTLV-1 母子感染対策のために HTLV-1 陽性の母親が出生前に選択した栄養法を完遂するには継続的な支援が必要である。それは短期母乳を選択した母親で特に認められた。
全国的な取り組みが開始された現在、HTLV-1 陽性の母親を支援する環境を迅速に改善していく必要がある。