Review Article

An attempt at building a database of children using donor human milk in Japan

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Abstract: A hospital-dedicated human milk bank was established in Japan at Koto Toyosu Hospital, Showa University in 2014. After a 3-year trial-and-error period, the Japanese Human Milk Bank Association was established in 2017. The supply of donor human milk (DHM) from the Japanese Human Milk Bank Association to various facilities nationwide has increased recently. However, as of 2021, there is only one human milk bank in Japan and the supply is limited. Therefore, there is an urgent need to understand the status of usage of DHM in the neonatal intensive care unit. Moreover, it is globally rare to build a database aimed at understanding the background and prognosis of all children supplied with DHM. In this paper, we have introduced the database and reported on aspects such as the salient points considered in building this database. The fundamental policy of this database included the following: (I) accessibility from the neonatal intensive care unit, (II) a simple input method, (III) reliability and continuity, (IV) safeguarding anonymity, (V) enriched search functionality, and (VI) enabling administration by the person in charge at each facility. In accordance with these six policies, the main items such as patient clinical information, DHM usage amount, and prognosis were set. In addition, the database was built to enable detailed search. The database was completed and became operational in November 2020. The input format was simplified as much as possible by adopting a selection-from-options approach. Enriched search functionality was implemented considering the function as a database in each facility. This database has enabled the proper operation of the human milk bank, and it would likely contribute further to perinatal care outcomes.

Keywords: Japanese Human Milk Bank Association; database; donor human milk (DHM)

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Introduction

In Japan, surveys on treatment results and prognoses are being conducted for very low-birth-weight infants using the Neonatal Research Network Database. From 2003 to 2015, neonatal intensive care unit (NICU) discharge mortality rate has improved. The survival rate of very preterm infants born at a gestational age of 22 weeks has also improved (1). However, an international comparative study has reported that although the mortality rate is low in Japan, there are many complications of retinopathy of prematurity and chronic lung disease in premature infants (2). Moreover, the association between nutritional management and various complications has been reported recently. This suggests that early nutritional strategies in the NICU are important in further improving the long-term prognosis of very low-birth-weight infants. Conventional nutritional strategies in Japan involve waiting for the general condition to stabilize

immediately after birth and fasting for a few postnatal days to ensure resting of the digestive tract. Then, small amounts of enteral nutrition are initiated. However, some recent studies have reported that unnecessary fasting periods promote atrophy of the gastrointestinal mucosa and cause bacterial translocation (3,4). The timing of the initiation of enteral nutrition has been reviewed mainly in Europe and North America. The facilities that used to initiate enteral nutrition several days after birth have now been initiating it within 24 hours after birth (5-7). In doing so, own mothers' milk (OMM) may not be available or the quantity of OMM may be insufficient. Therefore, in some countries, human milk banks have been established and systems have been put in place to make donor human milk (DHM) available at all times (8,9). The DHM described here is human milk that is properly processed and managed by the same procedure used in other countries. Since there were no human milk banks established in Japan until 2014, the initiation of enteral nutrition tended to be delayed while waiting for OMM. Therefore, we established a human milk bank at Koto Toyosu Hospital of Showa University in 2014. After going through a trial period, the Japanese Human Milk Bank Association (JHMBA) was then established in 2017 to supply DHM to other facilities. Currently, DHM supply to each facility in Japan is gradually increasing. However, there is only one human milk bank in Japan, and the situation is far from providing enough supply to all infants for whom it is necessary. There is an urgent need to understand the actual usage status and utilization of the human milk bank operation. Hence, the right quantity can be supplied to the children who need it. Moreover, we believe that it is necessary to build a database (DB) that can help in the understanding of the clinical course and nutritional management because it is difficult to utilize existing DBs in Japan to investigate detailed items concerning DHM usage and nutritional methods. Building a DB that is aimed at understanding the total number of children who received such DHM supply are globally rare. Hence, we have introduced the DB of children who received the DHM prepared by us. We have also reported on aspects such as the salient points that are considered in building this DB.

Database overview

Basic concept of the DB

The following shows the six policies considered in building the DB.

(I) The DB shall be accessible from all NICUs in Japan.

NICUs in Japan, depending on the size of the facility, are classified into general perinatal centers and regional perinatal centers. However, very preterm infants who require DHM are often admitted to both types of facilities. Therefore, as a rule, without identifying the size of the facility, it is possible to access the DB from all NICUs via the internet. Moreover, in principle, this DB is a complete survey of the infants in Japan who have used DHM.

(II) The input method shall be simple and utilize hassle-free input.

The medical clerical system in Japan is not robust, and often the neonatal clinicians perform the input work. Therefore, consideration was given to minimize the burden on clinical work at the NICUs. Specifically, input using not only the personal computer but also smartphones and tablets was enabled. Regarding the input, descriptive input was minimized, and the method of selection using multiple options or pull-down lists was adopted as much as possible.

(III) Reliability and continuity of data shall be ensured.

It was assumed that the neonatal clinicians perform the input work. Moreover, DB administrators can also view items other than personal identification information (patient name/ medical record number), enabling measures against inadvertent non-entry of data. Most data can be entered during NICU stay or at the time of discharge. However, for follow-up data, it is necessary to enter data after discharge from the NICU; at the age of 1.5, 3, and 6 years; and at the third-grade of elementary school. Continuity of data input was ensured by setting up reminder emails to the person in charge in case the data for the infants were not entered after they reach the respective ages for new data entry.

Additionally, the system was set to dispatch reminder emails automatically to the person in charge when the follow-up data items necessary to be entered at specified ages for each of the cases were not completed on time to avoid input omissions or oversight due to changes in the person in charge.

Limitations of this database include (i) lack of

control data, absence of information about babies who do not have donor breast milk. (ii) To ensure reliability, the data input by two different people is compared. However, the input of this database does not make a request. Instead, database management is regularly viewed by neonatologists so that personnel can be emailed to confirm if clinically apparently inconsistent data has been entered.

(IV) The anonymity of personal information shall be ensured.

Information such as name and personal ID was made accessible only at the facility where it was entered. It was designed such that even the DB administrator cannot access such personal identification information.

(V) The search functions shall be enriched.

The point that the person in charge at each of the facilities should be able to search patient information was considered beneficial for capturing the trend of DHM usage in the facility. Accordingly, searching all data on clinical items were enabled. However, it was limited to the data entered at the concerned facility only. The reason why the information described by other facilities is not accessible is to protect personal information. Only breast milk bank managers can search the entire database. A detailed search was enabled by allowing the combination of multiple items in the search. The DB administrator was allowed to search data on the facility number, setting of periods based on the date of birth, reason for DHM usage, and weight at birth, for all patients registered.

(VI) Administration by the person in charge at each facility shall be enabled.

A system is in a place where the DB administrator is notified through access from designated places in case of forgotten passwords or change of the person in charge.

Registration system

For the facility that wants to use DHM as a new user, the person in charge of the facility needs to register the user on the JHMBA website. When new user registration is initiated, an email is automatically sent to the DB administrator, notifying that a request for new user registration has been made. The DB administrator, using the user administration screen, then approves the request after checking the name of the facility making the request, the name of the person in charge, and the email address. Note that the use of DHM in Japan requires prior approval from the clinical ethics committee of the facility. The DB administrator and the person in charge of the facility communicate with each other via email in advance for preparing documents such as research plans. Therefore, as a rule, the entered data must match the content of the relevant documents. As a general rule, when using donor milk from a breast milk bank, it is required to be registered in the database. Once approved, one ID and password are automatically issued for one facility, and a notification is sent to the person in charge of the facility through the email address provided at the time of registration initiation. The person in charge at each of the facilities uses this ID and password on the login page to login to the DB. Next, using the new user registration screen, the patient information is entered. The information entered here includes personal information, such as patient ID and name. However, such information that is used for personal identification is accessible only by using the respective facility ID. It is not accessible to the DB administrator. Moreover, at each facility, it is only possible to access the information entered at that facility, and information entered at other facilities cannot be accessed. Note that when the name of the patient cannot be entered using the internet because of compliance with policies in place at each of the facilities, a specific symbol is entered into the DB. In addition, the provision was made to ensure anonymity by linking this symbol to a facility-specific corresponding list of patient names that cannot be accessed via the internet. In such circumstances, a case number is assigned to each patient according to the order of registration. The DB administrator and person in charge can check the case details using the case number (*Figure 1*).

Setting and implications of main items and sub-items

Nine main items were set, and for each item, sub-items were set. The system was set to proceed to the input of the next main item once the input for one main item was completed. Moreover, the input can be commenced for any of the main items, and editing of the input is always enabled. The main and sub-items are shown in *Tables 1-3*. Specifically, the following are characteristic items for the human milk bank DB.

(I) Background: to start using DHM, a method of selection from the following options was set: (i) extremely low birth weight, infants (ii) very low

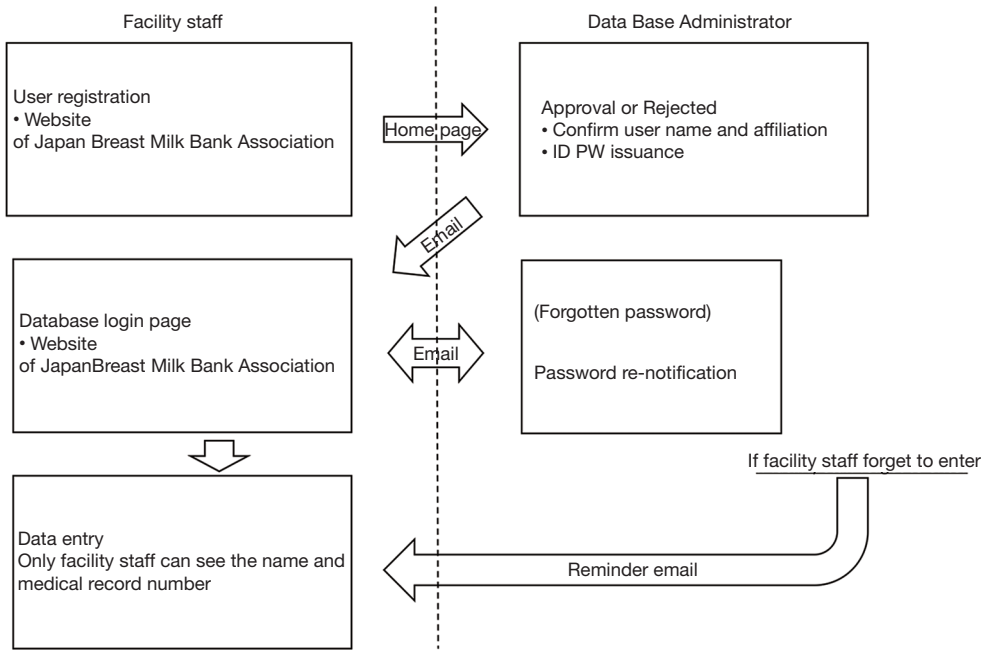

Figure 1 Registration system.

Table 1 Database items: basic patient data

Category	Main items	Sub-items (○: select from pull-down or description)
Background	Facility number	Autofill
	Case no.	Autofill
	sex	Man/woman/unknown
	Gestational age	○Week ○ Day/Unknown
	Birth weight	○g
	Head circumference at birth	○cm
	Height at birth	○cm
	Apgar score	1min ○, 5m in ○
	Floatation number	Single /twin (MD DD, etc.:)/etc.
	Delivery style	Vaginal delivery/Caesarean section
	Pregnancy and delivery history	Prenatal/Multiparous
	Pregnancy complications	Preeclampsia/pregnancy with diabetes/gestational diabetes/premature rupture/placental abruption of the placenta/help syndrome/fetal asphyxia/fetal growth restriction/imminent premature birth/chorioamnionitis/other
	Maternal complications	Thyroid disease/collagen disease/asthma/infection/other
	Maternal drug	Steroids/ritodrine hydrochloride/magnesium preparations/antibacterial drugs/antihypertensive drugs/psychotic drugs/etc.
	Reasons for starting donor milk	Very low birth weight infant/very low birth weight infants (excluding very low birth weight infants)/gastrointestinal diseases (other than allergies)/heart disease/unable to use breast milk (reason stated)/other

Table 2 Database items: nutrition, treatment, complications, side effects

Category	Main items	Sub-items (○: select from pull-down or description)
Enteral nutrition	Date of consent for donor milk use	○/○/○
	First own mother's milk start time or age (not including oral application)	○Hour/○ day
	First donor milk start time or age	○Hour/○ day
	First artificial milk start date	Age ○
	Age when enteral nutrition reached 100 mL/kg/day	Age ○
	Use of fortified breast milk	Use, not used
	Types of fortified milk	HMS1/HMS2
	Complications after starting breastfeeding	Yes (abdominal distension/increased gastric residue/milk allergy/ fecalith formation/etc.), none
	Donors	a single donor/multiple donors
	END of donor milk use	Age ○
	Total amount of donor milk use	1-50/51-100/101-500/501-1,000/1,001-2,000/2,001-5,000/5,001 mL or more
Intravenous nutrition	Age at which intravenous nutrition was started	○Day
	Age at which intravenous nutrition was completed	○Day
Method of treatment	Artificial ventilation period (excluding nasal positive pressure ventilation)	○Day
	Days of oxygen use	○Day
	Drugs used	Iron/erythropoietin caffeine/methylxanthine/surfactant/Vitamin D (oral/venous)/antibacterial steroids/circulatory agents/ COX inhibitors/ diuretics/sedatives/narcotics/muscle relaxants blood products (transfusion/blood products)
	Surgical procedure	Yes (patent ductus arteriosus/cardiovascular disease/gastrointestinal disease/cranial nerve disease /retinopathy of prematurity: laser treatment/etc.), none
Complications	Complications	Neonatal respiratory distress syndrome/severe jaundice (exchange transfusion)/necrotizing enterocolitis/gastrointestinal perforation/ meconium plug syndrome/other intestinal diseases/symptomatic patent ductus arteriosus/late circulatory insufficiency/neonatal persistent pulmonary hypertension/bile stagnation/acquired bacterial infection/catheter-related infection/Intraventricular hemorrhage/ periventricular leukomalacia/chronic lung disease/retinopathy of prematurity/hearing loss/etc.
Side effects of donor milk	DHM-related side effects	Yes, no
	Hepatitis B virus infection	Yes, no
	Hepatitis C virus infection	Yes, no
	HIV	Yes, no
	HTLV-1	Yes, no

Table 3 Database items: body measurement, outcome, follow-up

Category	Main items	Sub-items (○: select from pull-down or description)
Body measurement value	Weight at 34 weeks of correction	○g
	Height at 34 weeks of correction	○cm
	Head circumference at 34 weeks of correction	○cm
	Corrected gestational age at discharge	○Weeks○day
	Weight at discharge	○g
	Height at discharge	○cm
	Head circumference at discharge	○cm
	1 and a half years old weight	○g
	1 and a half years old Height	○cm
	1 and a half years old Head circumference	○cm
	3 years old weight	○g
	3 years old height	○cm
	3 years old head circumference	○cm
	6 years old weight	○g
	6 years old height	○cm
	6 years old head circumference	○cm
	3rd grade elementary school weight	○g
	3rd grade elementary school height	○cm
	3rd grade elementary school head circumference	○cm
Outcome	Breast milk rate at discharge: average breast milk rate for one week before discharge	○%
	Outcome to hospitalization	Healing, transfer, death
	Re-hospitalization	Yes No (1 year after discharge from NICU)
Follow-up	Breastfeeding rate one month after discharge	○%
	Breastfeeding duration	○Weeks
	New edition K type (developmental examination in Japan)	
	1 and a half years old	
	3 years old	
	WISC-IV	
	6 years old	
	Third grade of elementary school	

birth weight infants (excluding extremely low birth weight), (iii) gastrointestinal disease (excluding allergy), (iv) infantile gastrointestinal allergy, (v) heart disease, (vi) unavailability of own mother's milk, (vii) other (free-form description).

(II) Enteral nutrition:

(i) Date of consent for DHM use: this was set to investigate whether prenatal consent was obtained after explanation to the mother or whether postnatal consent was obtained for

emergency use.

(ii) First OMM start time, first DHM use time, age in days at the first artificial milk start date, age in days at end of DHM use: the JHMBA has not formulated any protocol for adaptation and usage of DHM. The actual use of DHM in the field is left at the discretion of the attending physician. While this is useful to enable usage without any hesitation for the infants who need it, it is difficult to estimate the demand without some level of understanding about the method of usage in the facilities. Therefore, these sub-items were set to understand the overview of nutritional administration in each facility.

(iii) Donors: whether the DHM use is from a single donor only or multiple donors was set here. At the JHMBA, the attending physician needs to decide whether to use DHM from a single donor or DHM mixed from multiple donors, and the judgment to differentiate the type to use is left to the attending physician. Moreover, when the duration of DHM use is long and supply from the same single donor cannot be secure, it is possible to select DHM from multiple donors.

(iv) Amount of DHM: total amount of DHM usage was made selectable from the options of 1–50, 51–100, 501–1,000, 1,001-2,000, 2,001-5,000, and over 5,001 mL to avoid complex numerical input or erroneous input.

(III) DHM side effects: in case of the presence of clinical symptoms that are confirmed through blood tests, the selection was made necessary for the presence or absence of hepatitis B virus, hepatitis C virus, HIV, and HTLV-1 diseases.

(IV) Outcome: the breastfeeding rate at discharge was defined by the following formula: (total own mother's milk dosage for one week ÷ total enteral nutrition dosage for one week) ×100. It set as an indicator to judge whether the introduction of DHM affects the breastfeeding rate in the NICU.

Current number of registered facilities and number of cases

Since the database became operational in November 2020, as of February 22, 2021, a total number of 59 cases have been registered at 20 facilities, and new cases are being sequentially registered.

Discussion

At the beginning of the operation of the human milk bank in Japan, we built a DB aimed at understanding the status of all children who used DHM. The items described in the basic policy were considered while building the DB. As applicable to all such DBs, it was considered that continuity of registration in the DB cannot be achieved without paying attention to convenience and benefits for the persons in charge at the facilities. Therefore, free-form description items were eliminated as much as possible and the selection-from-options approach was adopted. Moreover, enriched search functions were implemented to enable the extraction of statistical data useful for the facilities. Since the operation of the DB has just started, we plan to keep a watch for future trends. Moreover, regarding the implications of the human milk bank DB itself, it is believed that a general understanding of the annual DHM usage of each facility is particularly important given that the supply was low in the early days after its inception. Once DHM supply is started, any suspension or discontinuation results is disadvantages for the patient. Human milk is a limited and valuable source of food and have an expiration date. Moreover, even after the pasteurization of human milk, if a certain number of bacteria is detected, it is not usable anymore. Utilization of the DB is believed to be important in obtaining a general understanding of annual usage at each facility and appropriately adjusting the balance between supply and demand. The current system is specialized for children who have received DHM supply. Thus far, there is only one human milk bank in Japan. However, when the number of such banks increases in the future, it would be more appropriate to create a donor-oriented system that will be necessary to enable efficient supply based on DHM inventory management at each such bank.

Conclusions

We believe that utilizing this DB will enable proper operation of the human milk bank, which will contribute further to preterm infants and perinatal medical care.

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Footnote

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