Repeatability and Reliability of Home-Based Stool Color Card Screening for Biliary Atresia Based on Results in China and Japan

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Biliary atresia (BA) is the most frequent hepatic cause of death in early childhood. Early referral and timely Kasai portoenterostomy are essential for the improvement of long-term native liver survival rate of BA patients. Screening with stool color card (SCC) has been implemented in Japan since 1994. Recently current digital edition of SCC consisted of seven digitally created images was introduced to China. Our study aimed to evaluate the repeatability and reliability of same edition of SCC used in Beijing, China and Sapporo, Japan. In Beijing from 2013 to 2014, SCCs were distributed to infants' guardians by trained nurses in maternal facilities during information sessions on neonatal screening programs. SCC was used at three checkpoints for each infant after birth for screening. The SCC data were collected from 27,561 infants (92.5%) in Beijing by 42-day health checkup, mobile phone and social network services. In Sapporo from 2012 to 2015, the SCCs with a postcard and guardian instructions were inserted into Maternal and Child Health Handbook and distributed to all pregnant women. The data were collected from a total of 37,478 (94.3%) infants in Sapporo via the postcard during the 1st month infant health checkup. We thus identified two BA patients in Sapporo and two BA patients in Beijing. High rates of sensitivity and specificity in both cities were observed. The frequency distribution of color images on SCC reported in both cities was similar. This study shows excellent repeatability and reliability of the current digital edition of SCC.

Keywords: biliary atresia; home-based screening; infants; stool color cards; repeatability

Introduction
The prevalence of biliary atresia (BA) has been reported to be approximately 1.1 in 10,000 live births in Japan and 1.3 in 10,000 live births in China (Gu et al. 2015; Kong et al. 2016). The prevalence in French Polynesia is 2.8 in 10,000 live births, and 0.5 in 10,000 live births in the United States of America, the United Kingdom, and France (Yoon et al. 1997; Chardot et al. 1999; McKiernan et al. 2000).

BA caused by a complete inability to excrete bile from the liver to the duodenum is a result of sclerosing inflammation of the extra- and intrahepatic bile ducts of unknown etiology in early infancy. The pathogenesis of BA is multifactorial, and the nature of BA is complex. Thus, the timing of BA onset varies among infants, but almost is within 4 months after birth.

BA is a progressive disease having various forms of...
clinical presentation including congenital abnormalities and presenting with the three following main clinical features: pale-pigmented stools, prolonged jaundice persisting beyond 2-3 weeks of age, and dark urine. However, these typical symptoms can appear relatively late in patients with BA. Untreated patients develop biliary cirrhosis and chronic liver failure and die within 2-3 years after birth. The Kasai portoenterostomy or Kasai Procedure is aimed at restoring bile flow (Kasai 1974). It is still the first line of treatment for almost all cases of BA, followed by liver transplantation if cirrhosis progresses (Kasahara et al. 2013). BA is the most frequent hepatic cause of death in early childhood, and is the most common indication for liver transplantation in the pediatric population (Kasahara et al. 2013). It has been reported that the Kasai portoenterostomy, performed at an early stage of BA, improves BA prognosis (Serinet et al. 2009; Gu et al. 2015; Gu and Matsui 2017). Therefore, some strategies have been attempted for early detection of BA. Detection of BA using stool color card (SCC) in Japan, China, and some other areas has been demonstrated to be effective and inexpensive (Hsiao et al. 2008; Gu et al. 2015; Kong et al. 2016; Gu and Matsui 2017). The strategy of early detection by SCC and followed by early Kasai portoenterostomy showed a significant improvement in the long-term native liver survival rate in Japan (Gu et al. 2015; Gu and Matsui 2017). However, SCC used in different countries or areas is varied, which makes it difficult to do quality of control and produce consistent result. Since 1994 various versions of SCC in Japan have been developed with the aim to enhance quality control and produce better reproducibility.

In 2012, a nationwide BA screening using an updated version of the SCC was initiated in Japan (Gu et al. 2018). The current edition of the SCC consists of seven digital photographic images (Fig. 1) to ensure quality control of the stool colors on the card and for greater reproducibility of printing, according to an official notice of the points for attention of printing the stool color card released on December 28, 2011 (Ministry of Health, Labour and Welfare of Japan 2011). The screening method has also been modified. Stool color is inspected at least three times, not only at 30 days of age as previously reported in Tochigi prefecture (Gu et al. 2015) but also at 14 days and 1-4 months of age. In Japan, however, only in Sapporo City the results of the SCC are collected from all infants at 1 month-health checkup, and in the other cities the data of the SCC are not collected at 1 month-health checkup. If images 1-3 (as positive results) were observed, even if only once, guardians were advised to bring the stool and the infant to the SCC office in Beijing or to a local clinic or hospital in Sapporo. In 2013, the current version of SCC used in Japan was introduced in Beijing, China (Fig. 1) (Kong et al. 2016).

In the present study, based on the data of home screening for infants using SCCs collected from Beijing and Sapporo, we aimed to reveal the reproducibility and reliability of current edition of the SCC by means of the sensitivity, specificity, the false positive and negative rates, and the frequency of each image color on SCC reported in two cities.

**Materials and Methods**

**Study design** A cross-sectional study was performed. The SCC data were collected from December 2013 to October 2014 in ChaoYang district of Beijing and from April 2012 to July 2015 in Sapporo during routine works in Sapporo City Institute of Public Health (Table 1). Participants in Sapporo were consented verbally. In Beijing, consent was signed by all guardians.

Subjects were infants born in livebirth in all 25 childbirth facilities of ChaoYang district and in Sapporo city (Table 1). ChaoYang district is the largest district in Beijing in terms of the number of live births in Beijing.

The study protocol was reviewed and approved by the
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Ethics Board of the National Center for Child Health and Development (numbers 13 and 24 in 2014) and Health and Science Section (Maternal and Child Screening), Sapporo City Institute of Public Health.

SCCs distribution, use, and data collection

The method of the current SCC with digital color images (Table 1) was described in our previous study (Kong et al. 2016; Gu et al. 2018). Briefly, the current SCC (the 2012 academic year edition) includes seven digital images of stool color ranging from infants of approximately 30 days of age with BA (images 1-3, abnormal range) to age-matched healthy infants (images 4-7, normal range) (Fig. 1).

The same version of the SCC in different languages with the same screening method was used in Sapporo (Japanese) and Beijing (Chinese). Fig. 1 shows a sample of current SCC in English.

In Beijing, the SCCs were distributed to the infants’ guardians by trained nurses in maternal facilities during information sessions on neonatal screening for phenylketonuria and congenital hypothyroidism. In Japan, the SCCs were inserted into Maternal and Child Health Handbook and distributed together with both post cards and maternal health checkup tickets to all pregnant women at the municipal office according to Maternal and Child Health Law (MCHL) released in 1965 by Japanese government (Ministry of Health, Labour and Welfare of Japan 1965). The guardians in Sapporo were received an explanation of usage. The guardians were advised to carefully compare their infants’ stool color. If infant’s stool color was similar to any of the images 1-3, the guardians in Beijing were advised to bring the stools and the infant to the SCC office (Beijing) or to a local clinic or hospital (Sapporo). Images 4-7 were considered a negative result, and the stool color was observed continuously up to 4 months after birth to ensure the color did not develop into that of images 1-3.

Confirming patients with BA or with other diseases after detection of positive and negative BA screening results using SCCs

BA patients of SCC screening were calculated by comparing the screen results with the existing congenital abnormality database retrospectively. In Beijing the database contains all of the records of BA patients in that area including those diagnosed beyond the neonatal period. In
Sapporo, the database of the Medical Aid Program for Chronic Pediatric Diseases of Specified Categories of Japan (Gu et al. 2008) was used to identify the patients with BA (Table 2). In Sapporo city, BA patients were beneficiaries and were registered into the Medical Aid Program for Chronic Pediatric Diseases of Specified Categories system (Gu et al. 2008).

Calculation of sensitivity, specificity, false positive, false negative and frequency of each image on current SCC

Calculation of sensitivity, specificity, false positive and false negative was based on results of each infant (Table 3). The frequency of the images provided by guardians was calculated based on replies of guardians including multiple replies (Table 4).

Results

Patients with BA diagnosed after early detection using SCC and without using SCC at each city

As shown in Table 2, during the study period, a total of 3 patients with BA were found in Sapporo and 4 patients with BA were found in Beijing. Among them one patient with BA in Sapporo and 2 patients with BA in Beijing were identified by clinical findings other than SCC screening after birth.

In Sapporo, three infants with BA were diagnosed. They were brought to a hospital at 16, 37 and 50 days after birth, respectively (Table 2). Among them an infant firstly presented a positive result of galactosemia by neonatal screening, and was subsequently diagnosed as having BA at 16 days after birth by further examinations in a hospital. The other was image 5 on SCC at 4-month health checkup, subsequently was brought to a hospital at 50th day and was received Kasai portoenterostomy at 53th day after birth. The details about the infants with BA in Sapporo were not provided because of Personal Information Protection Law of Japan implemented on May 23, 2003 (Personal Information Protection Law of Japan 2003).

In Beijing, two infants with BA showed severe jaundice from the first two days after birth, and were immediately referred to a neonatal intensive care unit. One was image 4 on SCC at 1-month health checkup, subsequently was brought to a hospital at 37th day and was received Kasai portoenterostomy at 55th day after birth. The other was image 1 on SCC at 1-month health checkup, subsequently was brought to a hospital at 50th day and was received Kasai portoenterostomy at 53th day after birth.

# The patient was born at 37 gestational weeks, and birth weight was 3,130 grams. On day 50 after birth biochemical examinations of liver function were performed (ALT, TBIL, DBIL, TBA and GGT was 70.0 IU/L, 121.4 μmol/L, 65.4 μmol/L, 97.0 μmol/L and 128.0 IU/L, respectively).

Table 2. Patients with BA and other diseases found during period of the present study in Sapporo and Beijing.

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Sapporo</th>
<th>Beijing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with BA</td>
<td>At 1-month health checkup</td>
<td>At two weeks after birth</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>(The infant firstly was a positive result of galactosemia by neonatal screening, and was subsequently diagnosed as having BA at 16 days after birth by further examinations in a hospital.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with BA diagnosed by other signs without using SCC at home</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>(Two patients with BA showed severe jaundice from the first two days after birth, and were immediately referred to a neonatal intensive care unit.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with BA diagnosed after using SCC</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>(One was image 4 on SCC at 1-month health checkup, subsequently was brought to a hospital at 37th day and was received Kasai portoenterostomy at 55th day after birth. The other was image 5 on SCC at 1-month health checkup, subsequently was brought to a hospital at 50th day and was received Kasai portoenterostomy at 53th day after birth.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with other diseases diagnosed after using SCC</td>
<td>1 patient with neonatal intrahepatic cholestasis caused by citrin deficiency; 1 patient with neonatal hepatitis; 1 patient with neonatal hepatitis (suspected); 1 patient with transient cholestasis</td>
<td>1 patient with Alagille syndrome</td>
</tr>
</tbody>
</table>

Result on dry blood spot by tandem mass spectrometry for determining citrullinemia was in a normal range in all infants with a positive result of SCC.

BA, biliary atresia; SCC, stool color card. ALT, alanine aminotransferase, normal range: 5-40 IU/L; TBIL, total bilirubin, normal range: 3.4-17.1 μmol/L; DBIL, direct bilirubin, normal range: 0-3.4 μmol/L; TBA, total bile acid, normal range: 0-12 μmol/L; GGT, gamma-glutamyl transferase, normal range: 11-50 IU/L.

* The patient was born at 37 gestational weeks, and birth weight was 3,130 grams. On day 50 after birth biochemical examinations of liver function were performed (ALT, TBIL, DBIL, TBA and GGT was 70.0 IU/L, 121.4 μmol/L, 65.4 μmol/L, 97.0 μmol/L and 128.0 IU/L, respectively).
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Table 3. Sensitivity, specificity, false positive and false negative rates of SCC in two cities calculated based on numbers of infants at 1 month and 1-4 months after birth.

<table>
<thead>
<tr>
<th></th>
<th>Sapporo, at 1 month after birth (number of infants)</th>
<th>Beijing, at 1 month after birth (number of infants)</th>
<th>Beijing, at 1-4 months after birth (number of infants)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BA</td>
<td>Total</td>
<td>BA</td>
</tr>
<tr>
<td>Positive</td>
<td>0</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Negative</td>
<td>37,466</td>
<td>37,466</td>
<td>27,558</td>
</tr>
<tr>
<td>Total</td>
<td>0</td>
<td>37,478</td>
<td>1</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.0%</td>
<td>100.0%</td>
<td>99.9%</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.9%</td>
<td>99.9%</td>
<td>99.9%</td>
</tr>
<tr>
<td>False positive rate</td>
<td>0.03%</td>
<td>0.01%</td>
<td>0.0%</td>
</tr>
<tr>
<td>False negative rate</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

SCC, stool color card; BA, biliary atresia. Positive, images on SCC were 1-3. Negative, images on SCC were 4-7.

*Sensitivity, specificity, false positive and false negative rates were calculated based on numbers of infants at 1 month and 1-4 months after birth.

Table 4. Frequency of each image on SCC in Sapporo and Beijing calculated based on guardians’ replies at each check point.

<table>
<thead>
<tr>
<th>Stool color reported in Beijing as a single color</th>
<th>Stool color reported in Beijing at least one time</th>
<th>Stool color reported in Sapporo at least one time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Image on SCC</td>
<td>1 month after birth n = 13,588 (%)</td>
<td>Image on SCC</td>
</tr>
<tr>
<td>1</td>
<td>0 (0.0)</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>0 (0.0)</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>0 (0.0)</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>3,141 (23.1)</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>8,487 (62.5)</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>1,410 (10.4)</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>550 (4.0)</td>
<td>7</td>
</tr>
</tbody>
</table>

SCC, stool color card.

*Number of guardians’ replies (including multiple replies).

*The patient with slight jaundice from 3-14 days after birth; at 23rd day after birth image on SCC was 2.

*A patient with biliary atresia.

The guardians brought the stools and the infant to the SCC office at the Department of Newborn Screening, Beijing Obstetrics and Gynecology Hospital and blood tests had been done (Table 2). The third and fourth patients were further introduced to liver specialists and laparoscopic surgery was performed after receiving further supportive results from laboratory tests. The diagnosis was confirmed as BA type III. The guardians of both patients refused Kasai portoenterostomy, because they expected to receive a domino liver transplant soon in China. The patients follow up were up to 4 months of age. The details of liver transplantation were not recorded.

Among 7 patients with BA, two in Sapporo were brought to a hospital at 37 and 50 days after birth, respectively; and one patient in Beijing were found at 48 days after birth. At the checkpoint of 1 month after birth normal images were shown for those three patients. We therefore calculated them as negative results and as infants without BA at the point of 1-month after birth (Table 3).
Sensitivity, specificity, false positive and false negative rates of the current edition of the SCCs

As shown in Table 3, the specificity was 99.9% at 1 month in two cities, and 1-4 months after birth in Beijing. The false positive rate was 0.03% and 0.01% at 1 month after birth in Sapporo and Beijing, respectively. The sensitivity was 100.0% in Beijing.

Although two patients with BA in Sapporo and one patient with BA in Beijing showed normal images of SCC at 1 month after birth, the guardians successfully identified the matching color of infants’ stool (SCC images 1-3 on the 37th, 50th day in Sapporo and 48th day of life in Beijing). The patients were subsequently confirmed in hospitals.

The frequency distribution of images on SCC reported by guardians and stool colors changed in some infants during observation period in two cities

As shown in Table 4, at 1 month after birth, image 5 on SCC was most frequently reported in infants from both cities, followed by image 4, image 6, and image 7. This pattern was also found at 2 weeks and 1-4 months after birth among infants in Beijing.

Regarding to multiple colors of image 3 (abnormal) and image 4 (normal) at 1 month after birth, in Sapporo images 2-3-4 and images 3-4 were reported in 0.008% (3/39,191) of replies. In Beijing images 3-4 were reported in 0.0% (0/19,605), 0.01% (2/17,223), and 0.02% (3/17,207) of replies at 2 weeks, 1 month, and 1-4 months after birth, respectively.

Moreover, among infants used SCC in Beijing besides the above-mentioned two patients with BA, there were a total of 22 false positive cases until 4 months after birth; 12 among patients with the later symptomatic onset in most previous reports, results were analyzed by age (Serinet et al. 2009) using univariate analysis (Kaplan-Meier method) without introducing other covariates such as type of BA and other congenital abnormalities. The distinction between “late onset” and “late diagnosis” of BA may be important. The late-onset patients with a shorter duration of disease are likely to have a favorable outcome after the Kasai procedure, even when the patient is over 1 month after birth (Schoen et al. 2001; Fontenele et al. 2016).

The observation period until 4 months after birth is one of methods to have an early detection of the late symptomatic onsets and reduce false negatives. In the present study, the guardians were given the SCC instruction by trained nurses in Beijing and followed through up to 4 months after birth. And patients with the later symptomatic onset after 1-month after birth were successfully identified. According to both the MCHL and rules for using the SCC released by the Ministry of Health, Labour and Welfare in Japan (Matsui 2012), an explanation of how to use the handbook and the SCC is given to pregnant women when the Maternal and Child Health Handbook is distributed in Sapporo city. In the present study, two BA patients had not presented abnormal image on SCC at 1-month health checkup, and subsequently were brought to a hospital at 37th, 50th day in Sapporo and 48th day after birth by SCC, although they showed negative results at 1-month health checkup via postcard. Similarly, a patient who was onset on 48 days after birth also tested positive (true positive) in Beijing at the 1-4 months check.

In our previous study, it has been noticed that not all BA patients could be identified at 1-month health checkup, because the timing of BA onset varies (Gu et al. 2015). On one side, in some patients, BA onset does not happen until 1 month after birth, on the other side a few BA patients are referred to a neonatal intensive-care unit due to severe jaundice or breeding after birth immediately (Gu et al. 2015; Gu and Matsui 2017). In our previous study, a total of 313,230 live born infants were screened (Gu et al. 2015). The sensitivity and specificity of stool color card screening at the 1-month check-up was 76.5% (95% CI 62.2-90.7) and 99.9% (95% CI 99.9-100.0), respectively (Gu et al. 2015). In Taiwan the sensitivity of detecting BA using stool color cards before 60 days of age was 72.5% in 2004, which was improved to 97.1% in 2005 (Hsiao et al. 2008). In the present study, screening at 1-4 months after birth yielded higher sensitivity (100.0%) and specificity (99.9%), and lower false positive and negative rates in comparison with the previous studies (Hsiao et al. 2008; Gu et al. 2015).

Onset in most patients with BA is in neonatal period. In the most previous reports, results were analyzed by age only (Serinet et al. 2009) using univariate analysis (Kaplan-Meier method) without introducing other covariates such as type of BA and other congenital abnormalities. The distinction between “late onset” and “late diagnosis” of BA may be important. The late-onset patients with a shorter duration of disease are likely to have a favorable outcome after the Kasai procedure, even when the patient is over 1 month after birth (Schoen et al. 2001; Fontenele et al. 2016).

The observation period until 4 months after birth is one of methods to have an early detection of the late symptomatic onsets and reduce false negatives. In the present study, the guardians were given the SCC instruction by trained nurses in Beijing and followed through up to 4 months after birth. And patients with the later symptomatic onset after 1-month after birth were successfully identified. According to both the MCHL and rules for using the SCC released by the Ministry of Health, Labour and Welfare in Japan (Matsui 2012), an explanation of how to use the handbook and the SCC is given to pregnant women when the Maternal and Child Health Handbook is distributed in Sapporo city. In the present study, two BA patients had not presented abnormal image on SCC at 1-month health checkup, and subsequently were brought to a hospital at
37th and 50th day after birth, respectively. The SCC screening program may play a role of increasing the guardians’ awareness of BA in this case, although the patients were not picked up at 1-month health checkup.

There were 7 patients with BA identified in the period of the present study in two cities. Among them, 3 were identified immediately after birth; namely, SCC was not used at home. The remaining 4 patients with BA were diagnosed after screening by showing abnormal stool colors from 23rd day to 50th days of life, while slight jaundice presented. SCC successfully detected BA before obvious clinical manifestations showed up.

During observation period stool colors changed in some infants in two cities, resulting in multiple data reported in a same infant. Moreover, images 3 and 4 presented in one infant at the same checkpoint were reported by some guardians in the present study, suggesting that more than 3-colour abnormal panel of SCC may be necessary. In fact, a SCC with 4-color abnormal panel has been used in Taiwan (Hsiao et al. 2008). Combining the SCC screening system with other methods, such as laboratory-based screening, should be further considered.

The SCC uses an objective referent (digital image colors) for estimating infants’ stool color quantitatively to reduce bias created subjectively by guardians’ observation. Information from daily stools is very important for pediatric professionals and guardians to identify an infant’s health condition. Several studies have described the frequency, color, and hardness of infant stools and their associations with diseases and feeding types (Tunc et al. 2008; Bakshi et al. 2012; den Hertog et al. 2012). However, few studies have examined stool color in infants using quantitative tools. It has recently been reported that one-third of patients with pale-pigmented stools were not correctly identified by pediatric professionals (Bakshi et al. 2012). The use of an objective referent to identify stool color, such as the SCC reported by our previous study (Matsui and Dodoriki 1995; Gu et al. 2015), has been recommended (Bakshi et al. 2012). In our previous cross-sectional study, we had reported the usefulness of a previous edition of the SCC as an objective referent for the early detection of BA in infants (Gu et al. 2015; Gu and Matsui 2017). In the present study, using the current, updated, digitally printed SCC, the similar pattern of frequency distribution was presented in one infant at the same checkpoint were reported except that in Japan, Taiwan and the Mainland of China. There are a number of variables that can affect the quality of SCCs, such as quality, type and remaining amount of ink, type of printer and photo paper. The current edition of SCC used in the present study consists of seven digital photographic images as internal control to enhance its reproducibility (Ministry of Health, Labour and Welfare of Japan 2011; Japan Association of Graphic Arts Technology 2011).

In Sapporo, the database of the Medical Aid Program for Chronic Pediatric Diseases of Specified Categories of Japan (Gu et al. 2008) was used to confirm the patients with BA. The prevalence of BA up to 4 months after birth was 0.8 (3/39,723; 95% CI, 0.0-1.6) in 10,000 live births in Sapporo in the present study, and this result was similar to that in our previous study in which the prevalence of BA was 1.1 (34/313,230; 95% CI, 0.7-1.5) in 10,000 live births in nationwide of Japan (Gu et al. 2015). Moreover, it was reported that the number of BA patients registered in the database of the Medical Aid Program for Chronic Pediatric Diseases of Specified Categories of Japan was greater than that in Japanese Biliary Atresia Registry suggesting that almost BA patients had been registered in the database of the Medical Aid Program (Nio 2012; Japanese Biliary Atresia Society and Office of Nationwide Registration of Biliary Atresia 2018).

Limitations of this study were that i) we did not have details about medical information of BA infants in two cities, especially the data of BA patients in Sapporo. ii) Number of participants was relatively small considering the prevalence of BA in the population. iii) Data collection in Sapporo was performed in one checkpoint (at 1-month health checkup), although guardians observed infants’ stool color until 4 months after birth.

In conclusion, the repeatability and reliability of the home-based SCC was demonstrated in both Japan and China. Furthermore, our results demonstrated that observation of stool color is useful for early detection BA, especially for BA patients without obvious clinical manifestations. We recommend that observation period should be up to 4 months after birth using SCC at home, if there is no obvious or slight jaundice after birth. Delivering SCC along with instruction should be performed.

Acknowledgments

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Conflict of Interest

The authors declare no conflict of interest.

References


