

Universal Screening for Biliary Atresia Using an Infant Stool Color Card in Taiwan

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Biliary atresia is the most common cause of death from liver disease in children. Although the Kasai operation before 60 days of age can significantly improve prognosis, delay in referral and surgery remains a formidable problem worldwide because of difficulties in differentiating it from benign prolonged neonatal jaundice. We established a universal screening system using an infant stool color card to promote the early diagnosis and treatment of biliary atresia. After a pilot regional study in 2002-2003, a national stool color screening system was established by integrating the infant stool color card into the child health booklet given to every neonate in Taiwan since 2004. Within 24 hours of the discovery of an abnormal stool color, this event is reported to the registry center. The annual incidence of biliary atresia per 10,000 live births in 2004 and 2005 was 1.85 (40/216,419) and 1.70 (35/205,854), respectively. The sensitivity of detecting biliary atresia using stool cards before 60 days of age was 72.5% in 2004, which improved to 97.1% in 2005. The national rate of the Kasai operation before 60 days of age increased from 60% in 2004 to 74.3% in 2005. The jaundice-free rate (<2 mg/dL) at 3 months after the Kasai operation among infants with biliary atresia in 2004-2005 was 59.5% (44 of 74), significantly higher than the historical data of 37.0% in 1976-2000 before the stool card screening program ($P = 0.002$). **Conclusion: Universal screening using the stool color cards can enhance earlier referral, which may ultimately lead to timely performance of the Kasai operation and better postoperative outcome in infants with biliary atresia. (HEPATOLOGY 2008;47:1233-1240.)**

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Biliary atresia (BA) is the most common life-threatening hepatobiliary disorder in children, with an incidence of 1 in 12,000-18,000 infants in Western Europe¹ and a higher incidence in Asia, including 1.04 per 10,000 in Japan²⁻³ and 3.7 per 10,000 in Taiwan.⁴ BA is characteristic of an idiopathic obliteration of all or part of the extrahepatic

biliary ductal system, leading to cholestasis and biliary cirrhosis. If untreated, prognosis is extremely poor, with death from liver failure occurring within 2 years.⁵

The commonly accepted treatment strategy for BA is the Kasai operation,⁶ which restores bile flow through the excision of extrahepatic biliary remnants, and reconstruction involving a hepatic portoenterostomy to a jejunal loop. Subsequent liver transplantation may be needed for failure of the Kasai operation and/or complications of cirrhosis.⁷ A successful Kasai operation may decrease the need for transplantation.

Abbreviation: BA, biliary atresia.

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It is generally accepted that the Kasai operation is more successful in children when performed earlier, before they are 60 days old.⁸ Age at Kasai operation has been confirmed as a main prognostic factor in infants with BA.⁹⁻¹² Successful bile flow rate after surgery is decreased by half for every 10 days of delayed surgery. Thereafter, the reported successful bile flow rate is 91%, 56%, 38%, and 17% in patients operated on before 60 days, in 61-70 days, in 71-90 days, and beyond 90 days, respectively.¹³ The 10-year survival rate for those treated before 60 days of age is significantly higher than that for those treated after 90 days (57% versus 13%).⁸ However, because most parents only have the concept of "benign" prolonged jaundice associated with breast-feeding beyond 4 weeks after birth, it is understandable that this is overlooked or not considered pathologic. Thus, affected infants referred beyond 60 days of age remain a substantial issue worldwide.¹⁴

Early identification and timely surgery are essential for better prognosis. Lai et al. reported that pale-pigmented stool was identified in 95.2% of infants with BA in early infancy.¹⁵ In Japan, Matsui et al. reported a pilot study in 1994 using an infant stool color card to increase the efficacy of the 1-month health check in identifying BA¹⁶ and had accomplished regional screening for BA in 17,641 infants from 1994 to 1995.¹⁷ Other screening programs for BA, including serum bile acid,¹⁸ serum direct bilirubin,¹⁹ urinary sulfated bile acid,²⁰ and fecal bilirubin and fat,²¹ have been proposed but have not been put into practice extensively. Screening with stool color cards is the most practical method because it is easy and inexpensive. Therefore, we promoted a preliminary education program that included regional screening for BA using an infant stool color card that took place from March 2002 to December 2003 in 95 hospitals and clinics covering the northern, middle, southern, and eastern regions of Taiwan.⁴

To emphasize to the public and to medical staff the importance of observing stool color in early infancy, we established an infant stool color screening system and a stool card registry center. In 2004 we extended the screening program nationwide. This is the first nationwide screening program for BA using an infant stool color card in the world.

Materials and Methods

Infant Stool Color Card. After a pilot regional study from 2002 to 2003, universal screening for BA using an infant stool color card was launched in 2004 (Fig. 1). To educate the parents and medical staff to accurately recognize stool color as normal or abnormal, we designed an

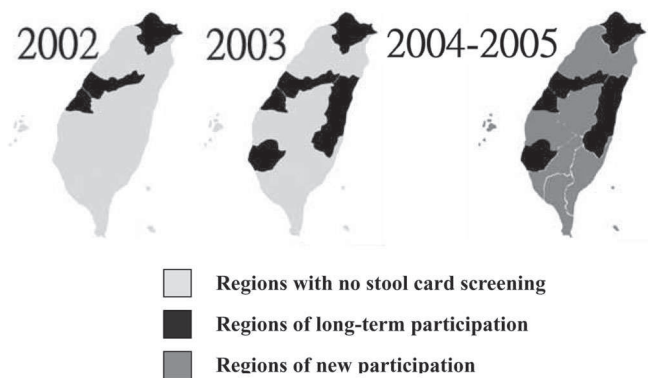


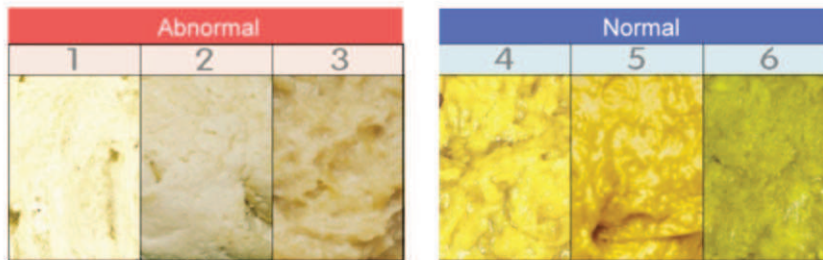
Fig. 1. Algorithm of the stepwise implementation of the infant stool card screening program in Taiwan.

infant stool color card with 6 photographs of different colored stool samples from Taiwanese infants. Three colors (1-3) on this card are labeled abnormal (clay-colored, pale yellowish, and light yellowish), whereas the other 3 (4-6) are labeled normal (yellowish, brown, and greenish; Fig. 2). Telephone and fax numbers for consultation were also printed on this card, and parents, guardians, or medical personnel were instructed to inform the stool card registry center within 24 hours of discovery and identification of abnormal stools, regardless of the baby's age.

Participants. All neonates born between January 2004 and December 2005 in Taiwan were our screening participants. All participants were divided into 2 groups according to region of birth. One group, the long-term participation group, included infants born in the 95 collaborating hospitals or clinics covering the northern, central, southern, and eastern parts of Taiwan and who participated in the pilot study of infant stool color card from March 2002 to December 2003. The other group, the new participation group, included those born in hospitals or clinics where the infant stool card had just been introduced at the beginning of January 2004. Ultimately, 216,419 neonates in 2004 and 205,854 neonates in 2005 were enrolled. The study protocol has passed the review of the institutional review board at the National Taiwan University Hospital's ethics committee.

Screening Method for BA. Since 2004, the infant stool color card has been integrated into the child health booklet that is given to every neonate in Taiwan for information and recording of the child's health and immunizations. Medical staff would observe the baby's stool color after birth while hospitalized and in a baby room, which usually takes 3 to 5 days in Taiwan. The parents were also educated to observe their baby's stool color using this stool color card before discharge from the nursery. If the stool color resembled colors 1-3 (acholic), either the parents or medical personnel were

Infant Stool Color Card



Careful Observation of Stool Color Is Helpful in Early Diagnosis of Biliary Atresia in Early Infancy

Though neonatal jaundice is very common, some babies may suffer from cholestasis if the jaundice is prolonged after the 3rd or 4th week of life. Cholestasis can be divided into intra-hepatic and extra-hepatic type. The most common intra-hepatic cholestasis is neonatal hepatitis, while the most common extra-hepatic cholestasis is biliary atresia. The infants with biliary atresia should be diagnosed within 50 days of age, and undergo surgery as quickly as possible before 60 days of age. The stasis of bile in the liver tends to result in liver cirrhosis, and most die before 2 years of age if left untreated.

How to Assist in Early Screening for Infantile Cholestasis?

The parents should observe the baby's skin and stool color. When the skin and sclera color becomes yellowish, it's necessary to carefully observe the baby's stool color. The color in pictures No. 4-6 above, belong to the normal stool color group. The color of stools without a mixture of bile will be light yellow or clay-colored, as in pictures No. 1-3 above. These colors belong to the abnormal stool color group. Babies with abnormal stools should be sent to a professional pediatric physician for consultation and transferred to a pediatric gastroenterologist if necessary, as early as possible.

Fig. 2. English version of the infant stool color card. The notice on this card educates parents about carefully observing stool color to help in the early diagnosis of biliary atresia in early infancy and to assist in early screening for infantile cholestasis.

<p>The baby's stool color is most like photo No.: _____</p> <p>The date when this kind of stool was first noticed: _____</p> <p>Name of the baby: _____ Date of Birth: _____</p> <p>Mother's Name: _____ Tel.: _____</p> <p>Address: _____</p> <p>The hospital or clinic where the baby was born: _____</p>	<p>If the baby's stool most closely resembles photos No. 1-3, please inform us by phone or fax immediately. We will provide you with related information and advice.</p> <p>Fax: 02-2388-1798</p> <p>Tel: 02-2382-0886</p>
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asked to immediately inform (within 24 hours) the stool card registry center by fax or telephone.

When the infants were brought to the hospitals or clinics for the 1-month health check and hepatitis B vaccination, the physicians would also check the number of the stool color chosen by the parents, and the medical staff had to inform the stool card registry center if colors 1-3 were chosen. Thereafter, the personnel of the registry center would contact the parents to pro-

vide related information for medical care as soon as possible. Each infant with an abnormal stool color would be followed up until a definite diagnosis was made.

In addition, the pediatric gastroenterologists in the medical centers of the 4 areas of Taiwan (north, middle, south, and east) were contacted to serve as core doctors for promotional work and case referral. We also promoted the stool color card and gave educational lectures to pedi-

atric and obstetric medical personnel in all the counties through the assistance of the Taiwan Pediatric Association and a grant from the Bureau of Health Promotion, Department of Health, Taiwan. Through a stool color card-teaching video compact disk, posters, and the mass media, the importance of the infant stool color was spread to the general population.

The diagnostic criteria of BA in this study had to meet either the radiological evidence of BA in operative cholangiography or the characteristic operative and histological findings of BA after laparotomy, when operative cholangiography had not been performed.

National Reporting System for BA. We have established 2 reporting systems for BA in Taiwan that have worked simultaneously since 2004. The first line of reporting is the Stool Color Card Registry System, in which BA infants identified by the stool card were reported to the stool card registry center either by the caretakers or the medical staff, as already mentioned.

The second line of reporting is the Taiwan Biliary Atresia Study Group, which collects information on BA infants reported by pediatric gastroenterologists. As members of the Taiwan Biliary Atresia Study Group, all pediatric gastroenterologists in the 21 major medical centers and hospitals in which the Kasai operation has been performed since 1999 were requested to report newly diagnosed infants at least twice a year. The staff of the study group collected data twice per year from pediatricians in the remaining 25 regional or local hospitals in Taiwan that had no pediatric surgeons to report infants with BA.

The annual incidence of BA was calculated by dividing the number of reported BA cases by the total number of annual live births in Taiwan, which is published on the Web site (<http://www.doh.gov.tw/statistic/index.htm>) of the Department of Health, Executive Yuan, Republic of China.

Definition of Successful Screening for BA by Stool Card. We collected basic data on the infants reported to have BA, including age when pale-colored stool was recognized, age at first hospitalization for differential diagnosis, and age at Kasai operation. The data collected on age at abnormal stool color recognition came from the verbal reports of either the parents or physicians. The data on age at first hospitalization and age at Kasai operation were both collected from review of the patients' medical records. We also asked the parents if they utilized the infant stool color card before visiting a physician.

Infants with BA successfully screened out by the infant stool color card were defined as: (1) patients who were identified with pale-colored stool (colors 1-3) before 60 days of age and reported through the Stool Color Card Registry System, and (2) patients reported by the Taiwan Biliary Atresia Study Group with pale-colored stool be-

fore 60 days of age and parents who utilized the stool color card before visiting a physician.

Historical Data of Infants with BA in 1976-2000.

To analyze differences in early Kasai operation rates and postoperative outcomes among infants with BA between the period of nationwide screening program using the infant stool color card and the period without stool card screening, we retrospectively reviewed the medical records of infants with BA who were admitted to the National Taiwan University Hospital from January 1976 to December 2000, using the same diagnostic criteria for BA, but excluding BA infants lost to follow-up before 1 year of age. All of the included patients were followed up until December 2002.

Jaundice-free status was defined as total serum bilirubin < 2.0 mg/dL (34 μ mol/L) with normal stool color at 3 months after the Kasai operation as in the stool color card study. The Kasai operation rate before 60 days of age and the jaundice-free rate were calculated.

Statistical Analysis. The chi-square test and Fisher's exact test for categorical variables and the Student *t* test for continuous variables were used. The relative risk was computed to compare 2 different rates. A *P* value < 0.05 was considered statistically significant.

Results

National Reported BA Infants. From 2004 to 2005, a total of 75 infants with BA were diagnosed in Taiwan. Forty were male, and the male-to-female ratio was 1.14:1. Four infants (5.3%) were prematurely born, and 2 (2.7%) had a heterozygous twin without BA. Ten (13.3%) were associated with congenital anomalies, including situs inversus in 1 patient, congenital heart disease in 4, congenital intestinal atresia in 2, anal atresia in 1, bilateral inguinal hernia in 1, and polydactyly in 1.

Of the 75 reported BA infants in 2004-2005, 63 patients (84%) were successfully screened out by the stool color card before 60 days of age (Fig. 3).

Infants Reported with Pale-Colored Stool. There were 148 infants in 2004 and 131 infants in 2005 reported as having pale-colored stool (colors 1-3) before 60 days of age. Among them, 29 (19.6%) in 2004 and 34 (26.0%) in 2005 were diagnosed as having BA. The underlying causes of pale-colored stool in 2004-2005 are listed in Table 1.

Screening Results for BA by Stool Card. In 2004, 29 of 40 reported infants with BA (72.5%) were successfully screened out by the stool card before 60 days of age, and the rate of successful screening was increased to 97.1% (34 of 35) in 2005 (*P* = 0.004). Furthermore, the rate of successful screening before 45 days of age was increased

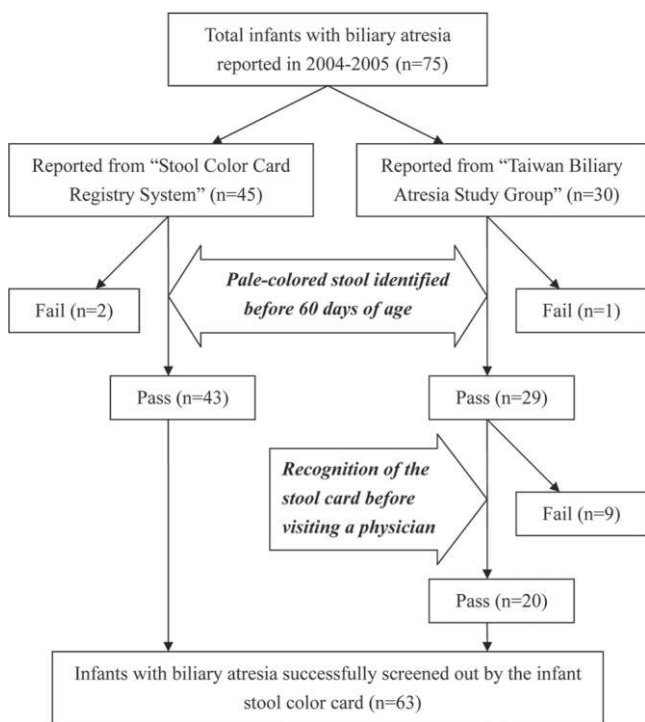


Fig. 3. Flowchart of successful screening using the infant stool color card among 75 reported infants with biliary atresia in 2004-2005.

from 62.5% (25 of 40) in 2004 to 82.9% (29 of 35) in 2005 ($P = 0.052$; Table 2).

The annual incidence rate of BA in Taiwan was 1.85 (40/216,419; 95% confidence interval [CI], 1.32-2.52) per 10,000 live births in 2004 and 1.70 (35/205,854; 95% CI, 1.18-2.37) per 10,000 live births in 2005. For detection of BA before 60 days, the sensitivity of the stool card in our national study was 72.5% (29 of 40) in 2004 and 97.1% (34 of 35) in 2005.

Historical Data of Infants with BA in 1976-2000.

Among 185 infants with a definite diagnosis of BA in a single center in 1976-2000, 41 were excluded because

Table 2. Summary of Screening Results for BA Using the Stool Card (2004-2005)

	2004	2005
Number of live births	216,419	205,854
Number of acholic stool (colors 1-3)	148	131
Number of nationwide reported BA	40*	35†
Number of cases screened out by stool card	29	34
Detection ≤ 30 days (%)	22 (55.0)	23 (65.7)
Detection ≤ 45 days (%)	25 (62.5)‡	29 (82.9)‡
Detection ≤ 60 days (%)	29 (72.5)§	34 (97.1)§
Sensitivity of stool card (before 60 days)	72.5%	97.1%
Annual incidence (95% CI) of BA (/104)	1.85 (1.32-2.52)	1.70 (1.18-2.37)

Abbreviations: BA, biliary atresia; CI, confidence interval.

*In 2004, 13 BA infants were born in long-term participation regions with early promotion of the stool card since 2002-2003, and 27 cases have been born in the new participation region since 2004.

†In 2005, 13 BA infants were born in long-term participation regions and 22 cases were born in the new participation region.

‡Relative risk, 1.3; 95% CI, 1.0-1.8; $P = 0.052$, overall rate of screening as BA patients before 45 days old by stool cards in 2005 versus 2004 (2004 group, relative risk of 1.0).

§Relative risk, 1.3; 95% CI, 1.1-1.6; $P = 0.004$, national detection rate of BA patients before 60 days old by stool cards in 2005 versus 2004.

they were lost to follow-up before 1 year of age. A total of 144 BA infants were enrolled, and 135 (93.8%) received the Kasai operation. Postoperative jaundice-free status was reached in 50 patients (37.0%).

Kasai Operation. Age at Kasai operation among BA infants in 2004-2005 were compared with the data of the preliminary regional study in 2002-2003⁴ and the historical data in 1976-2000 (Table 3).

The national Kasai operation rate before 60 days of age was 60% in 2004 and increased to 74.3% in 2005, which was higher than the 47.2% in 1976-2000 ($P = 0.004$). In contrast, the delayed operation rate beyond 90 days was decreased gradually with time, from 15.3% in 1976-2000 to 10.3% in 2002-2003 and 0% in 2004 and 2005 after mass screening with stool cards.

Outcomes of Kasai Operation. Table 4 shows the outcomes of the Kasai operation. Among infants with BA who received the Kasai operation, the jaundice-free rate was 59.5% (44 of 74) in 2004-2005 with the nationwide stool card screening program, which was significantly higher than the historical data of 37.0% (50 of 135) in 1976-2000 with no stool card screening. In 2004-2005, BA infants who received an early Kasai operation, before they were 60 days old, had a higher jaundice-free rate (72% versus 33.3%, $P = 0.002$) than those operated on after 60 days. The jaundice-free rate after surgery was 72%, 45.5%, and 23.1% in patients operated on before 60 days, in 61-70 days, and in 71-90 days, respectively.

Table 1. Causes of Pale-Colored Stool Screened by the Stool Card before 60 Days of Age (2004-2005)

Diagnosis	No. of cases in 2004	No. of cases in 2005
Biliary atresia	29	34
Neonatal hepatitis	7	5
PFIC	2	3
Choledochal cyst	1	1
TPN cholestasis	2	5
Intestinal perforation	1	0
Urinary tract infection	1	0
Enterovirus infection	0	1
Transient pale-colored stool	105	82
Total	148	131

Abbreviations: PFIC, progressive familial intrahepatic cholestasis; TPN, total parenteral nutrition.

Table 3. Age at Surgery among BA Infants (2002–2005) Versus the Era of No Stool Card (1976–2000)

	1976–2000*	2002–2003†	2004	2005
Number of cases of BA	144	29	40	35
Received Kasai operation	135 (93.8%)	28 (96.6%)	39 (97.5%)	35 (100%)
≤60 days	68 (47.2%)‡§	17 (58.6%)‡	24 (60.0%)§	26 (74.3%)
61–90 days	45 (31.3%)	8 (27.6%)	15 (37.5%)	9 (25.7%)
≥91 days	22 (15.3%)	3 (10.3%)	0 (0%)	0 (0%)
Without Kasai operation	9 (6.2%)	1 (3.4%)	1 (2.5%)	0 (0%)

Abbreviation: BA, biliary atresia.

* From 1976 to 2000, 185 infants with BA received treatment and follow-up at the National Taiwan University Hospital, and 41 patients were excluded because they were lost to follow-up at 1 year old.

† A pilot regional screening program for BA by the infant stool card covering 4 regions of Taiwan from 2002 to 2003.⁴

‡ Relative risk, 1.2; 95% confidence interval (CI), 0.9–1.8; $P = 0.264$, early Kasai operation rate ≤ 60 days in 2002–2003 versus 1976–2000 (1976–2000 group, relative risk of 1.0).

§ Relative risk, 1.3; 95% CI, 0.9–1.7; $P = 0.154$, early Kasai operation rate ≤ 60 days in 2004 versus 1976–2000.

| Relative risk, 1.6; 95% CI, 1.2–2.0; $P = 0.004$, early Kasai operation rate ≤ 60 days in 2005 versus 1976–2000.

Mean Age of Recognized Pale-Colored Stool, First Hospitalization, and Surgery. The mean age when pale-pigmented stool was recognized among 75 infants with BA nationwide in 2004–2005 was 27.8 ± 17.6 days (range: 1–64 days). The overall mean age at first hospitalization and Kasai operation was 43.6 ± 22.1 days (range: 1–90 days) and 54.6 ± 17.1 days (range: 11–90 days), respectively. In addition, the overall mean age at Kasai operation was 55.1 ± 15.8 days (range: 24–84 days) in 2004 and 54.1 ± 18.7 days (range: 11–90 days) in 2005 ($P = 0.821$).

Comparison between Long-Term Versus New Participation Groups. The long-term participation group included 13 BA infants in 2004 and 13 in 2005, whereas the new participation group included 27 patients in 2004 and 22 in 2005. BA infants in the long-term participation group with a longer duration of promoting the stool cards had a significantly higher rate of utilizing this card before visiting a physician (96.2% versus 69.4%; relative risk, 1.4; 95% CI, 1.1–1.7; $P = 0.007$) and a higher reporting rate through the Stool Color Card Registry System than

those in the new participation group (76.9% versus 51.0%; relative risk, 1.5; 95% CI, 1.1–2.1; $P = 0.030$).

Causes of Delayed Surgery. In 2004, 15 of 40 BA infants (37.5%) received the Kasai operation beyond 60 days of age. Causes of delayed surgery included a lack of recognition of stool cards in 8 patients, difficulty in diagnosis for BA by physicians in 1, incorrect judgment of stool color in 2, delayed identification of pale-colored stool in 2, and delayed visit to a physician in 2.

In 2005, 9 of 35 BA infants (25.7%) received delayed surgery, beyond 60 days of age. The causes of delay included difficulty in diagnosis in 1, incorrect judgment of stool color in 1, delayed identification of pale-colored stool in 4, and delayed visit to a physician in 3.

Discussion

The national screening program for BA using the infant stool color card has been successfully launched and promoted for early diagnosis and timely surgery before 60

Table 4. Outcomes of BA Infants after Kasai Operation in 2004–2005 (National Stool Color Card Screening Program) Versus Outcomes in 1976–2000 (Era of No Stool Card Screening)

	Jaundice-free* rate in 1976– 2000†	Jaundice-free* rate in 2004– 2005	Relative risk‡ (95% CI)	P
Received Kasai operation	50/135 (37.0%)	44/74 (59.5%)	1.6 (1.2–2.1)	0.002
≤60 days old	30/68 (44.1%)	36/50 (72.0%)§	1.6 (1.2–2.2)	0.003
>60 days old	20/67 (29.9%)	8/24 (33.3%)§	1.1 (0.6–2.2)	0.752
61–70 days	10/23 (43.5%)	5/11 (45.5%)		
71–90 days	5/22 (22.7%)	3/13 (23.1%)		
≥91 days	5/22 (22.7%)	0/0 (0%)		
Without Kasai operation	0/9 (0%)	0/1 (0%)		

Abbreviations: BA, biliary atresia; CI, confidence interval.

* Total serum bilirubin < 2.0 mg/dL (34 μmol/L) with normal stool color 3 months postoperatively.

† From 1976 to 2000, 185 infants with BA received treatment and follow-up at the National Taiwan University Hospital, and 41 patients were excluded due to loss of follow-up at 1 year old.

‡ Relative risk is for the jaundice-free rate in 2004–2005 compared with the jaundice-free rate in 1976–2000 (1976–2000 group, relative risk of 1.0).

§ Relative risk, 2.2; 95% CI, 1.2–3.9; $P = 0.002$, jaundice-free rate after Kasai operation ≤ 60 days versus > 60 days in 2004–2005.

days of age. Before implementation of the screening program, a significant number of BA infants were referred at a delayed age, beyond 60 days.^{2,14,22} According to historical data from 1976 to 1989 in Taiwan, only 23.3% of BA infants in a medical center received surgery before 60 days of age in the era of no stool card screening.²³ The Japanese Biliary Atresia Registry from 1989 to 1999 reported that the Kasai operation rate before 60 days of age was 43%, with no remarkable change in the trend of age at operation since 1990.²

Regional screening for BA by stool cards in Taiwan, launched in 2002-2003, has increased the rate of the Kasai operation being performed early by up to 58.6%.⁴ After the national screening by stool cards, this rate has further increased, from 60% in 2004 to 74.3% in 2005. Through the infant stool color card, not only parents but also medical personnel have been educated about the significance of observing stool color, which hopefully will lead to early referral and ultimately to the Kasai operation being performed in a timely manner.

In addition, universal screening by stool color cards has effectively improved prognosis in infants with BA. The jaundice-free rate after surgery was significantly improved, from 37.0% in the era of no stool card screening (1976-2000) to 59.5% in 2004-2005 with universal screening. However, it is possible that some of the improvements in the current era might reflect improved surgical and medical interventions and not simply earlier intervention because of the use of this screening approach. In this national study, we also proved that BA infants receiving the Kasai operation before 60 days of age had a better jaundice-free outcome.

Our national study revealed that the annual incidence rate of BA in Taiwan ranged from 1.70 to 1.85 per 10,000 live births, which was lower than the previously reported 3.7 per 10,000 live births from the 2002-2003 regional study.⁴ The incidence rate of the regional study obtained through collecting the returned cards might have been overestimated because the return rate of the stool cards was below 70%, and the parents of infants with an abnormal stool color had a higher trend of returning the cards. The incidence of BA from this national study is more reliable, despite the possibility of underestimation because of unreported BA infants or infants with cholestasis who died before a definite diagnosis.

In analyzing the impact of promoting stool cards from 2002 to 2003, BA infants from the long-term participating regions had higher reporting rates through the Stool Color Card Registry System and higher rates of utilizing the stool card before visiting a physician than those from the new participating regions ($P = 0.030$ and 0.007 , respectively). This implies that the long-term promotion of

stool cards from 2002 to 2003 played an essential role as a cornerstone in the later success of nationwide screening for BA by stool color card.

In our national study, we found a long lag from the identification of pale stools (mean: 27.8 days) to the actual Kasai procedure (mean: 54.6 days). This lag consisted of 15.8 days from identification of pale stools to the first hospitalization and another 11 days from the first hospitalization to the actual Kasai procedure. The infant stool color card has promoted early referral because of early identification of pale stools. However, a significant number of parents whose children had abnormally colored stool still hesitated in seeking medical aid because of their emotional denial, which might explain why there was a delay from identification of pale stools to first hospitalization. In addition, the variable lag period from hospitalized survey to Kasai operation depended on the level of experience of different physicians and whether there was difficulty in diagnosing BA.

Although we have conducted a 3-day protocol since 1982 regarding a fast and feasible method for diagnosing BA that can shorten the interval between referral and surgery,²⁴ on many occasions a significant period was still needed to exclude infective, genetic, metabolic, and biliary disorders that might mimic BA in order to avoid children with intra-hepatic cholestasis having to undergo unnecessary laparotomy. Furthermore, some parents delayed accepting surgery when the Kasai operation was suggested. Therefore, it is essential to further reinforce the efficacy of the infant stool card registry system in order to shorten delays in seeking medical aid through close follow-up of infants with abnormal stool color and through continuing medical education for early surgery.

In analyzing the causes of delayed surgery, a lack of utilizing stool cards played a major role in 2004 but not in 2005, after efforts to educate the general population regarding the significance of the infant stool color card. However, delayed identification of pale stools and delayed visits to a physician remained significant causes of delayed surgery. In the future, for a higher national rate of the Kasai operation being performed before 60 days of age, we should enhance early screening for BA by distributing stool cards before 30 days of age, so that timely referral can be achieved within 45 days.

In conclusion, this universal screening program for BA by an infant stool color card can promote earlier referral, which may ultimately lead to timely surgery and better postoperative outcomes.

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