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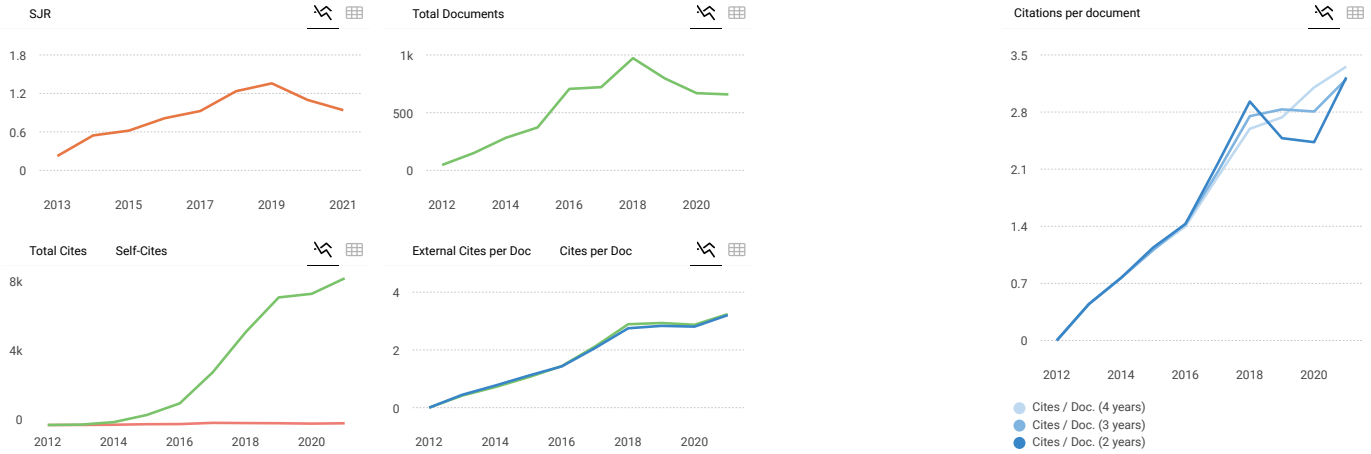

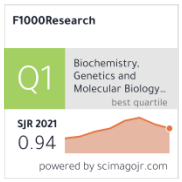

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Early detection of biliary atresia in primary health care: still a problem [version 1; peer review: awaiting peer review]

Bagus Setyoboedi, Rendi Aji Prihaningtyas, Martono Tri Utomo, Sjamsul Arief

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Early detection of biliary atresia in primary health care: still a problem [version 1; peer review: awaiting peer review]

Bagus Setyoboedi, Rendi Aji Prihaningtyas, Martono Tri Utomo, Sjamsul Arief

Child Health Department, Airlangga University, Surabaya, Indonesia

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Abstract

Background: Biliary atresia is the leading cause of liver transplantation in children. Early detection of biliary atresia is crucial for diagnosis and disease progression. The purpose of this study was to analyze knowledge about biliary atresia and the effectiveness of health education in increasing the knowledge of primary health care providers.

Methods: A quasi-experimental study with pretest and posttest designs was carried out in Sidoarjo, East Java using a self-administered questionnaire. The intervention using health education was delivered by pediatrician and consultant of pediatric gastro hepatology. There were 13 questions on the questionnaire, question numbers 1 to 6 were about normal and abnormal neonatal jaundice, question numbers 7 to 13 were about biliary atresia.

Results: A total of 252 participants were involved, the mean age of the participants was 40.7 ± 9.4 years old. Most of the participants were midwives (61.9%) and 77.8% of participants have years of service in primary health care > 5 years. A total of 40.5% participants stated that newborns may have physiological jaundice, which was characterized by icteric sclera, pale stools, and dark urine. A total of 27,4% and 24,2% participants said that all jaundice in newborn will always improve on their own and newborn with prolonged jaundice does not need further examination, respectively. There was an increase in the median value in the pretest and posttest knowledge scores after interventional health education ($p < 0,05$).

Conclusions: The primary health care provider understands about biliary atresia, however, the initial knowledge about early detection of biliary atresia is not evenly distributed in all primary health care providers. These findings suggest that improving knowledge to early detection of biliary atresia is needed. Health education can be used effectively in increasing knowledge about biliary atresia.

Keywords

Biliary atresia, knowledge, primary health care provider, early detection

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Introduction

Biliary atresia (BA) is the most common cause of pediatric end-stage liver disease and is the leading cause of liver transplantation in children. It remains a challenge for clinicians.[1] BA is found worldwide, with incidence rates of 1 in 10-19,000 in Europe and North America, and higher incidence rates of 1 in every 3,000 infants in East Asia.[2–4]

Biliary atresia is manifested with abnormal narrowing of the bile ducts, blockage of the bile ducts to the absence of bile ducts in the liver.[2] Early detection of biliary atresia is crucial for diagnosis and the rate of disease progression. Currently, increasing evidence has shown that the development of BA is associated with infections, such as perinatal viral infections. The presence of infection can trigger neonatal cholestasis which begins with progressive inflammation of the intrahepatic and extrahepatic bile ducts.[2] Biliary obstruction can happen within the first few weeks after birth.[1] The best prognosis of BA remains dependent on early diagnosis and surgical treatment.[5]

There are two clinical forms of BA, perinatal and congenital. In the perinatal form of BA, the infant has no congenital abnormalities and the onset of jaundice begins during or after the second week of life. This contrasts to the congenital form, in which signs of cholestasis appear soon after birth and associated with non-hepatic congenital anomalies.[5] Most cases (80%) are considered perinatal form.[3]

Clinically, in infants with biliary atresia, cholestatic jaundice develops in the first few weeks of life followed by acholic stools, dark urine, hepatomegaly, poor growth, progressing to cirrhosis, portal hypertension, and liver failure.[2,5] The symptoms of BA continue to worsen two weeks after birth. It is different with physiological jaundice. Physiological jaundice will improve within two weeks and get better. Meanwhile, in cholestasis that occurs due to biliary atresia, jaundice will worsen.[3] Unfortunately, identification of infants with cholestatic jaundice is quite difficult because it appears similar to the physiological jaundice that is very common in early infancy.[1] Currently, the Stool Color Card has been introduced as an early detection tool for biliary atresia in infants which can diagnose earlier, shorten surgical treatment time, and improve the long-term prognosis of children with biliary atresia.[5]

Unfortunately, early diagnosis of biliary atresia is still challenging. The delay in diagnosing BA is the main problem, especially in Indonesia. The lack of knowledge and awareness about early detection of BA among primary healthcare providers is the important cause of delayed diagnosis of BA.[6] This study aims to analyses the knowledge about BA and evaluate the effectiveness of health education to increase knowledge of primary health care providers in early detection of BA in infants. Increasing primary health care awareness by conducting an educational seminar on early detection of BA was expected in this study.

Methods

Participants

A quasi-experimental study with a pretest and posttest design was performed to analyses the knowledge about BA and evaluate the effectiveness of health education to increase the knowledge of primary healthcare providers about early detection of BA in infants. An educational seminar on early detection of BA was performed. A total of 252 health care providers at seven primary healthcare centers in Sidoarjo, East Java during the period from April to August 2022 were involved in this study. The inclusion criteria in this study were healthcare providers who provided health services and were willing to participate in the study. Exclusion criteria in this study were healthcare providers who were not involved in patient health care.

Intervention

The evaluation of knowledge about BA was performed using a self-administered questionnaire. The intervention using health education of BA in this study was performed by a pediatrician and a consultant of pediatric gastro hepatology who already has more than 10 years of experience in treating patients with biliary atresia in a teaching center hospital. The interventional health education was delivered by a face-to-face meeting with health care provider in primary healthcare centers. A pretest questionnaire was first delivered to evaluate the participant's initial level of knowledge about BA ten minutes before conducting the health education seminar. The health education was then performed followed by an interactive discussion, including the basics of jaundice, BA, early detection of BA, and how to use the stool color card as a screening tool of BA. The health education was delivered within a total duration of two hours. Afterward, the posttest questionnaire was given to evaluate post educational health intervention. There were 13 questions on the questionnaire, question numbers 1 to 6 were about normal and abnormal neonatal jaundice, question numbers 7 to 13 were about BA (symptoms, early detection, management and complications of BA).

Ethical clearance

This study was carried out in accordance with the Declaration of the Helsinki World Medical Association. This study was undertaken with the understanding and written consent of respondents. Before the study, a permit was obtained from the

Sidoarjo District Health Office and all primary healthcare centers agreed to participate in the study. This study was previously reviewed and independently approved by an ethical board of Faculty of Medicine, Airlangga University, Surabaya (No. 60/EC/KEPK/FKUA/2022).

Data analysis

Pre- and post-test questionnaire results were obtained to evaluate the initial knowledge of BA and effect of health education on the participants. Normality test was conducted to evaluate the normality of data distribution. If the data was not normally distributed, non-parametric test analysis was performed such as using the Wilcoxon Signed Ranks Test. The difference in pre-test and post-test scores was obtained by analysis using chi Square (Fisher's Exact Test) with a significant $p < 0.05$. The data analysis was done using SPSS version 21.0.

Results

In this study, there were 252 participants involved and the majority (92.9%) were female. The mean age of the participants was 40.7 ± 9.4 years old (Min-Max: 22-71 years old). Most of the participants were midwives (61.9%) with a diploma graduate (82.5%). A total of 77.8% of participants have years of service in primary health care > 5 years as described in Table 1.

Questionnaire analysis

Question (1): Newborns < 28 days old may have normal (physiological) jaundice, which is characterized by icteric sclera, pale stools, and dark urine.

There were 18.7% of participants who consistently answered correctly, although 21.8% answered incorrectly on the post test. Overall, there were 40.5% of the pre-test who answered correctly, down to only 28.6% who answered correctly. There was a difference in pre and post values for question 1, using chi Square (Fisher's Exact Test) obtained a p-value of 0.000 (Table 2).

Table 1. Basic characteristics of participants.

	Total participants (n =)	(%)
Sex		
Male	18	7.1
Female	234	92.9
Age group		
20-30 years old	32	12.7
30-40 years old	94	37.3
40-50 years old	73	29.0
50-60 years old	49	19.4
>60 years old	4	1.6
Occupation		
Medical doctor	22	8.7
Nurse	65	25.8
Midwifery	156	61.9
Others (pharmacist, laboratory officer)	9	3.6
Education		
Undergraduate	44	17.5
Diploma	207	82.5
Years of service		
<3 years	25	9.9
3-5 years	31	12.3
>5 years	196	77.8

Table 2. **Analysis of question 1.**

Pre test	Post test				P value*
	True	False	Unknown	Total	
True	47 (18.7%)	55 (21.8%)	0 (0%)	102 (40.5%)	0.000
False	25 (9.9%)	120 (47.6%)	0 (0%)	145 (57.5%)	
Unknown	0 (0%)	4 (1.6%)	1 (0.4%)	5 (2%)	
Total	72 (28.6 %)	179 (71%)	1 (0.4%)	252 (100%)	

p value < 0.05.
*Chi square test.

Table 3. **Analysis of question 2.**

Pre test	Post test				P value*
	True	False	Unknown	Total	
True	27 (10.7%)	42 (16.7%)	0 (0%)	69 (27.4%)	0.000
False	7 (2.8%)	165 (65.5%)	0 (0%)	172 (68.3%)	
Unknown	3 (1.2%)	7 (2.8%)	1 (0.4%)	11 (4.4%)	
Total	37 (14.7%)	214 (84.9%)	1 (0.4%)	252 (100%)	

p value < 0.05.
*Chi square test.

Question (2): All jaundice that occurs in babies aged < 28 days will always improve on its own.

There were 10.7% of participants who consistently answered correctly, although 16.7% answered incorrectly on the post test. Overall, there were 27.4% pre-test who answered correctly, down to only 14.7% who answered correctly. There was a difference in pre and post values for question 2 obtained a p-value of 0.000 (Table 3).

Question (3): A yellow baby > 2 weeks old does not need further examination, it is enough to just expose to the sun.

There were 6.7% of participants who consistently answered correctly, although 17.5% answered incorrectly on the post test. Overall, the pre-test was 24.2% who answered correctly, down to only 10.7% who answered correctly. Therewas a difference in pre- and post-values for question 3 obtained a p-value of 0.000 (Table 4).

There were 77.4% of participants who consistently answered correctly in question 9, although 0.8% answered incorrectly on the post test. Overall, the pre-test there were 78.2% who answered correctly, increasing to 96.8% who answered correctly. There is a difference in pre and post values for question 9, using chi Square (Fisher's Exact Test) obtained a p-value of 0.000 (Table 5). There were 67.1% of participants who consistently answered correctly in question 11, although 1.6% answered incorrectly on the post test. Overall, the pre-test there were 69.0% who answered correctly, increasing to 94.0% who answered correctly. There was a difference in pre and post scores for question 11, using chi Square (Fisher's Exact Test) the p-value is 0.004 (Table 5).

Table 4. **Analysis of questions 3.**

Pre test	Post test			P value*
	True	False	Total	
True	17 (6.7%)	44 (17.5%)	61 (24.2%)	0.000
False	10 (4.0%)	179 (71.0%)	189 (75%)	
Unknown	0 (0%)	2 (0.8%)	2 (0.8%)	
Total	27 (10.7%)	225 (89.3%)	252 (100%)	

p value < 0.05.
*Chi square test.

Table 5. Differences in pre test and post test scores.

Question	Pre test	Post test	P value
(1)	102 (40.5%)	72 (28.6%)	0.000
(2)	69 (27.4%)	37 (14.7%)	0.000
(3)	61 (24.2%)	27 (10.7%)	0.000
(4)	233 (92.5%)	249 (98.8 %)	0.000
(5)	23 (9.1%)	15 (6.0%)	0.000
(6)	226 (89.7%)	246 (97.6%)	0.010
(7)	148 (58.7%)	163 (64.7%)	0.000
(8)	238 (94.4%)	251 (99.6%)	NA
(9)	197 (78.2%)	244 (96.8%)	0.000
(10)	237 (94%)	250 (99.2%)	0.116
(11)	174 (69%)	237 (94%)	0.004
(12)	242 (96%)	250 (99.2%)	1.000
(13)	226 (90%)	250 (99.6%)	1.000

Table 6. Differences in knowledge level of biliary atresia.

	Median (Min–Max)	P value*
Pre test	15 (5-20)	0.000
Post test	17 (12-21)	

P value < 0.05.
*Wilcoxon sign ranks test.

Table 7. Differences in improvement scores by gender, education, age group, and years of service.

	P value
Sex	0.078[1]
Education	0.610[1]
Age group	0.467[2]
Years of service	0.272[2]

[1]Mann-Whitney test.
[2]Kruskal-Wallis test.

There is no difference in pre and post scores for questions 10,12,13, using chi Square (Fisher's Exact Test) p-values are 0.0116, 1.000, and 1.000 (Table 5). There was a significant difference between the posttest and pretest scores (p value 0.000). The post test score (median 17) was higher than the pretest score (median 15) (Table 6).

There was no significant difference between the participants' pre and post test scores based on gender, education, age, and years of service (Table 7). This is indicated by p value > 0.05.

Discussion

Biliary atresia is present with findings: (1) the occurrence of total extrahepatic bile duct obstruction (2) the presence of proliferation of the intrahepatic bile ducts, and (3) the discovery of intrahepatic fibrosis that occurs at an early age.[7] BA is found worldwide, and incidence rate is 1 in 10-19,000 infant in Europe and North America, up to 6.5 to 7.5 in 100 000 infant in the US mainland until high incidence rate to 1 in 3,000 infants in East Asia.[1–4] But no official data on the incidence of BA has been published in Indonesia.[8]

Although BA is a rare disease, BA is the leading cause of liver transplantation in children and the most common cause of death from liver disease in infants.[9] The prognosis of BA in infants is influenced by several factors, including age at the time of surgical intervention and the anatomy of the bile duct remnant. Nearly half of all infant with BA survive into adolescence if Kasai surgery is carried out early.[10]

Unfortunately, the challenge remains in recognizing that infants with jaundice may have BA, not a common physiologic jaundice. Delayed diagnosis is still a problem worldwide.[11] Delayed diagnosis and Kasai procedure performed after three months of age have a significantly poor prognosis for survival of the original liver.[12] Kasai surgery can improve long-term liver survival and reduce the need for a liver transplant if performed before 60 days of age.[13,14] Liver cirrhosis is major morbidity resulting from untreated BA, requires very costly liver transplantation that Indonesia has limited facilities. Not all centers in Indonesia can perform liver transplants. Therefore, the most likely thing to do is to carry out the Kasai procedure as early as possible.[15]

An early diagnosis of biliary atresia is difficult. Delay in diagnosing BA is also a major source of problems in therapy, especially in Indonesia. Global efforts are urgently needed to increase the rate of BA diagnosis as early as possible.[15] The lack of knowledge and awareness about early detection of BA among primary healthcare providers is the important cause of delayed diagnosis of BA.[6]

In this study, there were 40.5% of the primary health care provider stated that newborns < 28 days old may have normal (physiological) jaundice, which is characterized by icteric sclera, pale stools, and dark urine. Infants suffering from BA generally appear as healthy as any other infant when they are neonates.[1,2] Clinically, in the early condition of BA, infants with BA are indistinguishable from infants with non-conjugated hyperbilirubinemia, such as physiologic jaundice and breast milk-associated jaundice. Then, making the diagnosis of infant jaundice other than physiologic or breast milk-related jaundice is still a challenge today.[1] However, in BA jaundice will extend beyond two weeks of age and infants will experience other complaints, such as pale stools, dark urine, poor growth, increased abdominal circumference due to ascites and splenomegaly, and other complications due to liver damage.[2,9]

Overall, there were 27.4% health care provider showed that all jaundice that occurs in newborn will always improve on their own in this study. A total of 24.2% primary health care provider stated that newborn with prolonged jaundice does not need further examination, it is enough to just expose to the sun. The evaluation of bilirubin serum should be done in infant with prolonged jaundice. Then the presence of BA should be considered for any jaundiced infant with acholic stools and accompanied by an increase in the serum conjugated bilirubin concentration.[1]

There was no difference in pre- and post- test scores for questions about complication of biliary atresia in this study and the need for liver transplantation. The primary health care provider understands about biliary atresia and its complications, however, in this study it was found that only 69.0% of participants understood that jaundice due to biliary atresia must be detected as early as possible and surgery performed before the age of two months.

Early diagnosis and treatment are necessary in infants with BA.[1] There was a significant difference between the pretest and posttest scores (p value 0.000). The post test score (median 17) was higher than the pretest score (median 15) after interventional health education. Improving knowledge to early detection of biliary atresia using screening with stool color cards is a promising and economically feasible strategy.[11,16] It is necessary to increase the awareness of primary healthcare providers to early detection of BA for improving the outcomes of the Kasai procedure and reduce the need for liver transplantation.[10] Therefore, it is very important to socialize how to early detection BA in Indonesia, especially in the regions to reduce the delay rate in the referral of infants with BA using interventional health education.

Serum conjugated bilirubin concentrations and stool color cards are the two BA screening methods currently in use.[1] A study in the United Kingdom stated that baby with conjugated bilirubin more than 20% of total bilirubin was followed up in a community setting, from this study several liver diseases such as neonatal hepatitis, extra-hepatic biliary atresia, Alagille syndrome, hypopituitarism, and alpha-1-antitrypsin deficiency were detected.[17] Another study showed that at 24 to 48 hours of life, subjects with BA had mean conjugated bilirubin levels significantly higher than those of controls, and it can happen shortly after birth.[18] Thus, serum conjugated bilirubin levels can be a valuable screening test for BA.[1]

Screening with stool color cards is currently an important strategy because it requires lower costs and better results.[16] Stool Color Cards have been used in China, Taiwan, and Japan to shorten the age at diagnosis and shorten the time between diagnosis and the Kasai procedure.[19,20] A 19-year cohort study in Japan showed that the sensitivity and specificity of stool color card screening at one-month evaluation were 76.5% and 99.9%, respectively.[21] In Taiwan, the stool color card screening had a sensitivity and specificity of 89.7% and 99.9%, respectively.[22] However, in this study,

it was found that 78.2% of health workers in primary health facilities understood the stool color card used as a screening tool for biliary atresia in infants. The optimization of biliary atresia screening is still needed using the health intervention to primary health care provider to reduce the need for liver transplantations.[13]

This study was the first research conducted and provides new information that one of the failures of early detection of biliary atresia is the uneven level of knowledge about jaundice and biliary atresia in primary health facilities which is the main milestone in public health services. The results of this study can be used as the basis for policies to carry out more massive socialization to health workers in primary health facilities about biliary atresia. The weakness of this study is the limited number of subjects. Further research with a larger number of subjects and a wider area is needed to determine the level of knowledge of early detection of biliary atresia in Indonesia.

Conclusion

The natural history of biliary atresia has been described. Early diagnosis provides a better prognosis for infants with biliary atresia. These findings suggest that improving knowledge to early detection of biliary atresia is needed to primary healthcare providers, including information about prolonged jaundice and screening with the stool color card for improving outcomes in BA in Indonesia. Health education interventions has significantly increased the knowledge of primary healthcare providers about early detection of BA. Further studies with larger subjects and area are needed to evaluate the effectiveness and feasibility of potential education for early identification of infants with biliary atresia in Indonesia.

Data availability

Underlying data

Figshare: Knowledge of Biliary Atresia, https://doi.org/10.6084/m9.figshare.20579820.v2.[23]

This project contains the following underlying data:

- knowledge of biliary atresia F1000.xlsx

Extended data

Figshare: Knowledge of Biliary Atresia, https://doi.org/10.6084/m9.figshare.20579820.v2.[23]

This project contains the following extended data:

- kuesioner pengetahuan atresia bilier_Indonesia.pdf (questionnaire in Indonesian)

- kuesioner pengetahuan atresia bilier_English.pdf (questionnaire in English)

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