



Factors Associated with Survival Rate in Biliary Atresia Patients Following Kasai Surgery

Agung Aji Prasetyo¹, Edwin Basyar¹, Rudi Yuwono Raharjo¹,
Agoes Wibisono¹, Avriana Pety Wardhani¹, Banundari Rachmawati², Ignatius Riwanto³

¹Division Pediatric Surgery, Department of Surgery, Kariadi Hospital /
Faculty of Medicine Diponegoro University, Semarang, Indonesia

²Department of Clinical Pathology, Kariadi Hospital / Faculty of Medicine Diponegoro University, Semarang, Indonesia

³Division Digestive Surgery, Department of Surgery, Kariadi Hospital /
Faculty of Medicine Diponegoro University, Semarang, Indonesia

Abstract

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Author Affiliation:

Division Pediatric Surgery, Department of Surgery,
Kariadi Hospital / Faculty of Medicine
Diponegoro University, Semarang, Indonesia

Author Correspondence:

Agung Aji Prasetyo
Dr. Sutomo Street No. 16, Semarang,
Central Java 50244, Indonesia

E-mail:

aaprasetyo82@gmail.com

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Background : Biliary atresia is the most frequent cause of obstructive jaundice leading to liver fibrosis, end-stage liver disease, and death. Kasai surgery offers a bridge to attenuate liver fibrosis progression through reconstruction of the biliary system. The success of the Kasai procedure depends on the presence of jaundice, age at the time of surgery, clay-colored stool, and bilirubin counts. This study aimed to investigate and predict the death incidence of Biliary atresia patients following Kasai Surgery in our institution.

Methods : We conducted a case-control study from March 2020 to January 2022 at Kariadi General Hospital, Semarang, Indonesia. We collected data related to gender, age at surgery, albumin level pre and post-surgery, total and direct bilirubin before and after surgery, and the presence of ascites. Bivariate analysis using the Chi-Square test with OR (95% CI) was performed to analyze the risk factors in BA patients following the Kasai procedure.

Results : 19 patients with biliary atresia underwent the Kasai procedure with a survival rate of 68.4%. Bilirubin levels ≥ 10 mg/dL before ($p=0.033$, OR 11.25) and after ($p=0.025$, OR 11.00) the Kasai procedure, and the presence of ascites ($p=0.005$) were significant factors associated with mortality cases. However, a combined multivariate analysis of these factors did not show any significant relationship with outcomes.

Conclusion : Bilirubin exceeding 10 mg/dL before and after the Kasai procedure and the presence of Ascites was a marker for poor outcomes for biliary atresia patients following the Kasai procedure.

Keywords : Biliary atresia, Kasai procedure, ascites

INTRODUCTION

Biliary atresia (BA) is the most commonly identified cause of obstructive jaundice in the first three months of life. Biliary atresia (BA) is a potentially fatal disease in infants, where there is progressive obliterative cholangitis that affects the intra and extrahepatic tracts as persistent cholestasis. This often results in liver fibrosis, end-stage liver disease, and death.^{1,2} The incidence rate of biliary atresia is 1:19000 compared to live births in Canada.³ The incidence rate in North America and Europe ranges from 1:8000–1:16000, while in Asia it ranges from 1:5000–1:8000.^{4,5} In Yogyakarta, Indonesia, the prevalence of BA is reported to be 1:7000.⁶ BA should be treated immediately in the early stages of life to avoid biliary cirrhosis and liver failure. The main surgical procedure used to treat BA is Kasai surgery. However, only 65% of BA patients remain alive after Kasai's surgery within 5 years.⁷ Only less than 30% of patients were able to survive long-term with their liver after Kasai, and most eventually died or received a liver transplant.⁸ Although liver transplants are constrained by a lack of donors, high costs, and the use of lifelong anti-rejection drugs after surgery, liver transplants from living donors to treat biliary atresia have made rapid progress in recent years. Various methods are used to identify the prognostic factors of Kasai surgery outcomes, such as age, bilirubin profile after surgery, aspartate aminotransferase (AST) after recovery from Kasai surgery, recurrent cholangitis, etc. However, the results still show some conflicting findings,⁹ so the prognosis of AB patients undergoing Kasai surgery is uncertain. Therefore, the researcher investigated the relationship between prognostic factors and the mortality rate of BA patients after Kasai surgery in the Indonesian population, especially in Kariadi Semarang Hospital.

MATERIALS AND METHODS

Patient samples

A retrospective study using the medical records of babies with BA who underwent Kasai surgery was conducted at Kariadi Hospital, Semarang, Indonesia. Researchers analyzed 19 BA patients, with 13 male patients and 6 female patients, from March 2020 to January 2022.

Prognostic factors

The researchers evaluated and correlated the following prognostic factors and the survival rate of BA patients after Kasai surgery: sex, age at Kasai surgery, and total bilirubin and albumin levels before and after the Kasai procedure. Researchers determined patients who survived with a survival rate of 1 year.

The researchers divided the total serum bilirubin (TB) levels from the samples before and after Kasai surgery into high (<10 mg/dL) and very high

(≥10 mg/dL). The researchers divided serum albumin levels from samples before and after Kasai surgery into normal (≥3.5 g/dL) and abnormal (<3.5 g/dL). Total serum bilirubin and albumin levels were measured in the first week before and after Kasai surgery. Ascites are categorized as present when they are clinically detected or found by sonography or intraoperative methods in quantities greater than *traces* or *scants*.

Statistical analysis

The data is presented as a frequency. Univariate analysis was carried out to obtain the frequency of each variable. Bivariate analysis using *the Chi-Square* test was carried out to determine the relationship between prognostic factors and the survival rate of BA patients. Multivariate analysis aims to find out which prognostic factors are more influential. This study was approved by Health Research Ethics Committee of RSUP Dr. Kariadi Semarang.

RESULTS

Nineteen BA patients were identified from March 2020 to January 2022. Researchers identified the survival rate after the Kasai operation to be 68.4%. [Table 1](#) presents basic clinical and biochemical data for BA patients.

First, the researchers analyzed the relationship between the characteristics of BA patients and their survival rates. Bilirubin greater than 10 mg/dL before ($p=0.05$, OR 11.25) and after ($p=0.046$, OR 11.00) Kasai procedure and the presence of Ascites ($p=0.021$) were significant factors in mortality cases. ([Table 1](#)).

Multivariate analysis using tests cox-regression in the three variables above, the mortality of the Kasai procedure in BA patients showed the following results ([Table 2](#)).

The results of *the cox-regression* test on the output of total bilirubin before surgery, total bilirubin after surgery, and ascites were found to be insignificant ($p>0.05$ value) to the mortality of the Kasai procedure.

DISCUSSION

The Kasai procedure aims to cut off the blocked extrahepatic bile ducts and restore bile flow.¹¹ If this procedure fails to eliminate jaundice and/or complications associated with biliary cirrhosis, a secondary liver transplant (LT) is required.¹² Overall, 20% of patients can reach the age of 20 with their original heart, and 10% can reach the age of 30.^{13,14} In developed countries, biliary atresia patients are generally referred to undergo Kasai surgery before the age of sixty days.

Albumin levels at one month and three months after surgery were able to predict the survival rate of BA patients after Kasai surgery at Sardjito Hospital Yogyakarta, Indonesia.¹⁵ Patients with albumin levels of

TABLE 1
Shows the basic clinical and biochemical data of BA patients

Variable		Outcome		p	OR (95% CI)
		Died (n=6) n (%)	Control (n=13) n (%)		
Gender	Man	4 (66.7)	9 (69.2)	0.911 ^α	0.89 (0.11 – 7.02)
	Woman	2 (33.3)	4 (30.8)		
Age at the time of surgery	< 60 days	1 (16.7)	4 (30.8)	0.516 ^α	0.45 (0.39 – 5.21)
	≥ 60 days	5 (83.3)	9 (69.2)		
Albumin before surgery	< 3.5 g/dL	1 (16.7)	2 (15.4)	0.938 ^α	0.90 (0.06 – 12.58)
	≥ 3.5 g/dL	5 (83.3)	9 (69.2)		
Albumin after surgery	< 3.5 g/dL	3 (50.0)	7 (53.8)	0.876 ^α	0.86 (0.12 – 5.94)
	≥ 3.5 g/dL	3 (50.0)	6 (46.2)		
Total bilirubin before surgery	≥ 10 mg/dL	5 (83.3)	4 (30.8)	0.033 ^{α*}	11.25 (0.97 – 130.22)
	< 10 mg/dL	1 (16.7)	9 (69.2)		
Total bilirubin after surgery	≥ 10 mg/dL	4 (66.7)	2 (15.4)	0.025 ^{α*}	11.00 (1.14 – 106.43)
	< 10 mg/dL	2 (33.3)	11 (84.6)		
Ascites	Yes	3 (50.0)	0 (0)	0.005 ^{α*}	–
	Not	3 (50.0)	13 (100)		

Description: *Significant bivariate test (p<0.05); ^α Chi-Square test

TABLE 2
Multivariate Test Results

Variable	p	OR	95% CI
Bilirubin total pre op	0.946	0.000	0.000 – 7.710
Bilirubin total post op	0.662	0.537	0.033 – 8.727
Ascites	0.230	0.190	0.013 – 2.865

Description: * Significant (p < 0.05)

<3.5 g/dL at one month and three months after surgery had worse prognosis (~4 and ~28-fold, respectively) compared to those with albumin levels of ≥3.5 g/dL.¹⁶ Low albumin causes ascites and increases the mortality rate of infants with chronic liver disease. Higher preoperative mean serum albumin levels and postoperative jaundice are associated with long-term survival for original liver transplant patients.¹⁷ Unfortunately, the researchers' statistical analysis stated that there was no significant association between albumin measured at 1 week before and after surgery on the survival rate of BA patients. Serum albumin and total bilirubin in the first month after Kasai surgery were not significant prognostic factors in determining the survival of BA patients at Sardjito Hospital.¹⁵ Total bilirubin

>2mg/dL and albumin <3.5g/dL at 3 months post-operative to Kasai are also significant predictors of future transplant needs.¹⁸

Although 60% of babies with BA will initially experience a recovery in bile flow after surgery, liver fibrosis is progressive, and portal hypertension (PHT) occurs in most children. Manifestations of PHT, including splenomegaly with hypersplenism, esophageal and gastrointestinal varicose veins, and ascites, are associated with significant morbidity and mortality. Ascites occur in about one-third of patients with PHT. Diuretic therapy and reduction of excess sodium intake are the main treatments in children. Ascites associated with low serum albumin levels may obtain good results from intravenous 20% or 25% albumin infusion followed by IV furosemide.

In diuretic refractory ascites associated with respiratory disorders, difficulty eating, or urine retention, recurrent large-volume paracentesis may be necessary. Researchers identified that ascites after surgery can predict the survival rate of BA patients after Kasai surgery. Ascites are a sign of liver cirrhosis. Patients with ascites after surgery have a worse prognosis compared to patients without ascites. Ascites and sepsis are strong prognosis factors against poor post-operative prognosis in Kasai.¹⁷⁻¹⁹

Although some conflicting results have been published regarding the impact of age during surgery, a series of large studies simultaneously show that the short-term outcomes of Kasai's surgery will be better when the surgery is performed early in life. Most of the research patients underwent Kasai surgery at more than 60 days of age. It has been proven that earlier surgical age has a good prognosis for the survival of BA patients.^{20,21} but this hypothesis is not always confirmed.^{14,22,23} An effective BA screening program is important because early diagnosis can allow for an earlier age for Kasai portoenterostomy, significantly improving short- and medium-term outcomes, including *jaundice clearance rates* (JCR), *native liver survival rates* (NLSR), and overall mortality.²⁴⁻²⁷ A retrospective study in 2015 also found that liver transplant rates were significantly lower in BA patients who underwent Kasai surgery at 60 days of age than those who underwent surgery at more than 60 days of age.²⁸ Researchers believe the need for LT could be reduced if the average age at Kasai surgery was reduced to age 50 or even 45 days. However, the best time for Kasai surgery to get better outcomes for BA patients is still controversial.^{10,16} Some studies have shown that age is not a determining factor in the success of the Kasai operation.^{14,29}

This study was able to predict the survival rate of biliary atresia patients after Kasai surgery based on data from 1 week after surgery. Although the sample was relatively small, this study could provide insight into postoperative management after Kasai surgery.

CONCLUSION

Bilirubin levels exceeding 10 mg/dL before and after the Kasai procedure and the presence of Ascites are markers of poor outcomes in biliary atresia patients after the Kasai procedure.

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