Factors influencing outcome after hepatic portoenterostomy among extrahepatic bile duct atresia patients in Hospital Sultanah Bahiyah, Alor Setar

Devkumar Namasemayam, MMED (Surg), Mohan Nallusamy, FRCS Edinburgh

Hospital Sultanah Bahiyah, Alor Setar Malaysia

ABSTRACT

Introduction: Biliary atresia implies high risk of mortality if not diagnosed and treated early. We undertook this study to assess the prognostic factors affecting the outcome of Kasai surgery.

Methods: A retrospective clinical study was conducted among 58 patients from Hospital Sultanah Bahiyah Alor Setar. Data were analysed with logistic regression analysis using SPSS. Factors studied included age during surgery, bile duct diameter at the porta hepatic, race of patient, preoperative total bilirubin level and cholangitis. These factors were analysed to determine its significance as a prognostic factor affecting the outcome of Kasai surgery.

Results: Older age group above 56 days of life, bile duct diameter at porta hepatis measuring <50µm, pre-operative total bilirubin >10mg% and cholangitis were found to be poor prognostic factors from univariate regression analysis. Variables having p value<0.025 were analysed using the multivariable regression analysis. Only age of patient and diameter of bile duct at the porta hepatis were eligible for this analysis. The final analysis showed that age 57 days of life and above (adjusted odd's ratio (aOR) = 9.412, p value = 0.042, 95% confidence interval (95%CI) = 1.079 to 82.104) and bile duct diameter <50µm (aOR = 13.812, p value = 0.016, 95%CI = 1.616 to 118.042) were significant factors affecting the outcome.

Conclusion: In conclusion, age of patient 56 days of life and younger and diameter of bile duct at porta hepatis ≥50µm gave a significantly better outcome after Kasai surgery.

KEY WORDS:
Kasai Surgery, prognostic factors

INTRODUCTION

Biliary atresia is a progressive inflammatory process that begins very soon after birth. In the most common form, called extrahepatic biliary atresia, the delicate ducts outside the liver are affected first. White blood cells invade the ducts, which become damaged and may whither or completely disappear. Bile is trapped inside the liver and rapidly causes damage and scarring to the liver cells. Further scarring of the liver tissue may result in cirrhosis. Management for biliary atresia became available in 1957 when Kasai introduced complete excision of the entire damaged biliary tree with bile drainage into a Roux-en-Y loop of jejunum, also known as hepatic portoenterostomy. Other surgeries performed are hepatic enterostomy and hepatic portocholecystostomy depending on the type of biliary atresia. There has since been some modification of this technique.[1]

Complications that patients could develop post operatively are failure of Kasai surgery, cholangitis, liver cirrhosis, portal hypertension and hepato-pulmonary syndrome. Outcome depends on prognostic factors, such as age during surgery, race, bile duct diameter, preoperative total bilirubin level and cholangitis. The aim of this study was to identify the factors affecting the outcome of Kasai surgery.

MATERIALS AND METHODS

A retrospective cohort study was performed among patients who underwent hepatic portoenterostomy (Kasai operation) in Hospital Alor Setar from 1998 to 2010. The inclusion criteria included all patients whom have undergone a Kasai procedure in Hospital Alor Star since 1998. The exclusion criteria was all patients whose records were incomplete or missing.

The sample size was calculated through Dupont and Plummer,[2] Power and sample size calculations, Version 1.0.13 (ά = 0.05, power = 0.80, m 1:1). The calculated sample size was 58 and this was taken as the sample size for this study.

Data collected was entered into SPSS 12 (Statistical Package for the Social sciences) software and analysed. Multivariable logistic regression analysis was used to identify the relationships between the variables included in the study. Statistical significance was assigned to a p value <0.05.

Independent study variables were bile duct diameter, pre-operative total bilirubin level, age of patient during surgery and cholangitis. Race was omitted because of its small sample size. Bile duct diameter was divided into three groups; no ducts, <50µm, and ≥50µm. Pre-operative total bilirubin level in mg% was divided into the following groups; 5.0-10.0mg%, 10.1-15.0mg% and >15mg%. Age of patients at operation was divided into the following groups; <28 days,

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Corresponding Author: Devkumar Namasemayam
Email: devkumarf18_26@yahoo.com

28-56 days, 57-84 days, and >84 days. The presence or absence of cholangitis included preoperative and postoperative episodes of cholangitis. Patients were divided into two groups; had one or more episodes of cholangitis either preoperatively or post operatively and had no episodes of cholangitis.

Dependant study variables (outcome variables) was post-operative total serum bilirubin level at four weeks. It was classified into three groups according to the clinical level of bile drainage and post-operative total bilirubin level (post operatively at four weeks); Group A: Bile flow restoration and free from jaundice (Total bilirubin level <2mg%), Group B: Bile flow restoration with jaundice (Total bilirubin level 2-5mg%), Group C: Minimal bile drainage with moderate jaundice (Total bilirubin level >5mg%) or failure to achieve bile flow (Total bilirubin level not decreased). Patients in group A and B was classified as satisfactory outcome while patients in group C was classified as unsatisfactory outcome. This study has received the approval of the relevant ethical committee from Hospital Universiti Sains Malaysia.

RESULTS

The preoperative patient's parameters and the outcome of the surgery categorised according to the postoperative total bilirubin levels are described in Table I.

Univariable regression analysis was performed. Older age group above 56 days of life, bile duct diameter less than 50µm, pre-operative total bilirubin level more than 10mg% and cholangitis were found to be poor prognostic factors (Table I).

Variables having p value less than 0.025 were analysed using the multivariable regression analysis. Age of patient and bile duct diameter were included for this analysis. Age of patients was regrouped into two categories, younger than 57 days of life and 57 days and above.

The goodness of fit of the model was tested by Hosmer and Lemeshow test statistics and it was found to be a good fit (p value >0.05).

DISCUSSION

Age of patient during surgery was found to be a significant factor for the outcome of Kasai surgery both in univariable and multivariable analysis. As in our study, most papers also report a better outcome before eight weeks of life or day 56 of life.

If the surgery is performed early, the acini recover and regenerate giving a better outcome. If surgery is delayed, then the acini develop scarring and fibrosis leading to a poor outcome after surgery. Fibrosis is believed to begin after four to six weeks of cholestasis and become third degree fibrosis after eight weeks.[3,4] This could be prevented if surgery is carried out before eight weeks of life and would enable the liver to drain bile after surgery.

Most patients with a preoperative total bilirubin level below 10mg% showed a satisfactory outcome while patients with preoperative total bilirubin level between 10 to 15mg% and above 15mg% showed unsatisfactory outcome postoperatively Table I.

Univariable analysis study found pre-operative total bilirubin level as a significant factor affecting the outcome but multivariable study could not be done on this variable due to a small sample size. Univariable analysis showed that patients with total pre-operative bilirubin levels more than 10mg% were at a significantly higher chance of an unsuccessful outcome compared to patients with pre-operative total bilirubin less than 10mg%.

In our study, almost 76% of patients had a diameter more than 50µm with the largest bile duct diameter measuring 207µm and smallest measuring 20µm. Many papers have studied on the outcome of Kasai surgery comparing various sizes of bile duct diameter at the porta hepatis. In this study, both univariable and multivariable analysis found that bile duct diameter more than 50µm showed a significantly better outcome compared to bile duct diameter less than 50µm (Table I, Table II).

Schweizer et al. reported that, if the total diameter of all the bile ducts at the porta hepatic was more than 400µm, it indicates a significantly better prognosis compared to patients with total bile duct diameter less than 400µm.[4] Mean while, Chandra et al. reported that larger ductal diameter more than 150µm had a significantly better bile flow post operatively compared to smaller diameter or absent bile ducts at porta hepatic.[5]

Cholangitis is a serious and common complication in patients after Kasai surgery. It is estimated that almost half of the patients would develop cholangitis within the first year after Kasai surger.[6] From a total of 58 patients in this study, 15 had one or more documented episodes of cholangitis while 43 patients had no episodes of cholangitis. There were no patients with a successful outcome in the group with cholangitis while 28 patients had a successful outcome in the group with no episodes of cholangitis (Figure 4). Univariate data analysis showed that patients who suffered cholangitis had a significantly poorer outcome (Table I). Multivariable analysis could not be performed for this variable due to a small sample size.

Progressive liver fibrosis after Kasai surgery is usually seen in patients with poor bile flow post operatively. Besides that, it occurs also in patients with episodes of cholangitis. This could also explain the reason for poor outcome in patients with episodes of cholangitis.[1,3]

Anyway, in a multicentre study in the United States from 1997 to 2000, it was found those patients with good bile flow had more episodes of cholangitis. This was possible because a patent bile duct allowed bacteria from the bowel to travel upwards into the biliary tree and cause infection.[7]

Late referral for biliary atresia continues to be a problem in Malaysia and other countries. A stool colour card system is being introduced to identify jaundiced infants with suspected biliary atresia so that referral for jaundiced infants who may have biliary atresia can be done early. Anyway, the

Table I: Preoperative patient's parameters and postoperative outcome categorised according to postoperative total bilirubin levels

Patient's parameters	Postoperative total bilirubin levels		
	<2mg% (satisfactory) n (%)	2-5mg% (satisfactory) n (%)	>5mg% (unsatisfactory) n (%)
Age (days of life)			
<56 days	1 (1.7%)	9 (15.6%)	1 (1.7%)
57-84 days	1 (1.7%)	12 (20.7%)	18 (31.0%)
>84 days	0 (0.0%)	5 (8.6%)	11 (19.0%)
Bile duct diameter			
≥50μm	2 (3.4%)	25 (43.1%)	17 (29.3%)
<50μm	0 (0.0%)	1 (1.7%)	13 (22.4%)
Cholangitis			
Present	0 (0.0%)	0 (0.0%)	15 (25.9%)
Absent	2 (3.4%)	26 (44.8%)	15 (25.9%)
Preoperative total bilirubin level (mg%)			
5.0 - 10.0 mg%	2 (3.4%)	26 (44.8%)	5 (8.6%)
10.1 -15.0 mg%	0 (0.0%)	10 (17.2%)	0 (0.0%)
>15.0 mg%	0 (0.0%)	0 (0.0%)	15 (25.9%)

Table II: Results from univariable regression analysis showing Crude odd ratio, p-value and 95% confidence interval of each factors studied upon

Variables		Crude OR	95% CI (Lower, Upper)	p-value
Age (days of life)	<56 days	1.0		
	57–84 days	13.846	1.572, 121.900	0.018
	>84 days	22.000	2.180, 221.900	0.009
Bile duct diameter (μm)	≥50μm	1.0		
	<50μm	20.647	2.472, 172.452	0.005
Cholangitis	Absent	1.0		
	Present	2.867	1.906, 4.312	<0.001
Pre-operative total bilirubin (mg%)	<10mg%	1.0		
	≥10mg%	2.681	-1.862, 3.964	<0.001

OR = odd's ratio. CI = confidence interval

Table III: Results from multivariable regression analysis showing adjusted odd ratio, p–value and 95% confidence interval of each factors studied upon

Variables		Crude OR	95% CI (Lower, Upper)	p-value
Age (days of life)	< 57 days	1.0		
	>57 days	9.412	1.079, 82.104	0.042
Bile duct diameter (μm)	≥50um	1.0		
	<50um	13.812	1.616, 118.042	0.016

OR = odd's ratio, CI= confidence interval

implementation of this needs the cooperation of our paediatric counterparts.

CONCLUSION

Patients with biliary atresia who underwent Kasai surgery in Hospital Alor Setar showed that older age group above 56 days of life, bile duct diameter less than 50μm, pre-operative total bilirubin level more than 10mg% and cholangitis were found to be poor prognostic factors. Univariable analysis in our study revealed that these factors significantly affected the outcome of Kasai surgery. Multivariable data analysis showed that age and bile duct diameter were significant factors that affected the outcome or patients.

LIMITATION OF STUDY

Not all cases which underwent Kasai's surgery since 1998 were included in this study. The records of some patients could not be traced as the identity card numbers were changed from the mother's identity card number during surgery to the child's identity card number during follow up. Some records were incomplete as in the case with many retrospective studies. Unfortunately hepatic histology was not included in this study because the pattern of pathological study varied according to the attending pathologist. The episodes of cholangitis could not be ascertained accurately for every patient because some cases were referred to Hospital Alor Setar just for the purpose of surgery. Some of these patients could have had cholangitis and treated at their respective hospitals and would not be recorded in our records.

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