RESEARCH PAPER

Outcome of Biliary Atresia After Kasai's Portoenterostomy: A 15-year Experience

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Objective: To study the outcome of Biliary atresia after Kasai's portoenterostomy and clinical and biochemical factors affecting the outcome.

Methods: Medical record review of patients of biliary atresia operated from January 2000 to December 2014. The following data were collected and analyzed - sex, age at surgery, liver function tests, associated congenital anomalies, and clearance of jaundice (at 3 months). Final outcome was classified as alive, dead, or jaundice-free at last follow-up (minimum 1 year).

Results: 121 patients (61.9% males) were included; 32 (26.5%) were lost to follow-up at 1 year. At last follow-up, out of the 89, 42 (47.2%) were alive, 29 (32.6%) were jaundice-free, and 47 (52.8%) had died. The native liver survival rate at last follow up was 43.8%. 42 (47.2%) patients had complete clearance of jaundice at 3 months post-procedure. Jaundice-clearance rate was significantly high in patients alive (83.3% *vs* 16.7%, *P*<0.001)) as compared to those who died later.

Conclusion: Jaundice clearance at 3 months post surgery is a good early indicator of long term success.

Keywords: *Conjugated hyperbilirubinemia, Jaundice, Management, Outcome.*

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Kasai portoenterostomy (KPE) is currently the surgical treatment of choice to restore bile flow and relieve jaundice in children with biliary atresia [1,2]. Outcomes from centers around the world show a lot of variability, with initial success of the KPE to achieve bile flow, ranging from 30-80% [1,3]. However, even with successful KPE, progressive inflammation and fibrosis of the intrahepatic bile ducts develops to varying degrees, leading to biliary cirrhosis and the need for liver transplantation in upto 80% of patients [4,5]. The ultimate success of KPE depends on several factors which include the patients age at the time of surgery, presence of cirrhosis, surgeon's experience with performing KPE, occurrence of postoperative cholangitis, and perhaps unknown genetic factors [3]. In this study, we present 15-year data of patients who underwent KPE at our center.

Methods

This is a retrospective chart study which included 121 patients of biliary atresia who underwent KPE, performed by a single surgeon at multiple institutions, from January 2000 to December 2014. The protocol included a clinical examination, examination of the stool color, and liver function tests to confirm the presence of obstructive jaundice. A Toxoplasmosis, Rubella virus, Cytomegalovirus, Herpes virus (TORCH) serology was done in most cases and Hepatobiliary iminodiacetic acid scan (HIDA) scan was carried out after priming with phenobarbitone. Ultrasound abdomen was routinely done to look for a distended gall bladder, the anatomy of the biliary tree, the liver echotexture, and exclude the presence of choledochal cyst. Patients in whom biliary atresia could not be excluded pre-operatively, underwent an Intra-operative cholangiogram (IOC) through a limited subcostal incision. On confirmation of biliary atresia, a KPE was performed. The portal dissection was wide and extended from the exposure of the origin of the umbilical vein from the left portal vein in the Rex fossa to the bifurcating right portal pedicle. A 45-cm Roux-en-Y loop of jejunum is created for anastomosis to the porta. All patients had a wedge liver biopsy and biopsy of the tissue from the portal plate. Post-operatively, the patients were followed up in the surgical clinic for a minimum period of one year. Patients who did not return for follow- up were contacted by telephone or letters and evaluated by a pediatric surgeon. All patients received prophylactic

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antibiotics (cotrimoxazole 2.5 mg/kg/day of trimethoprim component for 6 months), choleretics (ursode-oxycholic acid 15mg/kg/day in 2 divided doses till bilirubin normalized or 1 year post-op) and fat-soluble vitamins during follow-up.

Non-improvement of jaundice within 3 months of surgery, persistence of clay colored stools with or without progression to liver cell failure (increasing jaundice, ascites or anasarca with hypoalbuminemia, altered coagulation profile, failure to thrive) was determined as failure of KPE. Patients who were jaundice-free (bilirubin <2 mg%) without liver cell failure were classified as successful response to KPE. Patients with a failed Kasai's surgery were counseled regarding liver transplantation.

The following data were collected for each patient: sex, age at KPE, liver function tests, associated congenital anomalies. At 3 months, clearance of jaundice was noted. During follow-up visits, complications including cholangitis, upper gastrointestinal bleed, liver failure and portal hypertension were noted. For the purpose of the study, at one year follow-up, the patients who expired were considered to have a poor outcome, while those alive were considered to have a good outcome. The patients with good outcome were separated into those who were jaundiced and those who were jaundice-free.

For statistical analysis, Student's t test was used for continuous variables and chi-square test (or Fischer's-exact test) for categorical variables.

RESULTS

Data for 121 infants (75, 61.9% males) was extracted. At the end of the one-year follow-up, records of 89 (73.5%) were available; 42 (47.2%) were alive and 29 (32.6%) were jaundice-free. The native liver survival-rate at 1-year follow-up was 43.8% (39/89). The oldest patient alive is presently aged 15 years.

Mean age at the time of surgery was 103 days, with a median of 96 (range, 40-217) days. The outcome in terms of survival and jaundice-free status at 1-year follow-up was better with younger age at surgery (***Table* I**), but there was no statistical difference in the outcome between the various groups.

At the time of presentation, all patients had pale stools and dark- coloured urine. Eighty five patients (70.3%) had splenomegaly and 17 (14%) of the patients had clinical ascites on admission. All patients had elevated total and direct bilirubin levels. The levels of the biochemical markers had no association with the final outcome (***Table* II**). Out of the 78 patients tested for TORCH, 39 had CMV IGM positive and were treated with gancicyclovir.

Thirty three (27.8%) patients had associated congenital anomalies, with 9 (7.5%) having more than one anomaly. The anomalies were as follows, polysplenia: 13 (10.7%), umbilical hernia: 13 (10.7%), situs inversus: 3 (2.5%), inguinal hernia: 4 (3.3%), Meckel's diverticulum, malrotation of gut, cardiac anomalies: 2 each (1.7%), and hepatic artery variations: 5 (4.1%). The jaundice clearance rate at 3 months post-KPE was 47.2% (42-89). Of the jaundice-free patients after 3 months, 35 (83.3%) are alive, while 7 (16.7%) are dead. The Jaundice clearance rate at 3 months post-operatively was significantly higher (P<0.001) in the patients who are alive to those who expired.

TABLE I ASSOCIATION OF AGE AT SURGERY WITH OUTCOME

Age, d	*Alive, No. (%)*	**Jaundice free, No.(%)*
<60 (*n*=11)	7 (63.6)	6 (54.5)
60-90 (*n*=31)	16 (51.6)	12 (38.7)
90-120 (*n*=28)	12 (42.9)	8 (28.6)
>120 (*n*=19)	7 (36.8)	3 (15.8)
Total (*n*=89)	42 (47.2)	29 (32.6)

**at one year after Kasai portoenterostomy.*

TABLE II BIOCHEMICAL PROFILE OF CHILDREN WITH BILIARY ATRESIA UNDERGOING KASAI PORTOENTEROSTOMY

Variable	*Total*	*Children alive at 1-year*		*Jaundice-free at 1-year*	
		Mean (SD)	*P-value**	*Mean (SD)*	*P-value#*
Total bilirubin (mg/dL)	11.4 (4.8)	10.8 (3.3)	0.8	10.6 (3.7)	0.9
Direct bilirubin* (mg/dL)	6.5 (2.9)	6.3 (2.6)	0.87	6.3 (2.8)	0.79
SGOT (IU/L)	276.2 (230.4)	279.3 (232)	0.95	281.4 (234.2)	0.83
SGPT(IU/L)	227.5 (338.9)	235.1 (177.6)	0.78	234.3 (202.5)	0.69
Alkaline Phosphatase(IU/L)	1234.3 (910.4)	1192.4 (829.4)	0.45	1212.4 (887.7)	0.54
GGTP(IU/L)	513.3 (357.8)	464.6 (357.8)	0.25	486.2 (348.8)	0.34

**Compares levels between those alive at 1 year and those died; #Compares levels between those jaundice-free at 1-year and those with jaundice.*

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WHAT THIS STUDY ADDS?

- Jaundice-clearance at 3-months post-operatively is a good early indicator of long-term success of Kasai portoenterostomy.

Of the patients who were alive, 13 patients had jaundice with yellow stools, 10 patients had ascites and 3 patients had portal hypertension with episodes of upper gastrointestinal bleed (being managed medically). Of the patients who were alive and jaundice-free, 6/29 (20.6%) had episodes of cholangitis (3 having multiple episodes) in the first year requiring admission and intravenous antibiotics. Three patients had undergone liver transplant and at present are jaundice-free with good growth and development for age.

Thirteen (26.5%) children died within two weeks of surgery with peri-operative complications (sepsis, hemorrhage, DIC, electrolyte imbalance, ventilator associated pneumonia). Another 13 died between 2 weeks and 3 months of surgery with persistent jaundice, cholangitis and sepsis. Twenty (40.8%) patients died beyond 3 months with initial clearance of jaundice, which recurred, with cause of death being liver cell failure or portal hypertension. Three of the patients who died beyond 3 months had complete clearance of jaundice after 3 months of surgery but died due to lower respiratory tract infections. In all the patients that died, only 7 patients had clearance of jaundice by 3 months after surgery.

DISCUSSION

In our series, the outcome of the patients was best when operated before 60 days of age and worsened with age. Inspite of a fairly good volume of cases in this study, a vast majority was operated after 60 days of age, with less than half being alive and about a third being jaundice-free after one year. The post-operative bilirubin values at 3 months had predictive value, with those with jaundice clearance at 3 months faring better than the rest.

The limitations in our study include loss of follow-up of a quarter of cases, non-inclusion of data of histopathological factors, and short follow up.

The recommendation, in European countries, to perform KPEs at centres doing at least 5 cases / year to achieve a better outcome was comfortably achieved in this series [6]. In most studies, the eventual outcome after KPE was better if done before 45-60 days of age [7-11]; though the age at KPE in majority of the patients was beyond 60 days in Indian studies [12-15], unlike international data [3,4,7-11]. Ten-year survival rates from 73%-92% have been reported in infants in whom jaundice cleared following KPE. Hence, the 3-month post-KPE jaundice clearance, was a useful early biomarker, reflecting the early-phase success. The outcomes after KPE across the world revealed overall survival at 2 years at 73-84%, while overall survival with the native liver being 30-60% [2,7]. Although, the survival figures in this series match the world wide figures with native livers, the overall survival figures (73-84%) cannot be compared because of poor percentage of patients undergoing liver transplantation.

In our study, the upper limit of the age of surgery was not fixed as we have seen patients responding to KPE done even after 90 days of age (upto 170 days of life). This is of particular importance because most of the patients requiring a liver transplant do not opt for it and eventually are lost to follow-up [15]. On the other hand, the major hurdle in performing early surgery was the late mean age of referral almost after 75 days of life. This factor of delayed presentation to a tertiary care center like ours which leads to delayed surgery, has been perhaps the major cause of poor outcome in terms of survival and jaundice free life in the Indian setting [13,14]. These tertiary care centres should not only offer KPE but liver transplant programs at economical packages to improve the overall situation in a developing country like ours.

Although, the overall outcome and jaundice clearance after KPE in BA is better with early surgery, it has moderate levels of success even in the best of hands. Jaundice clearance at 3months post-operatively is a good early indicator of long term success.

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