Post Kasai prognosis factor

Articles review

- A 2013 systematic review found that survival rates with native liver following Kasai portoenterostomy ranged from 20 to 76% at 1–3 years and 24–53% at 10 years .
- In cases where Kasai portoenterostomy is either not performed or deemed to have failed, liver transplantation is the only definitive therapeutic option.

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PEDIATRIC GASTROENTEROLOGY (S ORENSTEIN, SECTION EDITOR)

Early and Peri-operative Prognostic Indicators in Infants Undergoing Hepatic Portoenterostomy for Biliary Atresia: a Review

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Histopathology

- **In the past few decades, a number of studies have been conducted seeking to establish histological findings which may predict outcome following hepatic portoenterostomy. In general, results have often been contradictory and thus far no consensus agreement exists.**

- Miyano et al. classified their group of 40 patients histologically according to the diameter of the ductal structure present in the remnant of the extrahepatic duct

- They showed a correlation between younger age at portoenterostomy and type 1 findings—described by them as luminal ductal diameter of ≥100 μ and a relative paucity of ductal inflammation and hepatic fibrosis. They proposed (without demonstrating) that greater lumen size and milder inflammatory change equated to better postoperative outcomes.

- These findings were supported by Chandra and Altman who in their retrospective review of 34 patients with biliary atresia found that the presence of a measurable lumen was favourably associated with post-operative biliary drainage

- **A Danish study involving 40 patients and reporting a single, national centre's 24-year experience found that the number, length and degree of proliferation of biliary ductal remnants was positively associated with jaundice-free native liver survival following portoenterostomy.**

- **The King's College Hospital group, however, found no relationship between either the number or size of biliary ductules in the proximal bile duct remnant and biliary drainage following portoenterostomy.**

- **retrospective review of 29 patients who had undergone portoenterostomy between 1999 and 2014 in Sydney, Australia, the absence of bridging fibrosis (defined as histological evidence of fibrosis between adjacent portal areas and central veins) was the only factor associated with improved native liver survival at 5 years.**

- **An innovative Japanese study attempted to draw a link between bile canalicular contraction and post-operative biliary drainage in infants who had undergone portoenterstomy . By measuring actin and myosin volumes using histochemical and immunocytochemical methods, the authors reported that in their sample of 13 patients, increased levels of bile canalicular membraneassociated filaments (particularly actin and myosin) were associated with either no or poor post-operative jaundice clearance. Another study to employ immunocytochemical staining in its methodology found a correlation between high proliferating cell nuclear antigen (PCNA) and poor jaundice clearance following portoenterostomy.The authors suggested that this finding reflected the more severely damaged liver trying to actively regenerate itself.**

- **A Brazilian study which performed immunohistochemical staining for cytokeratin 7 (CK7) on wedge liver biopsies obtained from 47 patients at the time of portoenterostomy showed a positive association between the extent of CK7 positivity (as a marker for biliary proliferation) and one-year native liver survival.**

- **Davenport and Howard described a macroscopic appearance at portoenterostomy (MAP) score to serve as an intraoperative prognostic variable .**

They found a significant association between higher MAP scores and the persistence of jaundice following portoenterostomy.

ORIGINAL ARTICLE

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

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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

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

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

Age

- Early age at portoenterostomy has been widely, though not universally, associated with successful biliary drainage and native liver survival.

A recently published cohort study involving 217 patients showed age ≥45 days at portoenterostomy was associated with poor native liver survival on univariate (but not multivariate) analysis

A large single-centre study which included 244 patients found that on multivariate analysis, an age cutoff of greater than 90 days at portoenterostomy was associated with poor native liver survival at 5 years.

Table 1 Recent national studies of outcome in biliary atresia

	n	Period	Age at surgery	Clearance of jaundice
National series				
England and Wales	439	1999–2009	54 days	55%
Finland, Sweden, Norway, and Denmark	148	2005–2016	64 days	64%
The Netherlands	104	1998–2008	59 days	38%
France	339	2003–2009	59 days	36%

Biomarkers

- A few studies have sought to identify non-invasive prognostic indicators in children with biliary atresia.

The aspartate aminotransferase (AST) to platelet ratio or APRI is calculated using the formula [AST/upper limit of normal (ULN)]/platelet count (expressed as platelets × 109 /L) × 100. This index was initially developed as a non-invasive means to predict hepatic fibrosis in patients with chronic hepatitis C

- In evaluating their retrospective cohort of up to 91 children, Yang et al.

found that pre-Kasai APRI correlated significantly with liver fibrosis based on Metavir scores and with persistence of jaundice following portoenterostomy. In their study, an APRI of 0.75 and 0.81 was able to predict significant fibrosis and cirrhosis, respectively, whereas an APRI of 0.60 predicted ongoing cholestasis with a sensitivity of 66.7% and a specificity of 83.3%, respectively.

- raised serum hyaluronic acid level before portoenterostomy strongly correlates with either death or need for liver transplantation by 5 years of age.

- urinary excretion of D-glutaric acid, a metabolite of the cytochrome P-450 pathway had significant correlation with degree of hepatic fibrosis and post-Kasai biliary drainage. In their small sample of 12 patients, 24-hour urinary collection was performed before portoenterostomy. The authors found that urinary D-glutaric acid levels were significantly lower in infants with persistent jaundice following, and more marked liver fibrosis at, the time of portoenterostomy.

Infections

- The aetiology of biliary atresia remains elusive. Hepatotropic viral exposure, either directly causing bile duct destruction or by eliciting an autoimmune reaction, has been proposed as a causative mechanism.

- A Chinese study published in 2012 demonstrated the presence of CMV DNA in 51 out of 85 liver bjopsy samples obtained at the time of Kasai portoenterostomy. The authors also showed in the same publication, an in-vitro cytopathic effect of CMV within intra-hepatic biliary epitheilial cells, thereby, according to them, suggesting a causal link between CMV infection and biliary atresia within their population.

- In a recent publication, Zani et al. suggested that infants with biliary atresia who were CMV IgM positive constituted a distinct aetiological and prognostic sub-group .

They compared a group of 20 infants who were CMV IgM positive with 111 who were CMV IgM negative, at initial presentation with biliary atresia. Over a median follow-up period of 2.75 years, the authors demonstrated significantly reduced jaundice clearance, native liver survival and true survival in the CMV IgM positive cohort following hepatic portoenterostomy. Other reports have similarly suggested a link between CMV infection and poor outcome following the Kasai procedure, with some proposing that anti-viral therapy may have a role in this setting.

- Conversely, however, in a 2012 German study, the presence of hepatotropic viruses on wedge liver biopsy at the time of the Kasai procedure was not found to be a significant prognostic indicator .

Their results included 66 prospectively enrolled infants whose biopsy samples were screened by polymerase chain reaction for common hepatic viruses. They found no difference in post-portoenterostomy survival (with or without native liver) nor laboratory parameters, including bilirubin, among the virus-positive and virus-negative groups.

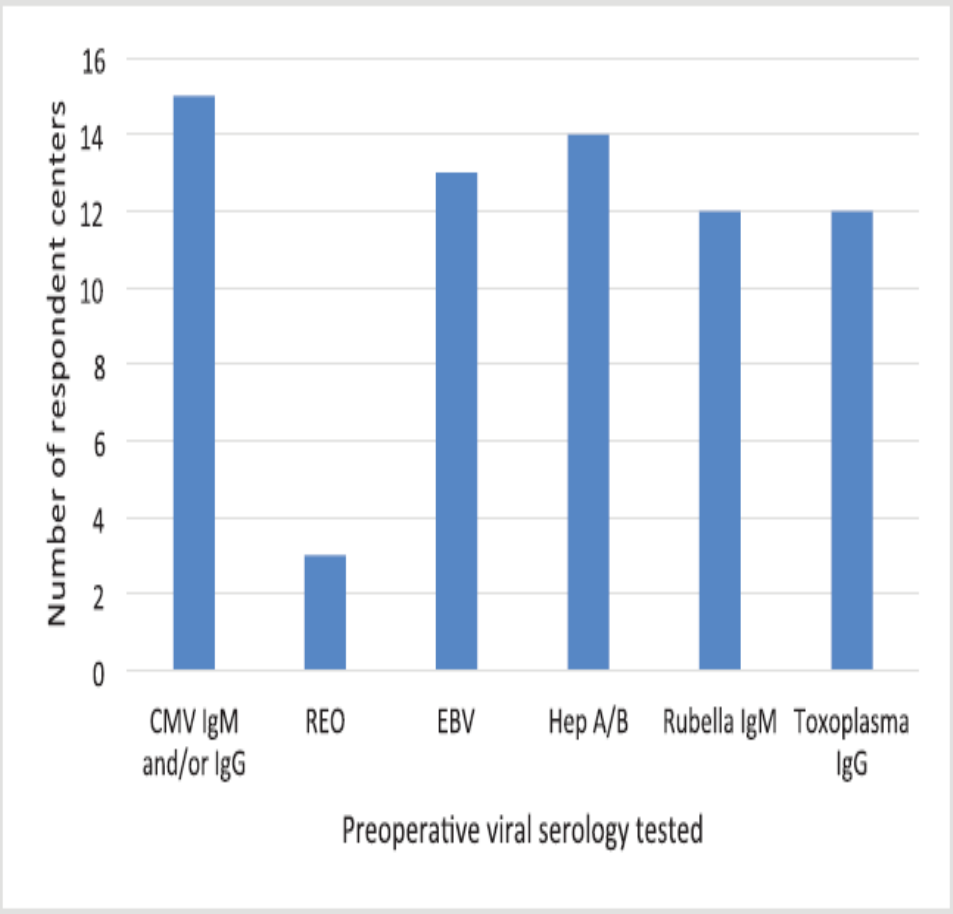

Fig. 2 Distribution of preoperative viruses tested. CMV, cytomegalovirus; Hep; hepatitis; IgG, immunoglobulin G; IgM, immunoglobulin M; REO, reovirus.

Research Article

EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

Long-term native liver fibrosis in biliary atresia: Development of a novel scoring system using histology and standard liver tests

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Background & Aims: Although liver fibrosis is an important predictor of outcomes for biliary atresia (BA), postsurgical native liver histology has not been well reported. Here, we retrospec-

Conclusions: In postsurgical BA patients aged ⩾1 year, the BALF score is a potential non-invasive marker of native liver fibrosis.

- Results: Natural logarithms of the serum total bilirubin, c-glutamyltransferase,and albumin levels, and age were selected as

significantly independent variables for the BALF score equation.

The BALF score had a good diagnostic power (AUROCs = 0.86–0.94, $p < 0.001$) and good diagnostic accuracy (79.4–93.3%) for each fibrosis grade.

The BALF score revealed a strong correlation with fibrosis grade ($r = 0.77$, $p < 0.001$), and was the preferable non-invasive marker for diagnosing fibrosis grades PF2. In a serial liver histology subgroup analysis, 7/15 patients exhibited liver fibrosis improvement with BALF scores being equivalent to histological fibrosis grades of F0–1.

- BALF score = 7:196 +1:438 * Loge TB mg/dl + 0:434* Loge (GGT (IU/L) -3:491 * Loge (albumin (g/dlÞ)
- 0:670 * Loge (age years)

Table 1. Baseline data, stratified by histological fibrosis grade, for the development of the biliary atresia liver fibrosis (BALF) score.

	F0 (n = 15)	F1 (n = 53)	F2 (n = 44)	F3 (n = 34)	F4 (n = 34)
TB (mg/dl)	0.5 (0.2-0.9)	0.7 (0.3-10.1)	0.8 (0.3-11.5)	1.9 (0.4-24.5)	7.2 (0.3-30.1)
AST (IU/L)	33 (25-83)	36 (18-550)	75 (22-251)	108 (35-1065)	181 (94-472)
ALT (IU/L)	22 (14-79)	35 (9-676)	64 (13-457)	86 (21-411)	133 (37-587)
GGT (IU/L)	44 (10-102)	68 (7-1108)	142 (8-1384)	204 (66-1456)	317 (32-1817)
Albumin (g/dl)	4.4 (3.7-4.7)	4.1 (3.1-5.1)	4.0 (3.0-5.1)	3.7 (2.4-4.6)	3.2 (1.5-4.5)
ChE (IU/L)	326 (220-598)	342 (97-567)	278 (122-581)	185 (46-335)	141 (43-323)
PT-INR	1.07 (1.00-1.21)	1.07 (0.91-1.47)	1.03 (0.86-1.25)	1.04 (0.86-2.01)	1.14 (0.89-1.48)
Platelet count (× 10^9/L)	141 (70-356)	165 (52-372)	127 (45-392)	113 (56-446)	152 (42-524)
Age (yr)	9.7 (1.1-18.8)	7.0 (1.2-19.9)	5.3 (1.2-19.2)	7.4 (1.1-25.4)	2.4 (1.0-33.6)

Data are presented as median (range).

TB, total bilirubin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ-glutamyltransferase; ChE, cholinesterase; PT-INR, prothrombin time-international normalized ratio.

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Long-term Outcome of Children With Biliary Atresia Who Were Not Transplanted After the Kasai Operation: >20-year Experience at a Children's Hospital

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ABSTRACT

Objective: Sequential strategies combining the Kasai operation as a first-line treatment and liver transplantation as a

already developed liver cirrhosis and its sequelae. Episodes of cholangitis and gastrointestinal bleeding occurred after

- Results: The 5-, 10-, and 20-year survival rates of patients with

their native livers were 63%, 54%, and 44%, respectively. The survival rates varied significantly depending on the type of BA, age at initial Kasai operation, era of surgery, and surgical method. By age 20, nearly half of the adult survivors had already developed liver cirrhosis and its sequelae.

Episodes of cholangitis and gastrointestinal bleeding occurred after 20 years of age in 37% and 17% of the adult patients,respectively, and 20% of the adult patients died of liver failure or underwent living-related partial liver transplantation in their 20s. Five female patients gave birth to a total of 9 children, and 1 male patient fathered a child.

Regards

- Doaa Alharazi
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