Cholangitis definition and treatment after Kasai hepatoportoenterostomy for biliary atresia: TRACK-BA study (TRacking Cholangitis post Kasai in Biliary Atresia)

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Summary

- Prospective, observational international feasibility study (NCT number pending, Protocol ID 2021-01251)
- Any hospital treating biliary atresia patients after Kasai hepatoportoenterostomy can participate.
- Inclusion: All patients presenting with suspected and confirmed cholangitis during the first year after Kasai hepatoportoenterostomy
- **Twelve months data collection** period. **No** changes should be made to normal patient care/ follow-up pathways.
- Primary outcome: Applicability of the cholangitis definition and management guidelines in a broad clinical setting.
- All collaborators will be included as PubMed-citable co-authors on resulting publications.

Background

- Acute cholangitis is one of the most serious complications after Kasai hepatoportoenterostomy for biliary atresia due to its negative impact on prognosis, repeated bouts of cholangitis decreasing patient survival.
- In the absence of standard criteria for diagnosis of acute cholangitis after Kasai hepatoportoenterostomy, practical treatment guidelines have never been established; over and under treatment might be avoided, reporting might be standardized.
- Definition and treatment of cholangitis after Kasai hepatoportoenterostomy were established through a Delphi method, an extensive literature review, iterative rounds of surveys and expert panel discussions*.
- This feasibility study will collect data about biliary atresia patients clinically diagnosed to have a cholangitis during the 1st year after Kasai, so that data for suspected and confirmed cholangitis can be assessed.

* **Cholangitis definition and treatment after Kasai hepatoportoenterostomy for biliary atresia: a Delphi process and international expert panel**

Cholangitis definition and treatment protocol version 4.0 (16 Avril 2025)

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Primary aim
To assess the applicability of the definitions (Figure 1) for suspected and confirmed cholangitis.

Primary analysis
Prospective application of diagnostic criteria to the patients suspected of acute cholangitis on a clinical basis.

Inclusion criteria: patients with a suspected diagnosis cholangitis within 1 year after Kasai hepatoportoenterostomy:

- This includes patients for whom (1) cholangitis will not be finally confirmed (**please do NOT exclude these patients!)**, (2) cholangitis is finally confirmed.

Exclusion criteria: recurrent cholangitis, cholangitis >1 year after Kasai.

In this study, patients were considered to have had an acute cholangitis based on three criteria:

1. clinical confirmation by clinicians.
2. clinical remission due to antimicrobial therapy.
3. laboratory values improvement after antimicrobial therapy.

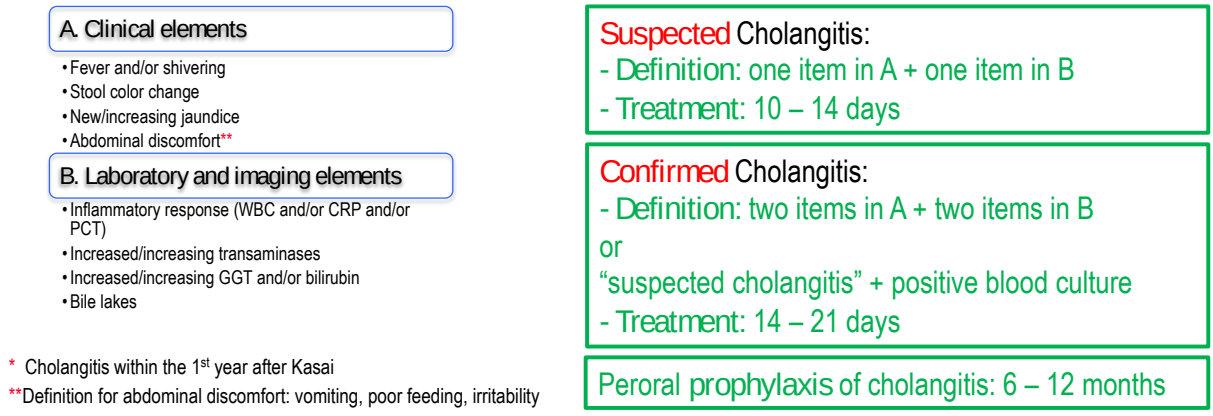

Figure 1: definitions of suspected and confirmed cholangitis, used in this study.

Bile lakes were defined as bile containing solitary or multiple cystic intrahepatic lesions following the portal tracts.

Secondary aims

- Validate the duration of treatment for suspected and confirmed cholangitis

Analysis

Assess the actual duration of treatment and compare it with the proposed duration of antibiotic treatment

Data will only be released at regional and country-level. No hospital-level outcomes data will be published.

Methodology

- Prospective observational feasibility study.
- All hospitals caring for patients with biliary atresia are eligible to participate.
- Collaborators will collect data on all consecutive eligible cases.
- **Data will be completely anonymized and subjects cannot be re-identified.**
- A mini-team of around three collaborators will collect data over 12 months:
    - The first day of data collection will be starting with 1st June 2025.
    - Multiple mini-teams may participate at the same hospital.
    - We suggest that at least one mini-team participating within your specialty should include a senior (consultant/ attending) doctor.

Inclusion criteria

- Any biliary atresia patient within 1 year after Kasai suspected to have a cholangitis.
- All connected specialties including: pediatric surgery, hepatology, pediatrics, emergency care, intensive care.
- Outpatient clinic and inpatient included.

Follow-up

This is an observational study and **no** changes should be made to normal patient pathways, and no additional patient follow-up is required. Patients should have clinical follow-up as per normal practice at their hospital. Follow-up data should be entered at the end of the study period following first presentation based on written patient notes, computer records, or telephone/in-person follow-up.

Data collection

Data will be collected and stored online through a secure server running the Research Electronic Data Capture (REDCap) web application. REDCap allows collaborators to enter and store data in a secure system. A designated collaborator at each participating site will be provided with REDCap project server login details, allowing them to securely submit data on to the REDCap system. The REDCap server is managed by the Geneva University Hospitals, Switzerland. Only anonymized data will be uploaded to the database. No patient identifiable data will be collected. The study will be carried out in accordance with national and international guidelines, as well as the basic principles of the protection of the rights and dignity of Human Beings, as set out in the Helsinki Declaration (75th Assembly Fortaleza, Brazil, in October 2024), and according to locally applicable legislation.

Local approvals

Principal investigators at each participating site is responsible for obtaining necessary local approvals in line with their hospital's regulations. Collaborators will be required to confirm that a local approval is in place at the time of uploading each patient record to the study database. Whatever approvals pathway is followed, it should be highlighted that this is an investigator-led, non-commercial, observational (no changes to normal patient care) study which is extremely low risk, as only routinely available non-identifiable data will be collected.

Possible pathways to register this study include:

- Research (e.g. research ethics committee or institutional review board approvals). Written patient consent should only be taken if required by your local ethics committee.
- Data from pre existing database
- Service evaluation.
- Clinical audit (e.g. approval process in the UK).

Authorship

Up to three collaborators may participate in each team that collects data over a 12-months period. Collaborators from each site who contribute patients will be recognized on any resulting publications as PubMed-citable co-authors.

Case Report Form

Baseline	
Age	< 1 month, 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 12 months
Age at Kasai	< 4 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, 16 weeks, >16 weeks
Sex	>Female >Male >Other
Cholangitis diagnosis	
Age at cholangitis	< 1 month, 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 12 months, 13 months, 14 months, 15 months, 16 months, 17 months, 18 months, 19 months, 20 months, 21 months, 22 months, 23 months
Were any of the following clinical elements present at the patients with suspected cholangitis *(tick all that apply)*	>Fever and/or shivering* >Stool color change >New/increasing jaundice >Abdominal discomfort** * Body temperature > 38° ** Vomiting, poor feeding, irritability
Were any of the following laboratory and imaging elements present at the patients with suspected cholangitis *(tick all that apply)*	>Inflammatory response (WBC and/or CRP and/or PCT) >Increased or increasing transaminases (1.5 VN) >Increased or increasing GGT (1.5 VN) and/or bilirubin >Bile lakes >Positive blood cultures
Suspected cholangitis diagnosis according to the physician's appraisal **w/o using the study definitions**	>Yes >No >If no: final diagnosis:……
Confirmed cholangitis diagnosis according to the physician's appraisal **w/o using the study definitions**	>Yes >No >If no: final diagnosis:……

If confirmed Cholangitis How was the diagnosis made? *(tick all that apply)*	>Clinical diagnosis >Responded to antibiotic treatment >Purulent bile discharge if bile lake drained >On liver biopsy if biopsy performed >Other (please specify): ……..
Were the study definitions for confirmed and suspected cholangitis used?	>Yes >No
What were the limitations you encountered in applying the provided definitions?	……. …….
Cholangitis prophylaxis and treatment	
Was the patient on prophylaxis when cholangitis occurred?	>Yes >No
When was prophylaxis initiated?	>After Kasai >After the 1st cholangitis episode >After the 2nd cholangitis episode >Other (please specify): ……..
What was the intended duration for prophylaxis after Kasai?	>3-6 months >6-9 months >9-12 months >More than 12 months >Other: please specify
If yes, what treatment was the patient getting?	>Sulfamethoxazole and trimethoprim >Oral cephalosporin >Amoxicillin and clavulanic acid >Other: please specify ……
What treatment did the patient get for this cholangitis episode?	>Tazobactam and piperacillin >Ceftriaxone >Ciprofloxacin >Other: please specify …..
For how long was the patient treated?	>Less than1 week >10 days >2 weeks >3 weeks >More than 3 weeks

Was the patient prescribed prophylaxis after this cholangitis episode?	>Yes >No
What was the intended duration for prophylaxis after this episode of cholangitis?	>3-6 months >6-9 months >9-12 months >More than 12 months >Other: please specify
Did the patient experience a new cholangitis episode during the study period?	>Yes >No
What was the patient ‘s status after this cholangitis episode?	>Dead >Alive
General information	
How many biliary atresia patients were diagnosed during the last 12 months in your center?	>…….
Do you have other comments or suggestions?	>……