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ORIGINAL ARTICLE

Incidence of Cholangitis and Impact of Antibiotic Prophylaxis after Kasai Portoenterostomy: A 15-Year Retrospective Study

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ABSTRACT

Objectives: This study evaluates the incidence, timing (early versus late), and clinical outcomes of post-Kasai cholangitis in a tertiary hospital over a 15-year period; the impact of oral antibiotic prophylaxis on the frequency of episodes, timing of onset, and duration of hospitalization; and to characterize the demographic, clinical, and microbiologic profiles of the cohort, including comparison of etiologic agents and antimicrobial resistance patterns between patients who received prophylaxis and those who did not.

Methodology: A retrospective cohort of 63 infants who underwent Kasai portoenterostomy (KPE) from January 2010 to March 2025 was analyzed. Demographic and clinical data, use of oral antibiotic prophylaxis (61.9%), as well as the incidence, timing, and outcomes of cholangitis and duration of hospitalization were evaluated. Associations were assessed using odds ratios (OR) with 95% confidence intervals (CI) and Fisher's exact test.

The primary outcome was the incidence of acute cholangitis following KPE, including its overall frequency (49.2%) and the impact of antibiotic prophylaxis on reducing its occurrence. Secondary outcomes included the timing of onset (early versus late), length of hospital stay, microbiologic profile (including causative organisms and culture results), antimicrobial resistance patterns (MDR, ESBL, XDR), and the clinical and demographic characteristics of the cohort, such as gestational age, sex, and baseline liver function at the time of surgery.

Results: Cholangitis occurred in 49.2% of patients, mostly within six months post-surgery. Antibiotic prophylaxis showed no significant reduction in incidence (46.2% vs. 54.2%; OR 0.73, p = 0.62) but was associated with shorter hospital stays (<10 days: 61.1% vs. 38.5%; OR 2.51, p = 0.29). Early cholangitis (<6 months) was less frequent with prophylaxis. Culture-proven infections were rare (10.3% vs. 8.3%). One patient without prophylaxis developed fatal extensively drug-resistant *Klebsiella pneumoniae* infection.

Conclusion: Cholangitis remains common after KPE, particularly within six months. Although prophylaxis did not significantly lower incidence, its link to shorter hospitalization suggests reduced severity or faster recovery; however, the lack of statistical significance in the primary outcome warrants further research to strengthen such findings. The emergence of resistant pathogens highlights the need for careful antibiotic stewardship and further prospective research on optimal prophylactic strategies.

KEYWORDS: Biliary atresia, Kasai portoenterostomy, cholangitis, antibiotic prophylaxis, native liver survival

INTRODUCTION

Biliary atresia (BA) is a rare but serious congenital condition in infants, characterized by obstruction or absence of the bile ducts, which prevents bile flow from the liver to the intestine. This leads to progressive cholestasis, hepatocellular damage, fibrosis, and, if untreated, liver failure and death.[1] The Kasai portoenterostomy (KPE) is the primary surgical treatment for BA. By excising the atretic extrahepatic ducts and anastomosing a Roux-en-Y jejunal loop to the porta hepatis, bile drainage is re-established.[2] Although not curative, the Kasai procedure can significantly prolong native liver survival, particularly when performed early in life. One of the most frequent and serious complications following KPE is acute cholangitis, a bacterial infection of the biliary tract.[2]

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Cholangitis not only increases short-term morbidity through recurrent hospitalizations and prolonged antibiotic therapy but also accelerates long-term liver injury, contributing to cirrhosis and the need for liver transplantation. Recurrent episodes, in particular, are strongly associated with reduced native liver survival.

Globally, the reported incidence of BA varies, from 1 in 5,000 live births in Taiwan to 1 in 20,000 in Europe, North America, and other regions.[1] Post-Kasai cholangitis is reported in 40–93% of patients, with most episodes occurring within the first year of life.[3] However, there remains a lack of data in the Philippine setting. While the Philippine Pediatric Society registry documented 585 cases of cholangitis from 2006 to 2025,[4] the etiology of these cases, particularly post-Kasai episodes, has not been well characterized. At our institution, 70 children underwent KPE between January 2010 and March 2025, with some receiving oral antibiotic prophylaxis and others not.

Given the variability in reported incidence and outcomes of post-Kasai cholangitis, along with the lack of consensus on the effectiveness of antibiotic prophylaxis after KPE, particularly in low- and middle-income settings, a better understanding of its clinical course and the role of prophylaxis in the local context is essential.

This study primarily aims to evaluate the incidence, timing, and clinical outcomes of cholangitis following the Kasai procedure in a tertiary hospital over a 15-year period, and to determine the effectiveness of oral antibiotic prophylaxis in reducing its occurrence. Secondarily, it aims to characterize the demographic and clinical profiles of infants with biliary atresia who underwent the Kasai procedure, and to compare those who developed cholangitis with those who did not, with particular focus on the use of oral antibiotic prophylaxis, timing of onset of acute episodes, and identified etiologic agents.

The development of vaccines and implementation of immunization programs have significantly prevented more than 20 life-threatening diseases worldwide.[1] Because of vaccination, morbidity has decreased by 90% to 100% compared to annual cases in the 20th century.[2] However, immunization campaigns were severely affected when the coronavirus disease 2019 (COVID-19) was declared a global pandemic in March 2020. Twenty-three (23) million children worldwide missed their recommended vaccines that year.[3] The greatest decline was observed in April 2020, when 33% fewer DTP3 doses were administered globally.[4] Measles vaccination campaigns were stopped in 27 countries and polio vaccination campaigns were postponed in 38 countries.[5] As a result, measles-containing vaccine (MCV1) coverage dropped to 84% in 2020, while the estimated DTP3 and polio global coverage dropped to 83%. This led to about 17.1 million zero-dose children recorded who did not receive the first dose of DTP, an increase of 3.5 million from 2019.[6]

In the Philippines, prior to the pandemic, the country's DPT3 vaccination coverage fell by 14 percentage points between 2010 and 2019. This resulted from vaccine stock-outs and vaccine hesitancy due to concerns about potential or real adverse effects of vaccination.[7] The country's immunization program however was further challenged when routine childhood vaccination was temporarily suspended due to the COVID-19 pandemic restrictions. As a result of global disruptions in childhood immunization programs, approximately 80 million children under the age of 1 are estimated to be at risk of VPDs.[5]

MATERIALS AND METHODS

This retrospective cohort study included all patients with biliary atresia who underwent the Kasai procedure and met the inclusion criteria from January 2010 to March 2025. No formal sample size calculation was performed, as all available cases were included, which may limit the ability to detect statistically significant differences between groups. To maintain confidentiality and reduce bias, patient anonymity was maintained by assigning codes and omitting identifiers. All eligible patients with Biliary Atresia who underwent KASAI procedure were included in this study, while patients with a history of cholangitis prior to surgery were excluded.

Independent variables in this study include age, sex, age at diagnosis, age at surgery, baseline liver function tests, and use of postoperative antibiotic prophylaxis. For patients included in the study, the initiation of post-Kasai antibiotic prophylaxis was upon the discretion of the attending gastroenterologist as to type of antibiotic (amoxicillin, cefalexin, co-amoxiclav, cotrimoxazole, cefuroxime, sultamicillin), timing of initiation and duration spanning from 6 to 12 months. Adherence to antibiotic prophylaxis was inferred from follow-up attendance at the gastroenterology clinic; however, due to the study design, true adherence could not be reliably assessed.

The decision to initiate antibiotic prophylaxis was left to the attending physician's clinical judgment based on perioperative conditions, as no standardized institutional protocol was in place.

The outcomes measured were timing of the first cholangitis episode, duration of illness, etiologic agents isolated, subsequent admissions, and outpatient follow-up visit as documented in the patient record. The diagnosis of cholangitis was based on published consensus criteria[3] and documented chart entries indicating a final diagnosis, all of which were confirmed by specialists.

Descriptive statistics such as mean and standard deviation were used to present continuous data while frequency and percentage were used for categorical data. Chi-Square test was used for sufficient categorical data, while Fisher's Exact test was applied to calculate data sets with smaller counts. DataStatPro (Version 2.2.3, DSRConsult LLC, Sheridan, WY, USA) a browser-based cloud-centric statistical analysis platform accessible for free via https://datastatpro.com was the software used in this study. The final sample included 63 of 70 patients (from both prophylaxis and non-prophylaxis groups), as 7 were excluded due to incomplete charts. Consequently, key clinical variables such as age at surgery, baseline liver function, and timing of diagnosis could not be adjusted for and may act as potential confounders.

This study adhered to the ethical guidelines and principles of the World Health Organization and the International Conference on Harmonization, Good Clinical Practice. It was conducted only after obtaining approval from the Institutional Review Board Ethics Committee of the institution. All collected data were stored in a password-protected Excel file and will be permanently deleted ten years after publication.

RESULTS

Majority of infants with biliary atresia were born at term (96.8%) and slightly more than half were female (57.1%). Most patients were diagnosed (77.8%) and underwent surgery (82.5%) beyond 2 months of life. Antibiotic prophylaxis was administered to 61.9% of the cohort. Mean baseline liver function tests showed elevated total bilirubin and transaminases, with slightly low albumin levels, reflecting significant hepatic dysfunction at the time of surgery (Table 1).

Table 2 summarizes the association between antibiotic prophylaxis and the occurrence of cholangitis following the Kasai procedure. Among patients who received prophylaxis, 46.2% developed cholangitis compared with 54.2% in those without prophylaxis,

Table 1. Demographic and clinical profile of infants with biliary atresia who underwent Kasai procedure (N = 63)

Variable	With Prophylaxis	Without Prophylaxis	Frequency (n=63)	Percentage (%)
Age of Gestation				
· Preterm (<37 weeks)	1	1	2	3.2
· Term (37–41 weeks)	38	23	61	96.8
· Post-term (>41 weeks)	0	0	0	0
Sex				
· Male	15	12	27	42.9
· Female	23	13	36	57.1
Age at Diagnosis				
· < 2 months of life	10	4	14	22.2
· ≥ 2 months of life	29	20	49	77.8
Age at Operation				
· < 2 months of life	7	4	11	17.5
· ≥ 2 months of life	32	20	52	82.5
Antibiotic Prophylaxis				
· With prophylaxis	-	-	39	61.9
· Without prophylaxis	-	-	24	38.1
Liver Function Tests (Mean values)				
· Total Bilirubin (mg/dL)	-	-	7.789	–
· Pro-time (INR)	-	-	1.58	–
· Albumin (g/L)	-	-	33.2	–
· ALT/AST (U/L)	-	-	45.0 / 119.3	–

Table 2. Association of antibiotic prophylaxis with the incidence of the first cholangitis episode following the Kasai procedure

Outcome	Prophylaxis (n=39)	No Prophylaxis (n=24)	Odds Ratio (95% CI)	p-value
Any cholangitis	18 / 39 (46.2%)	13 / 24 (54.2%)	0.73 (0.26 – 2.02)	0.62
Early (<6 mos.)	15 / 39 (38.5%)	12 / 24 (50.0%)	0.63 (0.22 – 1.75)	0.35
Late (>6 mos.)	3 / 39 (7.7%)	1 / 24 (4.2%)	1.92 (0.19 – 19.6)	0.62

yielding an odds ratio (OR) of 0.73 (95% CI: 0.26–2.02, p = 0.62). For early cholangitis (<6 months), the incidence was 38.5% with prophylaxis and 50.0% without, with an OR of 0.63 (95% CI: 0.22–1.75, p = 0.35). For late cholangitis (>6 months), 7.7% of patients with prophylaxis and 4.2% without prophylaxis were affected, corresponding to an OR of 1.92 (95% CI: 0.19–19.6, p = 0.62). The p-value and wide confidence interval do not provide sufficient evidence of an association between prophylaxis and the first incidence of cholangitis following Kasai procedure.

Among the prophylactic regimens, **Cotrimoxazole and Co-amoxiclav** were the most commonly prescribed (Table 3). Both were associated with higher rates of cholangitis within 6 months (54.5% and 44.4%, respectively). In contrast, **Cefuroxime and Sultamicillin** had no recorded cases of cholangitis, though the sample sizes were very small. This suggests variability in outcomes depending on the choice of prophylactic antibiotic, but this should be interpreted with caution and considered exploratory, as the study was not powered to detect differences between specific antibiotic regimens.

Table 3. Type of antibiotic prophylaxis and incidence of the first cholangitis episode in infants with biliary atresia following Kasai procedure (n = 39)

Antibiotic used	Cholangitis <6 mos.				Cholangitis ≥6 mos., n (%)	No cholangitis, n (%)
	≤1 mo.	1 to 3 mos.	>3 to 6 mos.	Sub-total, n (%)		
Cotrimoxazole (n=11)	1	2	3	**6** (54.5%)	**0** -	**5** (45.5%)
Co-amoxiclav (n=18)	3	3	2	**8** (44.4%)	**1** (5.6%)	**9** (50.0%)
Cefixime (n=3)	0	1	0	**1** (33.3%)	**0** -	**2** (66.7%)
Amoxicillin (n=4)	0	1	0	**1** (25.0%)	**1** (25.0%)	**2** (50.0%)
Cefuroxime (n=2)	0	0	0	**0** -	**0** -	**2** (100.0%)
Sultamicillin (n=1)	0	0	0	**0** -	**0** -	**1** (100.0%)
Total (n=39)	4	7	5	**16** (41.0%)	**2** (5.1%)	**21** (53.9%)

Table 4. Length of hospital during the first episode of cholangitis following Kasai procedure (n = 31)

Group	< 10 days	≥ 10 days	Total	OR	p-value
With prophylaxis (n=18)	11	7	18		
Without prophylaxis (n=13)	5	8	13	2.51	0.29
Total (n=31)	16	15	31		

Table 5. Microbiologic profile of first cholangitis episode in patients with and without antibiotic prophylaxis

Group	Culture-proven, n (%)	Isolated organisms (n)	Culture-negative, n (%)
With antibiotic prophylaxis (n=39)	4 (10.3%)	*Klebsiella pneumoniae* (1) *Klebsiella pneumoniae* ESBL (1) *Klebsiella pneumoniae* MDR (1) *Staphylococcus hominis* (1)	14 (35.9%)
Without antibiotic prophylaxis (n=24)	2 (8.3%)	*Klebsiella pneumoniae* XDR (1)† Coagulase negative *Staphylococcus* (1)	11 (45.8%)

†One patient developed *Klebsiella pneumoniae* that was extensively drug-resistant (XDR) and subsequently demised.
ESBL = extended-spectrum beta-lactamase; MDR = multidrug-resistant; XDR = extensively drug-resistant.

Table 4 shows the distribution of hospital stay duration among infants who underwent Kasai procedure, stratified by antibiotic prophylaxis use. The length of hospital stay was computed by deducting the date of admission from the date of discharge yielding the total number of days admitted at the ward. In the group with prophylaxis (n = 18), 61.1% (11/18) were discharged in less than 10 days, while 38.9% (7/18) stayed for 10 days or longer. In contrast, among those without prophylaxis (n = 13), only 38.5% (5/13) stayed for less than 10 days, whereas 61.5% (8/13) had prolonged hospitalization (≥10 days). Fisher's exact test showed no statistically significant association between prophylaxis use and shorter hospital stay (<10 days) (two-sided p = 0.29). Although the odds of shorter stay were higher in the prophylaxis group (OR = 2.51), this did not reach statistical significance.

Table 5 compares the occurrence of culture-proven and culture-negative cholangitis between infants who received antibiotic prophylaxis and those who did not following Kasai procedure. Among patients with prophylaxis, 10.3% (4/39) had culture-proven cholangitis and 35.9% (14/39) had culture-negative cholangitis. In contrast, in the group without prophylaxis, 8.3% (2/24) developed culture-proven cholangitis and 45.8% (11/24) developed culture-negative cholangitis. Notably, among those without prophylaxis, one patient developed XDR *Klebsiella pneumoniae* infection that ultimately led to death.

DISCUSSION

This 15-year single-center cohort confirms that post-Kasai cholangitis is a frequent complication, occurring in nearly half of children after portoenterostomy. Our overall incidence of 49.2% is consistent with the wide international range of 40% to 93%, with most episodes occurring within the first six months of surgery, a pattern well described in global literature.[3] In Malaysia, Selvalingam et al. reported that 57% of patients developed cholangitis within the first year, most within the initial six months, which closely mirrors our temporal findings.[5] In contrast, a Korean cohort by Baek et al. demonstrated a substantially higher cumulative incidence, 75.5% at one year and 84.2% at five years, with more than 90% of episodes clustering in the first year and recurrences in 76% of patients.[6] Meanwhile, earlier data from the United States, such as the report by Lally et al., showed a lower crude incidence of 22%; however, these findings predated current perioperative care standards and included smaller cohorts with differing definitions, which likely account for the discrepancy.[7] Taken together, our incidence falls mid-range, closer to Southeast Asian experience, but below the very high Korean rates, reflecting differences in surveillance practices, definitions, timing of surgery, and postoperative management across centers.

Antibiotic prophylaxis did not significantly reduce the incidence of cholangitis in our cohort, though a modest trend toward fewer early episodes was observed among those who received prophylaxis (46.2% vs. 54.2%, OR 0.73, 95% CI 0.26–2.02, $p = 0.62$). This equivocal finding mirrors the inconsistent results reported internationally. Random assignment of prophylaxis to patients may yield different results, as opposed to this study wherein specialists' discretion was the basis for prophylaxis management. A systematic review that included four studies involving 329 post-Kasai biliary atresia patients (196 with and 133 without prophylaxis) from the United States, Taiwan, and the Netherlands likewise found conflicting evidence. Lally et al. (U.S.) reported a significantly lower cholangitis rate with prophylaxis (15% vs. 57%, $p < .03$), while de

Vries et al. (Netherlands) found no benefit (62% vs. 51%, p = .15). Wu et al. (Taiwan) observed that patients who developed cholangitis had a lower rate of prophylactic antibiotic use, although detailed data were lacking.[8] Similarly, Ramachandran et al. (India) reported that 51.8% of infants developed cholangitis within the first month despite receiving cyclical amoxicillin–clavulanate or cefpodoxime for six months.[9] The absence of a statistically significant benefit in our study may reflect small sample size, heterogeneous antibiotic regimens, and adherence limitations inherent to retrospective designs. Despite these uncertainties, an international Delphi consensus still recommends six to twelve months of prophylaxis, underscoring its potential role in supporting native liver survival.[3]

An important observation in this study is the predominance of culture-negative cholangitis, with culture-proven cases occurring in only 10.3% of patients on prophylaxis and 8.3% without. This mirrors findings from other centers, where a large proportion of cases yield no growth. Possible explanations include prior antibiotic exposure before sampling, infection with fastidious organisms, or non-bacterial inflammatory processes that clinically mimic cholangitis.[5,6,9] When cultures are positive, organisms such as *Enterococcus faecium* and Gram-negative bacilli including *E. coli*, *Klebsiella*, and *Enterobacter* are commonly reported, particularly in Asian cohorts.[6] In our setting, *Klebsiella pneumoniae* was the most frequent pathogen isolated, including ESBL- and MDR-producing strains among prophylaxis recipients. Importantly, one patient without prophylaxis developed *Klebsiella pneumoniae* that was extensively drug-resistant (XDR) and eventually succumbed to the infection. This case underscores the grave clinical implications of antimicrobial resistance in post-Kasai cholangitis and highlights the urgent need for judicious antibiotic use, robust antimicrobial stewardship, and early detection strategies in high-risk patients.

While prophylaxis did not reduce the overall incidence of cholangitis, it was associated with shorter hospital stays; although the odds of shorter stay were higher in the prophylaxis group (OR = 2.51), this did not reach statistical significance. The study showed that 61.1% of patients with prophylaxis were discharged in under 10 days compared to 38.5% without; the prolonged hospital stays, as reflected in the records, were primarily due to the need to complete the antibiotic regimen and ensure the patient's overall clinical stability. In several cases, delays were also attributed to the necessity of stepping up or adjusting antibiotic therapy in response to the patient's condition. Gradual improvement was observed only after these adjustments were made, contributing to the extended duration of hospitalization. This suggests that prophylaxis may mitigate disease severity or facilitate earlier discharge, outcomes that remain clinically meaningful even in the absence of strong incidence reduction. Reducing the duration of hospitalization has important implications for resource use, family burden, and risk of hospital-acquired infections, particularly in resource-limited settings.

Overall, our findings reinforce that cholangitis most frequently occurs within the first six to twelve months following the Kasai procedure, highlighting this interval as the most critical for close surveillance and preventive strategies, consistent with journals cited in this study.[5,6,10] Accordingly, cholangitis was classified as early when occurring within six months post-Kasai and late when occurring thereafter, following the most commonly used timeframe reported in the literature. Although antibiotic prophylaxis did not significantly reduce the incidence in our cohort, interpretation is limited by the inability to verify adherence to oral regimens, an inherent limitation of the retrospective design. Nonetheless, its potential to attenuate disease severity and reduce hospitalization supports its continued use, consistent with current consensus guidelines. Future research should aim to clarify the true protective effect of prophylaxis through larger, prospective multicenter studies. Moreover, integrating advanced microbiologic techniques may improve pathogen detection in culture-negative cases and better inform empiric treatment. Finally, comparative studies assessing different prophylactic agents and durations, and their effects on patient-centered outcomes such as recurrent cholangitis, hospital stay, and native liver survival, would provide stronger evidence for standardizing care.[8,9]

CONCLUSION

This study demonstrates that cholangitis remains a frequent complication following Kasai portoenterostomy, affecting nearly half of patients, with the majority of episodes occurring within six months after surgery. Antibiotic prophylaxis had no significant effect on the overall incidence of post-operative cholangitis. This may be due to small sample size, the absence of standardized protocol for post-Kasai antibiotic prophylaxis and uniform documentation of all necessary variables.

It was observed that patients who developed cholangitis and received prophylaxis had shorter hospital stays, and that prophylaxis may have a protective effect against early cholangitis. The predominance of culture-negative episodes highlights the limitations of current diagnostic methods. Importantly, one patient without prophylaxis developed cholangitis caused by extensively drug-resistant *Klebsiella pneumoniae* and eventually demised, underscoring the serious consequences of antimicrobial resistance in this population.

RECOMMENDATIONS

In light of these findings, despite the absence of a statistically significant association between antibiotic prophylaxis and cholangitis incidence, the benefits observed in this study such as shortened hospital stay and a possible protective effect against early cholangitis may support the continued use of antibiotic prophylaxis as part of early postoperative management for 6–12 months. This is consistent with recommendations from consensus guidelines, given its potential to reduce severity and improve recovery. Close surveillance during the first year, particularly the initial six months, remains critical. Empiric antibiotic regimens should include coverage for both Gram-negative organisms and *Enterococcus*, guided by local resistance patterns, while institutional protocols should prioritize timely recognition and management of suspected cholangitis. Caregiver education and nutritional support are also essential to improve patient outcomes.

For research purposes, standardization of prophylaxis management and hospital-wide adherence of recommendations from recognized consensus guidelines is best. The use of standard definition for operational terms such as cholangitis, is recommended for all cases of biliary atresia. Future research should focus on prospective multicenter studies to encompass varied hospital settings and patient population; as well as identify the most effective prophylactic regimens, while integrating advanced microbiologic diagnostics (e.g. PCR) to improve detection of pathogens in culture-negative cases. The emergence of XDR organisms calls for stronger antimicrobial stewardship, regional surveillance, and the development of standardized protocols to harmonize post-Kasai care and improve native liver survival.

Conflicts of Interest

None declared.

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