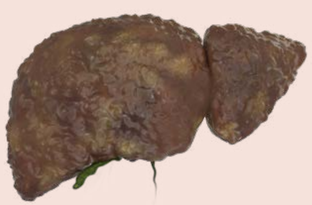
The Burden of Biliary Atresia

WHAT IS BILIARY ATRESIA?

Biliary atresia: a severe, progressive, neonatal disease that affects the hepatobiliary system[1]

- Hallmarks of biliary atresia are inflammation, fibrosis, and obstruction of the bile ducts, which rapidly leads to liver cirrhosis[1]
- Biliary atresia typically progresses to liver failure and death within 2 years in the absence of intervention[2,3]; therefore, **patients require swift diagnosis and surgical treatment**[1]



The incidence of biliary atresia varies by geographical region, but occurs in approximately **1 in 10,000** to **1 in 20,000** children[9–11]

Symptoms of biliary atresia can include prolonged jaundice, acholic stools, hepatosplenomegaly, and elevated levels of biliary components (sDBil, sBA, GGT, ALT, AST)[1]

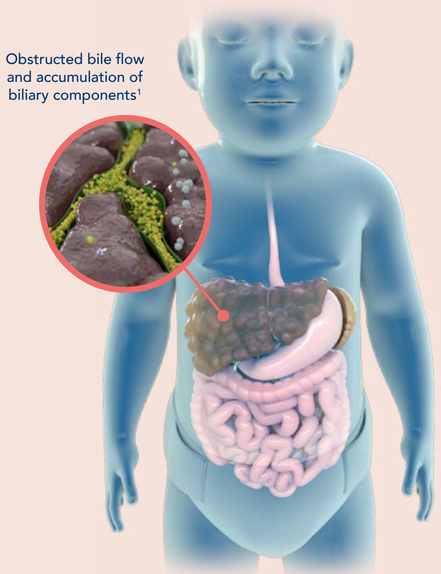
Biliary atresia is the **leading cause of neonatal cholestasis** and **pediatric liver transplantation worldwide**[1]

LIVER FUNCTION

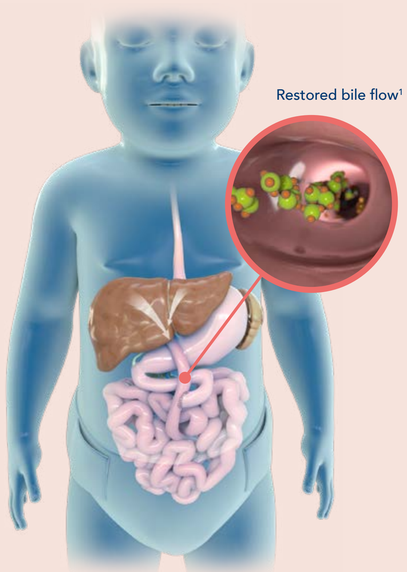
In biliary atresia, **obstruction of bile flow leads to an accumulation of biliary components** (e.g., bilirubin, bile acids) **in the liver**. This can cause a spillover into the systemic circulation and rapid progression to advanced liver disease[1]

Kasai portoenterostomy (KPE) is the standard surgical intervention for infants with biliary atresia. In this procedure, which **aims to restore bile flow,** the extrahepatic biliary tree is surgically removed and a limb of the intestine is connected directly to the liver[1]

Pathogenic Consequences of Cholestasis in Biliary Atresia[1]



Liver Function After Successful KPE[1]



DISEASE PROGRESSION AND BURDEN

Patients who undergo a KPE **within the first 3 months of life** have the **greatest chance of restored bile flow.** There is a sharp decline in patient outcomes when surgery is performed later[3,4]

Following KPE, **patients with lower total bilirubin levels have better native liver survival (NLS)** at 2 years than those with higher total bilirubin levels[5]

An analysis of data from **137 children with biliary atresia** was supported by the Childhood Liver Disease Research Network (ChiLDReN). This analysis showed that patients with lower sBA levels after KPE had **less liver injury at 2 years of age** and **improved NLS** versus those with higher levels[6]

However, even with successful KPE, patients with biliary atresia can experience ongoing liver damage and may **eventually require liver transplantation**[1,7]

After KPE, approximately **40% of patients need a liver transplant by 2 years of age,** which rises to more than **70% by 15 years of age**[8]

Indications for transplantation post-KPE include failure to thrive due to ongoing malnutrition, pruritus, or another clinical sequelae[12]

Patients with biliary atresia **may have reduced quality of life** compared to healthy individuals in the general population as it can impact school, social, and physical functioning[13–15]

Non-surgical treatment options for biliary atresia that lower serum bilirubin and bile acid levels, slow disease progression, and/or extend NLS would be valuable[1]

ALT, alanine transaminase; **AST**, aspartate transferase; **GGT**, gamma-glutamyl transferase; **sBA**, serum bile acid; **sDBil**, serum direct bilirubin.

1. Karpen SJ, et al. *Hepatol Int.* 2020;14(5):677–689. doi:10.1007/S12072-020-10070-W; 2. Liu MB, et al. *Surgery.* 2017;161(2):533–537. doi:10.1016/J.SURG.2016.08.012; 3. Mieli-Vergani G, et al. *Lancet.* 1989;1(8635):421–423. doi:10.1016/S0140-6736(89)90012-3; 4. Altman RP, et al. *Ann Surg.* 1997;226(3):348–355. doi:10.1097/00000658-199709000-00014; 5. Shneider BL, et al. *J Pediatr.* 2016;170:211–217.e2. doi:10.1016/J.JPEDS.2015.11.058; 6. Harpavat S, et al. *Hepatology.* 2023;77(3):862–873. doi:10.1002/HEP.32800 ; 7. Kumagi T, et al. *Liver Int.* 2012;32(3):510–518. doi:10.1111/J.1478-3231.2011.02668.X; 8. Serinet MO, et al. *Pediatrics.* 2009;123(5):1280–1286. doi:10.1542/PEDS.2008-1949; 9. Jimenez-Rivera C, et al. *J Pediatr Gastroenterol Nutr.* 2013;56(4):344–354. doi:10.1097/MPG.0b013e318282a913; 10. Schreiber RA, et al. *J Clin Med.* 2022;11(4). doi:10.3390/jcm11040999; 11. Cavallo L, et al. *Journal of Pediatrics.* 2022;246:89–94.e2. doi:10.1016/j.jpeds.2022.03.038; 12. Sundaram SS, et al. *Liver Transpl.* 2017;23(1):96–109. doi:10.1002/LT.24640; 13. Naghashi S, et al. *Iranian Journal of Pediatrics* 2019 29:3. 2019;29(3):83559. doi:10.5812/IJP.83559; 14. Wong CWY et al. *J Pediatr Gastroenterol Nutr.* 2018;66(4):570–574. doi:10.1097/MPG.0000000000001854; 15. Hukkinen M, et al. *Best Pract Res Clin Gastroenterol.* 2022;56–57:101764. doi:10.1016/J.BPG.2021.101764.

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ALLSC-US-001324
July 2024