Burden of Disease

CHOLESTATIC PRURITUS IS A CONSEQUENCE OF CHRONIC CHOLESTASIS[1-5]

76% to 100% **Cholestatic pruritus has been correlated with elevated serum bile acids (sBAs) and could affect as much as 76% up to 100% of patients with later-course progressive familial intrahepatic cholestasis (PFIC)[5]**

It can be difficult to identify, but has been recognized as the most debilitating symptom[2,6]

Cholestatic pruritus can lead to[6-11]:

Skin damage

Irritability

Physical discomfort

Inability to concentrate

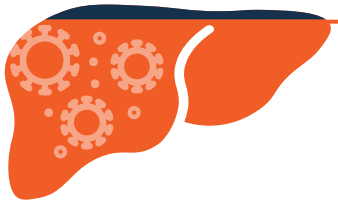
Sleep disturbances

Negative impact on social activities

References: 1. Cai S-Y, Li M, Boyer J. The role of bile acid-mediated inflammation in cholestatic liver injury. In: Arias IM, Alter HJ, Boyer JR, et al, eds. *The Liver: Biology and Pathobiology.* 6th ed. Wiley; 2020:728-736. doi:10.1002/9781119436812.ch56 **2.** Kamath BM, Stein P, Houwen RHJ, Verkade HJ. Potential of ileal bile acid transporter inhibition as a therapeutic target in Alagille syndrome and progressive familial intrahepatic cholestasis. *Liver Int.* 2020;40(8):1812-1822. doi:10.1111/liv.14553 **3.** Karpen SJ, Kelly D, Mack C, Stein P. Ileal bile acid transporter inhibition as an anticholestatic therapeutic target in biliary atresia and other cholestatic disorders. *Hepatol Int.* 2020;14(5):677-689. doi:10.1007/s12072-020-10070-w **4.** Li T, Chiang J. Bile acid-induced liver injury in cholestasis. In: Ding WX, Yin XM, eds. *Cellular Injury in Liver Diseases.* Springer; 2017:143-172. *Cell Death in Biology and Diseases.* **5.** Baker A, Kerkar N, Todorova L, Kamath BM, Houwen RHJ. Systematic review of progressive familial intrahepatic cholestasis. *Clin Res Hepatol Gastroenterol.* 2019;43(1):20-36. doi:10.1016/j.clinre.2018.07.010 **6.** Kamath BM, Abetz-Webb L, Kennedy C, et al. Development of a novel tool to assess the impact of itching in pediatric cholestasis. *Patient.* 2018;11(1):69-82. doi:10.1007/s40271-017-0266-4 **7.** Srivastava A. Progressive familial intrahepatic cholestasis. *J Clin Exp Hepatol.* 2014;4(1):25-36. doi:10.1016/j.jceh.2013.10.005 **8.** Kamath BM, Baker A, Houwen R, Todorova L, Kerkar N. Systematic review: the epidemiology, natural history, and burden of Alagille syndrome. *J Pediatr Gastroenterol Nutr.* 2018;67(2):148-156. doi:10.1097/MPG.0000000000001958 **9.** Kamath BM, Chen Z, Romero R, et al. Quality of life and its determinants in a multicenter cohort of children with Alagille syndrome. *J Pediatr.* 2015;167(2):390-396.e3. doi:10.1016/j.jpeds.2015.04.077 **10.** Elisofon SA, Emerick KM, Sinacore JM, Alonso EM. Health status of patients with Alagille syndrome. *J Pediatr Gastroenterol Nutr.* 2010;51(6):759-765. doi:10.1097/MPG.0b013e3181ef3771 **11.** Cohran VC, Heubi JE. Treatment of pediatric cholestatic liver disease. *Curr Treat Options Gastroenterol.* 2003;6(5):403-415. doi:10.1007/s11938-003-0043-4

CHOLESTATIC PRURITUS REMAINS A SIGNIFICANT INDICATION FOR LIVER TRANSPLANT

Many patients with PFIC with uncontrolled cholestatic pruritus continue to opt for surgical biliary diversion and/or liver transplant[1,2]



92%

Among 38 pediatric patients with PFIC who underwent surgical biliary diversion, the most common indications were cholestatic pruritus (92%) and progression of liver disease (59%).[1]

End-stage liver disease (80%) was the most common indication for liver transplant in pediatric patients with PFIC, followed by refractory cholestatic pruritus (20%).[2]

In PFIC1 and BSEP, it has been reported that ~50% of patients are alive and have their native liver at 10 years old (Van Wessel 2018)[3*]

In BSEP specifically, only 32% of patients are alive and have their native liver by 18 years old (Van Wessel 2020)[4*]

For patients with PFIC, there is a need to help reduce bile acid buildup and relieve cholestatic pruritus[5]

BSEP=bile salt export pump; PFIC=progressive familial intrahepatic cholestasis.

*NAtural course and Prognosis of PFIC and Effect of biliary Diversion (NAPPED) Consortium is a large, international, multicenter observational study designed to define the natural history and prognosis of genetically confirmed FIC1 (PFIC1) and BSEP (PFIC2) deficiency.

- Retrospective follow-up data on native liver survival at age 10 in 42 FIC1-deficient and 192 BSEP-deficient patients from European and Asian centers
- Retrospective data on native liver survival at age 18 for 264 patients with homozygous or compound heterozygous pathological *ABCB11* mutations causing BSEP deficiency from European, Middle Eastern, and Asian centers

These data are from 2 different publications.

References: 1. Wang KS, Tiao G, Bass LM, et al. Analysis of surgical interruption of the enterohepatic circulation as a treatment for pediatric cholestasis. *Hepatology.* 2017;65(5):1645-1654. **2.** Vasudevan AK, Shanmugam N, Rammohan A, et al. Outcomes of pediatric liver transplantation for progressive familial intrahepatic cholestasis. *Pediatr Transplant.* 2023;27(8):e14600. **3.** van Wessel DBE, Thompson RJ, Grammatikopoulos T, et al. The natural course of FIC1 deficiency and BSEP deficiency: initial results from the NAPPED Consortium. *J Hepatol.* 2018;68(suppl 1):S626. **4.** van Wessel DBE, Thompson RJ, Gonzales E, et al; NAPPED Consortium. Genotype correlates with the natural history of severe bile salt export pump deficiency. *J Hepatol.* 2020;73(1):84-93. **5.** Kamath BM, Stein P, Houwen RH, Verkade HJ. Potential of ileal bile acid transporter inhibition as a therapeutic target in Alagille syndrome and progressive familial intrahepatic cholestasis. *Liver Int.* 2020;40(8):1812-1822. doi:10.1111/liv.14553

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