

# Pediatric Liver Biopsy: Dos and Don'ts

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Received on: 17 August 2022; Accepted on: 20 August 2022; Published on: 27 September 2022

*Annals of Pediatric Gastroenterology and Hepatology ISPGHAN* (2022); 10.5005/jp-journals-11009-0104A

Liver biopsy is a valuable but invasive tool in the diagnosis, prognosis, monitoring of disease progression, and response to treatment of liver diseases in children. Different techniques of liver biopsy are percutaneous (blind), image (sonological, fluoroscopic, or CT) guided, transjugular (TJLB) or surgical (laparoscopic or laparotomy). The ultimate endpoint is the proper interpretation of the histology. Most patients have a limited window of opportunity for the biopsy before the disease progresses. Details of how to perform a liver biopsy are beyond the scope of this review. From personal experience, some practical tips and tricks with their nuances are highlighted below.

## GENERAL INFORMATION

With the availability of genetics, many genetic-metabolic liver diseases presently do not require liver biopsy for diagnosis anymore. Common indications and techniques of liver biopsy are given in [Tables 1](#) and [2](#). Mandatory prebiopsy testing comprises hemoglobin, platelet count, international normalized ratio (INR), and ultrasonography of the abdomen (to look for ascites, size, and morphology of liver, vascular abnormalities, and intrahepatic biliary radicle dilatation). Family history of concomitant bleeding or coagulation disorders must be carefully looked for and evaluated.

## Dos

- **Justify the Indication:** There are numerous indications (acute and chronic) that may be benefited from liver biopsies. However, the fundamental question a physician must wisely ask himself or herself before the procedure is, "Will the biopsy add anything extra and change the decision-making of the index patient?" Only if positive or negative histology guides the further management and adds to the algorithm of the patient's workup, then this invasive procedure justified.
- Biopsy should not be encouraged simply to confirm a diagnosis that is obvious on noninvasive tests. For example, finding features of steatohepatitis on liver function tests and ultrasonography does not warrant an immediate biopsy just to confirm fatty liver unless there are compelling reasons.
- Biopsy should not be performed if the diagnosis is obvious and its natural history is well known. For example, it is not wise to perform a biopsy in acute viral hepatitis with prolonged cholestasis, since its spontaneous resolution after a few weeks is well known.
- Biopsy should not be performed prematurely before the thorough completion of the workup. For example, proceeding with a biopsy just based on seropositivity for

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**How to cite this article:** Badarinath S, Sen Sarma M. Pediatric Liver Biopsy: Dos and Don'ts. *Ann Pediatr Gastroenterol Hepatol* 2022;4(3):40–42.

**Source of support:** Nil

**Conflict of interest:** None

autoimmune markers is not correct. The physician should have thoroughly ruled out chronic viral diseases and Wilson disease as potential etiologies before the premature conclusion of autoimmune hepatitis.

- Biopsy should not be performed in haste. For example, do not proceed for biopsy in a child presenting with severe ascites. If the likely cause is chronic Budd-Chiari syndrome and the diagnosis is initially unyielding, it is then advisable to reconfirm the Doppler with a sound sonologist or perform a CT venography.
- **Choose an experienced team of pediatric sonologist, anesthetists, and liver pathologists ahead of the biopsy**
  - Most liver biopsies today are sonologically or radiologically guided. A trained sonologist is accustomed to the pediatric liver size, and will cautiously avoid the vascular structures, biliary system, and sample with precision from the masses and nodules.
  - Children with chronic liver diseases may have borderline or minimal hepatic encephalopathy which may worsen on sedatives like benzodiazepines. An anesthetist finely balances the sedation.
  - A sound liver pathologist's role is to assess the gross tissue at the time of sampling, ask for a repeat pass in the same setting if found inadequate, process the sample swiftly, carefully interpret the histology in light of the clinical dilemma, reserve some tissue for further analysis like immunohistochemistry and store the slides and the paraffin blocks for future review. An ideal core should be approximately 20 mm long and 1.8 mm thick. Unambiguity in reporting is advised. Some research centers may blind the pathologist as per project protocol.

**Table 1:** Common indications for liver biopsy in children

Older children	
<ul style="list-style-type: none"> <li>• Persistently abnormal liver function tests and/or hepatomegaly</li> <li>• Diagnosis of autoimmune hepatitis as a part of diagnostic criteria</li> <li>• Withdrawal of immunosuppression in autoimmune hepatitis</li> <li>• Diagnosis of Wilson disease for hepatic copper (optional, not mandatory)</li> <li>• Staging and prognosis of chronic hepatitis</li> <li>• Evaluation of hepatic tumors, nodules,</li> <li>• Suspicion of autoimmune liver failure</li> <li>• Cryptogenic cirrhosis or portal hypertension of unknown etiology</li> <li>• Suspicion of small duct sclerosing cholangitis</li> <li>• Drug-induced liver disease</li> <li>• Post-liver transplantation rejection</li> <li>• Veno-occlusive liver disease</li> <li>• Graft vs host disease</li> <li>• Fever of unknown origin with considerable hepatic involvement</li> </ul>	
Neonates/infants	
<ul style="list-style-type: none"> <li>• Suspected biliary atresia with a good sized gall bladder</li> <li>• Prior to biliary diversion to rule out cirrhosis</li> <li>• Persistent organomegaly despite resolution of jaundice</li> <li>• Indeterminate cause (if genetics unyielding)</li> <li>• Suspected CMV hepatitis (for documentation of inclusion bodies)</li> <li>• Liver space occupying lesion in conditions such as tyrosinemia</li> </ul>	
Can preferentially avoid liver biopsy in atretic gallbladder or cyst at porta (proceed directly for a per-operative cholangiogram) and in all the genetic-metabolic causes (unless indicated)	

**Table 2:** Techniques of liver biopsy

Technique	Indications
Percutaneous "blind"	Most conditions of enlarged liver except those listed in text and table
Percutaneous image-guided	Sonological preferred in all settings Biliary dilatation Liver tumors, nodules and space occupying lesions Left side enlarged liver Shrunken liver span Normal liver span Soft enlarged liver
Percutaneous image-guided plugged tract	Borderline coagulopathy or thrombocytopenia Vascular tumors
TJLB	Thrombocytopenia Coagulopathy Ascites
Laparoscopic or laparotomy (surgical)	Risk of bleeding Large tissue samples Ascites without any etiology Abdominal mass Poor sonological window of space occupying lesions Failure of percutaneous liver biopsies or TJLB During shunt surgeries or devascularization

TJLB, transjugular liver biopsy

- **Give a local anesthetic:** In addition to the intravenous sedation, a local anesthetic at the site of biopsy prevents the body's reaction of the "menace reflex." When the needle enters the unanesthetized skin, there is an expected lateral flexion of the right side of the body in response to the noxious stimulus. This alters the plan of the needle pathway, diverting from the targeted liver parenchyma and causes erroneous or inadequate sampling.

- **Pressure from left side:** An assistant's palm must firmly cover the left interaxillary area or flank with a sustained mild counter pressure exerted towards the right. This allows the abdomen to be fixed firmly when the needle enters from the right side into the liver.
- **Hold the biopsy gun steadily:** With a core biopsy needle (disproportionate to the size of the abdomen in neonates and smaller children), always rest the handle on the volar aspect of your hand, the cutting cannula on the palm. The beveled edge of the inner stylet should be pointing downwards. This allows steady control during insertion.
- **Perform a dry run:** For core biopsy needles, plungers should be retracted and fired (*ex vivo*) before insertion to see if the equipment is well functioning.
- **Insert the needle as per protocol:** Biopsy specimens are best obtained if the needle points to the opposite clavicle and the throw or depth of the needle is approximately 2–3 cm from the skin surface. Except for tumors, intercostal entry is recommended as it provides natural tamponade by the ribs.
- **Always give manual pressure:** Immediately after the procedure, the entry site should be given sustained pressure with the thumb or ball of the palm for at least 5 minutes before tincture and tape is applied. Manual tamponade is the most effective tamponade.
- **Always examine the specimen personally:** Examine the specimen for color, length, fragmentation, and most importantly, buoyancy. A floating tissue is usually a lung. Liver tissue should sink to the bottom.
- **Mandatory monitoring for complications:** Despite alleviation of pain, if there is tachycardia and tachypnea, then this may be the earliest indication of a brewing complication. All efforts should be made to rule out pneumothorax, hemothorax, hemobilia, hemoperitoneum, and puncture of any other organ.
- **Careful informed consent in India:** Parental awareness in India is generally poor with myths and speculations. The consent must be sought before the procedure with explanatory diagrams, estimated risks (<3%), possible outcomes, and a choice of alternatives. Care must be taken neither to over-highlight nor underplay the risks. There should be a fair balance. In many conditions, the biopsy is ancillary and not diagnostic. There may be issues with nonrepresentative areas in the first attempt.

**Don'ts**

- **Do not attempt the subcostal approach:** To avoid potential chest complications of intercostal liver biopsy, a subcostal approach is often chosen. However, this is not recommended as a subcostal approach has three dangers: poor tamponade, chances of overshooting, and ending up in damaging the biliary apparatus, and chances of erroneous biopsy from the upper pole of the right kidney.
- **Do not perform a percutaneous blind liver biopsy in a soft palpable liver or those without hepatomegaly:** Firm livers have a subjective "give way" gritty feeling when the biopsy needle is inserted blindly. With soft livers, this feeling is absent and the depth may be miscalculated. Soft liver biopsy indications are asymptomatic hypertransaminasemia, immunotolerant hepatitis B, hepatitis C, Dubin-Johnson syndrome (rarely), etc. It is recommended to perform sonologically guided biopsies.
- **Do not perform a percutaneous blind liver biopsy in a special population with platelet dysfunction:** These conditions are children with chronic renal failure, Alagille syndrome,

Arthrogryposis-cholestasis syndrome, and low birth weight babies. It is recommended to perform sonologically guided plugged tract biopsies.

- **Do not perform any kind of percutaneous biopsy in ascites:** Moderate-severe ascites are a contraindication till the patient is dry. Mild ascites may track along the perihepatic space, give an erroneous assessment of the liver and impede tamponade. Moreover, the fluid can leak or get infected causing peritonitis. TJLB is recommended.
- **Do not perform a percutaneous blind liver biopsy in tumors:** In low-resource settings, it may be tempting to attempt blind liver biopsy in palpable tumors as a desperate measure for tissue diagnosis. However, all liver tumors (primary or secondary) are known to be highly vascular and may bleed profusely. Moreover, hemangioendothelioma, a vascular tumor may be a close differential diagnosis in any palpable liver tumor. Attempting blind biopsies in this situation may be catastrophic. Plugged biopsies are recommended.
- **Avoid liver biopsy in liver cysts:** If there is a doubt of hydatid liver disease due to potential anaphylaxis.

- **Do not make more than three passes:** In percutaneous liver biopsy as it can increase the risk of complications.

## SUGGESTED READING

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