

Original Articles

Liver Biopsy in Children in Dhaka Shishu Hospital A Study of 30 Cases

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Abstract

Background: Liver biopsy is an established procedure to diagnose disease, to assess prognosis and to follow up of liver diseases. Although liver biopsy is a confirmatory diagnostic procedure of majority of the hepatological disorders, it carries the risk of complications. Though major complications rarely occur, minor complications are common. To minimize complications, several biopsy techniques have been developed. The present study was intended to correlate the clinical diagnoses with histological diagnoses and to observe the complications encountered by the children with percutaneous liver biopsy procedure.

Patients and Methods: A total of 30 paediatric patients of suspected liver diseases, based on predefined eligibility criteria, were subjected to biopsy for confirmation of diagnosis. An ultrasound of liver was routinely performed before the procedure to mark the site for percutaneous biopsy. The field was prepared with alcohol-based solution (povidone-iodine) and sterile drapes were placed over the patient. Local anaesthetic was administered with 2% lidocain solution 20mg/ml (preferably levobupivacaine 2.5mg/ml) in both superficial and deep planes. A blind liver biopsy was done at the point of maximum dullness by percussion over the right trunk. We used cutting needle. The diameter of the needle used in our study was 14-gauge (1.4 mm) which allowed adequate collection of tissue for diagnosis. The biopsy material was taken in a very small amount of sterile normal saline and was immediately sent to the laboratory for evaluation.

Results: Half (50%) of the patients was more than 5 years of age with median age being 5.0±3.9 years. Majority (80%) was male. Ninety percent of the patients belonged to poor socioeconomic class. Clinically the cases were diagnosed as having chronic hepatitis (23.3%) followed by CLD (16.7%), isolated hepatomegaly (16.7%), liver cirrhosis (13.3%) and storage disease (13.3%). Hepatosplenomegaly and congenital hepatic fibrosis, each was 6.7%. Histological diagnoses of biopsy material obtained from the liver confirmed that one-sixth (16.7%) of the cases had liver cirrhosis. Storage disease and glycogen storage disease each comprised 13.3% of the cases and congenital biliary atresia 10%. Very few cases had moderate fatty changes with cholestasis, congenital hepatic fibrosis, chronic inflammatory cells, chronic viral hepatitis and secondary biliary cirrhosis. Nearly half (46.7%) patients had mild pain and discomfort at the site of biopsy, most of which spontaneously went away. However, some 3 (10%) patients developed major complications needing management.

Conclusion: Liver biopsy is a well established procedure in the diagnosis and follow up of liver diseases. But it is not without risk of complications. So, before deciding for a liver biopsy, the indications and risks must be assessed cautiously for each patient.

Key words: Percutaneous liver biopsy, clinical diagnoses, histological diagnoses, complications.

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Introduction

Liver biopsy (LB) is now a days a powerful clinical tool to establish a diagnosis, to assess prognosis and to follow up liver diseases¹. The use of liver biopsy declined during the 1980s due mainly to increasing availability of new imaging techniques and the development of accurate serological tests². However,

evaluation of liver histology remains very important as LB can change the clinical diagnosis in 8-14%, the management in 12-18 % and the frequency of liver test monitoring in 36% of cases³. In the last 10-15 years the number of liver biopsy have increased dramatically due to emerging liver transplantation and the identification of hepatitis C virus^{2,4}. However, liver biopsy is an invasive technique that carries a risk of complications¹. So, before deciding for a liver biopsy, the indications, risks and benefits for individual patients must be weighed with utmost caution.

To prevent complications, several techniques (automatic needles, ultrasound guidance, conscious sedation, laparoscopic transjugular LB) have been developed. Although traditionally performed 'blindly', there is growing evidence to suggest that US guidance in identifying the puncture site decreases the complication rate^{5,6} and is cost-effective^{7,8}. In a recently published survey of liver biopsy practice in France, US guidance was used by 56% of gastroenterologists and hepatologists⁹. The Patient Care Committee of the American Gastroenterological Association has stated that the liver biopsy "appears to be more accurate and perhaps more safe when performed in conjunction with ultrasound guidance"¹⁰. Most hepatologists agree that all patients should undergo ultrasonography of the liver before a percutaneous biopsy is performed. However, it is debatable whether the routine use of ultrasonography to guide the biopsy reduces the rate of complications, provides a higher diagnostic yield, or is cost effective¹¹⁻¹⁴. Nevertheless, it is still debatable whether routine use of US to guide percutaneous liver biopsy should be considered as the standard of care. The present study was conducted to correlate the clinical diagnoses with histological diagnoses as well as to see the complications associated with percutaneous liver biopsy.

Materials and Methods

It is a prospective study done in Dhaka Shishu Hospital, a tertiary care 530 bedded paediatric hospital, during the period February, 2004 to December, 2006. A total of 30 paediatric patients (age up to 13 years) of suspected liver diseases (based on following eligibility criteria) were subjected to biopsy for confirmation of diagnosis. Patients with evidence of liver disease, e.g., enlargement of liver and/or spleen, abnormal liver function tests, an abnormal appearance of the liver on a scan, raised blood ammonia, pyrexia

of unknown origin (PUO) with hepatomegaly, metabolic liver disease/storage disease, suspected hepatic neoplasm and cholestatic liver diseases were included in the study. However, patients with increased prothrombin time (international normalized ratio (INR) >1.6, thrombocytopenia (platelet count <80,000/cumm of blood) and ascites were excluded from the study. Besides these, unstable or critically ill or uncooperative child were discouraged to undergo the procedure. An ultrasound of liver was routinely performed before the procedure to mark the site for percutaneous biopsy. Ultrasonography performed before a liver biopsy identifies mass lesions that are clinically silent and defines the anatomy of the liver and the relative positions of the gallbladder, lungs, and kidneys. US information is also useful in selecting the spot for insertion of needle.

After explaining the nature of the disease, details of the procedure of liver biopsy and risk of complications to the parents, written consent was taken before doing the procedure. Position of the child while doing biopsy is an important determinant of safety. Younger children and babies were placed in a supine position. Older children were also placed in a supine position with pillows removed and the right arm elevated behind the head. A blind liver biopsy was done at the point of maximum dullness by percussion over the right trunk during both inspiration and expiration. Once a space below the onset of the hepatic dullness, between the mid axillary and anterior axillary line was located, the location was marked with a surgical pen. The field was prepared with alcohol-based solution (povidone-iodine) and sterile drapes were placed over the patient. Local anaesthetic was administered with 2% lidocain solution (preferably levobupivacaine 2.5mg/ml) in both superficial and deep planes. A small nick in the skin was made with a surgical blade, using a subcostal approach to allow introduction of the biopsy needle. The investigator then advanced the biopsy needle (a single pass of an outer needle) through the chest wall, between the mid axillary and anterior axillary line until the saline flows out freely. Suction was applied to the biopsy needle, advanced quickly into the liver and was taken out immediately (usually 3-4 firings of the biopsy needle). Two types of needle – suction needle (Menghini needle) and cutting needle (Tru-cut needle) can be used, but we used only tru-cut needle here. When cirrhosis was suspected on clinical grounds, the cutting needle was used to avoid fragment of fibrotic tissue. For both needle-types there were spring loaded

devices (so called guns) with a built-in triggering mechanism available. The diameter of the needle used in our study was 14-gauge (1.4 mm) which allowed adequate collection of tissue for diagnosis. The biopsy material was obtained in a very small amount of sterile normal saline in a sterile specimen pot. The sample was clearly labeled with the patient's details, sample type, date and time, prior to sending it to the appropriate laboratory. The sample was transported immediately to the laboratory, so that it could be processed correctly, e.g., some fixed in formalin, some in glutaraldehyde, some frozen.

As soon as the needle was taken out, pressure was applied to the site, followed by a wound closure strip and an adhesive dressing. The patient was rolled onto the right side and an instruction was given for them to remain in this position for one hour to help prevent bleeding or bile leakage complications.

The detailed procedure was recorded in the child's health care record including: 1) how many passes were made, 2) any medication administered, 3) any apparent complications and 4) specific post-operative care requirements. The patient was then followed up for any rise in pulse rate, fall in blood pressure, respiratory distress every 15 minutes for 1 hour, every 30 minute for next 2 hours and every 4 hours for the next 24 hours. Anuria / oliguria was notified immediately to the registrar / present investigator by 'on-duty doctor'. The possible need for blood transfusion, clotting factors, platelets, etc. was assessed. The actual site of the biopsy was looked for any signs of bleeding and the vital signs were checked and recorded, for the first 12-hour period after the procedure. An intravenous cannula was kept in situ for the 24-hour period post biopsy. Analgesics were given if needed. Patients were allowed to eat and drink 2 hours post procedure if awake and orientated. Patients remained on bed rest for 24 hours post procedure. However, the child was allowed to respond natural calls under supervision by a nurse or a responsible family member during this period provided their vital signs were stable. Older children were slowly mobilized 24 hours post procedure.

Results

Out of 30 patients of liver disease, 1(3.3%) was below 1 year, 14(46.7%) between 1-5 years and 15 (50%) more than 5 years of age. The median age of the patients was 5.0 ± 3.9 years and the minimum and maximum ages were 3 months and 13 years respectively (Table-I). Majority (80%) of the patients was male, giving a male to female ratio of 4:1 (Fig.-1).

Ninety percent of the patients belonged to poor socioeconomic class and none of the children came from higher social class (Table-II).

Table-I
Distribution of patients by age (n=30)

Age (yrs)	Frequency	Percentage
<1	1	3.3
1-5	14	46.7
>5	15	50

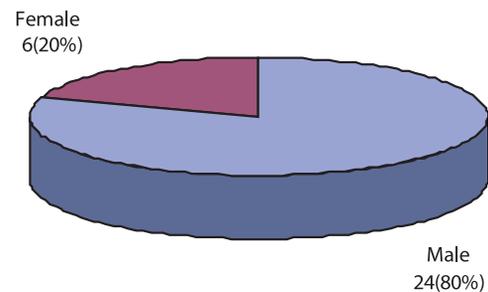


Fig.-1: *Distribution of patients by sex (n=30)*

Table-II
Distribution of patients by socioeconomic status (n = 30)

Socioeconomic status	Frequency	Percentage
Poor	27	90
Middle class	3	10

Clinically the cases were diagnosed as having chronic hepatitis (23.3%) followed by CLD (16.7%), isolated hepatomegaly without definite diagnosis (16.7%), liver cirrhosis (13.3%), storage disease (13.3%), hepatosplenomegaly and congenital hepatic fibrosis each was 6.7% (Fig.-2). Histological diagnoses of biopsy material obtained from the liver confirmed that

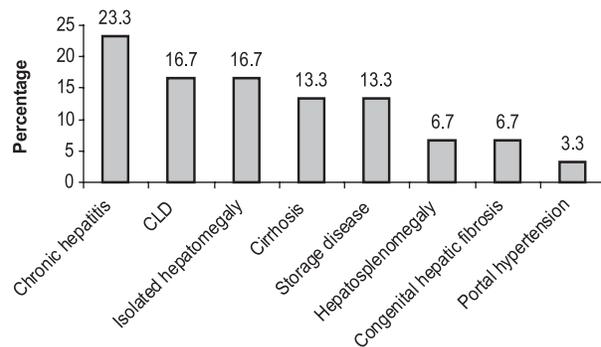


Fig.-2: *Distribution of patients by clinical diagnoses*

one-sixth (16.7%) of the total 30 cases had liver cirrhosis followed by storage disease and glycogen storage disease each comprised 13.3% of the cases, congenital biliary atresia 10%, and moderate fatty changes with cholestasis, congenital hepatic fibrosis, chronic inflammatory cells, chronic viral hepatitis and secondary biliary cirrhosis each consisted of 6.7% of the cases. Other cases of least frequency were hepatoblastoma with small anaplastic cells, cholestatic hepatitis, mild peripheral lymphatic infiltration and chronic triaditis (each 3.3%) (Table-III).

Table-III

Distribution of patients by biopsy diagnosis (n=30)

Biopsy diagnosis	Frequency	Percentage
Liver cirrhosis	05	16.7
Storage disease	04	13.3
Glycogen storage disease	04	13.3
Congenital biliary atresia	03	10.0
Moderate fatty changes with cholestasis	02	6.7
Secondary biliary cirrhosis	02	6.7
Chronic inflammatory cells (Chronic hepatitis)	02	6.7
Chronic viral hepatitis	02	6.7
Congenital hepatic fibrosis	02	6.7
Chronic triaditis	01	3.3
Cholestatic hepatitis	01	3.3
Mild peripheral lymphatic infiltration	01	3.3
Hepatoblastoma with small anaplastic cells	01	3.3

After biopsy, 3 (10%) patients complained of diffuse pain over the liver requiring analgesics, while 11(36.7%) patients had mild pain and discomfort at the site of biopsy which spontaneously went away. Only 3 (10%) patients experienced major complications, sustained major bleeding (6.7%) and peritonitis (3.3%) (Table-IV).

Table-IV

Complications after liver biopsy

Complications	Frequency	percentage
Mild pain did not require medication	11	36.7
Diffuse pain required analgesics	3	10
Major sustained bleeding	2	6.7
Peritonitis	1	3.3

Discussion

Some of the findings of liver need to be interpreted further to arrive at a conclusion. The clinical diagnosis of liver cirrhosis (13.3%) and storage disease (13.3%) correlated well with histological diagnosis of liver cirrhosis (16.7%) and storage disease (13.3%) and histopathologist did not mention the type of storage disease. Of the 5(16.7%) cases of CLD (diagnosed clinically), 4(13.3%) were histologically confirmed to have glycogen storage disease and 1(3.3%) exhibited moderate fatty changes with cholestasis. Out of 7 cases (23.3%) of chronic hepatitis diagnosed clinically, 2(6.7%) had congenital biliary atresia, 2(6.7%) chronic inflammatory cells, 1(3.3%) mild peripheral lymphatic infiltration, 1(3.3%) cholestatic hepatitis and another 1(3.3%) chronic triaditis was histologically confirmed. Clinical diagnosis of congenital hepatic fibrosis was done by unexplained hard isolated hepatomegaly matched well with histological diagnosis. Of the 2 (6.7%) cases of hepatosplenomegaly, 1(3.3%) had moderate fatty change with cholestasis and another 1(3.3%) hepatoblastoma. Overall, the clinical diagnoses matched well with the histological diagnosis. In 23.3% cases diagnoses made histologically were quite different from those diagnosed clinically. These findings are more or less consistent with those of Sheela and associates³ who reported that liver biopsy can change the clinical diagnosis in 8-14%. The findings emphasize the necessity of liver biopsy in disputed diagnosis before initiating a therapy, particularly if the therapy is costly and is to be continued for longer duration. However, liver biopsy is not without risk of carrying complications. Although the rate of major complications was low, minor complications may occur more frequently¹.

Sixty percent of complications occur within 2 hours, 82% in the first 10 hours and 96% within 24 hours after LB¹⁵. In our patients 3 (10%) patients complained of diffuse pain over the liver requiring analgesics, while 11(36.7%) patients had mild pain and discomfort at the site of biopsy which spontaneously went away. Post biopsy pain is the most common complication of LB, although the incidence varies depending on the severity. Less severe pain frequently indicates a small amount of blood or bile stretching the liver capsule and occurs in 30-50% patients¹⁶. There are two factors

demonstrated to be associated with an intense pain requiring analgesics: cutting biopsy needles and less experienced operators¹⁷⁻¹⁹.

The risk of major complications (such as bleeding requiring transfusion or further surgical intervention, penetration of adjacent organs, peritonitis and death) occur less frequently (0.13-5.4%), the most important being bleeding^{2,9,16,20}. In our series 3 (10%) patients experienced major complications. Two sustained major bleeding, one peritonitis. All of them improved with specific management. The higher rate of major complications might be due to "blind biopsy" which is liable to penetrate adjacent organ or major vessels. Besides, liver cirrhosis cases are more prone to bleed²¹ and in our study 16.7% of the patients had liver cirrhosis. Whatever the reason be, an ultrasound-guided percutaneous liver biopsy could minimize the major complications to a great extent.

Conclusion

Liver biopsy is a well established procedure in the diagnosis and follow-up of liver diseases. However, it is an invasive technique that carries a risk of complications. Although major complication is a rare occurrence, minor complications may occur very often. So, before deciding for a liver biopsy, the indications and risks must be assessed carefully for each patient and an account should be taken of the results of other routine investigations.

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