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SAFETY OF OUTPATIENT BLIND PERCUTANEOUS LIVER BIOPSY (OBPLB) IN CHILDREN AND DOCUMENTATION OF THE SPECTRUM OF CHILDHOOD LIVER DISEASE

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Abstract:

Aim: *To determine the safety of Outpatient Blind Percutaneous Liver Biopsy (OBPLB) in children and to document the spectrum of pediatric liver disease.*

Material and Methods: *This retrospective study was conducted in the Department of Pediatric Gastroenterology, Sir Ganga Ram Hospital Lahore for three-year duration from November 2017 to November 2020. Liver biopsies were performed using the Menghini aspiration technique. Histological diagnosis was documented. Complications were classified into minor (excessive crying and / or irritability, pain at the biopsy site, excessive sedation, and minor external hemorrhage from the biopsy site) or major (major external biopsy site hemorrhage, intraperitoneal hemorrhage, intrahepatic bleeding, biliary peritonitis, haemobilia, injury lungs, shock and death).*

Results: *Seven hundred and sixty-eight biopsies were performed on an outpatient basis in our department over the period of 3 years. Five hundred and five (65.8%) are men and 263 (34.2%) are women. The age range was from one month to 16 years. The liver biopsy fragment was diagnostic in 700 (91.1%) of the cases, 4.6% of the biopsies were normal, and 4.3% of the biopsies were inconclusive. The most common histological diagnosis was neonatal hepatitis (20.3%), followed by a decreasing frequency of chronic hepatitis (14.3%), glycogen storage disorders (13.7%), biliary atresia (13.4%), steatosis (10.8%), progressive familial intrahepatic cholestasis. (6.6%), lipid storage disorder (4.8%), cirrhosis 17 (2.2%), granulomatous hepatitis (0.7%), secondary haemochromatosis (0.7%), hepatosplenic aspergillosis (0.4%) and hepatoma (0.4%). One patient was diagnosed with each hepatocellular carcinoma, sclerosing hemangioma, metastatic non-Hodgkin's lymphoma, biliary cyst, cholangitis, and Budd-Chiari syndrome (0.1%). Seven (0.7%) biopsies were performed in six patients after liver transplantation. In our study, 45 had minor complications (5.8%) and no major complications were observed.*

Conclusion: *This study suggests that ambulatory percutaneous liver biopsy is relatively safe and well-tolerated with minimal complications in young infants and older children, and the results provide important diagnostic information. The most common histological diagnoses were neonatal hepatitis, chronic hepatitis, glycogen storage disorders, biliary atresia, steatosis, and progressive familial intrahepatic cholestasis.*

Key words: *liver biopsy, ambulatory, percutaneous, histological diagnostics*

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INTRODUCTION:

There are various liver diseases in the pediatric age group that can be broadly categorized as infectious, metabolic, developmental and neoplastic. These disorders are mostly age specific. The most common diagnoses in infancy are atresia of the bile ducts and neonatal hepatitis. Wilson's disease occurs around the age of 5, and autoimmune hepatitis can be found at any age. Early diagnosis is required for proper treatment and better outcomes. In the diagnosis of liver disease, in addition to clinical data, hematology and biochemistry tests, enzyme tests, and imaging techniques are helpful in establishing the diagnosis, but liver biopsy is often a critical component and enables the diagnosis of many forms of liver disease. Liver biopsy is indicated in many situations and can provide valuable information on diagnosis, prognosis, and treatment. Paul Ehrlich performed the first percutaneous liver biopsy in 1883 in Germany. Schupfer in 1907 developed a larger needle for liver biopsy, providing tissue for histological evaluation. The procedure became widely used after Menghini described the technique of "one-second liver needle biopsy" in 1958. Percutaneous liver biopsy may be performed blindly or under ultrasound guidance, and may be performed in both inpatient and outpatient settings. An outpatient procedure must be effective and economical as well as safe. Overnight hospitalization of patients costs about twice as much as sending them home in kindergarten. Ambulatory percutaneous liver biopsy (OPLB) was described in adults in 1978 and studies were conducted in a pediatric population considered to be a safe and cost-effective procedure. It is now standard practice to perform an outpatient liver biopsy if the recommendations and regulations published by the North American Society of Pediatric Gastroenterology and Nutrition Committee of Patient Care are followed. There are no data on the safety of ambulatory liver biopsy in children and adolescents. In our ward, outpatient liver biopsies typically take much longer than 15 years, and we reviewed our medical records of pediatric liver biopsies to determine the complication rate at our facility. We aim to investigate the safety of the outpatient blind Percutaneous liver biopsy (OBPLD) in pediatric population and to document the spectrum of the different histological diagnoses of liver disease.

MATERIAL AND METHODS:

This retrospective study was conducted in the Department of Pediatric Gastroenterology, Sir Ganga Ram Hospital Lahore for three-year duration from November 2017 to November 2020. A total of 768 biopsies were performed during this period. The medical records of all patients who underwent liver biopsy were reviewed. Information was collected retrospectively from graphs, laboratory results, imaging studies, and pathology reports. BPLB was performed on an outpatient basis using the Menghini Technique aspiration technique for the diagnosis of liver dysfunction. Basic vital signs including heart rate (HR), respiratory rate (RR), arterial blood pressure (BP), and core body temperature were recorded 1 hour prior to biopsy. All patients were treated with midazolam at a dose of 0.2 mg / kg body weight 10 minutes before the procedure as a sedative. Right intercostal access to the middle jaw was used under infiltration anesthesia with lidocaine hydrochloride. The needle was inserted in the right midaxillary line above the rib, just 1 intercostal space below the maximum blunting of the liver. After piercing the skin and subcutaneous tissues, reaching the surface of the liver, the trocar was withdrawn using the attached syringe, creating a vacuum, and 3–7 cm of the entire needle was inserted into the liver substance and was quickly withdrawn within 1 sec. originally described by Menghini. After the biopsy, the patients were placed in the right lateral position. A four-hour fast was carried out before and after surgery, and observation for up to 6 hours was carried out in order to early detect possible complications. Vital signs were monitored for 15 minutes in the first hour, for 30 minutes in the next 2 hours and every hour for the remaining 3 hours. Patients were discharged the same day, if there were no complications. Previous blood test including hemoglobin above 10 g, platelets> 70,000, PT extended for no more than 3 seconds compared to control and initial ultrasound to see vascular or cystic changes, situs reversal and ascites. An infectious needle lesion, clinical ascites, and examination disorder were contraindications for ambulatory liver biopsy. Complications were classified into minor (excessive crying and / or irritability, pain at the biopsy site, excessive sedation, and minor external hemorrhage from the biopsy site) or major (major external biopsy site hemorrhage, intraperitoneal hemorrhage, intrahepatic bleeding, biliary peritonitis, haemobilia, injury lungs, shock and death). Data collected for analysis in this study included age, gender, histological diagnosis, and advanced complications.

RESULTS:

Seven hundred and sixty-eight biopsies were performed on an outpatient basis in our department over the period of 3-years. The total number of patients was 767. One liver transplant patient underwent two biopsies on two separate occasions to rule out transplant rejection. Five hundred and five (65.8%) are men and 263 (34.2%) are women. The

age range was from one month to 16 years. The most common age group was <1 year (48.7%) followed by 1-5 years (35%). Eighty patients (10.4%) were 5-10 years of age, and there was a less frequent age group> 10 years (5.9%). The liver biopsy fragment was diagnostic in 700 (91.1%) of the cases, 4.6% of the biopsies were normal, and 4.3% of the biopsies were inconclusive. Histological diagnosis with age distributions is presented in Table 1.

TABLE 1- Distribution of Histological Diagnosis according to Age Groups

Histological Diagnosis	Age Groups of Patient				Total (%)
	<1Yr (%)	>1-5 Yrs(%)	>5-10 Yrs (%)	>10 Yrs(%	
Neonatal Hepatitis	143(18.6)	13(1.7)	0	0	156(20.3)
Chronic Hepatitis	6(0.8)	49(6.4)	34(4.4)	21(2.7)	110(14.3)
Glycogen Storage Disorder	18(2.3)	71(9.2)	13(1.7)	3(0.4)	105(13.7)
Biliary atresia	95(12.4)	8(1.0)	0	0	103(13.4)
Steatosis	47(6.1)	27(3.5)	5(0.7)	4(0.5)	83(10.8)
PFIC	29(3.8)	19(2.5)	1(0.1)	2(0.3)	51(6.6)
Lipid Storage Disorder	10(1.3)	25(3.3)	2(0.3)	1(0.1)	38(4.9)
Cirrhosis	1(0.1)	10(1.3)	4(0.5)	2(0.3)	17(2.2)
Granulomatous Hepatitis	2(0.3)	3(0.4)	1(0.1)	2(0.3)	8(1)
Post Liver Transplant Biopsy	0	7(0.9)	0	0	7(0.9)
Congenital Hepatic Fibrosis	0	1(0.1)	4(0.5)	0	5(0.7)
Secondary Hemochromatosis	0	4(0.5)	1(0.1)	0	5(0.7)
Hepatosplenic Aspergilosis	1(0.1)	2(0.3)	0	0	3(0.4)
Hepatoblastoma	1(0.1)	2(0.3)	0	0	3(0.4)
Hepatocellular Carcinoma	0	0	0	1(0.1)	1(0.1)
Sclerosed Hemangioma	0	1(0.1)	0	0	1(0.1)
Metastatic Non-hodgkin Lymphoma	0	0	1(0.1)	0	1(0.1)
Normal	9(1.2)	14(1.8)	9(1.2)	3(0.4)	35(4.6)
Inconclusive	11(1.4)	12(1.6)	5(0.7)	5(0.7)	33(4.3)
Choledochal Cyst	1(0.1)	0	0	0	1(0.1)
Cholangitis	0	1(0.1)	0	0	1(0.1)
Budd Chiari Syndrome	0	0	0	1(0.1)	1(0.1)
Total	**374(48.7)**	**269(35)**	**80(10.4)**	**45(5.9)**	**768(100)**

The most common histological diagnosis was neonatal hepatitis (20.3%), followed by a decreasing frequency of chronic hepatitis (14.3%), glycogen storage disorders (13.7%), biliary atresia (13.4%), steatosis (10.8%), progressive familial intrahepatic cholestasis. (6.6%) and lipid storage disorders (4.8%). Liver cirrhosis was found in 17 (2.2%) cases. Less frequent diagnoses were granulomatous hepatitis (0.7%), secondary haemochromatosis (0.7%), hepatosplenic aspergillosis (4%) and hepatoma (4%). In each case, one patient was diagnosed with hepatocellular carcinoma, sclerosing hemangioma, metastatic non-Hodgkin's lymphoma, biliary cysts, cholangitis and Buddha-Chiari syndrome, accounting for 1% each. Seven (7%) biopsies were performed on six liver transplant patients due to transplant rejection indications, and one patient underwent two biopsies. Thirty-five (4.6%) had normal liver biopsy results, which were taken in patients with hepatitis B and C as a baseline, and in patients with undiagnosed systemic diseases in whom ALT was elevated, liver biopsy was performed for diagnosis. Thirty-three (4.3%) had ambiguous histological reports. Forty-five had minor complications (5.8%). Twenty-six (58%) patients in the <1-year group were irritable and over-sedated. Thirteen (28.8%) patients in the 1-5 years age group, 1 (2.2%) in the 5-10 years age group and 5 (11%) in the> 10 years age group have minor complications, including irritability and pain.

TABLE 2 – Incidence of Complications in Different Age Group

Age groups of Patient	Complications		
	Major	Minor (%)	None (%)
<1Year	0	26(7.0)	348(93.0)
1-5 Years	0	13(4.8)	256(95.2)
5-10 Years	0	1(1.3)	79(98.7)
>10 years	0	5(11.1)	40(88.9)
Total Number of Liver Biopsies(768)	**0**	**45(5.8)**	**723(94.2)**

TABLE 3: Distribution of Histological Diagnosis according to Gender

Histological Diagnosis	Male	Female	Total
Neonatal Hepatitis	122	34	156
Chronic Hepatitis	74	36	110
Glycogen Storage Disorder	58	47	105
Biliary atresia	60	43	103
Steatosis	52	31	83
PFIC	36	15	51
Lipid Storage Disorder	27	11	38
Cirrhosis	12	5	17
Granulomatous Hepatitis	5	3	8
Post Liver Transplant Biopsy	5	2	7
Congenital Hepatic Fibrosis	5	0	5
Secondary Hemochromatosis	3	2	5
Hepatosplenic Aspergilosis	3	0	3
Hepatoblastoma	3	0	3
Hepatocellular Carcinoma	0	1	1
Sclerosed Hemangioma	1	0	1
Metastatic Non-hodgkin Lymphoma	1	0	1
Normal	18	17	35
Inconclusive	20	13	33
Choledochal Cyst	0	1	1
Cholangitis	0	1	1
Budd Chiari Syndrome	0	1	1
Total	**505**	**263**	**768**

DISCUSSION:

The main causes of liver disease observed in infancy are neonatal cholestasis, including biliary atresia, neonatal hepatitis, and progressive familial intrahepatic cholestasis, followed by toxic, infectious, metabolic, autoimmune, vascular and infiltrative disorders after infancy. The relative frequency of each disorder will vary with the patient's age. The most common disorder in our study was neonatal hepatitis (20.3%) with a predominance of men (M / F ratio 3.6: 1). One hundred and forty-three were <1 year old, and 13 patients> 1 year of age. Similarly, higher incidence of neonatal hepatitis was reported in other studies of 28.9% by Akinbami et al. From Oman 10 and 18% by Ramakrishna et al from India. In contrast, the frequencies of 10% and 10.9% were reported by Ahmed et al. From Pakistan and Monajemzadeh, et al. From Iran. This difference is likely due to the higher incidence of secondary haemosiderosis due to thalassemia in their studies. Another related diagnosis of neonatal cholestasis, biliary atresia was the fourth common diagnosis in our study (13.4%) with a male to female ratio (1.4: 1). Only 31 patients (30%) were under 2 months of age, the rest were older, and eight patients (7%) were over one year of age. This proves a reduced awareness of the disease and late referral to appropriate centers, thus monitoring the prognosis. At this stage, managing the patient also becomes difficult, as a procedure similar to a liver biopsy is associated with an increased risk of complications. A similar incidence of biliary atresia was reported by Monajemzadeh et al. (11.8%) and Akinbami et al. (12%), but the overall number of patients is higher (n = 103) in our study compared to these two studies, respectively n = 38 and n = 9. Earlier local studies from Pakistan showed incidence rates with variable rates of 20%, 8%, 5% and 9%, but again the number of patients was higher in our study. Chronic hepatitis was the second most frequent diagnosis in our study (14.3%) with an M: F ratio (2: 1). Ten patients were with chronic hepatitis B and eight with chronic hepatitis C. The incidence is quite high compared to previous local studies in Pakistan - 6% and 5%. Monajemzadeh et al. They published the incidence of chronic hepatitis (10.6%). Liver cirrhosis was detected in 17 patients (2.2%). Contrary to higher studies, higher frequencies of 10%, 6%, 23.4%, and 14% were recorded in Pakistan, 20% in India and 8.1% in Iran. Granulomatous hepatitis was found in 8 patients (01%), 5 men and 3 women. One patient died of miliary tuberculosis and one patient had drug-resistant tuberculosis, which initiated second-line anti-tuberculosis. The rest were diagnosed as tuberculosis and treated appropriately. There were 3 cases of hepatosplenic granuloma (0.4%). One was diagnosed with chronic granulomatous disease and two were immunodeficient. Five cases of secondary haemochromatosis (0.7%) were diagnosed, they were patients with thalassemia. We have a separate hematological unit and they usually deal with them separately, so the incidence of secondary

hemochromatosis was lower. Ahmed et al. From Pakistan showed the most common diagnosis of this disease because they have a bone marrow transplant center and an increased number of thalassemia patients undergoing liver biopsy prior to bone marrow transplantation. Hepatic fibrosis was diagnosed in 5 patients (0.7%). In our study, 374 (48.1%) were under the age of one year. 26 patients (7.5%) experienced minor complications including irritability and sedation that were transient and recovered without major complications in this age group. Amaral et al. Minor complications were reported in 4.6% (minor bleeding) and serious complications in 4.6% in infants. These data show that liver biopsy is relatively safe in this age group. Overall, forty-four in our study had minor complications (5.8%) in all patients. Twenty-six (58%) patients in the <1-year group were irritable and over-sedated. Thirteen (28.8%) patients in the 1-5 years age group, 1 (2.2%) in the 5-10 years age group and 5 (11%) in the> 10 years age group have minor complications, including irritability and pain and only pain medication is required and sent home after six hours of monitoring. Except in one patient, no bleeding to the point requiring transfusion has been reported in any other patient. Careful patient selection is essential for an outpatient liver biopsy, especially of the coagulation profile.

CONCLUSION:

This study suggests that outpatient percutaneous liver biopsy is relatively safe and well tolerated with minimal complications in small infants and older children and the results yield important diagnostic information. The most common histological diagnoses were neonatal hepatitis, chronic hepatitis, glycogen storage disorders, biliary atresia, steatosis, and progressive familial intrahepatic cholestasis. The incidence of glycogen storage disorders and progressive familial intrahepatic cholestasis has been found to be higher in our population and individual studies should be conducted for these below-reported disorders.

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