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Clinical Findings in Biliary Atresia: A Literature Review

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Abstract

Biliary atresia is an obstructive disease affecting the biliary tract. Patients with biliary atresia often appear similar to normal infants, leading to delayed detection in many cases. There are several clinical symptoms and typical laboratory findings that typically manifest in patients with biliary atresia. As the age of the patient advances, the manifestations worsen, potentially leading to the development of cirrhosis, liver failure by the age of 1, and other complications. The aim of this review is to understand the clinical finding of biliary atresia patients, facilitating early detection and intervention to reduce the likelihood of the disease progressing to a more severe stage. Delay in the diagnosis of biliary atresia can result in a poor prognosis.

Keywords: Biliary Atresia; Clinical sign; Laboratory result; Treatment

1. Introduction

Biliary atresia is an obstructive disease of the biliary tract that results in the inability of bile to reach the intestinal tract [1]. Biliary atresia is found in 1 in every 8000 to 18000 births and is more prevalent in Asian and African populations compared to Europeans [2]. Biliary atresia has some common symptoms include jaundice, pale stools, and hepatomegaly. Untreated biliary atresia can lead to liver cirrhosis, liver failure by the first year of life, and other complications [3,4].

Biliary atresia presents in two forms based on associated anomalies: perinatal and embryonic. The embryonic type has an earlier onset and is often accompanied by abnormal developments. The perinatal type is suspected to result from postnatal cholangiopathy obstruction and presents with alcoholic stools [3,5]. The Japanese Association of Pediatric Surgeons categorizes biliary atresia into three main types based on the location of obstruction. Type I involves atresia in the common bile duct, while the gallbladder and hepatic

ducts remain patent (referred to as distal biliary atresia). Type II further divides into IIA and IIb. In Type IIA, the gallbladder and common bile duct are patent, whereas Type IIb involves obstruction in the gallbladder, cystic duct, and common bile duct. Type III, the most prevalent condition at 73%, is characterized by obliteration of all extrahepatic bile ducts (complete biliary atresia) [6].

Biliary atresia results from inflammation and fibrous tissue formation, leading to obstruction of the extrahepatic bile ducts, disrupting bile flow [7]. Simultaneously, intrahepatic bile ducts undergo hyperplasia. There is substantial evidence indicating that viruses, toxins, and genetic variations contribute to the etiology of biliary atresia, eliciting an inflammatory response affecting the epithelial layer. Immune cells activate the expression of type 2 cytokines, inducing epithelial cell proliferation and the formation of matrix cells from non-parenchymal cells [1,8].

2. Clinical Manifestation

The most prevalent clinical manifestation in patients with Biliary Atresia is jaundice. This occurs due to the accumulation of bile fluid in the body, resulting in a yellowish appearance in the sclera, skin, and mucous membranes. Biliary atresia patients experience post-hepatic jaundice, a condition where the blocked bile ducts affect the amount of conjugated bilirubin [9]. This leads to the buildup of bilirubin in the circulation, soluble in fat beneath the skin, causing the appearance of jaundice [10]. Many infants exhibit jaundice in the early stages of life, making it challenging to differentiate if the jaundice physiological or not. [11]. Jaundice in biliary atresia patients differs from physiological jaundice. Physiological jaundice typically improves with exposure to UV light, whereas pathological jaundice, as in biliary atresia, does not improve even with sunlight exposure and worsens over time. [12].

Additionally, biliary atresia patients typically present with pale stools. This is because bilirubin, which should reach the intestines, fails to do so. Bilirubin in the digestive tract serves as a colorant for feces. Some countries have started implementing fecal color detection cards for early biliary atresia detection,

including at RS DR. Soetomo Surabaya. These cards display various stool colors ranging from pale to normal, aiding parents in identifying alarming signs of their child's stool color. [13,14].

Another common symptom in biliary atresia patients is dark-colored urine. Normally, urine does not contain bilirubin. However, in biliary atresia cases, conjugated bilirubin is excreted through the kidneys, giving the urine a dark color [15]. Another commonly observed symptom is hepatomegaly [16]. Jaundice, pale stools, and dark-colored urine are an early signs of biliary atresia, so there is no difference between early and late diagnosis symptoms in biliary atresia. [14].

3. Laboratory Result

Patients with biliary atresia typically exhibit elevated levels of conjugated bilirubin, a slight increase in serum gamma-glutamyl transferase (GGT), ALP, and elevation in serum transaminases [17]. The increase in conjugated bilirubin is indicate of liver cell damage or cholestasis. Although the measurement of conjugated bilirubin is effective in detecting liver diseases in neonates, it is not entirely accurate for biliary atresia, necessitating further examination. Several studies have explored early detection strategies for infants, with commonly used methods worldwide including the measurement of conjugated bilirubin levels and the use of color stool cards provided to parents [18].

Patients also tend to exhibit elevated levels of GGT [19]. Elevated GGT levels can serve as a crucial parameter to rule out other diagnoses related to neonatal cholestasis. Infants with biliary atresia tend to have higher GGT levels compared to those without biliary atresia. However, it's important to note that GGT measurements are most effective when performed in infants aged less than 120 days [20].

Various enzymes, including SGPT, SGOT, ALP, among others, can indicate liver function. In this context, liver function tests aim to identify the source of liver damage. An increase in the SGPT and SGOT ratio to alkaline phosphatase (ALP) and bilirubin indicates hepatocellular disease. Conversely, disproportionate increases in SGPT and SGOT to ALP and bilirubin suggest a cholestatic condition,

prompting the consideration of differential diagnoses. SGPT and SGOT are part of serum aminotransferases, which are markers of liver cell damage [21,22].

4. Diagnosis

Early diagnosis, ideally within the first 3 months, is crucial. This is because cirrhosis can begin to develop at around 3 months of age, leading to poorer outcomes. Hepatosplenomegaly and ascites tend to appear in patients older than 3 months, indicating cirrhosis [23]. Late diagnosis is considered when the patient is over 90 days old [24].

Abdominal ultrasonography is the first and non-invasive imaging examination of choice for suspected biliary atresia patients [25]. One of the findings in the ultrasonography (USG) of patients with biliary atresia is the presence of the triangular cord sign [26]. Another diagnostic option is percutaneous cholecysto-cholangiography, which is more accurate as it directly observes the progressive filling of iodine in the bile ducts, confirming biliary atresia in challenging cases. The absence of retrograde contrast filling in the intrahepatic bile ducts is also indicative of biliary atresia. In patients without biliary atresia, clarity in both intrahepatic and extrahepatic bile ducts is always observed [27].

Histopathological examination findings in biliary atresia patients reveal bile duct proliferation (BDP), bile duct obstruction, portal infiltration with lymphocytes, neutrophils, and eosinophils, hepatocyte transformation, and liver cell swelling [28].

5. Treatment

Infants with biliary atresia can have a better prognosis if detected and treated early, ideally within the first 8 weeks of life. The procedures used to manage biliary atresia include the Kasai Procedure (KP) and liver transplantation.

5.1 Kasai Procedure

The Kasai Procedure aims to restore bile flow between the liver and the intestine, helping to reduce the progression of liver disease using a Roux-en-Y jejunal limb. Kasai Procedure can successfully restore bile ducts from the liver to the intestine especially when performed within the first 60 days of life. The success of the Kasai Procedure is determined by the restoration of bile flow, the return of normal stool color, and the disappearance of jaundice [25,29]. It is advisable to perform the Kasai Procedure before the age of 3 months to prevent further liver damage or progression to cirrhosis [23].

5.2 Liver Transplantation

Liver transplantation (LT) is considered in various conditions, including Kasai Procedure failure, significant malnutrition, recurrent cholangitis, portal hypertension, hepatopulmonary syndrome, and malignancies. Unfortunately, patients with biliary atresia often face long waiting times for liver transplantation [23] . The Pediatric End-stage Liver Disease (PELD) score is used to allocate liver transplants in children, considering factors such as albumin levels, bilirubin levels, prothrombin time, and growth failure [30]. Early detection and appropriate intervention significantly impact the prognosis and quality of life for patients with biliary atresia.

6. Conclusions

Biliary atresia is a neonatal disease that requires early diagnosis. Commonly observed symptoms include jaundice, pale stools, dark urine, and hepatomegaly. Laboratory test results in patients with biliary atresia tend to show elevated levels of conjugated bilirubin, GGT, and serum transaminases. The later the diagnosis, the more likely patients are to experience clinical deterioration, and the efficacy of treatment is compromised. Ultrasonography (USG) is routinely performed in the early stages of diagnosis to assess the patient's biliary tract condition. A more accurate diagnostic procedure is percutaneous cholecysto-cholangiography. Treatment options for biliary atresia include the Kasai Procedure and Liver Transplant. Therefore, it is imperative to prioritize early diagnosis for biliary atresia.

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