Biliary Atresia in Infants with Cholestasis

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ABSTRACT

Background: *Cholestasis is a pathological condition due to impaired secretion and excretion of bile into the duodenum. The etiology should be found within golden period age (< 10 weeks of life) in order to get better outcome. Biliary atresia is characterized by total obstruction of extrahepatic biliary system. The cause is unknown. The only effective treatment is Kasai procedure, which should be done at 8 weeks age or less. The aim of this study was to observe the pattern of cholestasis cases in infants.*

Method: *A descriptive study was conducted on 63 patients with cholestasis at the Harapan Kita Woman and Children Hospital, Jakarta between January 2008 and December 2009. Data was obtained from the computerized medical record database system. Statistical analysis was performed using SPSS program.*

Results: *There were 63 infants, include of 40 (63.5%) boys. Age at admission were 80.2 (30-207) days. The laboratory findings included mean serum levels of hemoglobin 8.9 g/dL, conjugated bilirubin 12 mg/dL, alanine transaminase 149 u/L, aspartate transaminase 236 u/L, alkaline phospatase 582 u/L and gamma-glutamyl transpeptidase level 326 u/L. Biliary atresia was diagnosed in 8 (12.7%) infants by abdominal ultrasonography examination, cholangiography and liver biopsy. Kasai procedure (portoenterostomy) was performed to all those infants. Two of those infants died.*

Conclusion: *Cholestasis has become one of the most common problem found in infants. Biliary atresia should always be considered as one of the cause, since early diagnosis and immediate treatment are needed to provide a good outcome.*

Keywords: *cholestasis, biliary atresia, Kasai procedure*

ABSTRAK

Latar belakang: *Kolestasis adalah suatu kondisi patologis akibat gangguan sekresi dan ekskresi empedu ke duodenum. Etiologi penyakit ini sebaiknya ditemukan pada usia < 10 minggu kehidupan untuk mendapatkan hasil yang lebih baik. Atresia bilier ditandai dengan obstruksi total sistem ekstrahepatik empedu dengan penyebab yang belum diketahui. Satu-satunya pengobatan yang efektif pada saat ini yaitu dengan prosedur Kasai yang sebaiknya dilakukan pada usia 8 minggu atau kurang. Penelitian ini bertujuan untuk melihat gambaran pola kasus kolestasis pada bayi.*

Metode: *Penelitian deskriptif dilakukan pada 63 pasien bayi dengan kolestasis di Rumah Sakit Anak dan Bunda Harapan Kita, Jakarta selama bulan Januari 2008-Desember 2009. Data diperoleh dari sistem komputerisasi rekam medis pasien. Analisis statistik dilakukan dengan program SPSS.*

Hasil: *Didapatkan 63 pasien bayi yang terdiri dari 40 (63,5%) bayi laki-laki. Rata-rata usia pasien saat masuk rumah sakit adalah 80,2 hari (30-207). Pada hasil laboratorium ditemukan rerata kadar hemoglobin darah 8,9 g/dL, bilirubin direk 12 mg/dL, alanin aminotransferase (ALT) 149 u/L, aspartat transaminase (AST) 236 u/L, alkali fosfatase 582 u/L dan rerata kadar gamma-glutamil transpeptidase 326 u/L. Atresia bilier didiagnosis pada 8 (12,7%) bayi dengan pemeriksaan ultrasonografi abdomen, kolangiografi dan biopsi hati. Prosedur Kasai (portoenterostomi) dilakukan pada semua bayi tersebut, namun terdapat dua bayi meninggal.*

Kesimpulan: *Kolestasis telah menjadi salah satu masalah yang paling sering ditemukan pada bayi. Atresia bilier dapat dipertimbangkan sebagai salah satu penyebabnya, untuk itu diperlukan diagnosis dini dan pengobatan segera agar memberikan hasil yang baik.*

Kata kunci: *kolestasis, atresia bilier, prosedur Kasai*

INTRODUCTION

Cholestasis is a pathological condition due to impaired secretion and excretion of bile into the duodenum. Clinically, the infants will have yellow discoloration of the skin, enlarged liver, pale stools and dark urine. The laboratory tests show conjugated bilirubin level of > 1 mg/dL in total bilirubin level < 5 mg/dL or conjugated bilirubin of > 20% of the total bilirubin > 5 mg/dL.[1] The etiologies of cholestasis are divided into extra and intrahepatic and each has specific etiology. Intrahepatic cholestasis is characterized by hepatocyte dysfunction and impaired patency of the extrahepatic biliary system, while the extrahepatic neonatal cholestasis is characterized by complete and persistent cholestasis.[2]

Infants with such clinical symptoms require further diagnostic evaluations since infants with conjugated hyperbilirubinemia is always abnormal and should be considered to have a liver dysfunction. Biliary atresia is the most common causes extrahepatic cholestasis in infants. The incidence has been reported to vary from 1 : 10,000 to 1 : 15,000 live birth.[2] Infants may have good clinical condition with white stool more than 7 days, hepatomegaly with no splenomegaly, and the bilirubin level is not always very high. Biliary atresia is an emergency condition that requires immediate surgery intervention.[1]

Prognosis of biliary atresia depends on several factors. Kasai procedure performed before 6 weeks of age infants would give 80% probability of 5-year jaundice-free survival rate.[1] Overall, the 10-year survival rate is 90%. Failures of Kasai procedure are influenced by control of nutrition (nutrition, vitamins) and timely liver transplantation.[2] Many infants with cholestasis have been hospitalized in women and children hospital; therefore, this study aimed to observe the pattern of infant cholestasis cases in Harapan Kita Women and Children Hospital.

METHOD

The present study was a descriptive study conducted in 63 infants who had been diagnosed with cholestasis at the Harapan Kita Woman and Children Hospital, Jakarta between January 2008 and December 2009. The data about the subjects was obtained from computerized database system of medical record unit including age, sex, hemoglobin level, serum levels of conjugated billirubin, alanine aminotransferase (ALT), aspartate transaminase (AST), alkaline phospatase (ALP), gamma-glutamyl transpeptidase (GGT), abdominal ultrasound, cholangiography, liver biopsy, and Kasai procedure. Statistical analysis was performed by SPSS.

RESULTS

Patients were mostly boys (63.5%) with an average age of 2.5 months. They had been suffered from anemia with mean hemoglobin levels less than 10 g/dL and conjugated bilirubin levels over 10 mg/dL. The mean serum levels of ALT and AST increased less than 10 times of the normal value (Table 1).

Table 1. Patient characteristics

Characteristic	Results
Age (days)	80.2 (1-207)
Sex (%)	
Boy	40 (63.5)
Girl	23 (36.5)
Laboratory findings	
Hemoglobin (g/dL)	8.9 (6-14.4)
Conjugated bilirubin (mg/dL)	12 (10-23)
ALT (u/L)	149 (13-454)
AST (u/L)	236 (24-850)
ALP (u/L)	582(102-1,459)
GGT (u/L)	326 (16-2,530)

ALT: alanine aminotransferase; AST: aspartate transaminase; ALP: alkaline phospatase; GGT: gamma-glutamyl transpeptidase

All had undergone ultrasound examination and 8 (12.7%) of them had presentation suggestive of biliary atresia. All those eight infants had also been undergone the cholangiography, liver biopsy and followed by Kasai procedure (Table 2).

Table 2. Diagnostic and Kasai procedure

Type of diagnostic procedure	n
Ultrasonography abdomen (n = 63)	
Atresia biler	8
Sludge (bile plaque syndrome)	48
Hepatitis	7
Cholangiography (n = 8)	
Confirmed biliary atresia	8
Liver biopsy (n = 8)	
Confirmed biliary atresia	8
Kasai procedure (n = 8)	
Died after several times of control	2
Lost of contact after several time of control	4
Could not be traced	2

DISCUSSION

Bilirubin is the final catabolism product of erythrocytes. Bilirubin is bound by albumin and transferred to the liver, which subsequently being conjugated with glucoronic acid to form conjugated bilirubin.[3] A condition of jaundice with direct bilirubin serum level more than 50% of total bilirubin is defined as conjugated hyperbilirubinemia. Such condition can be caused by intrahepatic (45%) or extrahepatic (5%) or intra and extrahepatic (45%) cholestasis. Hyperbilirubinemia of intrahepatic cholestasis occurs when there is a blockage of the bile flow or hepatocyte excretion transport failure of bile duct obstruction.[4]

After birth, the clinical triad of biliary atresia are jaundice, alcoholic stool and dark urine, and hepatomegaly. The general condition of the child is usually good. There is no failure to thrive, at least in the first month of life. Jaundice at two weeks of life is relatively common (up to 15%), however it is not always associated with liver disease. Jaundice infants with dark urine (conjugated /direct bilirubin) are always abnormal. Normal prothrombin time (PT) after giving parenteral vitamin K is considered as cholestasis or abnormality in bile formation or excretion and low PT as liver insufficiency. The color of stool is also important. About 98% of infants with white stool more than 7 days has been confirmed to have biliary atresia. On this study, most of cholestasis infants were diagnosed at the age of 2.5 months.[1]

Anemia can be found in infants with cholestasis due to reduced hepatocytes function or micro-hematochezia.[5] In this study, most infants were anemic with mean level of hemoglobin was 8.9 (6 to 14.4) g/dL. Therefore, the possibility of hepatocyte damage in those infants should be considered. The laboratory result of ALT serum level can be used as an indicator of hepatocyte damage.[6] The present study demonstrated increased mean levels of ALT and AST. Some infants had ALT and AST levels above 10 times of the normal value, which indicated severe liver damage.

Increasing levels of GGT suggests biliary obstruction since the GGT enzymes are located in the canaliculi. Obstruction may cause further hepatocyte damage. GGT level is more sensitive to detect obstructive jaundice than ALP, ALT, and AST.[7] The mean serum level of GGT in this study was 326 (16-2,530) u/L, which could a marker of biliary obstruction in some infants.

Biliary atresia is characterized by total obstruction of extrahepatic biliary system; however, the cause is uncertain.[8] One of the diagnostic procedures is abdominal ultrasonography (USG).[9] The abdominal USG was performed in two-phase procedure. The first phase was done after 12-hour fasting and the second phase was completed in 2 hours after giving breast milk or formula milk. The presence of the triangular cord sign above the portal vein bifurcation could be a sensitive radiologic marker for biliary atresia.[9] Abdominal ultrasound has some advantages since it carries minimal risk and no time delay. Experts in ultrasound examination could point to biliary atresia by demonstrating an irregularly shaped or absent gall bladder.[10] Eight infants (12.7%) in this study were diagnosed on ultrasound as biliary atresia.

Cholangiography followed by liver biopsy and Kasai procedure are mandatory in biliary atresia infants. Biliary atresia could be diagnosed by histopathologic examination at the age of 4-7 weeks.[2]

Edema or expanded portal tracts, bile duct damage and reduplication, as well as fibrosis are strongly suggested a large bile duct obstruction, which biliary atresia is the most common cause.[11] Percutaneous liver biopsy is a reliable, definitive, and safety technique. Experienced pathologist may yield diagnosis in 90-95% of cases.[12] In this study, 8 infants had suggestive results of biliary atresia on abdominal USG, cholangiography and liver biopsy as shown in Table 2. All infants had undergone Kasai procedure.

The current management of biliary atresia patients involves two steps, i.e. Kasai operation (in neonatal period) which aim to restore bile flow and liver transplantation in children for whom the Kasai procedure has failed in its primary aim or for whom complications of biliary cirrhosis have supervened. Time plays a major role in the treatment of biliary atresia. The biliary tract between liver and intestines is completely blocked and bile retention then causes destruction of the liver itself. Kasai conducted in older infants would reduce the success of the outcome, because it may have been a process of hepatic cirrhosis.

There were two-year survival rate of 65% and 80% of jaundice-free period when Kasai is performed before 60 days of age. If the Kasai is done after the age of 60 days, the survival rate is 22% and there is 20-35% of jaundice-free period.[13] Of eight infants with biliary atresia who had undergone Kasai procedure, two infants died after several times of visits; while the outcome of the other six infants were unknown due to lost contact or could not be traced. Porto-enterostomy performed by an experienced surgeon would give promising results of good bile flow with normal serum bilirubin, which can be achieved in more than 80% of infants with biliary atresia operated on 60 days of age.[13,14]

Treatment after the Kasai procedure such as treatment with phenobarbital and ursodeoxycholic acid or chloretic also affect the long-term survival rate.[12] Bile flow after portoenterostomy is 25-35% at 10-year survival rate.[14] Death is usually caused by liver failure, sepsis, acidosis, or respiratory failure secondary to intractable ascites, and esophageal variceal hemorrhage.[1] Cholangitis, which is an important post-operative complication due to a wide range of micro-organisms, may occurs in more than 50% of patients in the first 2 years after surgery.[3]

CONCLUSION

Cholestasis has become one of the circumstances that are often found in infants. Although the prevalence is not high, biliary atresia should always be considered as one of the cause, since early diagnosis and immediate treatment are required in order to provide a good outcome.

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