

## RESEARCH NOTE

# PREVALENCE OF HEPATITIS A VIRUS INFECTION IN CHILDREN WITH BILIARY ATRESIA

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**Abstract.** This study aimed at identifying the prevalence of hepatitis A virus (HAV) infection in children with biliary atresia (BA). Blood samples were collected from children with BA whom had undergone portoenterostomy and attended the pediatric liver clinic, King Chulalongkorn Memorial Hospital between May 2002 and May 2003. Seventy-seven patients, 45 females and 32 males, ages ranging from 0.2-19 years (mean  $\pm$  SD = 5.9  $\pm$  4.6 years) were enrolled in the study. The HAV seropositivity rate of patients aged <10 years and  $\geq$  10 years were 13.1% and 25%, respectively. The seropositivity rate of patients with favorable outcomes (total bilirubin level  $\leq$  2 mg/dl) and unfavorable outcome (total bilirubin level  $>$  2 mg/dl) were 17.5% and 13.5%, respectively, which were not statistically different ( $p = 0.6$ ). Children suffering from BA with failed portoenterostomy are at risk of developing severe liver damage at an early age. In these patients a superimposed acute liver infection due to a hepatitis virus, including HAV, may affect liver function and lead to particularly severe disease. The effectiveness of HAV immunization in this particular group of children merits further study.

Biliary atresia (BA) is a severe neonatal liver disease resulting from a sclerosing cholangiopathy of unknown etiology. Hepatic fibrosis and portal hypertension still occur despite disappearance of jaundice following successful hepatic portoenterostomy. Patients who fail to clear jaundice after portoenterostomy eventually develop secondary biliary cirrhosis and end-stage liver disease.

In Thailand, both the prevalence and incidence of hepatitis A infection is decreasing, especially amongst the younger age group, as sanitation and socio-economic conditions improve. This has resulted in an increasing proportion of susceptible young adults, and is thus changing the demographics of this disease. Although it is a self limited, relatively mild illness, hepatitis A infection can cause serious and even fatal disease with an overall mortality rate of 0.1% (O'Grady, 2000). It is the main etiology of acute liver fail-

ure in normal children (Debray *et al*, 1997; Ciocca, 2000; Moreira-Silva *et al*, 2002). Patients with underlying chronic liver disease and older individuals are at increased risk of fulminant hepatitis when infected with hepatitis A virus (HAV) (Keeffe, 1995; Vento *et al*, 1998; Pramoolsinsap *et al*, 1999). If BA patients are infected with HAV, they may be at high risk for developing severe hepatitis and/or of worsening their chronic liver disease.

This study aims at identifying the prevalence of HAV infection in children with biliary atresia.

Blood samples were collected from children with biliary atresia whom had undergone portoenterostomy and attended the pediatric liver clinic, King Chulalongkorn Memorial Hospital between May 2002 and May 2003 under the study on cytokines and genetic polymorphism in children with biliary atresia project. Serum samples were stored at -20°C until tested for anti-HAV IgG by ELISA (Abbott Laboratories, North Chicago, Illinois). Liver function testing was performed by an automated machine (Hitachi, 912). We obtained the permission from the director of the hospital to use the stored sera in this study. The

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study was approved by the Ethics Committee of the Faculty of Medicine, Chulalongkorn University. Comparison between groups was made by chi-square analysis.

Seventy-seven patients, ages ranging from 0.2-19 years (mean  $\pm$  SD = 5.9  $\pm$  4.6 years) were enrolled in the study. There were 45 females and 32 males. The distribution of detectable anti-HAV antibodies is shown in Table 1. There was no statistical difference in seropositivity rates in patients with favorable outcomes (total bilirubin level  $\leq$  2 mg/dl) and unfavorable outcomes (total bilirubin level  $>$  2 mg/dl) (Table 2, p = 0.6).

Improvement in sanitation and socioeconomic conditions in Thailand has led to a decline in natural immunity against HAV. Our study revealed that the HAV seroprevalence in children aged <10 and  $\geq$  10 years of age has declined from 24.8% and 51.2%, respectively, in 1988 to 6.8% and approximately 13%, respectively, in 1996 (Poovorawan *et al*, 1997a, b). It is clear that certain factors predispose patients to more severe disease and increased mortality. The age at which infection occurs clearly influences the outcome, with the risk of severe hepatitis increasing sharply after the age of 40 years (O'Grady, 2000). Individuals with chronic liver disease are at increased risk of severe disease. As reported in numerous studies on adult patients, hepatitis A can have a more serious course in patients with preexisting liver disease, resulting in greater impairment of liver function, more severe complications, such as fulminant hepatitis, and higher mortality rates (Keeffe, 1995; Vento *et al*, 1998; Pramoolsinsap *et al*, 1999). A study from King's College Hospital showed 17.7% of patients with chronic liver disease and HAV infection developed acute liver failure, with 4.4% of patients dying (O'Grady, 2000).

HAV infection in children is considered to be mild, or even a silent disease, in most instances. However, HAV has been identified as the main cause, ranging from 26-83%, of fulminant liver failure in children in many countries (Debray *et al*, 1997; Ciocca, 2000; Moreira-Silva *et al*, 2002). Fulminant hepatitis A is rare, but often fatal (Ciocca, 2000). A study from Pakistan found that of 2,735 children with hepatitis A, 30 (1%) developed liver failure and 11 (0.4%) died (Shah *et*

Table 1  
Age-specific prevalence of anti-HAV among biliary atresia patients.

Age	Anti- HAV	
	No. and (%)	No. examined seropositive
< 10 years	8 (13.1)	61
$\geq$ 10 years	4 (25)	16
Total	12 (15.6)	77

Table 2  
Hepatitis A seroprevalence in biliary atresia patients with different outcomes.

	Anti- HAV	
	No. and (%)	No. examined seropositive
Favorable outcome	7 (17.5)	40
Unfavorable outcome	5 (13.5)	37
Total	12 (15.6)	77

*al*, 2000). Despite good intensive care, children with acute liver failure have mortality rates as high as 40-60% (Arora *et al*, 2003).

Children suffering from BA with failed portoenterostomy are at risk for developing severe liver damage at an early age. In these patients a superimposed acute liver infection due to a hepatitis virus, including HAV, may affect liver function and lead to particularly severe disease. BA is the most common indication for liver transplantation in children.

HAV infection was more prevalent among our subjects, in both the <10 years (13.1%) and  $\geq$  10 years (25%) of age groups, than normal children from comparable age groups studied in 1996 (Poovorawan *et al*, 1997a,b). Despite the fact that BA patients in this study had seropositive rates higher than normal children, those without immunity are still at risk for HAV infection. The Advisory Committee on Immunization Practice (ACIP) recommended the hepatitis A vaccination for susceptible subjects with chronic liver disease (Anonymous, 1999). Hepatitis A vaccine is well-tolerated and induces a satisfactory immune re-

sponse in children affected by various metabolic liver diseases (Giacchino *et al*, 2001). To date, studies regarding the efficacy of hepatitis A vaccine in BA patients, especially in those with unfavorable outcome and end-stage liver disease, are still limited.

Although HAV infection is usually subclinical in childhood, individuals with chronic liver disease, including BA patients, are at increased risk of severe disease and liver failure. The effectiveness of HAV immunization in this particular group of children merits further study.

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