
# รายงานการวิจัย

# โครงการ การศึกษาพยาธิสรีรวิทยาของโรคทางเดินน้ำดีตีบตันในเด็ก

## The study of pathophysiology of biliary atresia in infants

หน่วยกุมารศัลยศาสตร์ ภาควิชาศัลยศาสตร์
คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

หัวหน้าโครงการ รองศาสตราจารย์ ไพศาล เวชชพิพัฒน์

CU-CLUSTER-Emerging H-38-98-53

# กิตติกรรมประกาศ
# Acknowledgement

โครงการวิจัยนี้ได้รับทุนอุดหนุนการวิจัยจาก
โครงการส่งเสริมการทำงานวิจัยเชิงลึกในสาขาวิชาที่มีศักยภาพสูง กองทุนรัชดาภิเษกสมโภช
(CU-CLUSTER-Emerging H-38-98-53)

# สรุปย่อ (Executive Summary)

**Study 1: Elevated hepatic expression of hepatocyte growth factor and C-met receptor in biliary atresia**

Hepatic HGF and C-met expression were studied from liver biopsies of 41 BA patients at the time of Kasai operation, and 17 non-cholestatic pediatric patients. The HGF and C-met expression of hepatocyte areas was scored as per its intensity and percentage of stained area. **Results:** Hepatic HGF and C-met staining scores of BA patients were higher than those of non-cholestatic patients ($P<0.0001$). Analysis of BA patients at 6 months post-Kasai revealed that there was no difference in either hepatic HGF or C-met expression at the time of surgery between the patients with good outcome and those with poor outcome. **Conclusions:** Strong expression of hepatic HGF and its receptor in BA patients was demonstrated. However, the expression was not associated with the early therapeutic outcome. These suggest that resultant actions of HGF involve in the liver pathology of BA but its expression cannot be used as a predictor for therapeutic outcome.

**Study 2: Can serum total bilirubin at 7th day post Kasai operation predict good outcome in biliary atresia?**

Biliary atresia (BA) is a seriously progressive inflammation of neonatal liver and ongoing obliterative process of the bile ducts with currently no predictable course nor certain prognosis. The study aimed to investigate the role of post-op serum total bilirubin (TB) as an early predictor for surgical outcome in BA. **Method:** BA patients between 2001 and 2009 were reviewed. Serum levels of TB were determined at 7th day after Kasai operation. The patients were categorized into two groups, good outcome (serum TB below 2 mg%) and poor outcome (serum TB above 2 mg%) at 6th month following surgery based on jaundice status. The data of serum TB were then analyzed to evaluate its predictive value for clinical outcome using descriptive study and Fisher's exact tests. **Results:** Ninety-four BA patients underwent Kasai operation. Median age at the operation was 80.5 days. Ascending cholangitis occurred in 40 (46%) patients. The outcome at 6th month could be assessed in 86 patients. Nevertheless, data of both serum TB and clinical outcome were able to be analyzed in only 80 patients (good: poor = 48:32). Fifty-four percent (26/48) of jaundice-free patients had a decrease in post-op serum TB levels at 7th day compared with only 25% (8/32) of those who remained jaundice. The drop of more than 20% in serum TB levels at 7th day was significantly associated with good outcome at 6th month ($p = 0.012$) showing predictive value of 76.5%. Further analysis revealed reduction in post-op serum TB at 7th day more than 50%, occurring in 6% (5/80), were all jaundice-free at 6th month. **Conclusions:** The data shown by evaluation of serum TB at 7th day after surgery showed a prognostic power to predict a short-term surgical outcome at 6th month. This early prediction using post-op TB concentration may be helpful as an adjunct in planning further management in these patients.

**ผลงานวิจัยที่ทำในรอบปีที่ผ่านมา**

ได้ทำการศึกษาวิจัย และสามารถเขียนนิพนธ์ฉบับเต็ม (Full manuscript) ทั้งสิ้น 2 เรื่องดังนี้

1. Elevated hepatic Expression of hepatocyte growth factor and C-met receptor in biliary atresia
2. Can serum total bilirubin at 7th day post Kasai operation predict good outcome in biliary atresia?

**Study 1: Elevated hepatic expression of hepatocyte growth factor and C-met receptor in biliary atresia**

**Introduction**

Biliary atresia (BA) is a devastating cholestatic disease in pediatric patients. Progressive liver fibrosis will lead to death within 2 years if left untreated [1, 2]. The patients who are left untreated will die from hepatic decompensation, esophageal variceal bleeding or infection [3]. Hepatic portoenterostomy or Kasai operation at the early age is indispensable to the successful management of infants with BA.

For years, extensive research on liver fibrosis in BA has been advocated in order to find the way to the improvement of long-term outcome. Several investigations regarding its pathophysiology have been explored. Although there have been a number of studies on pathophysiology of BA, including serum levels of various inflammatory markers [4-8], serum growth factors [9, 10], and the apoptosis of bile duct cells [11], the exact mechanism is still unclear.

Hepatocyte growth factor (HGF) has been shown to induce hepatocyte proliferation. HGF is a paracrine cellular growth factor. It is secreted by mesenchymal cells and targets and acts primarily upon epithelial cells and endothelial cells, but also acts on haemopoietic progenitor cells. It has been shown to have a major role in embryonic organ development, in

adult organ regeneration and in wound healing [12]. HGF regulates cell growth, cell motility, and morphogenesis by activating a tyrosine kinase signaling cascade after binding to the C-Met receptor. Its ability to stimulate mitogenesis, cell motility, and matrix invasion gives it a central role in angiogenesis, tumorogenesis, and tissue regeneration [13].

In addition, our previous results showed that there was an elevation in serum HGF in BA patients was associated with the poor therapeutic outcome [10]. However, there is little information available regarding the role of HGF/C-met in BA. Since progressive liver fibrosis is an important development in BA together with the possible role of HGF/C-met pathway in liver reparative process, it is of our interest to study the links between the expression of hepatic HGF/C-met and BA.

Therefore, the aims of this study were to investigate the expression of hepatic HGF and its receptor, C-met, in BA and to associate HGF and C-met expression with early therapeutic outcome using immunohistochemistry (IHC) technique.

## Methods

### Liver tissues and patients

Liver samples of BA patients undergoing Kasai operation and non-BA patients undergoing liver biopsies between July 2005 and July 2008 were retrospectively investigated. All patients were operated by one team of surgeons (PV and SC). The non-BA patients, who had no clinical jaundice, were served as controls. All non-BA patients underwent exploratory laparotomy as the therapeutic means for their diseases. Liver biopsies in this group of patients were an additional procedure and were indicated for medical reasons.

### Immunohistochemistry of liver tissues for HGF

Liver samples were fixed in formalin for 24 hours and kept in paraffin embedded blocks using standard procedure. New sections of 4 μm thickness were cut from the formalin-

fixed paraffin embedded blocks and mounted on glass slides coated by aminopropyltriethoxysilane (APES; Sigma Chemical Co., St Louise, MO, USA).

Sections were deparaffinized and rehydrated. Endogenous peroxidase activity was blocked with 10-minute incubation in 3% $H_2O_2$. Antigen retrieval was done by immersing the sections in 0.4% pepsin (Sigma Chemical Co., St Louise, MO, USA) in 0.01 M HCL at 37°C, one hour. After washing with 0.1% Tween 20 (MERCK-Schuchardt, Hohanbrunn, Germany) in phosphate buffered saline (PBS), the sections were treated with 5% bovine serum albumin (BSA; Sigma Chemical Co., St Louise, MO, USA) in PBS for 30 minutes and then treated with primary antibodies for two hours at room temperature. The primary antibodies used in this study were against HGF (Santa Cruz, USA) diluted at 1:20. The primary antibodies were diluted in PBS. After thorough washing in 0.1% Tween 20 in PBS, labeled polymer (Dako Envision System, Dako Corporation, Carpinteria, CA, USA) was applied to the sections for 30 minutes and followed by three washes of 0.1% Tween 20 in PBS. Color was developed in freshly made diaminobenzidine (Sigma Chemical Co). Sections were washed briefly in running tap water and lightly stained with Mayer's hematoxylin.

A negative control omitting the primary antibody was included for each specimen. In addition, negative controls of some sections were incubated with non-immune rabbit serum. Furthermore, sections of liver cancer, known to have strong cytoplasmic staining were stained at the same run as positive controls.

**Immunohistochemistry of liver tissues for C-met**

Sections were deparaffinized and rehydrated. Endogenous peroxidase activity was blocked with 10-minute incubation in 3% $H_2O_2$. Antigen retrieval was done by immersing the sections in 0.4% pepsin (Sigma Chemical Co., St Louise, MO, USA) in 0.01 M HCL at 37°C, one hour. After washing with 0.1% Tween 20 (MERCK-Schuchardt, Hohanbrunn, Germany) in phosphate buffered saline (PBS), the sections were treated with 5% bovine serum albumin

(BSA; Sigma Chemical Co., St Louise, MO, USA) in PBS for 30 minutes and then treated with primary antibodies for two hours at room temperature. The primary antibodies used in this study were against C-met (Santa Cruz, USA) diluted at 1:100. The primary antibodies were diluted in PBS. After thorough washing in 0.1% Tween 20 in PBS, labeled polymer (Dako Envision System, Dako Corporation, Carpinteria, CA, USA) was applied to the sections for 30 minutes and followed by three washes of 0.1% Tween 20 in PBS. Color was developed in freshly made diaminobenzidine (Sigma Chemical Co). Sections were washed briefly in running tap water and lightly stained with Mayer's hematoxylin.

A negative control omitting the primary antibody was included for each specimen. In addition, negative controls of some sections were incubated with non-immune rabbit serum. Furthermore, sections of normal intestine were stained at the same run as positive controls.

*Evaluation of hepatic HGF and C-met expression*

Immunostained sections were evaluated independently by 2 investigators who were unaware of the diagnosis or clinical outcome of the patients. Two quantitative methods were used, based on the extent and intensity of the antibody stain. Areas of hepatic lobules excluding portal triads and central veins were evaluated using visual scoring method.

Visual scores for HGF and C-met expression were assessed based on its intensity and percentage of staining areas. Expression of HGF and C-met intensity was categorized into 3 levels as weak (intensity score =1), moderate (intensity score =2), and strong (intensity score =3). In addition, the percentage of staining areas of hepatocytes was graded into 4 levels (Grade 1; 0-25% of hepatocyte areas was stained; Grade 2: 26-50% of hepatocyte areas was stained; Grade 3: 51-75% of hepatocyte areas was stained; and Grade 4: 76-100% of hepatocyte areas was stained). Any differences in scores were resolved by a conference. Total

scores of hepatic HGF and C-met expression, were calculated as intensity score times staining grade.

Categorization of the BA patients

In order to associate hepatic HGF and C-met expression with clinical outcome at 6 months post-op among BA patients, they were divided into 2 groups according to the status of jaundice (TB <2 mg/dL; good outcome vs. TB ≥2 mg/dL; poor outcome). Subgroup analysis of hepatic HGF/C-met expression based on early clinical outcome in BA patients was carried out.

*Statistical analyses*

The comparisons of HGF and C-met expression among the two groups (BA and non-BA patients) were performed using Mann-Whitney U tests (visual score). Spearman correlation analysis of HGF with C-met was performed. Association between outcome of BA patients at 6 months post-op and hepatic HGF and C-met expression was analyzed using univariate analysis.

Significant differences were established at $P<0.05$. For all statistical analyses, either GraphPad Prism version 3.02 (GraphPad Software Inc., California, USA) or SPSS software version 10.0 (SPSS Inc., Chicago, IL) was used. Data are expressed as median and range.

**Results**

Hepatic HGF and C-met expression was determined using immunohistochemistry from liver biopsies of 41 BA patients at the time of Kasai operation, and 17 non-cholestatic pediatric patients whose liver tissues were needed in the treatment process. All non-BA patients had no clinical jaundice. The diagnosis of non-BA patients were as follows: 6

choledochal cysts, 5 thalassemias, 3 neuroblastomas, 2 portal vein thromboses, and 1 hepatoblastoma.

Hepatic HGF and C-met staining scores of BA patients were significantly higher than those of non-cholestatic patients (HGF; 9 [2, 12] versus 2 [1, 12], C-met; 8 [1, 12] versus 1 [1, 6], both $P<0.0001$), as shown in Figure 1. There was a correlation between HGF and C-met (spearman $r = 0.77$, $P<0.0001$).

Regarding the clinical outcome at 6 months post-Kasai among BA patients, there were 24 patients with good outcome (serum TB < 2.0 mg/dL) and 17 patients with poor outcome (serum TB >2.0 mg/dL). Subgroup analysis showed that there was no association between either hepatic HGF or C-met expression and early clinical outcome in BA patients.

**Discussion**

Biliary atresia (BA) is a rare disease characterized by progressive sclerosing fibrous obliteration of the intra- and extra-hepatic biliary systems. Without hepatic portoenterostomy or Kasai operation, the resultant cholestasis leads to hepatic fibrosis and death within a few years [1, 14].

Our results clearly demonstrated that there is an overexpression of hepatic HGF and C-met in BA patients compared to other non-BA patients. Overexpression of hepatic HGF and C-met found in BA patients suggested that HGF and C-met production by the liver in BA is increased. This is consistent with our previous studies in post-operative BA patients illustrating that there is an elevation of serum HGF compared to normal children. In addition, this study demonstrated that most of the HGF stained within the liver tissues was from the area of hepatocytes. It is therefore likely that hepatocytes, not cholangiocytes or endothelial cells or inflammatory cells, are the major source of hepatic HGF production in BA patients.

Strong expression HGF and C-met in BA patients reflected the high activity of HGF/C-met pathway.

Subsequent analysis among BA patients revealed that either hepatic HGF or C-met expression at the time of Kasai operation was not associated with early clinical outcome in BA at 6 months post-Kasai. Therefore, the levels of hepatic HGF/C-met expression cannot be used as a prognostic marker for predicting the early outcome at 6 months post-op.

We are also aware of some limitations in this study. Firstly, we do not know whether the overexpression of HGF/C-met found in BA patients is a cause or is an effect to the disease pathology caused by cholestasis. If it is an effect, their expression will decrease in BA patients with good outcome. The study of hepatic HGF/C-met expression in post-Kasai patients with different clinical outcomes will be able to answer this research question. Secondly, overexpression of hepatic HGF/C-met may be just the non-specific findings of cholestasis. More studies on non-BA infants with cholestasis will solve this concern. Thirdly, the sample size of BA patients was probably too small in terms of statistical analysis. However, with the rarity of this disease, the results of a study of liver tissues from 41 BA patients cannot be underestimated.

In conclusion, strong expression of hepatic HGF and C-met receptor in BA patients was demonstrated. However, the expression was not associated with the early therapeutic outcome. These suggest that resultant actions of HGF involve in the liver pathology of BA but its expression cannot be used as a predictor for therapeutic outcome.

**Acknowledgments**

This study was supported by Chulalongkorn University (Grant No. CU-CLUSTER-Emerging H-38-98-53). We are grateful to the Thailand Research Fund for the support (Grant No. RMU-4980017). Also, we would like to thank Faculty of Medicine, Chulalongkorn

University for the permission to conduct the research work. The authors also thank Ms. Meesakul O for her technical assistance.

## References


1. Ohi R (2001) Surgery for biliary atresia. Liver 21:175-182.
2. Davenport M (2005) Biliary atresia. Semin Pediatr Surg 14:42-48.
3. Kobayashi H (2003) Biliary atresia. Sem Neonatol 8:383-391.
4. Narayanaswamy B, Gonde C, Tredger JM, Hussain M, Vergani D, Davenport M (2007) Serial circulating markers of inflammation in biliary atresia--evolution of the post-operative inflammatory process. Hepatology 46:180-187.
5. Chongsrisawat V, Chatchatee P, Samransamruajkit R, Vanapongtipagorn P, Chottivittayatarakorn P, Poovorawan Y (2003) Plasma endothelin-1 levels in patients with biliary atresia: possible role in development of portal hypertension. Pediatr Surg Int 19:478-481.
6. Kobayashi H, Horikoshi K, Long L, Yamataka A, Lane GJ, Miyano T (2001) Serum concentration of adhesion molecules in postoperative biliary atresia patients: relationship to disease activity and cirrhosis. J Pediatr Surg 36:1297-1301.
7. Honsawek S, Chongsrisawat V, Vejchapipat P, Thawornsuk N, Tangkijvanich P, Poovorawan Y (2005) Serum interleukin-8 in children with biliary atresia: relationship with disease stage and biochemical parameters. Pediatr Surg Int 21:73-77.
8. Vejchapipat P, Jirapanakorn N, Thawornsuk N, Theamboonlers A, Chongsrisawat V, Chittmittrapap S, Poovorawan Y (2005) There is no association between K469E ICAM-1 gene polymorphism and biliary atresia. World J Gastroenterol 11:4886-4890.
9. Yoshida S, Nio M, Hayashi Y, Ohi R, Kawamura I, Goto T (2003) Serum insulinlike growht factor-I in biliary atresia. J Pediatr Surg 38:211-215.
10. Vejchapipat P, Theamboonlers A, Chaokhonchai R, Chongsrisawat V, Chittmittrapap S, Poovorawan Y (2004) Serum hepatocyte growth factor and clinical outcome in biliary atresia. J Pediatr Surg.
11. Liu C, Chiu J-H, Chin T, Wang L-S, Li AF-Y, Chow K-C, Wei C (2000) Expression of Fas ligand on bile ductule epithelium in biliary atresia - a poor prognostic factor. J Pediatr Surg 35:1591-1596.
12. Cramer T, Schuppan D, Bauer M, Pfander D, Neuhaus P, Herbst H (2004) Hepatocyte growth factor and c-Met expression in rat and human liver fibrosis. Liver Int 24:335-344.
13. Nakamura T (1991) Structure and function of hepatocyte growth factor. Prog Growth Factor Res 3:67-85.
14. Davenport M (2006) Biliary atresia: outcome and management. Indian J Pediatr 73:825-828.

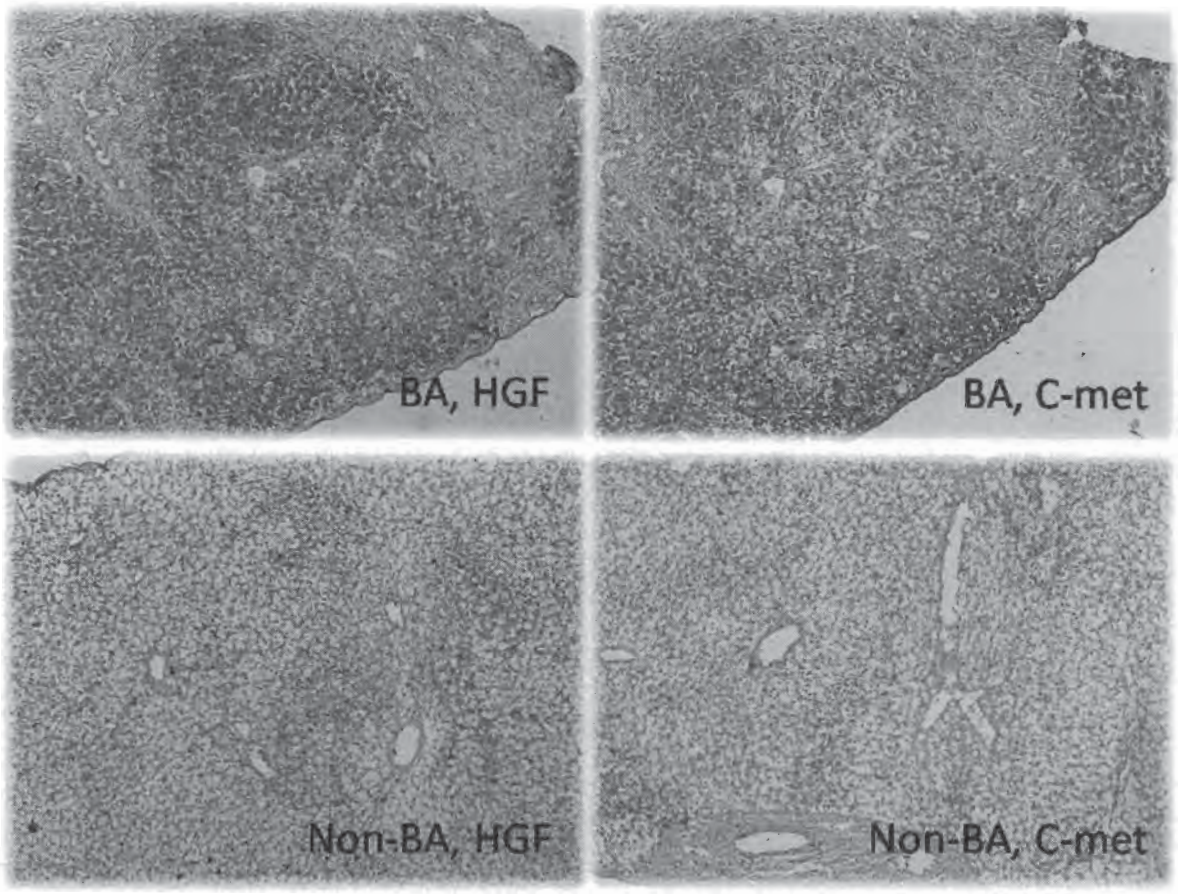
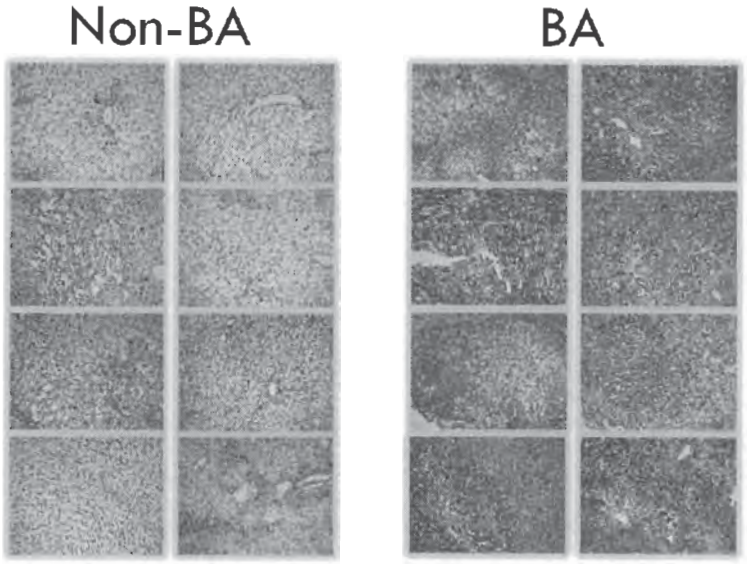
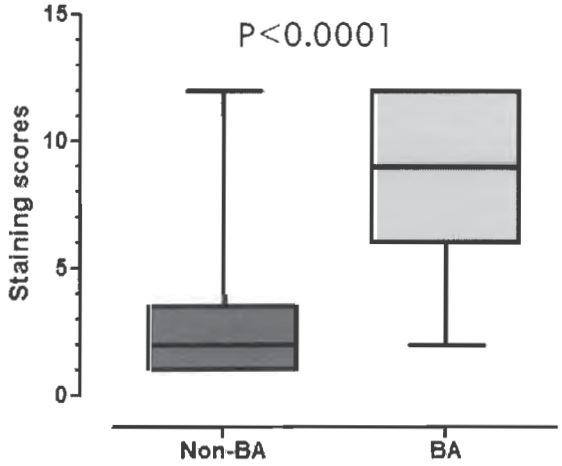



Figure 1: Representative immunohistochemical features of the livers from a BA patient and a non-BA patient. Note the strong expression of HGF and C-met stained on hepatocytes in BA patients

# RESULTS: HEPATIC HGF

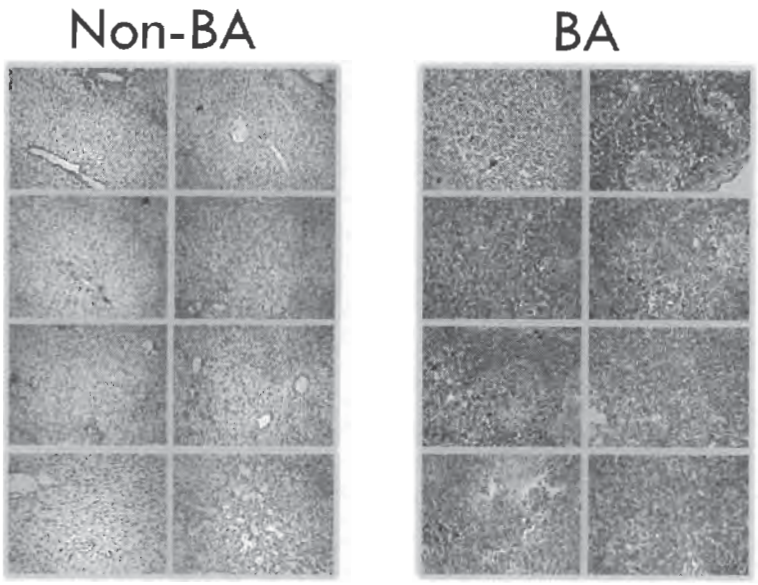



# RESULTS: HEPATIC HGF

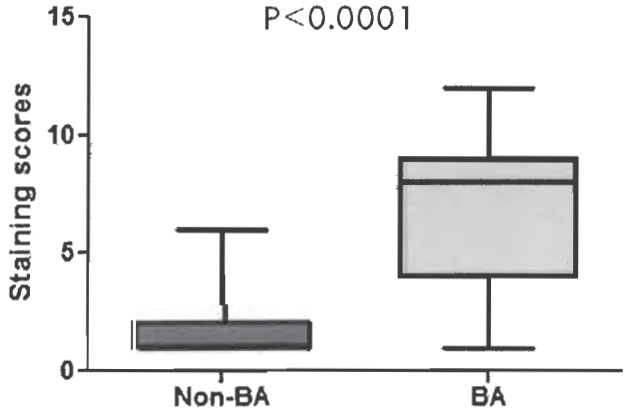



- Hepatic HGF staining scores of BA patients were significantly higher than those of non-cholestatic patients

# RESULTS: HEPATIC C-MET




# RESULTS: HEPATIC C-MET




- Hepatic C-met staining scores of BA patients were significantly higher than those of non-cholestatic patients

## Study 2: Can serum total bilirubin at 7th day post Kasai operation predict good outcome in biliary atresia?

### Introduction

Biliary atresia (BA) is a serious neonatal hepatobiliary disorder of unknown cause with progressive inflammation of liver and ongoing obliterative process of the bile ducts. Untreated patients ultimately die of end-stage liver decompensation. The renown hepatic portojejunostomy procedure by Morio Kasai restoring extrahepatic biliary drainage can rescue 20-30% of BA patients [1,2]. The remaining or the majority of children will eventually suffer from biliary cirrhosis and being listed for liver transplantation.

The post-op course of the disorder, however, is currently not predictable and uncertain, even after a successful Kasai operation. A number of prognostic markers of post-op success after the operation have been investigated [3-7]. As liver function test, particularly total bilirubin (TB) concentration is routinely used to evaluate post-op icteric status, the implement of this factor as an early predictor is very simple and save. In addition, the use of serum TB to predict a surgical outcome is rarely reported in the literature [8-10]. The present study was to investigate the prognostic value of post-op serum TB at $7^{th}$ day, focusing on the short-term results at $6^{th}$ month after operation.

### Methods

The ethical approval was granted by the International Review Board of the Faculty of Medicine, Chulalongkorn University. A total of 94 consecutive BA patients who underwent Kasai operation at King Chulalongkorn Memorial Hospital between 2001 and 2009 were retrospectively reviewed. The diagnosis of all BA patients following ultrasonography and liver scintigraphy was confirmed by coeliotomy with intraoperative cholangiography and when the diagnosis was made the original hepatic portoenterostomy was carried out. The

operation techniques, roughly including liver mobilization, magnification using a surgical loupe, lateral dissection of the fibrous portal mass, liver biopsy, and Roux-en-Y portojejunostomy as described in the literature previously, was performed by one team of surgeons. Postoperatively, all BA patients received intravenous antibiotics followed by long-term oral cotrimoxazole, ursodeoxycholic acid, vitamin A, D, E, and K, and short-term high-dose prednisolone.

In order to investigate the prognostic role of post-op serum TB, the specimens of peripheral venous blood postoperatively collected at $7^{th}$ day (± 2 days) were determined for serum TB concentration using an automated chemical analyzer (Hitachi 911) at our central laboratory. The patients were then classified into two groups depending on their icteric status at $6^{th}$ month after surgery; good (serum TB below 2 mg%) and poor outcome (serum TB above 2 mg%). The correlations between serum TB levels and surgical outcomes at that period of time were analyzed using descriptive study and Fisher's exact test. Demographic data including age, gender, complications, and other hepatic enzymes were also analyzed. The statistical calculation was performed using Statistical Package of the Social Science software version 10.0 (SPSS Inc., Chicago, IL, USA). A significant difference was defined as p value of $<0.05$.

**Results**

Male to female ratio was about 1.2:1. The median age of infants at the time of surgery was 80.5 days (range, 21 to 209 days). Approximately 85.1% in the series underwent Kasai operation beyond 60 days of life. The age and gender, however, were not significantly different between those with jaundice and those who were jaundice-free at $6^{th}$ month. Ascending cholangitis was the most common post-op complication, accounting for 46% of cases in the study. There was no peri- and post-op mortality.

Mean pre-op TB concentration of 11.82 ± 3.44 mg% slightly declined to 10.90 ± 4.46 mg% at post-op day 7. At sixth month, the icteric status could be assessed in 86 patients. Nevertheless, data of both serum TB levels at $7^{th}$ day and $6^{th}$ month were able to be analyzed in only 80 patients. Forty-eight patients (60%) were jaundice-free (classified as good outcome), whereas the remaining 32 patients remained jaundice (poor outcome).

Fifty-four percent (26/48) of jaundice-free patients had a decrease in post-op serum TB levels at $7^{th}$ day compared with only 25% (8/32) of those who were in poor outcome. The 20% or more drop of serum TB levels at $7^{th}$ day was significantly associated with good outcome at $6^{th}$ month ($p = 0.012$). And also, the predictive value where the decrease in post-op serum TB at $7^{th}$ day was used as a predictor for good outcome was 76.5%. Further analysis revealed reduction in post-op serum TB at $7^{th}$ day more than 50%, which found in 6% (5/80) of all patients, were all jaundice-free at $6^{th}$ month. Although none in poor outcome obtained half drop in post-op serum TB at $7^{th}$ day, the difference between the half concentration reduction and outcome was not statistically significant ($p = 0.08$).

Twenty percent drop in post-op serum glutamic pyruvic transaminase (SGPT) and glutamic oxaloacetic transaminase (SGOT) at day 7 accounted for 37.8% and 46.4% of patients in good outcome, respectively. However, both SGPT and SGOT were found no strong correlation between post-op levels and surgical outcome as serum TB.

**Discussion**

It has been accepted that the standard treatment of BA involves early diagnosis, successful Kasai operation, and prompt aggressive prevention and treatment of post-op ascending cholangitis. With this sequential therapy, approximately half of BA patients at our institution are jaundice-free at one year follow-up [11]. However, the post-op course of this disorder is exactly unpredictable and uncertain, thus providing not all post-op improvement

will achieve long-term survival. Apart from the unsuccessful operation, some patients with post-op jaundice-free still insidiously develop biliary cirrhosis and eventually suffer end-stage liver decompensation. As a result, only about one-third of BA patients after surgery can reach the cure [1,2].

Several prognostic features, including histoimmunological findings of the liver and fibrous portal mass, portal pressure index and hepatobiliary imaging, that determined at the time of surgery have been proposed to predict the ultimate outcome after surgery [5,12-15]. Although the authors had found correlation between them and the surgical outcome, all these characteristics are subjective or depend upon the experience and skill of the persons who are responsible for the measurement. Thus, to obtain more objective value, it would rather that the prognostic parameters are measured by means of serum biochemistry.

Since some trace elements such as copper and zinc are involved in several hepatic metabolism and stored in a significant amount in hepatic parenchyma [16,17], they were included in a calculation of BA prognostic index [18]. The interpretation showed that the serum copper to zinc ratio was the most reliable parameter among other liver function variables, including TB, cholinesterase, and gamma-glutamyl transpeptidase, in predicting the severity of liver deterioration in BA. Nevertheless, these trace elements do not directly reflect the status of liver function. Although the serum cholinesterase levels might correspond more sensitively with the improvement of synthetic liver function, its value in predicting the prognosis after surgery was not demonstrated [19].

A predictive value of the serum TB levels has been proposed and determined as an indication for liver transplantion [10, 20, 21]. The earliest prediction of ultimate outcome was three months post surgery [10]. Some authors estimate the post-op prognosis by serum TB clearance or measurement [22] of TB excretion from direct limb of portoenterostomy [23]. All studies were conducted for the purpose that providing unsuccessfully patients an early

referral to liver transplantation. Although the present study determine the outcome at $6^{th}$ month that too early to interpret the success of Kasai operation, the prediction time at 1 week after surgery will serve an early advice to the parents or provision of a great concern to aggressively treat BA patients whose results are suspected to be unsuccessful. As we have shown, the 20% or more decrease in serum TB levels at $7^{th}$ day was significantly associated with good outcome at $6^{th}$ month. According to our knowledge, this relationship was found at the earliest time following surgery. The further analysis that more than half TB concentration reductions were all jaundice-free would reflect the satisfying bile drainage from the wide range of the liver. Unfortunately, such patients accounted for a minority of our cases.

We can conclude from our findings that the drop in post-op serum TB at one week showed a strong prognostic power to predict our patients' short-term outcome. Although this early prediction cannot be used as a parameter of long-term survival or, in the long run, an indication for liver transplantation, at least, our findings will help in planning further management in these patients.

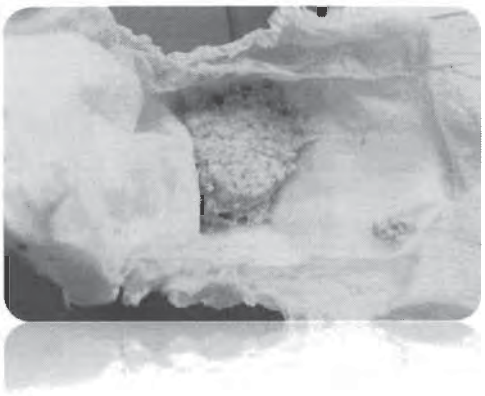
**References**

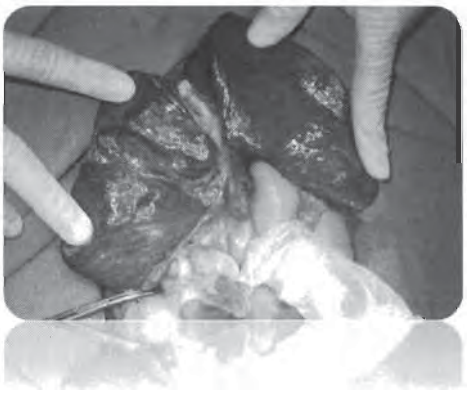

1. Okazaki T, Kobayashi H, Yamataka A, Lane GJ, Miyano T. Long-term postsurgical outcome of biliary atresia. J Pediatr Surg. 1999 Feb;34(2):312-5.
2. Davenport M. Biliary atresia. Semin Pediatr Surg. 2005 Feb;14(1):42-8.
3. Altman RP, Lilly JR, Greenfeld J, Weinberg A, van Leeuwen K, Flanigan L. A multivariable risk factor analysis of the portoenterostomy (Kasai) procedure for biliary atresia: twenty-five years of experience from two centers. Ann Surg. 1997 Sep;226(3):348-53; discussion 353-5.
4. Chardot C, Carton M, Spire-Bendelac N, Le Pommelet C, Golmard JL, Auvert B. Prognosis of biliary atresia in the era of liver transplantation: French national study from 1986 to 1996. Hepatology. 1999 Sep;30(3):606-11.
5. Duché M, Fabre M, Kretzschmar B, Serinet MO, Gauthier F, Chardot C. Prognostic value of portal pressure at the time of Kasai operation in patients with biliary atresia. J Pediatr Gastroenterol Nutr. 2006 Nov;43(5):640-5.
6. Sanghai SR, Shah I, Bhatnagar S, Murthy A. Incidence and prognostic factors associated with biliary atresia in western India. Ann Hepatol. 2009 Apr-Jun;8(2):120-2.

7. Vejchapipat P, Theamboonlers A, Poomsawat S, Chittmittrapap S, Poovorawan Y. Serum transforming growth factor-beta1 and epidermal growth factor in biliary atresia. Eur J Pediatr Surg. 2008 Dec;18(6):415-8. Epub 2008 Nov 14.
8. Rodeck B, Becker AC, Gratz KF, Petersen C. Early predictors of success of Kasai operation in children with biliary atresia. Eur J Pediatr Surg. 2007 Oct;17(5):308-12.
9. Lang T, Kappler M, Dietz H, Harms HK, Bertele-Harms R. Biliary atresia: which factors predict the success of a Kasai operation? An analysis of 36 patients. Eur J Med Res. 2000 Mar 27;5(3):110-4.
10. Ohhama Y, Shinkai M, Fujita S, Nishi T, Yamamoto H. Early prediction of long-term survival and the timing of liver transplantation after the Kasai operation. J Pediatr Surg. 2000 Jul;35(7):1031-4.
11. Sookpotarom P, Vejchapipat P, Chittmittrapap S, Chongsrisawat V, Chandrakamol B, Poovorawan Y. Short-term results of Kasai operation for biliary atresia: experience from one institution. Asian J Surg. 2006 Jul;29(3):188-92.
12. Azarow KS, Phillips MJ, Sandler AD, Hagerstrand I, Superina RA. Biliary atresia: should all patients undergo a portoenterostomy? J Pediatr Surg. 1997 Feb;32(2):168-72; discussion 172-4.
13. Kinugasa Y, Nakashima Y, Matsuo S, Shono K, Suita S, Sueishi K. Bile ductular proliferation as a prognostic factor in biliary atresia: an immunohistochemical assessment. J Pediatr Surg. 1999 Nov;34(11):1715-20.
14. Kotb MA, Sheba M, El Koofy N, Mansour S, El Karaksy HM, Dessouki NM, Mostafa W, El Barbary M, El-Tantawy HE, Kaddah S. Post-portoenterostomy triangular cord sign prognostic value in biliary atresia: a prospective study. Br J Radiol. 2005 Oct;78(934):884-7.
15. Castagnetti M, Davenport M, Tizzard S, Hadzic N, Mieli-Vergani G, Buxton-Thomas M. Hepatobiliary scintigraphy after Kasai procedure for biliary atresia: clinical correlation and prognostic value. J Pediatr Surg. 2007 Jun;42(6):1107-13.
16. Cywes C, Millar AJ. Assessment of the nutritional status of infants and children with biliary atresia. S Afr Med J. 1990 Feb 3;77(3):131-5.
17. Sato C, Koyama H, Satoh H, Hayashi Y, Chiba T, Ohi R. Concentrations of copper and zinc in liver and serum samples in biliary atresia patients at different stages of traditional surgeries. Tohoku J Exp Med. 2005 Dec;207(4):271-7.
18. Endo M, Masuyama H, Watanabe K, Hagane K, Ikawa H, Yokoyama J, Kitajima M. Calculation of biliary atresia prognostic index using a multivariate linear model. J Pediatr Surg. 1995 Nov;30(11):1575-9.
19. Popović L, Batinica S, Mestrović T, Zupancić B, Antabak A, Petrunić M, Davila S. The value of cholinesterase activity after Kasai operation. Pediatr Surg Int. 2003 Oct;19(8):605-7. Epub 2003 Sep 6.
20. Kasai M, Mochizuki I, Ohkohchi N, Chiba T, Ohi R. Surgical limitation for biliary atresia: indication for liver transplantation. J Pediatr Surg. 1989 Sep;24(9):851-4.
21. Yanchar NL, Shapiro AM, Sigalet DL. Is early response to portoenterostomy predictive of long-term outcome for patients with biliary atresia? J Pediatr Surg. 1996 Jun;31(6):774-8.
22. Grosfeld JL, Fitzgerald JF, Predaina R, West KW, Vane DW, Rescorla FJ. The efficacy of hepatoportoenterostomy in biliary atresia. Surgery. 1989 Oct;106(4):692-700; discussion 700-1.

23. Vazquez-Estevez J, Stewart B, Shikes RH, Hall RJ, Lilly JR. Biliary atresia: early determination of prognosis. J Pediatr Surg. 1989 Jan;24(1):48-50; discussion 50-1.

- Biliary atresia (BA) is a disease characterized by progressive liver fibrosis with fatal consequences





**CURRICULUM VITAE**
***(August 2011)***

**PAISARN VEJCHAPIPAT**

# PERSONAL DETAILS

| | |
|---|---|
| Address | Department of Surgery, Faculty of Medicine<br>Chulalongkorn Hospital<br>Rama IV road, Patumwan<br>Bangkok 10330, Thailand |
| Telephone | +66-(0)2-256-4117, +66-(0)2-256-4907 |
| FAX | +66-(0)2-256-4194 |
| E-mail | pvejchap@yahoo.co.uk; paisarnv@gmail.com |
| Sex | Male |
| Nationality | Thai |

## EDUCATION AND QUALIFICATIONS

| | |
|---|---|
| 2001 | Doctor of Philosophy, Field of Study: Pediatric Surgery<br>Institute of Child Health, University College London, UK |
| 1998 | Certificate in Pediatric Advanced Life Support<br>Resuscitation Council, UK |
| 1998 | Personal License to carry out regulated procedures on living animals<br>The Home Office, UK |
| 1997 | Certificate in training for Personnel working under the Animals (Scientific Procedures) Act 1986, UK<br>Royal Veterinary College, London, UK |
| 1997 | Certificate of Proficiency in English for Academic Purposes<br>University College London, UK |
| 1995-1997 | Diploma of Medical Practice in Pediatric Surgery<br>Medical Council of Thailand |
| 1992-1995 | Diploma of Medical Practice in General Surgery<br>Medical Council of Thailand |
| 1992-1993 | Diploma of Clinical Sciences in Surgery<br>Chulalongkorn University, Thailand |
| 1992 | License of Medical Practice<br>Medical Council of Thailand |
| 1986-1992 | Doctor of Medicine (Second)<br>Chulalongkorn University, Thailand |
| 1980-1986 | High School Diploma<br>Assumption College, Bangkok, Thailand |

# EMPLOYMENT

2004- now Associate Professor in Pediatric Surgery
Department of Surgery, Faculty of Medicine
Chulalongkorn University, Bangkok, Thailand

2001-2004 Assistant Professor in Pediatric Surgery
Department of Surgery, Faculty of Medicine
Chulalongkorn University, Bangkok, Thailand

1997-2001 Clinical Research Fellow and PhD student
Department of Surgery, Institute of Child Health
University College London, UK

1995-1997 Lecturer in Pediatric Surgery
Department of Surgery, Faculty of Medicine
Chulalongkorn University, Bangkok, Thailand

**LIST OF PUBLICATIONS** (2000-2010)

## *FIRST AUTHOR*

1. Vejchapipat P, Theamboonlers A, Poomsawat S, Chittmittrapap S, Poovorawan Y. Serum transforming growth factor-beta1 and epidermal growth factor in biliary atresia. Eur J Pediatr Surg 18:415-8, 2008
2. Vejchapipat P, Sookpotarom P, Theamboonlers A, Chittmittrapap S, Poovorawan Y. Elevated serum soluble E-selectin is associated with poor outcome and correlated with Serum ALT in biliary atresia. Eur J Pediatr Surg 18:254-7, 2008
3. Vejchapipat P, Poomsawat S, Imvised T, Chongsrisawat V, Chittmittrapap S, Poovorawan Y. Overexpression of hepatic inducible nitric oxide synthase in biliary atresia. Hepatol Res 38:1018-25, 2008
4. Vejchapipat P, Passakonnirin R, Sookpotarom P, Chittmittrapap S, Poovorawan Y. High-dose steroids do not improve early outcome in biliary atresia.J Pediatr Surg 42:2102-5, 2007
5. Vejchapipat P, Theamboonlers A, Chongsrisawat V, Poovorawan Y. An evidence of intestinal mucosal injury in dengue infection. Southeast Asian J Trop Med Public Health 37:79-82, 2006
6. Vejchapipat P, Poomsawat S, Poovorawan Y, Proctor E, Pierro A. The effects of moderate hypothermia on energy metabolism and serum inflammatory markers during laparotomy. Pediatr Surg Int 22:66-71, 2006
7. Vejchapipat P, Chongsrisawat V, Theamboonlers A, Chittmittrapap S, Poovorawan Y. Elevated serum nitric oxide metabolites in biliary atresia. Pediatr Surg Int 22:106-9, 2006
8. Vejchapipat P, Leawhiran N, Poomsawat S, Theamboonlers A, Chittmittrapap S, Poovorawan Y. Amelioration of intestinal reperfusion injury by moderate hypothermia is associated with serum sICAM-1 levels. J Surg Res 130:152-7, 2006
9. Vejchapipat P, Jirapanakorn N, Thawornsuk N, Theamboonlers A, Chongsrisawat V, Chittmittrapap S, Poovorawan Y. There is no association between K469E ICAM-1 gene polymorphism and biliary atresia. World J Gastroenterol 11:4886-90, 2005

10. Vejchapipat P, Tangkijvanich P, Theamboonlers A, Chongsrisawat V, Chittmittrapap S, Poovorawan Y. Association between serum hepatocyte growth factor and survival in untreated hepatocellular carcinoma. J Gastroenterol 39:1182-8, 2004
11. Vejchapipat P, Theamboonlers A, Chaokhonchai R, Chongsrisawat V, Chittmittrapap S, Poovorawan Y. Serum hepatocyte growth factor and clinical outcome in biliary atresia. J Pediatr Surg 39:1045-9, 2004
12. Vejchapipat P, Proctor E, Ramsay A, Petros A, Gadian DG, Spitz L, Piero A. Intestinal energy metabolism after ischemia-reperfusion: effects of moderate hypothermia and perfluorocarbons. J Pediatr Surg 37:786-90, 2002
13. Vejchapipat P, Eaton S, Fukumoto K, Parkes HG, Spitz L, Pierro A. Hepatic glutamine metabolism during endotoxemia in neonatal rats. Nutrition 18:293-7, 2002
14. Vejchapipat P, Williams SR, Proctor E, Lauro V, Spitz L, Pierro A. Moderate hypothermia ameliorates liver energy failure after intestinal ischaemia-reperfusion in anaesthetized rats. J Pediatr Surg 36:269-75, 2001
15. Vejchapipat P, Williams SR, Spitz L, Pierro A. Intestinal metabolism after ischaemia-reperfusion. J Pediatr Surg 35:759-64, 2000

## *CO-AUTHOR*

1. Poomsawat S, Punyasingh J, Vejchapipat P, Larbcharoensub N. Co-expression of hepatocyte growth factor and c-met in epithelial odontogenic tumors. Acta Histochem. 2011 Aug 18 Epub ahead of print
2. Chongsrisawat V, Vejapipat P, Siripon N, Poovorawan Y. Transient elastography for predicting esophageal/gastric varices in children with biliary atresia. BMC Gastroenterol 18;11:41, 2011
3. Honsawek S, Chayanupatkul M, Chongsrisawat V, Theamboonlers A, Praianantathavorn K, Udomsinprasert W, Vejchapipat P, Poovorawan Y. Serum adiponectin and transient elastography as non-invasive markers for postoperative biliary atresia. BMC Gastroenterol 28;11:16, 2011
4. Honsawek S, Praianantathavorn K, Chongsrisawat V, Vejchapipat P, Theamboonlers A, Poovorawan Y. High serum matrix metalloproteinase-3 and liver stiffness in postoperative biliary atresia. Pediatr Surg Int 27:681-7, 2011
5. Honsawek S, Vejchapipat P, Chongsrisawat V, Thawornsuk N, Poovorawan Y. Association of circulating osteopontin levels with clinical outcomes in postoperative biliary atresia. Pediatr Surg Int 27:283-8, 2011
6. Honsawek S, Chayanupatkul M, Chongsrisawat V, Vejchapipat P, Poovorawan Y. Increased osteopontin and liver stiffness measurement by transient elastography in biliary atresia. World J Gastroenterol 16:5467-73, 2010
7. Sookpotarom P, Nimanussornkul K, Luecha O, Poolsavatkitikool R, Vejchapipat P. Isolated tuberculosis of tunica vaginalis in a child. Pediatr Surg Int 26:763-5, 2010
8. Preativatanyou K, Honsawek S, Chongsrisawat V, Vejchapipat P, Theamboonlers A, Poovorawan Y. Correlation of circulating endoglin with clinical outcome in biliary atresia. Eur J Pediatr Surg 20:237-41, 2010
9. Sookpotarom P, Porncharoenpong S, Vejchapipat P. Topical steroid is effective for the treatment of phimosis in young children. J Med Assoc Thai 93:77-83, 2010
10. Honsawek S, Klaikeaw N, Vejchapipat P, Chongsrisawat V, Ruangvejvorachai P, Poovorawan Y. Cyclooxygenase-2 Overexpression is Associated with Clinical Outcome in Biliary Atresia. Eur J Pediatr Surg 2010 [Epub ahead of print]
11. Ausavarat S, Leoyklang P, Vejchapipat P, Chongsrisawat V, Suphapeetiporn K, Shotelersuk V. Novel mutations in the STK11 gene in Thai patients with Peutz-Jeghers syndrome. World J Gastroenterol 15:5364-7, 2009

12. Sookpotarom P, Vejchapipat P. Primary transanal Swenson pull-through operation for Hirschsprung's disease. Pediatr Surg Int 25:767-73, 2009
13. Poomsawat S, Punyasingh J, Vejchapipat P. Immuno-histochemical expression of p53 protein and iNOS in odontogenic cysts. J Med Assoc Thai 92:952-60, 2009
14. Nattee P, Honsawek S, Chongsrisawat V, Vejchapipat P, Thamboonlers A, Poovorawan Y. Elevated serum macrophage migration inhibitory factor levels in post-operative biliary atresia. Asian J Surg 32:109-13, 2009
15. Chayanupatkul M, Honsawek S, Vejchapipat P, Chongsrisawat V, Poovorawan Y. Elevated serum bone morphogenetic protein 7 levels and clinical outcome in children with biliary atresia. Eur J Pediatr Surg 19:246-50, 2009
16. Honsawek S, Chaiwatanarat T, Vejchapipat P, Chongsrisawat V, Thawornsuk N, Poovorawan Y. Relationships between OPG, RANKL, bone metabolism, and bone mineral density in biliary atresia. Pediatr Surg Int 25:261-7, 2009
17. Trinavarat P, Sasiwimonphan K, Sansopha L, Vejchapipat P, Sosothikul D. Xanthogranulomatous adrenalitis in a neonate: CT and US findings. Pediatr Radiol 39:286-9, 2009
18. Honsawek S, Chongsrisawat V, Vejchapipat PI, Thawornsuk N, Poovorawan Y. High levels of serum basic fibroblast growth factor in children with biliary atresia. Hepatogastroenterology 55:1184-8, 2008
19. Chittmittrapap S, Imvised T, Vejchapipat P. Resection for primary liver tumors in children: an experience of 52 cases at one institution. J Med Assoc Thai 91:1206-11, 2008
20. Honsawek S, Chaiwatanarat T, Chongsrisawat V, Thawornsuk N, Vejchapipat P, Poovorawan Y. Circulating leptin levels and bone mineral density in children with biliary atresia. Acta Paediatr 97:206-11, 2008
21. Honsawek S, Chongsrisawat V, Vejchapipat P, Thawornsuk N, Tangkijvanich P, Poovorawan Y. Elevation of serum stem-cell factor in postoperative biliary atresia. Pediatr Int 49:888-93, 2007
22. Sookpotarom P, Vejchapipat P.Non-correctable biliary atresia with large extrahepatic cyst: a report of two cases. Eur J Pediatr Surg 17:295-7, 2007
23. Sookpotarom P, Siriarchawatana T, Jariya Y, Vejchapipat P. Demonstration of nasogastric intubation using video compact disc as an adjunct to the teaching processes. J Med Assoc Thai 90:468-72, 2007
24. Sa-nguanmoo P, Vejchapipat P, Chongsrisawat V, Chirathaworn C, Honsawek S, Theamboonlers A, Poovorawan Y. Analysis of connective tissue growth factor promoter polymorphism in Thai children with biliary atresia. J Med Assoc Thai 90:251-7, 2007
25. Chiengthong K, Somboonnithiphol K, Kittipinyovath P, Chongsrisawat V, Poovorawan Y, Panyakhamlerd K, Vejchapipat P. Pregnancy in biliary atresia after kasai operation complicated by portal hypertension. J Med Assoc Thai 89:1961-4, 2006
26. Poomsawat S, Punyasingh J, Vejchapipat P.Expression of basement membrane components in odontogenic tumors.Oral Surg Oral Med Oral Pathol Oral Radiol Endod 104:666-75, 2007
27. Honsawek S, Chongsrisawat V, Vejchapipat P, Thawornsuk N, Poovorawan Y.Association of serum levels of tissue inhibitors of metalloproteinase-1 with clinical outcome in children with biliary atresia.Asian Pac J Allergy Immunol 24:161-6, 2006
28. Sookpotarom P, Vejchapipat P, Chittmittrapap S, Sookpotarom P, Chongsrisawat V, Chandrakamol B, Poovorawan Y. Short-term results of Kasai operation for biliary atresia: experience from one institution. Asian J Surg 29:188-92, 2006

29. Sookpotarom P, Vejchapipat P, Chongsrisawat V, Mahayosnond A. Gastric volvulus caused by percutaneous endoscopic gastrostomy: a case report. J Pediatr Surg 40:e21-3, 2005
30. Honsawek S, Chongsrisawat V, Vejchapipat P, Thawornsuk N, Tangkijvanich P, Poovorawan Y. Serum interleukin-8 in children with biliary atresia: relationship with disease stage and biochemical parameters. Pediatr Surg Int 21:73-7, 2005
31. Chongsrisawat V, Kongtawelert P, Tongsoongnoen W, Tangkijvanich P, Vejchapipat P, Poovorawan Y. Serum hyaluronan as a marker reflecting the severity of cirrhosis and portal hypertension in postoperative biliary atresia. Pediatr Surg Int 20:773-7, 2004
32. Stefanutti G, Vejchapipat P, Williams SR, Pierro A, Eaton S. Heart energy metabolism after intestinal ischemia and reperfusion. J Pediatr Surg 39:179-83, 2004
33. Vinardi S, Pierro A, Parkinson EJ, Vejchapipat P, Stefanutti G, Spitz L, Eaton S. Hypothermia throughout intestinal ischaemia-reperfusion injury attenuates lung neutrophil infiltration. J Pediatr Surg 38:88-91, 2003
34. Proctor E, Vejchapipat P, Fuller B. A Guide to the effective protection by hypothermia against ischaemic depolarisation in the gerbil brain. Cell Preserv Tech 1:205-10, 2002

**GRANTS AND FUNDINGS**

1. The Thailand Research Fund (2010-2012) for the study of the pathophysiology of biliary atresia
2. The Thailand Research Fund (2006-2009) for the study of HGF, EGF, and steroid receptor in biliary atresia
3. The Thailand Research Fund (2004-2006) for the study of nitric oxide and inducible nitric oxide synthase in biliary atresia
4. The Rachadapisek Sompoth Fund, Faculty of Medicine, Chulalongkorn University year 2004, 2005, and 2006

**PRESENTATIONS AT INTERNATIONAL MEETINGS**

## *ORAL PRESENTATIONS*

1. 12th European Congress of Pediatric Surgeons, June 2011, Barcelona, Spain
2. 95th Clinical Congress American College of Surgeons, October 2009, Chicago, USA
3. 10th European Congress of Pediatric Surgeons, June 2009, Vienna, Austria
4. 9th European Congress of Pediatric Surgeons, June 2008, Istanbul, Turkey
5. 44th International Meeting of the Japanese Society of Pediatric Surgeons, May 2007, Tokyo, Japan
6. 40th Congress of the Pacific Association of Pediatric Surgeons, April 2007, Queenstown, New Zealand
7. 20th Congress of the Asian Association of Pediatric Surgeons, November 2006, New Delhi, India
8. 18th International Symposium of Pediatric Surgical Research, October 2005, Stockholm, Sweden
9. 19th Congress of the Asian Association of Pediatric Surgeons, November 2004, Hong Kong, Republic of China
10. 18th Congress of the Asian Association of Pediatric Surgeons, October 2002, Singapore

11. Annual Meeting of British Association of Parenteral and Enteral Nutrition, November 2000, Harrogate, UK
12. 13th International Symposium of Pediatric Surgical Research, November 2000, Ann Arbor, Michigan, USA
13. Annual Meeting of British Association of Pediatric Surgeons, July 2000, Sorrento, Italy
14. Annual Meeting of International Society for Magnetic Resonance in Medicine, March 2000, Denver, Colorado, USA
15. Annual Meeting of British Association of Parenteral and Enteral Nutrition, December 1999, Bournemouth, UK
16. Annual Meeting of Canadian Association of Pediatric Surgeons, September 1999, Montreal, Canada

## *POSTER PRESENTATIONS*

1. 22nd Congress of the Asian Association of Pediatric Surgeons, February 2010, Kuala Lumpur, Malaysia
2. 19th Congress of the Asian Association of Pediatric Surgeons, November 2004, Hong Kong, Republic of China
3. Annual Meeting of International Society for Magnetic Resonance in Medicine, May 2004, Kyoto, Japan
4. Annual Meeting of International Society for Magnetic Resonance in Medicine, May 2002, Honolulu, Hawaii, USA
5. Annual Meeting of British Association of Pediatric Surgeons, July 2001, London, UK
6. Annual Meeting of International Congress of Nuclear Magnetic Resonance Spectroscopy, July 2001, Durham, UK
7. Annual Meeting of International Society for Magnetic Resonance in Medicine April 2001, Glasgow, UK
8. The Glutamine Workshop at the Sir Hans Krebs Centenary Symposium, September 2000, Oxford, UK
9. Annual Meeting of British Chapter of International Society for Magnetic Resonance in Medicine, June 2000, Liverpool, UK
10. Annual Meeting of British Association of Pediatric Surgeons, July 1999, Liverpool, UK
11. Annual Meeting of British Chapter of International Society for Magnetic Resonance in Medicine, December 1999, London, UK
12. Annual Meeting of International Society for Magnetic Resonance in Medicine, April 1999, Philadelphia, Pennsylvania, USA

## SELECTED HONOURS AND AWARDS

| | |
|---|---|
| 2009 | International Guest Scholarships, American College of Surgeons |
| 2004 | Young Investigator Award at the 19th Congress of the Association of Pediatric Surgeons, Hong Kong, Republic of China |
| 2004 | Poster Prize at the 19th Congress of the Association of Pediatric Surgeons, Hong Kong, Republic of China |
| 2000 | The Best Paper in Metabolism at the Annual Meeting of Clinical Nutrition and Metabolism Group of The British Nutrition Society, Harrogate, UK |
| 1999 | The Resident Best Paper Award: Book Prize for Best Basic Science Research Paper at The Annual Meeting of Canadian Association of Pediatric Surgeons, Montreal, Canada |

| | |
|---|---|
| 1998 | Young Clinician Program Award, the World Congress of Gastroenterology, Vienna, Austria |
| 1997 | PhD Scholarship from Royal Thai Government |
| 1990 | Outstanding Medical Student Award in Pediatrics |
| 1987 | Deputy Head of the Musical Club of Faculty of Medicine |

**SELECTED CERTIFICATES OF ATTENDANCE**

| | |
|---|---|
| 2001 | Masterclass in Advanced Pediatric Laparoscopy<br>Institute of Child Health, London, UK |
| 2000 | Annual Meeting of American Academy of Pediatrics<br>Chicago, Illinois, USA |
| 2000 | Diseases of the Visceral Circulation<br>Imperial College of Science, Technology and Medicine, London, UK |
| 2000 | Simpson Smith Symposium (Pediatric Surgery)<br>Institute of Child Health, London, UK |
| 2000 | Surgical Treatment of Anorectal Malformations (by Dr Alberto Pena)<br>Institute of Child Health, London, UK |
| 2000 | Annual Meeting of Nuclear Magnetic Resonance Symposium<br>London, UK |
| 1998 | Training Course in Magnetic Resonance Imaging and Spectroscopy<br>The Institute of Physics and Engineering in Medicine, UK |
| 1998 | Pediatric Intensive Care Workshop<br>Institute of Child Health, London, UK |
| 1998 | Advanced Life Support<br>Great Ormond Street Hospital NHS Trust, UK |
| 1998 | Annual Meeting of British Association of Pediatric Surgeons, Bristol, UK |
| 1998 | World Congress of Gastroenterology<br>Vienna, Austria |

## SUBJECTS OF INTEREST

Biliary atresia, intestinal ischemia-reperfusion, necrotizing enterocolitis, anorectal malformation, and Hirschsprung's disease