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Biliary Alkaline Phosphatase Isoenzyme in Biliary Obstruction.

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Abstract:

Alkaline phosphatase (ALP; EC 3.1.3.1) is mainly derived from the liver, bones and in lesser amounts from intestines, placenta, kidneys and leukocytes. A raised level of alkaline phosphatase in the blood frequently indicates a variety of diseases. The examination of the ALP isoenzyme can be performed by electrophoresis. This examination can be helpful in disease classification of those cases with hyperalkalinephosphatasemia. Of several ALP isoenzymes, biliary ALP isoenzyme is mentioned for its clinical usefulness in detection of biliary obstruction. Here, the authors performed a study to investigate the clinical usefulness of biliary alkaline phosphatase isoenzyme in biliary obstruction. Of interest, there is no significant difference of serum ALP level between malignant and benign biliary obstruction group. But there is a significant difference of serum biliary - ALP isoenzyme between malignant (range 28 U/L – 365 U/l) and benign biliary obstruction (range 20 – 140 U/L). Nevertheless, the average biliary - ALP level of the cholangiocarcinoma cases (range 105 – 365 U/L) is significant higher than the other malignant biliary obstruction cases (range 28 – 50 U/L). According to our study, the biliary - ALP isoenzyme determination can be use as a marker for malignant biliary obstruction.

Key Words: Biliary, alkaline Phosphatase, Isoenzyme, Obstruction.

Introduction:

Presently, the malignant biliary tract obstructions are common cancerous diseases among the people in the Southeast Asia, with the world highest prevalence at the northeastern Thailand and Laos [1]. The major manifestations of these diseases are severe jaundice, weight loss and abdominal distension [2].

Concerning the laboratory investigations, abnormalities of the liver function tests are the hallmark of these disorders. According to the study of Wiwanitkit, cholangiocarcinoma, a malignant biliary tract obstruction is the most common cause of the hyperalkalinephosphatasemia among the Thai hospitalized patients [3]. The ingestion of uncooked fishes infected with liver fluke, a rooted culture, is believed to be the major risk factor for developing of cholangiocarcinoma among this population.

Unfortunately, most patients came to see the physician when the symptoms are severe progressive. Early diagnosis of this disease seems necessary. Here, we reported our experience in determination of the biliary - Alkaline phosphatase (ALP) isoenzyme in the subjects with the problem of biliary tract obstruction. The studied biliary - ALP isoenzyme is a biochemical substance, which is mentioned as a sensitive marker of cholestasis

[4 - 5]. This isoenzyme is generated from the pathological biliary lining epithelium and rarely found in normal individuals [4 - 5]. Here, the authors performed a study to investigate the clinical usefulness of biliary alkaline phosphatase isoenzyme in biliary obstruction.

Materials and Methods:

Subjects: A total of 33 hospitalized patients who admitted to Department of Surgery, King Chulalongkorn Memorial Hospital between year 1998 were recruited. All were diagnosed to have biliary tract obstruction and admitted for further investigations and proper surgery. All patients in this study had dilated intrahepatic duct and/or common bile duct on imaging study.

Laboratory analysis: The pre-surgery blood samples from each subjects were collected. Classified by definitive diagnosis after surgery, two groups of subjects can be divided. The first group consisted of 15 patients with malignant biliary obstruction, cholangiocarcinoma and other periampullary tumors. The second group consisted of patients with benign biliary obstruction (n = 18). All patients in this group had the stones obstructing the common bile duct. Blood sample from each subjects was analyzed for serum alkaline phosphatase (ALP) level by automated clinical chemistry analyzer, Hitachi (Boehringer Mannheim). Each sample was analyzed for the level of biliary -

ALP isoenzyme by cellulose electrophoresis method (Helena Laboratory, Beaumont USA).

Results:

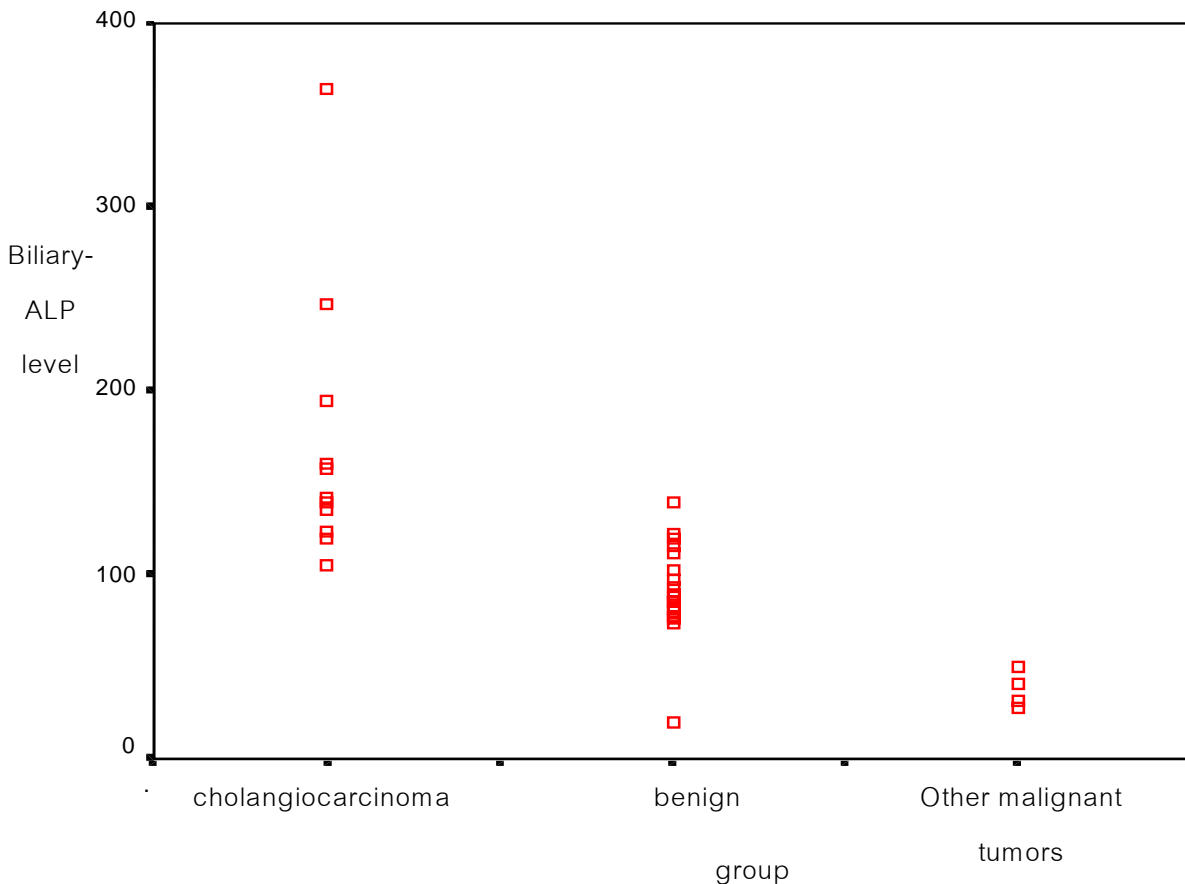
Of interest, there is no significant difference of serum ALP level between malignant and benign biliary obstruction group (Table 1). But there is a significant difference of serum biliary

- ALP isoenzyme between malignant (range 28 U/L – 365 U/L) and benign biliary obstruction (range 20 – 140 U/L) ($P = 0.04$) (Table 1). Nevertheless, the average biliary - ALP level of the cholangiocarcinoma cases (range 105 – 365 U/L) is significant higher than the other malignant biliary obstruction cases (range 28 – 50 U/L) ($P = 0.01$) (Table 1)

Table 1. Serum biochemical parameters in studied groups expressed as mean + standard deviation.

Group	Serum ALP (U/L)	Serum biliary - ALP (U/L)
Malignant (N = 15)	733.00 + 158.84	136.20 + 88.58
Cholangiocarcinoma (N = 11)	772.73 + 169.15	172.00 + 75.29
Other tumors (N = 4)	623.75 + 25.86	37.75 + 9.81
Benign (N = 18)	730.68 + 468.68	92.44 + 25.89

Figure 1. Biliary-ALP of the subjects.



Discussion:

Alkaline phosphatase (ALP; EC 3.1.3.1) is mainly derived from the liver, bones and in lesser amounts from intestines, placenta, kidneys and leukocytes [6]. A raised level of alkaline phosphatase in the blood frequently indicates a variety of diseases, although sometimes the rise is transient and the level returns to normal after one to three months without a clinical cause being found [7]. Various disorders are mentioned for the correlation with abnormal high serum ALP levels [8 – 9]. The wide range of clinical conditions associated with raised ALP include liver disease, heart problems, benign bone disease, treatable malignancy, sepsis, and acquired immunodeficiency syndrome – AIDS [8 – 9].

The examination of the ALP isoenzyme can be performed by electrophoresis. This examination can be helpful in disease classification of those cases with hyperalkalinephosphatasemia [4 – 5]. Of several ALP isoenzymes, biliary ALP isoenzyme is mentioned for its clinical usefulness in detection of biliary obstruction [4 – 5]. However, there has been no report on its usefulness in classification for subtype of obstruction. Here, the author tested if the biliary ALP isoenzyme could be used for this purpose.

According to our study, the biliary - ALP isoenzyme determination can be use as a

marker for malignant biliary obstruction. Indeed, the malignant biliary obstruction, especially cholangiocarcinoma is high prevalent in our setting, Southeast Asia and it is one of the most important problematic cancer in this area [10]. Clinical diagnosis of this cancer is hard and must have supportive investigations [10]. It may be useful as an adjunct to diagnosis when non-invasive imaging assessment is inconclusive. Nevertheless, it may be a useful tumor marker for cholangiocarcinoma. In fact, this ALP isoenzyme has been reported to be of merit as a tumor marker for hepatic metastasis even in the absence of jaundice [11]. However, some limitations due to the few cases in this study must be mentioned. A further larger studies to evaluated the sensitivity of biliary - ALP as the tumor marker for cholangiocarcinoma should be done.

References:

1. Wiwanitkit V. Etiological study of hyperalkalinephosphatasemia among the Thai hospitalized cancerous patients, a two-year retrospective in a Thai Tertiary hospital. Presented at the 22nd Annual Meeting of The International Association of Cancer Registries; 2000. Nov 8 - 10, Khon Kaen. Khon Kaen: International Association of Cancer Registries, 2000
2. Simcock R. Hepatobiliary tumours. Practitioner 2001;245:668-74

3. Wiwanitkit V. High serum alkaline phosphatase levels, a study in 181 Thai adult hospitalized patients. *BMC Fam Pract.* 2001;2:2
4. Crofton PM. Biochemistry of alkaline phosphatase isoenzymes. *CRC Crit Rev Clin Lab Sci* 1982; 16: 161 – 94
5. Siede WH, Seiffert UB. Relative merits of the biliary alkaline phosphatase isoenzyme and lipoprotein X complex in cholestasis and hepatic malignancy. *Clin Chem* 1983; 29: 698 – 700
6. Reichling JJ, Kaplan MM. Clinical use of serum enzymes in liver diseases. *Dig Dis Sci* 1988 33: 1601 – 1614
7. Lieberman D, Phillips D. "Isolated" elevation of alkaline phosphatase: significance in hospitalized patients. *J Clin Gastroenterol* 1990; 12, 415-419
8. McIntyre N, Rosalki S. Biochemical investigations in the management of liver disease. In: ?McIntyre, ed. *Oxford Textbook of Clinical Hepatology.* Oxford: Oxford University Press, 1991: 293 – 309
9. Neuschwander-Terti BA. Common blood tests for liver disease. Which ones are most useful? *Post Grad Med J* 1995 98: 49 - 56
10. Kullavanijaya P, Tangkijvanich P, Poovorawan Y. Current status of infection-related gastrointestinal and hepatobiliary diseases in Thailand. *Southeast Asian J Trop Med Public Health* 1999; 30: 96-105
11. Nishio H, Sakuma T, Nakamura SI, et al. Diagnostic value of high molecular weight alkaline phosphatase in detection of hepatic metastasis in patients with lung cancer. *Cancer* 1986; 57: 1815 – 9