



Ultrasonographic investigation of cholangiocarcinoma in Lao PDR

Ju Yeong Kim^{a,i}, Tai-Soon Yong^{a,*}, Han-Jong Rim^b, Jong-Yil Chai^c, Duk-Young Min^d, Keeseon S. Eom^e, Woon-Mok Sohn^f, Jae Hoon Lim^g, Dongil Choi^g, Sithat Insisiengmay^h, Bounlay Phommasack^h, Bounnaloth Insisiengmay^h

^a Department of Environmental Medical Biology, Institute of Tropical Medicine, Arthropods of Medical Importance Resource Bank, Yonsei University College of Medicine, Seoul 03722, Republic of Korea

^b Department of Parasitology, College of Medicine, Korea University, Seoul 02841, Republic of Korea

^c Department of Parasitology and Tropical Medicine, Seoul National University College of Medicine, Seoul 03080, Republic of Korea

^d Department of Microbiology and Immunology, Eulji University College of Medicine, Daejeon 34824, Republic of Korea

^e Department of Parasitology and Medical Research Institute, Parasite Resource Bank, Chungbuk National University School of Medicine, Cheongju 28644, Republic of Korea

^f Department of Parasitology and Tropical Medicine, and Institute of Health Sciences, Gyeongsang National University College of Medicine, Jinju 52727, Republic of Korea

^g Department of Radiology and Center for Imaging Science, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul 06351, Republic of Korea

^h Department of Hygiene and Prevention, Ministry of Health, Vientiane Municipality, Lao Democratic People's Republic

ⁱ Brain Korea 21 PLUS Project for Medical Science, Yonsei University College of Medicine, Seoul 03722, Republic of Korea

ARTICLE INFO

Keywords:

Opisthorchis viverrini
Cholangiocarcinoma
Abdominal ultrasonography
Opisthorchiasis
Stool ova examination
Lao PDR

ABSTRACT

Opisthorchis viverrini is a group 1 carcinogen that causes cholangiocarcinoma (CCA). Although opisthorchiasis is known to be severely endemic to several areas along the Mekong River in Lao PDR, the CCA status of residents of this region is still under investigation. In this study, we analyzed the results of abdominal ultrasonography (US) performed on 6113 residents in 9 provinces (Vientiane Municipality, Savannakhet, Phongsaly, Khammouane, Saravane, Champasak, Vientiane, Xieng Khuouang, and Luang Prabang provinces) of Lao PDR from 2007 to 2011. Overall, 51 cases (0.83%) were detected with suspected CCA. The CCA rates in Vientiane Municipality and in Savannakhet and Khammouane provinces were 1.45%, 1.58%, and 1.09%, respectively. However, in the other 6 provinces, the rate of CCA averaged only 0.26%. In the 3 provinces with higher rates of CCA, bile duct dilatation (grade ≥ 2) was also significantly more prevalent ($P < 0.0001$). These results are concordant with previous reports showing a higher endemicity of opisthorchiasis in Vientiane Municipality and in Savannakhet and Khammouane provinces.

1. Introduction

Recent reports have suggested that over 2 million individuals are infected with *Opisthorchis viverrini* in Lao People's Democratic Republic (PDR), with the infection rate in children being 10.9% (Andrews et al., 2008; Rim et al., 2003; Shin et al., 2010; WHO, 1995). *O. viverrini* is heavily endemic along the Mekong River because many Laotians eat undercooked freshwater fish, which is the second intermediate host of *O. viverrini* (Sripa et al., 2011).

O. viverrini lives in the bile ducts of humans or other reservoir hosts, such as dogs and cats. *O. viverrini* has been classified as a group 1 carcinogen that causes cholangiocarcinoma (CCA) or bile duct cancer (Bouvard et al., 2009). In addition, opisthorchiasis is a chronic, neglected tropical disease that affects individuals for decades, finally

causing morbidity and then death (Sripa et al., 2011).

The conventional diagnosis of *O. viverrini* is made by examining the stool of the patient for the presence of ova. However, a stool ova examination does not provide information on the pathological changes in the liver caused by *O. viverrini*. Moreover, the eggs of *O. viverrini* cannot be distinguished from minute intestinal flukes (MIFs) by stool ova examination (Kato–Katz method) in a field setting, which complicates the assessment of *O. viverrini* infection status.

Abdominal ultrasonography (US) is a powerful means of examining the lesions caused by *O. viverrini* in a field setting, such as in the rural areas of Laos, which lack appropriate systems for CT, MRI, pathological inspection, and laboratory support. Although recent studies have found several biomarkers of CCA such as 8-oxo-7,8-dihydro-2'-deoxyguanosine, miR-192, miR-21, and IL-6 (Saichua et al., 2015; Silakit

Abbreviations: CCA, cholangiocarcinoma; MIF, minute intestinal fluke; US, ultrasonography; HCC, hepatocellular carcinoma

* Corresponding author.

E-mail address: tsyong212@yuhs.ac (T.-S. Yong).

<https://doi.org/10.1016/j.actatropica.2018.02.031>

Received 12 April 2017; Received in revised form 7 February 2018; Accepted 23 February 2018

Available online 24 February 2018

0001-706X/ © 2018 Published by Elsevier B.V.

et al., 2014, 2017; Sripa et al., 2012b; Thanan et al., 2008; Yongvanit et al., 2014), abdominal US is much more useful than biomarkers if laboratory support is not readily available. Abdominal US is a non-invasive technique that has a high level of community acceptance and is relatively simple to perform (Mairiang et al., 2006). Abdominal US can rapidly detect pathological changes in the liver and bile duct, without causing pain. Using abdominal US, the lesions caused by *O. viverrini* such as CCA and other abdominal findings can easily be assessed by a medical professional.

In this study, we performed abdominal US examinations in 9 provinces of Laos using portable US devices. We assessed hepatobiliary lesions related to *O. viverrini* infection, such as CCA and bile duct dilatation, by abdominal US examination, and determined their association with *O. viverrini* infection by stool ova examination.

2. Materials and methods

2.1. Ethical considerations

This study was approved by the Ministry of Public Health, Lao PDR, under the agreement of the Korea-Lao PDR International Collaboration on Intestinal Parasite Control in Lao PDR (2007–2011). All participants provided written informed consent before participation in the study. Patients were informed of the US results and of any infection diagnosed during the examination, and were referred for treatment according to standard healthcare procedures. All patients with lesions suggesting CCA were given additional counseling. All individuals found to be positive for *O. viverrini* infection were treated with praziquantel (40 mL/kg, single oral dose).

2.2. Study area and population

From December 2007 to December 2011, a cross-sectional abdominal US study was performed in 110 villages in 42 districts within 9 provinces in Lao PDR (Fig. 1). Surveys were conducted in Vientiane Municipality (n = 546) in December 2007, Savannakhet Province (n = 1210) in June 2008, Savannakhet (n = 586) and Phongsaly (n = 76) provinces in December 2008, Khammouane Province (n = 877) in June 2009, Saravane Province (n = 819) in December 2009, Champasak Province (n = 759) in June 2010, Champasak Province (Khong Island) (n = 296) and Vientiane Province/Nam Ngum Dam (n = 145) in December 2010, Xieng Khuouang Province (n = 663) in June 2011, and Luang Prabang Province (n = 559) in December 2011. The study initially recruited 6536 voluntarily participating residents. Of the initially recruited 6536 residents, individuals who did not undergo either abdominal US (140 people) or stool ova examination (263 people) were excluded. Of the 6139 subjects who underwent both abdominal US and stool ova examination, only 6113 subjects had complete records of sex and age (Table 1).

2.3. US examination of hepatobiliary morbidity

Abdominal US examination was performed in each village using a portable US machine (Voluson E, General Electric, Boston, MA, USA). The criterion for suspected CCA by abdominal US was the presence of a mass located in the bile duct and/or dilatation of intrahepatic bile ducts. Intrahepatic bile duct dilatation is one of the specific characteristics of opisthorchiasis, and the degree of dilatation varies according to the quantity of infecting *O. viverrini* and disease progression (Lim et al., 2008; Mairiang, 2017). We therefore considered bile duct dilatation to be an important parameter of opisthorchiasis and defined grades for it. Bile duct dilatation grades were defined as follows: grade 1, minimal dilatation with few differences from healthy tissue; grade 2, mild changes, with 3 or more peripheral bile duct dilatations and thicknesses; grade 3, moderate dilatation, with prominent bile duct dilatation and thicknesses; and grade 4, severe dilation, with

parenchymal tissue damage caused by dilatation of the bile duct.

US examination was performed by local radiologists, Korean radiologists, and parasitologists experienced with the US detection of liver lesions caused by liver flukes. US examiners were blinded to the parasite infection status of the subjects. US images were stored as image files.

2.4. Stool ova examinations

Fecal specimens were examined for *O. viverrini* and MIF eggs using the Kato–Katz smear technique, recorded collectively as Ov/MIF.

2.5. Statistical analysis

The chi-square test, Fisher's exact test, and multiple logistic regression were performed using R package, version 3.1.3 (<http://www.R-project.org>). P-values below 5% were considered significant.

3. Results

3.1. Rate of suspected CCA

Among 6113 subjects in 9 provinces of Lao PDR who were examined by abdominal US, 51 cases of suspected CCA (0.83%) were detected. In Vientiane Municipality and the Savannakhet and Khammouane provinces, 7 (1.45%), 27 (1.58%), and 9 (1.09%) cases of suspected CCA were detected, respectively. However, only 8 cases (average of 0.26%) of suspected CCA were detected in the other 6 provinces combined (Table 1, Fig. 2).

The 9 provinces surveyed can be divided into 2 groups in 255 possible ways. The difference in CCA rates between the 2 groups was maximized (1.17%) when Vientiane Municipality and the Savannakhet and Khammouane provinces were assigned to 1 group and the other 6 provinces were assigned to the other. In this manner, Vientiane Municipality and the Savannakhet and Khammouane provinces were assigned to the group with a relatively higher CCA rate for analysis using the multiple logistic regression model.

Multiple logistic regression analysis indicated that individuals who live in Vientiane Municipality and the Savannakhet and Khammouane provinces have an approximately fivefold greater risk of CCA than that of individuals living in the other provinces (Table 2). Among the cases detected with suspected CCA, 32 were male (1.28%) and 19 were female (0.53%). The incidence was significantly higher in males than in females, with an odds ratio (OR) of 2.398. The rate of suspected CCA was the highest in individuals in their 60s (13/799, 1.63%), followed by those in their 50s. The regression model indicated that the cases of suspected CCA increased by 1.028-fold as age increased by 1 year. *O. viverrini*/MIF egg detection in stool was not associated with CCA by the chi-square test ($P = 0.3669$); therefore, it was not assigned as a variable in the multiple regression model for CCA (Table 1).

3.2. Prevalence of bile duct dilatation

We examined bile duct dilatation in subjects because it is an important US marker of *O. viverrini* infection and pathological progress. The presence of liver flukes in the bile ducts causes dilatation, as well as chronic inflammation followed by adenomatous hyperplasia (Lim et al., 2007).

The pattern of prevalence of bile duct dilatation was very similar to that of CCA in that significantly more cases were detected in Vientiane Municipality and the Savannakhet and Khammouane provinces than in the other 6 provinces (Table 3). For statistical analysis of bile duct dilatation, grade ≥ 2 was used as the dependent variable because it is relatively easily detected by US.

Overall, 592 cases of bile duct dilatation grade ≥ 2 were detected by abdominal US (Fig. 3). The prevalence rates of bile duct dilatation of

Download English Version:

<https://daneshyari.com/en/article/8744297>

Download Persian Version:

<https://daneshyari.com/article/8744297>

[Daneshyari.com](https://daneshyari.com)