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Predictive risk factors towards liver fluke infection among the people in Kamalasai District, Kalasin Province, Thailand

Woragon Wichaiyo[1], Wirat Parnsila[1], Wisit Chaveepojnkamjorn[2] and Banchob Sripa[3]

Abstract

Background: Liver fluke disease caused by *Opisthorchis viverrini* remains a major public health problem with its crucial risk factors caused by some individual habits or false beliefs among the people in northeastern Thailand concerning the consumption of raw fish meat dishes.

Objectives: This study explores the predictive risk factors for the infection of liver fluke disease.

Methods: The sample consisted of 400 people aged 30 years and above in Thanya sub-district, Kamalasai district, Kalasin province. A cross-sectional analytic study, using the χ^2 test, odds ratio and 95% confidence interval, was used to find the influence of each variable, along with the use of multiple logistic regression ($p = 0.05$). A questionnaire form was used as the research instrument.

Results: Factors found in the results are as follows: households with a cat were 7.00 times more at risk than households without a cat; eating raw fish dishes prepared by themselves increases the risk of infection by 2.58 times; eating raw fish dishes prepared by family members increases the risk by 4.74 times; and raw fish dishes bought from a community market increases the risk by 2.33 times.

Conclusion: A campaign should be launched to educate people not to eat raw or undercooked fish dishes, but to fully cook fish dishes before eating, as the food is still delicious, but also safe, healthy, and free from liver fluke infection.

Keywords

Liver fluke, factors liver fluke, raw fish, liver fluke disease, *Opisthorchis viverrini*

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Introduction

Pathologists consider that liver fluke disease has become one of the most serious diseases in public health. The World Health Organization (WHO) believes that liver fluke disease is a result of the eating habits of the people in the community and can lead to serious illness in the future.[1,2] In northeastern Thailand, liver fluke infection is endemic and is caused by *Opisthorchis viverrini* resulting from the cultural custom of eating uncooked fish dishes. This area has the highest reported incidence of opisthorchiasis[3] due to the consumption of raw or undercooked fish containing liver fluke within the contaminating contact period (metacercaria).[4] There are some alarming statistical records of the infection in the population of provinces nearby the selected area of this study. Sakon Nakhon province has 0.0154% infected people, Khon Kaen province has 0.0046%, Mukdahan province has 0.0003%, and Nakhon Phanom province has 0.0001%.[1,2]

Furthermore, in data collected on the incidence of liver fluke disease in Thailand by the Ministry of Public Health from 2009 to 2013, it was found that the percentage of infection of liver fluke disease among Thai people was 8.7%, or

[1]Faculty of Public Health, Mahasarakham University, Maha Sarakham, Thailand
[2]Department of Epidemiology, Faculty of Public Health, Mahidol University, Bangkok, Thailand
[3]Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Corresponding author:
Woragon Wichaiyo, Faculty of Public Health, Mahasarakham University, Kantarawichai District, Maha Sarakham 44150, Thailand.
Email: woragon.wi@ksu.ac.th

around 6 million people, and that they tended to have risk behaviour in their daily life.[4] Whereas, in the region of northeast Thailand, 16.6% of the people were infected, especially those living in the area of 'Roi Kean SaRa Sin' (shortened form for the provinces of Roi Et, Maha Sarakham, Khon Kaen, and Kalasin). Here, the percentage of people infected with liver fluke infection was found to be as follows: Kalasin province 27.4%, Khon Kaen province 14.2%, Roi Et province 11.8%, and Maha Sarakham province 11.6%.[5]

Thai people infected with liver fluke have the disease 'opisthorchiasis' or 'opisthorchiosis'. This is caused by *O. viverrini*. So, infection by *O. viverrini* is an important factor for the prediction of liver fluke disease. Besides, a survey on the prevalence of liver fluke diseases in other provinces near the river (Chee River) were found similar to the results investigation in Kalasin Province, such as Khon Kaen province showed that children under the age of 14, including newborn babies, can be infected with liver fluke and are four times more likely to become infected than children between the ages of 14 and 19. People aged 55–64 years are most likely infected with a morbidity rate of between 0.001% and 0.0008%.[2,5]

Up to now, there has been a continual high infection ratio of liver fluke disease. People can get infected again once they completely recover from the disease. It is difficult to treat this disease properly.

It has been found that the custom of eating raw, undercooked, or under-fermented cyprinoid freshwater fish in different menus still exists. The life cycle of the liver flukes is as follows. Eggs of the liver fluke are shed in faeces and are ingested by the Bithynia snail.[6] The eggs encyst, reproduce asexually, and are then released into the water as free-swimming cercariae which penetrate cyprinoid fish and encyst to become metacercariae. When the raw, uncooked, or under-fermented infected fish are eaten by definitive hosts, the metacercariae excyst and develop as adult liver flukes in the bile duct.[7–9]

Since liver fluke disease is associated with the eating culture of rural people living in the northeast region of the country, the researcher was interested in conducting a study about predictive risk factors for liver fluke infection of people in Kamalasai district, Kalasin province.

Materials and methods

Study design and data collection

The study was conducted with a cross-sectional analytic study, and data were collected from January 2016 to December 2016.

Study population and sample size

The study concerned predictive risk factors for liver fluke disease of people in Thanya sub-district, Kamalasai district, Kalasin province. The population in the study was 6462 people aged 30 years and over, and the sample size comprised 400 people.

Selection of the study area

1. The characteristics of samples to be studied were specified, and the responsible areas were in eight sub-districts of Kamalasai district.
2. The sub-district to be studied was randomly selected according to the target population using cluster random sampling and simple random sampling techniques through a method of drawing lots, and Thanya sub-district was selected as the area of the study.
3. Villages to be studied were randomly selected. The villages had to have a large freshwater source where people could find food, have water stored all year round and populated principally by farmers who grow rice twice a year. Due to the geography of Thanya sub-district, people usually settle near water sources, and they most likely find scaled fish for consumption in streams, freshwater swamps, and the Chi River.

Selecting sample for the study based on the following criteria

1. People who consume food likely to cause liver fluke infection.
2. Males or females aged 30 years and over.
3. People who are not detected with parasite eggs of the liver fluke.
4. People who have lived in Kamalasai district, Kalasin province for 6 months and over.

Infection confirmation of liver fluke

Infection confirmation was done by detecting liver fluke eggs in the stool by the method of Kato–Katz thick (KKT) smear technique.

Study instrument

Interview forms were used to collect data about predictive factors for liver fluke. One form was used to collect general information and another form for behavioural risk factors for liver fluke disease. Face-to-face interview technique was used in field surveys. The quality of the study instrument was tested by content validity handled by three experts. The index of item objective congruence (IOC) was used to screen the items, and it was found that all items had scores higher than 0.5. The reliability test was conducted with 50 interview forms to calculate Cronbach's alpha coefficient which was equal to 0.80. The directions of informed consent form (ICF) were explained regarding research purposes and distributed to each of the respondents.

Data analysis

Data analysis was performed using STATA (version 10.0), and Statistical Analysis software was employed. The statistics included number, percentage, mean, standard deviation, and high and low values. Crude analysis was used to find the influence of risk factors on those suffering from liver fluke disease with χ^2 test (chi-squared test). The statistical significance was determined at $p < 0.25$ to find an influence between two paired variables (bivariate analysis). The obtained factors were analysed to find interaction effect of variables with multivariate analysis. Multiple logistic regression analysis was used to estimate the statistical significance at 0.05 and odds ratio (OR) with 95% confidence interval (CI).

Results

Demographics and characteristics

This study showed the most common characteristics in the sample as follows: female (55.0%); over 60 years of age (31.00%), average age was 54.50 years; married (81.50%); finished primary education level (65.75%); main job – farmer (70.50%); second job or extra job – farmer (21.50%); taken anthelmintic drugs (51.00%); households without a cat (88.00%); taking raw or undercooked fish dishes prepared by themselves (69.00%); not eating raw or undercooked fish dishes prepared by family members (84.75%); and not eating raw or undercooked fish dishes bought from a community market (65.00%).

Predictors with the risk

After crude analysis was used to assess the relationship between dependent variables (risk and non-risk groups) and independent variables (factors) of each pair (bivariate analysis), the relationship was considered from $p < 0.25$ so as to carry out a multivariate analysis (Table 1). The predictive risk factors for liver fluke infection of people in the risk group based on the multiple logistic regression, with a statistical significance level at 0.05% and 95% CI, shows that there is only one factor being a preventive factor for liver fluke infection. The other four are risk factors for liver fluke infection. Details of the factors are as follows:

- The rice farmers were 3.88 times more at risk of getting infected with the disease (95% CI = 1.25–12.07), and other careers were 12.62 times more at risk of getting infected with the disease (95% CI = 1.65–96.53).
- People who have taken anthelmintic drugs were 0.43 times more at risk of getting infected with the disease (95% CI = 0.22–0.88).
- Households with a cat were seven times more at risk of getting infected with the disease (95% CI = 1.36–36.09).
- It was found that people taking raw or undercooked freshwater fish dishes which were (1) prepared by themselves were 2.58 times more at risk of getting infected with the disease (95% CI = 1.26–5.29), (2) prepared by family members were 4.74 times more at risk of getting infected with the disease (95% CI = 1.20–18.85), and (3) bought from a market were 2.33 times more at risk of getting infected with the disease (95% CI = 1.07–5.10). This is shown in Table 2.

Risks and prediction of liver fluke disease

In order to employ the model or equation to separate the risk group of liver fluke disease from this study and to apply for classifying people in the risk group who live in the risk areas, the researcher recommends that it would be better to use it for supporting the separation of a new risk group that is going to happen with two equations as follows:

1. Logistic regression equation can be written as risks of liver fluke disease.

Z = –3.17 0.47 (sex) + 0.10 (age 40–49 years) + 0.50 (age 50–59 years) + 0.41 (age 60) + 0.22 (widow, divorced, separate) + 0.70 (single) + 0.29 (primary school) – 0.03 (high school) + 0.98 (up to diploma) + 1.36 (main job of farming) – 0.90 (primary career: contractors) + 2.54 (other occupation) + 2.33 (secondary career: paddy) – 1.39 (secondary career: contractors) + 0.80 (secondary career: other career) + 1.95 (cat) – 0.83 (medication, quietly won) + 0.95 (to make raw by self) + 1.56 (sister/brother make to raw dishes) + 0.85 (raw dishes bought from the market).

2. Risk prediction equation to identify those at risk of liver fluke disease

$$P(X) = \frac{Exp^{(0.11 + X1 + X2 + X3 + X4 + X5)}}{1 + Exp^{(0.11 + X1 + X2 + X3 + X4 + X5)}} = \frac{Exp^{(0.11 + 1.95X1 + 1.56X2 + 0.95X3 + 0.85X4 - 0.83X5)}}{1 + Exp^{(0.11 + 1.95X1 + 1.56X2 + 0.95X3 + 0.85X4 - 0.83X5)}}$$

where P(x) = risk of getting liver fluke disease; X1 = the value of households with cats (with cats, substitute 1 and without cats, substitute 0); X2 = their family members make raw fish dishes (if they make raw fish dishes, substitute 1, and if they do not make raw fish dishes, substitute 0); X3 = they make raw fish dishes themselves (if they make raw fish dishes, substitute 1, and if they do not do, substitute 0); X4 = they eat raw fish dishes from a market (if they eat fish dishes from a market, substitute 1, and if they never eat raw fish dishes from a market, substitute 0); and X5 = anthelmintic drugs (if they have taken anthelmintic drugs, substitute 1, and if they have never taken anthelmintic drugs, substitute 0).

Discussion

The study results revealing the predictive factor for liver fluke disease of people in the risk group based on multiple

Table 1. A determination of the relationship between the general information and the predictors for the risk of liver fluke disease among the risk group using multiple statistics logistic regressions.

Variables	N (400)	OV risk group n (%)	Crude OR	Adj OR	95% CI OR_{adj}		p-value
					Lower	Upper	
Gender							
Female	220	130 (64.55)	1	1	–	–	0.195
Male	180	142 (72.22)	1.42	0.63	0.31	1.27	
Age group (years)							
30–39	77	59 (76.62)	1	1	–	–	0.470
40–49	96	59 (61.46)	0.49	1.10	0.31	3.91	
50–59	103	73 (70.87)	0.74	1.65	0.42	6.45	
⩾60	124	81 (65.32)	0.57	1.51	0.35	6.43	
Marital status							
Married	326	212 (65.03)	1	1	–	–	0.367
Divorced	35	28 (80.00)	2.15	1.25	0.24	6.44	
Single	39	32 (82.05)	2.45	2.02	0.44	9.30	
Education level							
Never studied	17	10 (58.82)	1	1	–	–	0.428
Finished primary school	263	172 (65.40)	1.32	1.34	0.32	5.50	
Finished secondary school	95	73 (76.84)	2.32	0.97	0.19	4.94	
Diploma and higher levels	25	17 (68.00)	1.49	2.67	0.24	30.28	
Main job							
Vendor	39	20 (51.28)	1	1	–	–	0.006*
Farmer	282	194 (68.79)	2.10	3.88	1.25	12.07	
Employee	49	37 (75.51)	2.92	0.41	0.08	2.10	
Other careers	30	21 (70.00)	2.21	12.62	1.65	96.53	
Second job or extra job							
Vendor	11	6 (54.55)	1	1	–	–	0.015*
Farmer	86	70 (81.40)	3.65	10.29	1.94	54.49	
Employee	63	42 (66.67)	1.67	4.01	0.81	19.88	
Other careers	85	54 (63.53)	1.45	2.23	0.48	10.28	
Have taken anthelmintic drugs							
No	193	137 (70.98)	1	1	–	–	0.021*
Yes	207	135 (65.22)	0.77	0.43	0.22	0.88	
Have a cat at home							
No	352	231 (65.63)	1	1	–	–	0.020*
Yes	48	41 (85.42)	3.07	7.00	1.36	36.09	
Eat raw or undercooked fish dishes prepared by themselves							
No	124	66 (53.23)	1	1	–	–	0.009*
Yes	276	206 (74.64)	2.59	2.58	1.26	5.29	
Eat raw or undercooked fish dishes prepared by family members							
No	339	217 (64.01)	1	1	–	–	0.027*
Yes	61	55 (68.00)	5.15	4.74	1.20	18.85	
Eat raw or undercooked fish dishes bought from a market							
No	260	157 (60.38)	1	1	–	–	0.033*
Yes	140	115 (82.14)	3.02	2.33	1.07	5.10	

OV: *Opisthorchis viverrini*; OR: odds ratio.
*Significant level at 0.05.

logistic regression analysis with a statistical significance level at 0.05% and 95% CI found that there is only one factor that can prevent liver fluke infection while the other four are risk factors causing liver fluke disease. Details of the factors can be described as follows. People living in households with a cat are 7.00 times more at risk of getting infected with the liver fluke disease than those who do not have cats.[4,5,7,10,11] Moreover, those who prepared raw or undercooked freshwater fish dishes for themselves are 2.58 times more at risk of getting infected with the disease.[1,3,8,12–16] However, when people did not make raw fish dishes themselves but their relatives made them to eat with their families, the risk of getting infected with the disease increased by 4.74 times.[1,3,4,8,16,17] When they did not have time to cook at home and bought

Table 2. Analysis using multiple linear regressions predicting the risk factors for liver disease among the risk group using the statistical multiple logistic regressions.

Variables	Coefficient	Adj. OR	95% CI for OR_{adj}		p-value
			Lower	Upper	
Have a cat	1.95	7.00	1.36	36.09	0.020*
Family members make raw fish dishes	1.56	4.74	1.26	18.85	0.027*
They make their own raw fish dishes	0.95	2.58	1.26	5.29	0.009*
They eat raw fish dishes from a market	0.85	2.33	1.07	5.10	0.033*
They have taken anthelmintic drugs	−0.83	0.43	0.22	0.88	0.021*
Constant		0.11	0.01	2.06	0.135

OR: odds ratio: CI: confidence interval.
Control by age, sex, education and status gives goodness of fit; Pearson chi-squared p = 0.320; Hosmer-Lemeshow chi-squared p = 0.7123 (data into the model).
*Significant level at 0.05.

raw fish dishes from a market in their community, the risk of getting infected with the disease increased by 2.33 times.[14–16] Moreover, it was found that the uncooked dishes tend to have greater risks of infection in the uncooked part of the fish's tail or the orange part of the fish that is not fully grilled.

It was also found that people in the risk group who had taken anthelmintic drugs were only 0.43 times more at risk of liver fluke disease,[4,3,18] while those who had never taken anthelmintic drugs had 2.33 times more risk of getting infected with the disease.[6,8,19] Since the taking of anthelmintic drugs resulted the prevention of Liver fluke disease at 57%,[6,12] these drugs should be made readily available to communities at risk of the disease.

This type of pathological study is important as it can be noted that taking raw fish from certain sources is more likely to affect people who eat the food if it is not cooked properly. It is also indicated that living near river banks and other water resources can lead to the infection of liver fluke in animals such as cats and dogs as they eat the raw fish. Furthermore, the parasite *O. viverrini* will live in the bile duct and gall bladder as well as in the ducts of the pancreas of the animals.[1,4,19–21] The infection passes from one animal to another and also to humans, particularly young children.

With regard to the limitations of the study, the liver fluke disease could infect people through the consumption of raw fish from as early an age as 10 years old. In contrast, the Ministry of Public Health screens risk groups of people who reside in northeastern Thailand and are older than 30 years. This might result in patient screening for the liver fluke disease being both incorrect and irrelevant.

Conclusion

An important consideration in the prevention of liver fluke disease is the consolidation of useful data collected from the people working in the field to find ways to help the people in the community realize the importance of solving the problem. It is important to create prevention campaigns to persuade people not to consume raw food, but to eat fully cooked dishes that are both tasty and healthy and free from liver fluke infection. For a healthy community, it is imperative to develop healthy eating behaviours and to teach the people how to protect themselves from the liver fluke disease.

Even a gradual change in the eating behaviour can be a good adjustment to remove the beliefs and habits of eating raw fish dishes among the people in the community. This will eventually decrease the risk of liver fluke disease. Step by step, we will have a healthy community without risky eating habits that lead to the infection of liver fluke. Such an outcome would be beneficial to everyone.

This study provides a model to predict the risk of liver fluke and is a useful tool to help in the detection and identification of vulnerable groups at risk of liver fluke with five risk indicators to be applied in disease prevention. Any reduction to the risk of morbidity and mortality from liver fluke disease is beneficial to Thailand and the world.

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Author contributions

W.W., who compiled this study as a requirement for her Doctoral degree, was the project leader. W.P., W.C., and B.S. were responsible for the project design. W.P. and W.C. drafted the article, were responsible for all calculations, were responsible for the project design and data collection, and collaborated to write this article.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

The study protocol was approved by the Faculty of Public Health, Mahasarakham University Ethics Committee, (No.PH 007/2559) and the Ministry of Public Health office in Kalasin Province, Thailand.

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Informed consent

Written informed consent was obtained from legally authorized representatives before the study.

ORCID iD

Woragon Wichaiyo https://orcid.org/0000-0001-8831-7931

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