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Assessing the burden of human cysticercosis in Vietnam

Dung Do Trung[1]*, Nicolas Praet[2]*, Thach Dang Thi Cam[1], Binh Vu Thi Lam[1], Hung Nguyen Manh[1], Sarah Gabriël[2] and Pierre Dorny[2]

1 *National Institute of Malariology, Parasitology and Entomology, Hanoi, Vietnam*
2 *Institute of Tropical Medicine, Antwerp, Belgium*

Abstract

OBJECTIVES To describe the occurrence of cysticercosis in patients living in rural areas of Northern Vietnam presenting clinical signs of neurocysticercosis.
METHODS Serological antigen detection, reflecting current infection with viable larval stages of *Taenia solium*, was used to estimate the prevalence of active cysticercosis in this patient population.
RESULTS The seroprevalence in epileptic patient population was <10%. However, antigen detection cannot detect dead cysticerci, which may also cause clinical signs. Therefore, the seroprevalence figures shown here may underestimate the role of neurocysticercosis as a causal agent of epilepsy and headaches in this population.
CONCLUSIONS Human and porcine cysticercosis remain public and veterinary public health problems in Northern Vietnam and probably in other parts of the country.

keywords *Taenia solium*, Vietnam, neurocysticercosis, clinical signs, burden

Introduction

Like many other Asian countries, Vietnam is endemic for *Taenia solium*, a zoonotic parasite causing porcine and human cysticercosis (CC) (Erhart *et al.* 2002; Somers *et al.* 2007; Willingham *et al.* 2003; Somers *et al.* 2006). While CC in pigs may cause considerable economic losses, establishment of the larval stage of the parasite (cysticercus) in the human central nervous system (neurocysticercosis (NCC)) may cause severe neurological disorders, such as epilepsy and headaches (Prabhakar & Singh 2002; Carabin *et al.* 2006; Praet *et al.* 2009).

Data on the occurrence of *T. solium* in Asia are limited. Some studies conducted in Asian countries have reported a prevalence of porcine and human CC ranging from 0.01% to 70.4% and 1.7% to 18.5%, respectively (Willingham *et al.* 2010; Murrell 2005). However, these prevalence figures should be interpreted carefully because the diagnostic tools used to detect infected individuals differ among the studies, which may considerably influence the estimates (Praet *et al.* 2010a). Willingham *et al.* (2003) reviewed the available information on human and porcine CC and taeniasis in Vietnam. Although some information on CC is available at hospital level, community-based data, which would permit a clearer estimation of the burden of the disease in rural areas where the major risk factors prevail, are lacking. Such risk factors for parasite transmission are freely roaming pigs, lack of properly used latrines and the habit of eating raw pork (Erhart *et al.* 2002; Willingham *et al.* 2003). Through community-based surveys conducted in 2006 in villages of Northern Vietnam, Somers and colleagues demonstrated the presence of circulating cysticercus antigens, suggesting active infection with the parasite, in 5.3%, 0.6% and 0.0% of the sampled individuals from the mountainous, coastal and urban regions, respectively (Dorny *et al.* 2004; Somers *et al.* 2006).

Besides prevalence and incidence figures, estimates of the proportion of NCC-associated health outcomes (epilepsy and headaches) are urgently needed to assess the burden of *T. solium* CC. Unfortunately, these figures are often lacking because studies to measure the attribution rate of CC require a complicated and expensive study design. Recently, a systematic review estimated a proportion of 29.0% of NCC among people with epilepsy living in *T. solium* endemic areas (Ndimubanzi *et al.* 2010). Asia-specific estimates are scarce, but studies in India estimate a proportion ranging from 18.0% to 38.6% of NCC-associated epilepsy (Rajshekhar *et al.* 2006; Ndimubanzi *et al.* 2010; Raghava *et al.* 2010; Goel *et al.* 2011; Raina *et al.* 2012; Singh *et al.* 2012). Asian estimates of the proportion of NCC-associated headaches are inexistent. One study conducted in Mexico estimated that about 0.1% of the population suffers from severe headaches due to NCC (Bhattarai *et al.* 2012; Carabin *et al.* 2011).

*Contributed equally.

We report here the results of investigative surveys conducted in seven provinces of Northern Vietnam to describe the occurrence of CC in selected epileptic, headache and subcutaneous cyst patient populations living in rural areas of Northern Vietnam.

Materials and methods

Between 2007 and 2010, seven provinces (Bac Giang, Bac Ninh, Dien Bien, Ha Giang, Laichau, Lang Son and Tuyen Quang; Figure 1) were selected based on preliminary questionnaire surveys indicating the presence of the major risk factors for *T. solium* transmission, that is, free-roaming pigs, lack of properly used latrines and raw pork-eating habits (data not shown; Erhart *et al.* 2002; Willingham *et al.* 2003). First, the populations were screened for the presence of the three major CC clinical manifestations, namely epilepsy, chronic headaches and presence of subcutaneous cysts (Prabhakar & Singh 2002). Epileptic, chronic headache patients and patients presenting subcutaneous cysts were identified using available registers at health centres and local hospitals. After informed consent, patients who were willing to participate were blood sampled. Blood was allowed to clot and centrifuged, and the serum was kept at −20 °C until analysis. Serum samples were tested using ELISA for detection of circulating antigens of the larval stage of *T. solium* (Ag-ELISA; Dorny *et al.* 2004). A sensitivity of 90% and a specificity of 98% were determined for the diagnosis of active CC using Ag-ELISA (Praet *et al.* 2010a).

Data were entered in Microsoft Excel software. For each NCC clinical manifestation, multivariate logistic regression analysis was used to identify significant relations between positivity to the Ag-ELISA (dependent variable) and age and sex (independent variables). The significance level was set at $P < 0.05$. Statistical analyses were conducted in STATA 11 ES software (Stata Corp., College Station, TX).

The study's protocol was approved by the Ethical Research Committee of the National Institute of Malariology, Parasitology and Entomology, Ministry of Health, Vietnam. Patients were included in the study upon written informed consent. A clinical follow-up of the Ag-ELISA positive patients was organised by the local health centres, and treatments were adjusted when needed.

Results

A total of 513, 758 and 83 patients suffering from epilepsy, chronic headaches and subcutaneous cysts,

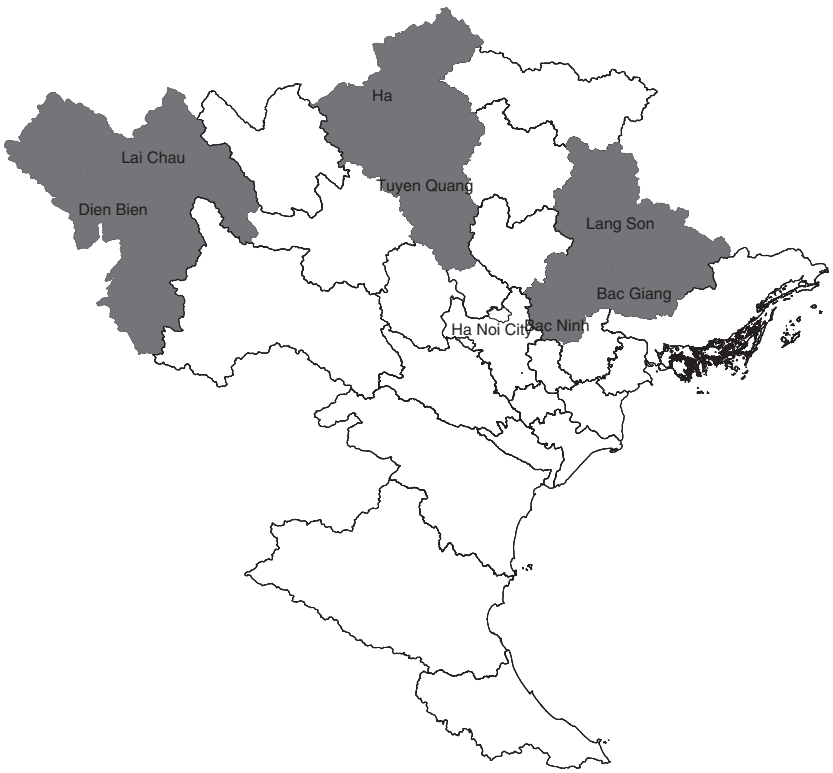

Figure 1 Map of Northern Vietnam showing the seven selected provinces where *Taenia solium* is endemic (shaded areas).

respectively, agreed to participate in the study. Patients were aged 6–89 years. The seroprevalence of CC in epileptic, headache and subcutaneous cyst patient populations and by province is detailed in Table 1.

Among patients suffering from epilepsy, 5% also had headaches and subcutaneous cysts, 58% had headaches only and 4% had only subcutaneous cysts. Logistic regression analysis did not show any significant difference of seroprevalence between males and females but revealed a positive correlation with age in both epileptic and headache patient populations (Figure 2).

Discussion

Taenia solium is endemic in Vietnam, but few studies allowed estimating the prevalence of the disease in the country. Moreover, little is known about the role of the parasite as a causal agent of epilepsy and headaches. The present study aimed at describing the occurrence of CC in selected epileptic, headache and subcutaneous cyst patient populations living in rural areas of Northern Vietnam. The Ag-ELISA, reflecting current infection with viable larval stages of the parasite, was used to estimate the prevalence of active CC in these populations, where risk factors for transmission are still present. The seroprevalence of CC in the epileptic patient population was relatively low (<10%) but within the range of values found in other countries (1.9% to 38.3%; Prado-Jean *et al.* 2007; Nitiéma *et al.* 2012; Willingham *et al.* 2010). A lower proportion of Ag-ELISA positives among epileptic patient may be linked to a lower overall CC prevalence in the region. However, as *T. solium*, *T. saginata* and *T. asiatica* are sympatric in South-east Asian countries; interspecific parasite competition may moderate *T. solium* transmission in this region, as suggested by Conlan *et al.* (2009). Yet, even though Gabriël *et al.* (2012) demonstrated that antigen detection can be of added value for diagnosing NCC in patients with epilepsy, one has to keep in mind that the Ag-ELISA is not able to detect dead cysticerci, which may also be responsible of clinical signs. Therefore, our seroprevalence figures probably underestimate the role of NCC as a causal agent of epilepsy and headaches in these populations. In contrast, using the Ag-ELISA may also overestimate the latter figure because the serological assay detects active CC and not exclusively NCC.

Data on the proportion of NCC-associated headaches are dramatically lacking, which precludes an accurate assessment of the burden of *T. solium* cysticercosis (Carabin *et al.* 2006, 2011; Praet *et al.* 2009; Bhattarai *et al.* 2012). Providing estimates of the proportion of active NCC among patients suffering from headaches in Northern Vietnamese provinces is a first attempt to fill this gap.

Table 1 Seroprevalence of CC (based on Ag-ELISA) in epileptic, headache and subcutaneous cyst patient populations by province

	Proportion of Ag-ELISA positives (95% CI)		
Provinces	Epilepsy	Headaches	Subcutaneous cysts
Bac Giang	0.06 (0.02–0.12)	0.08 (0.07–0.23)	0.33 (0.00–0.91)
Bac Ninh	0.12 (0.07–0.18)	0.12 (0.06–0.20)	0.04 (0.00–0.18)
Dien Bien	0.04 (0.00–0.13)	0.07 (0.03–0.14)	0.09 (0.00–0.41)
Ha Giang	0.07 (0.02–0.15)	0.09 (0.03–0.19)	0.18 (0.02–0.52)
Laichau	0.11 (0.04–0.23)	0.05 (0.02–0.10)	0.00 (0.00–0.71)
Lang Son	0.13 (0.05–0.27)	0.05 (0.03–0.10)	0.09 (0.11–0.29)
Tuyen Quang	0.00 (0.00–0.21)	0.03 (0.01–0.07)	0.00 (0.00–0.52)
Mean Prev.	0.09 (0.06–0.11)	0.06 (0.05–0.08)	0.08 (0.03–0.17)

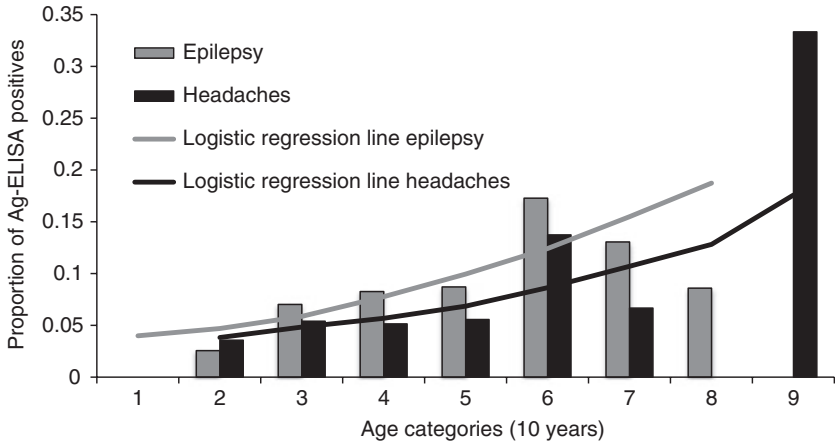

Figure 2 Proportion of Ag-ELISA positives in both epileptic and headache patient populations by age category (9 age categories of 10 years).

Our study indicates that human and porcine CC still remain public and veterinary public health problems in Northern Vietnam and probably in other parts of the country and neighbouring countries sharing the same pig breeding and raw pork-eating habits, and lacking functioning sanitations. The prevalence of CC in both epileptic and headache patient populations significantly increased with age of the patients. This observation could indicate that susceptibility to become infected increases with age as hypothesised in other studies (Fleury *et al.* 2004; Cavellani *et al.* 2007; Praet *et al.* 2010b).

The design of this study has limitations mainly due to the selection of patients, which is based on registers at health centres and local hospitals. Therefore, the number of patients suffering from CC symptoms may have been underestimated. Moreover, due to the lack of appropriate tools at local level, the diagnosis of epilepsy, chronic headaches and subcutaneous cysts may be inaccurate. However, this study underlines the importance of conducting community-based studies in the region using available serological tools to study the relation between clinical manifestations of CC and infection with the parasite. Further investigations should include the use of imaging techniques such as Magnetic Resonance Imaging and/or Computed Tomography scan allowing to determine the role of NCC as causal agent of epilepsy and headaches. These neuroimaging methods are starting to become available in hospitals in Vietnam, also at the provincial level. Adult tapeworm detection tests such as coprology, coproantigen ELISA, tapeworm recovery after treatment and molecular identification should be simultaneously used with CC detection tools to fully understand the transmission dynamics of the parasite in this *Taenia* spp. co-endemic region, to assess its impact on public and veterinary public health and to combat CC (Willingham *et al.* 2010; Murrell 2005).

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Corresponding Author Nicolas Praet, Institute of Tropical Medicine, Nationalestraat 155, 2000 Antwerpen, Belgium.
E-mail: npraet@itg.be