



Human Cysticercosis in Asia: A Systematic Review and Meta-Analysis

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Abstract

Background: Cysticercosis is among the neglected tropical diseases caused by eating the egg of the parasite *Taenia solium*. In this review, we aimed to verify the prevalence of human cysticercosis in different countries of Asia using a systematic review and meta-analysis approach.

Methods: Based on the protocol, reliable databases including PubMed, SCOPUS, Science Direct, Embase, and Cochrane Library from 1990-2018 were searched using a panel of keywords. Overall, 48 countries of Asia were searched in turn and data were analyzed using a category of statistical tests.

Results: Out of 28 included studies, 586175 samples were collected and included in the data analysis. Based on the meta-analysis results, the overall pooled percent of cysticercosis was estimated 3.8% (95% CI: [2.0, 7.0]). According to the result of heterogeneity statistics including I-squared, chi-square, and tau-squared, it was statistically significant ($Tau^2 = 2.94$, $chi^2 = 12733.31$, $P < 0.001$, $I^2 = 100\%$) therefore a random effect model was used to handle the heterogeneity of studies. To evaluate the trend of cysticercosis over time, cumulative meta-analysis was performed and the result showed that there was a minor upward tendency in the prevalence of cysticercosis over time.

Conclusion: Although, considering the religious culture and food habits in Asia, we might have expected to witness a low prevalence of human cysticercosis, but we noticed more or less significant infection in some countries of the region. Regarding the new feature of immigration and travel between countries, all authorities are advised to take measures on controlling and monitoring the disease.

Keywords: Cysticercosis; *Taenia solium*; Human; Neglected tropical disease; Prevalence; Asia

Introduction

One of the diseases regarded as Neglected Tropical Diseases (NTD) by WHO is cysticercosis (1). Cysticercosis is a parasitic disease established after ingestion of *Taenia solium* egg through contaminated food (2). Both humans and pigs might be infected with the disease. After ingestion of the egg,

oncospheres hatch in the small intestine, invade the intestinal wall and afterwards migrate to internal organs including striated muscles, brain, liver, and other tissues. There, cysticerci develop and result in cysticercosis (2). Many people in Asia consume pork, so it is possible that para-

site's eggs are spread everywhere, therefore cysticercosis might be occurred in Asia especially southeast Asia countries (3-6).

One of the most dangerous form of cysticercosis is Neurocysticercosis (NCC), which is occurred when the larvae of *T. solium* migrate to brain (2, 7, 8).

Considering that *T. solium* is transmitted via eating pork, and it is unusual in many Muslim countries in Asia, we expect to detect cysticercosis mostly in south-east countries including China (9, 10), Vietnam (11), India (12), Indonesia (4), Thailand (3) Korea (13), etc.

In this study, we aimed to collect and analyze data concerning the situation of human cysticercosis in Asia countries through searching authentic databases from 1990-2018. Animal cysticercosis and the prevalence of *T. solium* itself was not searched.

Methods

Search strategy

The databases including PubMed, SCOPUS, Science Direct, Embase, and Cochrane Library were searched using a panel of keywords, including, but not limited to, human cysticercosis, prevalence, epidemiology, and all Asia countries in turn (<https://www.worldatlas.com/articles/how-many-countries-are-in-asia.html>). The searched countries included Afghanistan, Armenia, Azerbaijan, Bahrain, Bangladesh, Bhutan, Brunei, Cambodia, China, Cyprus, East Timor, Georgia, India, Indonesia, Iran, Iraq, Israel, Japan, Jordan, Kazakhstan, Kuwait, Kyrgyzstan, Laos, Lebanon, Malaysia, Maldives, Mongolia, Myanmar, Nepal, North Korea, Oman, Pakistan, Philippines, Qatar, Saudi Arabia, Singapore, South Korea, Sri Lanka, State of Palestine, Syria, Tajikistan, Thailand, Turkey, Turkmenistan, United Arab Emirates, Uzbekistan, Vietnam and Yemen.

We included studies conducted between 1990-2018 published in English and relevant to the aim of the study. We screened at first the studies based on their title and abstract followed by availability of full text. For availability of abstracts only, we used them for Discussion section, if appropriated. Items such as books and Letter to the Editors were excluded from the study.

Inclusion criteria were studies 1) Conducted from 1990-2018; 2) Studies of English language 3) Availability of the full text; 4) Studies of Original or Review Article kind and 5) Human studies.

Exclusion criteria were 1) Studies conducted regarding animals only; 2) Case Report studies.

According to Prisma guideline (14), altogether, 2050 records were initially found through searching the databases mentioned already (Fig. 1).

After the initial screening, 77 articles were checked to verify the eligibility according to inclusion criteria, and eventually, 28 studies were included into the study.

Statistical analysis

In the present study, the data were evaluated using R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria.). The overall prevalence of cysticercosis was estimated using a point estimate and 95% confidence interval. The heterogeneity of studies were analysis using I-squared, Chi-square, and Tau-squared tests. The results with *P* value less than 0.05 were set statistically significant.

Results and Discussion

As mentioned earlier, we noticed that cysticercosis is found mostly in Southeast Asia countries. The prevalence varied from 0.80% in Indonesia (15) to 41.8% in Thailand (3). The whole distribution of human cysticercosis is demonstrated in Fig. 2.

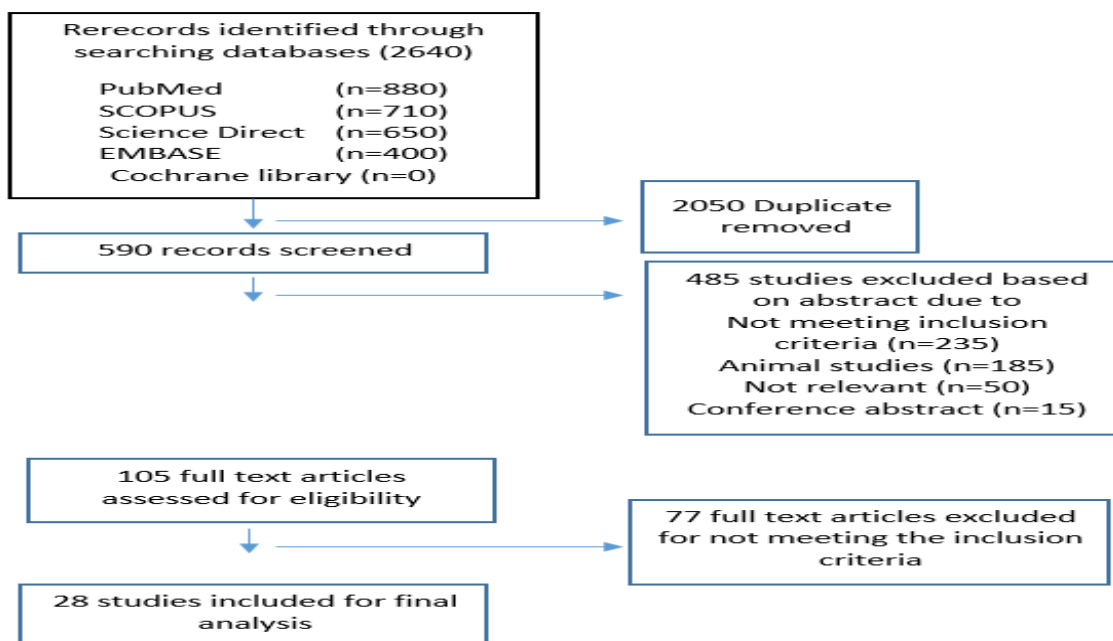


Fig. 1: The flow diagram of search and selection of relevant articles

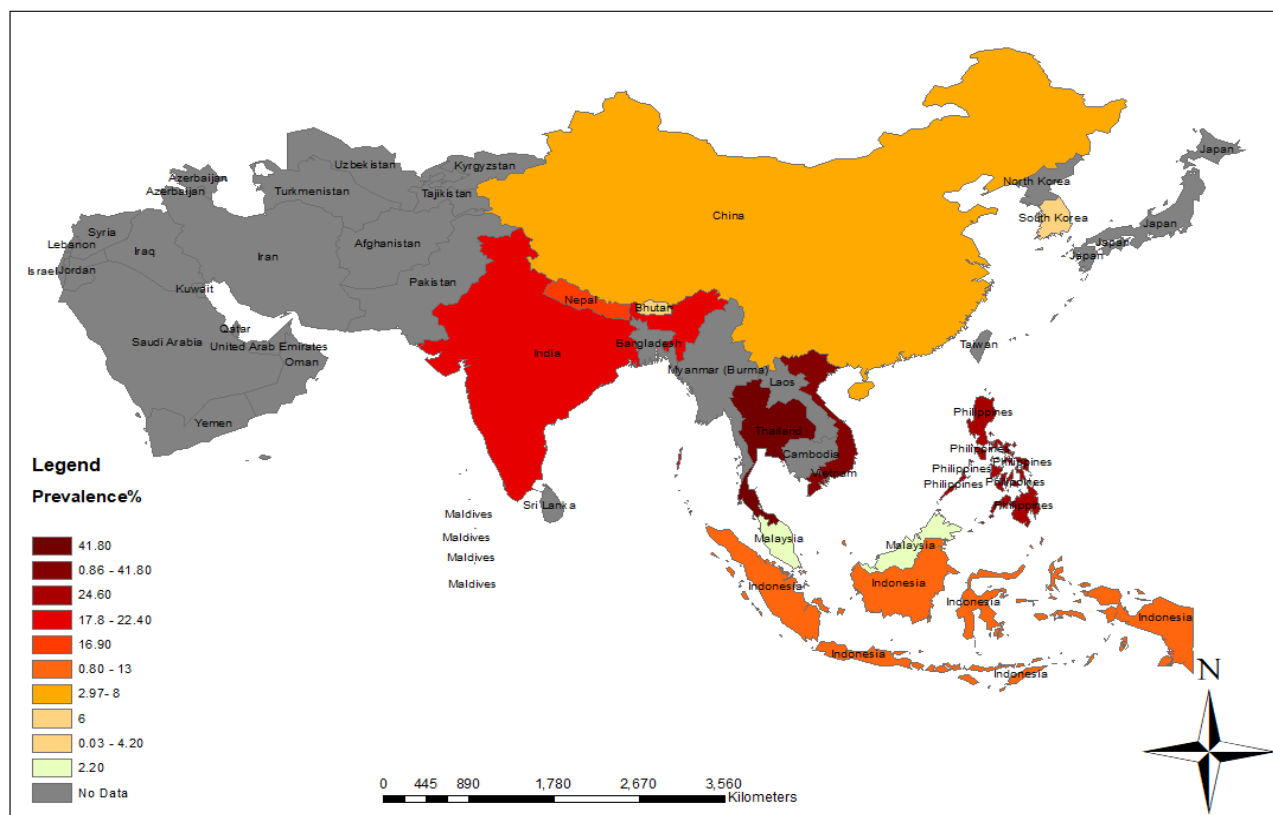


Fig. 2: Distribution map of cysticercosis in Asia

Result of meta-analysis

Out of 28 included studies, 586175 samples were collected and included in the data analysis. Based on the meta-analysis results, the overall pooled percent of cysticercosis was estimated 3.8% (95% CI: [2.0, 7.0]). According to the result of heterogeneity statistics including I-squared, chi-square, and tau-squared, it was statistically significant (Tau2 = 2.94, chi2 = 12733.31, P value <0.001,

I2 = 100%) therefore a random effect model was used to handle the heterogeneity of studies (Fig. 3).

To evaluate the trend of cysticercosis over the time, Cumulative meta-analysis was performed and the result showed that there was a minor upward tendency in the prevalence of cysticercosis over the time (Fig. 4).

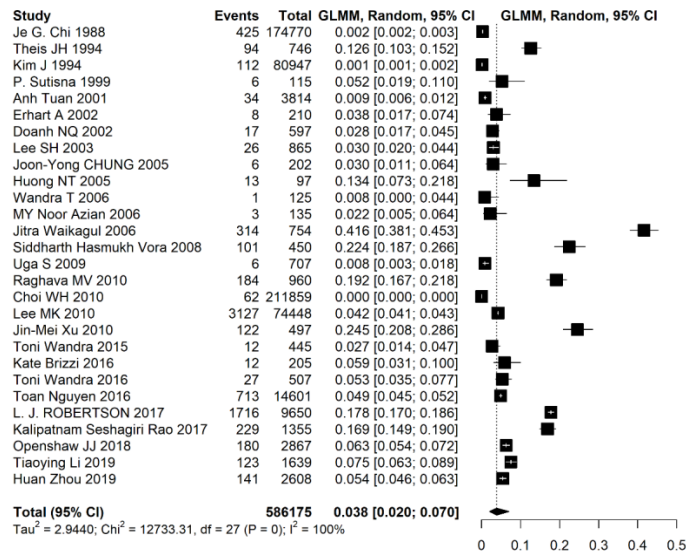


Fig. 3: Forest plot showing the pooled prevalence of cysticercosis in Asia

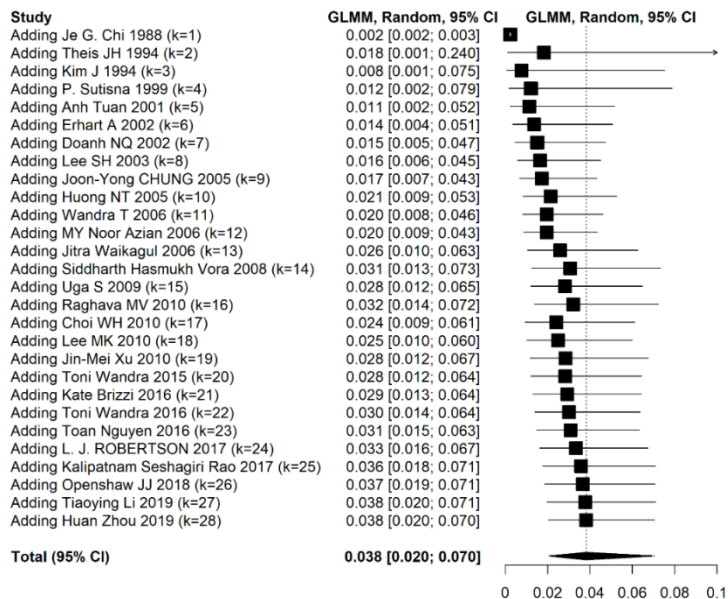


Fig. 4: Cumulative forest plot showing the trend of cysticercosis prevalence in Asia

China

NCC has been reported in China as affecting about 7 million people (16, 17). During a study on 2867 students in China, it was found that antibody to *T. solium* cysticercosis was present in 6% of subjects. In some schools, the prevalence was even 15% (16). Other studies showed human cysticercosis in China as 2.97% (10), 2.29% (18), and 4.32% (19). In minority areas of western Sichuan, China, from 2016 to 2017 a large study was conducted to detect the seroprevalence of cysticercosis in primary school-aged children. ELISA was used as serologic test. Eventually, from 1639 children examined, seropositivity was detected from 2.3% to 15.6% (overall 7.5%). It was found that children infected with *T. solium* showed more seropositivity than children without it (43.6% vs. 6.6%) (20). Zhou et al surveyed the rate of seropositivity for NCC in three mountainous areas in Sichuan Province of western China. From 2608 students, the seroprevalence of cysticercosis IgG antibodies was detected as 5.4%. The authors declared that sociodemographic factors, sources of pork and pig husbandry, as well as behavioral factors were contributed to establishing NCC (21).

Vietnam

Cysticercosis has been reported from Vietnam as well. Although *T. solium* is endemic in this country but from 1994 to 2002 the prevalence of cysticercosis was less than 1% (11, 22). Of course, the reported prevalence was mostly based on animal cysticercosis. However, as for human cysticercosis a review article reported 13% prevalence (22). Altogether, about 250-400 patients infected with cysticercosis have been reported from Vietnam from 2006-2011 (23). Another study reported a prevalence of human cysticercosis of 5% (average 2.2%-7.2%) from 1999-2000 (24). Erhart et al reported human cysticercosis as 5.7% in a village in 1999, from them 9 cases had NCV (25). The only study in south of Vietnam reported 4.3% seropositivity among people for cysticercosis (26). These data show that Vietnam has problem with the disease and should monitor it. A formal report testifies that males were significant-

ly more involved and the age group of 30-6 yr old had the highest rate of infection (23). Among risk factors mentioned for the disease in Vietnam, “the consumption of raw vegetables, drinking unboiled water, not washing hands before eating and outdoor defecation” may be considered (22).

India

Although India has a low portion of consuming pork, but considering that the pigs are present in this country, we should expect infection with cysticercosis there. Especially that mostly poor people raise pigs so the sanitation is not observed properly (12). A prevalence of 4.5/1000 for NCC, has been reported in the people infected with epilepsy in Jammu and Kashmir, Northwest India (27). During a serological study in south India, 391 patients were examined from January 2011 to December 2015. Altogether 32.5% of cases were found seropositive for NCC, of which male cases with 59.1% seropositivity showed higher rate than females (40.9%) (28). Another study in south India, reported a seroprevalence of 1.28/1000 in urban areas and 1.02/1000 in rural areas for NCC (29). In all these studies, NCC has been attributed as a major cause of epilepsy. Considering the estimation of the health and economic burden of neurocysticercosis on people in India, a comprehensive study was conducted by Sing et al in India (30). The results showed that in terms of DALYs it was 1.73 per thousand people. An annual economic burden of 12.03 billion rupees was calculated as well. Vora et al reported 22.4% seroprevalence for 450 people from rural Goa, India examined for cysticercosis (31). The prevalence increased in parallel with age.

Korea

Different seroprevalence rate has been reported for cysticercosis in Korea. A study by Lee et al Using ELISA test in 2001, detected 3.0% (26 cases) seropositivity for cysticercosis among 865 studied samples (32). Another long period study conducted in Korea from 1993 to 2006, examined 74448 samples using ELISA test. It was showed that seropositivity was decreased from

8.3% (1993) to 2.2% (2006) for cysticercosis (33). Age group of 50-59 years encompassed the highest positivity as 21.2%, besides to people coming from the Seoul (Capital) as 55.9%. It shows that tissue invading parasitic infections is an important issue in Korea and should be regarded as significant phenomenon. Cho et al analyzed 211859 biopsy specimens in Seoul, Korea during 1984-2005 and found 62 cases of cysticercosis (34), out of them, 55 cases were detected in subcutaneous tissues or the central nerve system. They reported that from the year 2000, no case of cysticercosis was found and all reported cases belonged to 1984-1988. During another long period study from 1980-89 with 80947 biopsy specimens conducted in Korea, 112 cases of cysticercosis were reported (35).

Indonesia

Altogether, from 1985 until 2006, the seroprevalence on cysticercosis has been reported as 5.2%-21% in this country (15, 36-38). From the early 1990s, *T. solium* was presented in Indonesia, therefore, cases of NCC were reported there more or less. However a joint project supported financially by Japan, regarding the control of NCC initiated from 1996 (39). Among the regions famous for NCC is Papua (formerly Irian Jaya), because of having some cases of outbreaks due to NCC (39). Although a 10-year project to control the disease has been started by the government from 1990, yet it is labeled as high endemic are for NCC and subcutaneous cysticercosis (36, 40). Besides, NCC was common in Bali from 1990s (39, 41). After taking health measurement by the government, the cases of NCC have been reduced significantly and considered as sporadic. The issue of immigrants infected with NCC or *T. solium* cause spreading the disease to different parts of Indonesia (39). Feeding from infected pigs, looking for job by many unemployed infected individuals especially in dry session have been mentioned as factors assisting to spread NCC (39). Moreover, a local food entitled *lawar*, prepared with uncooked beef or pork is reported as another factor in the region. Bali is a favorite place for tourists so there is the risk of

infection with the disease. Theis et al conducted a study on 746 residents in Bali to find the anti-Cysticercus antibodies, from which, 94 cases (13%) showed seropositivity (37). They concluded that epilepsy might be an output of NCC in the area. Another study from rural areas of Bali showed seroprevalence of human cysticercosis by immunoblot as 1.65% (6/363) (38). Some undocumented cases of subcutaneous cysticercosis have been reported from the local clinics as well. Other reports showed that 45.8% of people, 70.4% of pigs, and 10.9% of local dogs were seropositive for cysticercosis in Papua (36, 42, 43). These figure shows that in terms of cysticercosis the situation in Indonesia and especially Papua needs more attention by local authorizes and international involved organizations.

Other countries

Considering that cysticercosis is transmitted via eating parasite's egg released by pig, we expect that the disease is present in only some limited countries depending on the religious and food habitats and cultures. Anyway, other countries in Asia, more or less show a degree of infection with cysticercosis.

In Bhutan, people with epilepsy were investigated for NCC by ELISA and EITB. Results showed that 6% were definitely infected with NCC (44). Twenty percent were reported as probable NCC. Rao et al conducted a study in Nepal from 2033-2015 on children. They reported 229 (16.90%) case of NCC among the 1355 cases of seizure disorders (8). The authors have expressed their satisfaction of the trend of NCC during the last years in Nepal. In Thailand we have report from Waikagul et al (3). Accordingly cysticercosis was reported as 41.8% via immunoblot technique from 2000-2005. They believe that the rate of infection already reported in literature is underestimate and needs more verification. In Thailand people are used to consume raw/half-cooked meat dishes so the risk of taeniasis and cysticercosis would be considered by authorities. Noor Azian et al verified the situation of cysticercosis in Malaysia among a rural village. They reported a seropositivity as 2.2% among 135 studied cases

(6). In the Philippine, we have the situation of endemic for cysticercosis (45). In a study conducted in rural areas, the seroprevalence of 24.6% was detected among 497 studies subjects (45). This shows more necessity for considering the disease in this country.

Conclusion

Indeed we might have expected a low prevalence of human cysticercosis in the region in comparison with other regions, but the rate of infection shows considerable range. It varied from 0.8% to 41.8%. Of course, countries where pork can be seen in the matrix of people lives, showed more infection. Increasing rate of travel and immigration between countries, looking for job and better job in countries where cysticercosis had not been reported already, changing food habits because of shortage of food materials, increasing political turmoils in most countries of the region which force people to move to other countries, and some similar reasons have caused to spread the NTDs, among them human cysticercosis and NCC are considered very important. It is due to pathological effects this disease brings for patients.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interests.

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