Minireview Article

A Review on Important Foodborne Zoonotic Parasites of Southeast Asia

ABSTRACT

Many neglected tropical diseases are foodborne parasitic zoonoses, which are typically transmitted to humans after consumption of contaminated food, soil or water, containing eggs or larval stages. This review focuses on the three main foodborne zoonotic helminths of Southeast Asia (SEA): *Taenia solium*, *Opisthorchis viverrini* and *Ascaris* species; describing their life cycle and clinical signs, distribution and prevalence, associated risk factors, key control and prevention strategies, and main challenges. This review highlights that despite the existence of recommended standardized and validated diagnostic methods, the range of available procedures can cause overreporting or underestimation of the prevalence and intensity of foodborne parasite infections, and directly impact the monitoring of the food chain and of control and prevention programs. These foodborne parasites and their intermediate hosts will be able to expand their geographic range and colonise new habitats due to ongoing increases in temperature, humidity and rainfall, as a result of climate change. Future interventions aiming to reduce the prevalence and impacts of foodborne parasitic zoonoses in SEA should thus be multi-dimensional and consider interactions between humans, animals, the food chain, and the environment, by adopting a One Health approach. In order to disrupt foodborne zoonotic helminthic transmission, this review underlines that animal reservoirs and high-risk human populations should be both the target of anthelmintic treatments; more remote and tribal areas should be included in health, hygiene and sanitation infrastructures and awareness programs; stricter national policies and control systems should be implemented to reinforce food safety monitoring and limit contamination of the food chain; while existing education and training campaigns should be further promoted.

KEYWORDS

Ascaris species, foodborne zoonotic parasites, Opisthorchis viverrini, Southeast Asia, Taenia solium

1. INTRODUCTION

Zoonoses are infectious diseases transmitted from animals to people, they are broadly distributed worldwide, but are more abundant in Eastern Africa and Southeast Asia (SEA) than other regions [1]. In SEA, bacterial, helminthic and viral pathogens are associated with more zoonoses than protozoa and fungi [1]. Pathogenic organisms do not equally infect all mammal groups, with rodents carrying the greatest number of zoonotic helminths, followed by carnivores and ungulates [1]. More specifically, dogs (carnivores), followed by aquatic animals (amphibians, birds, fish and reptiles) and pigs (ungulates) can be definitive hosts to more zoonotic helminths infections than other animal groups [2]. Interestingly, the common sources of infections in the animal groups with the bigger diversity of zoonotic helminths (namely dogs, as companion animals, aquatic animals and pigs, as livestock animals) and humans include poor hygiene, environmental contamination and consuming improperly cooked or raw meat [2]. In SEA, many neglected tropical diseases (NTDs) are foodborne parasitic zoonoses, which are typically transmitted to humans after consumption of cruciferous vegetables, improperly cooked or raw crustaceans, fish and meat, containing parasitic larval stages [3]. The occurrence of foodborne parasitic zoonoses in this region correlates with poor hygiene and sanitation, and traditional cooking practices [3].

Using multi-criteria decision analysis, the global ranking of foodborne parasites listed the following as the five most important helminth species [4]: *Taenia solium* (commonly called the pig tapeworm), *Echinococcus* species (hydatid tapeworms), *Trichinella spiralis* (referred to as the pork worm), *Ascaris* species (*A. lumbricoides* and *A. suum*, respectively called the large roundworms of humans and pigs) and Opisthorchidae parasites, which encompass three trematode species: *Clonorchis sinens*is, *Opisthorchis viverrini*, and *O. felineus* (referred to as the Chinese, Southeast Asian and cat liver flukes respectively).

This ranking was published after a meeting held close to 10 years ago and since then, global measures were implemented to try to reduce the prevalence of these foodborne parasites and limit their impact on humans [3-5]. Reducing prevalence was and is still a global priority because these organisms represent a major threat to public health, both globally and in SEA [3, 5, 6]. In fact, every year, approximately 420 000 people die worldwide due to foodborne diseases [3] with 22% of illnesses, 55% of deaths, and 61% of DALYs (Disability-Adjusted Life Year) estimated to be due to foodborne parasites [7]. More precisely, foodborne zoonotic helminths cause the majority (60%) of DALYs and deaths, with the largest disease burdens occurring in Africa, in developing America and in SEA [7]. In SEA, the main parasites associated with DALYs are *Taenia solium, Opisthorchis* and *Ascaris* species [7].

This paper will thus provide an overview of these three helminth parasites in SEA in their order of importance; focusing on their life cycle and clinical signs, distribution and prevalence, associated risk factors, relevant key control and prevention strategies and associated challenges.

2. *TAENIA SOLIUM*

2.1 Life cycle and clinical signs

T. solium, or the pig tapeworm, is a cestode which larval stages cause cysticercosis in pigs and humans (Fig. 1). Both intermediate hosts can become infected after consumption of human faeces-contaminated food (vegetables), water or soil, containing eggs or proglottids (Fig. 1). Humans can also acquire this helminth as a result of poor hand hygiene, while pigs can also get exposed via direct coprophagy. After ingestion of eggs or tapeworm segments, oncospheres penetrate the intestinal wall, reach different organs via the bloodstream, and develop into cysticerci (Fig. 1) [4, 8, 9].

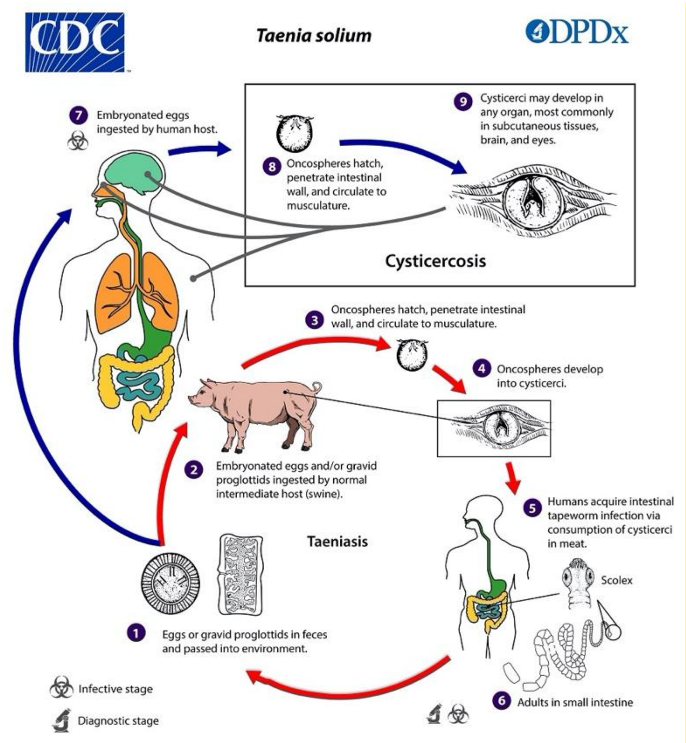

Figure 1. Life cycle of *Taenia solium* [8].

Formation of cysticerci in human brains can result into neurocysticercosis and is associated with neurological problems such as epilepsy, seizures, and death. Porcine cysticercosis cases are usually asymptomatic, as cyticerci are typically embedded in striated muscles, but heavily infected pigs can display lingual cysts. *T. solium* adult stages can also cause taeniasis in humans, who can get infected after consumption of undercooked cysticerci-contaminated pork meat, or via autoinfection. Through digestion, cysticerci hatch and develop to adult tapeworms in the small intestine of definitive human hosts, who will shed eggs and proglottids in their faeces, perpetuating the parasite life cycle and further contaminating the environment (Fig. 1). Intestinal infections can cause mild digestive symptoms including abdominal pain, constipation or diarrhea, decreased appetite, intestinal inflammation, and nausea; but most cases tend to be asymptomatic [4, 8, 9].

2.2 Distribution and prevalence

Previously, the distribution of *Taenia solium* cysticercosis in Cambodia, Laos, Thailand, and Vietnam was extensively described [10] and further details about studies conducted in SEA communities were provided; but also included data about other *Taenia* species reports [11, 12]. In a recent review, confirmed cases of *Taenia solium* infections in humans and pigs between 2000 and 2018 were comprehensively reviewed: porcine cysticercosis was reported from Cambodia, East Timor, Indonesia, Laos, Myanmar, Thailand, and Vietnam, while no data was available for human *T. solium* infections, except for Cambodia, East Timor, and Indonesia. In the Philippines, only human cases were documented, probably because no proper epidemiological survey in pigs was performed [13]. Further details are provided here below.

In Cambodia, a single study reported porcine cysticercosis after inspection of pork meat, suggesting 6.7% prevalence (29/432), positive animals originated from Banteay Mean Chey, Battambang, Kampong Cham, Kampong Chhnang, Kampong Speu, Kampong Thom, Kandal, Koh Kong provinces [12, 14]. The World Health Organisation (OIE) reported porcine cysticercosis cases between 2005 and 2017 in East Timor but no published paper was found for porcine or human *T. solium* infections [13].

In Indonesia, four studies detected *T. solium* from pigs: two of them reported porcine cysticercosis after inspection of pork meat, suggesting 77.1% prevalence (27/35) and 100% (6/6) respectively, while two others detected cysts during pig postmortem examinations; positive animals originated from Bali, Lampun and Papua provinces [13, 15-18].

The OIE reported porcine cysticercosis cases between 2005 and 2017 in Laos and a single paper found positive cases after inspection of pork meat (5/590), indicating only 0.85% prevalence from pigs originating from Huaphana and Luangprabang provinces [13, 19]. In addition, *T. solium* infections were detected in 3.1% (5/163) of tested humans originating from Savannakhet province [20].

In Myanmar, a single study reported porcine cysticercosis after inspection of pork meat, suggesting 23.7% prevalence (71/300), positive animals originated from Naypyidaw province [13, 21]. Porcine and human cysticercosis, as well as taeniosis cases, were also detected from the border between Myanmar and Thailand [13, 22].

No porcine cysticercosis report was found from the Philippines; however, *T. solium* infections were detected in 25% of tested humans originating from Leyte Island [13, 23].

In Thailand, a single study reported porcine cysticercosis from serology screening, suggesting 19.7% prevalence (37/188), post-mortem detection of cysts was confirmed from all seropositive animals examined (n=10), infected swine originated from Tak province [24]. Human taeniosis and cysticercosis were also found in two villages from Kanchanaburi province [13, 25].

The OIE reported porcine cysticercosis cases between 2005 and 2017 in Vietnam and a single paper found positive cases after examination of pig tongues (109/172 087), indicating only 0.06%

prevalence from swine originating from Bac Kan, Bac Giang, Lao Cai, Nghe An and Yen Bai provinces [13, 26]. Moreover, *T. solium* infections were detected in 5% of tested humans originating from Dak Lak province [27].

In Brunei and Malaysia, no report of porcine or human *T. solium* infection was found during the examined period, most likely because these two countries are predominantly Muslim [11-13]. In contrast, human cysticercosis cases from migrants have been previously described from Singapore while this country imports pork meat products from other countries [11-13]. This parasite is thus not considered a problem in these three countries although some communities (foreign workers, non-Muslim people) may be at higher risk of exposure [11-13].

2.3 Risk factors

Swine production is crucial to most rural communities of SEA, except for Muslim countries including Brunei, Indonesia, and Malaysia. Pork meat is often the principal source of protein and income, with the majority being produced from small mixed farming systems. Consumption of pork meat has increased tremendously but swine production, husbandry and farming systems are still rudimentary and mostly unmonitored. Furthermore, in SEA, pigs are often reared as free-range, which increase their risk of exposure to *T. solium* contaminated faeces, as a result of coprophagy [4, 6, 11, 12].

T. solium transmission is also enhanced by poor hygiene and sanitation practices including improper handwashing habits, limited domestic use of clean and safe water, primitive or lack of toilets such as latrines, consumption of improperly cooked or raw pork meat, no disease transmission awareness, letting pigs scavenge and feed on human food and faecal wastes, use of human solid and liquid faecal wastes as crop fertilizer, direct or indirect contact with a household carrier, and limited abattoir inspection of pork meat [4, 6, 11, 12].

3. *OPISTORCHIS VIVERRINI*

3.1 Life cycle and clinical signs

O. viverrini, or the Southeast Asian liver fluke, is a trematode which inhabits the hepatobiliary system of cats, dogs, pigs and humans. People and mammals are definitive hosts, they become infected after consumption of fermented, raw or undercooked metacercariae-contaminated freshwater fish (Fig. 2).

After ingestion, metacercariae excyst in the intestine, migrate to the bile duct where they mature to adult flukes, and produce eggs which are shed in faeces (Fig. 2).

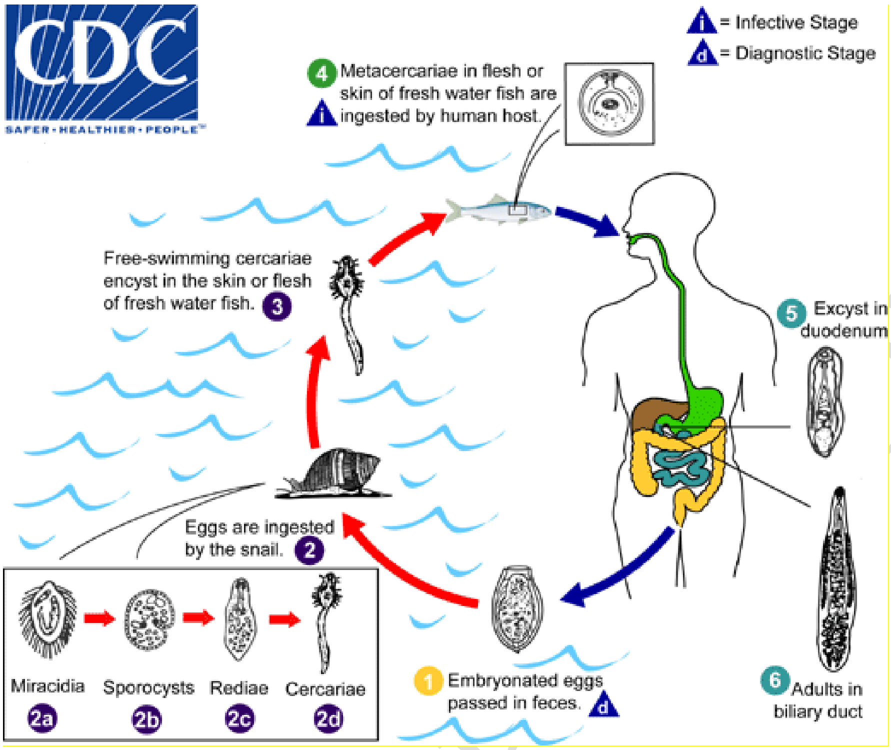

Figure 2. Life cycle of *Opisthorchis viverrini* [8].

Eggs are eaten by freshwater *Bithynia* species snails, the first intermediate hosts, in which they release miracidia prior to developing to sporocysts, rediae and cercariae (Fig. 2). Cercariae then get ingested by cyprinid fish (carp family), the second intermediate hosts, and encyst as metacercariae into their muscles, subcutaneous tissues, and under their scales (Fig. 2) [4, 8, 12, 28-30].

Heavy burdens of flatworms can obstruct the gall bladder and bile duct of humans, causing abdominal pain, constipation or diarrhea, dyspepsia, fever, malabsorption and malnutrition; but most acute light intensity cases tend to be asymptomatic. Similar clinical signs are observed in other mammalian hosts carrying severe fluke infections. Chronic opisthorchiasis can also cause hepatobiliary symptoms in humans such as gallstones, hepatomegaly; while prolonged infections can lead to cholangiocarcinoma, cholangitis, and cholecystitis [4, 8, 12, 28-30].

3.2 Distribution and prevalence

O. viverrini is endemic to continental SEA, it is prevalent in all countries bordering the Lower Mekong Basin but has been more frequently reported from Cambodia, Central and Southern Lao PDR, North and Northeast Thailand, and Central and Southern Vietnam [30-32]. *O. viverrini* infections have also been recently detected from Myanmar, while sporadic cases from Malaysia and the Philippines have been previously recorded [30-35]. Its geographic range matches the distribution of its first intermediate hosts, the freshwater snails *Bithynia sp.* [31, 36] while 31 cyprinid fish species, its second intermediate hosts, are found in Cambodia, Lao PDR, Thailand and Vietnam; 21, 11, 7 species are also prevalent in Malaysia, Myanmar and Singapore respectively [34, 37].

A recent review suggested that *O. viverrini* was found across Cambodia and was particularly prevalent in the flood plain of the Mekong River [34, 38]. High infection rates have been recorded from Kampong Cham (18%, 23.9-28.5% and 44.8%), Kandal (7.9%, 10.7% and 20.2%), Takeo (26.9%, 32% and 47.5%) provinces [32, 34, 39-43]. Two national surveys were performed in the past decade: one study detected a 4.1% prevalence for *O. viverrini* infections from schoolchildren, while the other reported a 5.7% prevalence for *O. viverrini* and minute intestinal flukes from the general population [34, 38, 44]. It was previously noted that national data were incomplete and limited, while contradictory infection rates have been reported for some provinces [32, 34, 38].

The national prevalence of *O. viverrini* was previously reported as 10.9% in Laos, with high infection rates detected from the lowland areas of the southern and central provinces of Khammuane (32.2.%), Savannakhet (25.9%) and Saravane (32.2%) [32, 34, 45, 46]. *O. viverrini* was also found in 64.3% (430/669) of faecal samples screened from Champasack province [32, 34, 46]. More recent cross-sectional studies indicated that *O. viverrini* remains very common in these areas, with reports of 51.1% (559/1095) in Chanpasack, Luangprabang and Savannakhet provinces, and of 54.8% (150/237) and 70.3% (90/128) in Khammuane province [34, 47-49].

A recent study assessed *O. viverrini* infections in human rural communities of three Southern Myanmar regions, prevalences of 18.9%, 5% and 3.6% were detected in the Bago, Mon state and Yangon regions respectively [33, 34]. These data indicated a 9.3% (34/364) overall prevalence, but the number of screened samples was limited; a subsequent study, which analysed a larger sample size, reported a much lower prevalence (14/2057; 0.7%) from the Yangon region [33-35].

Historically, the national prevalence of *O. viverrini* was very high in Thailand (14%); but it has been considerably reduced (2.2%) after 40 years of opisthorchiasis control programs [32, 34]. Its prevalence decreased from 34.6% to 4.98% in the Northeast; from 6.3% to 0.87% in the Centre and from 5.6% to 1.79% in the North between 1980 and 2019, while it remained very low (0.01%) in the South [34, 50]. Nonetheless, *O. viverrini* was recently detected from 19.4% (75/387) of faecal samples screened from Khon Kaen province; suggesting that it is still common in Northeast rural villages [34, 51].

O. viverrini was previously found in 11 provinces of Southern Vietnam including Binh Dinh (11.9 %), Da Nang (0.3%), Dac Lac (7.6 %), Khanh Hoa (1.4%), Phu Yen (36.9 %), Quang Nam (4.6%), Quang Tri (32%) and rare cases reported from Thua Thien Hue [32, 34, 52-54]. Infection rates reaching up to 40% were also detected in 6 Central Vietnam districts, namely Buon Don, Mhu My, Mo Duc, Nui Thanh, Song Cau and Tuy An [32, 34, 54]. These earlier data may have overestimated opisthorchiasis prevalence by misdiagnosing morphologically similar minute intestinal fluke eggs: *Clonorchis* or *Opisthorchis* species infections are thought to be less prevalent in Vietnam than *Haplorchis* species cases, while mixed trematode species infections are common [34, 55]. An unpublished recent survey conducted in 2015-2018 by the National Institute of Malariology, Parasitology and Entomology detected moderate to high *O. viverrini* infections rates of 6.8%, 4.8%, 15.3%, and 8.9% in Dac Lac, Binh Dinh, Phu Yen, and Quang Trị provinces respectively [34].

3.3 Risk factors

Fish is the main protein source of Southeast Asian rural communities, with cyprinid fish often being consumed daily because they are easy to raise and catch, readily affordable and available [56, 57]. The Lower Mekong Basin is flooded every year, shaping most of this region as wetlands, which is majorly being exploited for rice and fish production [57, 58]. Lakes, ponds, swamps and rice fields provide a highly productive fish habitat, fishing is a common practice amongst those communities [56-58]. Fish consumption is thus central to the diet of rural people of the Lower Mekong Basin, who will eat traditional raw fish dishes such as *Gỏi cá*, *Koi-pla, Laap-pla* (spicy minced salads) and process leftovers into fermented fish dishes including *Maam chao*, *Pla-som, Pla-ra* (moderately to extensively fermented and salted dishes), which are shared with other family members, friends or villagers [32, 34, 56, 57, 59].

As a result, consumption of fermented, raw or undercooked cyprinid fish is the major risk factor for opisthorchiasis; other related risk factors include land and water-based activities (fishing, fishermen, laborers and rice farmers), food-sharing habit, household subjected to flooding, located close to the Mekong corridor or within two kilometres of food and water sources. *O. viverrini* transmission is also associated with limited sanitation practices, water source contamination, uncontained disposal of food wastes, presence of cats or dogs in the household, limited or no liver fluke health education, and persistent smoking and consumption of alcohol (red whiskey) by older men [57, 60].

4. *ASCARIS* SPECIES

A. lumbricoides, or the large roundworm of humans, is an intestinal nematode infecting humans worldwide, while *Ascaris suum,* or the large roundworm of pigs, mostly infects swine; but cross-infections have been reported. These two parasites are genetically related and morphologically similar, and with the identification of hybrids, experts have been questioning whether they should be considered as distinct species. Because of this controversy, most prevalence studies use '*Ascaris* species' when referring to either organism, this term will thus be used in this paper from here forward [4, 8, 61].

4.1 Life cycle and clinical signs

Ascaris spp. cause ascariasis in pigs and humans, both definitive hosts can become infected after consumption of faeces-contaminated food (fruits and vegetables), water or soil, containing eggs (Fig. 3). Humans can also acquire this helminth as a result of poor hand hygiene, while pigs and dogs can also get exposed via direct coprophagy. After ingestion of embryonated eggs, infective larvae hatch, and invade the intestinal wall prior to migrating to the liver and lungs (Fig. 3). Upon maturation, larvae further migrate via the alveoli, bronchi, and trachea, before being swallowed back into the in the gastrointestinal tract, where they further develop to adults in the small intestine and ileum (Fig. 3). Eggs are excreted in host faeces and contaminate the environment, perpetuating the life cycle of these parasites (Fig. 3) [4, 8, 62, 63].

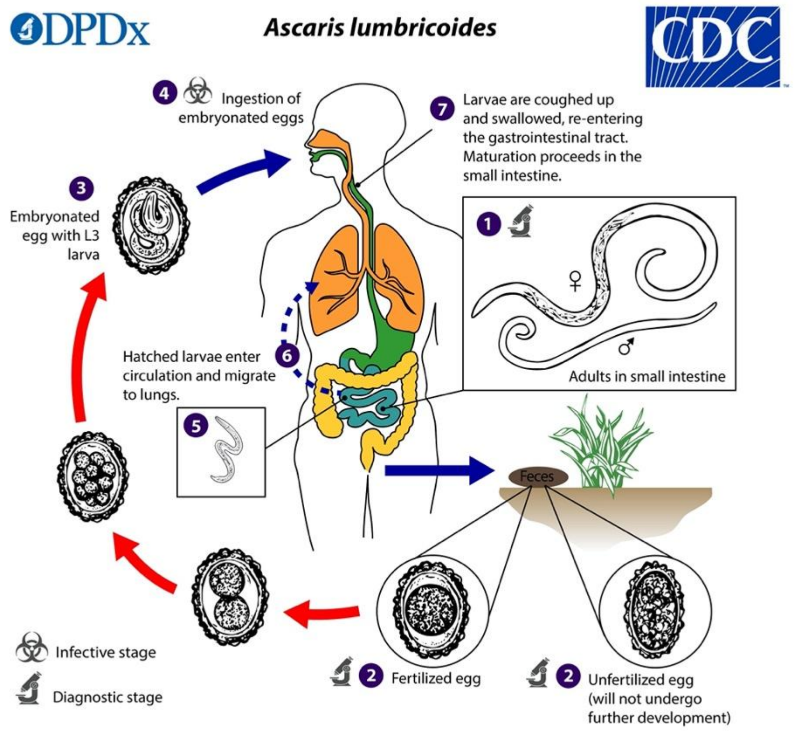

Figure 3. Life cycle of *Ascaris lumbricoides* [8].

In humans, heavy worm burdens can cause abdominal pain, anorexia, malabsorption and malnutrition, as a result of the damage of the intestinal villi and inflamed lamina propria; intestinal blockage, perforation or rupture can also occur in extreme cases, while light infections are usually asymptomatic. Other symptoms can be observed following adult or larval worm migration including appendicitis, nasopharyngeal expulsion, death following obstruction of the biliary and pancreatic tracts, damage to the liver and peritoneum. Pulmonary larval migration can also initiate a life-threatening immune response called 'Loeffler's Syndrome' [4, 8, 62, 63].

Ascariasis usually causes more severe clinical signs in young than adult pigs. Swine can present with diarrhea, pendulous abdomen, rough hair coat, unthriftiness and weight loss; intestinal blockage may occur in heavy infections. Larval migration through the liver can induce haemorrhages and fibrosis, but most commonly cause white lesions called 'milk spots', resulting from the accumulation of lymphocytes. Abdominal breathing ('thumping'), coughing, fibrosis, pneumonia, and pulmonary consolidation, haemorrhage or oedema can manifest when larvae migrate through the lungs [4, 8, 62, 63].

4.2 Distribution and prevalence

Both *Ascaris* spp. are globally distributed and particularly prevalent in subtropical and tropical regions, which include SEA, where moist and warm environmental conditions enhance the survival and development of eggs. As *Ascaris* pp. are Soil-Transmitted Helminths (STHs) and part of the NTD group, thousands of studies have been previously published. However, the varying population sample size, the range of laboratory tests used to diagnose parasites, and the methodology applied to evaluate prevalence and intensity of infections have often complicated the perception of the STH status in SEA, due to the inadequacy of available data [4, 54].

Brooker et al. (2003) previously provided an estimate of the total disease burden in SEA for each STH and applied Geographical Information Systems to map surveys published between 1962 and 1999, in order to identify the populations at risk of infection and evaluate proportions requiring treatment. The predicted prevalence of ascariasis was 22% in Cambodia, 35.8% in Laos, 28.8% in Myanmar, 23.2% in Thailand, and 54% in Vietnam [64].

Similarly, a comprehensive review including data from 1997 to 2008 on helminth infections in the Western Pacific Region, was performed by WHO, in order to assist parasite control interventions [54]. Epidemiological surveys were not available from each Southeast Asian country, but the following prevalences of ascariasis from schoolchildren were reported: 26% in Cambodia, 34.9% in Lao, 23.2% in the Philippines, and 68.8%, 37.4% and 14.6% from North, Central and Southern Vietnam respectively [54]. The Ministry of Health of Brunei, Malaysia and Singapore indicated that STH infections were not common nor considered as a major public health problem in their countries [54]. However, three studies performed on school children from aboriginal and remote Malaysian communities detected *Ascaris* spp. in 16 to 61.9% of tested faecal samples; it was also suggested that high STH and *Ascaris* spp. infection rates were common in islands, fishing villages, forest areas and plantations of rural Malaysia [54].

Such publications guided national public health preventive and control programs, which were largely implemented by the World Health Organization (WHO) in order to reduce the impact of STH infections, including *Ascaris* spp., in SEA, with a particular focus on children and rural communities.

Recently, a systematic review included 174 STH studies published between 1990-2015 in order to assist the planning of future mass drug administration (MDA) campaigns [65]. Low to moderate prevalence of ascariasis were reported from Thailand (1%, 0-6%), Cambodia (5%, 1-19%), Laos (12%, 5-25%) and Indonesia (22%, 16-31%); Vietnam (36%, 23-52%) and Malaysia (39%, 31-48%)

had high *Ascaris* spp. prevalences while the highest *Ascaris* spp. infections rates were from Myanmar (55%, 37-71%) and the Philippines (59%, 46-72%) [65]. The overall prevalence of *Ascaris* spp. in South and SEA was 18% (14-23%) indicating that ascariasis is the most common STH in this region [65].

Interestingly, this review also analysed published literature by community types and found that urban and rural populations had lower prevalence of *Ascaris* spp. compared to tribal communities, which can act as a human reservoir of transmission when migrating, for work purposes for example [65]. In fact, in Thailand, *Ascaris* spp. infection rates of 19.23% (189/923) were detected from Karen (tribal group) people from the Tak province, while screening of faecal samples collected from pregnant migrants and refugees living in camps at the Thai-Myanmar border (majority of Karen ethnicity) reported prevalences of 5.4% (470/8517) and 23.3% (943/3909) for ascariasis [66, 67].

Another newly published paper estimated that the overall prevalences of STH infections were 61.4% (50.8-71.4%) and 32.3% (25.7-39.3%) for ascariasis in minority indigenous communities of SEA and West Pacific Region [68]. *Ascaris* spp. infection rates in indigenous populations of 26% (22.95, 29.18%) for Indonesia; 10.64% (7.78-13.87) for Laos; 38.26 % (31.79-44.94) for Malaysia, 44.72% (9.67-83.17) for the Philippines, 13.61% (3.79- 27.99%) for Thailand, and 27.13% (25.63-28.66) for Vietnam [68].

These recent publications suggest that future public health interventions in SEA should focus on indigenous and tribal populations, where STH and *Ascaris* spp. infection rates may be much more important than what has been disclosed by latest national epidemiological surveys.

4.3 Risk factors

As most epidemiological studies have been assessing *Ascaris* spp. and other STH spp. concurrently, most risk factors associated with these parasites cannot be easily separated per causative organism.

The main mode of transmission of the most important STH (hookworms, roundworms, whipworms) occurs via the faecal to oral route; many risk factors are thus linked to poor personal hygiene and sanitation practices, including access to clean water, outdoor defecation, no sewage or waste disposal system, no use of soap for handwashing, proximity with domestic and livestock animal species, use of human faeces and wastewater as fertilizer or for the irrigation of field crops [8, 63, 69,70].

As a result, humans get infected by accidentally ingesting eggs contaminating water sources or raw fruits and vegetables; particularly if the water is not boiled, and if fruits or vegetables are not properly peeled or washed prior to consumption.

Children are at higher risk of STH infection because they also play with contaminated soil and can ingest eggs by putting their hands into their mouths; particularly if they do not have the habit of washing their hands before eating and/or after defecation; but also if they bite their nails or suck their thumbs [8, 63, 69, 70].

People from rural and tribal communities, of low socio-economic status, living in overcrowded settings, in poverty or in substandard conditions, and having limited health education are also more at risk of STH infection [8, 63, 69, 70].

In addition, pig farming, pig ownership and the use of pig manure as fertilizer increase the risk of exposure to *Ascaris suum* eggs [8, 63, 69, 70].

5. CONTROL AND PREVENTION OF FOODBORNE PARASITES

5.1 Key strategies

Three key strategies have been globally adopted to control and prevent foodborne parasites: deworming humans and animals, improving health, hygiene and sanitation, and monitoring the food chain. These strategies rely on successful concurrent education and training programs targeting professionals, consumers and children in order to enhance food safety awareness and practices.

<u>5.1.1 Deworming</u>

Deworming, or delivery of anthelmintic medicines, aims to decrease morbidity by reducing worm burdens; considering human impacts of foodborne parasites here discussed, most Southeast Asian countries which reported high helminth prevalence, particularly in children, were targeted by different WHO MDA programs.

The main objectives of MDA programs are to provide anthelmintic medicines to a large proportion of targeted populations, in order to eliminate infections in asymptomatic carriers, to prevent reinfection during post-exposure prophylaxis and to interrupt parasite transmission. MDA programs can quickly reduce the prevalence and incidence of helminth infections, but if transmission is not interrupted, worm burdens can quickly come back to their pre-intervention levels. When parasitic infections are not completely eliminated, MDA programs may initiate selective pressure for the emergence of anthelmintic resistance, such programs should therefore not be initiated without evidence that complete elimination is achievable in targeted populations.

Efficient MDA programs require high to entire coverage of targeted human populations (which implies community commitment and compliancy), disruption of the life cycles of the parasites (including control and treatment of intermediate hosts), concurrent health education, hygiene and sanitation improvements (such as access to safe water); as well as regular monitoring and evaluation of chemotherapy efficiency [54, 71, 72].

5.1.2 Health, hygiene and sanitation

Improving health and safety awareness, hygiene and sanitation practices and infrastructures, together with promoting clean water accessibility are fundamental requirements to stop parasitic transmission and reinfection via the faecal to oral route. Global Water, Sanitation and Hygiene (WASH) programs have thus been implemented by the CDC (Centers for Disease Control and Prevention), the United Nations Children's Fund (UNICEF) and the WHO in developing regions, including SEA.

Actions supporting better health and hygiene practices include making water available, clean and safe to drink and use (source, collection, treatment and storage), promoting proper handwashing habits (use of soap; before preparing, handling or eating food, after defecating, before feeding children and after changing a diaper) and the use of footwear, building accessible handwashing facilities, providing education and training via schools, governmental agencies and health facilities.

Discouraging open defecation, teaching how to safely handle and dispose of human faeces, providing improved latrines, septic tanks and sewage systems, managing properly wastewater, as well as separating children from soil and domestic or livestock animal faeces are essential measures to improve sanitation [8, 73, 74].

5.1.3 Food safety and food chain

Monitoring of the food chain from primary production (pre-harvest) to consumption (post-harvest) is also crucial to stop parasitic disease transmission and to ensure the safety and quality of food products for consumers.

In order to prevent faecal to oral transmission of foodborne parasitic infections pre-harvest, assessing faecal contamination of raw food products, ensuring on-farm sanitation infrastructures (handwashing facilities, latrines, sewage systems) and monitoring the use and composition of organic fertilizers are important considerations. Stopping the zoonotic transmission of foodborne parasites from primary production can be enhanced by administering regular anthelminthic treatments to aquatic, domestic and livestock animals, controlling access to aquaculture ponds and farms by reservoir and intermediate hosts (including feral and stray animals), discouraging feeding raw meat, animal carcasses and offal to aquatic, domestic and livestock animals, monitoring the water quality given to livestock animals and used to irrigate crop fields, and by enabling traceability of food products back to primary producers.

Control of foodborne parasites post-harvest should focus on the processing of food products: freezing and cooking raw food products with the appropriate temperature and time combination will kill most infective parasitic stages while curing, drying, marinating, pickling, salting or smoking processed food should be evaluated for the survival of specific parasites. Education and training of abattoir workers, farmers, food handlers and consumers should cover hygienic animal husbandry production systems (location and design of farms and ponds, manure use, risk of faecal run-off, slaughter techniques), disease awareness, as well as safe food handling practices (high risk food products, handwashing, adequate cooking) to further break the transmission of foodborne parasitic diseases.

In addition, improving veterinary sanitary measures such as disease management and control, performing risk-based inspection of the food chain by identifying hazards (Hazard Analysis and Critical Control Point or HACCP), harmonizing surveillance, monitoring and testing of foodborne parasites (including thorough meat inspection and postmortem examinations) are needed to further prevent and control foodborne parasite contamination and promote international trade of food products [3, 4, 75].

5.2 Main challenges

Two main challenges should be taken in account by future studies in SEA: choice of adequate diagnostic tests to monitor the food chain and the efficacy of control and prevention programs; and climate change impacts, which will further affect the transmission and life cycle of foodborne parasites.

5.2.1 Diagnostic testing

The diversity of diagnostic techniques applied to the monitoring foodborne parasites can affect their detection levels and prevalence data. Microscopic tests including Kato-Katz (gold-standard), formalin-ether concentration technique, flotation methods (including FLOTAC, faecal egg counts, McMaster technique; using saturated sodium chloride, sodium nitrate, sugar or zinc sulfate solutions), and Stoll's dilution technique aim to assess egg numbers in faecal samples. These methods are widely used as they are relatively low cost and convenient for cross-sectional and epidemiological studies, but they are known to lack sensitivity and specificity.

Immunological tests, including ELISA and other serological assays, are sometimes used to evaluate population and herd infection rates; they have also been reported to lack specificity: cross-reactions with other species than targeted organisms are common, while detection of antibodies does not provide any information about current infection status. Molecular tools, in particular Polymerase Chain Reaction (PCR) and real-time PCR tests, have been gaining popularity, as they are more specific than other methods and allow to concurrently detect and quantify multiple parasite species. However, these tests require appropriate storage of samples and specific equipment and expertise, making them more costly and less adapted to large-scale field surveys.

Because of the range of methods available, prevalence and intensity of foodborne parasite infections can be overestimated or underreported, which directly impacts the monitoring of the food chain and of control and prevention programs, despite the existence of recommended standardized and validated procedures [61, 69].

5.2.2 Climate change

Climate change directly influences the life cycles of foodborne parasites, as it modifies their ability to survive in the environment, the geographic range of their hosts and increases the risk of transmission. Temperature determines the development of helminth eggs to larvae in the environment: increasing temperatures accelerate egg embryonation, reduce the time needed to reach infective larval stages, and thus shorten the life cycle of foodborne parasites. Higher temperatures also affect the survival time of helminth eggs and larvae in the environment, as it accelerates desiccation; *Ascaris* spp. and

T. solium eggs are highly resistant to this type of stress, as they are protected by thick shells, while *O. viverrini* eggs and intermediate stages require high humidity levels to survive.

Climate change will increase rainfall and humidity levels in tropical and subtropical regions, higher humidity levels will further enhance helminth eggs and larvae survival in the environment and favour the development of aquatic parasitic stages (like those of *O. viverrini*). Increased rainfall will facilitate the spread of eggs, larvae and aquatic parasitic stages via water, but also augment the risk of faecal contamination of water sources (flooding, water runoff, sewer overflow).

Increased temperature, humidity and rainfall will provide new habitats for helminth eggs, larvae and aquatic stages, as well as expand the geographic range of intermediate hosts like snails; resulting into the establishment of foodborne parasites in areas where they are not currently prevalent. Climate change will thus most definitely enhance the levels of transmission of foodborne parasites in SEA, which has been acknowledged as one of the most vulnerable regions to global warming, unless governments reduce dramatically their greenhouse gas emissions, while political agendas of most countries do not always include climate change as a national priority [2, 74, 76].

5.3 One Health Approach from a Veterinary Public Health Perspective

Considering that human anthelmintic treatments are also used in animals and were initially developed for the veterinary sector, MDA programs can impact animal parasitic populations, their evolution and spread through selective pressure, potentially increasing drug resistance and limiting available treatment options [77, 78]. Parasites previously thought to be host-specific have been found to infect different species (such as *Ascaris* and *Trichuris* spp.) highlighting that cross-infection and cross-transmission of zoonotic parasites between animals and humans can occur, re-defining STH and foodborne pathogens as multi-host parasites [77, 78, 79]. With this in mind, recent surveillance activities have tried to identify wildlife animal reservoirs and prevent spill-over events into livestock and human populations and food chains by monitoring pathogens from farm or forest to fork [77, 79].

Adequate control strategies of foodborne parasitic zoonoses thus not only require a sound understanding of life cycles and transmission routes, but also necessitate a One Health approach and the multisectoral involvement of key professionals with animal, environmental and public health, food safety, vector control and sanitation expertise (Fig. 4) [77, 78, 79, 80]. Animal health professionals (veterinarians and veterinary governmental bodies) play a critical role in the active surveillance of these infections by reporting and monitoring animal cases in suspected or affected areas, which are key to organise public health interventions, collaboratively with other expert sectors [81].

The animal health sector can use several complementary methods in order to control and prevent neglected zoonotic parasites under the One Health approach (Fig. 4) including raising public awareness (animal technicians, community, farmers, pet owners, schools), implementing affordable and applicable biosecurity measures (outbreak management plan, disinfection, pest control, quarantine, vaccination), recommending good animal husbandry, management and farming practices (antimicrobial use, diagnostic testing, food safety, pasture management, personal hygiene, preventive treatment), enhancing communication (with field, official, regional and national animal health experts as well as with professionals from other sectors) of case reports, outbreaks and policies [79-81].

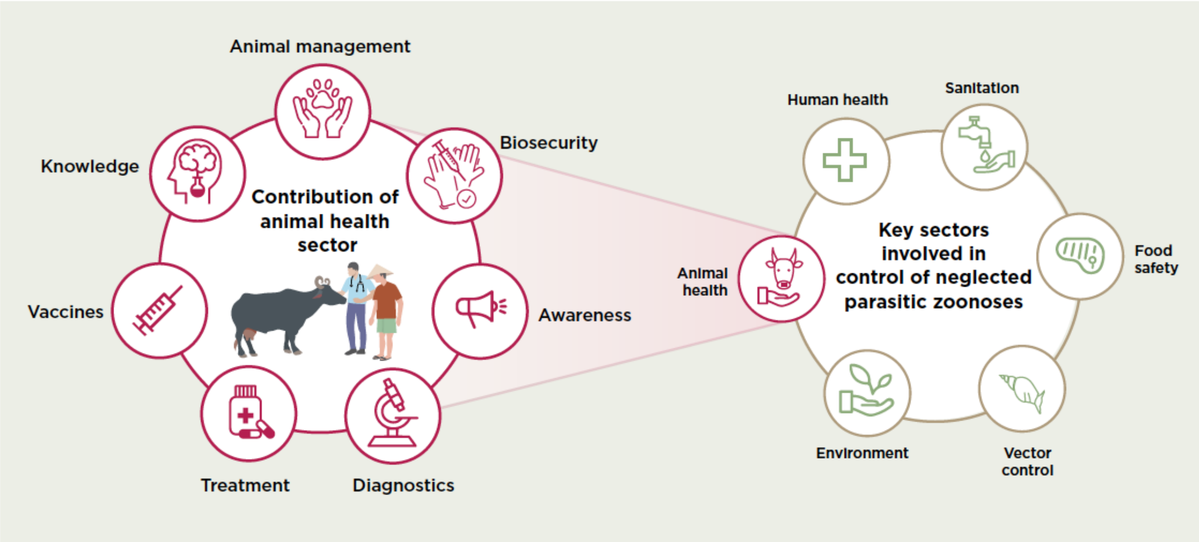

Figure 4. Methods available to the Animal Health sector to control and prevent neglected zoonotic parasites under the One Health approach [81].

Looking specifically at *Taenia solium*, animal health professionals can explain to pig farmers the benefits of rearing pigs in pens in order to prevent them from roaming and reduce the risk of egg ingestion from the environment and human faeces. In addition, veterinarians should promote intramuscular administration of the TSOL19 antigen vaccine (Cysvax®) to further prevent porcine cysticercosis. As some animals may already have developed cysts at the time of vaccination, they should also recommend simultaneous treatment with oxfendazole, the sole efficient single dose drug option, and inform pig farmers that this anthelmintic does not prevent reinfection while drug residues make meat unsafe for consumption 3 weeks post-treatment. Veterinarians should be involved in meat inspections in slaughterhouses, local butcheries and markets, and perform multiple incisions in organs most likely to harbor cysts in order to increase the chances of detecting infections. After detecting cysts, veterinarians should report their findings to the relevant governmental bodies, which will trace the source of infection and implement adequate control measures in the affected area. Animal health professionals should inform consumers in affected and at-risk areas about safe meat consumption i.e. cooking pork at high temperature in order to kill the parasite and avoiding transmission to humans [81].

Recently, it was suggested that to achieve control and elimination of *T. solium*, a multisectoral One Health stepwise approach was needed. Firstly, obtaining accurate porcine cysticercosis prevalence data is needed in order to establish an accurate estimation of the parasite distribution and disease burden in order to recognise the pathogen as a public health threat in a given area. Such awareness is required to involve relevant governmental bodies and stakeholders in order to generate intervention funding. Governmental involvement should then promote a One Health coordination unit, which should be responsible for data management, control measures, and strategic actions across all expert sectors. With respect to the 'international tripartite agreement', this unit will set out control goals and select appropriate intervention measures to facilitate these goals, but also promote the programme to local institutions and communities, provide education and staff training and secure needed resources including drug treatments and vaccines. Simultaneously, continuous evaluation of porcine cysticercosis disease prevalence, implementation of compulsory animal and human case reporting, monitoring of animal movements and development of disease surveillance systems should be implemented [82].

Previously, the 'Lawa model', a multidimensional integrated One Health approach, was successfully applied to the control of *O. viverrini* infections in Thailand, by interrupting the transmission of this parasite at every stage of its life cycle after assessing its prevalence in all host species (humans, snails, fish, small animals). From a human health perspective, targeted praziquantel treatment was administered to infected people while latrines were installed to reduce environmental contamination by faecal wastes containing liver fluke eggs. Intensive health education was provided to initiate cultural changes in traditional food-eating habits at a population level. Waste management, sanitation and hygiene improvements were implemented to further limit transmission to intermediate and reservoir hosts. These actions involved a range of stakeholders including medical professionals, local health and religious authorities, teachers and volunteers. From an intermediate host perspective, *Bithynia* spp. snail biodiversity was assessed, and control was achieved by using a combination of molluscicide treatment and environment modification techniques with the help of ecologists, engineers and malacologists. The prevalence of Cyprinid fish species and parasite burden was established using the expertise of fish biologists and parasitologists while food technicians and restaurant owners were involved in the design of safely cooked fish recipes. With regards to reservoir host species, faecal examination from cats and dogs were performed, followed by animal treatment administered by veterinarians, and development of policies for the control and surveillance of feral and stray animals by governmental bodies. Using this approach, the prevalence of opisthorchiasis was reduced from 60% to 10%, fish infection rates were lowered from 70% to 1% while no parasite was detected from snails in subsequent field surveys in the area targeted by this program; suggesting that a multisectoral collaborative One Health approach empowering animal, environmental and public health, food safety, vector control and sanitation experts, as well as community stakeholders, is essential to the success of foodborne parasitic zoonoses control and prevention strategies [83].

6. CONCLUSION

This paper provided a detailed overview of the current available data for the three main zoonotic parasites of SEA, namely *T. solium*, *O. viverrini* and *Ascaris* spp. Considering clinical signs, DALYs and deaths associated with these organisms, they are still major public health threats in this region. Their respective life cycles involve livestock or aquatic animal species as intermediate hosts, which contaminate directly or indirectly the environment and the food chain. In fact, the risk factors here reviewed all revolved around poor hygiene practices, limited sanitation and traditional food habits, which allow parasitic eggs or larval stages to contaminate food, soil or water consumed by humans.

In order to stop their transmission, administration of anthelmintic drugs need to target animal reservoirs and high-risk human populations; better health, hygiene and sanitation infrastructures and awareness programs should be maintained and extended to remote and tribal areas; while governments should aim to reinforce food safety monitoring via implementing stricter national policies and control systems to limit contamination of the food chain. Existing education and training campaigns should also be promoted and expanded to enhance the chances of success of these key strategies.

To further control and prevent foodborne parasites, future interventions in SEA should be multi-dimensional and focus on the food chain, human populations, animal intermediate hosts and their interactions with the environment, by adopting a One Health approach, while considering the challenges caused by diagnostic testing and climate change.

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ABBREVIATIONS

SEA: Southeast Asia

NTDs: Neglected Tropical Diseases

DALYs: Disability-Adjusted Life Years

OIE: World Organisation for Animal Health

STHs: Soil-Transmitted Helminths

WHO: World health Organization

MDA: Mass Drug Administration

WASH: Global Water, Sanitation and Hygiene

CDC: Centers for Disease Control and Prevention

UNICEF: United Nations Children's Fund (UNICEF)

HACCP: Hazard Analysis and Critical Control Point

PCR: Polymerase Chain Reaction