Consumption of invasive apple snails (*Pomacea* spp.): a public health concern for neuroangiostrongyliasis in Taiwan

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Abstract

Angiostrongylus cantonensis(Rat Lungworm) is a major pathogen of Eosinophilic Meningitis in humans worldwide. *Angiostrongylus cantonensis* generally completes its life-cycle in two hosts: the rats as definitive and the gastropods as intermediate hosts. Among the wide range of intermediate hosts is the critically invasive *Pomacea canaliculata* (Golden apple snails), which have caused numerous outbreaks of neuroangiostrongyliasis worldwide, especially China and Taiwan. While there have been numerous surveys on the prevalence of *Angiostrongylus cantonensis* larvae in *P. canaliculata* in China, there are an inadequate number of studies in Taiwan.This review gives an overview of the current status of *A. cantonensis* prevalence and infection in general, along with focusing on the status and developments regarding neuroangiostrongyliasis in Taiwan. Additionally, we investigate the implications of a well-known invasive vector of *A. cantonensis*, *Pomacea* spp., and its effects on disease transmission to humans. Results show that *P. canaliculata* has been the source of approximately 15.5% infections in Taiwan. Furthermore, due to rapidly growing invasive freshwater snail populations (specially *Pomacea* spp.), indirect transmission through water cannot be neglected. Thus, as a precautionary measure, we suggest environmental DNA based monitoring should be implemented to detect parasites.

Keywords: Foodborne disease; invasive species; *Angiostrongylus cantonensis*; *Pomacea* spp.; neuroangiostrongyliasis; Taiwan

Introduction

Angiostrongylus cantonensis (the rat lungworm), the primary causative agent for several outbreaks of eosinophilic meningitis in humans (Tseng et al., 2011), was first described by Chen (1935) based on the worms collected from the pulmonary arteries of infected rats in Guangzhou, China. The first human infection by this nematode was reported in Taiwan, by Nomura and Lin, 10 years later (Beaver and Rosen, 1964). *Angiostrongylus cantonensis* infection typically presents as eosinophilic meningitis; however, other manifestations in the form of ocular angiostrongyliasis, encephalitis, and radiculomyelitis have also been reported. Primary symptoms include acute headaches, eosinophilia in the blood and cerebrospinal fluid (CSF), and other symptoms ranging from fever, hyperesthesia, paresthesia, nausea, vomiting and in some rare cases even coma and death (Cowie et al., 2022). There is an additional risk of developing chronic sequelae, which is majorly debilitating. Definitive diagnosis of this infection has proved to be challenging; given visual detection of parasite in patient samples is rare; and the amplification of the ITS1 region of the parasite DNA from the patient's CSF has a detection rate of merely 65.3% (Jarvi et al., 2023). Hence, spreading awareness for prevention is just as important as finding a cure.

Angiostrongylus cantonensis nematode is a parasite, its synanthropic definitive and intermediate hosts being rodents (particularly *Rattus* spp.) and a diverse range of gastropods, respectively; however, animals such as shrimp, frogs, and lizards can act as paratenic hosts (Turck et al., 2022) (Figure 1). Consumption of such hosts have given rise to further cases and outbreaks of*Angiostrongylus cantonensis* infection in humans in several countries, including Taiwan (Tseng et al., 2011), Thailand (Eamsobhana, 2014), China (Lv et al., 2009), Brazil (Morassutti et al., 2014), USA (Cowie et al., 2017), Vietnam (McBride et al., 2017), Australia (Barratt et al., 2016), and India (Pandian et al., 2023). A number of cases have occurred in travelers to endemic areas, where consumption of exotic dishes and contaminated foodstuffs result in infection (Federspiel et al., 2020), which highlights the necessity for further awareness about this disease and its causative agent. Indeed, there are concerns as to the extent of infection the rat lungworm can inflict upon humans, where cases have shown presence of the parasite in the lungs of human patients (Prociv et al., 2000). Nevertheless, as the presence of*Angiostrongylus cantonensis* in human feces have not yet been identified, hence the spread of *Angiostrongylus cantonensis*depends largely on its natural hosts; rats and gastropods.

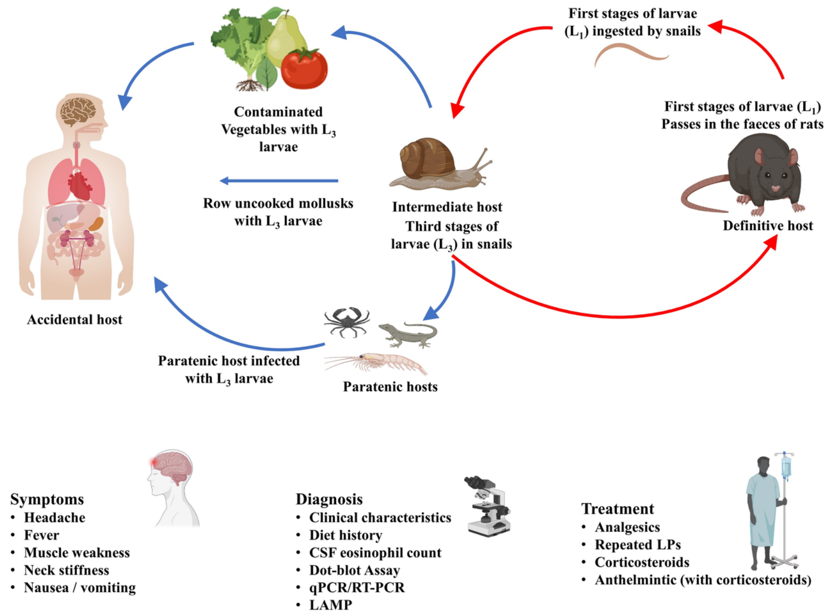

Figure 1: **Figure 1.** *Angiostrongylus cantonensis* disease cycle-*Angiostrongylus cantonensis* as human parasite; simplified life cycle with modes of transmission, symptoms, diagnosis and treatment.

The species in the genus *Pomacea* spp., specially *P. canaliculata* and *P. maculata* , also known as Golden apple snails, are among the world's most critical invasive species, which had been introduced to Taiwan during the 1980's for dietary protein supplementation and commercial utilization (Cheng and Kao, 2006; Hayes et al., 2008). The rapid proliferation due to high reproduction rate, fast growth, and stress tolerance created a widespread sympatric distribution of two cryptic species of *Pomacea* in Taiwan:*Pomacea canaliculata* (Lamarck 1819) and *P. maculata*(Perry, 1810) (Banerjee et al., 2022; Hayes et al., 2008; Qin et al., 2022). These snails cause destruction to local agriculture as well as to the native ecological balance, besides acting as intermediate host to the dangerous parasite: *Angiostrongylus cantonensis* . Furthermore,*Pomacea* spp. are actively consumed in countries such as Taiwan, Thailand, and China, which, when consumed raw or undercooked, contribute to the transmission of *Angiostrongylus cantonensis* to humans and cause neuroangiostrongyliasis outbreaks, especially in China and Taiwan (Lv et al., 2009; Song et al., 2016; Tsai et al., 2013). However, on the basis of our recent understanding of the distribution of *Pomacea*spp. in Taiwan (Banerjee et al., 2022), an in-depth look at the prevalence of this nematode and its implications in Taiwan is required.

2. Methods

In order to evaluate the current status, we performed an advanced PUBMED and Google Scholar search (December 2023), with the combination (and/or) of keywords "*Angiostrongylus cantonensis"* "eosinophilic meningitis" "*Pomacea* " and "Taiwan". We also searched journals, reports from Ministry of Health and Welfare of Taiwan (http://www.mohw.gov.tw/) and newspapers (http://www.taiwannews.com.tw). The results obtained from this investigation were filtered in order to identify the clinical cases reported from Taiwan and obtain a brief understanding of the current scenario of *Angiostrongylus cantonensis* infection. Additionally, a clearer picture was obtained relating to the risk associated with the massively growing invasive*Pomacea* spp. populations in Taiwan.

3. Results and Discussion

3.1 *Angiostrongylus cantonensis*outbreaks in Taiwan

Instances of human infection by *Angiostrongylus cantonensis* have been reported in Taiwan and details of those cases including clinical manifestation, diagnosis and treatments are provided in Table- 1, including whether direct or indirect involvement of gastropod species was reported. The first outbreak in this review occurred during 1968-1969 (Table 1) among whom many patients displayed severe manifestations. Three patients suffered from permanent sequelae from the infection including blindness, and there were four deaths (Yii, 1976). Sequelae were noted in only two other reports; one toddler among the 37 cases presented in Tseng et al. (2011) with weakness in lower limbs, and a 15-year old with pica disorder who presented with urine retention (Hsueh et al., 2013). In addition, a case study of a 66-year old homeless man who presented with neuroangiostrongyliasis in 2022 mentioned transfer of the patient to long term care post-treatment, however the reason for transfer was not clear (Luo et al., 2023).

Children appeared to be more vulnerable to severe manifestations, as well as had greater chances of parasite recovery from the CSF, as seen in the 87 cases of children reviewed by Hwang et al. (1994). They were found to be more likely to get infected, and quicker to manifest symptoms than adults. This implies the large populations of invasive gastropod vectors, including *Achatina fulica* and *Pomacea*spp. pose a high infection risk to children.

Mode of infection appeared to be highly variable among cases (Table 1), where direct consumption of raw *Pomacea* sp. alone or with wine (Tsai et al., 2001; Wang et al., 2011) as well as boiled *Pomacea*sp. (http://www.mohw.gov.tw/), and even raw vegetable juice without any apparent involvement of a host (Tsai et al., 2004) have resulted in cases of neuroangiostrongyliasis. Involvement of paratenic hosts in causing infection, such as the Eastern Golden Frog *Rana plancyi* , which was consumed as Chinese medicine by a 70-year old man, have also been reported (Lai et al., 2007). Interestingly, in a case reported by Wan and Weng (2004), a 10-year old boy displayed intermittent headache, low grade fever, and blurred vision after raising*Pomacea* spp. as pets, suggesting an indirect infection route.

Since the first reported case in 1945, there has been a number of neuroangiostrongyliasis cases in Taiwan, including four outbreaks. While recently within the past three decades, there have been relatively fewer cases reported, there is still a high risk of infection from consuming raw or undercooked snails, or even through close contact with infected gastropod hosts (Tsai et al., 2013). As seen in Table- 1, a considerable number of cases have resulted from infection through handling or consuming gastropods such as *Pomacea canaliculata* and*Achatina fulica* , which may be attributed to the prevalence of these snails in Taiwanese cuisine, or to the large population sizes of these invasive snails. This implies a high prevalence of *A. cantonensis* among the gastropod species in Taiwan (Banerjee et al., unpublished data).

3.2 Disease spread via invasive golden apple snails (*Pomacea* spp.) in Taiwan

The primary mode of spread of *Angiostrongylus cantonensis* are through their hosts, particularly rats and gastropods, some of which are highly invasive, readily transport the parasite beyond its endemic zones. Although a broad range of species can act as intermediate hosts, recent studies have found that some hosts naturally hold more*Angiostrongylus cantonensis* larvae than others (e.g.,*Parmarion martensi*), (Medeiros et al., 2020; Rollins et al., 2021), however prevalence of larva may also depend on size, availability, physiological and immunological capability of the hosts. The frequency of association of *Angiostrongylus cantonensis* with*Pomacea* spp., as well as other vector gastropods such as*Achatina fulica* differs among countries; for example,*Pomacea* spp. has low contribution to parasite prevalence in Thailand (Vitta et al., 2016), and Brazil (Carvalho et al., 2012), however, in contrast *Pomacea* spp., particularly *Pomacea canaliculata* have been shown to have considerable parasite prevalence in Vietnam and Cambodia (Lv et al., 2018), and also be major contributors of the spread of neuroangiostrongyliasis in China (Song et al., 2016) and Taiwan (Tsai et al., 2013).

Another species of *Pomacea* , *P. maculata* has also been involved in spreading the disease, as for example, a study in the USA reported that *P. maculata* shows notable prevalence and exhibits competence in acting as intermediate host to *Angiostrongylus cantonensis* (Teem et al., 2013). The *Pomacea* spp. were introduced in many places as a result of global trade of snails in Asia, and they turned invasive. However, due to the cryptic shell morphology with *P. canaliculata* , *P. maculata* has often been misidentified and thus this association has been less evaluated worldwide. In Taiwan, both species of *Pomacea* are now widely distributed (Banerjee et al., 2022), thus causing a potential threat of increased infection. According to the reviewed articles, approximately 15.5% of cases have been known to be caused by Pomacea spp. and 23% of cases have an unknown cause, which underlines the dire situation growing populations of invasive species have on the spread of neuroangiostrongyliasis (Table 1).

Studies conducted by Howe et al. (2019) and Modrý et al. (2021) held further implications for transmission of the parasite via the aquatic*Pomacea* spp. The infectivity of L_3*Angiostrongylus cantonensis* larvae released into water from drowned gastropod hosts have demonstrated that the parasite has potential for spread without involving a host's body, to some extent. Additionally, the process of intermediesis being successfully demonstrated for *Angiostrongylus cantonensis* larvae suggests greater range and frequency of parasite transmission, particularly in aquatic habitats (Modrý et al., 2021). This greatly impacts control strategies to reduce the prevalence of the parasite in the environment. However, the characteristics of such water-based transmission modes with live (uninjured) aquatic gastropod hosts such as *Pomacea* spp. have not been adequately investigated.

3.3 Clinical manifestations and diagnosis

In most cases for patients suffering from neuroangiostrongyliasis, a presumptive diagnosis has to be made by using several observations such as; symptoms, history of travel and diet, analysis of CSF or serum samples, and serological tests (Ansdell et al., 2021). Nevertheless, in regions where the rat lungworm is not endemic or it has been very recently introduced, there may be a delay in considering neuroangiostrongyliasis as diagnosis by the medical practitioners, which may hinder treatment effectiveness (Cowie et al., 2022; Luo et al., 2023).

Generally, the incubation period of *Angiostrongylus cantonensis*is 1-2 weeks; however it may vary. The symptoms associated with*Angiostrongylus cantonensis* may also vary; nevertheless, some common indicators are headache, neck stiffness, Brudzinski's sign/ Kernig's sign, hyperesthesia/paresthesia, fever, muscle weakness, facial palsy and paralysis of the external muscles (Cowie et al., 2022; Tseng et al., 2011). The symptoms and severity of the disease may be dependent on parasite strain (Lee et al., 2014), parasite load, and the patient's tolerance level towards their immune response (Watthanakulpanich et al., 2021). For example, severe headache was the most common symptom in Thailand, fever and neck stiffness in China, and headache and fever in Taiwan (Khamsai et al., 2020). Whether the variation in symptoms sheds light on the severity of the infection is unclear; the majority of cases resolve spontaneously, though more serious cases may result in death (McAuliffe et al., 2019). Nevertheless, given that none of the symptoms are distinctive enough to be diagnostic, most cases require laboratory testing to obtain a definitive diagnosis.

In Taiwan, a study by Lee et al. (2014) investigated the genetic differences among *Angiostrongylus cantonensis* populations, and discovered the presence of two primary strains showing infectivity in non-permissible hosts such as humans. The more common strain showed low genetic diversity and high infectivity, whereas the new strain isolated from Hualien showed considerable genetic difference from the other strains, and much lower infectivity in their mouse models. This is corroborated by another metagenomic study concluding that there is low genetic diversity in infective invasive *Angiostrongylus cantonensis* strains globally (Červená et al., 2019). Hence, the large variety of symptoms may possibly arise from other factors such as larval development in the human host, and interaction with the individual immune systems.

Definitive diagnosis is possible with visual confirmation of*Angiostrongylus cantonensis* larvae in the blood or cerebrospinal fluid (CSF); however it is rarely successful (Ansdell et al., 2021). Detection of blood eosinophilia, and studying CSF characteristics e.g., high CSF pressure, CSF white blood cell count (especially eosinophils), and CSF proteins are often used as initial indicators (Wang et al., 2011). Radiography such as magnetic resonance imaging (MRI) and computed tomography (CT) scans are also used as supplementary tests, particularly MRI of the brain where lesions, leptomeningeal enhancement, or increased signal intensity in the subcortical white matter may be detected after the first few weeks of infection (Ansdell et al., 2021). MRI of the spine is recommended for patients with myeloradicular symptoms. Furthermore, CT scans of the chest have shown nodular lesions, indicative of migratory larvae or young adult parasites, but is ineffective in most cases. Nevertheless, it is recommended to undergo a chest CT scan only if there are respiratory symptoms (Ansdell et al., 2021).

Serological methods such as dot immunogold filtration assay (DIGFA) developed by Eamsobhana et al. (2021), are already in use in hospitals of endemic regions, such as Thailand. The disadvantage of serological methods is the delay in formation of antibodies; however serological tests are still a common procedure, both as a method of diagnosis, as well as to rule out the presence of other parasites (Carvalho et al., 2022).

Detection of parasite DNA in CSF or serum of patient by polymerase chain reaction (PCR) is currently used for conclusive results (Carvalho et al., 2022). Molecular techniques have a number of benefits over other methods (e.g., visual detection or serological methods) where early detection can be done from parasite fragments without need of antibody formation (Qvarnstrom et al., 2016). There are a number of molecular assays that are currently in use or under development which can be used for high sensitivity or specificity (Carvalho et al., 2022). There is a possibility of a negative PCR result despite strong clinical suspicion if the sample is taken from early infection stages, however it is recommended that the test be repeated in 5-10 days in such a scenario (Ansdell et al., 2021). Recently, a novel method, metagenomic next-generation sequencing (mNGS) used for the presence of multiple parasites simultaneously, has also been used to detect*Angiostrongylus cantonensis* in some case studies (Carvalho et al., 2022). Additionally, the AcanR3990 qPCR assay developed by Sears et al. (2021), shows potential for success as a diagnostic tool for neuroangiostrongyliasis, with greater accuracy and sensitivity than conventional PCR with ITS primers (Jarvi et al., 2023). Genetic characterization of the obtained *A. cantonensis* larvae as done by Dumidae et al. (2023) provides substantial reference data for more robust molecular identification methods.

In Taiwan, the current method of *Angiostrongylus cantonensis*detection is by use of PCR on CSF samples (Luo et al., 2023). In addition, alternative markers for easier detection of*Angiostrongylus cantonensis* infection are being tested, such as IgE antibody levels in *Angiostrongylus cantonensis* infected mouse models (Lee et al., 2023), and microRNA upregulation in meningoencephalitis caused by *Angiostrongylus cantonensis*infection (Chen and Lai, 2023).

3.4 Detection of the parasite from intermediate and paratenic hosts

Surveys of known definitive, intermediate, and paratenic hosts are instrumental in the tracking and quantifying of *Angiostrongylus cantonensis* prevalence in the environment, and also to develop an accurate risk assessment. Currently, surveys have been known to employ visual methods for detection in hosts (Xie et al., 2023), as well as molecular methods (Gamiette et al., 2023). Molecular tools such as PCR-based detection and analysis are accurate and have the additional benefit of being effective with both fresh and frozen snail tissue, and with low parasite numbers (high ct value in qPCR) (Qvarnstrom et al., 2010). The assay developed by Qvarnstrom et al. (2010) demonstrated specificity of detection when tested against *Angiostrongylus costaricensis* and *A. vasorum* , both known mammalian parasites, and was thus a commonly used protocol in many subsequent studies. However, a relatively cheaper and more accessible qPCR assay using SYBR green was more recently developed by Jakkul et al. (2021), which bypasses the need for probes. Apart from PCR, loop-mediated isothermal amplification (LAMP) assays have been developed for providing low-cost and sensitive detection of *Angiostrongylus cantonensis* from invasive *P. canaliculata* hosts, which is an effective strategy for large scale prevalence detection (Chen et al., 2011). However, the specificity of this protocol against other species of*Angiostrongylus* remains to be tested.

Rapid and accurate methods of identifying *Angiostrongylus cantonensis* larvae within mollusk hosts as well as patient samples have gained a substantial amount of interest as the number of outbreaks of eosinophilic meningitis continues to rise (Rollins et al., 2021). Furthermore, newly developed environmental DNA (eDNA) based methods may be applied to detect many infectious diseases from environmental samples (eg: standing water from paddy fields) which could also be applied for*Angiostrongylus cantonensis* detection and quantification (Bass et al., 2023).

3.5 Recent advancements in treatment and control measures

3.5.1 Treatment

There is no official treatment protocol, however, the treatment is generally performed according to the symptoms (Carvalho et al., 2022). Hence, courses of analgesics and regular lumbar punctures to relieve the severe headaches typical of neural angiostrongyliasis cases is a common course of action (Cowie et al., 2022). Corticosteroids, such as prednisolone, are effective in management of inflammation that causes headaches, and further reduce duration of headache persistence. Other anti-inflammatory drugs, such as nonsteroidal anti-inflammatory drug (NSAID) options may have increased risk of gastrointestinal and intracranial bleeding, particularly if used concomitantly with corticosteroids (Ansdell et al., 2021). Anthelmintics as treatment must be administered carefully, because the increased death rate of the parasites in the tissues may trigger an increased immune response, particularly for more severe infections. However, in reality, the use of ivermectin, levamisole, albendazole (which shows highest absorption among benzimadoles) have shown improvement of symptoms in many cases (Ansdell et al., 2021; McAuliffe et al., 2019). Nevertheless, albendazole has displayed decreased efficacy when used after L_4 stage larval development (McAuliffe et al., 2019). In Taiwan, research is currently being conducted in order to protect the brain from the harmful inflammatory effects of albendazole being administered in the later infection stages. In BALB/c mouse models, Chen et al. (2023b) investigated the combined effects of benzaldehyde with albendazole; Lu et al. (2023) explored the efficacy of an active compound, calycosin, extracted from a herb commonly used in Chinese medicine known for its anti-inflammatory effects. Therapeutic use of Tanshinone IIA (TSIIA) to reverse cell damage to mouse astrocytes are being investigated using the excretory-secretory products of A. cantonensis as an effective way to induce host immune responses to the infection (Chen et al., 2023a).

There is scarce information available about management of chronic symptoms that emerge in some cases of neural angiostrongyliasis (McAuliffe et al., 2019). However, there are cases with debilitating sequelae after treatment such as erectile dysfunction, strabismus, intellectual disability, prolonged severe pain, hyperalgesia, and even death (Carvalho et al., 2022; McAuliffe et al., 2019). Treatment varies case-by-case; however the corticosteroids may cause adrenal suppression and albendazole may elevate liver transaminases if used long-term, hence they are unsuitable for chronic care (Ansdell et al., 2021). Thus, more research is required to develop effective management strategies for sequelae.

3.5.2 Control

The broad range of hosts, as well as the invasive nature of many of them, has resulted in the widespread occurrence of *Angiostrongylus cantonensis* (Carvalho et al., 2012; Kim et al., 2014; Morassutti et al., 2014; Thiengo et al., 2022). Nevertheless, some factors limit the spread of the disease; such as rainfall, temperature and close association/interactions between definitive and intermediate hosts (Gamiette et al., 2023; Rollins et al., 2021). Given the nematode is tropical by nature, their spread has been limited to tropical zones with warm temperatures and humidity. The gastropod hosts commonly associated with *Angiostrongylus cantonensis* display a preference for a similar climate (Cowie et al., 2022; Rollins et al., 2021). Therefore, the spread of the nematode can be considered to be severely restricted by the availability of its hosts. The life cycle of*Angiostrongylus cantonensis* involves direct transfer of larvae from rat to the gastropod via rat feces, and vice versa via consumption of the gastropod by rats, instead of indirect transmission via gastropod mucus (Kramer et al., 2018). Nevertheless, despite the general containment of the parasite within its hosts' bodies, parasitic contamination of water from dead/injured infected hosts is quite possible, and must be accounted for (Howe et al., 2019; Modrý et al., 2021).

The intermediate hosts precede the definitive hosts in priority during survey, as the infectious larval stage of the parasite (L_3) develops in the intermediate hosts (Lv et al., 2018). This is particularly important for Taiwan, where snails form part of a regular diet. The invasive nature of *Pomacea* spp. and*Achatina fulica* imply increased chances for accidental consumption, particularly considering their proximity to agricultural fields. In general, human infection is seen to occur via three modes: (i) consumption of intermediate or paratenic hosts; (ii) indirect contact by handling infected gastropods or rat feces; and (iii) usage of contaminated water (Carvalho et al., 2022). Widespread surveys of gastropods, testing for the prevalence of *Angiostrongylus cantonensis,* have taken place in numerous regions/countries where cases of infection have been reported, such as China (Lv et al., 2009), Brazil (Carvalho et al., 2012), Thailand (Vitta et al., 2016), Vietnam (Lv et al., 2018), Hawaii (Kim et al., 2014), French Polynesia (Fontanilla and Wade, 2012), USA (Teem et al., 2013), Spain (Martin-Alonso et al., 2015), and Taiwan, where surveys have investigated the prevalence of the nematode in gastropods, particularly *Pomacea canaliculata* (Yen et al., 1990) (Banerjee et al., unpublished data), *Achatina fulica*(Lee et al., 2014), and rats (Yang and Lu, 2000).

Another major source of infection in Taiwan is the consumption of infected paratenic hosts, such as frogs (Tseng et al., 2011). Other paratenic hosts, eaten raw (e.g. shrimp, crabs, monitor lizards and frogs) in some other countries, are also quite frequent sources of infection (Carvalho et al., 2022; Turck et al., 2022). Therefore, any raw animal products intended for direct consumption should be regulated carefully for presence of parasites. Cooking has been shown to eliminate the infectivity of the *Angiostrongylus cantonensis* larvae, and there should be a general caution around eating raw foods (Hollingsworth et al., 2013).

Regarding the eradication of the nematode, there are particular considerations that need to be made in case of the aquatic snail host*Pomacea* spp. The general mode of control of this invasive snail is via hand-picking of the snails, commercially available pesticides, pesticidal agents made from plant extracts or by-products, and biocontrol using ducks or fish (Yang et al., 2013). However, given the chances of increased parasite spread from injured or dead gastropod hosts in aquatic media (Modrý et al., 2021), special care needs to be taken to remove the dead gastropod bodies from the field and dispose safely. Additionally, with regards to biocontrol, birds and fish have been known to get infected or act as paratenic hosts for the disease, thus aiding in spreading the disease (Burns et al., 2014; Turck et al., 2022).

Genetic characterization and phylogenetic study have been performed on*Angiostrongylus cantonensis* populations in multiple studies to understand the distribution and aid in control measures (Gamiette et al., 2023; Lee et al., 2014; Lv et al., 2020). In Taiwan, Lee et al. (2014) had discovered two major strains present in Taiwan; the more common and infectious P strain, and the less infectious H strain, which had been discovered only in Hualien. Further analyses of the distribution of the parasite and its hosts may aid in developing a model to predict the spread of parasite, and result in targeted eradication strategies (Lv et al., 2020).

4. Conclusion

- Although low in occurrence, eosinophilic meningitis from neural angiostrongyliasis can cause severe outbreaks in the near future with continued negligence. Thus, regular monitoring and awareness are necessary for prevention.
- The use of molecular methods to detect *Angiostrongylus cantonensis* has many benefits over conventional methods; however further development (e.g., PCR primer, modelling of parasite distribution, and rapid detection methods) is needed.
- Implementation of novel detection and quantification approaches using environmental DNA (eDNA)

has an immense potential in surveying*Angiostrongylus cantonensis* in the environment, that will help to avoid direct contact with hosts during laboratory testing.Extraction of eDNA can be done from environmental samples such as water, soil and host feces (may include high concentration of larval DNA) for periodic monitoring. Indeed, there have been studies that have attempted to use eDNA metabarcoding methods to test abundance of parasites in an ecosystem; however, some drawbacks remain, such as lack of reference sequences in the databases.

- Furthermore, the improvement of treatment methods is necessary for the patients who are more severely infected with neuroangiostrongyliasis. Further progress in the investigation into mitigation of harmful side effects of albendazole when administered in later infection stages is required. Progress is similarly required in the treatment of permanent sequelae.
- Lastly, awareness among the public about consumption of meat only after careful processing, and avoidance of raw meat is necessary. Tourists should avoid adventurous eating in the endemic zones. Nevertheless, inadvertent consumption should not be neglected. Proper hygiene should be maintained, avoiding the persistence of rats and other pests in food preparation areas.

CRediT authorship contribution statement

Pritam Banerjee- Conceptualization, Data curation, Formal analysis, Investigation, Visualization, Roles/Writing - original draft, Writing - review & editing; **Nalonda Chatterjee-** Data curation, Formal analysis, Investigation, Visualization, Roles/Writing - original draft, Writing - review & editing; **Jung-Sheng Chen-** Software, Project administration, Resources; **Gobinda Dey-** Formal analysis, Resources, Writing - review & editing; **Raju Kumar Sharma-** Visualization, Resources, Writing - review & editing;**Jyoti Prakash Maity-** Resources, Writing - review & editing;**Chin-Wen Wang-** Data curation, Investigation, Resources;**Chayada Jaidee-** Data curation, Formal analysis, Investigation;**Thanyalak Kammeerak-** Data curation, Formal analysis, Investigation; **Marut Tangwattanachuleeporn-** Project administration, Resources; **Kulwara Poolpol-** Project administration, Resources; **Michael W.Y. Chan-** Project administration, Resources; **Kuan Hsien Lee-** Conceptualization, Funding acquisition, Project administration, Resources;**Chien-Yen Chen-** Conceptualization, Funding acquisition, Project administration, Supervision, Resources, Writing - review & editing.

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Data Availability

No data was used for the research described in the article.

Declarations of interest

None

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Figure Caption

Figure 1. *Angiostrongylus cantonensis* disease cycle-*Angiostrongylus cantonensis* as human parasite; simplified life cycle with modes of transmission, symptoms, diagnosis and treatment.

Table Caption

Table 1. *Angiostrongylus cantonensis* infections in Taiwan with possible sources, symptoms, diagnosis and treatment; data collected from advanced PUBMED and Google Scholar search for published articles and ministry of health and welfare of Taiwan and newspaper reports for additional cases up to December 2023.

Year	Patients infected/died	Symptoms
1968-69	125/0	N/A
1985	9/4	Headache, fever, double vision and muscle pain, neck stiffness, Kemis' sign, asymm
1985	4/0	Fever, headache, vomiting, and tiredness
1991-2009	37/2	Headache, fever, nausea/vomiting, muscle weakness, abdominal pain, dizziness, nec
1998-99	17/0	Headache, neck stiffness, fever, paresthesia, muscle weakness, orbital/retro-orbital p
2001	5/0	Headache, fever, neck stiffness, paresthesia/hyperaesthesia, nausea/vomiting, abdor
2003	1/0	Headache, mild fever, vomiting, diarrhea, blurred vision, acute gastroenteritis, acut
2006	1/0	Headache, bilateral upper abdominal pain, nausea, vomiting, vertigo
2009	3/0	N/A
2009	5/0	Headache, muscle pain, tiredness, neck pain, diarrhea, inability to turn your eyes to
2010	1/0	Diarrhea, dizziness, headache, inability to stand, and altered consciousness
2011	1/0	Processing conscious disturbance for 2 weeks, paucity of speech, decrease engageme
2012	1/0	Body aches and discomfort, abnormal behavior, confusion and trance
2012	8/0	Headache, neck pain, Symptoms of facial paralysis and quadriplegia
2013	1/0	Headache and neck stiffness
2022	1/0	Fever, dizziness, headache, chest tightness

Note: N/A= not applicable

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