1 **The prevalence of *Angiostrongylus cantonensis* in rodent hosts in** 2 **China and several Asian countries: a systematic review and** 3 **meta-analysis**

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14 **Abstract**

15 **Introduction**

16 *Angiostrongylus cantonensis* (*A.cantonensis*) is a zoonotic parasitic nematode, with a
17 worldwide distribution, causing eosinophilic meningitis or meningoencephalitis in
18 human. Human infection with *A.cantonensis* typically occur from intentional or
19 unintentional ingestion of infected intermediate or paratenic hosts, sometimes due to
20 contaminated produce. Although the biology of *A.cantonensis* is relatively well
21 known, little is understood about the transmission level in different zoogeographical
22 regions, especially in Asia. Here, to evaluate the prevalence of *A.cantonensis* in

rodent hosts in China and several Asian countries, we conducted a systematic review registered with PROSPERO (CRD42020161665).

Methods

Records were selected systematically from 7 database (Medline via to Pubmed, Web of science, Scopus, Google Scholar, CNKI, Wangfang, CBM). Forest plots and random-effects model were used to display pooled estimates. The Freeman-Tukey double arcsine transformation of R software was used to conduct meta-analysis and statistical significance was set at 0.05.

Results

A total of 67 studies met the inclusion criteria and were included in the systematic review and meta-analysis. The pooled prevalence estimates of *A.cantonensis* infection in rodents was 0.1003 (95%CI: 0.0765, 0.1268). There was significant heterogeneity in reported outcomes ($p < 0.0001$). And we considered that there was no publication bias in the included studies.

Conclusion

The *A.cantonensis* infection rate among rodent hosts were still high in Asia, particularly in China, especially in *Rattus norvegicus*, and thus comprehensive measures should be taken for rodent hosts control to avoid an angiostrongyliasis outbreak. Due to the wide distribution and movement of rodent hosts, people in all regions of China, even in other Asia area live at risk of an infection. Hence, the development of more reliable diagnostic tests will be key for an effective identification of cases as well as improved patient care. Consequently, further studies

are required to updated strategies for controlling *A.cantonensis* infection among human population.

Author summary

Angiostrongylus cantonensis (*A.cantonensis*) is a zoonotic parasitic nematode, with a worldwide distribution, causing eosinophilic meningitis or meningoencephalitis in human. Human infection with *A.cantonensis* typically occur from intentional or unintentional ingestion of infected intermediate or paratenic hosts, sometimes due to contaminated produce. Information about angiostrongyliasis burden, including its prevalence and incidence and geographic distribution in Asia, which is necessary to guide in planning appropriate control measures. In this study, we performed a systematic review and meta-analysis of published studies in China and several Asian countries on *A.cantonensis*. Our approach allowed evidence-based approximation to the estimations of the burden of *A.cantonensis* infection, for different rodent hosts groups, geographic regions, publication years and so on. At the same time, our review showed the *A.cantonensis* infection rate among rodent hosts were still high in Asia, particularly in China, especially in *Rattus norvegicus*. Finally, much bigger and longer-term studies are required to updated strategies for controlling *A.cantonensis* infection among human population.

Background

Angiostrongylus cantonensis (*A.cantonensis*) is a zoonotic parasitic nematode, with a worldwide distribution, causing eosinophilic meningitis or meningoencephalitis in human. Human infection with *A.cantonensis* typically occur from intentional or

unintentional ingestion of infected intermediate or paratenic hosts, sometimes due to contaminated produce.

Traditionally, with the wider domain of climate and health, the neglected tropical diseases (NTDs), a collection of infectious diseases affected hundreds of millions of individuals living in tropical and subtropical countries. Recently, such dramatic habitat changes are linked to accelerated biodiversity loss, which has been linked to major changes in the epidemiology of human diseases: increased disease risks and the emergence of novel pathogens resulting from increased contacts among wildlife, domesticated animals, and humans[1-3]. In particular, angiostrongyliasis, as a kind of NTDs, was found in the Pacific Islands, Southeast Asia, parts of South and Central America and the Caribbean, even in European countries[4-6]. Recently, although researchers gradually pay more attention to investment towards reducing the burden of NTDs, they still collectively contribute to productivity loss, illness and suffering in many countries[7,8]. Recent estimates of their overall burden suggest NTDs kill over 350,000 people per annum and cause the loss of between 27 and 56 million disability-adjusted life years[9]. To date, more than 2000 cases of eosinophilic meningitis have been recorded in China, even 100 cases in Taiwan and most human cases of angiostrongyliasis (~1300 cases) have been reported in Thailand[5,10], where between 0.3 and 2 people per 100,000 become infected annually[11,12]. These findings indicate that the extensive distribution of *A.cantonensis* in global world is high, human will be at high risk of *A.cantonensis* infection.

In recent decades, more than 20 species of feral rodents have been categorized as

89 pests in tropical and subtropical countries, and these species cause tremendous losses
90 and damages to crops and food stocks[13]. Feral rodents are known to transmit
91 diseases and act as reservoir hosts to many zoonotic parasites that pose health risks to
92 humans, including *A.cantonensis*, hantaviruses, *Leptospira spp.*, *Bartonella spp.*,
93 *Trypanosoma spp.*, and *Babesia spp.*[14-16]. For *A.cantonensis*, at least 17 rodent
94 species may behave as definitive hosts, capable of passing first stage (L1) larvae in
95 their feces. Simultaneously, snails and slugs (intermediate hosts) ingest these
96 larvae, which mature into the third stage (L3) larvae (infective form) that are passed
97 on to the definitive hosts again when the definitive hosts consume infected
98 intermediate hosts. Then, the worms travel to brain, especially in the subarachnoid
99 space, elicits an intense eosinophilic inflammation and causes acute eosinophilic
100 meningitis. Finally, it will become a molluscs-rodents cycle to lead infectious.
101 Humans become the incidental hosts by consuming the infected intermediate or
102 paratenic hosts (or ingestion of snail slime)[17]. Importantly, the development of
103 control methods against zoonotic parasites depends on knowledge of their life cycles
104 and transmission patterns in different zoogeographical regions. Therefore, it is
105 essential to survey the relationship between parasites and rodents in order to identify
106 the sources of zoonotic infections[18].

107 Surprisingly, despite rodents being the dominant vertebrate species in many of these
108 altered tropical systems and the key hosts for numerous zoonotic microparasites
109 (viruses, bacteria, and protists), consistent patterns between habitat fragmentation and
110 environment change with the epidemiology of multiple parasite diseases have yet to

be determined, and studies that address the context of pathogen circulation are lacking. Indeed, simultaneous to the technical and targeted approaches being, recommended by WHO are much wider attempts at sustainable development, most visible through the lens of the sustainable development goals[19]. Meanwhile, there are little diagnostic methods and effective treatment methods. Furthermore, we need do more research to solve this challenge. Here, in this study, we aim to identify the prevalence of *A.cantonensis* in rodent hosts in China and several Asian countries, provided essential recommendations for the researchers and policy makers.

Materials and methods

The protocol for this systematic review was defined in advance and registered with PROSPERO (CRD42020161665). This study was conducted in accordance with the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-analysis) for systematic review and meta-analysis. The PRISMA checklist (Table S1) was used to ensure inclusion of relevant information in the analysis.

Literature search

To evaluate the prevalence of *A.cantonensis* in rodent hosts in China and several Asian countries, we carried out a systematic review of the literature (full-text) published online in the English and Chinese between May 1946 and December 2019. Records were selected systematically from 7 database (Medline via to Pubmed, Web of science, Scopus, Google Scholar, CNKI, Wangfang, CBM). This range of years was important to study the prevalence since the first study was reported. The modified searches were performed by various combinations of the following terms using

Boolean operator “AND” and “OR”: (rat lungworm OR *Angiostrongylus cantonensis* OR *Angiostrongyliasis* OR *Angiostrongylidae*) AND (prevalence OR distribution OR epidemic OR incidence OR frequency OR occurrence OR detection OR identification OR characterization OR investigation OR survey OR rate) AND Asia. The reference lists of selected articles also were screened manually and appropriate articles were included. Full text articles were downloaded or obtained through library resources.

Study selection

All selected articles had to meet the following inclusion criteria: (i) a cross-sectional study or descriptive study; (ii) the study published between May 1946 and December 2019; (iii) the language was limited in Chinese or English; (iv) full-text article; (v) infection cases in Asia, provided geographical location; (vi) reported as animal level prevalence data; (vii) exact total numbers and positive cases numbers; (viii) rodent hosts numbers higher than fifty.

Investigations without these criteria were excluded. Also, if the same study data were published in both English and Chinese sources, the articles with less detailed information would be excluded from this study. When any authors found articles different to judge, the first author was consulted and eventual differences discussed to reach a consensus decision on whether to include or exclude the article.

Quality assessment

The included articles were evaluated using a 10-items quality appraisal checklist (File S1). An item would be scored ‘0’ if it was answered ‘no data available’ or ‘unclear’;

if it was answered ‘yes’, then the item scored ‘1’. Article quality was assessed as follows: low quality = 0–3; moderate quality = 4–7; high quality = 8–10.

Data extraction

For the data extraction, the two independent assessors applied the inclusion criteria selected the articles and extracted the data. Discrepancies were resolved by consensus. The detailed characteristics of each study were extracted using a pre-designed data-collection excel form. Information was collected as followings: first author, year of publication, location, geographical region, sample size, number of positive cases, diagnostic methods, types of rodent hosts, quality score of each study.

Statistical analysis

The statistical software used in the analysis was R software version (3.6.3). Estimated pooled prevalence and 95% confidence intervals (CI) were calculated with the Freeman-Tukey double arcsine transformation. Heterogeneity testing was performed using the I^2 and Cochran’ Q statistic methods. A significant value ($p < 0.05$) in the analysis suggested a real effect difference. The I^2 values of 25%, 50% and 75% were considered as low, moderate and high heterogeneity, respectively. The risk of study bias was assessed using the funnel plots, and the Egger’s regression test. Furthermore, subgroup analysis were done if the heterogeneity were overlapping moderate I^2 . Four potential sources of heterogeneity were examined: country, animal species, publication year, quality score. The Q and I^2 statistics values were calculated for each subgroup to determine the effective factors on the prevalence *A.cantonensis* and heterogeneity about all the included studies.

Results

Study search and included studies

A total of 2103 articles were screened in the initial and 67 were obtained for the final analysis. Fig 1 showed our systematic workflow for identifying, screening and including studies in this study. Hence, 59 articles from China, 1 from Japan, 4 from Thailand, 1 from India and 2 from Philippines. The complete list of included articles with the extracted data can be found in the Fig 2 and Supporting information (File S2). A total of 45196 rodents were dissected and 4954 were identified with *A.cantonensis* infection. The detailed characteristics of each study were provided in Table 1.

Fig 1. Flow-chart of systematic review of *A.cantonensis*

Fig 2. Map of the geographical distribution in Asian countries of the surveys

Table 1. Characterizatics of the eligible studies

Study	Location	Method	Number	Positive rate	quality score
(Zhang et al. 2017)	Fujian	NE	5266(541)	10.30%	7
(Huang et al. 2017)	Guangdong, Shenzhen	NE	238(22)	9.24%	8
(Hu et al. 2017)	Guangdong, Nan'ao island	NE, PCR	110(32)	29.10%	8
(Lin et al. 2016)	Fujian, Zhangzhou	NE	1551(142)	9.20%	9
(Eamsobhana et al. 2016)	24 provinces in Thailand	NE	669(46)	6.90%	7
(Ribas et al. 2016)	Udon Thani province	Staining	98(3)	3.10%	5
(Yang et al. 2015)	Yunnan	ELISA	304(0)	0.00%	6
(Tujan et al. 2016)	Nueva Ecija, Philippines	PCR	209(64)	29%	8
(Zhang et al. 2014)	Yunnan	NE	174 (0)	0.00%	7
(Castillo et al. 2018)	Nueva Ecija, Philippines	NE	600(600)	100%	9
(Liang et al. 2014)	Guangdong, Shenzhen	NE	195(21)	10.80%	6
(Hu et al. 2018)	Guangdong, Nan'ao island	NE, PCR	110(32)	29.10%	8
(Xie et al. 2013)	Guangxi, Beihai	NE	58(1)	1.70%	5
(Huang et al. 2019)	Guangdong, Shenzhen	NE, ELISA	238(22)	9.20%	8

(Yang et al. 2012)	Guangdong, Guangzhou	NA	432(23)	5.30%	8
(Chen et al. 2011)	Guangdong	NE	1391(132)	9.50%	9
(Huang et al. 2011)	Guangdong, Shenzhen	NE	331(50)	15.10%	7
(Hu et al. 2011)	Hainan island	NA	118(13)	11.00%	6
(Vitta et al. 2011)	Phitsanulok province	NE	62(1)	1.60%	7
(Zeng et al. 2011)	Jiangxi	Microscopy	502(12)	2.40%	4
(Zhu et al. 2010)	Fujian, Nanping	NE	291(42)	14.40%	7
(Li et al. 2010)	Fujian	NE	4890(434)	8.90%	6
(Fu et al. 2010)	Guangxi	NE	149(5)	3.40%	5
(Deng et al. 2010)	Guangdong	NE	491(56)	11.40%	7
(Zhang et al. 2009)	Guangdong, Yangchun	NE	192(11)	5.70%	4
(Renapurkar et al. 1982)	Bombay	NA	937(12)	1.30%	6
(Lan et al. 2010)	Zhejiang, Lishui	NE	1937(70)	3.61%	6
(Zhang et al. 2008)	Guangdong, Shenzhen	NE	248(22)	8.90%	7
(Li et al. 2008)	Yunnan	NE	124(4)	3.20%	4
(Ye et al. 2008)	Fujian, Fuzhou	NE	1964(269)	13.70%	6
(Wang et al. 2008)	Fujian, Ximen	NE	957(64)	6.70%	4
(Zeng et al. 2007)	Jiangxi	Microscopy	187(3)	1.60%	3
(Luo et al. 2005)	Fujian, Fuzhou	NE	1487(246)	16.50%	9
(Shen et al. 2004)	Guangdong, Zhaoqing	NE	221(12)	5.40%	8
(Yang et al. 2003)	Fujian	NE	625(52)	8.30%	6
Chen et al. 2003)	Fujian, Changle	Microscopy	112(44)	39.30%	3
Pan et al. 2002)	Zhejiang, Wenzhou	NE	87(17)	19.50%	4
(Yang et al. 2001)	Fujian	NE	579(40)	6.90%	5
(Liang et al. 2000)	Zhejiang, Wenzhou	NE	2069(316)	15.30%	9
(Zhang et al. 1999)	Fujian, Fuzhou	NE	113(18)	19.50%	7
(Tung et al. 2013)	Taiwan, Taichung	NE	51(8)	15.70%	5
(Tokiwa et al. 2013)	Ogasawara Archipelago,				
	Japan	NE	136(46)	33.80%	5
(Pipitgool et al. 1997)	Ubon Ratchathani	NE	272(3)	1.10%	7
(Lv et al. 2009)	China	NE	711(32)	4.50%	6
(Zhang et al. 2008)	Guangdong, Jiangmen	NE	229(10)	4.40%	8
(Deng et al. 2012)	Guangdong	NA	491(56)	11.40%	7
(Barratt et al. 2016)	Guangdong, Guangzhou	NA	432(23)	5.30%	7
(Duan et al. 2008)	Hunan	NE	60(1)	1.70%	6
(Ma et al. 2008)	Guangdong, Shenzhen	NE	248(22)	8.90%	8
(Lin et al. 2007)	Fujian, Lianjiang	NE	178(27)	15.20%	6
(Pan et al. 2011)	Guangdong	NE	5820(496)	8.50%	8
(Lan et al. 2009)	Zhejiang, Lishui	NE	218(12)	5.50%	6

(Feng et al. 2008)	Guangdong, guangzhou	NE	113(4)	3.50%	7
(Yu et al. 2008)	Guangdong, shenzhen	NE	1510(301)	19.90%	9
(Wang et al. 2007)	Fujaing, xiamen	NE	957(64)	6.70%	5
(Lin et al. 2010)	Guangdong, qingyuan	NE	387(37)	9.60%	8
(Tan et al. 2008)	Guangdong, jiangmen	NE	229(10)	4.40%	7
(Li et al. 2008)	Guangxi, wuzhou	NE	193(4)	2.10%	7
(Chen et al. 2009)	Guangdong, maoming	NE	196(21)	10.70%	5
(Tong et al. 2011)	Hainan	NE	124(14)	11.30%	8
(Lin et al. 2011)	Guangdong, jiangmen	NE	113(30)	26.50%	7
(Geng et al. 2011)	Guangdong, shenzhen	ELISA	331(40)	12.10%	10
(Huang et al. 2010)	Guangdong	NE	293(24)	8.20%	7
(Zhang et al. 2009)	Guangdong, maoming	NE	148(15)	10.10%	7
(Lin et al. 2011)	Guangdong, qingyuan	NE	844(96)	11.40%	9
(Qu et al. 2011)	Guangdong, qingyuan	NA	288(27)	9.40%	6
(Zhang et al. 2008)	Guangdong, shenzhen	NA	307(38)	12.40%	4

191 Pooling and heterogeneity analysis

192 The pooled prevalence estimates of *A.cantonensis* infection in rodent hosts with
193 individual studies were shown in a forest plot (Fig 3). A substantial heterogeneity was
194 observed among studies ($\chi^2=4979.77$, $P<0.05$; $I^2=99.0\%$). When calculated using a
195 random-effects model, the overall infection rate was 0.1003 (95%CI: 0.0765,0.1268).

196 The estimates of infection rates for different subgroups and heterogeneities were
197 presented in Table 2 and Fig 4. All pooled infection rates for each subgroup were
198 calculated using a random-effects model because of the observed high heterogeneity
199 among studies within subgroups. Base on study periods, the estimate had been
200 significantly increased since 2008 (≤ 2008 : 0.0834 (95%CI: 0.0595, 0.1107) vs > 2008 :
201 0.111 (95%CI: 0.0758, 0.1518)). In terms of the rodent hosts species, the estimate was
202 highest in *Rattus norvegicus* (0.1441, 95%CI: 0.1100, 0.1818), followed by *Rattus*
203 *flavipectus* (0.0428, 95%CI: 0.0062, 0.0987), *Bandicota indica* (0.0409, 95%CI:

0.0000, 0.1240), *Mus musculus* (0.0101, 95%CI: 0.0041, 0.0187), *Rattus rattus* (0.0093, 95%CI: 0.0004, 0.0299), *Rattus losea* (0.0044, 95%CI: 0.0000, 0.0176), and the lowest was *Suncus Murinus* (0.0006, 95%CI: 0.0000, 0.0086). In terms of Asia region, China (0.0893, 95%CI: 0.0773, 0.1020) was higher than Thailand (0.0299, 95%CI: 0.0053, 0.0700). Finally, in terms of score, the estimate was highest in high score (0.1266, 95%CI: 0.1021, 0.1560), followed by low score (0.0892, 95%CI: 0.0420, 0.1509), the lowest was middle score (0.0728, 95%CI: 0.0583, 0.0888).

Fig. 3 Random-effects model meta-analysis of *A.cantonensis* infection in Asian countries

Fig. 4 Subgroup forest plot of infection *A.cantonensis* in Asian countries

Table.2 Subgroup meta-analysis of *A.cantonensis* in Asian countries

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variable	population	No.of infected rodents	No. of total rodents	Pooled estimate Prevalence (%)	95%CI	Heterogeneity(Q)			Egger'test	
						Q	I ² (%)	P-value	t	P
Asia region										
China	42213(4179)	4179	42213	0.0893	(0.0773,0.1020)	1005.38	95.1	<0.0001	-0.5678	0.5724
Thailand	1101(53)	53	1101	0.0299	(0.0053,0.0700)	19.67	93.9	0.0002	-1.0502	0.4038
Japan	136(46)	46	136							
Philippines	809(664)	664	809							
india	937(12)	12	937							
Score										
≤4 (low)	2469(192)	192	2469	0.0892	(0.0420,0.1509)	139	96.8	<0.0001	1.0588	0.3304
>4 to ≤7 (middle)	24578(2103)	2103	24578	0.0728	(0.0583,0.0888)	674.28	95.4	<0.0001	-0.8451	0.4035
>7 to ≤10 (high)	18149(2659)	2659	18149	0.1266	(0.1021,0.1560)	421.26	96.5	<0.0001	0.4219	0.6781
Host species										
<i>Rattus norvegicus</i>	18479(3048)	3048	18479	0.1441	(0.1100,0.1818)	2320.32	98	<0.0001	-0.4383	0.663
<i>Rattus flavipectus</i>	7840 (918)	918	7840	0.0428	(0.0062,0.0987)	2230.08	98.3	<0.0001	-0.409	0.6846

<i>Suncus</i>	5758 (179)	179	5758	0.0006	(0.0000,0.0086)	164.89	87.2	<0.0001	-0.7805	0.4416
<i>Murinus</i>										
<i>Mus musculus</i>	1137 (22)	22	1137	0.0101	(0.0041,0.0187)	34.88	44.6	0.2469	-2.2943	0.0292
<i>Rattus losea</i>	1697 (69)	69	1697	0.0044	(0.0000,0.0176)	25.5	62.3	0.0841	1.8715	0.0797
<i>Bandicota indica</i>	800 (66)	66	800	0.0409	(0.0000,0.1240)	90.17	93.1	<0.0001	0.3826	0.7109
<i>Rattus rattus</i>	797(19)	19	797	0.0093	(0.0004,0.0299)	35.34	79.3	0.0008	0.8389	0.4179
other species	4269(415)	415	4269							
publication year										
≤2008	14007(1602)	1602	14007	0.0834	(0.0595,0.1107)	665.2	97.1	<0.0001	-1.833	0.0798
>2008	31189(3352)	3352	31189	0.111	(0.0758,0.1518)	4311.74	99.1	<0.0001	0.6216	0.5377
Overall	49156(4954)	4954	49156	0.1003	(0.0765,0.1268)	4979.77	99.0	<0.0001	0.1075	0.9147

Publication bias

Despite the significant heterogeneity, the funnel plot displayed a symmetric spread of studies in terms of relative weight and effect size, thereby we could not directly judge whether there was publication bias in the included studies (Fig. 5). The results of Egger's test showed $P=0.9147$ ($P>0.05$) (data not shown). Therefore, we considered that there was no publication bias in the included studies. Notably, the total number of studies was reasonable, and the individual studies were of variable sample size. Moreover, Duval and Tweedie's trim and fill procedure for the detection of publication bias did not support the possibility of missing studies from the analysis.

Fig. 5 Funnel plot of the arcsine transformed infection rates of *A.cantonensis* in Asian countries

Discussion

In previous study, rodents may play an important role in the transmission of certain zoonotic parasites to humans[18]. For *A.cantonensis*, the estimate was highest in *Rattus norvegicus*, *Rattus flavipectus* and *Bandicota indica*, followed by *Mus musculus*, *Rattus rattus*, *Rattus losea*, and *Suncus Murinus*. The difference of the

infection rates among seven kinds of rats may be relative to the factors: the susceptibility to *A. cantonensis*, rat's habitat, activity range and hunted objects, and so on. For example, the front several rodents : (i) be considered as dominant species in several Asian countries[20,21]; (ii) live close to human dwellings[22]; (iii) they were also known to prey on snails not plants[23]. The outcome is comparable to the previous report[24].

Before 2008, there were outbreaks in Beijing, Wenzhou, Guangzhou and so on in China, particularly, 160 cases infected in Beijing[25]. Then, investigator did more research across China by the national angiostrongyliasis control programme. They found this phenomenon was supported by the environment change, including soil, water and air. The climate changes influence global air and land surface temperatures. Also, soil and water are important to the natural history of many parasite or their vectors. In such environments, a high prevalence of parasite infection (hantavirus, *Yersinia pestis*) is often found in various rodents species[26]. In normal, *Rattus spp.* feces could be in water or soil. The major intermediate hosts (e.g. *Pomacea canaliculata* and *Achatina fulica*)[27] maybe infected by ingesting feces. Typically, soil and water properties' changes will affect the intermediate hosts and definitive hosts living time. Their living stages are an essential component of the *A.cantonensis* infection life cycle. Moreover, with the wide habitat alternation, the hosts may adapted and mitigated quickly to modify emissions and habitats. Finally, all factors mentioned earlier leads cases increased year by year.

Limitations

Though this study provided information for the prevalence of *A.cantonensis* in rodent hosts in Asia, several limitations may merit attention. First, the estimations of infection rates using a random-effect model was unavoidable, then subgroup analysis was employed but could not fully explain the source of heterogeneity. Secondly, our study didn't included all Asian countries because the relevant data were not available or incomplete. Finally, in this study, we only focused on *Rattus norvegicus*, *Rattus flavipectus*, *Bandicota indica*, *Mus musculus*, *Rattus rattus*, *Rattus losea* and *Suncus Murinus*, because they were common and most important rodent hosts. However, other rodents, like *Rattus tiomanicus*, *Rattus exulans* and so on, though difficulty to collect them but should not be neglected. To fully elucidate the prevalence of angiostrongyliasis, further studies should pay attention to the other species rodent hosts.

Conclusion

In conclusion, our systematic review and meta-analysis estimated a national prevalence of *A.cantonensis* in rodent hosts in Asia, particularly in China, which provided a scientific basis for prevention a control of the spread of angiostrongyliasis. The *A.cantonensis* infection rate among rodent hosts were still high in China, especially in *Rattus norvegicus*, and thus comprehensive measures should be taken for rodent hosts control to avoid an angiostrongyliasis outbreak. Due to the wide distribution and movement of rodent hosts, people in all regions of China, even in other Asia area live at a risk of an infection. Moreover, public health officials, epidemiologists, researchers, clinical technicians, medical practitioners,

parasitologists, and veterinarians, as well as the general public, should be aware of such risks, and integrated strategies should be taken to reduce or eliminate such risks[28]. Hence, the development of more reliable diagnostic tests will be key for an effective identification of cases as well as improved patient care. Consequently, further studies are required to updated strategies for controlling *A.cantonensis* infection among human population.

Supporting information

Table S1. PRISMA checklist.

(DOC)

File S1.Quality assessment checklist.

(DOCX)

File S2. References of the selected articles included in the systematic review.

(DOCX)

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Declaration of interests

We declare no competing interests.

Author Contributions

Conceptualization: Huifang Bai, Huiyuan Bai, Fei Bai.

Data curation: Huifang Bai, Huiyuan Bai, Fei Bai.

Formal analysis:Huifang Bai, Huiyuan Bai.

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298 Methodology: Huifang Bai, Huiyuan Bai, Fei Bai.

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304 References

305 1. Luis AD, Hayman DT, O'Shea TJ, Cryan PM, Gilbert AT, Pulliam JR, et al. A

306 comparison of bats and rodents as reservoirs of zoonotic viruses: are bats special?

307 Proc Biol Sci. 2013; 280(1756): 20122753. pmid:23378666

308 2. Civitello DJ, Cohen J, Fatima H, Halstead NT, Liriano J, McMahon TA, et al.

309 Biodiversity inhibits parasites: Broad evidence for the dilution effect. Proc Natl

310 Acad Sci U S A. 2015; 112(28): 8667-8671. pmid:26069208

311 3. Olival KJ, Hosseini PR, Zambrana-Torrel C, Ross N, Bogich TL, Daszak P. Host

312 and viral traits predict zoonotic spillover from mammals. Nature. 2017; 546(7660):

313 646-650. pmid:28636590

314 4. Rosen L, Chappell R, Laqueur GL, Wallace GD, Weinstein PP. Eosinophilic

315 meningoencephalitis caused by a metastrongylid lung-worm of rats. Jama. 1962;

316 179(620-624. pmid:14493905

317 5. Wang QP, Lai DH, Zhu XQ, Chen XG, Lun ZR. Human angiostrongyliasis. Lancet

318 Infect Dis. 2008; 8(10): 621-630. pmid:18922484

- 319 6. Thiengo SC, Simões Rde O, Fernandez MA, Maldonado A, Jr. *Angiostrongylus*
320 *cantonensis* and rat lungworm disease in Brazil. *Hawaii J Med Public Health*. 2013;
321 72(6 Suppl 2): 18-22. pmid:23901376
- 322 7. Molyneux D, Sankara DP. Guinea worm eradication: Progress and challenges-
323 should we beware of the dog? *PLoS Negl Trop Dis*. 2017; 11(4): e0005495.
324 pmid:28426663
- 325 8. Conteh L, Engels T, Molyneux DH. Socioeconomic aspects of neglected tropical
326 diseases. *Lancet*. 2010; 375(9710): 239-247. pmid:20109925
- 327 9. Hotez PJ. Ten global "hotspots" for the neglected tropical diseases. *PLoS Negl*
328 *Trop Dis*. 2014; 8(5): e2496. pmid:24873825
- 329 10. Wang QP, Wu ZD, Wei J, Owen RL, Lun ZR. Human *Angiostrongylus*
330 *cantonensis*: an update. *Eur J Clin Microbiol Infect Dis*. 2012; 31(4): 389-395.
331 pmid:21725905
- 332 11. Suankratay C, Wilde H, Berger S. Thailand: country survey of infectious diseases.
333 *J Travel Med*. 2001; 8(4): 192-203. pmid:11703902
- 334 12. Eamsobhana P, Lim PE, Yong HS. Genetic diversity of the rat lungworm,
335 *Angiostrongylus cantonensis*, the major cause of eosinophilic meningitis. *Hawaii J*
336 *Med Public Health*. 2013; 72(6 Suppl 2): 15-17. pmid:23901375
- 337 13. Claveria FG, Causapin J, de Guzman MA, Toledo MG, Salibay C. Parasite
338 biodiversity in *Rattus* spp caught in wet markets. *Southeast Asian J Trop Med*
339 *Public Health*. 2005; 36 Suppl 4(146-148. pmid:16438200

- 340 14. Tangkanakul W, Smits HL, Jatanasen S, Ashford DA. Leptospirosis: an emerging
341 health problem in Thailand. Southeast Asian J Trop Med Public Health. 2005;
342 36(2): 281-288. pmid:15916031
- 343 15. Truc P, Büscher P, Cuny G, Gonzatti MI, Jannin J, Joshi P, et al. Atypical human
344 infections by animal trypanosomes. PLoS Negl Trop Dis. 2013; 7(9): e2256.
345 pmid:24069464
- 346 16. Watt G, Pachirat O, Baggett HC, Maloney SA, Lulitanond V, Raoult D, et al.
347 Infective endocarditis in northeastern Thailand. Emerg Infect Dis. 2014; 20(3):
348 473-476. pmid:24572588
- 349 17. Sohal RJ, Lui F (2020) Angiostrongylus Cantonensis (Angiostrongyliasis).
350 StatPearls. Treasure Island (FL): StatPearls Publishing
351 Copyright © 2020, StatPearls Publishing LLC.
- 352 18. Tung KC, Hsiao FC, Wang KS, Yang CH, Lai CH. Study of the endoparasitic
353 fauna of commensal rats and shrews caught in traditional wet markets in Taichung
354 City, Taiwan. J Microbiol Immunol Infect. 2013; 46(2): 85-88. pmid:22516746
- 355 19. Griggs D, Stafford-Smith M, Gaffney O, Rockström J, Ohman MC, Shyamsundar
356 P, et al. Policy: Sustainable development goals for people and planet. Nature. 2013;
357 495(7441): 305-307. pmid:23518546
- 358 20. Lv S, Zhang Y, Liu HX, Zhang CW, Steinmann P, Zhou XN, et al.
359 Angiostrongylus cantonensis: morphological and behavioral investigation within
360 the freshwater snail Pomacea canaliculata. Parasitol Res. 2009; 104(6): 1351-1359.
361 pmid:19172296

- 362 21. Salibay C. Distribution of Native and Non-native Rats (*Rattus* sp) Along an
363 elevational gradient in the tropical Rainforest of Southern Luzon, Philippines.
364 *Ecotropica*. 2008; 14(129-136.
- 365 22. Hu QA, Lv S, Guo YH, Liu HX, Zhang Y. Genetic diversity of *Angiostrongylus*
366 *cantonensis* in Nan'ao Island of Guangdong Province. *Chin J Parasitol Parasit Dis*.
367 2017; 35(2): 130-135.
- 368 23. Hu QA, Zhang Y, Guo YH, Lv S, Xia S, Liu HX, et al. Small-scale spatial
369 analysis of intermediate and definitive hosts of *Angiostrongylus cantonensis*. *Infect*
370 *Dis Poverty*. 2018; 7(1): 100. pmid:30318019
- 371 24. Chen D, Zhang Y, Shen H, Wei Y, Huang D, Tan Q, et al. Epidemiological survey
372 of *Angiostrongylus cantonensis* in the west-central region of Guangdong Province,
373 China. *Parasitol Res*. 2011; 109(2): 305-314. pmid:21301874
- 374 25. MacDonald R. Eating raw snails leads to *angiostrongylus* meningitis in Beijing.
375 *The Lancet Infectious Diseases*. 2006; 6(10): 622.
- 376 26. McCauley DJ, Salkeld DJ, Young HS, Makundi R, Dirzo R, Eckerlin RP, et al.
377 Effects of land use on plague (*Yersinia pestis*) activity in rodents in Tanzania. *Am J*
378 *Trop Med Hyg*. 2015; 92(4): 776-783. pmid:25711606
- 379 27. Lv S, Zhang Y, Steinmann P, Zhou XN. Emerging *angiostrongyliasis* in Mainland
380 China. *Emerg Infect Dis*. 2008; 14(1): 161-164. pmid:18258099
- 381 28. Zhang RL, Chen MX, Gao ST, Geng YJ, Huang DN, Liu JP, et al. Enzootic
382 *angiostrongyliasis* in Shenzhen, China. *Emerg Infect Dis*. 2008; 14(12): 1955-1956.
383 pmid:19046534

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