Angiostrongylus cantonensis in the Definitive Rodent Host

Subjects: Parasitology

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Human angiostrongylosis is an emerging zoonosis caused by the larvae of three species of metastrongyloid nematodes of the genus *Angiostrongylus,* with *Angiostrongylus cantonensis* (Chen, 1935) being dominant across the world. Its obligatory heteroxenous life cycle includes rats as definitive hosts, mollusks as intermediate hosts, and amphibians and reptiles as paratenic hosts. In humans, the infection manifests as *Angiostrongylus* eosinophilic meningitis (AEM) or ocular form.

Keywords: human angiostrongyliasis ; Indian subcontinent ; *Angiostrongylus cantonensis*

1. Introduction

Angiostrongylus cantonensis is thought to be largely associated with three invasive species of Rattini: *R. rattus, R. norvegicus,* and *R. exulans*, with local involvement of a few other rodent hosts [1]. The frequency with which infection spreads to other rodent species is largely unknown. An infection of *Sigmodon hispidus* (Say & Ord, 1825), a rodent host in the rather distant family Cricetidae, has been reported in North America [2].

Current knowledge about the distribution of species of the Rattini in the Indian subcontinent is very inconsistent. Most data relate to a few highly adaptable synanthropic species, while most taxa are endemic rodents with a virtually unknown natural history. According to the comprehensive concept of Rattini (as defined by Lecompte et al.) [3], 32 species of 10 genera (*Bandicota*, *Berylmys*, *Chiropodomys*, *Dacnomys*, *Leopoldamys*, *Micromys*, *Nesokia*, *Niviventer*, *Rattus*, *Vandeleuria*) of rats inhabit the Indian subcontinent [4][5][6][7]. The highest rat diversity occurs in the northeast of the subcontinent (e.g., 15 species in West Bengal, **Figure 1**), where areas overlap with several species from Southeast Asia (including the *A. cantonensis*). This is followed by Sri Lanka, the Western Ghats, and the Andaman and Nicobar Islands (8–9 species each); the diversity there is due to a high degree of local endemism [4]. Although many *A. cantonensis* records are known from the Western Ghats and Sri Lanka, the involvement of endemic species in the life cycle of this parasite has never been studied.

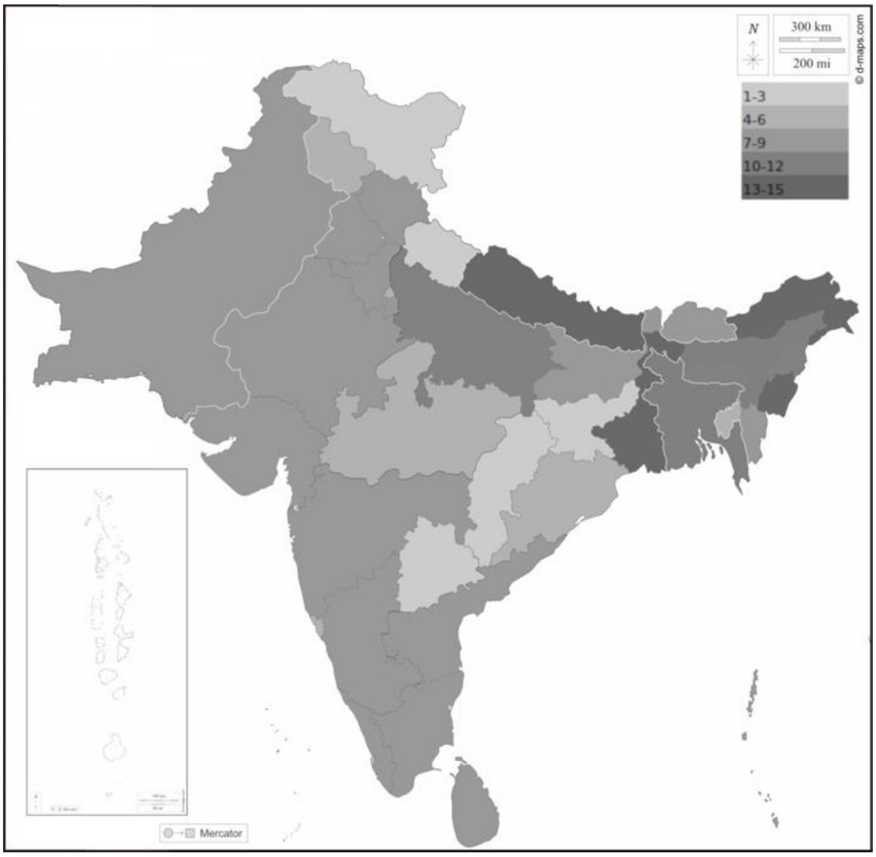

Figure 1. Diversity of rat species (Rattini) on the Indian subcontinent. The grayscale corresponds to the number of rat species described from each country or state, as indicated in the figure. Borders between countries white; coast, borders between Indian states, and outline of the subcontinent black. The map background was downloaded from https://d-maps.com, accessed on 8 November 2022.

Six species of rats inhabiting the Indian subcontinent were confirmed as *A. cantonensis* definitive hosts. Three species (*Bandicota indica*, *R. rattus*, *R. norvegicus*) are reported as hosts in studies directly from the subcontinent (**Table 1**) [8][9][10][11][12][13][14][15], while three others (*Berylmys bowersi, Niviventer fulvescens, Rattus exulans*) are known hosts in different parts of their distribution range [16]. From an ecological perspective, four of these species (*B. indica* (Bechstein, 1800)*, R. rattus, R. norvegicus, R. exulans*) are synanthropic pests that frequently encounter humans [7]. The other species *B. bowersi* (Anderson, 1879), and *N. fulvescens* (Gray, 1847) [16], avoid human settlements. From the proven definitive hosts, *R. rattus* probably represents a major source of *A. cantonensis* infections and should be investigated; *R. exulans* is of minor importance due to its limited range in the subcontinent; *R. norvegicus* is typically found in large urban areas and seems unlikely to spread infection in rural areas [4]. On the other hand, data are lacking for several other synanthropic species. A total of 437 *Bandicota bengalensis* (Gray & Hardwicke, 1833) were examined by Alicata, Renapurkar et al. [10][12], and Limaye et al. [13], with no single *A. cantonensis* record. According to Agrawal (2000), this species displaces *R. norvegicus* in large urban areas, especially in Kolkata. If there is a difference in host competence between *B. bengalensis* and *R. norvegicus*, this could be the theoretical reason why only one human case is known from Kolkata, compared to Mumbai or Delhi. *Rattus tanezumi* (Temminck, 1845) has only recently been separated from *R. rattus* [17][18], so in the case of *R. rattus* records, it cannot be clearly determined which species was examined. From a geographic perspective, *A. cantonensis* in rats was never surveyed in most of the subcontinent. The most conspicuous areas for further study are in the northeast of the subcontinent and associated islands (e.g., Andaman and Nicobar Islands, *R. rattus* was introduced in the Maldives [19]. (**Figure 1**). In general, the gaps in knowledge about the definitive hosts of *A. cantonensis* in the Indian subcontinent are compelling, considering that *A. cantonensis* is easily diagnosed and mainly associated with rats.

Table 1. List of records of *A. cantonensis* from hosts other than humans, as published from the Indian Subcontinent.

Country	State	***Bandicota indica*** **(Rodentia: Muridae)**	***Rattus norvegicus*** **(Rodentia: Muridae)**	***Laevicaulis alte*** **(Gastropoda: Veronicellidae)**	***Macrochlamys indica*** **(Gastropoda: Ariophantidae)**	Reference
India	**Kerala**	**+**				[11]

Country	State	*Bandicota indica* (Rodentia: Muridae)	*Rattus norvegicus* (Rodentia: Muridae)	*Laevicaulis alte* (Gastropoda: Veronicellidae)	*Macrochlamys indica* (Gastropoda: Ariophantidae)	Reference
India	Maharashtra		+	+	+	[13][14]
India	Tamil nandu	+				[9][12]
Sri Lanka	Ceylon	+	+			[9][12]

"+"—Definitive and intermediate hosts were investigated in the Indian subcontinent by region.

2. *Angiostrongylus cantonensis* in Intermediate Hosts

Like most other metastrongylids, the life cycle of *A. cantonensis* invariably involves mollusks as obligate intermediate hosts. However, the nematode can develop in a wide range of gastropods, with extreme variation in prevalence among different populations [9][20][21]. Environmental factors, rat density, and the ecology of specific snail or slug species are likely responsible for the observed differences [1][20][22]. Importantly, *A. cantonensis* exploits both aquatic and terrestrial mollusks, which is one of the reasons for the differences in the local epidemiology of human infections [23][24]. As for gastropods in the Indian subcontinent, Tripathy and Mukhopadhyay (2015) provided a list of the freshwater mollusks of India [25], and Sen et al. summarized the diversity of terrestrial snails in India [26]. Their conclusion that there are 1129 species of terrestrial snails in India alone shows how difficult it is to grasp an enormous diversity of these invertebrates in the Indomalayan region. In addition, there are several smaller studies that list gastropods from different geographic or ecological parts of the subcontinent, such as mangrove mollusks from India [27] or terrestrial snails from Sri Lanka [28]. Many others also attempt to characterize diversity without providing indicative lists [29][30]. Given the low host specificity so far known in *A. cantonensis*, it is easy to imagine that virtually any of these species could play the role of an *A. cantonensis* intermediate host.

In most studies, invasive snail species are considered more important than native fauna due to their ecology and high population density. The spread of *Lissachatina fulica*, one of the most detrimental invasive mollusk species, is commonly referred to as the gateway for the global spread of *A. cantonensis* [31][32]. *Bradybaena similaris* (A. Férussac, 1822), *Cornu aspersum* (O. F. Müller, 1774), *Parmarion martensi* (Simroth, 1893), *Pila* spp., *Pomacea canaliculata* (Lamarck, 1822), and *P. maculata* are associated with *A. cantonensis* in Southeast Asian countries, Australia, and the Caribbean islands [1][33][34][35][36][37][38][39]. Barrat et al. [1] provide a detailed overview of the prevalence and intensity of infection in species where they are known.

L. fulica and *P. canaliculata* are described as invasive in the Indian subcontinent [40][41][42], along with *Laevicaulis alte* (Férussac, 1822), *Physa acuta* (Draparnaud, 1805), and several other species [42][43][44][45][46][47]. *L. fulica* is common in almost all states, locally at densities, with negative impacts on agriculture [48]. *P. canaliculata* has invaded various water bodies in the Indian subcontinent [40], *L. alte* is widely reported in India and is known to have negative impacts on native snail species in the area [49]. Although there is no comprehensive study summarizing mollusk invasion across the subcontinent, the online data (www.iNaturalist.org, accessed on 8 November 2022) show a wide occurrence of the major invasive snails and slugs in India.

To date, few studies have addressed *A. cantonensis* in mollusks in the Indian subcontinent. Limaye et al. reported *A. cantonensis* infection in *Macrochlamys indica* (Godwin-Austen, 1883) [13]; the other few studies in the subcontinent [10][14][50][51] focused on a single species, the invasive slug *L. alte* [50].

3. Snail Consumption

Limited information is available on the scale of edible snail consumption in the Indian subcontinent. Snail consumption is well-known in some parts of India, such as the northeastern region, West Bengal, and other places such as Bihar, Karnataka, Kerala, Madhya Pradesh, and Tamil Nadu [52][53][54][55]. In these regions, snail meat is well known among urbanites and rural tribal communities for its therapeutic and culinary uses [56]. Although the Indian Council of Agricultural Research (ICAR) has supported the introduction of snail farming, there are few snail farms in the country. Instead, snails are collected from the wild rather than being cultivated [57]. Freshwater snails, *Pila globosa* (Swainson, 1822), *Bellamya bengalensis* (Lamarck, 1822), *Viviparus viviparus* (Linnaeus, 1758), and several species of terrestrial snails are among the snails reported to be most consumed in many parts of India [56][58][59][60]. Sharma et al. reported a case of angiostrongylosis in humans after consumption of raw slugs *L. alte* [50] but this species has not been mentioned in studies on the consumption of edible mollusks.

Consumption of raw or insufficiently cooked snails is a common source of human infection in Southeast Asian countries such as China, Taiwan, Thailand, and Hong Kong, including reports of associated clusters of infection [23][61]. However, nematode larvae are sensitive to high temperatures, and even short boiling kills L3 of *A. cantonensis* in infected mollusks [62]. Snails used in reviewed traditional Indian dishes are always prepared by boiling or frying for 5–10 min with various flavors and spices. Technically, following these procedures prevents the presence of live infectious larvae in cooked dishes. Importantly, many recipes recommend soaking the snails in water for 24 h before use. Together with the initial cleaning, this is a critical moment that deserves attention from an epidemiological point of view. The L3 actively escape from snails [63] and can contaminate cooking surfaces and utensils in high numbers [64]. Reportedly, the water from the soaked snails is used as eye drops to treat conjunctivitis as a traditional remedy [65], which may pose an additional risk of angiostrongylosis since larvae may enter the digestive system through the nasolacrimal duct.

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