

The helminth community of a population of *Rattus norvegicus* from an urban Brazilian slum and the threat of zoonotic diseases

Research Article

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Abstract

Urban slums provide suitable conditions for infestation by rats, which harbour and shed a wide diversity of zoonotic pathogens including helminths. We aimed to identify risk factors associated with the probability and intensity of infection of helminths of the digestive tract in an urban slum population of *Rattus norvegicus*. Among 299 rats, eleven species/groups of helminths were identified, of which *Strongyloides* sp., *Nippostrongylus brasiliensis* and the human pathogen, *Angiostrongylus cantonensis* were the most frequent (97, 41 and 39%, respectively). Sex interactions highlighted behavioural differences between males and females, as eg males were more likely to be infected with *N. brasiliensis* where rat signs were present, and males presented more intense infections of *Strongyloides* sp. Moreover, rats in poor body condition had higher intensities of *N. brasiliensis*. We describe a high global richness of parasites in *R. norvegicus*, including five species known to cause disease in humans. Among these, *A. cantonensis* was found in high prevalence and it was ubiquitous in the study area – knowledge which is of public health importance. A variety of environmental, demographic and body condition variables were associated with helminth species infection of rats, suggesting a comparable variety of risk factors for humans.

Introduction

Economic development has led to an increase in urbanization, as people migrate from rural areas in search of job and education opportunities (UN-Habitat, 2016). In many developing countries, this has, in turn, led to an increase in urban poverty, reflected in poor housing, infrastructural support, and social and health services – characteristics that define slum settlements (UN, 2003; Ooi and Phua, 2007). Although there have been initiatives to reduce poverty, such as the strategies undertaken in pursuit of the Millenium Development Goals, the number of slum residents increased by 28% from 1990 to 2014 (from 689 to 881 million) (UN, 2005; UN-Habitat, 2016).

The conditions imposed on urban slum residents, such as lack of adequate sanitation and garbage collection, provide resource-rich environments supporting large populations of rats (Riley *et al.* 2007; Costa *et al.* 2014a). The Norway rat, *Rattus norvegicus* Berkenhout (1769), has been the most successful invasive mammalian species, exhibiting tolerance to a wide range of temperatures, a high reproductive rate and adaptability to rural and urban environmental modification (Long, 2003; Vadell *et al.* 2014; Panti-May *et al.* 2016; Puckett *et al.* 2016). This species has been associated with economic losses due to its eclectic diet, contamination of food stores with feces and urine, and infrastructure damage inflicted through gnawing and burrowing (Childs *et al.* 1998; Singleton *et al.* 2003; Almeida *et al.* 2013). Additionally, *R. norvegicus* is a host for several agents that can infect humans (Webster and Macdonald, 1995; Ko *et al.* 1999; de Faria *et al.* 2008; Costa *et al.* 2014b) including the bacteria *Leptospira* (primarily of the Icterohaemorrhagiae serogroup). These pathogens impart a large burden of disease in human populations, with leptospirosis being by far the most important with an estimated 1 000 000 annual human cases and 60 000 deaths (Costa *et al.* 2015a). Norway rats are also reservoir hosts of several helminths that cause disease in humans (Rafique *et al.* 2009; Hancke *et al.* 2011; Walker *et al.* 2017). For example, the cestode *Hymenolepis nana* is associated with diarrhoea cases, whereas the nematode *Angiostrongylus cantonensis* can cause eosinophilic meningitis (EoM) (Alicata, 1965; Schantz, 1996; Alruzug *et al.* 2016).

Notwithstanding the importance of the descriptive work in characterizing helminth communities of *R. norvegicus* (Gómez Villafañe *et al.* 2008; Kataranovski *et al.* 2010; Hancke *et al.*

2011; Nursyazana *et al.* 2013), it is additionally important to understand the potential risk factors structuring these communities (Mohd Zain *et al.* 2012; Simões *et al.* 2016), enabling understanding of the risk of spillover to humans. This is especially relevant to slum settlement since the peridomestic habits of Norway rats and high human densities lead to frequent human–rodent contact and human exposure to environments contaminated with the infectious stages of parasites shed in rat excreta (McGarry *et al.* 2015; Costa *et al.* 2015b). Despite the effort to characterize the risk factors aforementioned, these studies have been especially concentrated on environmental variables and demographic variables of the rats. However, individuals in natural populations will also vary in their ability to acquire necessary resources, which can affect their body condition, and fitness, by influencing vulnerability and resistance to infection (Beldomenico and Begon, 2010). In this sense, susceptible hosts are more likely to get an infection, further reducing their body condition, in a vicious circle. This, in turn, may influence the concentration of parasites excreted in the environment (e.g., Costa *et al.* 2015b), raising the chance for infection of other hosts, including humans. In this study, therefore, we combined environmental variables, variables of rat demography and body condition, and signs of rat infestation (as proxies for rat density), to identify potential risk factors that are associated with the probability and intensity of infection of helminths of the digestive tract in an urban population of *R. norvegicus*.

Materials and methods

Study area

The study area was located in the periphery neighbourhood of Pau da Lima (13°32'53.47" S; 38°43'51.10" W) in the city of Salvador (BA – Brazil), which has a high human population density, varying from 13 742 to 128 997 inhabitants km⁻² (IBGE, 2010). The area, 0.17 km² in extent, covers residential areas in three valleys characterized by poor sanitation conditions, with open sewers and lack of refuse collection (Reis *et al.* 2008). The valleys are occupied by people commonly living in an informal infrastructure of houses (determined by residents' patterns of settlement and permeable to rats), also lacking access to officially-provided services (Riley *et al.* 2007). The area was selected for study as it presents high annual incidence of *Leptospira* asymptomatic infection (35.4 per 1000 person-years) and of severe leptospirosis cases (19.8 per 100 000 pop.) (Felzemburgh *et al.* 2014; Hagan *et al.* 2016), acquired from spirochetes shed in the contaminated urine of Norway rats, and residents are therefore at high risk of infection by intestinal parasites maintained by the same reservoir host.

The sampling design has been reported previously (Panti-May *et al.* 2016). Briefly, it included a randomized sample, from spatial maps, of 150 trapping points in the three valleys of Pau da Lima. However, in slum environments, such as in Pau da Lima, residents and visitors are subject to violence due to drug traffic and hence there is restricted access, so that the trapping locations were reduced to 101 (valley 1: 25 points, 2: 36 and 3: 40) (see Supplementary Fig. S1). Each of the 101 trapping points included three different trapping sites within an area of 30 m².

Trapping methods and tissue sampling

Rodents were trapped with Tomahawk traps (45 × 16 × 16 cm³) from the three valleys during two sampling campaigns in 2014: a rainy season (March to July 2014) and a dry season (October to December 2014). In each campaign, two trapping sessions were performed at each of the 101 points, at least one month apart. One of three sites randomly chosen within the area of 30 m² was sampled; a sampling scheme previously described

(Panti-May *et al.* 2016). In each site, two traps were set and baited at 9:00 am, and checked within 24 h. The expected number of trap-nights was of 2424 and 1616 (points × sessions × traps × nights) for the rainy and the dry seasons, respectively. The trapping efforts were shortened for the dry season sampling (from 6 to 4 nights) due to a complementary analysis performed with trapping information from previous campaigns, which showed that the mean abundance estimations of rats did not change significantly when reducing sampling effort for four nights. This was consistent with the previous expectation of capturing a higher number of rats during the first days of sampling (Hacker *et al.* 2016).

Previously developed environmental surveys were conducted at each point of capture once in each session (Costa *et al.* 2014a; Santos *et al.* 2017). Variables, subsequently included as covariates in our model development, were used to assess evidence of the presence of rats (presence of feces and trails, and number of burrows) and availability of food and harbourage sites for rats (pet food, human garbage, water sources and vegetation coverage by number of trees), in addition to assessing information relevant to helminth parasite survival and potential for human exposure (completely permeable or partially paved ground, and site proximity of at least 10 m to an open sewer). Daily rainfall data (mm) was obtained from the Environment and Water Resources Institute of the state of Bahia (INEMA) station, and the total rainfall (mm) per month was computed for the campaigns of active trapping and for lags of 30, 60 and 90 days. Traps containing individuals of *R. norvegicus* were placed in plastic bags and transported to a field laboratory, where individual rats were anesthetized and humanely killed. For each individual rat we obtained characteristics informative of population demography (mass, body length, sex and reproductive status) and of body condition (weight and length – for the estimate of an index later described – presence of wounds and internal fat – visceral or subcutaneous) (see Supplementary Table S1) (Glass *et al.* 1988; Costa *et al.* 2014b; Himsworth *et al.* 2014). These were recorded in an online database (REDCap). During the necropsies, performed for purposes of a larger project on leptospirosis (Costa *et al.* 2015b; Panti-May *et al.* 2016), fecal samples were collected directly from the intestines and placed in 10% formalin for subsequent analysis. Trapping and handling of rodents followed protocols previously validated and described (Mills *et al.* 1995; Costa *et al.* 2014b, 2015b) and approved by the Ethical Committee of the Animal Use (CEUA) protocol 003/2012 of the CPqGM – Oswaldo Cruz Foundation (Fiocruz).

Data collection

Formalin-fixed fecal samples were taken to a laboratory of parasitology for identification of helminth eggs by sedimentation (Hoffman *et al.* 1934), taking into account helminth lists previously described for *R. norvegicus* (Martins and Pessôa, 1977; Vicente *et al.* 1997). Subsequently, Gordon and Whitlock's (1939) flotation technique with McMaster chambers was carried out for the quantification of helminth eggs in eggs per gram of feces (EPG). Because fecal samples had already been processed for the previous method, to perform the flotation technique we discarded the supernatant (10% formalin) and mixed the fecal content with a saline solution (Zinc Sulphate, gravity: 1.20), as recommended (Faust *et al.* 1938; Bartlett *et al.* 1978; Schnyder *et al.* 2011). The volume of saline solution added to each fecal sample varied with fecal weights since it was not always possible to collect 2 g of feces from the rats (we adapted the technique by adding a proportional volume of saline solution).

Statistics

The variable mass was used as a surrogate estimate of rat 'age' (Table 1) as used by other studies to allow for direct comparisons

Table 1. Demographic characterization of *R. norvegicus* populations in the two campaigns of capture

	Rainy season		Dry season		<i>p</i>
	Total <i>n</i> of rats	<i>n</i> (%) or Median (IQR)	Total <i>n</i> of rats	<i>n</i> (%) or Median (IQR)	
<i>n</i> of trapped rats	179		120		
Age categories	179		120		
Young (<200 g)		40 (22.4)		25 (20.8)	0.87
Subadult (200–399 g)		113 (63.1)		72 (60.0)	0.67
Adult (≥400 g)		26 (14.5)		23 (19.2)	0.37
Scaled mass index (Smi) ^a	179	262.3 (236.6–289.0)	120	272.9 (237.6–304.8)	0.14
Sex	179		120		
Male		87 (48.6)		65 (54.2)	0.41
Female		92 (51.4)		55 (45.8)	0.41
Female	92		55		
Placental scars		44 (47.8)		32 (58.2)	0.30
Pregnant		33 (35.9)		18 (32.7)	0.84
Lactating		23 (25.0)		20 (36.4)	0.20
Male	87		65		
Scrotal testes		77 (88.5)		57 (87.7)	1.00
Coiled seminal vesicles		72 (82.8)		51 (78.5)	0.65

IQR, Interquartile range.

^aPeig and Green (2009).

(Glass *et al.* 1988; Costa *et al.* 2014a). However, we also estimated age in days [age(d)] using a statistical model derived from published age–weight growth curve for wild rats (Calhoun, 1962), as described by Panti-May *et al.* (2016) (see Supplementary Fig. S2). We also improved the use of a weight/length ratio index of overall body condition variable, by using a scaled mass index (Smi), which accounts for the effect of age (Peig and Green, 2009). Then, to assess whether the demographic features of the populations sampled in the two seasons were similar, we compared age categories, sex and reproductive status through two-way contingency tables using chi-squared (χ^2) test, and Smi using Wilcoxon rank sum test (since the assumption of normality was not met) (Table 1) (Crawley, 2007). Variables of reproductive status (e.g., presence of placental scars in females or presence of coiled seminal vesicle in males) were used to create a single three-level categorical variable of maturity for males and females – classified as immature, young-mature (first pregnancy; only females) or mature – to be assessed as a risk factor later (for details see Supplementary Table S1).

Helminth richness (the number of species present) was estimated for each individual rat and means were compared between sex and maturity, using Wilcoxon rank sum test and permutation ANOVA (Fisher LSD post-test), respectively, as richness distributions between sexes or maturity categories did not follow the normal distribution. Whether helminth richness varied with rats age (d) was also assessed by a generalized linear model (GLM) with Poisson family errors. The prevalence of each helminth species or group (see below) was estimated (% positive of feces sampled) and compared between sampling campaigns through two-way contingency tables using χ^2 test. The laboratory technique used to estimate eggs in feces produces an estimate of EPG, rounded to the nearest 50, hence estimated zeros correspond to EPG between zero and 25. Samples in which a helminth egg infection was identified during sedimentation (presence/absence method), but found to be absent during McMaster counting are ‘false negatives’. By this definition, approximately 25% of the rats found

positive to one helminth species were false negatives. For these, we replaced the zero by an imputed value as follows. Cumulative plots of the recorded EPG showed a variety of shapes. We assumed that the lower tail of the cumulative distribution for each species followed a power law, i.e. a linear relationship on a log-log scale. We fitted this relationship to each species ignoring the false negatives, then shifted the false negatives to the corresponding *x*-value on the fitted line, and back-transformed this value to the original scale to give an imputed value (see Supplementary Fig. S3).

To investigate the risk factors associated with the probability (dependent binary variable) and intensity (dependent continuous variable, including only positive individuals) of infection of each helminth species, GLMs with binomial or Gamma errors, respectively, were applied (Crawley, 2007). Because the EPG values are proxies for the intensity of helminth infestation in *R. norvegicus*, the EPG values were log₂ transformed for ease of interpretation. Additionally, we included the time interval (in months) between fecal sampling and laboratory quantification analysis – Interval-sampling-analysis – as a covariate in the intensity models to control for any effect of formalin fixation in the egg quantification. Initially, univariate analyses were applied and only variables with values of *P* < 0.1 were included in subsequent models, which were developed in steps. First, a model was built with statistically significant environmental variables, collected during the application of the environmental surveys as previously described. Then, model simplifications were conducted using a threshold of 2 Akaike Information Criterion, corrected for small samples [corrected Akaike’s information criterion (AICc)] according to Hurvich and Tsai (1989), to generate a minimal adequate model of environmental predictors. Next, the rat demographic variables [sex, maturity and age(d)] were added and the model simplifications were re-run. Finally, to the minimal adequate model containing both environmental and rat demographic predictors, variables of rat body condition (Smi, the presence of wounds and internal fat) were added and model simplifications

Table 2. Prevalence of helminth species of the digestive tract identified, by eggs or larvae, in an urban population of *R. norvegicus*

Species	Total (n = 299)	Rainy season (n = 179)	Dry season (n = 120)
	% (n)	% (n)	% (n)
<i>Strongyloides</i> sp. ^a	96.6 (289)	97.8 (175)	95.0 (114)
<i>Nippostrongylus brasiliensis</i> ^b	40.8 (122)	30.2 (54)	56.7 (68)
<i>Angiostrongylus cantonensis</i>	39.1 (117)	43.0 (77)	33.3 (40)
<i>Hymenolepis diminuta</i>	13.4 (40)	13.4 (24)	13.3 (16)
Trichuridae ^c	9.0 (27)	7.3 (13)	11.7 (14)
<i>Gongylonema neoplasticum</i>	6.4 (19)	5.6 (10)	7.5 (9)
<i>Aspicularis tetraptera</i>	0.3 (1)	0.6 (1)	0.0 (0)
<i>Hymenolepis nana</i>	0.3 (1)	0.0 (0)	0.8 (1)
<i>Syphacia muris</i>	0.3 (1)	0.6 (1)	0.0 (0)
<i>Toxocara</i> sp.	0.7 (2)	0.6 (1)	0.8 (1)
<i>Ascaris</i> sp.	1.7 (5)	0.0 (0)	4.2 (5)

Species potentially pathogenic to humans are shown in bold.

^a*S. ratti* or *S. venezuelensis*.

^bPrevalence was significantly higher in the dry season ($P < 0.0001$).

^c*Capillaria gastrica* or *Trichuris muris*.

again re-conducted. The most parsimonious model was chosen with a $\Delta AICc < 2$ compared with the final minimum model (indistinguishable explanatory power). We present the odds ratio (OR) and rates (Rate) of the significant variables in the binomial and gamma models, respectively. For all models, observations with missing values for any of the variables under evaluation were excluded. All the analyses were performed in R (R Development Core Team, 2011), considering a significance level of $P < 0.05$.

Results

Samples from 299 individuals of *R. norvegicus* were obtained: 179 in the rainy season, and 120 in the dry season, after an effort of 2318 and 1494 trap-nights, respectively. The demographic features of rats did not differ between campaigns of capture (Table 1).

Eleven species/groups of helminths were identified in the feces of *R. norvegicus* (Table 2). Richness ranged from zero to five helminth species per individual rat, with a median of two

(interquartile range of 1–2 species) ($n = 299$ rats). Mean richness did not differ between sex or age (d), however mature rats presented with higher richness than immature and young mature rats (5000 iterations; $P < 0.0001$) (Fig. 1). Overall, the most frequent species were *Strongyloides* sp., *A. cantonensis* and *Nippostrongylus brasiliensis*. For *N. brasiliensis*, the prevalence in the dry season was significantly higher than in the rainy season ($\chi^2 = 19.802$, $df = 1$, $P < 0.0001$). The five potential pathogenic species for humans are shown in bold in Table 2. Of these, *A. cantonensis*, which in feces occurs in the larval stage (L1), was among the most prevalent species and *Hymenolepis diminuta* also moderately common. Eggs of *Toxocara* sp. and *Ascaris* sp. were also observed in feces samples, but not included in any analysis as rats do not serve as natural reservoirs.

Aspicularis sp. infection was likely to have been incidental (Falcón-Ordaz et al. 2010) and, together with *Syphacia muris* was excluded from the statistical models later performed due to the low prevalence. Positive results for *H. nana* were pooled with those of *H. diminuta*, because of phylogenetic proximity and mode of transmission; this group will be referred to, hereafter, as *Hymenolepis* spp. The summaries of model selections for the probabilities and intensities of infection of each helminth species or families of helminth species are provided in Table 3. Details of each final model are available in Supplementary Table S2.

Variables of the environmental features and the demography and condition of the rats were significantly associated with the probabilities and intensities of infection of the helminth species, except for *Gongylonema neoplasticum*. Valleys 2 and 3 within the study area were significantly associated with higher probabilities of infection by *A. cantonensis* [Valley 3: OR, 3.67 (95% CI, 1.44–9.91)] and *Hymenolepis* spp. [Valley 2: 4.57 (1.80–14.07)] relative to valley 1 (Fig. 2A and B). On the other hand, compared with valley 1, valley 3 was significantly associated with lower probabilities of infection by Trichuridae [Valley 3: OR, 0.18 (95% CI, 0.05–0.57)] (Fig. 2C). The dry season was significantly associated with higher intensities of *Strongyloides* sp. [Rainy season: Rate, 0.24 (95% CI, 0.14–0.41)] (Fig. 3A).

For infections of both *Strongyloides* sp. and *N. brasiliensis* (females only) age(d) was only significant if combined with age²(d), indicating curvilinear associations. For *Strongyloides* sp., the fact that age(d) was positive and age²(d) negative indicates an increased probability of being infected that levelled off or even declined in older individuals (see Supplementary Table S2). For *N. brasiliensis*, on the other hand, age(d) in females, when considered alone, was positive and the inclusion of age²(d) also represented a positive association, indicating an increased probability of being infected that accelerated with age (see Supplementary Table S2). Maturity, a similar variable to age²(d), was also significantly associated with the infection by *A. cantonensis* [Mature: OR, 5.20 (95% CI, 2.65–10.89)], and therefore, after reaching maturity all individual rats shared a

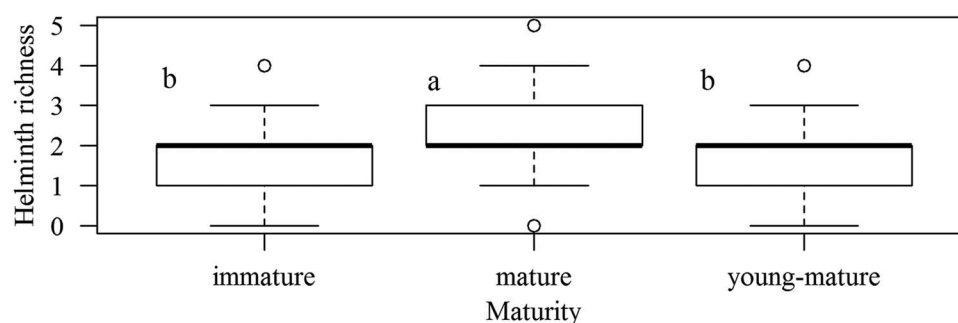


Fig. 1. Boxplots of richness by the maturity of rats ($n = 299$). Different letters mean statistical significance.

Table 3. Summary of model performances in explaining the probability of infection (glm, family = binomial) and intensity [glm, family = Gamma(link = 'identity')] of each helminth species

Parasite	Models for infection				Models for intensity of infection			
	Models	AICc	Δ AICc	wi	Models	AICc	Δ AICc	wi
<i>Strongyloides</i> sp.	i. y ~ Burrows + Sewer + Sex + Age(d) + Smi + Age ² (d) + Sex:Sewer	80.99	0.00	0.54	i. log2(y) ~ Season + Cumulative rain + Ground + Burrows + Sex + Age(d) + Sex:Ground + Sex:Age(d)	963.62	0.00	0.57
	ii. y ~ Burrows + Sewer + Sex + Age(d) + Age ² (d) + Sex:Sewer	82.27	1.28	0.28	ii. log2(y) ~ Season + Cumulative rain + Ground + Sex + Age(d) + Sex:Ground + Sex:Age(d)	964.56	0.94	0.36
	iii. y ~ Burrows + Sewer + Sex + Age(d) + Smi + Sex:Sewer	83.25	2.27	0.17	iii. log2(y) ~ Season + Cumulative rain + Ground + Burrows + Sex + Sex:Ground	967.88	4.26	0.07
	iv. y ~ 1	89.63	8.64	0.01	iv. log2(y) ~ 1	1021.37	57.75	0.00
<i>Nippostrongylus brasiliensis</i>	i. y ~ Season + Trails + Sex + Age(d) + Age ² (d) + Sex:Trails + Sex:Age(d)	368.59	0.00	0.79	i. log2(y) ~ Season + Fat presence + Interval-sampling-analysis	412.92	0.00	0.51
	ii. y ~ Season + Trails + Sex + Age(d) + Sex:Trails + Sex:Age(d)	371.24	2.65	0.21	ii. log2(y) ~ Fat presence + Interval-sampling-analysis	413.42	0.50	0.40
	iii. y ~ Season + Trails + Sex + Sex:Trails	378.95	10.37	0.00	iii. log2(y) ~ Season + Interval-sampling-analysis	416.44	3.52	0.09
	iv. y ~ 1	403.50	34.91	0.00	iv. log2(y) ~ 1	434.99	22.08	0.00
<i>Angiostrongylus cantonensis</i>	i. y ~ Valley + Sex + Maturity + Smi + Sex:Valley	361.09	0	0.69	i. log2(y) ~ Cumulative rain + Tree + Burrows + Sex + Sex:Cumulative rain	497.13	0.00	0.36
	ii. y ~ Valley + Sex + Maturity + Sex:Valley	362.72	1.628	0.31	ii. log2(y) ~ Cumulative rain + Tree + Burrows + Sex + Smi + Sex:Cumulative rain	497.20	0.07	0.35
	iii. y ~ Valley + Sex + Sex:Valley	383.85	22.76	0	iii. log2(y) ~ Cumulative rain + Tree (n) + Sex + Sex:Cumulative rain	497.65	0.52	0.28
	iv. y ~ 1	392.67	31.58	0	iv. log2(y) ~ 1	502.96	5.84	0.02
<i>Hymenolepis</i> spp.	i. y ~ Valley	226.20	0.00	0.99				
	ii. y ~ 1	240.74	14.54	0.00				
Trichuridae	i. y ~ Valley + Sex + Maturity + Sex:Maturity	172.19	0.00	0.55				
	ii. y ~ Valley	172.73	0.54	0.42				
<i>Gongylonema neoplasticum</i>	iii. y ~ 1	178.32	6.13	0.03				
	i. y ~ 1	143.51	0.00	0.62				
	ii. y ~ Smi + Sex + Sex:Smi	144.46	0.95	0.38				

AICc, corrected Akaike's information criterion; Δ AICc, difference between AICc score and lowest AICc score; wi, Akaike's model weight. The most parsimonious models are shown in bold.

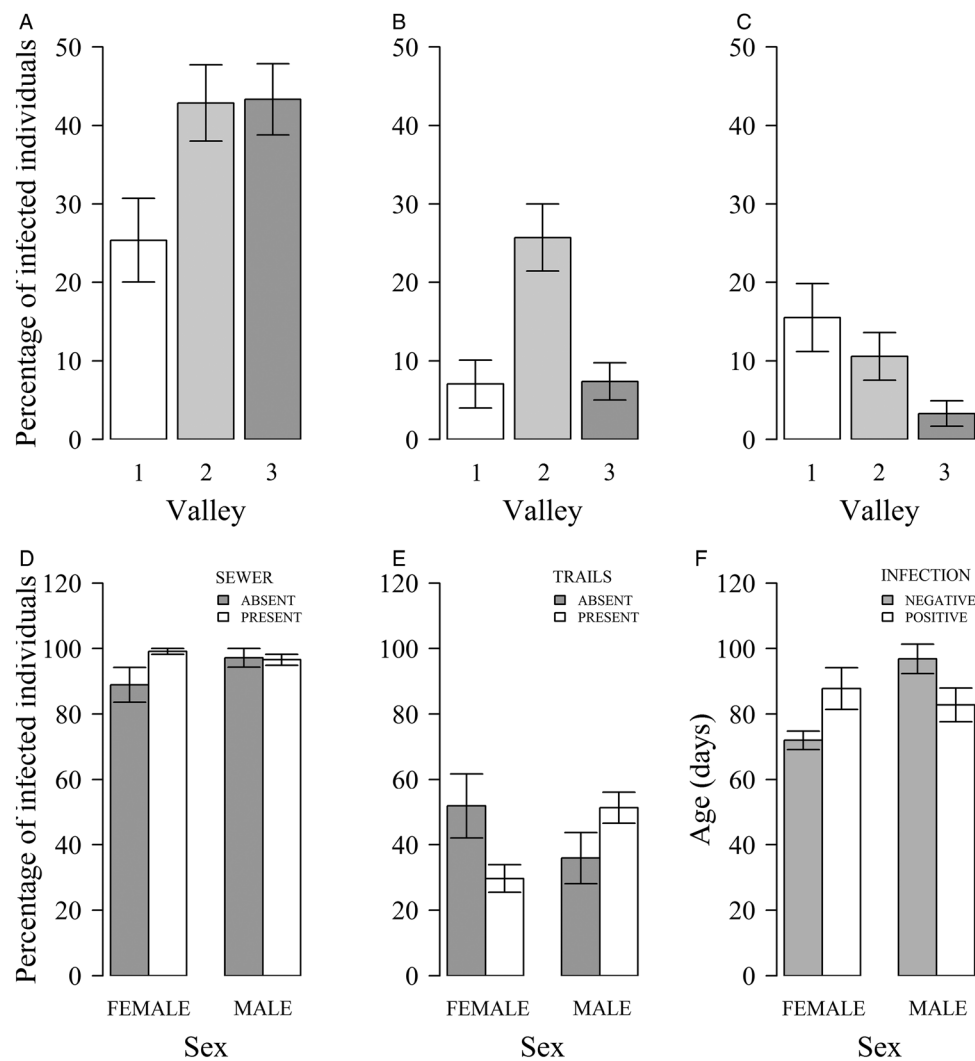


Fig. 2. Mean percentages of infected rats (A–E). Infections by *A. cantonensis* (A), *Hymenolepis* spp. (B) and Trichuridae (C) per valley; by *Strongyloides* sp. (D) per sex and presence of sewer; by *N. brasiliensis* (E) per sex and presence of trails. F – Mean ages (days) of *N. brasiliensis* infected and not infected individuals by sex. Whiskers represent standard errors.

similar probability of being infected by this lungworm. Associations with sex alone only bordered significance. Nonetheless, with the probability of infection by *Strongyloides* sp. and *N. brasiliensis*, interactions terms with other variables (females used as reference in the analyses) indicated, first, that it was more likely to find *Strongyloides* sp. in females if there was an open sewer within 10 m of the trapping site [Male:Sewer: OR, 0.01 (95% CI, 0.00–0.41)] (Fig. 2D). Also, it was more likely to find male rats infected with *N. brasiliensis* if rat trails were present [Male: Trails: 5.02 (1.49–17.25)] or if males were younger [Male:Age (d): 0.97 (0.96–0.99)] (Fig. 2E and F). Once infected, male rats were significantly associated with high intensities of *Strongyloides* sp. [Rate, 4.324 (1.640–11.343)] compared with females, especially if the ground was permeable [2.501 (1.155–5.414)] (Fig. 3B and C). Among the variables used as a proxy for rat body condition, the only significant association was the presence of internal fat being significantly associated with lower intensities of *N. brasiliensis* [Rate, 0.39 (95% CI, 0.15–0.85)] (Fig. 3D).

Discussion

A high global richness of enzootic parasites was identified in urban populations of *R. norvegicus*, including five zoonotic species. Helminth species were differently associated with a variety

of risk factors, including environmental features, and demographic and body condition variables of the rat population, together with sex interactions. The potential zoonotic transmission of some of these parasites to humans is significant in the environments studied, illustrated by the high prevalence, and ubiquity, of *A. cantonensis* (almost 40%) in the population of urban rats of the study area.

The fact that rats have been found infected by *A. cantonensis* indicates that the lungworm is able to complete its life cycle in the area. This may be due to the expansion of intermediate hosts distributions in Brazil (Thiengo *et al.* 2007; Carvalho *et al.* 2012; Moreira *et al.* 2013). Humans are accidental hosts of *A. cantonensis*, becoming infected after ingesting contaminated raw or undercooked intermediate hosts (snails or slugs), vegetables or paratenic hosts, such as crustaceans and other molluscs (Wang *et al.* 2008). The infective third stage larvae, then, migrate to the central nervous system, where they trigger a strong inflammatory response caused by the increased production of eosinophils, leading to EoM (>10% of eosinophils in the cerebrospinal fluid), alternatively they may move to the eye chamber leading to ocular angiostrongyliasis (Lo Re and Gluckman, 2003; Wang *et al.* 2012). This has been considered an emerging disease in Brazil – the first case was reported in 2006 (Garcia *et al.* 2008) – and it is probably under-recognized due to lack of proper diagnostics and the scarcity of information on the distribution of

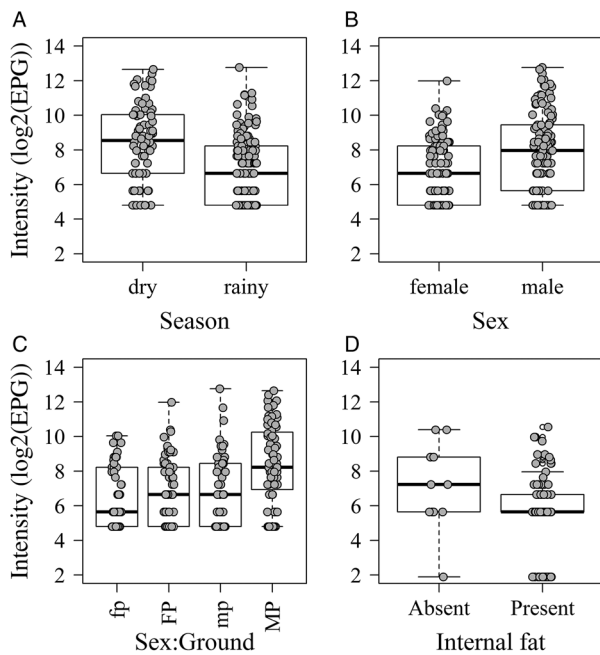


Fig. 3. Boxplots of helminths' intensities ($\log_2(\text{EPG})$). *Strongyloides* sp. by season (A); *Strongyloides* sp. by sex (B) and by sex and ground (C); *N. brasiliensis* by internal fat (D). In 'C', fp, female:partially-permeable-ground; FP, female:permeable-ground; mp, male:partially-permeable-ground; MP, male:permeable-ground.

A. cantonensis in the country (Morassutti *et al.* 2014), and of its intermediate host species, which can vary at local scales. Apart from *A. cantonensis*, a moderate prevalence of *H. diminuta* and low prevalence of *H. nana* were identified in the rat population. While the first is considered to rarely infect humans with asymptomatic or mild symptoms (Tena *et al.* 1998; Kunwar *et al.* 2005; Patamia *et al.* 2010; Tiwari *et al.* 2014), the second can cause diarrhoea, especially in children (Mirdha and Samantray, 2002).

Of the 299 rat feces examined, all except for five were infected by at least one helminth species. Higher richness was observed among mature rats, which are likely to be more susceptible to infection due to reproductive expenditure (Zuk, 1990). The overall helminth richness found in our study, with a community mostly formed by nematodes, is consistent with helminth richness and community characteristics in *R. norvegicus* worldwide (richness range of four to eleven species) (Araújo, 1967; Waugh *et al.* 2006; Gómez Villafaña *et al.* 2008; Rafique *et al.* 2009; Kataranovski *et al.* 2010; Hancke *et al.* 2011; Mohd Zain *et al.* 2012). However, the distribution of parasites within an area can vary at small scales, since it depends on local environmental conditions, host densities and, in some cases, on the presence of intermediate hosts. In this study, we found that *A. cantonensis*, *Hymenolepis* spp. and Trichuridae infections were significantly associated with different geographic valleys, and this might be due to differences in the distribution of intermediate hosts within these valleys, which require further investigation.

Nippostrongylus brasiliensis was the only helminth species that presented with differing prevalence between campaigns of capture, being higher in the dry season. Moreover, the other high prevalent soil-transmitted helminth found in this study, *Strongyloides* sp., interestingly, presented with higher intensities in the dry season of capture compared with the rainy season. This finding is contrary to what might be expected, given *Strongyloides* species' dependency on moist environments for larval viability (Gillespie and Chapman, 2006). Because this was a cross-sectional study, a potential explanation may be that in the rainy season, where there are more humid spots for infection, more rats were caught with recent acquired *Strongyloides* infections, which might have dragged down the intensity estimates in that season; whereas in

the dry season, rats might have been caught mostly carrying old infections, which were therefore more intense.

Sex interactions associated with differing probabilities of infection or intensities of helminths in the rat population highlight behavioural differences in space use between males and females (Wolff, 2003). The fact that more females were found to be infected with *Strongyloides* sp. where an open sewer was close may indicate that they spend more time in burrows situated close to sewers which offer more access to humid environments. Males, in turn, have a larger home range than females, which might increase their rate of contact with contaminated environments. Moreover, males are more susceptible to infection, owing to more energy-costly reproductive behaviours and to hormones that can both reduce immunocompetence and affect genes which determine infection resistance (Zuk, 1990; Klein, 2000). Therefore, it is reasonable to have found more intense *Strongyloides* sp. infections in males, and more males infected with *N. brasiliensis*. This parasite was also found more in younger males. Adult rats are more capable of triggering an immune response for the expulsion of *N. brasiliensis* than younger rats, which, if exposed to *N. brasiliensis*, may have a persistent infection until adulthood (Jarret *et al.* 1966, 1968; Dineen and Kelly, 1973). Moreover, rats in poorer body condition (absence of fat) were found to be carrying higher intensities of *N. brasiliensis*. Despite this seeming an intuitive conclusion, body condition is often neglected when assessing the risk factors for the probability or intensity of infection of parasites in the field. This result suggests the importance of adding body condition (as a proxy of health) variables in the models, given that individuals vary within natural populations and, therefore, in their susceptibility to infection by a parasite. However, it is worth noting that rather than previous poor condition has caused the infection, *N. brasiliensis* may have reduced the body condition of infected rats, as the parasite can cause anorexia (Mercer *et al.* 2000).

Aside from these results, the observation of eggs of *Toxocara* sp. and *Ascaris* sp. in the feces of *R. norvegicus* indicates recent contact with these parasites' eggs. While *Ascaris* sp. is likely to be a pseudoparasite for rats, presumably after ingesting human feces (Pinto *et al.* 2014), *R. norvegicus* are considered paratenic hosts for *Toxocara* sp., as after ingesting animal feces, mature eggs hatch and larvae migrate into rats' tissues, where they do not mature (Lescano *et al.* 2004; Santos *et al.* 2009). These findings indicate the circulation of these pathogens in the study area – knowledge which is of public health importance, as both can infect humans.

The sample size was a limitation of this study. With one campaign *per* season, the confirmation of seasonal patterns of probability and intensity of infection of the helminth species may have been prevented. Apart from that, this study was limited by the method of assessing the helminth infection (eggs in feces), which, in terms of intensity, only allowed the use of proxies by EPG. However, fecal egg counts in EPG give reliable estimates of parasite burden for a diversity of host species and are an essential tool when other intensive methods are impractical (Cringoli *et al.* 2004; Adejinmi and Emikpe, 2011; Lynsdale *et al.* 2015). Moreover, the McMaster technique applied has been considered a robust method (accurate multiplication factor) and sensitive enough to allow comparisons between different laboratories (Levecke *et al.* 2011).

This study provides relevant information about the helminth community of rats in a tropical slum settlement. Among the helminths, it is important to highlight the presence of species pathogenic to humans, such as *A. cantonensis* found in high prevalence, a finding of notable public health system importance. Along with the prevalence of helminths, the main risk factors associated with the probabilities and intensities of infection of these parasites among rats included a variety of environmental features and the demography and body condition variables of the rat population. This potentially suggests different risk factors involved in the

routes for human infection. Given the high richness of helminth species found within the rat population, further work should take co-infection into account in seeking to understand how potential associations between parasites may explain their probabilities and intensities of infection and the subsequent risk of transmission to humans.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S0031182017001755>

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