Pakistan J. Zool., pp 1-3, 2022. DOI: https://dx.doi.org/10.17582/journal.pjz/20210428030426

Short Communication

Effects of Altitude on the Transmission of Alveolar Echinococcosis

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Article Information
Received 28 April 2021
Revised 05 June 2021
Accepted 25 June 2021
Available online 07 January 2022 (early access)

Authors' Contributions
KY designed and directed the study. KY and YZ carried out investigations, analysed and wrote the manuscript.

Key words
Alveolar echinococcosis, *Echinococus multilocularis*, Intermediate hosts, Plateau pika, *Ochotona curzoniae.*

ABSTRACT

Alveolar echinococcosis is an important cestode diseases with a huge public health impact, it caused by larval of *Echinococus multilocularis,* whose life cycle requires a variety of canids and small mammals as hosts. The terminal hosts have received a lot of attention, while there are few studies on the distribution and abundance of intermediate hosts. A structural equation model was produced to demonstrate the effects of habitat factors on the distribution and abundance of intermediate hosts of *E. multilocularis*. Plateau pika (*Ochotona curzoniae*) act as the main intermediate hosts of *E. multilocularis*, whose effective cave density was 0.03/m^2 to 0.32/m^2, and it was negatively correlated with altitude at a high value (p = 0.010). Altitude regulates the distribution and abundance of plateau pika by influencing food resources and their fertility, which in turn affects the transmission of alveolar echinococcosis.

Alveolar echinococcosis (AE) is a parasitic disease caused by larval of *Echinococus multilocularis*, whose life cycle requires a variety of canids and small mammals as hosts. As the lack of obvious symptoms in 60%-75% of the patients, the disease has a high mortality due to the delayed start of treatment (Belard *et al*., 2016). The one-year postoperative mortality of AE patients was higher than that of cystic echinococcosis, another important cestode diseases with a huge public health impact globally, and the 10-year mortality of untreated AE patients was 94% (Mengyuan *et al*., 2018). AE has been described as a kind of parasitic cancer, the most serious zoonosis in temperate and Arctic regions of the Northern Hemisphere, and one of the top ten parasitic diseases by the World Health Organization (Jenkins, 2001; Zhenghuan *et al*., 2008; Guoqiang *et al*., 2019).

In China, *E. multilocularis* is mainly seen in Tibet Plateau, where not only has a large number of mammals as hosts, but also has low temperatures as well as dry climatic conditions, which can help their eggs survive. As a result, the AE prevalence in Tibetan plateau was significantly higher than that in non-Tibetan plateau areas (Weiping *et al*., 2018; Sihui *et al*., 2020). Shiqu County, located on the southeastern margin of Tibet Plateau, is one of the most seriously endemic areas in the world, with the serological positive rate among residents was as high as 95.4% in 2008, and the morbidity rate was 12.09% in 2007-2013 (Deyou *et al*., 2008). Although humans are unsuited and dead-end intermediate hosts for *E. multilocularis*, people who live there suffer a lot.

Serve as a source of infection, the terminal hosts have received a lot of attention. Fox is a kind of main terminal hosts for *E. multilocularis* in Tibet Plateau. But in fact, the Tibetan fox has been listed as the second class in the List of Wildlife under Key State Protection of China (Ministry of Agriculture and Rural Affairs of the People's Republic of China, 2021). In addition, there are many stray dogs and domestic dogs in the Tibetan Plateau act as terminal hosts. It has been found that the spread of infected dogs plays an important role in transmission of AE (Junli *et al*., 2017). Then, a comprehensive control of echinococcosis in Shiqu County has been launched by the Chinese government since 2015. On the one hand, stray dogs in large numbers have been captured or killed. On the other hand, the expelling parasite control for domestic dogs was strictly enforced monthly. By building a harmless treatment tank for dog feces, it was cut off that the channel of environmental pollution through *E. multilocularis* eggs from dog fecal (Mingzhong *et al*., 2017). Besides, there are more than 40 kinds of small mammals that act as intermediate hosts for *E. multilocularis* in China. The infection rate of genus *Microtus* was 0.1% and that of genus *Ochotona* was close to 10% (Tang *et al*., 2004; Zhenghuan *et al*., 2008). They also play an important role in transmission of AE. However, there are few studies on the distribution and abundance of intermediate hosts. Therefore, it would be necessary to analyze the relationship between intermediate hosts and habitat factors, which will help to clarify the

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0030-9923/2022/0001-0001 $ 9.00/0

distribution and abundance of intermediate hosts, and provide a theoretical basis for the AE prevention.

Materials and methods

The intermediate hosts density was determined by the block-open method. 32 sample sites were choosed at random in Shiqu County, Sichuan province, China.

The sample sites were 25 m×25 m squares, with an altitude of 3924 m to 4249 m. The number of blocked caves was 47 to 226 among 32 sample sites, which depended on the number of caves in the sites (Supplementary Table I). Some indicators were recorded the next day, including the number of effective caves, the intermediate hosts species, and the distances from the sample sites to rivers, roads and human settlements. Caves provide mall mammals with shelter and protection, thus the number of effective caves can represent their density to some extent.

Then a structural equation model (SEM) was constructed by Amos software to analyze the relationship between the number of effective caves and other factors.

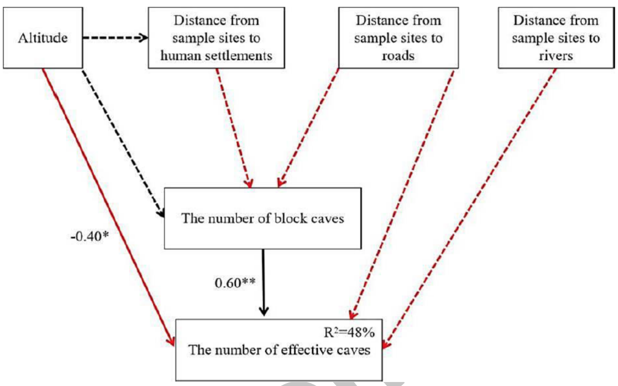

Fig. 1. The SEM of the number of effective caves and habitat factors. The solid line indicates a significant correlation; * indicates p<05; ** indicates p<01; direction of the arrow changes from the latent variable to dependent variable; black arrow indicates a positive influence, red arrow indicates a negative influence; the full line indicates a significance, the dotted line indicates no significance; the number on the arrow is the normalized estimated coefficient.

Results

In our study, as shown in Supplementary Table I, the number of effective caves was 17 to 201 per sample sites. That is to say, the effective cave density of the intermediate hosts was 0.03/m^2 to 0.32/m^2. As for the species, the investigation found that all intermediate hosts were plateau pika except in one sample quadrat that had rodent mammals (*Lasiopodomys fuscus*), thus plateau pika is the main intermediate hosts for *E. multilocularis* in Shiqu County.

In addition, the distances from the sample sites to the rivers, roads and human settlements were 30 m to 3000 m, 10 m to 800 m, and 0.21 m to 3000 m, respectively. Our SEM fits well with the following parameters: p = 0.411, RMSEA = 0.029, CFI = 0.945, CHI/DF = 1.025 (Fig. 1), because a SEM is regarded to match the data when p > 0.05, RMSEA < 0.08, 0.9 < CFI < 1, 1 <CHI/DF <3 (1 <CHI/DF < 2 is better). The model shows that the number of effective caves was directly affected by altitude with standardization coefficients of -0.40 (p = 0.010), and 48% of the number of effective caves explained by this model.

Discussion

Since the terminal hosts were strictly controlled in Shiqu County, we need to think about the effects of intermediate hosts for *E. multilocularis*. In this study, plateau pika is the main intermediate hosts in Shiqu County. According to the literature (Shijie *et al*., 2018), the density of plateau pika (103.80/hm^2) were higher than that of rodent (83.35/hm^2), and AE infection rate of plateau pika (6.50%) were also higher than that of rodent (3.01%) in Shiqu County. Moreover, plateau pika was detected in 99% of Tibetan fox food and accounted for 53.7% of its stomach contents (Harris *et al*., 2014). As the plateau pika is preyed upon by the fox, *E. multilocularis* can develop from larval stage to adult worms which lay eggs, then becoming a source of infection. Therefore, plateau pika play an important role in the transmission of AE.

Plateau pika prefer some habitats, altitude and rivers are the main factors affecting their habitat selection (Ye *et al*., 2014). Our SEM indicated that the number of effective caves was negatively correlated with altitude at a statically significantly level. Plateau pika are more widely distributed at low altitudes, thus we speculated that the pika select habitats by depending on oxygen concentration and temperature. On the one hand, oxygen concentration affects the physiological structure in male and the foetuses number in female among pikas (Lian *et al*., 2014). Thus, the oxygen level, decreasing with altitude increases, regulates population quantity of this species. On the other hand, the temperature also decreasing with altitude increases. Plateau pika may fail to reproduce at low temperatures during the breeding season (Shengqing *et al*., 2015). Low temperature makes pikas consume a large amount of heat to resist the cold, which leads to an increasing demand for food resources- often limited and shortage supply at high altitude.

Conclusions

In Shiqu County, the main intermediate hosts are Plateau pika, whose distribution and abundance are regulated by altitude, and it is speculated that the pikas select habitats depending on temperature and oxygen concentration.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (31070380), the Fundamental Research Funds for the Central Universities, Southwest Minzu University (2019XMJXPY07), funded by Science and Technology Department of Sichuan Province (2020YFH0107). In addition, the authors are most grateful to Hongqi Xie (Station master of Ganzi Grassland Workstation) for his support of this work.

Supplementary material

There is supplementary material associated with this article. Access the material online at: https://dx.doi.org/10.17582/journal.pjz/20210428030426

Statement of conflict of interest

The authors have no potential conflict of interest.

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Pakistan J. Zool., pp 1-3, 2021. **DOI**: https://dx.doi.org/10.17582/journal.pjz/20210428030426

Supplementary Material

Short Communication: Effects of Altitude on the Transmission of Alveolar Echinococcosis

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Supplementary Table I. Field investigation of the host cave.

Sample sites No.	Latitude	Longitude	Altitude (m)	No. of blocked caves	No. of effective caves
1	N 32°59.915′	E 098°21.361′	3989	60	30
2	N 32°59.461′	E 098°39.247′	4131	60	30
3	N 32°59.434′	E 098°39.239′	4134	71	24
4	N 32°59.432′	E 098°39.198′	4133	134	73
5	N 32°53.029′	E 098°36.612′	3994	154	61
6	N 32°52.961′	E 098°36.618′	3982	79	36
7	N 32°52.864′	E 098°36.612′	3968	49	20
8	N 32°52.767′	E 098°36.610′	3958	67	27
9	N 32°49.922′	E 098°33.811′	3927	77	45
10	N 32°49.945′	E 098°33.761′	3928	71	26
11	N 32°49.977′	E 098°33.729′	3924	81	36
12	N 32°49.912′	E 098°33.709′	3925	47	17
13	N 32°49.856′	E 098°33.735′	3925	79	28
14	N 33°03.956′	E 097°57.989′	4194	108	33
15	N 33°03.964′	E 097°57.955′	4194	191	42
16	N 33°03.945′	E 097°57.923′	4194	226	38
17	N 33°04.888′	E 097°53.467′	4080	114	29
18	N 33°05.630′	E 097°54.776′	4165	83	59
19	N 33°05.663′	E 097°54.772′	4163	83	47
20	N 33°05.683′	E 097°54.800′	4163	113	87
21	N 33°10.843′	E 097°58.217′	4102	163	54
22	N 33°03.893′	E 097°58.871′	4192	115	21
23	N 33°05.291′	E 097°57.030′	4161	-	18
24	N 33°05.284′	E 097°57.057′	4162	-	21
25	N 33°05.287′	E 097°57.088′	4162	-	48
26	N 33°05.198′	E 097°57.153′	4161	-	24
27	N 33°05.220′	E 097°57.282′	4162	-	31
28	N 33°05.241′	E 097°57.195′	4157	-	48
29	N 32°54.528′	E 098°34.352′	3952	-	169
30	N 32°59.027′	E 098°20.480′	3959	-	119
31	N 33°03.314′	E 097°59.919′	4249	-	75
32	N 33°03.314′	E 097°59.919′	4062	-	201

No. of blocked caves has a few missing values due to snow covering the ground and no need to block holes.

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0030-9923/2022/0001-0001 $ 9.00/0