The Spatial-Demographic Association Between Water Contact and Schistosomiasis Reinfection

Eunice Yujung Lee

Abstract Despite the progress in controlling and eradicating schistosomiasis in disease prevalent areas, the disease has reemerged in some regions. Poor sanitation and waste treatment contribute to higher risk of disease transmission to humans and host snails. Snails were collected from irrigation ditches during the summer and GPS was used to create a ditch map for each village. Based on this information, and a survey of human parasitological examinations, a GIS was created. I used the GIS to assess the correlation between village prevalence mean eggs per gram and non-spatial and spatial predictors. I found village level human infection rate to be strongly associated with the number of infected snails and the average distance of infected snails from the residential area, with higher numbers of infected snails found close to the residential area in villages with high human prevalence. In addition, a spatial analysis of location and intensity of individual-level water contact patterns assessed individual-level human exposure to the parasite. The intensity of water contact and the individual-level exposures were not strong indicators for infection risk. The village-level results have implications for surveillance near residential areas. However, individual-level human water contact patterns must be further investigated.

Introduction

Schistosomiasis is a water-borne infectious disease that affects humans in 74 developing countries. The disease is caused by adult blood flukes that mate in humans and lay eggs in the blood vessels surrounding the bladder or gut of the infected host. These eggs are excreted from the host in urine or feces, depending upon whether the worms prefer to mate in the urinary or intestinal tract (Ross et al, 2001). Symptoms of the disease include damage to the urinary tract, blood in urine and stool, and enlargement of the liver and spleen. Intestinal infection and damage to the bladder and kidney can be fatal. *Schistosoma japonicum* is the species of the parasite that causes schistosomiasis in China, and has existed in the country for over 2,100 years. It remains one of the most serious public health problems in many areas of China (Seto et. al., 2002). Despite the progress in controlling and eradicating schistosomiasis in disease-prevalent areas, the disease has re-emerged in some regions. There are still 800,000 people infected with schistosomiasis annually and 60 million people at risk of infection (Liang et al, 2005).

Humans become infected via contact with water, which is contaminated with the parasite. *S. japonicum* is one of the three major schistosome species that infects humans. The parasite enters directly through the skin while a person is having water contact. S. japonicum causes the intestinal form of schistosomiasis, so once a human becomes infected, worms mature to adulthood, and lay eggs which are excreted in feces. Eggs hatch in freshwater to become miracidia, a new form of the parasite. Miracidia infect the intermediate host snails. The parasite asexually reproduces in infected snails, and is reintroduced as cercariae back into the water. The cercarial form of the parasite is what re-infects human.

Although the mechanism of transmission via water contact is fairly clear, few studies have attempted to accurately quantify water contact intensity and its relationship to infection. In fact, recent studies have not found a relationship between water contact and infection (J.T Scott et al. 2003). One reason for this may be that water contact alone does not completely account for risk. Instead, it may be necessary to consider where and when water contact occurs, and how this relates to cercariae and snails in the environment. Geographic Information Systems (GIS) may be helpful in this regard. Previous GIS and remote sensing studies have focused on environmental factors influencing snail density and spatial distribution of snail and cercaria within a village as a means to detect clusters of high snail density and locations of infected snails in the village. However, these studies have not closely examined the spatial relationship between distance from the residential area and infected snail.

A previous study has found that reemergence of schistosomiasis in the region is due to a snail outbreak resulting from abundant snail habitat in the area (Seto et al., 2003). This study suggests that the presence of snails in the region indicates that there is an increased possibility for disease transmission to humans. Due to a lack of sanitation and adequate waste treatment, I hypothesize that in villages with higher human infection, there are a higher number of infected snails near the center of the residential area. Thus, people who have more water contact near the residence area will have a higher chance of getting infected. Human water contact in irrigation ditches and fertilization practices in the village are the main factors that lead to disease transmission. In this paper, I use a GIS to explore the spatial relationship between water contact intensity and infection. I consider both a village-level analysis of schistosomiasis prevalence (percentage of people in the village who are infected) and individual-level analysis of infection intensity (number of eggs in feces) versus water contact.

Methods

To examine the proximity effect of snails and villages, I chose twenty villages near the city of Xichang in southwestern of Sichuan, China. Ninety percent of the villages are located in the mountainous region. The living and working habits of the people in the village are primarily agricultural and their housing and living areas are all adjacent to the fields. The climate is subtropical with annual average temperature of 17°C and annual average rainfall is 1000 mm (Seto et. al., 2002).

Snail populations (August). Snails from irrigation ditches were collected during wet season during the summer. "Kuang" sampling frames that are about 0.11 m^2 in area were placed at 10-meter intervals in the irrigation ditches. All the snails were collected from within each kuang, placed in paper envelopes, and transferred to the laboratory of Deyang Institute of Parasite Disease in Deyang city where they were tested for their infectious status. To test for infection, each snail was crushed between glass microscope slides and then inspected with dissecting microscopes for presence of the parasite.

Ditch map. GPS was used to create a ditch map for each village. Remote sensing images were used to identify the potential snail habitat in each village, and show irrigation ditches in agricultural fields, mountains, hills and residential areas within the region. When we collected the snails from the ditches we also recorded the position (longitude and latitude) of each snail points by using global positioning system (GPS) to create a map for irrigation ditches, the primary snail habitat for the intermediate snail host. Various attributes of ditch type (width, depth) and identifying data such as time, date, and collection ID were recorded as well.

Human infection survey. For each villager in the 20 villages, infection status was determined via parasitological examination. Fecal samples were examined for the presence of parasite eggs.

Human water contact survey. A 25% random sample of the village population was interviewed and asked to recall the frequency, duration, and location of their water contact over a period of up to seven months in the past (Spear et. al., 2004). The questionnaire includes eight different water activities: swimming, washing hands, washing clothes or vegetables, washing agricultural tools, ditch operation, plowing, rice cutting, and fishing.

Cercarial bioassay. The cercarial bioassay aims to quantify cercarial concentrations in surface water systems. The bioassay is performed by setting a cage of five mice at the surface of the water for 10 hours, typically at locations where people have frequent water contact. The feet and abdominal part of mice is submerged in the water so that they can become infected by cercariae. After exposure, mice are held for 35 days to allow for parasite maturation and afterwards dissected and the worms are counted (Spear et. al., 2004).

__**Village-level Analysis:**__

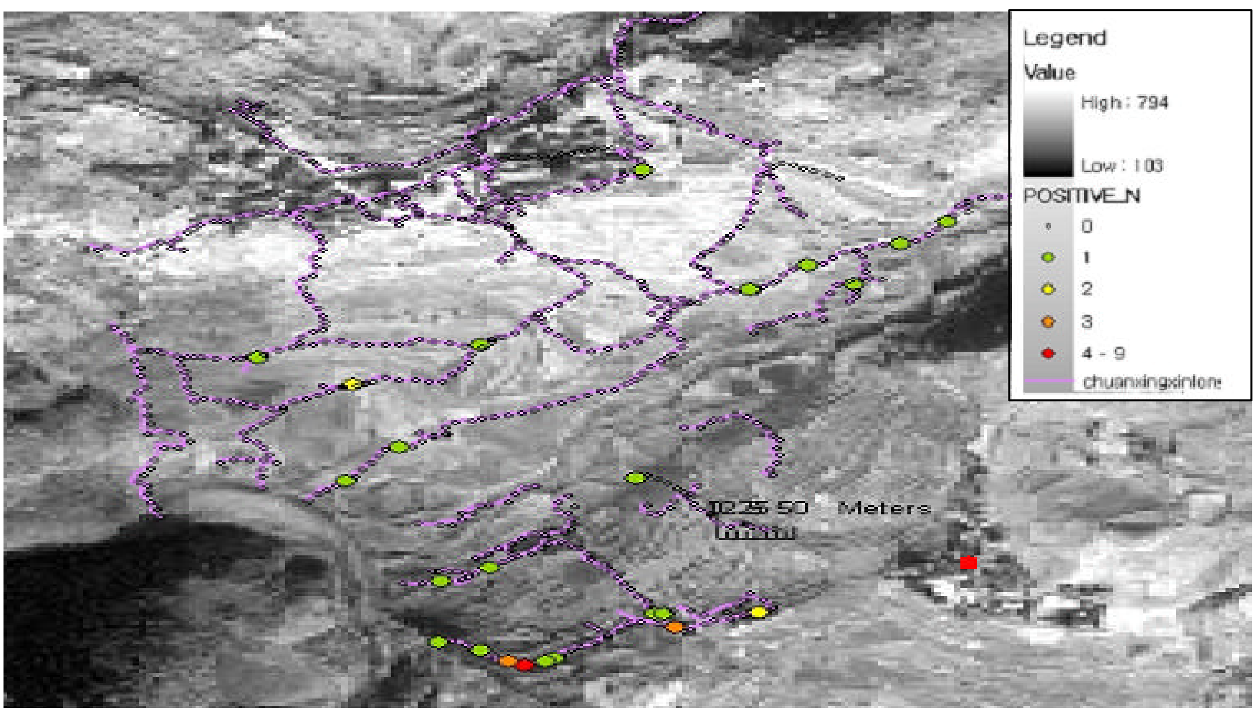


Figure 1. Satellite image of Chuanxing village and irrigation ditch with positive snail points found along the ditch line in southwestern Sichuan Province in China.

The GIS database, which includes the snail survey, human survey, a satellite image of village, and ditch map was analyzed to determine high snail density and locations of infected snails in the village (Figure 1). I made a focal point in the center of each residential area and computed the distance between each positively infected snails and residential area. To analyze the village-level schistosomiasis prevalence, I chose to investigate the correlation between two outcomes (village prevalence and mean egg per gram) with non-spatial and spatial predictors. These predictors include the total number of snails, number of infected snails, number of infected snails over number of samples (non-spatial), average distance between infected snails and village, number of infected snails multiplied by average distance, % infected snails times average distance (spatial).

Individual-level Analysis:

Instead of making simple assumption about water contacts being close to the village, actual data of individual person's water contacts and activities was investigated. Monthly exposure data between April to October, 8 different activities (swimming, fishing, wash, farming, etc), 25% representative sample of villages, demographics (infection history), frequency, duration of water contacts (survey), and ditch ID (upper, middle, lower) were used for computing the total exposure from each water contact from each site. Different scales for each activity to exposure area and adjustment factor for children (<15 years old) and for adults (>15 years old) were applied.

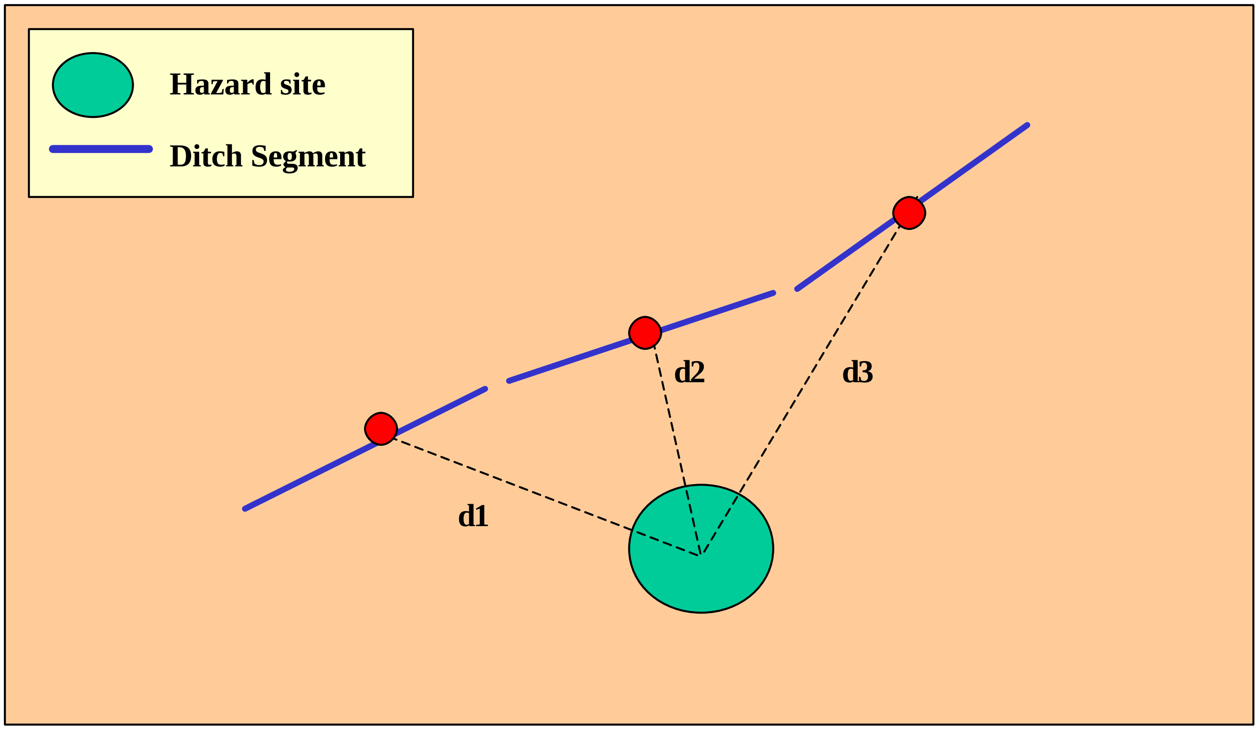


Figure 2. Spatial analysis of individual water contacts from each hazard source to each ditch segment where the water contact occurs.

First, each segment of ditch was divided into three parts (upper, middle, and lower) to specify the location of contacts (Figure 2). The distances between each ditch and each "hazard source"- either the location of a kuang with positive snails or the location of a positive mouse bioassay site were computed in GIS. For each person, I first computed the amount of water contact at each ditch location:

$$W(i, t) = ?_i \; frequency_{ik}\ (t) * duration_{ik}\ (t) * surface\ area_k\ (m^2 * minute)$$

where W(i,t) is water contact for each month (t) and each ditch (i). The units of W (i,t) are in m^2 minutes.

Exposure at a particular site is a function not only of the person's water contact, but also the concentration of cercariae found at that site. The concentration of cercariae was compute as:

$$C\ (i, t) = ?_j \; C_j\ (t)\ e^{-?dij}$$

where *dij* is the distance between each ditch and each hazard source, C_j is either the number of positive snails in the kuang or the mean number of worms per mouse, and lambda, ? (0.014381) is used to calculate the exponential decay of cercariae as it travels downstream.

Taking into account both cercarial concentration and water contact, a person's exposure for each month t is then calculated:

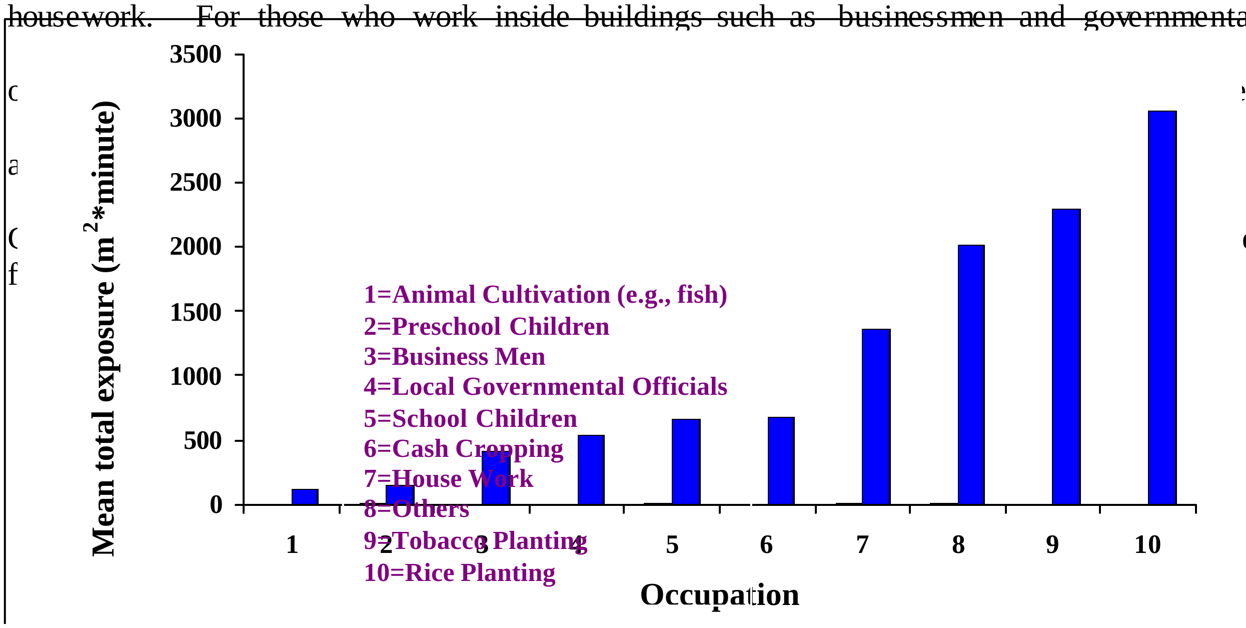
$$E(t) = ?_i C(i,t) * W(i,t)$$

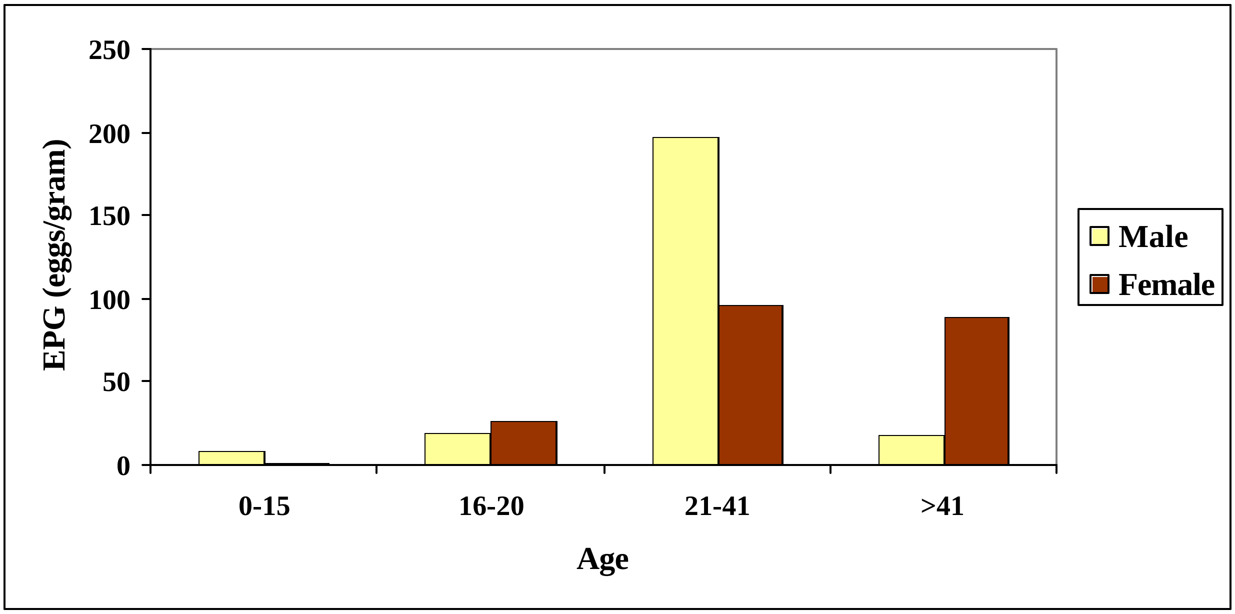
I then compared this exposure amount to the intensity of infection (i.e., the number of eggs per gram of feces, or epg) for the person. I considered both negative binomial regression model of epg based on the total season's exposure, as well as exposure broken down by month and by village. I also considered a logistic regression model looking only at binary outcome (infected versus uninfected), using similar predictor variables.

Result

1. Description of demographics

The mean total exposure to schistosomiasis by water contacts and the occupation distribution (Graph 1) was used to determine the infection variation between different occupations among all 20 villages. The graph generally shows that the group that has the highest mean total exposure is those who participate in the agricultural activities such as rice and tobacco planting followed by housework. For those who work inside buildings such as businessmen and governmental



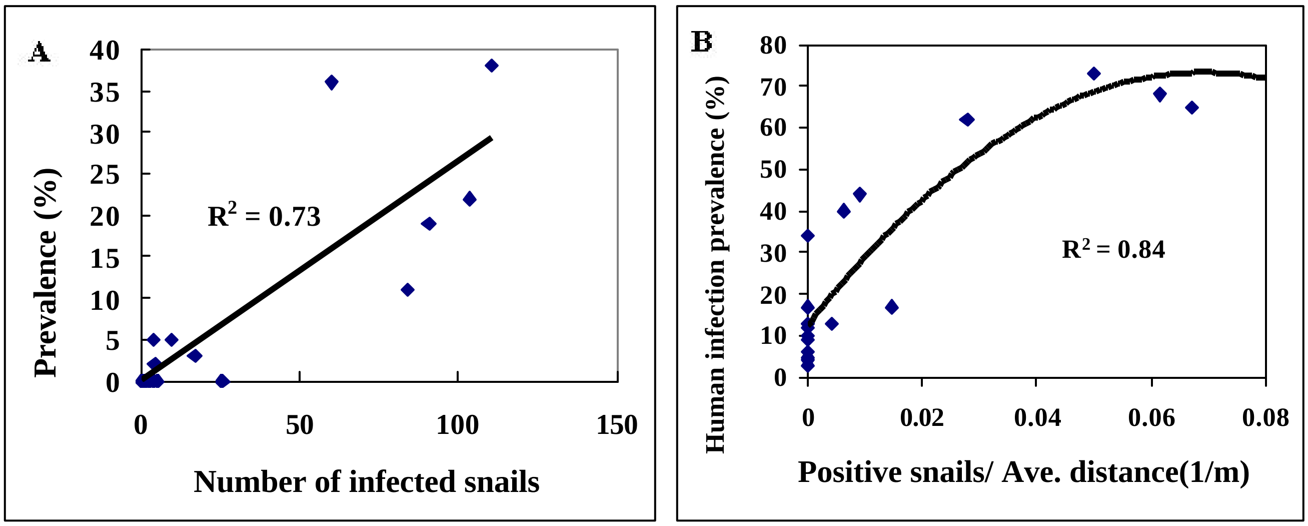


Graph 2. Schistosomiasis infection ratio between female and male with different range of age distribution over all 20 villages.

Over all 20 villages, there are more males than females. Males age less than 15 years old have higher epg level than females (Graph 2). The infection level difference is relatively small for the age between 16 to 20 years old. However, males in the age of 21 to 41 have a significantly high infection level compare to females in the same age range. Most of males aged of 21 to 41 participate in agricultural activities and they have more water activities such as washing tools, operating irrigation ditches and planting crops. Females have higher epg than males in age greater than 41.

2. Village level analyses

Of the village level analyses, the strongest relationships with infection prevalence were found using analyses involving infected (or positive) snails. The non-spatial relationship between number of positive snails and village-level schistosomiasis prevalence (Graph 3) is approximately linear with a R^2 =0.73. In an attempt to determine if positively infected snails and their distance from the residential area are associated with village-level prevalence, the polynomial regression model was used which resulted in an improved R^2 = 0.84.



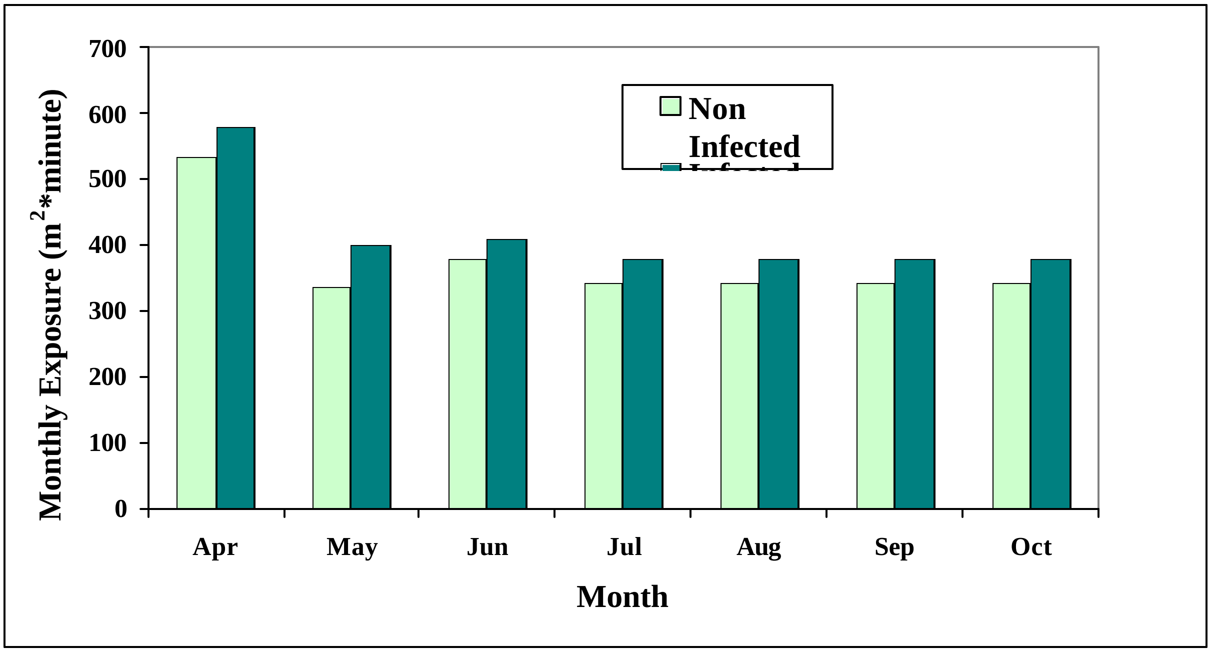
Graph 3. **A**, Linear regression model shows the village prevalence of infection with *Schistosomiasis* infected snails. **B**, Polynomial regression model represents the intensity of village infection with spatial relation of infected snails from the residential area.

The total number of snails (infected and uninfected) does not seem to be associated with the disease prevalence of a village. Different snail infection rates between villages suggest that the higher numbers of snails does not result in higher numbers of infected snails nor affects disease prevalence of a village. Positively infected snails and their distance from the residential area are strongly associated with village-level prevalence. The results show that the higher numbers of infected snails were found close to the residential area. High number of infected snails and the close distance from the village are strong determinants of disease transmission to people in village. However, the polynomial model suggests that at a certain level, the prevalence of disease does not increase infinitely. This may be due to the development of immunity amongst those who frequently harbor a large number of worms.

3. Individual-level analyses

A. Negative Binomial Model	EPG (R^{2})
Total Exposure	0.0026
Monthly Exposures	0.0075
Separately by village	
Total Exposure	0.0015-0.035
Monthly Exposure	0.041-0.22
B. Logistic models of infected vs. not infected	
Total exposure	0.021
Monthly exposure	0.030
Separated by village	
Total exposure	0.0001-0.067
Monthly exposure	0.13-0.53

Table 1. A negative binomial and logistic model found a non-significant correlation between the intensity of water contacts patterns of individual people with their EPG level.



Graph 4. Monthly cercarial exposure of infected and not infected people found in Shian village

The results of the individual-level regression models were not statistically significant. Hence, higher exposure to cercariae was not strongly associated with human infection. Both the negative binomial and logistic regression show low R^2 values, which suggest that there may or may not be a correlation (Table 1). However, a better correlation is found for the total exposure with individual epg after separating them by village and by month. Therefore, if there is a relationship between individual-level exposure to cercaiae and epg, it is most likely subject to seasonal variation and variation between villages as well. Despite lack of statistical significance, if we look only at the Shian 5 village (Graph 4), the village with the highest R^2 value, we find that exposures each month are on average higher among the infected versus the non-infected.

Discussion

From the snail spatial analysis, I found that the number of total snail (infected and non-infected) does not relate to the prevalence of infected snails because each village has a different snail infection rate. However, positively infected snails and their distance from the residential area strongly associated with the village-level prevalence of disease in humans. There were more infected snails detected in the irrigation ditches near the residential area than far away from the village center. Moreover, the village prevalence increased as the number of positively infected snails increased. Nevertheless, the intensity of water contact patterns and cercarial exposure of individual persons does not explain the transmission and intensity of disease. There is no clear or significant correlation between the intensity of water contact and human infection of schistosomiasis.

Regardless of the fact that I considered both where and when the water contacts occur, the assumption that we made earlier about the risk of infection near the hazard source does not prove anything about the intensity of schistosomiasis infection to humans. Although I considered both seasonal variation for the exposure and variation between villages, I still found a weak correlation. There are potential problems that might have resulted in this weak correlation. During survey, people may not have provided an accurate report of their water activities. Because the study was retrospective, participants were asked to remember what they did in April when it was already in October and many people may not have been able to accurately recall where exactly they had water contacts and activities (recall bias). Moreover, only 25% of the villagers participated in the study. In the future, a larger sample of villagers may be able to clarify the individual-level relationship between exposure and epg.

Despite the lack of a clear individual-level result, the village-level result is promising, and has practical public health relevance. In the future it may be possible to use distance form village center to infected snail locations to identify villages at risk. This may be particularly useful for re-emerging villages, where there is no historical human prevalence data to characterize whether a village is a high or low prevalence village. In these re-emerging villages, as positive infected snails are found, their distance to the center of the village may provide a clue as to the risk within the village.

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