



Commentary Article

Cyclospora cayetanensis Infection in the Developing World: The Venezuelan Perspective

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Citation: Leonor Chacin-Bonilla (2023) *Cyclospora cayetanensis* Infection in the Developing World: The Venezuelan Perspective. Rep Glob Health Res 6: 153. DOI: 10.29011/2690-9480.100153

Received Date: 28 March, 2023; **Accepted Date:** 01 April, 2023; **Published Date:** 04 April, 2023

Abstract

Significant gaps remain on the biology and epidemiology of *Cyclospora cayetanensis* including its modes of transmission in endemic areas. The aim of this article is to share the lessons learned from findings on cyclosporiasis in impoverished settings from Venezuela to better understand new challenges and propose future avenues of research and strategies for infection control. The most outstanding finding was the explicit correlation of infection with poverty and soil transmission; there was a strong association of infection with living in huts where infections were clustered. These results carry pertinent connotations for public health actions. An in-depth study to assess the links between social marginalization and *Cyclospora* positivity is needed. Sampling strategies with longitudinal and spatial analyses are crucial to determine the impact of poverty on infection and to guide intervention actions.

Keywords: *Cyclospora cayetanensis*; Cyclosporiasis; Epidemiology; Social health determinants; Soil-borne transmission; Venezuela

Introduction

Cyclospora cayetanensis is a leading cause of diarrheal disease affecting humans globally. In endemic areas, the infection and illness occur more often in children and AIDS patients [1]. Predominance of infection in school children and high percentages of asymptomatic carriers have been documented [2-7]; in Peruvian shanty towns, no infections were detected after 11 years of age suggesting that early infections afford immunity [8]. A notable seasonality of infection with different patterns has been reported [2,9]. Significant gaps remain about *Cyclospora*, principally in its biology and epidemiology.

In developed regions, cyclosporiasis outbreaks have largely been associated with fresh produce imported from endemic areas, and *Cyclospora* is considered a food-waterborne pathogen [10]. However, the dynamics for infection transmission in lower-income countries is unclear. These areas have different lifestyles, hygiene levels, and agricultural intensity which favor the anthroponotic transmission of pathogens. Thus, the sources and dissemination routes of the parasite could differ. Variables related to water, eating fresh produce, agricultural occupations, poor personal hygiene,

deficient sanitary facilities [3,5-7,11], and contact with soil [12] or animals [1] have been linked to infection.

Cyclosporiasis, as other parasitic infections, is a public health problem in Venezuela [13-16]. However, there is a dearth of information concerning the epidemiology of infection in the general population. Infection rates and asymptomatic carriers percentages up to 40.7% and 100%, respectively, have been reported [2,17,18]. We have studied the prevalence, pathogenic role, and potential environmental sources of contamination in health centers and impoverished populations from Zulia and Falcon States, Northwestern Venezuela, to provide a comprehensive description of the epidemiology of *Cyclospora* [19-24]. In this article we have critically reviewed and reflected upon our experience on communities where poverty has a severe impact on the infection; several aspects emerge as epidemiologically remarkable and biologically interesting and are therefore highlighted here. The aim is to share the lessons learned to better understand new challenges, and to propose future avenues of research and strategies for the control of cyclosporiasis.

Relevant Findings and Implications

We have found *Cyclospora* infection rates from 6.1 to 9.9%, suggesting that cyclosporiasis is endemic and common in Venezuela. The age distribution of infection indicates that children are exposed to the parasite at an early age, with the odds

of infection being significantly higher in children ≤ 10 years old, declining abruptly in adults. The highest prevalence of diarrhea was noted in children ≤ 5 years old with a tendency toward lower prevalence with increasing age; the proportion of asymptomatic infections was notably high (86.1-94.5%) and scarce infections were observed in adults [20,21,24]. In AIDS patients, the high infection rate noted (9.8%) [19] suggests that the parasite is an important opportunistic pathogen in the area.

The prevalence of infection showed monthly variation from 0% to 35.3%; children had a higher risk of getting the infection during the rainfall time [23], as documented [2-9]. A striking finding was the bimodal distribution of infection corresponding with the two months when the highest rainfall was observed. There was a marked correspondence between the tendency of increasing infection rate and the growing intensity of rainfall, serving as a significant forecaster of cyclosporiasis. Although one year of surveillance could be insufficient to affirm what pattern of *Cyclospora* infection will be yearly, the bimodal distribution of infection suggests that this is the seasonality pattern of infection in Venezuela. Given the semiarid condition of the area, we can assume that moisture of the soil is essential for the endurance and load maintenance of oocysts [22].

Several socio-economic and environmental factors were found to be independently associated with the infection; living in huts, not having a toilet or latrine, and having contact with human feces-contaminated soil were strong predictors for cyclosporiasis. These factors may be understood as poverty proxies and their association with the infection indicates that household socioeconomic level is correlated with *Cyclospora*. Exceptional outcome was the strong association of cyclosporiasis with environments conducive to fecal contamination and clustering of infections in sectors and residences of extreme poverty, suggesting that the patterns of transmission can vary in adjacent areas [21,24]. This finding could explain the presence of scant infections in adults, likely immunologically naive, contrasting with studies from Peruvian shanty towns where immunity becomes complete by adolescence [8].

The ≤ 10 years old group was also associated with infection, as documented [1-7]; the reasons for this finding are not clear. Our results suggest that the greater susceptibility to infection in these children is due to other factors associated with socio-economic status, rather than age alone. Their play activities and poor hygiene standards indicate that they often come into contact with feces-contaminated soil inside the households and are more exposed to infection; transmission of the parasite could have occurred often in the dwellings of case patients. Lifestyle in huts is itself risky due to a deficient infrastructure with earthen floors and limited sanitation which likely increase exposure to oocysts through contact with contaminated soil potentially fostering the spread and dy-

namic epidemiology of *Cyclospora*. Indeed, *Ascaris lumbricoides*, *Trichuris trichiura*, *Cryptosporidium* spp. and *Toxoplasma gondii* infections were also clustered in sectors of extreme poverty in one of the communities [14,15,21]. An interesting observation was a statistically significant interaction between *Cyclospora* and *Ascaris lumbricoides* [24], indicative of a similar dissemination potentially explained by concurrences in the biology of these species, sharing soil transmission and predominating in school children. The detection of *Cyclospora* oocysts in 9/50 (18%) soil specimens [24] indicates the potential spread of infection by this vehicle, and supports our hypothesis that this is the primary mode of *Cyclospora* spread in these neighborhoods.

Variables related to water played a role in the transmission of cyclosporiasis in a setting [24]. Drinking well water and untreated water were associated with elevated odds of infection, as described [2,3,5]. The link between the infection and well water suggests that this water contaminated by oocysts washed from the soil by the rain could be a significant factor in the dissemination of infection that would affect equally all household members. *Cyclospora* oocysts were identified in 4/14 (28.6%) water samples, suggesting the waterborne infection in the area [24]. Poultry exposure increased the likelihood of getting cyclosporiasis, as reported [1-4], probably reflecting mechanical transport of oocysts. Eating fresh produce was not linked with the infection. Nevertheless, the detection of *Cyclospora* in 3/77 (3.9%) of local produce samples [24] backs the credibility of this exposure route.

The most outstanding finding of our investigations was a clear association of infection with extreme poverty and soil transmission; it is the first evidence that soil contaminated with feces is an important risk factor, and poverty a predisposing condition for cyclosporiasis. Our data suggest that the dominant mode of spread is through this vehicle. However, there is an interplay of geographical, household- individual- and parasite-related factors in the transmission of *C. cayetanensis*, and multiple routes for the spread of the infection surely exist. The association of infection with factors associated with water and poultry and the detection of oocysts in soil, water, and produce samples in one of the settings [24] suggest the likely transmission of the coccidium by these means. Nevertheless, we could not ascertain the relative relevance of the variables determining the prevalence of *Cyclospora* infection. The present findings allow us to hypothesize that, besides water and food, soil may be a major source for the dissemination of *Cyclospora* in low-income areas. Poverty and deficient sanitation may facilitate fecal contamination of the environment. The potential links between poverty and *Cyclospora* positivity, and the current scenario of humanitarian crisis in Venezuela, could contribute to a significant spread of infection exaggerating intra-household transmission and would explain the present findings.

Reflections and Lessons Learned

1. *Cyclospora* infection is endemic and common in Venezuela, predominates in children ≤ 10 years old, the disease prevails in infants and AIDS patients, and a remarkable high percentage of asymptomatic carriers exists.
2. Cyclosporiasis has a marked seasonality with high endemicity during the rainy time.
3. There is a categorical correlation between *Cyclospora* infection and poverty; infections cluster in families living in sub-standard housing developments.
4. Patterns of distribution and transmission can differ in adjacent areas.
5. Multiple modes of spread for infection exist; water, food, and soil are reservoirs and routes of spread of *Cyclospora*.
6. Soil transmission may be the predominant mode of spread.

Although the lessons learned can not be generalized to all populations, they will be useful for similar settings and need to be thoroughly investigated. Given the emerging threat of cyclosporiasis, understanding interactions between socioeconomic and environmental conditions will aid address the complicated relationships between social discrimination, environmental factors, and *Cyclospora* exposure.

Potential Future Research

Forthcoming work should include an in-depth study to assess the potential links between social marginalization and *Cyclospora* positivity and the potential role of soil as a reservoir and avenue of infection. Assuming that poverty and its proxies are a risk factor for the infection, it emerges that more meticulous research is essential to detect exposure factors, especially if the households with clustering of infections become the epidemiological study target. The high concentration of cases in a few huts suggests that control approaches should be focused to better control infection. Sampling strategies in combination with longitudinal and spatial analyses will be crucial for understanding *Cyclospora* specific relationships with poverty and to guide intervention actions against infection. The biology, sources, modes of spread, environmental distribution, transportation, and destiny of the parasite should be studied more extensively. Temporal variability and the effects of climate change scenarios for infection should also be investigated when developing exposure-assessment plans.

Potential Strategies for Prevention and Control

The relationship of *Cyclospora* infection with poverty and the uneven distribution of infections bear pertinent connotations for public health actions in low-income areas. Integrated control strategies should focus on development of infrastructure and environmental sanitation, especially the implementation of water,

sanitation, and hygiene services in the communities. A major challenge of these actions is that they require huge efforts in vulnerable settings, a constant behavior change, and infrastructure maintenance to be effective over extended periods of time.

Conclusion

Cyclospora infection clearly associates to poverty and soil transmission, suggesting the correlation between household socioeconomic level and cyclosporiasis; sustainable development is essential in low-resource settings to avoid such widespread of the infection. Additional studies are needed to confirm and expand these findings in analogous environments.

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