

Study of Nonoutbreak Giardiasis: Novel Findings and Implications for Research

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ABSTRACT

BACKGROUND: The burden of nonoutbreak-related *Giardia* infections in the US is poorly understood, with little information on its impact on people's lives and on unusual manifestations of infection. This study was designed with the objectives of better defining the impact of infection, examining the occurrence of extraintestinal manifestations, and determining risk factors for delayed treatment of infection.

METHODS: Foodborne Diseases Active Surveillance Network surveillance was used to identify persons with nonoutbreak-related, laboratory-confirmed *Giardia* infection. People were enrolled into the Risk Factor arm and the Delayed Enrollment arm. Detailed questionnaires collected information on clinical manifestations, impact on activities of daily living, health care utilization, and treatment.

RESULTS: The study enrolled 290 people. Multivariate predictors of delayed study enrollment, a surrogate for delayed diagnosis of *Giardia*, included intermittent diarrheal symptoms, delayed time to first health care visit, and income. Decreased ability to participate in one's activities of daily living was reported by 210 (72.4%) participants. Appropriate therapeutic agent for *Giardia* was received by 237 (81.7%) by the time of study enrollment. Extraintestinal manifestations of *Giardia* were reported by 72 (33.8%) persons who enrolled in the Risk Factor arm.

CONCLUSIONS: The presence of intermittent diarrhea contributes to delayed health-seeking behavior and to delayed diagnosis of *Giardia*. More study is needed to determine if this symptom can help distinguish *Giardia* from other causes of infectious diarrhea. The occurrence of extraintestinal manifestations of *Giardia* infection does not appear to be rare, and merits further study.

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The protozoan parasite *Giardia intestinalis* (also known as *G. lamblia* or *G. duodenalis*) is a major cause of diarrheal illness worldwide.¹ In the US, *Giardia* is identified in 4%-7% of stool specimens from patients with diarrheal illness.²⁻⁶ Although approximately 20,000 *Giardia* infections were reported to the Centers for Disease Control and Prevention (CDC) during 2006-2008,⁷ the true burden of giardiasis is thought to approach 1.3 million infections annually.⁸

Giardia is transmitted by the fecal-oral route and results in asymptomatic infection, acute self-limiting diarrhea, or chronic diarrhea. Symptoms include diarrhea (89%), malaise (84%), flatulence (74%), foul-smelling greasy stools

(72%), abdominal cramps (70%), bloating (69%), nausea (68%), anorexia (64%), and weight loss (64%).⁹ Extraintestinal symptoms have been reported rarely.¹⁰ Skin symptoms include urticaria, angioedema, atopic dermatitis, and erythema nodosum.¹¹⁻²⁰ Reactive arthritis in a variety of joints has been described in case reports and series.²⁰⁻³⁰ Ophthalmologic involvement includes vision loss, uveitis, chorioretinitis, retinal arteritis, and retinal changes.³¹⁻³⁶ Urethritis also has been rarely reported.³⁷ Most extraintestinal symptoms resolve with appropriate therapy for giardiasis, although the retinal changes seen in children do not always resolve.³⁵ Reactive arthritis is typically resistant to nonsteroidal anti-inflammatory treatment.

In 2003 and 2004, the Foodborne Diseases Active Surveillance Network (FoodNet) sites in Colorado and Minnesota and the CDC conducted the case-control Risk Factor (RF) Study to assess the risk factors for nonoutbreak giardiasis. This article will focus on examination of the case series created as a component of the larger case-control study.

METHODS

FoodNet (<http://www.cdc.gov/foodnet>) staff in Colorado and Minnesota identified study participants in their respective catchment areas over a 1-year period by monitoring reports of laboratory-confirmed *Giardia* infections not linked to outbreaks. Laboratory confirmation could be based on microscopy or fecal antigen testing. Due to a higher incidence of giardiasis and larger catchment area, only every second case in Minnesota was eligible for the study. The exclusion criteria for the RF study are listed in Table 1. Cases enrolled

within 42 days of symptom onset were enrolled in the RF arm of the study and were included in the case-control study. Those enrolled after 42 days were enrolled in the Delayed Enrollment (DE) arm and were not included in the case-control study.

CLINICAL SIGNIFICANCE

- One third of persons with nonoutbreak giardiasis reported extraintestinal manifestations of the infection.
- Up to 20% of persons with laboratory-confirmed *Giardia* infection had not received appropriate chemotherapy.
- Intermittent diarrhea, which was reported by 48% of patients with more acute symptoms and 76% of patients with more chronic symptoms, may have contributed to a delay in diagnosis and may be an important clue for the diagnosis of *Giardia* infection

A structured telephone questionnaire was administered by trained staff to participants ≥ 12 years of age or to the parent or guardian of participants < 12 years of age. RF arm participants were asked about demographic information, chronic medical conditions, *Giardia* exposures, symptoms—including extraintestinal symptoms, health care utilization, impact of illness on activities of daily living, and treatment. DE arm participants were asked the same questions, using the same wording, except that no information on chronic medical conditions, *Giardia* exposures, or extraintestinal symptoms was collected. This research was conducted using a CDC and state Institutional Review Board-approved protocol.

Data were analyzed by using SAS v9.2 (SAS Institute, Cary NC). DE arm cases (DE cases) were compared with RF arm cases (RF cases) by demographics, symptoms, health care utilization practices, and treatment. Chi-squared and Fisher's exact tests were used to examine differences in categorical variables and the 2-sample median scores test to examine differences in continuous variables. A model of multivariable predictors was created using demographic variables, statistically significant univariate predictors, and interaction terms.

RESULTS

The FoodNet sites identified 653 people for the RF study; 350 (53.6%) were excluded for the following reasons: 192 (54.9%) were identified > 6 weeks after symptoms onset, 54 (15.4%) were recent immigrants, 41 (11.7%) were asymptomatic, 29 (8.3%) were not English speaking, and 10 (2.9%) were part of a family cluster. Of the 303 eligible for inclusion, 213 (70.3%) enrolled. Reasons for nonenrollment included: 56 (62.2%) refused, 32 (35.6%) unable to be contacted, and 2 (2.2%) did not complete the interview. After the DE arm was added, 77 (40.1%) of the 192 initially excluded because symptoms began > 6 weeks before being contacted were enrolled. The RF and DE cases were similar in sex, age, education, and income (Table 2). They differed significantly by state and setting of residence, with more DE cases living in Minnesota ($P < .0001$) and in rural areas or on farms ($P = .04$).

Table 1 Exclusion Criteria for the Risk Factor Study

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| Case-patients were excluded from the study if |
| They were not reached after 15 telephone attempts |
| They had unavailable telephone numbers |
| They were physically or emotionally unable to answer questions |
| They were recent immigrants, adoptees, or refugees |
| They were non-English speakers |
| They had asymptomatic infection |
| They had unknown illness onset date |
| They had a repeat infection within the past 3 months |
| They were associated with a family cluster of giardiasis but were not the earliest laboratory-confirmed case |

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