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ORIGINAL ARTICLE

Prevalence and Predictors of Giardia in the United States

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Abstract
Background Infection with *Giardia lamblia* is a common cause of diarrheal disease in the developing and industrialized world.
Aims We aimed to assess the prevalence of giardiasis in the United States (US) among patients with duodenal biopsies, investigating demographic and clinical factors associated with this condition.
Methods We conducted a cross-sectional study of patients with duodenal biopsies submitted to a national pathology laboratory between January 2, 2008, and December 31, 2015. The prevalence of giardiasis was calculated and categorized by the following patient sociodemographic and clinical data: age, sex, ethnicity, endoscopy indication, season, year, urban–rural setting, region, and presence of *H. pylori* and atrophic gastritis.
Results Among all patients ($n = 432{,}813$), the mean age was 52.2 years. The prevalence of giardiasis was 0.11%. Patients with giardiasis were more likely to be male (57.8 vs. 34.1%, $p < 0.0001$). Among patients who had a gastric biopsy ($n = 363{,}788$), those with giardiasis were more likely to be colonized with *H. pylori* (25.7 vs. 9.4%, $p < 0.0001$). There was no statistically significant association with age, endoscopy indication, urban–rural setting, ethnicity, season, or the presence of atrophic gastritis. On multivariate analysis, male sex, Southern region, and the presence of *H. pylori* were independently associated with giardiasis.
Conclusions To our knowledge, this is the largest study to date to assess predictors of giardiasis in the US. We found that male sex, being colonized with *H. pylori,* and residing in the Southern US are independently associated with giardiasis infection.

Keywords Giardia · Endoscopy · Epidemiology · Diarrhea

Abbreviations

AIDS	Acquired immunodeficiency syndrome
CDC	Centers for Disease Control
CI	Confidence interval
EGD	Esophagogastroduodenoscopy
HIV	Human immunodeficiency virus
OR	Odds ratio
US	United States

Introduction

Giardia lamblia (also known as *Giardia intestinalis and Giardia duodenalis*) is a protozoan organism that is a common cause of diarrheal disease in both the developing and industrialized world [1–3]. Estimated 2.8×10^8 cases of *Giardia* occur annually worldwide [4], with 1.2 million cases occurring annually in the United States (US) [5]. The annual hospitalization cost related to giardiasis in the US is estimated at $34 million [6].

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Symptoms of giardiasis can range from a self-limited acute diarrheal illness to one of persistent malabsorption [2, 3, 7, 8]. Other symptoms of giardiasis include non-specific gastrointestinal symptoms such as abdominal cramps, epigastric pain, dyspepsia, gas, flatulence, weight loss, anorexia, nausea, vomiting, and hematochezia, as well as systemic symptoms of headache, fever, and chills [3, 7–9]. Though diarrhea is usually thought of as a necessary component of giardiasis, up to 80% infected individuals may be asymptomatic chronic carriers [2, 7, 10], and diarrhea may not even be a clinically identified symptom [3, 7, 11]. The organism can be recovered from duodenal aspirates taken at endoscopy in patients undergoing endoscopy for a variety of causes [12].

To our knowledge, there are no recent studies that have investigated factors associated with giardiasis in the United States. While the Centers for Disease Control (CDC) has published a surveillance report on giardiasis since 1992 [3, 13–17], these reports do not include a control population and thus do not draw conclusions regarding predictive factors. Additionally, the CDC's reports lack details regarding patient ethnicity [3, 13–17].

Given the relative paucity of data on the current epidemiology of giardiasis in the United States, we measured the prevalence of giardiasis among 432,813 patients undergoing duodenal biopsy during an 8-year period using a national pathology database, and investigated demographic and clinical factors associated with this condition.

Methods

We conducted a cross-sectional study of all patients with duodenal biopsies from January 2, 2008 to December 31, 2015, submitted from endoscopy centers to Miraca Life Sciences, a commercial pathology laboratory that receives specimens from endoscopists throughout the US, including all 50 states, Puerto Rico, and the District of Columbia. All samples were processed centrally in one of three laboratories and examined by gastrointestinal pathologists. A central database contained biopsy reports, including date of procedure and indication for endoscopy as well as patient demographic information (age, sex, ZIP code of residence, and endoscopy practice).

Giardia was diagnosed when the characteristic pear or sickle-shaped, binucleate organisms were detected either attached to small intestinal enterocytes or, most frequently, in the intervillous spaces. The detection of *Giardia* organisms was facilitated by the periodic acid–Schiff/alcian blue stain routinely used on all duodenal biopsy specimens at the Miraca Life Sciences laboratory.

Duodenal specimens exhibiting reduced villous height were classified as partial villous atrophy (corresponding to Marsh class 3a) and subtotal/total villous atrophy (corresponding to Marsh 3b and Marsh 3c) [18]. Specimens were classified as duodenal intraepithelial lymphocytosis if their duodenal biopsy exhibited $\geq$25 lymphocytes per 100 enterocytes in the presence of a normal villous height/crypt depth ratio.

Of the patients in our data set, 363,788 also had gastric biopsies performed on the same date as their duodenal biopsy; gastric biopsies were evaluated by the updated Sydney System [19]. The diagnosis of *H. pylori* gastritis was made when *H. pylori* organisms were detected on gastric biopsies that were stained by a specific polyclonal immunochemical stain (Cell Marque Corporation, Rocklin, California), as is routine practice.

Patient ethnicity was classified using a computer algorithm that analyzed patient first and last name. This is a previously described method [20, 21] for classifying patients into ethnic categories and is modified from similar models [22, 23]. This model reached greater than 95% specificity by continuously adjusting the algorithm against lists of persons of known ethnicity [21]. The specificity reached by this model is similar to that of other self-reported ethnic classifications [24, 25]. Using this method, patients were grouped into the following categories: African, Armenian, East Asian, Indian, Latino, Jewish, Middle Eastern, North European, South European, Portuguese, Slavic, and Other American. The group Other American consisted of individuals who were not classified into any of the other ethnic groups. Patients whose ethnicity was unknown or whose names suggested more than one ethnicity were classified into the unknown category.

To assess whether the diagnosis of giardiasis varied over different seasons, we classified each procedure as occurring in the winter (December–February), spring (March–May), summer (June–August), or fall (September–November) [26].

We classified patients' locations as urban and rural, using an online research tool (Social Explorer) that provides access to current and historical census data [27]. We used data based on the US Census Bureau's 2010 urban and rural classification. This data source provides the percentage of a population in each US ZIP code that is in a rural or urban area. We classified each patient's ZIP code as urban if greater than 50% of the population residing in that ZIP code lived in an urban area, otherwise that ZIP code was classified as rural, in keeping with convention [28]. When available we used a patient's ZIP code of residence. When residential ZIP code was not available ($n = 151{,}394$), or if the patient's residential ZIP code did not correspond with available census data ($n = 4265$), we used the ZIP code of the gastroenterology practice from which the specimen was sent. When neither patient nor provider ZIP code was listed, or if neither ZIP code corresponded to available census

data, such patients ($n = 1138$) were excluded from the analysis concerning urban and rural setting.

Regions were defined based on the classification outlined in the CDC's 2011–2012 giardiasis surveillance report, as follows: Northeast (Connecticut, Maine, Massachusetts, New Hampshire, New Jersey New York, Pennsylvania, Rhode Island, Vermont), Midwest (Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin), South (Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, West Virginia, Virginia), Northwest (Alaska, Idaho, Montana, Oregon, Washington, Wyoming), and Southwest (Arizona, California, Colorado, Hawaii, Nevada, New Mexico, Utah) [3]. Patients were sorted into regional categories based on their ZIP codes. The same ZIP codes used for the urban and rural classification described above were used to classify the patients into regional categories. As Puerto Rico was not categorized into a region in the CDC's report, we excluded patients ($n = 481$) residing in Puerto Rico from the regional analysis. In total 1620 were excluded from our regional analysis.

Patient sociodemographic and clinical data (age, sex, ethnicity, endoscopy indication, urban–rural, region, season, year, and presence of *H. pylori*, atrophic gastritis, and giardiasis) were calculated and expressed as either a mean or a percentage of the total study population, where applicable. We used the Chi-square and Fisher's exact tests to compare the distributions of these characteristics among patients with giardiasis to those with normal duodenal biopsies. We then performed multiple logistic regression to assess for independent associations of giardiasis with each characteristic, using odds ratios (ORs) and their 95% confidence intervals (CIs). In the first multivariate model, we included age, sex, ethnicity, endoscopy indication, urban versus rural, region, season, and year. The second model was restricted to those individuals who underwent gastric biopsy and the presence of *H. pylori* and atrophic gastritis was added. All p values are two-sided. We used SAS version 9.4 (Cary, NC) for all analyses. This research was deemed "non-human subjects research" by the Columbia University Medical Center's Institutional Review Board as patient data were de-identified before use by the investigators.

Results

During the time period of the study (January 2, 2008 through December 31, 2015), 433,677 patients underwent duodenal biopsy. Of this population, 864 patients were excluded for possible erroneous age (recorded as greater than 90 years). The 432,813 patients remaining served as our study population. Demographic information is shown in Table 1. The mean age was 52.2 years, and the majority of patients (76%) were older than 40 years. For 429 patients, sex was not recorded. Out of the remaining 432,384 patients, 66% were female. The most common indication for endoscopy was gastroesophageal reflux disease (34%), followed by diarrhea (15%) and anemia (13%). Most of the study population lived in urban areas (93%), and a plurality was located in the Southern US (35%). Giardiasis was diagnosed in 457 patients, 0.11% of the study population. *H. pylori* was diagnosed in 34,205 patients and atrophic gastritis in 2167 patients, which made up 9.4% and 0.6%, respectively, of those who underwent gastric biopsy ($n = 363,788$).

Univariate analysis of characteristics of those with giardiasis compared to those without giardiasis is shown in Table 2. Patients with giardiasis had a mean age of 50.4 years compared to a mean age of 52.2 years in those with normal duodenal biopsies ($p = 0.029$). As compared to patients with normal duodenal biopsies, patients with giardiasis were far more likely to be male (57.8 vs. 34.1%, $p < 0.0001$). On multivariate analysis (Table 3), there was a strong association between giardiasis and male sex (OR 2.64; 95% CI 2.19–3.18; $p < 0.0001$).

Giardiasis was more common among those with Middle Eastern ($p = 0.0248$) and Latino ($p = 0.0348$) ethnicity on univariate analysis; however, this did not meet statistical significance on multivariate analysis, compared to other Americans (Middle Eastern; OR 2.39; 95% CI 0.98–5.81) (Latino; OR 1.36; 95% CI 0.94–1.97). None of the endoscopy indications were significantly associated with giardiasis. There was also no statistically significant seasonal variation nor variation by year of endoscopy procedure.

Among patients who had a gastric biopsy, patients with giardiasis were significantly more likely to be colonized with *H. pylori* compared to those without giardiasis (25.7 vs. 9.4%, $p < 0.0001$). On multivariate analysis, the odds of having giardiasis were increased in patients with *H. pylori* (OR 3.28; 95% CI 2.61–4.12; $p < 0.0001$). There was no significant association between the presence of atrophic gastritis and giardiasis (OR 1.72; 95% CI 0.55–5.38; $p = 0.3544$).

While there was no urban or rural difference observed between patients with giardiasis compared to those with normal duodenal biopsies on univariate analysis ($p = 0.1628$), there was a statistically significant variation in the regional distribution of giardiasis ($p = 0.0069$). Both patients with giardiasis and those with normal biopsies were more likely to live in the Southern US (41 vs. 35%), followed by the Northeast (23 vs. 21%). When compared to patients in the Southwest on multivariate analysis, those in the South had an increased odds of giardiasis (OR 1.50;

Table 1 Patient characteristics

Clinical characteristic	Number of patients (%)
Age (in years)	
Mean age (±SD)	52.24 (±17.78)
≤18	12,967 (3.00)
19–29	42,871 (9.91)
30–39	49,554 (11.45)
40–49	73,135 (16.90)
50–59	91,058 (21.04)
≥60	163,228 (37.71)
Sex (unknown = 429)	
Males	147,372 (34.08)
Females	285,012 (65.92)
Ethnicity	
Undetermined/unknown	73,471 (16.98)
African	69 (0.02)
Middle Eastern	1539 (0.36)
Armenian	62 (0.01)
East Asian	3815 (0.88)
Indian	1609 (0.37)
Jewish	14,912 (3.45)
Latino	23,473 (5.42)
Portuguese	1036 (0.24)
North European	3069 (0.71)
South European	12,838 (2.97)
Slav	6672 (1.54)
Other American	290,248 (67.06)
EGD indication/clinical symptoms	
Anemia	57,774 (13.35)
Dyspepsia	36,635 (8.46)
Diarrhea	64,772 (14.97)
Weight loss	29,753 (6.87)
Vomiting	51,724 (11.95)
Hematemesis	1841 (0.43)
GERD	148,940 (34.41)
Dysphagia	40,715 (9.41)
Epigastric pain	25,007 (5.78)
Unknown/other	122,732 (28.36)
ZIP Code (unknown = 1138)	
Urban	398,968 (92.52)
Rural	32,241 (7.48)
Region (unknown = 1620)	
Northeast	92,046 (21.35)
Midwest	55,341 (12.83)
South	150,267 (34.85)
Northwest	46,615 (10.81)
Southwest	86,924 (20.16)
Season	
Winter	100,956 (23.33)
Spring	109,050 (25.20)
Summer	110,972 (25.64)
Fall	111,835 (25.84)
Year	
2008	37,057 (8.56)
2009	44,859 (10.36)
2010	56,543 (13.06)
2011	58,506 (13.52)
2012	57,802 (13.35)
2013	57,865 (13.37)
2014	60,579 (14.00)
2015	59,602 (13.77)
Presence of *H. pylori* (among those with gastric biopsy $n = 363,788$)	34,205 (9.40)
Presence of *Giardia*	457 (0.11)
Atrophic gastritis (among those with gastric biopsy $n = 363,788$)	2167 (0.60)

95% CI 1.14–1.97; $p = 0.0108$). Figure 1 shows the correlation of giardiasis with *H. pylori* in each region, with the South and Northeast having the highest prevalence of both diagnoses.

Villous architecture of patients with giardiasis is enumerated in Table 4. Among 457 patients with giardiasis, the majority (96%) had normal villous architecture. Diffuse intraepithelial lymphocytosis with normal villous architecture was present in 14 patients (3%), while partial villous atrophy was present in 3 patients (0.7%) and subtotal/total villous atrophy was present in 1 patient (0.22%).

Discussion

In this study, we identified three independent factors associated with giardiasis: male sex, residing in the Southern US, and colonization with *H. pylori*. An increased male prevalence of giardiasis has been reported in studies from Canada and Germany [29, 30], and by the European Center for Disease Prevention and Control in 2008 [31] but not in 2010 [32]. In the US, the CDC only reported a male predominance in giardiasis from 1998 to 2012 [3, 14–17] but not from 1992 to 1997 [13].

Our finding that males are more likely to be infected with *Giardia* is also found with other parasitic diseases: *Cyrptosporidum* [30], *Entamoeba histolytica*, *Plasmodium* species, *Leishmania* species, *Schistosoma* species, *and Paracoccidioides brasiliensis* [33]. Hormonal differences between the sexes may be a cause of this increased prevalence as more severe infection profiles have been

Table 2 Univariate analysis: association of *Giardia* with sociodemographic and clinical characteristics

Clinical characteristic	Normal duodenal biopsy ($n = 432,356$)	Giardiasis ($n = 457$)	p value
Age (in years)			
Mean age (±SD)	52.24 (±17.78)	50.42 (±18.15)	0.029
≤18	12,948 (2.99)	19 (4.16)	0.1720
19–29	42,824 (9.90)	47 (10.28)	
30–39	49,487 (11.45)	67 (14.66)	
40–49	73,065 (16.90)	70 (15.32)	
50–59	90,966 (21.04)	92 (20.13)	
≥60	163,066 (37.72)	162 (35.45)	
Sex			
Male	147,109 (34.06)	263 (57.68)	<.0001
Female	284,819 (65.94)	193 (42.32)	
Ethnicity			
Undetermined/Unknown	73,410 (16.98)	61 (13.35)	0.0388
African	69 (0.02)	0	1.000
Middle Eastern	1534 (0.35)	5 (1.09)	0.0248
Armenian	62 (0.01)	0	1.000
East Asian	3810 (0.88)	5 (1.09)	0.6092
Indian	1605 (0.37)	4 (0.88)	0.0926
Jewish	14,900 (3.45)	12 (2.63)	0.3365
Latino	23,438 (5.42)	35 (7.66)	0.0348
Portuguese	1034 (0.24)	2 (0.44)	0.2988
North European	3069 (0.71)	0	0.0850
South European	12,824 (2.97)	14 (3.06)	0.9024
Slav	6661 (1.54)	11 (2.41)	0.1330
Other American	289,940 (67.06)	308 (67.40)	0.8787
EGD indication/clinical symptoms			
Anemia	57,719 (13.35)	55 (12.04)	0.4088
Dyspepsia	36,599 (8.47)	36 (7.88)	0.6520
Diarrhea	64,709 (14.97)	63 (13.79)	0.4793
Weight loss	29,717 (6.87)	36 (7.88)	0.3964
Vomiting	51,668 (11.95)	56 (12.25)	0.8416
Hematemesis	1840 (0.43)	1 (0.22)	1.0000
GERD	148,767 (34.41)	173 (37.86)	0.1211
Dysphagia	40,682 (9.41)	33 (7.22)	0.1092
Epigastric pain	24,973 (5.78)	34 (7.44)	0.1276
Unknown/other	122,616 (28.36)	116 (25.38)	0.1582
ZIP code (unknown = 1139)			
Urban	398,995 (92.54)	415 (90.81)	0.1628
Rural	32,222 (7.46)	42 (9.19)	
Region (unknown = 1620)			
Northeast	91,940 (21.34)	106 (23.35)	0.0069
Midwest	55,295 (12.84)	46 (10.13)	
South	150,079 (34.84)	188 (41.41)	
Northwest	46,574 (10.81)	41 (9.03)	
Southwest	86,851 (20.16)	73 (16.08)	
Season			
Winter	100,848 (23.33)	108 (23.63)	0.8656
Spring	108,928 (25.19)	122 (26.70)	
Summer	110,858 (25.64)	114 (24.95)	

Table 2 continued

Clinical characteristic	Normal duodenal biopsy ($n = 432,356$)	Giardiasis ($n = 457$)	p value
Fall	111,722 (25.84)	113 (24.73)	
Year			
2008	37,023 (8.56)	34 (7.44)	0.2351
2009	44,820 (10.37)	39 (8.53)	
2010	56,480 (13.06)	63 (13.79)	
2011	58,438 (13.52)	68 (14.88)	
2012	57,729 (13.35)	73 (15.97)	
2013	57,800 (13.37)	65 (14.22)	
2014	60,512 (14.00)	67 (14.66)	
2015	59,554 (13.77)	48 (10.50)	
Presence of *H. pylori*	34,102 (9.38)	103 (25.69)	< 0.0001
Atrophic gastritis	2164 (0.60)	3 (0.75)	0.5187

found in male animal models of *E. histolytica,* malaria, leishmaniasis, and paracoccidioidomycosis (but not schistosomiasis) [33]. Alternatively, the increased male prevalence of giardiasis could be influenced by environmental risk factors. Staphylococcus and tuberculosis, two other infectious diseases more common in males, have been linked to increased male performance of contact sports and occupational exposure to lung damaging toxins, respectively [34–36]. A third possibility may be an association between HIV and giardiasis [37–39], given that males make up 67% of US HIV diagnoses [40]. As we did not have access to patients' medical conditions, we could not take into account HIV or AIDS diagnoses into our multivariate analysis.

We found an association between giardiasis and residing in the Southern US. This differs from the CDC's finding of the highest incidence in the Northwest, at a rate of 9.4 per 100,000 in 2011 and 8.5 per 100,000 in 2012 [3]. The CDC acknowledges that its geographic distribution of the disease is incomplete because giardiasis is not a reportable disease in six southern states (Texas, Oklahoma, Mississippi, Kentucky, Tennessee, and North Carolina) [3]. As our study included giardiasis cases from these six states ($n = 87$), our sample might reflect a true geographic predominance in the Southern states. In fact, 14.6% (63,118/431,193) of all specimens and 19% (87/457) of giardiasis specimens included in our analysis are from states that are not tracked by the CDC. This could explain the difference in the prevalence of giardiasis in our study compared to that published by the CDC.

Our third finding of a strong association between giardias*i*s and *H. pylori* has been previously reported in the literature [41–44], though not in the US. As *H. pylori* and *Giardia* are known to spread by the fecal–oral route, it is likely that common environmental exposures are responsible for co-infection. Another possibility is that one of the pathogens creates a more favorable environment for co-infection with the other pathogen. One study found that co-infection with *Schistosoma japonicum* and *H. pylori* was associated with reduced *H. pylori* antibody titers compared to *H. pylori* infection alone [45]. Another study found that co-infection with *H. pylori* and *Salmonella typhimurium* in mice caused reduced severity of inflammation in both the stomach and cecum compared to either infection alone [46]. It is therefore possible that the presence of *H. pylori* in the stomach produces a favorable environment for infection with *Giardia* in the duodenum, or vice versa. The lack of association between atrophic gastritis and giardiasis within our study suggests that gastric acidity may not influence duodenal giardia infection. More research is needed to clarify the interplay of these co-infections on the gastrointestinal tract.

We found normal duodenal villous architecture in 96% of patients with giardiasis, which has been previously reported by Oberhuber et al. [47]. Though partial villous atrophy with intraepithelial lymphocytes, which is a characteristic of celiac disease, has been found in giardiasis [48], these features are very uncommon, comprising less than 5% of the histological characteristics of our sample and that of Oberhuber et al. [47]. In addition, we found no specific procedural indication which predicted the presence of giardiasis in duodenal biopsies.

Our study has several limitations. We lacked data regarding comorbid conditions (especially HIV), severity of symptoms, or outcome of treatment. This information would have allowed us to explore the relationship between giardiasis and immunocompromised status, travel history, or other exposures that have been reported in other studies [29]. Our lack of information about state-specific giardiasis outbreaks due to contaminated food or water sources, could have altered our regional analysis. Our classification of season by months may not have adequately addressed the

Table 3 Multivariate analysis: predictors of giardiasis on duodenal biopsy

Variable	OR	95% CI	*p* value
Age (in years)			
≤18	1.0	–	0.2707
19–29	0.92	0.53–1.58	
30–39	1.12	0.67–1.89	
40–49	0.80	0.48–1.36	
50–59	0.83	0.50–1.38	
≥ 60	0.80	0.49–1.30	
Sex			
Male	2.64	2.19–3.18	<.0001
Female	1.0	–	–
Ethnicity			
Other American	1.0	–	0.4858
African	NC	NC	
Middle Eastern	2.39	0.98–5.81	
Armenian	NC	NC	
East Asian	1.24	0.51–3.00	
Indian	1.90	0.70–5.11	
Jewish	0.76	0.43–1.36	
Latino	1.36	0.94–1.97	
Portuguese	1.79	0.44–7.21	
North European	NC	NC	
South European	1.02	0.59–1.75	
Slav	1.56	0.85–2.86	
EGD indication/clinical symptoms			
Anemia	0.85	0.60–1.19	0.3393
Dyspepsia	0.85	0.57–1.27	0.4394
Diarrhea	0.89	0.66–1.19	0.4207
Weight loss	1.03	0.72–1.49	0.8590
Vomiting	1.02	0.75–1.39	0.9152
Hematemesis	0.42	0.06–2.99	0.3848
GERD	1.01	0.77–1.31	0.9607
Dysphagia	0.70	0.48–1.02	0.0600
Epigastric pain	1.16	0.79–1.69	0.4458
Unknown/other	0.87	0.60–1.26	0.4562
ZIP code			
Urban	0.80	0.58–1.11	0.1838
Rural	1.0	–	–
Region			
Northeast	1.25	0.91–1.69	
Midwest	0.99	0.69–1.45	
South	1.50	1.14–1.97	
Northwest	1.03	0.70–1.51	
Southwest	1.00	–	0.0108
Season			
Winter	1.0	–	0.8914
Spring	1.07	0.82–1.38	
Summer	0.97	0.74–1.27	
Fall	0.98	0.75–1.27	
Year			
2008	1	–	0.5275
2009	1.02	0.64–1.63	
2010	1.29	0.84–1.98	
2011	1.39	0.91–2.12	
2012	1.48	0.98–2.25	
2013	1.31	0.86–2.01	
2014	1.29	0.85–1.97	
2015	1.14	0.55–2.37	
Presence of *H. pylori*[a]	3.28	2.61–4.12	<.0001
Atrophic gastritis[a]	1.72	0.55–5.38	0.3547

[a] Among patients who had gastric biopsies

NC not calculated due to low number of cases

variation in climate across regions of the US. Additionally, our study's use of duodenal biopsy to identify patients with giardiasis may have induced selection bias. While duodenal biopsy has a sensitivity of 82.5–100% for the diagnosis of giardiasis, diagnosis by stool examination is far more common, due to its noninvasive nature [7]. The lack of association between younger age and giardiasis in our study (in contrast to previous studies) [3, 13–17, 30] may be due to the fact that children are more likely to be diagnosed via the noninvasive stool examination as compared to adults. To our knowledge, this is the largest study to date to assess predictive factors for giardiasis in the US. In addition to the sample size, strengths include its geographic breadth (including all 50 states, the District of Columbia and Puerto Rico), the inclusion of a previously validated ethnicity categorization, and the systematic classification of duodenal histology.

We additionally acknowledge that the method we used for the ethnic classification of our patients is not perfect. Since we were most interested in relatively recent generations of immigrants, whose customs may still incorporate traditions (including dietary) that could affect the prevalence of certain conditions, our algorithms were guided by the principle that specificity was to take priority over sensitivity. Thus, we included in any given ethnic group only subjects with concordant first and last names, using the working theory that people with concordant names were more likely to be either first-generation immigrants or the children of two such immigrants. In addition, we used country-specific information to adapt our criteria. Of course, since this is an approximation and many cases would be incorrectly classified, we created the category "undetermined," which includes persons with names that have their roots in different languages.

In conclusion, we have identified predictive factors for giardiasis among patients with duodenal biopsies in the US

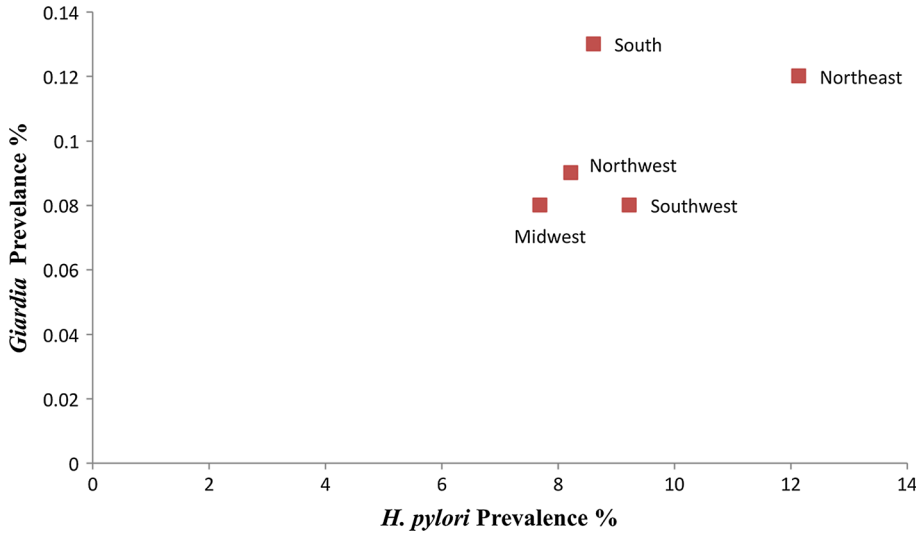

Fig. 1 Correlation between *H. pylori* gastritis and duodenal giardiasis by region in the United States

Table 4 Characterization of duodenal biopsies in giardiasis patients

Villous architecture	Duodenal biopsies ($n = 457$)
Normal	439 (96.06)
Duodenal intraepithelial lymphocytosis	14 (3.06)
Partial villous atrophy	3 (0.66)
Subtotal/total villous atrophy	1 (0.22)

over an 8-year period, using a national pathology database. We found that male sex, being colonized with *H. pylori,* and residing in the Southern US put an individual at an increased risk of infection with giardiasis. These clinical and demographic findings may aid medical practitioners in the assessment and testing of patients' symptoms compatible with this infection.

Author's contribution HMZ, PHRG, RMG, KOT, and BL were involved in study concept and design. RMG and KOT acquired the data. HMZ, PHRG, RMG, KOT, and BL analysed and interpreted the data and critically revised the manuscript for important intellectual content. HMZ and BL drafted the manuscript and involved in statistical analysis. BL supervised the study. All authors approve the final manuscript submitted and they approve the authorship list.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflicts of interest and nothing to declare.

Ethics approval This analysis was submitted to the Institutional Review Board of Columbia University and was deemed non-human subjects research, since all data were de-identified prior to being provided to the investigators.

References

1. Adam RD. Biology of *Giardia lamblia*. *Clin Microbiol Rev*. 2001;14:447–475.
2. Muhsen K, Levine MM. A systematic review and meta-analysis of the association between *Giardia lamblia* and endemic pediatric diarrhea in developing countries. *Clin Infect Dis*. 2012;55:S271–S293.
3. Painter EJ, Gargano JW, Collier SA, Yoder JS. Centers for Disease Control and Prevention (CDC) Giardiasis Surveillance: United States 2011–2012. *MMWR Surveill Summ*. 2015;64:15–25.
4. Lane S, Lloyd D. Current trends in research into the waterborne parasite *Giardia*. *Crit Rev Microbiol*. 2002;28:123–147.
5. Scallan E, Hoekstra RM, Angulo FJ, et al. Foodborne illness acquired in the United States—major pathogens. *Emerg Infect Dis*. 2011;17:7–15.
6. Collier SA, Stockman LJ, Hicks LA. Direct healthcare costs of selected diseases primarily or partially transmitted by water. *Epidemiol Infect*. 2012;140:2003–2013.
7. Lebwohl B, Deckelbaum RJ, Green PHR. Giardiasis. *Gastrointest Endosc*. 2003;57:906–913.
8. DuPont HL. Persistent Diarrhea: a Clinical Review. *Jama*. 2016;315:2712–2723.
9. Canteu PT, Roy S, Lee B, et al. Study of nonoutbreak giardiasis: novel findings and implications for research. *Am J Med*. 2011;124:1175.e1–1175.e8.
10. Hellard ME, Sinclair MI, Hogg GG, Fairley CK. Prevalence of enteric pathogens among community based asymptomatic individuals. *J Gastroenterol Hepatol*. 2000;15:290–293.
11. Stolte M, Vogele-Dirks H. Giardiasis: a simple diagnosis that is often delayed. *Z Gastroenterol*. 1991;29:373–377.
12. Carr MF Jr, Ma J, Green PH. Giardia lamblia in patients undergoing endoscopy: lack of evidence for a role in nonulcer dyspepsia. *Gastroenterology*. 1988;95:972–974.
13. Furness BW, Beach MJ, Roberts JM. Centers for Disease Control and Prevention (CDC) giardiasis surveillance: United States 1992–1997. *MMWR Surveill Summ*. 2000;11:1–13.

14. Hlavsa MC, Watson JC, Beach MJ. Centers for Disease Control and Prevention (CDC) giardiasis surveillance: United States 1998–2002. *MMWR Surveill Summ*. 2005;54:9–16.
15. Yoder JS, Beach MJ, Roberts JM. Centers for Disease Control and Prevention (CDC) giardiasis surveillance: United States 2003–2005. *MMWR Surveill Summ*. 2007;56:11–18.
16. Yoder JS, Harral C, Beach MJ. Giardiasis surveillance: United States, 2006–2008. *MMWR Surveill Summ*. 2010;59:15–25.
17. Yoder JS, Gargano JW, Wallace RM, Beach MJ. Centers for Disease Control and Prevention (CDC) giardiasis surveillance: United States 2009–2010. *MMWR Surveill Summ*. 2012;61:13–23.
18. Marsh MN. Gluten, major histocompatibility complex, and the small intestine: a molecular and immunologic approach to the spectrum of gluten sensitivity ('celiac sprue'). *Gastroenterology*. 1992;102:330–354.
19. Dixon MF, Genta RM, Yardley JH, et al. Classification and grading of gastritis: the updated Sydney System. International Workshop on the Histopathology of Gastritis, Houston 1994. *Am J Surg Pathol*. 1996;20:1161–1181.
20. Turner K, Genta RM, Sonnenberg A. Ethnic distribution of microscopic colitis in the United States. *Inflamm Bowel Dis*. 2015;21:2634–2639.
21. Krigel A, Turner KO, Makharia GK, Green PHR, Genta RM, Lebwohl B. Ethnic variations in duodenal villous atrophy consistent with celiac disease in the United States. *Clin Gastroenterol Hepatol*. 2016;14:1105–1111.
22. Elliott MN, Morrison PA, Fremont A, et al. Using the Census Bureau's surname list to improve estimates of race/ethnicity and associated disparities. *Health Serv Outcomes Res Methodol*. 2009;9:69–83.
23. Elliot MN, Fremont A, Morrision PA, et al. A new method for estimating race/ethnicity and associated disparities where administrative records lack self-reported race/ethnicity. *Health Serv Res*. 2008;43:1722–1736.
24. Saunders CL, Abel GA, El Turabi A, et al. Accuracy of routinely recorded ethnic group information compared with self-reported ethnicity: evidence from the English Cancer Patient Experience survey. *BMJ Open*. 2013;3:e002882.
25. Mathur R, Bhaskaran K, Chaturvedi N, et al. Completeness and usability of ethnicity data in UK-based primary care and hospital databases. *J Public Health*. 2014;36:684–692.
26. Jensen ET, Shah ND, Hoffman K, Sonnenberg A, Genta RM, Dellon ES. Seasonal variation in detection of oesophageal eosiniphilia and eosinophilic oesphagitis. *Alliment Pharmacol Ther*. 2015;42:461–469.
27. US Census Bureau. Census of Population and Housing, 2010. Prepared by Social Explorer. Accessed July 2016.
28. Hall SA, Kaufman JS, Rickets TC. Defining urban and rural areas in US epidemiologic studies. *J Urban Health Bull NY Acad Med*. 2006;82:162–174.
29. Espelage W, an der Heiden M, Stark K, Alpers K. Characteristics and risk factors for symptomatic *Giardia lamblia* infections in Germany. *BMC Public Health*. 2010;10:41.
30. Laupland KB, Church DL. Population-based laboratory surveillance for *Giardia* sp. and Cryptosporidium sp. infections in a large Canadian health region. *BMC Infect Dis*. 2005;5:72.
31. European Centre for Disease Prevention and Control. *Annual Epidemiological Report on Communicable Diseases in Europe 2008*. Stockholm: European Centre for Disease Prevention and Control; 2008.
32. European Centre for Disease Prevention and Control. *Annual Epidemiological Report on Communicable Diseases in Europe 2010*. Stockholm: European Centre for Disease Prevention and Control; 2010.
33. Bernin H, Lotter H. Sex bias in the outcome of human tropical infectious diseases: influence of steroid hormones. *J Infect Dis*. 2014;209:S107–S113.
34. Humphreys H, Fitzpatick F, Harvey BJ. Gender differences in rates of carriage and bloodstream infection caused by methicillin-resistant Staphylococcus aureus. Are they real, do they matter and why? *Clin Infect Dis*. 2015;61:1708–1714.
35. Neyrolles O, Quintana-Murci L. Sexual inequality in tuberculosis. *PLoS Med*. 2009;6:e1000199.
36. Nhamoyebonde S, Leslie A. Biological differences between the sexes and susceptibility to tuberculosis. *J Infect Dis*. 2014;2014:S100–S106.
37. Schmerin MJ, Jones TC, Klein H. Giardiasis: association with homosexuality. *Ann Intern Med*. 1978;88:801–803.
38. Moolasart P. *Giardia lamblia* in AIDS patients with diarrhea. *J Med Assoc Thai*. 1999;82:654–659.
39. Esfandiari A, Swartz J, Teklehaimanot S. Clustering of giardiosis among AIDS patients in Los Angeles County. *Cell Mol Biol (Noisy-le-grand)*. 1997;43:1077–1083.
40. Centers for Disease Control and Prevention. HIV at a glance [Internet]. Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral hepatitis, sexual transmitted diseases and tuberculosis prevention. http://www.cdc.gov/hiv/statistics/overview/ataglance.html. Accessed July 2016.
41. Zeyrek D, Zeyrek F, Cakmak A, Cekin A. Association of *Helicobacter pylori* and *giardiasis* in children with recurrent abdominal pain. *Turkiye Parazitol Derg*. 2008;32:4–7.
42. Moreira ED Jr, Nassri VB, Santos RS, Matos JF, de Carvalho WA, et al. Association of *Helicobacter pylori* infection and giardiasis: results from a study of surrogate markers for fecal exposure among children. *World J Gastroenterol*. 2005;11:2759–2763.
43. Ankarklev J, Hestvik E, Lebbad M, et al. Common coinfections of *Giardia intestinalis* and *Helicobacter pylori* in non-symptomatic ugandan children. *PLoS Negl Trop Dis*. 2012;6:e1780.
44. Doglioni C, De Boni M, Cielo R, et al. Gastric giardiasis. *J Clin Pathol*. 1992;45:964–967.
45. Du Y, Agnew A, Ye XP, Robinson PA, Forman D, et al. *Helicobacter pylori* and *Schistosoma japonicum* co-infection in a Chinese population: helminth infection alters humoral responses to *H. pylori* and serum pepsinogen I/II ratio. *Microbes Infect*. 2006;8:52–60.
46. Higgins PD, Johnson LA, Luther J, Zhang M, Sauder KL, et al. Prior *Helicobacter pylori* infection ameliorates *Salmonella typhimurium*-induced colitis: mucosal crosstalk between stomach and distal intestine. *Inflamm Bowel Dis*. 2011;17:1398–1408.
47. Oberhuber G, Kastner N, Stolte M. Giardiasis: a histologic analysis of 567 cases. *Scand J Gastroenterol*. 1997;32:48–51.
48. Gillon J. Clinical studies in adults presenting with giardiasis to a gastro-intestinal unit. *Scott Med J*. 1985;30:89–95.