

Prevalence of Irritable Bowel Syndrome and Chronic Fatigue 10 Years After *Giardia* Infection

Sverre Litleskare,^{*,‡} Guri Rortveit,^{*,‡} Geir Egil Eide,^{*,§} Kurt Hanevik,^{||,¶} Nina Langeland,^{||,¶} and Knut-Arne Wensaas^{*,‡}

^{*}Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway; [‡]Research Unit for General Practice, Uni Research Health, Bergen, Norway; [§]Centre for Clinical Research, Haukeland University Hospital, Bergen, Norway; ^{||}National Centre for Tropical Infectious Diseases, Haukeland University Hospital, Bergen, Norway; [¶]Department of Clinical Science, University of Bergen, Bergen, Norway

BACKGROUND & AIMS: Irritable bowel syndrome (IBS) is a complication that can follow gastrointestinal infection, but it is not clear if patients also develop chronic fatigue. We investigated the prevalence and odds ratio of IBS and chronic fatigue 10 years after an outbreak of *Giardia lamblia*, compared with a control cohort, and changes in prevalence over time.

METHODS: We performed a prospective follow-up study of 1252 laboratory-confirmed cases of giardiasis (exposed), which developed in Bergen, Norway in 2004. Statistics Norway provided us with information from 2504 unexposed individuals from Bergen, matched by age and sex (controls). Questionnaires were mailed to participants 3, 6, and 10 years after the outbreak. Results from the 3- and 6-year follow-up analyses have been published previously. We report the 10-year data and changes in prevalence among time points, determined by logistic regression using generalized estimating equations.

RESULTS: The prevalence of IBS 10 years after the outbreak was 43% (n = 248) among 576 exposed individuals and 14% (n = 94) among 685 controls (adjusted odds ratio for development of IBS in exposed individuals, 4.74; 95% CI, 3.61–6.23). At this time point, the prevalence of chronic fatigue was 26% (n = 153) among 587 exposed individuals and 11% (n = 73) among 692 controls (adjusted odds ratio, 3.01; 95% CI, 2.22–4.08). The prevalence of IBS among exposed persons did not change significantly from 6 years after infection (40%) to 10 years after infection (43%; adjusted odds ratio for the change 1.03; 95% CI, 0.87–1.22). However, the prevalence of chronic fatigue decreased from 31% at 6 years after infection to 26% at 10 years after infection (adjusted odds ratio for the change 0.74; 95% CI, 0.61–0.90).

CONCLUSION: The prevalence of IBS did not change significantly from 6 years after an outbreak of *Giardia lamblia* infection in Norway to 10 years after. However, the prevalence of chronic fatigue decreased significantly from 6 to 10 years afterward. IBS and chronic fatigue were still associated with giardiasis 10 years after the outbreak.

Keywords: Epidemiology; Bacteria; Microbiota; Long-Term Outcome.

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder that constitutes a substantial economic burden to society.¹ It is a common condition, with a pooled prevalence of 11.2%.¹ Chronic fatigue (CF) is another common complaint among patients seeking primary care, and 1 study found a prevalence of 24% in this population.² Despite its potentially debilitating features, it is less investigated. Fatigue is more commonly studied as part of the less prevalent CF syndrome (CFS).³ IBS and CF or CFS share a lack of consistent biologic findings and both conditions are often categorized as functional disorders.⁴

Etiology for both IBS and CF is incompletely understood, but both conditions have been associated with

previous infections.^{3,5} Postinfectious IBS (PI-IBS) has been described following outbreaks, among travelers returning from abroad, or as sporadic cases.^{5–10} The rate of recovery from PI-IBS varies between studies, and bacterial infections seem to be associated with more

Abbreviations used in this paper: AFE, attributable fraction among the exposed; aOR, adjusted odds ratio; CF, chronic fatigue; CFS, chronic fatigue syndrome; CI, confidence interval; IBS, irritable bowel syndrome; OR, odds ratio; PI-IBS, post-infectious irritable bowel syndrome.

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1542-3565/\$36.00
<https://doi.org/10.1016/j.cgh.2018.01.022>

prolonged symptoms than viral infections.¹⁰ One study after an outbreak of bacterial dysentery reported that IBS was associated with exposure up to 8 years after the acute infection.⁶ A more recent study found that IBS was associated with shigellosis after 1 and 3 years' post-exposure follow-up, but not after 5, 8, or 10 years.⁷ Postinfectious CF as part of CFS has been reported as a complication after various acute viral and bacterial infections.^{3,11–14}

In the autumn of 2004, the parasite *Giardia lamblia* contaminated 1 of the municipal drinking-water reservoirs in Bergen, likely due to broken sewage pipes. This is one of the largest waterborne outbreaks ever recorded in Norway,¹⁵ and 1252 patients had laboratory confirmed giardiasis that was linked to the outbreak.⁹ Several post-infectious conditions have been studied in this cohort over time, and our research group has previously found an association between *Giardia lamblia* infection and IBS and CF both 3 and 6 years after the acute illness.^{8,9} The prevalence fell from 3 to 6 years for both conditions.

The primary aim of the current study was to estimate the prevalence and odds ratio of IBS and CF 10 years after acute giardiasis relative to a control cohort. The secondary aims were to investigate changes in prevalence from 3 to 10 and from 6 to 10 years and to estimate incidence, recovery, and persistence of these conditions.

Methods

Participants

This study was a prospective follow-up of a cohort of 1252 patients (the exposed group) and a control group 3,

6, and 10 years after laboratory verified *Giardia* infection during a waterborne outbreak in the autumn of 2004. On our request, Statistics Norway established a 2:1 control group of 2504 individuals from Bergen matched by age and sex. There was a predominance of women in the exposed target population (61%, 764 of 1252). Children under 18 years of age were excluded from the data collection at the 10-year follow-up, and hence these children were retrospectively also excluded from all analyses based on the data collections at the 3- and 6-year follow-ups (Table 1). Analyses of prevalence changes from 3 to 6 years⁸ have been published previously, but were calculated anew for this study. The Regional Committee for Ethics in Medical Research approved the study (ref. no. 2014/1372).

Variables

The primary outcome variables were IBS and CF 10 years after giardiasis in the exposed and the control group, as well as the following subgroup categories: severe IBS, severe CF, IBS, and CF combined, IBS only and CF only. Secondary outcomes were changes in prevalence of IBS and CF from 3 to 10 years (for IBS and CF only), and from 6 to 10 years (all subgroup categories). Respondents who had either IBS or CF at all 3 follow-ups were defined as having a persistent condition.

IBS was defined according to the Rome III criteria,¹⁶ where respondents who had recurrent abdominal pain or discomfort at least 3 days/month in the last 3 months were defined as having IBS if their pain or discomfort was also associated with 2 or more of the additional IBS criteria. These symptoms must also have had an onset at

Table 1. Cohorts Available for Analyses 3, 6, and 10 Years After a *Giardia lamblia* Outbreak in Bergen, Norway, 2004

Cohort	Exposed ^a		Control Subjects ^b		Total	
	n	%	n	%	n	%
Original target population 2007	1252	100	2504	100	3756	100
Children removed ^c	34		68		102	
Target population 2007	1218	100	2436	100	3654	100
Study population 2007	802	66	843	35	1645	45
Lost to follow-up ^d	13		58			
Target population 2010	1205	100	2378	100	3583	100
Study population 2010	731	61	852	36	1583	44
Lost to follow-up ^d	29		48			
Target population 2015	1176	100	2330	100	3506	100
Questionnaires returned 2015	592	50	709	30	1301	37
<i>Giardia</i> during outbreak			6			
Incomplete response	2		6			
Withdrawn questionnaire			1			
Nonresponders	584		1622		2206	
Study population 2015	590	50	696	30	1286	37
Responded at all follow-ups	427	36	365	16	792	23

^a*Giardia* exposed in 2004.

^bSex and age matched controls from Bergen, Norway.

^cChildren younger than 18 years of age in 2015 were removed from original (and subsequent) target populations.

^dEmigrated, died, withdrawn, or address not found.

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