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## Excessive daytime sleepiness, sleep need and insomnia 3 years after *Giardia* infection: a cohort study



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#### ABSTRACT

*Objective:* To investigate whether prior infection with *Giardia lamblia* is associated with excessive daytime sleepiness, insomnia, and level of sleep need.

Design: A questionnaire was sent to all confirmed cases of giardiasis 3 years after the outbreak and a control group matched on age and gender. Associations were evaluated by use of multiple regression analysis. Results: Excessive daytime sleepiness (score ≥11 on the Epworth Sleepiness Scale) was reported by 31.5% of the Giardia-exposed and 14.1% of the controls. In multivariate analysis, excessive daytime sleepiness was independently associated with Giardia exposure, with an adjusted odds ratio of 1.40 (95% confidence interval [CI], 1.06-1.86). Insomnia was reported by 15.4% of Giardia-exposed and 8.8% of controls, adjusted odds ratio was 0.93 (95% CI, 0.65-1.35). Mean (SD) self-reported sleep need was 8 (1.4) hours among Giardia-exposed and 7.5 (1.1) hours in the control group (P<.001). The adjusted regression coefficient was 0.12 (95% CI, 0.01–0.24).

Conclusion: Being exposed to Giardia was independently associated with excessive daytime sleepiness and larger sleep need, but not with insomnia.

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#### Introduction

It is commonly believed that infections may interfere with sleep patterns. Some infections have been associated with sleep disorders, and a change in sleep pattern has been shown for streptococcal infection, Epstein-Barr infection and HIV.<sup>1–3</sup> Some of these infections are also associated with chronic fatigue syndrome (CFS).<sup>4,5</sup>

In 2004, there was an epidemic of giardiasis in the city of Bergen, Norway, and it has been estimated that 2500 inhabitants received treatment. Our group has previously reported a high prevalence and relative risk of irritable bowel syndrome (IBS) and chronic fatigue (CF) in giardiasis patients as compared with a control group 3 and 6

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years after the outbreak.<sup>7,8</sup> We have not found any studies investigating a possible connection between *Giardia* infection and sleep disorders.

The relationship between fatigue and sleepiness is not entirely clear. Sleepiness deals with the probability of actually falling asleep, whereas one can be fatigued without being sleepy, for instance, after strenuous exercise. It has previously been shown that patients with CFS are both more fatigued and sleepier than a healthy control group, but only more fatigued than a group with excessive daytime sleepiness. <sup>9</sup> In addition to sleepiness and fatigue, insomnia symptoms and self-reported sleep need may be changed after severe infection.

Against this backdrop, we explored the association between sleep problems and sleepiness as outcomes with a specific infectious agent as the risk factor. The aim of the study was to compare the prevalence of excessive daytime sleepiness, insomnia, and self-reported sleep need 3 years after *Giardia* infection with a matched control group. We also analyzed how these outcomes were related to CF and IBS.

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#### Methods

The study was developed as a cohort study. Data acquisition was performed by mailed questionnaires 3 years after the outbreak to all 1252 patients who had a positive fecal test result for *Giardia lamblia* during the outbreak and a control group of 3598 individuals. The population hit by the outbreak was younger and had a higher proportion of females compared with the general population. Consequently, the control group was randomly sampled with 2 persons with the same age and gender from the entire population in Bergen, thus establishing a 2:1 matched control cohort. The control group was selected by the help of Statistics Norway.

Questionnaires were sent to participants by regular mail in October 2007, and nonrespondents were mailed again after 1 month. In an effort to reduce possible bias caused by a low response rate among controls, this group was expanded by adding 2 more controls for each exposed individual when none of the first 2 controls had responded. As a result, the questionnaire was mailed to 1094 additional controls in May 2008.<sup>7</sup>

Detected G lamblia in stool samples during the outbreak in 2004 was the exposure in this study. We had 3 main outcome variables. The first was daytime sleepiness measured by the Epworth Sleepiness Scale (ESS) 3 years after Giardia exposure. 10 ESS evaluates subjective sleepiness and consists of 8 questions. Each question describes different situations and the participant is asked to rate their probability to doze off or fall asleep on a 4-point Likert scale where the responses are assigned values from 0 to 3. The responses are added to give the total ESS score, which indicates the level of sleepiness that the participant experiences. The maximum score is 24, and a value of ≥11 is classified as excessive daytime sleepiness. 10,11 Where there was a missing value on any of the 8 questions, the ESS was deemed invalid. The Norwegian version of this scale has been validated. 11 The second outcome variable was insomnia measured by the question "During the last month, how often have you experienced insomnia?" This question had 4 options ranging from "never or seldom," "1-2 times per month," "about once a week," and "more than once a week." "More than once a week" was classified as having insomnia, and this outcome was analyzed as a dichotomous variable. The third outcome variable was self-reported sleep need measured by the question "How much sleep do you need to feel rested?" where the participants could fill in the number of hours they needed to sleep.

CF was defined by the response to the Fatigue Questionnaire (FQ) developed by Chalder et al. <sup>12</sup> The FQ consists of 11 questions measuring both physical and mental fatigue and has previously been used in its translated form in a study on fatigue in the general Norwegian population. <sup>13</sup> CF was defined as a dichotomised score of 4 or more, given that the participant had experienced fatigue for the last 6 months. IBS was defined according to the Rome III diagnostic criteria for functional gastrointestinal disorders <sup>12,14</sup> as abdominal pain or discomfort of certain regularity linked to alterations in bowel movements, also described in a previous article from this study. <sup>7</sup>

#### Statistical analyses

The  $\chi^2$  test was applied to test differences between proportions. T-test was applied to compare means. Results were adjusted for IBS, CF, age, gender, marital status, education, employment status, and student status in 2004. Logistic regression analysis was used to investigate the association between excessive daytime sleepiness (ESS score  $\geq 11$ ) and Giardia exposure, and between insomnia and Giardia exposure. The results are reported as odds ratio (OR) and confidence interval (CI). Multiple linear regression analysis was applied to self-reported sleep need (in hours) to study main effects from and interactions between Giardia status and the presence of IBS and CF.

Interaction was tested using interaction terms. Regression was also used to estimate differences in mean and SD between the groups. All analyses were performed in SPSS version 22.

#### Ethical approval

This study was approved by the Regional Committee for Medical and Health Research Ethics (project 150.07) and by the Ombudsman for Privacy in Research, Norwegian Social Science Data Services (project 17014).

#### Results

The overall response rate was 40.1% (1945/4850), with a 65.3% (817/1252) response rate among exposed and 31.4% (1128/3598) among controls. Characteristics of the exposed group and controls are shown in Table 1. The ESS was incomplete in 78 cases. In addition, 18 cases had missing value on insomnia, and 30 cases on sleep need. There were missing data on IBS and CF in 70 and 33 cases, respectively.

Excessive daytime sleepiness was reported by 31.5% of *Giardia*-exposed (245/777) and 14.1% of controls (154/1090; P < .001). The mean ESS score in the *Giardia*-exposed group was 8.5 compared with 6.6 in the control group (P < .001). Among the *Giardia*-exposed with IBS, 41.8% (143/342) had excessive daytime sleepiness as compared with 28.2% (42/149) in the control group with IBS (P = .005). Among the *Giardia*-exposed with CF, 50.6% (175/346) had excessive daytime sleepiness as compared with 36.9% (48/130) in the control group with CF (P = .010; Table 2).

Insomnia was reported by 15.4% of *Giardia*-exposed (125/811) and 8.8% of controls (98/1116; P<.001). Among the *Giardia*-exposed with IBS, 22.9% (81/354) had insomnia as compared with 17.5% (27/154) in the control group with IBS (P=.195). Among the *Giardia*-exposed with CF, 26.6% (97/364) had insomnia as compared with 31.1% (41/132) in the control group with CF (P=.365; Table 3).

Self-reported sleep need was reported to a mean (SD) of 8.0 (1.4) hours in the *Giardia*-exposed and 7.5 (1.1) hours in the control group

**Table 1**Characteristics of patients with verified *Giardia* infection during an outbreak in 2004 and a control group who did not contract the infection.

Characteristics	Giardia group (n = 817)		Control group (n = 1128)		Р
Female, n (%)	540	(66.1)	738	(65.4)	.759ª
Age (y), mean (range)	36.0	(4-94)	36.3	(4-89)	.667 <sup>b</sup>
Age groups, n (%)					
Age 0-19 y	39	(4.8)	36	(3.2)	.108ª
Age 20-39 y	526	(64.4)	736	(65.2)	
Age 40-59 y	187	(22.9)	276	(24.5)	
Age 60-79 y	56	(6.9)	76	(6.7)	
Age 80-99 y	9	(1.1)	4	(0.4)	
Marital status, n (%)					
Single	271	(33.5)	293	(26.1)	$.004^{a}$
Married	497	(61.4)	778	(69.3)	
Divorced	33	(4.1)	41	(3.7)	
Widowed	9	(1.1)	11	(1.0)	
Education (highest level), n (%)					
Primary school	37	(4.7)	59	(5.3)	$.004^{a}$
Secondary school	169	(21.3)	308	(27.7)	
University	587	(74.0)	746	(67.0)	
Main employment status, n (%)					
Worker	576	(71.1)	881	(78.7)	<.001 <sup>a</sup>
Student	137	(16.9)	121	(10.8)	
Unemployed/retired	70	(8.6)	96	(8.6)	
Other	27	(3.3)	22	(2.0)	
Student during the outbreak, n (%)	299	(37.3)	269	(24.2)	<.001 <sup>a</sup>

Exposed and controls were matched by gender and age.

a Pearson  $\chi^2$  test from  $2 \times k$  table.

<sup>&</sup>lt;sup>b</sup> Gosset *t* test for independent samples.

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