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The Incidence and Risk of Celiac Disease in a Healthy US Adult Population

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Abstract

OBJECTIVES—Celiac disease (CD) is an increasingly common disease that may affect as many as 1% of the North American population. Recent population-based data suggest a substantial increase in the prevalence of CD over the last several decades. Several factors are hypothesized as possible disease triggers including intercurrent illnesses, such as gastroenteritis, surgeries, and trauma. We used the active duty US military, a unique healthy worker population with essentially complete medical diagnostic coding, as an opportunity to describe trends in CD and deployment-related risk factors.

METHODS—Using electronic medical encounter data (1999–2008) on active duty US military (over 13.7 million person-years), a matched, nested case–control study describing the epidemiology and risk determinants of CD (based on 2 ICD-9 medical encounters) was conducted. Incidence and duration of CD-related medical care were estimated, and conditional logistic regression was utilized to evaluate CD risk following infectious gastroenteritis (IGE) occurring within 3 years before CD diagnosis while controlling for other risk factors.

RESULTS—A total of 455 incident cases of CD were identified and age, gender, and time matched to 1,820 controls. The incidence of CD increased five-fold from 1.3 per 100,000 in 1999 to 6.5 per 100,000 in 2008, with the highest rates of increase among those over 34 years of age (average annual increase of 0.8 cases per 100,000). A total of 172 IGE episodes, predominately of “viral etiology” (60.5%), were documented. In multivariate models, a significant association between IGE and CD was found (Odds ratio (OR): 2.06, 95% confidence interval (CI) 1.43, 2.97). Risk generally increased with temporal proximity to, and non-viral etiology of, exposure. Other notable risk factors for CD in multivariate models were Caucasian race (OR: 3.1, $P < 0.001$), non-Army service (OR: 1.5, $P = 0.001$), and greater than a high-school education (OR: 1.3, $P = 0.05$).

CONCLUSIONS—Incidence of CD diagnosis in the US military is increasing, particularly among those in the fourth and fifth decades of life and appears higher than other population-based estimates. An association between antecedent IGE and risk of CD was noted, but the potential for exposure misclassification cannot be ruled out and further study is needed to link pathogen-specific exposure to incident CD anti-gluten antibody development or symptom onset.

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CONFLICT OF INTEREST

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INTRODUCTION

Celiac disease (CD) is an increasingly common disorder that may affect as much as 1% of the North American population. It is known to affect all ages, including young adults, and may be more prevalent in Caucasians (1). The rate of diagnosis in other racial groups is largely unknown. However, due to the broad spectrum of clinical presentation, and, until recently, the unavailability of sensitive and specific diagnostics, most affected individuals are never diagnosed (2). The consequence of the disease may be diverse in terms of issues such as bone fragility, depressed resistance to bacterial and fungal infections, reduced ability to respond to vaccinations, and a variety of other nutritional, immunological, and inflammatory comorbidities. The majority of CD patients have 1 of 2 HLAs encoded by genes that are also found in approximately one-third of the North American population. Considering that virtually the entire population consumes food containing significant amounts of the primary exogenous trigger (i.e., gluten), yet only 1% of the population may get the disease, research has been conducted to identify other factors triggering disease onset, or associated with increased CD risk among genetically susceptible individuals. Several factors have been suggested including early introduction or large consumption of gluten early in life after weaning and childhood (3), and infant infections (4). Other triggers include the seasonality of birth and risk of disease (5). In addition, intercurrent illnesses, such as surgeries, and trauma, are potential triggers. The role of infection early in life, especially in those that overlap with the introduction of high-dose gluten follow-on formulas that are often used after weaning, may be particularly likely to increase the rate of disease.

Recent population-based data suggest a substantial increase in the prevalence of CD over the last several decades (6–9). This increase is unlikely to be due to a change in human genetics or population changes in wheat consumption, but may reflect a change in other environmental factors. It has also recurred in adults, a phenomenon that may be more marked in North America than in Europe. In this study, we aim to explore the recent incidence and risk factors of CD in one of the largest and best documented adult populations in North America of active service personnel. This population includes substantial diversity of race and ethnicity and education level.

METHODS

Database information

Data were obtained from the Defense Medical Surveillance System, the main repository for medical data of Department of Defense beneficiaries maintained by the Armed Forces Health Surveillance Center (10, 11). All subjects were active duty US military personnel who served between 1999 and 2008. Medical information was derived from ambulatory and inpatient claims data for care provided within the Military Health System. Demographic data were derived from personnel information; deployment data were derived from deployment rosters and deployment health assessments. Included data were linked at the individual level and compiled into a single de-identified data set, which was provided to the study investigators. The study was reviewed and approved by the Naval Medical Research Center Institutional Review Board in compliance with all applicable regulations governing the protection of human subjects.

CD case identification and control selection

A CD case was identified when the service member had at least two ICD9-CM (579.0) specific medical encounters for a CD diagnosis within 6 months. Subsequent medical encounters were determined to be related to the CD if the International Classification of

Diseases, Ninth Revision, Clinical Modification (ICD9-CM) code was included in any of the diagnostic positions. Each case was matched by time (a medical encounter within 1 calendar year), sex, and age (within 1 year) with up to four controls with an unrelated diagnosis randomly selected from the population that produced the cases (i.e., active duty military personnel). Baseline medical encounters for the control subjects included vaccinations, procedures, or other unrelated diagnoses. Incident CD was defined as the first documented ambulatory or inpatient medical encounter with the ICD9-CM code listed above. Given that the military generally would not enlist or commission a service member with known CD, it is unlikely that many of the incident CD diagnoses would include individuals who have a prior diagnosis of CD, though undiagnosed disease could be prevalent among both cases and controls selected.

Exposure

The primary exposure variable of interest was infectious gastroenteritis (IGE) at any time before a diagnosis of an incident CD (cases) or censure (controls). An IGE exposure was defined by ICD9-CM codes for specific pathogens and non-specific infectious enteritis as previously reported (12). Non-specific IGE codes were included due to the lack of routine microbiology performed on patients with IGE in similar health-care settings (13). Both specific and non-specific codes were utilized to classify an exposure as a specific bacterial, non-specific bacterial, protozoal, or viral etiology. We also evaluated exposures at 24, 18, 12, and 6 months before CD diagnosis or censure (controls) to assess the temporal relationship between exposure and outcome. While previous studies have evaluated associations of exposure up to 1 year, we chose to extend exposure windows up until 24 months to account for potential in diagnostic delay due to patient's care seeking behavior and/or provider diagnosis (14), and we saw no significant changes in effect estimates with differential exposure windows. Due to similarities in clinical presentation between the primary exposure (IGE) and symptoms of the CD outcome of interest, we evaluated a 6-month diagnostic delay window whereby exposures occurring within 6 months before CD diagnosis (or censoring for controls) were excluded (12). In addition to IGE exposure, other demographic variables available in the data were evaluated, including race, military rank, educational attainment, marital status, and branch of service.

Analysis

CD incidence was estimated using the number of incident cases in a given year and the total number of active duty service members for that same year. The associations between CD, IGE, and covariates were initially explored by univariate methods. All analyses evaluated each CD independently. Univariate and multivariate conditional logistic regression models were used to evaluate the relationship between IGE, other covariates, and CD. For multivariate models, a backwards elimination approach was used, whereby all variables were initially added to the models. The variable with the largest insignificant *P* value was removed, and the models were refit. This process was continued iteratively until all variables retained in the models were significant at the $\alpha = 0.15$ level (15). Effect modification was assessed statistically utilizing a multiplicative approach. The association of psychological comorbidity among cases and controls was also evaluated, but limited to concomitant diagnosis for initial CD visit of incident diagnosis and at censure visit for controls.

Statistical analyses were performed using SAS v. 8.2 for Windows (SAS Institute, Cary, NC). Two-tailed statistical significance was evaluated using an α of 0.05.

RESULTS

As shown in Table 1, a total of 455 cases of incident CD were identified in active duty US military personnel between 1999 and 2008 with an overall incidence of 3.55 per 100,000 person-years (p-yrs) (95% confidence interval (CI): 3.24, 3.90; Table 1). Rates were higher in females (7.70 per 100,000 p-yrs) compared with males (2.78 per 100,000 p-yrs) ($P < 0.001$). Incidence for CD was noted to rise from 1.32 per 100,000 p-yrs in 1999 to 6.54 per 100,000 p-yrs in 2008, and this rise was highest in the older age strata (Figure 1). While incidence increased at a higher rate per annum in whites, those classified as other race (i.e., non-white and non-black) also showed year-over-year increases of ~0.8 per 100,000 per year.

The majority of cases and controls were male (65.9%), white (66.4%), and married (69.4%) (Table 2). Cases were noted to have education beyond high school (54.7%), which was higher than controls (45.8%) ($P < 0.001$). The three major branches of the US Military Armed Forces (Army, Navy, and Air Force) comprised the majority (88.6%) of the study population, with most classified as enlisted personnel, though a higher proportion of officers were noted among CD cases compared with controls (32.5 vs. 22.1%, $P < 0.001$). Overlap with functional and other gastrointestinal disorders were assessed among cases and included dyspepsia (8/455, 1.8%), constipation (10/455, 2.2%), irritable bowel syndrome (20/455, 4.4%), and functional diarrhea (4/455, 0.9%). There was no overlap with gastroesophageal reflux disease. Overall, 38 (8.4%) had one or more visit associated with these gastrointestinal disorders. One-hundred seventy-two subjects had one or more IGE exposures with etiological category distributed as follows: bacterial pathogens ($n = 4$, 2.3%), protozoal ($n = 2$, 1.2%), viral ($n = 104$, 60.5%), and other ($n = 74$, 43.0%).

Among incident CD cases followed, the median number of visits was two (interquartile range: 2, 4) with no significant difference based on exposure. Data were not available on the proportion of CD cases that resulted in discharge from medical service, though this is often known to occur in these cases (personal communication, Brooks Cash, US Navy).

Initial univariate analyses (Table 3) found that the following covariates were independently associated with an increased risk of CD: Caucasian race, non-Army branch of service, greater than high-school education, and previous IGE episode. Prior deployment to Operation Iraqi Freedom deployment had lower risk of CD compared with non-Operation Iraqi Freedom deployers. The odds ratio (OR) for incident CD following an antecedent episode of IGE increased as the time frame allotted for exposure decreased. When limiting the IGE episodes to only those of non-viral origin in the 24 months before censure, the associated OR increased for CD. In a multivariate model, after controlling for the other covariates, being married, having less than a Bachelor's Degree, being in the Army, having an episode of IGE in the 24 months before censure significantly increased the risk of each functional gastrointestinal disorder (FGD) (Table 4). In contrast, being in the Marines appeared to be protective (Navy referent). Being classified as non-Caucasian decreased the risk of CD.

DISCUSSION

This study demonstrates a substantial increased incidence and diagnosis rate of CD in a large, generally healthy young adult population for which there is excellent capture of diagnosis and ready access to health care. This rise in incidence is consistent with what has been reported in other western industrialized population-based studies (9, 16) and likely represents a combination of both increased diagnoses due to increased suspicion but also may reflect a true increase in incidence possibly related to environmental changes in cereal

processing including wheat genetics, bread processing, and enzymatic modification of wheat prolamins resulting from changes in industry processes (17). It is interesting that this increase in incidence seemed to be more marked in individuals in the third, fourth, and fifth decades in life, among those who would have already been in the military service for many years, suggesting that this is a true new onset of disease or the emergence of longstanding silent disease. We did not have data available on secular trends for number of serological CD tests performed, which should be done to inform the potential bias associated with increased testing that could partially explain the increased incidence (studies planned) (16).

Clearly, environmental, genetic, and immunological factors have a role in the pathogenesis of CD. It is well accepted that the common HLA genotype encoding HLA types DQ2 or DQ8 is necessary for CD to occur (18). However, as almost 30% of the Caucasian population carries these genotypes, and virtually all eat gluten, there must be other factors including genetics, immune dysfunction, and environmental exposures that trigger the disease. Extensive genetic analysis has revealed a large number of other genes that all have very small attributable risks that cumulatively only add 10% of risk (19). The balance of genetic and environmental influences in risk of disease is also supported by the 75% concordance in monozygous twin studies (20). Although the only well-documented environmental trigger is gliadin, it has been proposed that the clinical expression of CD can be modulated by environmental factors. It is possible that in genetically susceptible patients, an infectious insult may contribute to trigger overt CD through increased intestinal permeability, or adjuvant effects of infection or inflammation, latent CD may be unmasked.

Given the potential for infections to act as triggers for developing gluten intolerance through molecular mimicry or other immune modulation mechanisms, efforts to identify an infectious association have been made. However, to date, there is no compelling evidence for such an association (21). Neonatal infections have been associated with increased risk of CD, and the role of adenovirus 12 virus remains controversial. Based on the 12 amino-acid homology sequence of adenovirus type 12 E1B protein and α -gliadin, it has been suggested that exposure to adenovirus type 12 E1B may sensitize individuals to gliadin and trigger CD. However, it is difficult to establish a causative relationship between adenovirus type 12 E1B and gliadin, because adenovirus type 12 E1B is also highly prevalent in the duodenal tissue of normal individuals (22). CD is epidemiologically associated with other viral infections, such as chronic hepatitis C, non-viral disorders including insulin-dependent diabetes, thyroid disease and cardiomyopathy, and HIV (22, 23). This suggests that the association may involve chronic immune stimulation, which in turn triggers an autoimmune reaction.

In the present study, we found an increased odds ratio of exposure to prior IGE twice as high among CD cases compared with matched controls (OR: 2.0, 95% CI: 1.4, 2.8). Non-viral IGE exposure odds were relatively higher (OR: 3.0, 95% CI: 1.9, 4.8), and odds of exposure were higher when looking at temporal proximity to CD diagnosis. Unfortunately, we do not have specific pathogen etiologies associated with these infections, and while these results are intriguing, the potential for misclassification of exposure given the conflated symptomatology of infectious diarrhea and CD confounds the potential association in this study. While much is known about the pathogenic adaptive and innate immune responses associated with the disease process, less is known about the initiating steps that are involved in disease onset. As demonstrated in animal models of gluten sensitivity (24, 25), gastrointestinal infection may trigger or facilitate the onset of clinical CD, either by increasing intestinal permeability or by enhancing uptake and dysfunctional anti-gliadin immune response in the genetically susceptible host (26, 27). It is reasonable to suspect that acute gastrointestinal infections could result in the translocation of luminal antigens, including incompletely digested gluten peptides, which in the background of proinflammatory anti-bacterial responses could trigger a maladaptive immune response (2).

Campylobacter jejuni, a leading cause of enterocolitis worldwide, has been shown experimentally to permit the translocation of normal, non-invasive microflora via novel processes that implicate epithelial lipid rafts and M-cell transport and induce a pro-inflammatory response (28–30). Thus, similarly to the epidemiological studies observing *Campylobacter* and *Salmonella* infections as a trigger of inflammatory bowel disease (31, 32) it is possible that such infections could also trigger luminal antigens, including gluten peptides, across the intestinal barrier, and in certain susceptible individuals prime a mucosal immune response toward such antigens resulting in loss of tolerance to these antigens due to an inappropriate inflammatory response (33, 34).

With regard to what is known about infectious diarrhea as a trigger for CD there are a few anecdotal reports and case series suggesting an association whereby some patients with CD often attribute the onset of classic symptoms to a stressful episode or gastroenteritis (35), and cases of CD have been reported as presenting as persistent travelers' diarrhea when no infectious cause could be documented (36, 37). It has also been described that exposure to three or more IGE events in young children at or around the time of introduction of follow-on formula was associated with a substantial increased risk of childhood diagnosis of CD (38). In addition, a birth cohort followed in Denver suggested that rotavirus infection in the first year of life was associated with subsequent risk for CD (3). More recently, a case of a healthy subject who developed sudden irritable bowel syndrome-like symptoms after a confirmed episode of *C. jejuni* enteritis was subsequently diagnosed with new onset CD (39). It is interesting that in this study, we found a higher risk of CD in subjects who were diagnosed with a "non-viral" IGE episode. While the ICD-9-based diagnosis is non-specific, it would suggest that bacterial infections could be more associated with subsequent diagnosis of CD. In total, the results we found lend support to the infectious trigger hypothesis, though this study relied on non-specific (and potentially misclassified) infectious gastrointestinal exposures, which needs confirmation through studies evaluating risk after pathogen-specific exposures.

While CD is known to predominantly affect Caucasians, less is known about the incidence of CD in non-Caucasians. As this cohort of active military service personnel incorporates large numbers of individuals who are non-Caucasian, with unhindered access to medical care, the low incidence seen in non-Caucasians likely reflects a true difference in biologic predisposition, although rates increased during the study period that may implicate secular trends in environmental influences which has been seen in inflammatory bowel disease rates among non-whites (40). It is unlikely that there would be significant differences in environmental exposures or diet due to common food and preparation and provision with the military service, though it is possible that there may be inherently lower suspicion for CD by the medical personnel caring for individuals who are non-Caucasian. Future active surveillance study should be considered including sampling of non-Caucasians to verify that incidence is truly lower and not simply undiagnosed. Other US military population specific differences were noted. The association of CD with officer rank and higher educational level begets the positive association with socioeconomic status. This has been suggested in an epidemiologic study from Finland wherein there is a higher rate of CD in the more developed population of Finland than the adjacent less developed population (41). It is, however, possible that educational levels may have lead to increased awareness of this diagnosis, and also there may be a negative association with smoking for which we could not control.

Interestingly, we found that deployment decreased the risk of CD that may be counterintuitive given the known high risk of infectious exposures, including gastrointestinal infections, and stress while deployed. Unfortunately, capture of deployment-related illness and injury into the Defense Medical Surveillance System (DMSS) medical encounter

databases is not complete; therefore, assessment of deployment-related illness effects (particularly minor ones) is incomplete. Furthermore, military members with underlying medical illness may not be deployed resulting in a type of “healthy worker” effect, which might also explain the lower rate of CD in deployed personnel compared with their non-deployed counterparts. Surgical stress has been described to trigger CD (42), and future studies should be designed to capture these data to further evaluate deployment-related infectious and non-infectious exposures of interest.

This study has several limitations. First, an important limitation is that CD diagnoses were based on a medical encounter database, and while we believe our strategy for determining case status is robust based on prior experience with other complex diseases (12, 43–45) it is not possible to review individual medical records to confirm. Additional studies are needed (and being planned) that use clinical procedure codes associated with upper endoscopy and histology, as well as serological evidence from linked Department of Defense serum repository specimens. Furthermore, given our reliance on clinically diagnosed CD, our incidence estimates should be considered as a gross underestimate of the true incidence in the population, though we feel the secular trends and differential rates among demographic subgroups are relevant observations. Second, as mentioned, the precise identification of enteropathogens associated with IGE visits was not described, due to the fact that laboratory work-up of these infections is infrequently carried out in US military as well as in civilian clinics and emergency rooms. Furthermore, our stratification of IGE into viral and non-viral categories is imprecise. It is further possible that these gastroenteritis episodes that were called IGE may actually have represented short-lived symptom events associated with subsequently diagnosed CD. To assess for such an effect, we utilized a 6-month exposure exclusion period before initial CD diagnosis (or control censoring) to prevent misclassification of initial CD presentation as an episode of IGE, and we did not see such effect (data not shown). However, if the duration between exposure and disease onset is short, then we may have underrepresented the true association biasing the results toward the null. Additionally, to minimize potential misclassification, this study excluded functional gastrointestinal disorders among controls and did not include such medical encounter visits before onset of incident CD. While not directly addressing this potential source of bias, excluding CD cases with functional gastrointestinal disorders co-diagnoses in this study did not change in the primary effect estimate of any IGE exposure (adjusted-OR: 2.00, 95% CI: 1.37–2.90). Finally, this study cohort does not address CD in the elderly or in the very young, and indeed individuals with chronic ill health are generally not admitted into military service; hence, this study may underestimate the true incidence in the general population.

In summary, our study shows a substantial increase in the rate of CD diagnosis in adult healthy Caucasian population with a much lower but increasing incidence in non-Caucasians. The disease is more likely to be diagnosed after a proximate IGE event of a non-viral nature and contribute to the emerging body of data that warrants further prospective or seroepidemiological studies linking pathogen-specific infectious diarrhea exposure attribution to incident CD. Studies that aim to evaluate the instigating exposures and mechanisms of CD-related antibody development, or initiation of disease in those who were previously asymptomatic but with pre-existence of positive celiac serology are needed (planned).

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Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Celiac disease (CD) is an increasingly common disease that may affect as much as 1% of the North American population.
- ✓ Recent population-based data suggest a substantial increase in the prevalence of CD over the last several decades.
- ✓ Several factors are hypothesized as possible disease triggers including intercurrent illnesses, such as gastroenteritis, surgeries, and trauma.

WHAT IS NEW HERE

- ✓ Incidence of CD diagnosis in a healthy US adult population is increasing, particularly among those in the fourth and fifth decades of life and appears higher than other population-based estimates.
- ✓ We found an association between antecedent infectious gastroenteritis (IGE) and risk of CD. Association appeared strongest in non-viral IGE.
- ✓ Prospective and/or seroepidemiological studies linking pathogen-specific exposure attribution to incident CD autoantibody development are warranted.

Figure 1.
Incidence of celiac disease in US military stratified by age group, 1999–2008.

Table 1

Estimates of clinically diagnosed (2 International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9) 579.0 medical encounters) of celiac disease in the US military, 1999–2008

year	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Total incidence (per 100,000)	1.32	1.32	2.05	2.59	2.41	3.61	3.56	4.11	5.51	6.54
<i>Age</i>										
<20	0.00	0.00	0.78	0.00	0.87	1.81	1.02	1.05	0.00	2.04
20–24	0.72	1.17	1.35	1.29	1.86	1.85	2.13	2.60	1.97	5.68
25–29	1.78	1.10	1.91	1.12	2.85	3.11	4.74	3.33	8.18	4.74
30–34	1.39	2.42	3.46	2.97	1.97	4.96	3.02	2.07	7.26	8.72
35–39	0.99	1.50	2.07	4.76	2.74	4.02	6.54	9.58	7.18	7.80
40	3.87	1.52	3.71	8.39	4.75	9.41	4.75	8.96	10.54	11.97
<i>Service</i>										
Army	0.85	0.42	1.48	2.50	1.84	1.63	3.08	3.04	3.92	4.71
Navy	1.37	1.37	1.63	2.92	1.59	4.32	2.51	3.76	7.18	6.42
Air force	1.96	2.56	3.16	1.94	4.08	5.36	5.94	6.38	6.29	9.87
Marines	0.58	0.58	2.33	2.91	1.70	2.27	1.12	1.12	3.28	4.13
<i>Race</i>										
Black	0.11	0.00	0.00	0.21	0.52	0.10	0.21	0.00	0.11	0.21
White	5.47	6.16	9.35	10.82	9.14	15.14	17.98	19.10	26.73	30.89
Other	1.30	0.62	1.19	2.29	2.23	5.54	1.13	5.67	6.28	8.62
<i>Gender</i>										
Male	0.69	0.95	1.64	2.03	1.83	2.75	2.38	3.69	4.63	4.92
Female	5.18	3.55	4.46	5.77	5.67	8.56	10.43	6.57	10.73	16.33

Table 2

Demographic characteristics of US military service members diagnosed with celiac disease between 1999 and 2008 and their matched controls

	Cases	Controls
<i>N</i>	455	1,820
Mean (s.d.) age	32.1 (8.5)	32.1 (8.5)
Male gender (<i>N</i> (%))	300 (65.9)	1,200 (65.9)
<i>Education category (N (%))</i>		
Less than high school	3 (0.7)	5 (0.3)
High school only	203 (44.6)	982 (54.0)
Some college	69 (15.2)	245 (13.5)
Bachelor's Degree	77 (16.9)	264 (14.5)
Master's Degree	71 (15.6)	211 (11.6)
Doctorate	17 (3.7)	53 (2.9)
Unknown	15 (3.3)	60 (3.3)
<i>Marital status (N (%))</i>		
Married	314 (69.0)	1,265 (69.5)
Single	118 (25.9)	427 (23.5)
Other	23 (5.1)	128 (7.0)
<i>Race category (N (%))</i>		
Black	14 (3.1)	358 (19.7)
White	380 (83.5)	1,130 (62.1)
Other	61 (13.4)	332 (18.2)
<i>Branch of service (N (%))</i>		
Army	117 (25.7)	647 (35.6)
Navy	116 (25.5)	463 (25.4)
Air force	165 (36.3)	508 (27.9)
Marines	36 (7.9)	158 (8.7)
Coast guard	21 (4.6)	44 (2.4)
<i>Grade (N(%))</i>		
E1–E4	102 (22.4)	394 (21.7)
E5–E9	199 (43.7)	978 (53.7)
Warrant officer	6 (1.3)	45 (2.5)
O1–O5	133 (29.2)	341 (18.7)
O6–O10	15 (3.3)	62 (3.4)
Prior deployment (<i>N</i> (%))	169 (37.1)	798 (43.9)
Median (IQR) number of deployments	1 (1, 2)	1 (1, 2)

IQR, interquartile range.

Table 3

Unadjusted odds ratios (95% confidence intervals) for exposure variables from a conditional logistic regression model evaluating the risk of celiac disease among active duty US military personnel from 1999 to 2008

	Odds ratio	95% CI
White	3.17	2.42, 4.15
Non-army	1.59	1.27, 2.00
Officer	1.71	1.34, 2.18
More than high school education	1.62	1.27, 2.05
No prior OIF deployment	1.52	1.16, 2.01
Any prior IGE	1.99	1.42, 2.79
Any prior non-viral IGE	3.00	1.87, 4.81
Any prior viral IGE	1.42	0.91, 2.23
Three years prior IGE	2.33	1.53, 3.54
Three years prior non-viral IGE	4.81	2.67, 8.68
Three years prior viral IGE	1.22	0.65, 2.28
Two years prior IGE	2.77	1.72, 4.45
Two years prior non-viral IGE	6.00	2.98, 12.07
Two years prior viral IGE	1.57	0.80, 3.09
One year prior IGE	3.13	1.74, 5.65
One year prior non-viral IGE	20.00	5.79, 68.96
One year prior viral IGE	1.05	0.42, 2.59

CI, confidence interval; IGE, infectious gastroenteritis; OIF, Operation Iraqi Freedom.

Table 4

Adjusted^a odds ratios (95% confidence intervals) for infectious gastroenteritis from a multivariate conditional logistic regression model evaluating the risk of celiac disease among active duty US military personnel from 1999 to 2008

	Odds ratio	95% CI
Any prior IGE	2.06	1.43, 2.97
Any prior non-viral IGE	3.27	1.96, 5.45
Any prior viral IGE	1.44	0.89, 2.32
Two years prior IGE	2.93	1.75, 4.89
Two years prior non-viral IGE	6.65	3.10, 14.26
Two years prior viral IGE	1.57	0.76, 3.22

CI, confidence interval; IGE, infectious gastroenteritis.

^a Adjusted for race, branch of service, rank, education, and deployment history.