

Onset of Irritable Bowel Syndrome, Dyspepsia, Diarrhea, Bloating, and Constipation in Deployed Gulf War Veterans

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To cite this article:

Zachary Thomas Verne, Jeremy Zachary Fields, George Nicholas Verne, Benjamin Buyi Zhang, Amber Leigh Thacker et al. (2024). Onset of Irritable Bowel Syndrome, Dyspepsia, Diarrhea, Bloating, and Constipation in Deployed Gulf War Veterans. *International Journal of Gastroenterology*, 8(1), 5-10. <https://doi.org/10.11648/ijg.20240801.12>

Received: January 15, 2024; **Accepted:** January 29, 2024; **Published:** February 5, 2024

Abstract: An estimated 694,550 United States service members were actively deployed to the Persian Gulf from 1990-1991. Many veterans who were deployed developed Persian Gulf War Syndrome along with chronic gastrointestinal symptoms after returning from the Persian Gulf. Our objective in this study was to determine the phenotypic expression of gastrointestinal symptom complexes in previously healthy veterans who had been stationed in the Persian Gulf. One hundred and four consecutive veterans (88 males, 16 females) who had previously been deployed in 1990-91 were evaluated for their bowel habits and gastrointestinal symptoms. A workup was completed to find identifiable causes of their symptoms and all veterans were asked to do a modified version of the Bowel Disease Questionnaire symptom survey. None of the veterans reported gastrointestinal symptoms before deployment. During deployment to the Persian Gulf: 22 veterans (21%) developed irritable bowel syndrome; 17 (16%) developed dyspepsia; 50 (48%) developed diarrhea; 11 (11%) developed bloating; and 4 (4%) developed constipation. The results of the current study suggest that the development of irritable bowel syndrome, dyspepsia, diarrhea, bloating, and constipation is frequently seen in deployed Gulf War Veterans and the gastrointestinal symptoms commonly persist upon returning home. These novel findings are very important for currently deployed veterans who are serving in the Middle East and are at a high risk of developing gastrointestinal disorders.

Keywords: Gulf War Syndrome, Gulf War, Irritable Bowel Syndrome, Dyspepsia, Constipation, Diarrhea, Bloating

1. Introduction

It has been over 32 years since more than 2.2 million United States military personnel served and an estimated 694,550 were stationed in the Persian Gulf and participated in Operation Desert Shield and Operation Desert Storm starting August 2, 1990 through July 31, 1991. The Persian Gulf Registry identified many veterans who served from 1990-1991 with chronic health disorders of undetermined etiology. [1-5] Following deployment to the Persian Gulf, over 25% of veterans returned home with chronic gastrointestinal symptoms. [6-11] The VA Environmental Epidemiology Service has noted that the evaluation and treatment along with indirect costs such as lost work have cost

over \$900 million. Of greater concern is that these costs continue to grow and many veterans currently stationed in the Persian Gulf are at increased risk for developing chronic gastrointestinal disorders.

Veterans with Gulf War Syndrome often complain of frequent muscle and joint pain, chronic fatigue, persistent headaches, and gastrointestinal symptoms. [2-4] The most common gastrointestinal complaints by these veterans include abdominal pain, diarrhea, constipation, dyspepsia, and bloating. [7-10] Disorders of gut-brain interaction are much more common in veterans deployed to the Persian Gulf who have been subject to a highly stressful environment. [6-8] These veterans with gastrointestinal symptoms have also been shown to have intestinal hyperpermeability, somatic

complaints, and hypersensitivity to experimental nociceptive pain stimuli. [12, 13] Several reports suggest that over 50% of veterans deployed in 1990-1991 developed acute gastroenteritis which could be an inciting event leading to chronic gastrointestinal disorders and persistent gastrointestinal symptoms. [3, 4] Although acute gastrointestinal symptoms from gastroenteritis often resolve within several weeks, a significant number of veterans have persistent abdominal pain, bloating and diarrhea. [6]

Common enteric infections often lead to transient small bowel and colonic inflammation which may lead to sensitization of enteric neurons which persists following resolution of the inflammation as has been observed in animal models of functional gastrointestinal disorders. [14, 15] Human and animal studies of post-infectious irritable bowel syndrome both indicate that disruption of the intestinal barrier is a potential mediating factor for chronic visceral and somatic pain. [16-18] Sensitization of enteric neurons sets up central and peripheral sensitization and can manifest as increased hypersensitivity to experimental somatic nociceptive stimuli, as we have shown in both veterans with gastrointestinal disorders and patients with irritable bowel syndrome. [6, 12]

In our current study, we studied veterans who had been stationed in the Persian Gulf from 1990-1991 and returned home with persistent gastrointestinal symptoms that they developed while deployed. Thus, our objective was to determine the specific phenotypes of gastrointestinal symptom complexes in these previously healthy veterans who were deployed to the Persian Gulf. These findings are important for future veterans who may serve in the Persian Gulf and may be at high risk of developing chronic gastrointestinal symptoms during and/or after deployment.

2. Materials and Methods

2.1. GW Veterans

The study was performed at the Veterans Affairs Medical Center in Cincinnati, OH, and after approval by their Institutional Review Board. Informed consent was signed by all veterans before being enrolled in the study. We enrolled 104 consecutive veterans previously deployed from 1990-1991 in the Persian Gulf that were seen in the VA outpatient clinics and developed persistent gastrointestinal symptoms during their tour, and had gastrointestinal symptoms that persisted and have not yet resolved. None of the veterans had gastrointestinal symptoms before being deployed to the Persian Gulf. Veterans who were redeployed to the Persian Gulf for a second tour were excluded from this study. The complaint that veterans presented to the clinic with was persistent gastrointestinal symptoms. The veterans all previously had upper both colonoscopy and endoscopy with biopsies. In addition, a capsule endoscopy was performed and bacterial overgrowth was excluded with the lactulose breath test. A serum tissue transglutaminase was performed to exclude celiac sprue and all veterans had negative stool studies including Giardia antigen along with normal

hematologic and biochemical studies. Excluded from the analysis were veterans with a history of pancreatitis, inflammatory bowel disease, gastrointestinal surgery, and liver disease. Veterans who were on a medicine that affected bowel symptoms and function were also excluded. [19, 20]

2.2. Experimental Questionnaires

A complete history was taken from each veteran and a modified version of the validated Bowel Disease Questionnaire was administered which examined gastrointestinal symptoms before, during, and after deployment. The Rome IV Criteria was used to stratify the predominant bowel symptoms experienced by the veterans, including irritable bowel syndrome, functional dyspepsia, diarrhea, bloating, and constipation. [22-24]

2.3. Gastrointestinal Symptom Clusters

The veterans' gastrointestinal symptoms were classified according to the Rome IV Criteria into 5 groups:

2.3.1. Irritable Bowel Syndrome

Recurrent abdominal pain on average persisting for at least 1 day/week in the last 3 months, associated with two or more of the following criteria:

- related to defecation
- associated with a change in the frequency of stool
- associated with a change in form (appearance) of stool

2.3.2. Dyspepsia

One or more of the following:

- postprandial fullness
- early satiation
- epigastric pain
- epigastric burning
- No evidence of structural disease (on upper endoscopy) that explains the symptoms

2.3.3. Diarrhea

Loose or watery stools, without predominant abdominal pain or bothersome bloating, occurring in more than 25% of stool samples.

2.3.4. Bloating

- recurrent bloating and/or distension occurring on average at least 1 day/week; abdominal bloating and/or distension that predominates over other symptoms
- There are insufficient criteria for a diagnosis of irritable bowel syndrome, functional constipation, functional diarrhea, or post-prandial distress syndrome

2.3.5. Constipation

Two or more of the following:

- straining during more than ¼ (25%) of defecations
- lumpy or hard stools: Bristol Stool Form Scale in more than ¼ (25%) of defecations
- sensation of incomplete evacuation more than ¼ (25%) of defecations
- sensation of anorectal obstruction/blockage more than ¼

(25%) of defecations

- e. manual maneuvers to facilitate more than ¼ (25%) of defecations (e.g., digital evacuation, support of the pelvic floor)
- f. fewer than three spontaneous bowel movements per week
- g. loose stools rarely present without the use of laxatives
- h. insufficient criteria for irritable bowel syndrome

2.3.6. Statistical Analysis

SAS software, Version 9.4 of the SAS system (SAS Institute Inc.), and Prism version 6 were used to complete the statistical analysis. The analysis included one between and two within-subject variables. Repeated measures command within the General Linear model module of SPSS was used to assess different bowel symptoms in veterans. Values were expressed as mean ± standard deviation (SD). All p-values were 2-tailed, and the alpha level of significance was <0.05.

3. Results

In total, 104 consecutive veterans (88 males, 16 females) (Table 1) were recruited and successfully enrolled in the study. All had been deployed to the Persian Gulf for a median of 16 months during 1990-1991. All 104 veterans had documented chronic gastrointestinal symptoms that they developed within 2-6 months after deployment and persisted

upon returning home from the Persian Gulf. Table 2 shows the primary gastrointestinal symptom complexes reported by the group of veterans. Table 3 illustrates gastrointestinal complexes grouped by race. Laboratory studies, stool studies, and endoscopic findings were normal in all veterans. Veterans did not report any history of gastrointestinal symptoms, functional bowel disorders, inflammatory bowel disease, celiac disease, or bacterial overgrowth prior to deployment.

Table 1. Demographics of Gulf War Veterans with Gastrointestinal Symptoms.

	Male	Female
Age-years	51.4±2.1	50.7±1.7
Sex-no. (%)	88 (85)	16 (15)
Ethnic group-no. (%)		
White	62 (70)	12 (75)
Black	23 (26)	3 (19)
Hispanic	3 (4)	1 (6)

Plus-minus values are means ± standard deviation.

Table 2. Gulf War Veterans with Gastrointestinal Symptom Complexes.

	Number of Participants	Percentage (%)
IBS	22	21%
Dyspepsia	17	16%
Diarrhea	50	48%
Bloating	11	11%
Constipation	4	4%

Table 3. Gulf War Veterans with Gastrointestinal Symptom Complexes by Race.

White	Black	Hispanic						
IBS		15	5	2	Dyspepsia	8	8	1
Diarrhea	41	9	0					
Bloating	9	1		1	Constipation	1	3	0
Total	74	26	4					

3.1. Irritable Bowel Syndrome

Irritable Bowel Syndrome (IBS) can manifest in different subtypes based on the predominant bowel habits. The subtypes include IBS with mixed bowel movements (IBS-M) where individuals experience both diarrhea and constipation [also known as alternating IBS (IBS-A)]; IBS with constipation (IBS-C); and IBS with diarrhea (IBS-D). Each subtype has its own set of symptoms and challenges. New-onset irritable bowel syndrome was reported in 22 out of 104 Gulf War veterans (21%) (Figure 1). A total of 17 out of 22 (77%) reported mixed irritable bowel syndrome (IBS-M). IBS-M is a subtype of IBS where individuals experience a combination of both constipation and diarrhea, with alternating periods of each. Potential contributing factors in veterans for IBS-M: 1) A complex interplay of stress, diet, and lifestyle factors; 2) Previous exposure to environmental factors during military service. Managing IBS-M, particularly in veterans, involves addressing the

unique factors that may contribute to the development or exacerbation of symptoms. The other 5 out of 22 (23%) developed diarrhea-predominant irritable bowel syndrome (IBS-D). Veterans with IBS-D typically have frequent bowel movements with loose or watery stools. Potential Contributing Factors in Veterans: 1) Dietary changes during deployment; 2) Exposure to infectious agents during service. 3) Stress, including post-traumatic stress disorder (PTSD), which is prevalent among veterans. None of the veterans reported IBS-C.

In addition to irritable bowel symptoms, 11 out of 22 (50%) of the veterans with irritable bowel syndrome also complained of intermittent bloating symptoms (Figure 1). Bloating is a common symptom associated with IBS, and it was also commonly present in the current Gulf War Veterans with IBS to experience intermittent bloating. Bloating can be caused by various factors, including abnormal gas accumulation in the digestive tract, altered gut motility, and heightened visceral sensitivity to gas or intestinal distension.

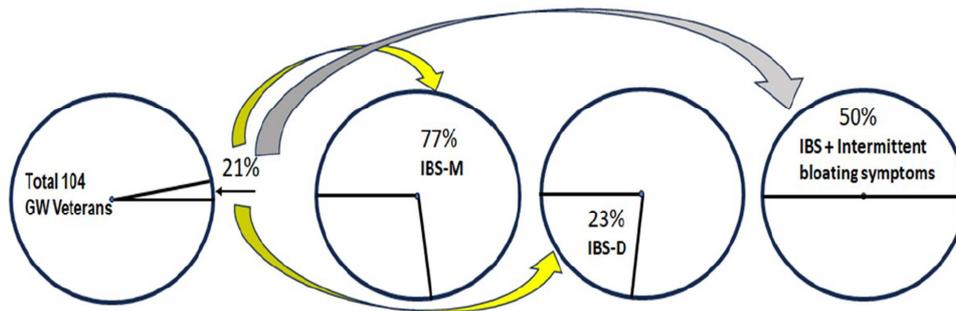


Figure 1. IBS Phenotype Subset Expression in Gulf War Veterans.

3.2. Dyspepsia

Dyspepsia, commonly referred to as indigestion, is characterized by symptoms such as epigastric pain or discomfort, bloating, early satiety (feeling full soon after starting a meal), and sometimes nausea. Veterans with IBS may also experience dyspepsia, as both conditions can involve disturbances in gastrointestinal motility and visceral sensitivity. New-onset dyspepsia was reported by 17 out of 104 (16%) of Gulf War veterans. Of the 17 veterans with dyspepsia, 6 out of 17 (35%) also had secondary bloating symptoms (Figure 2). Dyspepsia is characterized by symptoms such as upper abdominal pain, bloating, and discomfort, while bloating refers specifically to the sensation of fullness and distension in the abdomen. Dyspepsia and bloating can have common causes, such as gastrointestinal motility issues, dietary factors, and stress. Veterans may have been exposed to various stressors during their military service, and stress can exacerbate both dyspepsia and bloating symptoms.

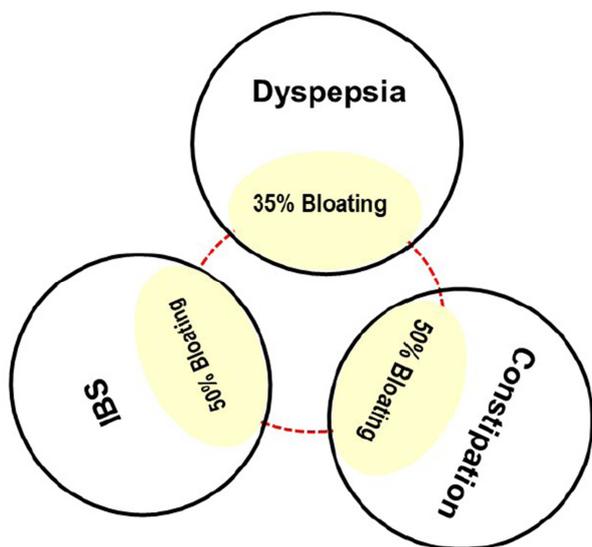


Figure 2. Overlap of bloating in veterans with irritable bowel syndrome, dyspepsia, and constipation.

3.3. Diarrhea

New-onset functional diarrhea was reported by 50 out of 104 (48%) of Gulf War Veterans. None of the veterans with

functional diarrhea reported overlapping bloating or dyspepsia. Diarrhea reported by Gulf War Veterans is one of the various health concerns associated with their military service during the Gulf War. Gulf War Veterans have reported a cluster of unexplained and a variety of symptoms, and gastrointestinal issues, such as diarrhea, have been reported. It's important for Gulf War Veterans experiencing persistent diarrhea or other health issues to seek medical attention.

3.4. Bloating

New-onset bloating was reported by 11 out of 104 (11%) of the Gulf War Veterans. None of the veterans with the primary symptom of bloating reported diarrhea, dyspepsia, irritable bowel syndrome, or constipation. The exact cause of GWI and the association with bloating are not fully understood. Various factors have been considered, including environmental exposures, chemical toxins, stress, and infectious agents experienced during deployment.

3.5. Constipation

Constipation is one of the gastrointestinal symptoms reported by some Gulf War Veterans experiencing Gulf War Illness (GWI). New-onset constipation was reported by 4 out of 104 (4%) of the Gulf War veterans. A total of 2 out of 4 veterans with constipation also complained of bloating as a secondary symptom (Figure 2). The symptoms for veterans with IBS-C may experience infrequent bowel movements, hard stools, and a sense of incomplete evacuation. The potential contributing factors in veterans for IBS-C: 1) Changes in diet and lifestyle during military service; 2) Stress and trauma related to military experiences; 3) Use of medications for service-related conditions. Given the variability of symptoms among GWI Veterans, including those with constipation, individualized care plans are crucial. Healthcare providers can tailor interventions based on the specific needs and challenges of each individual.

4. Discussion

We investigated veterans who were deployed to the Persian Gulf between 1990-1991 and returned home from active duty with chronic gastrointestinal symptoms. To our knowledge, this is the first study to stratify the phenotypic expression of functional gastrointestinal disorders in veterans deployed to

the Persian Gulf. Our study provides several new findings: (1) veterans developed phenotypically distinct gastrointestinal symptom complexes during deployment to the Persian Gulf; (2) irritable bowel syndrome, dyspepsia, diarrhea, bloating, and constipation were the most common gastrointestinal disorders identified among Gulf War Veterans; and (3) bloating is a common symptom that was shown to often overlap with other gastrointestinal symptom complexes.

The pathophysiologic mechanisms underlying the gastrointestinal symptoms in veterans who served in the Persian Gulf War are unclear but cause significant morbidity. Investigators at the Boston Veterans Affairs Medical Center conducted one of the earliest studies. [11] They evaluated 57 deployed and 44 non-deployed individuals at a National Guard unit. After a 6-12 month deployment in the Persian Gulf, up to 80% of the deployed veterans reported new gastrointestinal symptoms. These symptoms included loose stools and/or >3 stools per day, increased flatulence, incomplete bowel evacuation, as well as loose bowel movements that coincided with abdominal pain relieved with defecation. Over 20% of the deployed veterans reported chronic gastrointestinal symptoms following deployment. [11] The investigators concluded that the development of gastrointestinal symptoms was coincidental with the veterans' deployment to a stressful wartime environment and may be comparable to patients with stress-induced functional bowel disorders.

The results of our current study are similar to those seen in a previous study conducted on patients who traveled abroad on missionary work. [25] That study revealed that travelers who went abroad develop gastrointestinal symptoms that include other symptoms than just diarrhea. Many of the participants in that study reported irritable bowel syndrome, bloating, and dyspepsia. Many of the subjects who had persistent bowel symptoms after traveling abroad had developed them while they were overseas. More specifically, the study found that 53% of subjects had developed diarrhea and 31% irritable bowel syndrome after traveling abroad. Another study evaluated 169 students who traveled to Mexico, where 63% reported diarrhea while in Mexico. A total of 18% had persistent diarrhea 6 months after traveling. The findings in our current study are more consistent with the earlier study at the Boston Veterans Affairs Medical Center, which included Gulf War veterans who were deployed for an extended period in a psychologically stressful Gulf War setting. [11] The timeframe and travel environment may explain differences between the civilian and Gulf War veteran populations.

Dyspepsia is another common gastrointestinal symptom experienced by both veterans and travelers abroad. In our returning Gulf War veteran population, 16% reported dyspepsia after deployment to the Persian Gulf. The pathogenesis of dyspepsia is uncertain, however, experimental data in clinical studies suggest that gastroenteritis and gastric inflammation can lead to chronic changes in the myenteric plexus and gastrointestinal smooth muscle function resulting in dysmotility and dyspepsia. Similarly, post-infectious dyspepsia was reported after a Salmonella gastroenteritis

outbreak. [26] Stress may play a role in the chronic response to enteric infection and, in so doing, may induce chronic functional gastrointestinal disorders. [16] Gastrointestinal inflammation sensitizes receptors gut receptors and silent nociceptors trigger at a lower pain threshold. [17]

Overall, our new findings give insight into the gastrointestinal symptoms that many veterans deployed to the Persian Gulf experience upon returning home. However, we acknowledge a few limitations of our study. Our studies focused on Gulf War veterans enrolled in the Gulf War Registry at the Cincinnati VAMC. It is unclear if these findings apply to Gulf War veterans at other VAMCs. Also, the use of patient records describing veterans who sought care may be biased and they may report a higher prevalence of disorders. A high prevalence of bowel disorders after the Gulf War may be due to increased healthcare utilization and higher reporting by the veterans after returning from deployment to the Persian Gulf.

5. Conclusion

In conclusion, our current study investigated veterans deployed to the Persian Gulf and returned from active duty with persistent gastrointestinal symptom complexes. Thus, the development of irritable bowel syndrome, dyspepsia, diarrhea, bloating, and constipation are common among deployed veterans with Gulf War Syndrome and these symptoms persist after returning from deployment. To our knowledge, this is the first study to stratify the phenotypic expression of functional gastrointestinal complexes in veterans deployed to the Persian Gulf. These results support other studies on travelers who develop gastrointestinal disorders after traveling abroad. The findings of this study may also apply to veterans returning from other deployment assignments, so future studies of veterans from other military conflicts are needed. The conclusions of our study are important as they may lead to earlier diagnosis of gastrointestinal symptom complexes for veterans who suffer from chronic gastrointestinal disorders upon returning from deployment from the Persian Gulf.

Abbreviations

IBS: Irritable Bowel Syndrome
SD: Standard Deviation
IBS-M: Mixed Bowel Movements
IBS-A: Alternating IBS
IBS-C: IBS with Constipation
IBS-D: IBS with Diarrhea

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Acknowledgments

Supported by the Department of Veterans Affairs (CX001477) to QZ and GNV; and the National Institute of

Diabetes and Digestive and Kidney Diseases (DK099052 & DK118959) to QZ and GNV.

Conflicts of Interests

The authors declare no conflicts of interest.

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