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Observational Study

Enduring association between IBS and war trauma in civilians from the Nicaragua Civil War period: A population-based study

War trauma and IBS in civilian populations

Abstract

BACKGROUND

Psychosocial and physical trauma are known risk factors for irritable bowel syndrome (IBS), including in war veterans, whereas war exposure in civilians is unclear. Nicaragua experienced two wars, 1970-1990: The Sandinistas Revolution (1970s) and The Contra War (1980s). Our aim was to investigate the role of exposure to war trauma in the subsequent development of IBS in the context of an established health surveillance system (11,000 households).

AIM

To investigate in a civilian population the relationship between exposure to war trauma and events and the subsequent development of IBS in the context of an established public health and demographic surveillance system in western Nicaragua.

METHODS

We conducted a nested population-based, cross-sectional study focused on functional gastrointestinal disease (FGIDs) based on Rome II criteria. 1617 adults were randomly selected. The Spanish Rome II Modular Questionnaire and Harvard Trauma Questionnaire were validated in Nicaragua. War exposure was assessed with 10

measures of direct and indirect war trauma and post-war effects. Multiple exposures were defined by ≥ 3 measures.

RESULTS

The prevalence of IBS was 15.2% (F 17.1%, M 12.0%), war exposure 19.3% (F 9.3%, M 36.7%), and PTSD 5.6% (F 6.4%, M 4.3%). Significant associations with IBS in the civilian population were observed (adjusted by gender, age, socioeconomic status, education): physical and psychological abuse (aOR 2.25; 95%CI, 1.1-4.5), witnessed execution (aOR 2.4; 1.1-5.2), family member death (aOR 2.2; 1.2-4.2), and multiple exposures (aOR 2.7; 1.4-5.1). PTSD was independently associated with IBS (aOR 2.6; 1.2-5.7).

CONCLUSION

An enduring association was observed in the Nicaragua civilian population between specific civil war-related events and subsequent IBS. Civilian populations in regions with extended armed conflict may warrant provider education and targeted interventions for patients.

Key Words: Irritable Bowel Syndrome (IBS); Functional Gastrointestinal Disorders (FGID); war trauma; civil war; post-traumatic stress disorder (PTSD); Central America

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Core Tip: What is known: Psychosocial and physical trauma are known risk factors for irritable bowel syndrome (IBS), including in war veterans. What is new: An enduring association was observed in the Nicaragua civilian population between specific civil war-related events and subsequent IBS. Civilian populations in regions with extended armed conflict may warrant provider education and targeted interventions for patients

INTRODUCTION

Irritable bowel syndrome (IBS) is an important functional gastrointestinal disorder (FGID) affecting 1.1% to 35.5% of the general population.¹ In North America, Europe, Australia and New Zealand the prevalence is estimated to be 8.1% (95%CI 7.0-8.3)^[1]. Recent data developed in North America and the United Kingdom (UK) estimated an IBS prevalence with Rome IV criteria in 4.6% (95%CI 4.1%-5.2%)^[2]. In Latin America, the prevalence may be 2-3 times higher (17.5%, 95%CI 16.9%- 18.2%)^[1]. Furthermore, in central America the IBS studies are scarce, and not reported prevalence of IBS according to subtype^[3]. The pathophysiology of IBS is a complex bio-psychosocial disease model. Variation in disease epidemiology may be explained by the heterogeneity of the biology, cultural and socioeconomic context, evolution of diagnostic criteria, and the microbiome, including parasite and viral infections^[1, 4-6] IBS is associated with multiple comorbidities, including somatic pain syndromes, other gastrointestinal disorders and psychiatric disorders, which affect patient quality of life and health care utilization^[1, 7]. IBS and war veterans Most studies of FGIDs and war trauma have focused on professional soldiers. Studies in deployed U.S. veterans identified a positive association between IBS, life stressors and gastroenteritis^[8-10]. An analysis from the Millennium Cohort study, antecedent infectious gastroenteritis, female gender, life stressors, and anxiety are significantly associated with IBS^[8]. This suggests that functional gastrointestinal disorders may develop following war exposure, and may exert significant longterm adverse effects. In addition, the risk of IBS in women veterans is nearly three times higher (OR 2.82, 95%CI 2.06-3.85) in those with posttraumatic stress disorder (PTSD)^[11]. A recent meta-analysis based on 8 studies found PTSD ³to be a significant risk factor for IBS (OR 2.80, 95%CI 2.06-3.54)^[12]. In Gulf War veterans, a case-control study found a positive association with IBS with chronic multisymptom illness (CMI) condition (OR 11.57, 95%CI 3.66-36.58)^[9,10]. Similarly, Tujeda *et al*, founded a long-term persistence of FGIDs up to 16 years post-deployment, and a positive association with psychological disorders, ⁶extra-intestinal symptoms, and lower of quality of life (QOL)^[10]. ⁶The Central America

Four (CA-4) region The Central America Four region (CA-4), Nicaragua, Honduras, El Salvador, and Guatemala, are interconnected by geography, history, language, and development indices^[13]. In 2006, the CA-4 opened borders, similar to the European Union, and has been in transition toward a union of many aspects of their infrastructure, which has had implications for the health systems. The development indices in the CA-4 rank among the lowest in the Western Hemisphere: multidimensional poverty approaches 20%, and nearly half (48%) of the CA-4 population lives in rural areas^[13]. Civil wars dominated the region from 1970-1996, centered in Nicaragua, El Salvador and Guatemala. Importantly, the CA-4 countries account for a large number of the recent immigrant population to the United States, which makes the region unique among global low/middle income countries (LMICs) from a U.S. perspective^[13]. A number equivalent to one quarter of the population of El Salvador lives in the United States, and most are foreign born. From the US viewpoint, research and prevention initiatives in the CA-4 may be informative for U.S. Hispanic populations, particularly for those from the region (> 5 million)^[13]. The Nicaragua Civil War period, 1970-1990 Nicaragua suffered through two civil wars in 1970s and 1980s: The Popular Sandinista Revolution in the 1970s, with peak combat intensity in 1975-79, and the counter-revolution “Contra War” in the 1980s. The Sandinista Revolution was an intense conflict throughout the country, with the greatest intensity in the western region in the cities of León and Chinandega. The civilian population of Leon lived with armed confrontations and aerial bombing^[14]. The Contra War developed after the Sandinista victory, in the context of regional conflicts in Central America and the Cold War. It is estimated that 50,000 people were killed in each of the two conflicts, and tens of thousands more were exposed to war events and trauma^[14,15]. Based upon the enduring oral history of the civil wars in the Leon region, and the emerging bio-psychosocial model of IBS, we hypothesized a potential association between civil conflict and IBS. Our aim was to investigate in a civilian population the relationship between exposure to war trauma and events and the subsequent development of IBS in the context of an established public health and demographic surveillance system in western Nicaragua.

MATERIALS AND METHODS

STUDY DESIGN We conducted a nested population-based, cross-sectional study of IBS and the FGIDs with the Rome II criteria in western Nicaragua, utilizing the León Health and Demographic Surveillance System (León-HDSS). The Centre of Epidemiology and Health Research (CIDS), within the National Autonomous University of Nicaragua-León (UNAN-León), oversees the Leon-HDSS, established in 1993. The municipality of León has an area of 820 km², including rural and urban populations^[16]. The Leon-HDSS encompasses 10,994 households with 54,647 individuals, distributed in 208 randomly-distributed geographical clusters, which encompass approximately 22% of the population of the municipality of León^[16]. The current study is nested within a comprehensive study of the population prevalence of the FGIDs, based upon Rome 2 criteria, with final enrollment of 1,617 persons randomly selected from urban and rural areas. (The sample size was based upon an estimated IBS prevalence of 11%, alpha 5%, and 5% losses to follow-up within the Leon-HDSS). Thereafter, individuals born before 1975 were selected to meet the criteria of having been at least 5 years of age during the peak war period of 1975-1979 in the Leon region ($n = 1,012$).

VARIABLES AND INSTRUMENTS Socioeconomic status was measured by a validated poverty index based on the United Nations (U.N.) unsatisfied basic needs index (UBN)^[16, 17]. This is a scale from 0 to 4 (0-1 non-poor, 2-3 poor, and 4 extremely poor) that is based on four indicators: household condition, water and sanitation services, school enrolment, and number of dependents in the household. This scale has been adapted and validated to specific conditions in Nicaragua^[16]. Educational level was categorized into four levels: no schooling or illiterate, primary school, secondary school and university/professional formation. The Rome II Modular Questionnaire (R2MQ) was used to identify IBS cases, which were confirmed by physician interview^[18,19]. To validate the R2MQ instrument in Nicaragua, we performed an independent selection of 400 individuals (not included in the study sample) for dual R2MQ assessments by trained field coordinators with an interval of 15 days (± 1 day) between the first and second interview. Alternate field

coordinators conducted the second R2MQ assessment. The study subjects were randomly selected per the Leon-HDSS standing protocol. 380 subjects completed the two R2MQ assessments. Case status was confirmed thereafter *via* interviews by trained physicians, who were blinded to the survey results. We documented an R2MQ accuracy of 88% and repeatability of 84% (data not shown). The assessment of war trauma included direct exposures, indirect exposures, and post-war effects. The direct exposures refer to those experienced by the individual and included forced conscription, service in combat, personal trauma and disability, witnessed executions, and physical or psychological abuse. Indirect exposures included experiences of family members, and death of a family member. The post-war effects were focused on unemployment, loss of personal property, and rejection by family members. Unemployment includes difficulty finding employment in the immediate post-war period, and extended unemployment. The Harvard Trauma Questionnaire (HTQ) was used as a proxy to measure posttraumatic stress disorder. The war trauma instrument was developed by Mollica *et al*^[20], and includes a section covering 30 symptoms likely to be present after traumatic experiences, scored from 1 (not at all) to 4 (extremely). The trauma symptoms section of the HTQ is derived from the Diagnostic and Statistical Manual IV (DSM-IV) criteria for PTSD, with some additional questions specific to refugee trauma. The HTQ was validated in victims after the 1974 earthquake in Nicaragua, achieved a sensitivity of 95% and specificity of 77% with a cut-off 50/51 out of a maximum score 120^[21].

STATSTICAL METHODS AND ETHICS The variable distribution by groups (gender and strata age [29-39, 40-49 and ≥50]) was analysed with Mantel-Haenszel chi square test for categorical variables. The prevalence of IBS across the exposure variables (gender, age, socioeconomic status, educational level, war exposure, and PTSD). The multiple logistic regression model was adjusted for age, gender, education, and poverty level. In the analysis, age [age of ≥ 45 years old (29-44 or 45-65)], socioeconomic status [non-poor (0 to 1) *vs* poor (2 to 4)], and educational level (elementary primary school or less educational level *vs* secondary school or more) were dichotomized. The model was used to examine the relationship between IBS and war events and exposures (direct and indirect exposures, and postwar

effects). A distinct analysis was conducted for PTSD with and without war exposure and the association with IBS. The 95% confidence interval and p value <0.05 is used for the reported values. All analyses were done using IBM SPSS Statistics for Mac, Version 20.0 (IBM Corp., Armonk, NY, USA). This study was approved by the Institutional Review Boards of the University of North Carolina, Chapel Hill (#02-MED-461) and UNAN-Leon. All Good Clinical Practice (GCP) standards were followed, including informed consent with each subject, participant confidentiality and anonymized data. There were no conflicts of interest with respect to industry or government.

RESULTS

The prevalence of IBS in the LMIC setting of in Central America is significant and consistent with studies in Latin America. An enduring association in the civilian population of IBS with prior exposure to specific war-related events is observed, in a region of extended civil conflict. Our findings have important implications for healthcare programs for providers and civilian populations in the post-war period^[35].

DISCUSSION

Our population-based study in the civilian population of Nicaragua demonstrates an association of direct and indirect exposure to war events with the subsequent development of IBS. IBS was associated with specific war exposures, including physical or psychological abuse, a witnessed execution, and the death of a family member. A 'dose effect' is also observed, with an increased risk of IBS among those with ≥ 3 types of war trauma. Riddel *et al* describe an increase association in relation with the numbers of life stressors and female gender^[7]. Notably, the majority of studies to date have evaluated the association between deployed veterans and risk of gastrointestinal symptoms or IBS, and from the first Gulf War in particular^[9, 22-24]. The prevalence of IBS was 14.2% (95%CI 12.1-16.5) in the general population (without war trauma exposures), which is similar to estimations in Latin America 17.5% (95%CI, 16.9-18.2), some of which hvw used different Rome instruments^[1]. The IBS prevalence in females (17.1%; 95%CI 14.4-20.2) was greater

than males (12.0%; 95%CI 9.0-15.7), also consistent with Latin America data^[1,25]. We observed a lower IBS prevalence in subjects ≥ 50 years old, similar to the findings by Lovell *et al* in a review of 14 studies (OR: 0.75; 95%CI: 0.62-0.92)^[26]. The IBS prevalence was not significantly different among levels of poverty. In this regard, Lovell *et al*, noted an insufficient number of studies ($n = 4$) of the IBS association with socioeconomic status, and insufficient for assessment of heterogeneity^[26]. We found that the abuse of civilians in a civil armed conflict setting, physical or psychological, was independently associated with IBS. The association of abuse and IBS is a consistent finding in patients^[27-29]. Talley *et al* reported likelihood abuse (physical, emotional and/or verbal) during adulthood in subjects with symptoms of IBS in contrast with controls^[29]. Kanuri *et al* demonstrated a higher prevalence of abuse in the IBS population in comparison with the non-FGID population. Specific forms of abuse, including physical, emotional and sexual, were higher in IBS groups^[28]. Abuse experiences have lasting effects on the mental and gastrointestinal health of individuals, thereby establishing a relationship between these experiences and IBS during the adulthood^[27-29]. In the Nicaraguan civilian population, IBS was associated with PTSD, likely linked to prior war events exposure (42.1%, 95%CI 30.2% - 55.0%, p value < 0.001). The increased risk of gastrointestinal syndromes among men and women is a consistent finding with warzone exposure^[23,30]. Increased rates of IBS among deployed U.S. veterans^[9, 22, 24]. In a population-based military survey in China, appreciable differences in the prevalence of IBS were noted between aircrew and ground personnel (5.72% *vs* 3.70%), $p < 0.05$ ^[31]. In one of the major cohort studies among U.S. military personnel from all service branch, Riddle *et al*, identified a strong association between IBS and PTSD^[8]. Maguen *et al* conducted a retrospective, cross-sectional analysis of >600,000 Iraq and Afghanistan War veterans, finding that IBS was more likely among both males and females among those with PTSD^[32]. A meta-analysis with 648,375 subjects reported a pooled IBS risk OR of 2.80 (95%CI 2.06 to 3.54; $P < 0.001$) with PTSD^[12]. Our finding demonstrated similar association in the logistic regression model. In 2016, the Institute of Medicine (IOM) confirmed that there was sufficient evidence demonstrating an association between deployment to the Gulf War and gastrointestinal

symptoms consistent with FGIDs such as IBS or functional dyspepsia^[22]. Conversely, a UK study on the Iraq War estimated that the prevalence of IBS was relatively low on return from Iraq, although it was significantly higher during deployment^[33]. Tuteja *et al*, demonstrated the long-term persistence of IBS with higher scores for all psychological disorders under study (depression, anxiety, somatization, and global symptoms index) in deployed Gulf War veterans^[10]. Our results in the Nicaragua civil conflict setting suggest a long-term risk of IBS and its association with PTSD and specific war exposures. Likewise, Riddel *et al* describe an increase in association in relation with the numbers of life stressors and female gender^[8]. Our study has several strengths including the random selection of a civilian population from an established health and demographic surveillance system, thereby minimizing selection bias. The variables under study were well defined and used instruments validated in the Nicaraguan population. Our study evaluated a general civilian population and therefore may generalize to civilians in prior or current war zones. The study focused on the period over 15 years after the ending of Contra-Revolution war, and consistent with studies suggesting longstanding risk for the development of clinical IBS^[10,34]. Several study limitations are noted. The cross-sectional design does not confirm causality between war exposure and IBS. Rome II criteria were used, which have different IBS sensitivity and specificity in comparison with Rome III and Rome IV criteria, but notably, each IBS case was verified by a physician interview in our protocol. Our study was conducted several years after war exposure and potentially subject to recall bias, although arguably these recollections are vivid. Lastly, the impact of gastrointestinal infections in this study population in the tropical environment was not evaluated^[6].

CONCLUSION

A total of 1,617 individuals were randomly selected and consented from the Leon-HDSS for household interviews, of whom 1,012 met age inclusion criteria (see Methods). Nearly two-thirds ($n = 644$), were women in table 1. The mean age was 43.8 years old (range 29-65). The distribution of poverty and educational level by gender was similar, with p

values of 0.175 and 0.933, respectively. Men were exposed to a greater number of war events than women (36.7% *vs* 9.3%, $p < 0.001$), and men were more likely than women to have three or more war exposures (16.3% and 1.1%, $p < 0.001$). Participants ages 40-49 were more likely to have war experiences (23.8%, $p = 0.022$) compared with the 29-39 age group (15.7%) and 50-65 years old group (18.6%).

IRRITABLE BOWEL SYNDROME PREVALENCE AND ASSOCIATIONS

The overall prevalence of IBS was 15.2% (95%CI, 13.1-17.6), and significantly higher among women (17.1% *vs* 12.0%, $P = 0.029$). No significant differences in IBS prevalence were noted by age, education, or poverty level. The IBS prevalence was greater among individuals with war exposure, but not statistically significant (17.9% and 14.6%, respectively, $P = 0.237$) in table 2. Three specific war exposures were significantly associated with over two times the future risk of IBS in the logistic regression model adjusted for age, gender, education, and poverty level in table 3. These included physical or psychological abuse (aOR 2.25, 1.1-4.5), a witnessed execution (aOR 2.4, 1.1-5.2), and the death of a family member (aOR 2.2, 1.2-4.2). In addition, a dose effect was noted, as participants with ≥ 3 war exposures also had over two times the IBS risk (aOR 2.7, 1.4-5.1), with a prevalence of 23.9%. The remaining war event exposures were not associated with IBS, including direct combat involvement, physical injury or disability, a wounded family member, and post-war events (loss of personal property, rejection by family and unemployment in table.

PTSD RELATIONSHIP TO WAR EXPOSURE AND IBS

The overall prevalence of PTSD was 5.6%, and without differences observed by gender or age. (Table 1). PTSD specifically caused by war exposure was 3.0% overall, and similar in men and women (3.0 *vs* 2.2, $P = 0.422$) and among the age strata (1.3% *vs* 3.8% *vs* 2.4%, $P = 0.095$) in table 1. Notably, 42.1% (95%CI, 30.2-55.0) and 56% (95%CI, 37.1-73.3) of subjects who fulfilled the criteria for IBS had PTSD and war-associated PTSD, respectively, in table 2. Adjusted for age, gender, education, and poverty level, a strong relationship was observed between IBS and war-associated PTSD (aOR 3.3, 1.1-10.0) in table 3.

ARTICLE HIGHLIGHTS

Research background

Other populations in the world could be affected by IBS as a result of PTSD originated in different stressful conflicts. Interventions in primary health care could be implemented to improve the gut and mental health.

Research motivation

PTSD and IBS symptoms are persistent over the time. The association between them is positive.

Research objectives

Positive association between IBS and PTSD by war exposure in civilians was obtained.

Research methods

A nested cross-sectional study was design. A population data set was used to develop a random selection. Different instruments were validated to collect data. The instruments were focused on IBS, PTSD and poverty. Logistic regression model was develop to respond to our aim.

Research results

To determinate the association between PTSD and IBS in civilians exposed to war.

Research conclusions

According to United Nations Refugee Agency (UNHCR) 108.4 millions of people were forced to flee their homes to escape conflicts in 2023. During this exodus the people are exposed to suffer different PTSD. The Nicaraguan population between 1970 and 1988 was part of this worldwide phenomena.

Research perspectives

Post-traumatic stress disorders (PTSD) in veterans, and the association with Irritable Bowel Syndrome (IBS) is well described, but the impact on civilian population is poor described.

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