

World Journal of *Gastroenterology*

World J Gastroenterol 2023 December 7; 29(45): 5945-6021



EDITORIAL

- 5945 Gut microbiota in women: The secret of psychological and physical well-being
Marano G, Traversi G, Gaetani E, Gasbarrini A, Mazza M

ORIGINAL ARTICLE**Observational Study**

- 5953 Enduring association between irritable bowel syndrome and war trauma during the Nicaragua civil war period: A population-based study
Peña-Galo EM, Wurzelmann D, Alcedo J, Peña R, Cortes L, Morgan D
- 5962 Association of low muscle strength with metabolic dysfunction-associated fatty liver disease: A nationwide study
Lee GB, Huh Y, Lee SH, Han B, Kim YH, Kim DH, Kim SM, Choi YS, Cho KH, Nam GE

Basic Study

- 5974 Thioridazine reverses trastuzumab resistance in gastric cancer by inhibiting S-phase kinase associated protein 2-mediated aerobic glycolysis
Yang ZY, Zhao YW, Xue JR, Guo R, Zhao Z, Liu HD, Ren ZG, Shi M
- 5988 Pien Tze Huang alleviates Concanavalin A-induced autoimmune hepatitis by regulating intestinal microbiota and memory regulatory T cells
Zeng X, Liu MH, Xiong Y, Zheng LX, Guo KE, Zhao HM, Yin YT, Liu DY, Zhou BG

LETTER TO THE EDITOR

- 6017 Intestinal barrier in inflammatory bowel disease: A bibliometric analysis
Luan WY, Yang Z, Chen XD, Zhang TT, Zhang F, Miao YD

ABOUT COVER

Editorial Board Member of *World Journal of Gastroenterology*, Andrew S Day, MB, ChB, MD, FRACP, AGAF, Professor of Paediatrics, Department of Paediatrics, University of Otago, Christchurch 8041, New Zealand. andrew.day@otago.ac.nz

AIMS AND SCOPE

The primary aim of *World Journal of Gastroenterology* (*WJG*, *World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. *WJG* mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

INDEXING/ABSTRACTING

The *WJG* is now abstracted and indexed in Science Citation Index Expanded (SCIE), MEDLINE, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 edition of Journal Citation Reports® cites the 2022 impact factor (IF) for *WJG* as 4.3; Quartile category: Q2. The *WJG*'s CiteScore for 2021 is 8.3.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Hua-Ge Yu*; Production Department Director: *Xiang Li*; Editorial Office Director: *Jia-Ru Fan*.

NAME OF JOURNAL

World Journal of Gastroenterology

ISSN

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LAUNCH DATE

October 1, 1995

FREQUENCY

Weekly

EDITORS-IN-CHIEF

Andrzej S Tarnawski

EXECUTIVE ASSOCIATE EDITORS-IN-CHIEF

Xian-Jun Yu (Pancreatic Oncology), Jian-Gao Fan (Chronic Liver Disease), Hou-Bao Liu (Biliary Tract Disease)

EDITORIAL BOARD MEMBERS

<http://www.wjgnet.com/1007-9327/editorialboard.htm>

PUBLICATION DATE

December 7, 2023

COPYRIGHT

© 2023 Baishideng Publishing Group Inc

PUBLISHING PARTNER

Shanghai Pancreatic Cancer Institute and Pancreatic Cancer Institute, Fudan University
Biliary Tract Disease Institute, Fudan University

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

POLICY OF CO-AUTHORS

<https://www.wjgnet.com/bpg/GerInfo/310>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

PUBLISHING PARTNER'S OFFICIAL WEBSITE

<https://www.shca.org.cn>
<https://www.zs-hospital.sh.cn>

Observational Study

Enduring association between irritable bowel syndrome and war trauma during the Nicaragua civil war period: A population-based study

Edgar M Peña-Galo, Daniel Wurzelmann, Javier Alcedo, Rodolfo Peña, Loreto Cortes, Douglas Morgan

Specialty type: Gastroenterology and hepatology**Provenance and peer review:** Unsolicited article; Externally peer reviewed.**Peer-review model:** Single blind**Peer-review report's scientific quality classification**Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0**P-Reviewer:** Zamani M, Iran;
Zheng H, China**Received:** July 7, 2023**Peer-review started:** July 7, 2023**First decision:** August 8, 2023**Revised:** September 13, 2023**Accepted:** November 27, 2023**Article in press:** November 27, 2023**Published online:** December 7, 2023**Edgar M Peña-Galo, Javier Alcedo**, Department of Digestive Diseases, Miguel Servet University Hospital, Zaragoza 50009, Aragon, Spain**Edgar M Peña-Galo, Javier Alcedo**, Aragon Health Research Institute, IIS Aragon, Zaragoza 50009, Aragon, Spain**Daniel Wurzelmann**, Department of Mental Health, Carolina Partners, Durham, NC 27707, United States**Rodolfo Peña**, Department of Data Analysis, CIDE (Research, Development and Epidemiology Center), Tegucigalpa 11101, Francisco Morazán, Honduras**Loreto Cortes**, School of Medicine, National Autonomous University of Nicaragua, Leon 21000, Leon, Nicaragua**Douglas Morgan**, Department of Gastroenterology and Hepatology, UAB University of Alabama Birmingham, Birmingham, AL 35233, United States**Douglas Morgan**, School of Medicine, The University of North Carolina, Chapel Hill, NC 9500, United States**Corresponding author:** Douglas Morgan, FACG, MD, Director, Professor, Department of Gastroenterology and Hepatology, UAB University of Alabama Birmingham, No. 373 Boshell Bldg, UAB, Birmingham, AL 35233, United States. drmorgan@uabmc.edu

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 (11000 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 disorders 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% [Female (F) 17.1%, Male (M) 12.0%], war exposure 19.3% (F 9.3%, M 36.7%), and post-traumatic stress disorder (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 [adjusted odds ratio (aOR): 2.25; 95% confidence interval: 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; Functional gastrointestinal disorders; War trauma; Civil war; Post-traumatic stress disorder; Central America

©The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights reserved.

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.

Citation: Peña-Galo EM, Wurzelmann D, Alcedo J, Peña R, Cortes L, Morgan D. Enduring association between irritable bowel syndrome and war trauma during the Nicaragua civil war period: A population-based study. *World J Gastroenterol* 2023; 29(45): 5953-5961

URL: <https://www.wjgnet.com/1007-9327/full/v29/i45/5953.htm>

DOI: <https://dx.doi.org/10.3748/wjg.v29.i45.5953>

INTRODUCTION

Irritable bowel syndrome (IBS) is an important functional gastrointestinal disorder (FGID) affecting 1.1% to 35.5% of the general population. In North America, Europe, Australia and New Zealand the prevalence is estimated to be 8.1% [95% confidence interval (95%CI): 7.0-8.3][1]. Recent data developed in North America and the United Kingdom 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 (QOL) 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 United States 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 FGIDs may develop following war exposure, and may exert significant long term adverse effects. In addition, the risk of IBS in women veterans is nearly three times higher [odds ratio (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 to 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 multi-symptom illness condition (OR: 11.57, 95%CI: 3.66-36.58)[9,10]. Similarly, Tuteja *et al*[10], founded a long-term persistence of FGIDs up to 16 years post-deployment, and a positive association with psychological disorders, extra-intestinal symptoms, and lower of QOL. 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 United States 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 United States viewpoint, research and prevention initiatives in the CA-4 may be informative for United States. 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 1975-1979, 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 50000 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, within the National Autonomous University of Nicaragua-León, oversees the León-HDSS, established in 1993. The municipality of León has an area of 820 km², including rural and urban populations[16]. The León-HDSS encompasses 10994 households with 54647 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 1617 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 León-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 ($n = 1012$).

Variables and instruments

Socioeconomic status was measured by a validated poverty index based on the United Nations 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 d (± 1 d) between the first and second interview. Alternate field coordinators conducted the second R2MQ assessment. The study subjects were randomly selected per the León-HDSS standing protocol. Three hundred and eighty 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 PTSD. 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 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].

Statistical 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

Table 1 Demographic, irritable bowel syndrome and war exposure summary

Variable	Total	Gender		P value ¹	Age group			P value ¹
	N (%)	Men, n (%)	Women, n (%)		29-39, n (%)	40-49, n (%)	50-65, n (%)	
Poverty				0.175				0.010 ²
Non-poor	657 (64.9)	229 (62.2)	428 (66.5)		227 (59.6)	224 (65.9)	206 (70.8)	
Poor/extremely poor	355 (35.1)	139 (37.8)	216 (33.5)		154 (40.4)	116 (34.1)	85 (29.1)	
Educational level				0.933				< 0.001 ²
Primary school	489 (48.3)	175	314 (48.8)		117 (30.7)	163 (47.8)	209 (71.8)	
High school	372 (36.8)	(47.6) 137	235 (36.5)		183 (48.0)	124 (36.5)	65 (22.3)	
Professional	151 (14.9)	(37.2) 56 (15.2)	95 (14.7)		81 (21.2)	53 (15.6)	17 (5.8)	
IBS				0.029 ²				0.593
No	858 (84.8)	324 (88.0)	534 (82.9)		320 (84.0)	286 (84.1)	252 (86.6)	
Yes	154 (15.2)	44 (12.0)	110 (17.1)		61 (16.0)	54 (15.9)	39 (13.4)	
PTSD				0.180				0.537
No	955 (94.4)	352 (95.7)	603 (93.6)		362 (95.0)	317 (93.2)	276 (94.8)	
Yes	57 (5.6)	16 (4.3)	41 (6.4)		19 (5.0)	23 (6.8)	15 (5.2)	
War				< 0.001 ²				0.022 ²
No	817 (80.7)	233 (63.3)	584 (90.7)		321 (84.3)	259 (76.2)	237 (81.4)	
Yes	195 (19.3)	135 (36.7)	60 (9.3)		60 (15.7)	81 (23.8)	54 (18.6)	
PTSD + War				0.422				0.095
No	987 (97.0)	357 (97.0)	630 (97.8)		376 (98.7)	327 (96.2)	284 (97.6)	
Yes	25 (3.0)	11 (3.0)	14 (2.2)		5 (1.3)	13 (3.8)	7 (2.4)	
Dose Effect				< 0.001 ²				0.199
0-2 exposures	945 (93.4)	308 (83.7)	637 (98.9)		358 (94.0)	311 (91.5)	276 (94.8)	
≥ 3 exposures	67 (6.6)	60 (16.3)	7 (1.1)		23 (6.0)	29 (8.5)	15 (5.2)	
Total	1012 (100.0)	368 (100.0)	644 (100.0)		381 (100.0)	340 (100.0)	291 (100.0)	

¹Mantel-Haenszel chi square test.²P value < 0.05.

IBS: Irritable bowel syndrome; PTSD: Post-traumatic stress disorder.

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%CI 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, United States). 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 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

A total of 1617 individuals were randomly selected and consented from the León-HDSS for household interviews, of whom 1012 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%, $P <$

Table 2 Irritable bowel syndrome prevalence by Rome II criteria among 1012 study participants

Variables	IBS		P value ¹
	N (%)	95%CI	
Gender			0.029 ²
Male	44 (12.0)	9.0–15.7	
Female	110 (17.1)	14.4–20.2	
Age group			0.593
29-39	61 (16.0)	12.7–20.0	
40-49	54 (15.9)	12.4–20.1	
≥ 50	39 (13.4)	9.9–17.8	
Socioeconomic status ³			0.298
Non-poor	97 (14.8)	12.3–17.7	
Poor/Extremely poor	57 (16.1)	12.6–20.24	
Educational level			0.701
Primary school/Lower	70 (14.3)	11.5–17.7	
High school	61 (16.4)	13.0–20.5	
University/Professional	23 (15.2)	10.4–21.8	
War			0.237
No	119 (14.6)	12.3–17.1	
Yes	35 (17.9)	13.2–23.9	

¹Mantel-Haenszel chi square test.²P value < 0.05.³Based on United Nations Poverty Index, adapted to Nicaraguan population.

95%CI: 95% confidence interval; IBS: Irritable bowel syndrome.

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%).

IBS 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 [adjusted OR (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.

Table 3 Association between Irritable bowel syndrome and specific war exposures

Condition	IBS, n (%)	Non-IBS, n (%)	Unadjusted ¹ , OR (95%CI)	Adjusted ² , OR (95%CI)
Direct Exposures				
War experience	35 (22.7)	160 (18.6)	1.28 (0.84-1.94)	1.30 (0.81-2.09)
Direct combat involvement	13 (8.4)	77 (9.0)	0.93 (0.50-1.72)	0.61 (0.27-1.38)
Abuse, physical or psychological ³	17 (11.0)	47 (5.5)	2.19 (1.19-3.83)	2.25 (1.12-4.49)
Witnessed execution ³	17 (11.0)	51 (5.9)	1.96 (1.10-3.50)	2.41 (1.11-5.23)
Physical injury or disability	3 (1.9)	8 (0.9)	2.11 (0.55-8.04)	1.29 (0.27-6.02)
Indirect Exposures				
Death of a family member ³	20 (13.0)	68 (7.9)	1.73 (1.01-2.94)	2.21 (1.17-4.17)
Family member wounded	9 (5.8)	42 (4.9)	1.20 (0.57-2.53)	0.80 (0.33-1.93)
Post-war effects				
Loss of personal property	3 (1.9)	19 (2.2)	0.87 (0.25-3.00)	0.86 (0.24-3.08)
Rejection by family	5 (3.2)	16 (1.9)	2.58 (0.88-7.54)	2.57 (0.82-8.07)
Unemployment	9 (5.8)	36 (4.2)	1.41 (0.66-3.00)	1.58 (0.69-3.65)
Dose effect				
≥ 3 exposures ³	16 (10.4)	67 (7.8)	1.83 (1.01-3.30)	2.67 (1.39-5.13)
PTSD				
PTSD ³	24 (15.6)	33 (3.8)	4.61 (2.64-8.05)	2.63 (1.21-5.73)
PTSD, war associated ³	14 (9.1)	11 (1.3)	7.70 (3.42-17.3)	3.31 (1.09-10.0)

¹Crude odds ratio.²Multiple logistic regression analysis adjusted by gender, age, poverty and educational level.³Significant association with IBS.

95%CI: 95% confidence interval; IBS: Irritable bowel syndrome; PTSD: Post-traumatic stress disorder.

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. Riddle *et al*[8] describe an increase association in relation with the numbers of life stressors and female gender. 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 have 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 and Ford[26] in a review of 14 studies (OR: 0.75; 95%CI: 0.62-0.92). The IBS prevalence was not significantly different among levels of poverty. In this regard, Lovell and Ford[26] noted an insufficient number of studies ($n = 4$) of the IBS association with socioeconomic status, and insufficient for assessment of heterogeneity. 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]. Koloski *et al* [29] reported likelihood abuse (physical, emotional and/or verbal) during adulthood in subjects with symptoms of IBS in contrast with controls. Kanuri *et al*[28] 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. 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 United States 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 United States military personnel from all service branch, Riddle *et al*[8], identified a strong association between IBS and PTSD. Maguen *et al*[32] conducted a

retrospective, cross-sectional analysis of > 600000 Iraq and Afghanistan War veterans, finding that IBS was more likely among both males and females among those with PTSD. A meta-analysis with 648375 subjects reported a pooled IBS risk OR of 2.80 (95%CI: 2.06-3.54; $P < 0.001$) with PTSD[12]. Our finding demonstrated similar association in the logistic regression model. In 2016, the Institute of Medicine 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 United Kingdom study on the Iraq War estimated that the prevalence of IBS was relatively low on return from Iraq, although it was significant higher during deployment[33]. Tuteja *et al*[10], 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. 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, Riddle *et al*[8] describe an increase association in relation with the numbers of life stressors and female gender. 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

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].

ARTICLE HIGHLIGHTS

Research background

Post-traumatic stress disorder (PTSD) in veterans, and the association with irritable bowel syndrome (IBS) is well described, but the impact on civilian population is poor described.

Research motivation

According to United Nations Refugee Agency 108.4 million 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 objectives

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

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 developed to respond to our aim.

Research results

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

Research conclusions

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

Research perspectives

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.

ACKNOWLEDGEMENTS

The authors acknowledge to the staff of the Centre for Health and Demographic Research (CIDS) at the Autonomous National University of Nicaragua in León (UNAN-León). The authors would like to thank to Chris Martin, MPH (School of Medicine, the University of North Carolina, Chapel Hill, United States) for his contributions to the study.

FOOTNOTES

Author contributions: Morgan D and Peña R designed the research; Peña-Galo EM, Peña R, and Cortes L contributed with data acquisition; Peña-Galo EM, Wurzelmann D, Peña R, Alcedo J, and Morgan D analyzed and interpreted of data; Morgan D, and Peña EM wrote manuscript; Peña-Galo EM, Peña R, Alcedo J, Wurzelmann D, Cortes L, and Morgan D performed a critical review.

Supported by the UNC UNAN FGID Epidemiology Study Project, No. 54-1808958.

Institutional review board statement: This study was approved by the Institutional Review Boards of the University of North Carolina, Chapel Hill (#02-MED-461) and UNAN-León. All Good Clinical Practice (GCP) standards were followed, including informed consent with each subject, participant confidentiality and anonymized data.

Informed consent statement: All study participants or their legal guardian provided informed written consent about personal and medical data collection prior to study enrolment.

Conflict-of-interest statement: There were no conflicts of interest with respect to industry or government.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country/Territory of origin: United States

ORCID number: Edgar M Peña-Galo 0000-0003-2858-3079; Javier Alcedo 0000-0001-6522-6682; Rodolfo Peña 0009-0008-8496-8452; Douglas Morgan 0000-0002-1136-0963.

Corresponding Author's Membership in Professional Societies: American College of Gastroenterology; American Gastroenterological Association; American Society for Gastrointestinal Endoscopy.

S-Editor: Lin C

L-Editor: A

P-Editor: Yu HG

REFERENCES

- 1 **Sperber AD**, Dumitrascu D, Fukudo S, Gerson C, Ghoshal UC, Gwee KA, Hungin APS, Kang JY, Minhu C, Schmulson M, Bolotin A, Friger M, Freud T, Whitehead W. The global prevalence of IBS in adults remains elusive due to the heterogeneity of studies: a Rome Foundation working team literature review. *Gut* 2017; **66**: 1075-1082 [PMID: 26818616 DOI: 10.1136/gutjnl-2015-311240]
- 2 **Palsson OS**, Whitehead W, Törnblom H, Sperber AD, Simren M. Prevalence of Rome IV Functional Bowel Disorders Among Adults in the United States, Canada, and the United Kingdom. *Gastroenterology* 2020; **158**: 1262-1273.e3 [PMID: 31917991 DOI: 10.1053/j.gastro.2019.12.021]
- 3 **Oka P**, Parr H, Barberio B, Black CJ, Savarino EV, Ford AC. Global prevalence of irritable bowel syndrome according to Rome III or IV criteria: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2020; **5**: 908-917 [PMID: 32702295 DOI: 10.1016/S2468-1253(20)30217-X]
- 4 **Svensen AT**, Bytzer P, Engsbro AL. Systematic review with meta-analyses: does the pathogen matter in post-infectious irritable bowel syndrome? *Scand J Gastroenterol* 2019; **54**: 546-562 [PMID: 31112663 DOI: 10.1080/00365521.2019.1607897]
- 5 **Shariati A**, Fallah F, Pormohammad A, Taghipour A, Safari H, Chirani AS, Sabour S, Alizadeh-Sani M, Azimi T. The possible role of bacteria, viruses, and parasites in initiation and exacerbation of irritable bowel syndrome. *J Cell Physiol* 2019; **234**: 8550-8569 [PMID: 30480810 DOI: 10.1002/jcp.27828]
- 6 **Morgan DR**, Benshoff M, Cáceres M, Becker-Dreps S, Cortes L, Martin CF, Schmulson M, Peña R. Irritable bowel syndrome and gastrointestinal parasite infection in a developing nation environment. *Gastroenterol Res Pract* 2012; **2012**: 343812 [PMID: 22474433 DOI: 10.1155/2012/343812]
- 7 **Shiha MG**, Aziz I. Review article: Physical and psychological comorbidities associated with irritable bowel syndrome. *Aliment Pharmacol Ther* 2021; **54** Suppl 1: S12-S23 [PMID: 34927759 DOI: 10.1111/apt.16589]
- 8 **Riddle MS**, Welsh M, Porter CK, Nieh C, Boyko EJ, Gackstetter G, Hooper TI. The Epidemiology of Irritable Bowel Syndrome in the US Military: Findings from the Millennium Cohort Study. *Am J Gastroenterol* 2016; **111**: 93-104 [PMID: 26729548 DOI: 10.1038/ajg.2015.386]

- 9 **Blanchard M**, Molina-Vicenty HD, Stein PK, Li X, Karlinsky J, Alpern R, Reda DJ, Toomey R. Medical Correlates of Chronic Multisymptom Illness in Gulf War Veterans. *Am J Med* 2019; **132**: 510-518 [PMID: 30576630 DOI: 10.1016/j.amjmed.2018.11.045]
- 10 **Tuteja AK**, Talley NJ, Stoddard GJ, Samore MH, Verne GN. Risk factors for upper and lower functional gastrointestinal disorders in Persian Gulf War Veterans during and post-deployment. *Neurogastroenterol Motil* 2019; **31**: e13533 [PMID: 30697884 DOI: 10.1111/nmo.13533]
- 11 **Dobie DJ**, Kivlahan DR, Maynard C, Bush KR, Davis TM, Bradley KA. Posttraumatic stress disorder in female veterans: association with self-reported health problems and functional impairment. *Arch Intern Med* 2004; **164**: 394-400 [PMID: 14980990 DOI: 10.1001/archinte.164.4.394]
- 12 **Ng QX**, Soh AYS, Loke W, Venkatanarayanan N, Lim DY, Yeo WS. Systematic review with meta-analysis: The association between post-traumatic stress disorder and irritable bowel syndrome. *J Gastroenterol Hepatol* 2019; **34**: 68-73 [PMID: 30144372 DOI: 10.1111/jgh.14446]
- 13 **Piñeros M**, Frech S, Frazier L, Laversanne M, Barnoya J, Garrido C, Gharzouzi E, Chacón A, Fuentes Alabi S, Ruiz de Campos L, Figueroa J, Dominguez R, Rojas O, Pereira R, Rivera C, Morgan DR. Advancing Reliable Data for Cancer Control in the Central America Four Region. *J Glob Oncol* 2018; **4**: 1-11 [PMID: 30241165 DOI: 10.1200/JGO.2016.008227]
- 14 **Farré JA**. Dos guerras en Nicaragua: 1978-1988. *Espacio, Tiempo y Forma, Serie V, Historia. Contemporánea* 1991; **4**: 291-312 [DOI: 10.5944/etfv.4.1991.2741]
- 15 **Garfield RM**, Frieden T, Vermund SH. Health-related outcomes of war in Nicaragua. *Am J Public Health* 1987; **77**: 615-618 [PMID: 3565659 DOI: 10.2105/ajph.77.5.615]
- 16 **Peña R**, Pérez W, Meléndez M, Källestål C, Persson LA. The Nicaraguan Health and Demographic Surveillance Site, HDSS-Leon: a platform for public health research. *Scand J Public Health* 2008; **36**: 318-325 [PMID: 18519303 DOI: 10.1177/1403494807085357]
- 17 **Boltvinik J**. Poverty Measurement and Alternative Indicators of Development. In: van der Hoeven R, Anker R, editor. *Poverty Monitoring: An International Concern*. London: Palgrave Macmillan, 1999 [DOI: 10.1007/978-1-349-23134-8_4]
- 18 **Caplan A**, Walker L, Rasquin A. Validation of the pediatric Rome II criteria for functional gastrointestinal disorders using the questionnaire on pediatric gastrointestinal symptoms. *J Pediatr Gastroenterol Nutr* 2005; **41**: 305-316 [PMID: 16131985 DOI: 10.1097/01.mpg.0000172749.71726.13]
- 19 **Kwan AC**, Bao T, Chakkaphak S, Chang FY, Ke M, Law NM, Leelakusolvong S, Luo JY, Manan C, Park HJ, Piyaniran W, Qureshi A, Long T, Xu GM, Xu L, Yuen H. Validation of Rome II criteria for functional gastrointestinal disorders by factor analysis of symptoms in Asian patient sample. *J Gastroenterol Hepatol* 2003; **18**: 796-802 [PMID: 12795751 DOI: 10.1046/j.1440-1746.2003.03081.x]
- 20 **Mollica RF**, Caspi-Yavin Y, Bollini P, Truong T, Tor S, Lavelle J. The Harvard Trauma Questionnaire. Validating a cross-cultural instrument for measuring torture, trauma, and posttraumatic stress disorder in Indochinese refugees. *J Nerv Ment Dis* 1992; **180**: 111-116 [PMID: 1737972]
- 21 **Caldera T**, Palma L, Penayo U, Kullgren G. Psychological impact of the hurricane Mitch in Nicaragua in a one-year perspective. *Soc Psychiatry Psychiatr Epidemiol* 2001; **36**: 108-114 [PMID: 11465781 DOI: 10.1007/s001270050298]
- 22 **National Academies of Sciences, Engineering, and Medicine**. Update of Health Effects of Serving in the Gulf War, 2016. In: *Gulf War and Health*. Washington, DC: The National Academies Press, 2016 [DOI: 10.17226/21840]
- 23 **Maule AL**, Janulewicz PA, Sullivan KA, Krengel MH, Yee MK, McClean M, White RF. Meta-analysis of self-reported health symptoms in 1990-1991 Gulf War and Gulf War-era veterans. *BMJ Open* 2018; **8**: e016086 [PMID: 29440208 DOI: 10.1136/bmjopen-2017-016086]
- 24 **Wang WF**, Guo XX, Yang YS. Gastrointestinal problems in modern wars: clinical features and possible mechanisms. *Mil Med Res* 2015; **2**: 15 [PMID: 26301101 DOI: 10.1186/s40779-015-0042-5]
- 25 **Lovell RM**, Ford AC. Effect of gender on prevalence of irritable bowel syndrome in the community: systematic review and meta-analysis. *Am J Gastroenterol* 2012; **107**: 991-1000 [PMID: 22613905 DOI: 10.1038/ajg.2012.131]
- 26 **Lovell RM**, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. *Clin Gastroenterol Hepatol* 2012; **10**: 712-721.e4 [PMID: 22426087 DOI: 10.1016/j.cgh.2012.02.029]
- 27 **Grinsvall C**, Törnblom H, Tack J, Van Oudenhove L, Simrén M. Relationships between psychological state, abuse, somatization and visceral pain sensitivity in irritable bowel syndrome. *United European Gastroenterol J* 2018; **6**: 300-309 [PMID: 29511560 DOI: 10.1177/2050640617715851]
- 28 **Kanuri N**, Cassell B, Bruce SE, White KS, Gott BM, Gyawali CP, Sayuk GS. The impact of abuse and mood on bowel symptoms and health-related quality of life in irritable bowel syndrome (IBS). *Neurogastroenterol Motil* 2016; **28**: 1508-1517 [PMID: 27151081 DOI: 10.1111/nmo.12848]
- 29 **Koloski NA**, Talley NJ, Boyce PM. A history of abuse in community subjects with irritable bowel syndrome and functional dyspepsia: the role of other psychosocial variables. *Digestion* 2005; **72**: 86-96 [PMID: 16127275 DOI: 10.1159/000087722]
- 30 **Wachen JS**, Shipherd JC, Suvak M, Vogt D, King LA, King DW. Posttraumatic stress symptomatology as a mediator of the relationship between warzone exposure and physical health symptoms in men and women. *J Trauma Stress* 2013; **26**: 319-328 [PMID: 23695839 DOI: 10.1002/jts.21818]
- 31 **Wu W**, Guo X, Yang Y, Peng L, Mao G, Qurratulain H, Wang W, Sun G. The prevalence of functional gastrointestinal disorders in the chinese air force population. *Gastroenterol Res Pract* 2013; **2013**: 497585 [PMID: 23653637 DOI: 10.1155/2013/497585]
- 32 **Maguen S**, Madden E, Cohen B, Bertenthal D, Seal K. Association of mental health problems with gastrointestinal disorders in Iraq and Afghanistan veterans. *Depress Anxiety* 2014; **31**: 160-165 [PMID: 23494973 DOI: 10.1002/da.22072]
- 33 **Goodwin L**, Bourke JH, Forbes H, Hotopf M, Hull L, Jones N, Rona RJ, Wessely S, Fear NT. Irritable bowel syndrome in the UK military after deployment to Iraq: what are the risk factors? *Soc Psychiatry Psychiatr Epidemiol* 2013; **48**: 1755-1765 [PMID: 23636672 DOI: 10.1007/s00127-013-0699-6]
- 34 **Ford AC**, Forman D, Bailey AG, Axon AT, Moayyedi P. Fluctuation of gastrointestinal symptoms in the community: a 10-year longitudinal follow-up study. *Aliment Pharmacol Ther* 2008; **28**: 1013-1020 [PMID: 18657131 DOI: 10.1111/j.1365-2036.2008.03813.x]
- 35 **Leaning J**, Guha-Sapir D. Natural disasters, armed conflict, and public health. *N Engl J Med* 2013; **369**: 1836-1842 [PMID: 24195550 DOI: 10.1056/NEJMr1109877]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: bpgoffice@wjgnet.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

