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Adverse Childhood Experiences are Associated with Irritable Bowel Syndrome and Gastrointestinal Symptom Severity

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Abstract

BACKGROUND & AIMS—Early adverse life events (EALs) are associated with irritable bowel syndrome (IBS). Exposure to EALs as assessed by the Adverse Childhood Experiences (ACE) questionnaire is associated with greater disease prevalence, but ACE has not been studied in gastrointestinal disorders. Study aims were to: 1) Estimate the prevalence of EALs in the IBS patients using the ACE questionnaire; 2) Determine correlations between ACE and Early Trauma Inventory Self Report-Short Form (ETI-SR) scores to confirm its validity in IBS; and 3) Correlate ACE scores with IBS symptom severity.

METHODS—148 IBS (73% women, mean age=31 years) and 154 HCs (59% women, mean age=30 years) completed the ACE and ETI-SR between June 2010 and April 2015. These surveys measured EALs before age 18 in the domains of physical, sexual, emotional abuse, and general trauma. IBS and abdominal pain severity was measured by a 20-point scale (0=none, 20=worst symptoms).

RESULTS—The ACE score increased the odds of having IBS (odds ratio (OR)=2.05 [95% confidence interval (CI): 1.21-3.48], $p=0.008$). Household mental illness ($p<0.001$), emotional

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abuse ($p=0.004$), and incarcerated household member ($p=0.019$) were significant predictors of IBS. ACE and ETI-SR scores were strongly correlated ($r=0.59$, $p<0.001$). ACE, but not ETI-SR, modestly correlated with IBS severity ($r=0.17$, $p=0.036$) and abdominal pain ($r=0.20$, $p=0.015$).

CONCLUSION—The ACE questionnaire is a useful instrument to measure EALs in IBS based on its use in large studies, its ability to measure prevalence across different EAL domains, and its correlation with symptom severity.

Keywords

Irritable Bowel Syndrome; Early Life Trauma; Adverse Childhood Experiences; Early Life Trauma Inventory; Abuse

INTRODUCTION

Adverse childhood experiences ACEs, also known as early adverse life events (EALs), include traumas experienced early in life, such as childhood abuse, household mental illness or domestic violence. Patients with irritable bowel syndrome (IBS), a functional gastrointestinal disorder characterized by abdominal pain associated with alterations in stool form and/or frequency,[1] report a higher prevalence of EALs in comparison to healthy controls (HCs). [2-6]

In the last decade, the study of the health and societal impact of EALs has transitioned from a topic of research to a public health imperative. This is largely due to the results of The ACE Study, conducted by investigators from the Centers for Disease Control and Prevention (CDC) and Kaiser Permanente, which demonstrated a dose response effect between the number of EALs as assessed by the ACE questionnaire and a variety of negative health outcomes in a cohort of over 17,000 members of a health maintenance organization.[7]

More recently, data on EALs has been collected in 22 states as part of the CDC's Behavioral Risk Factor Surveillance System, the largest ongoing health survey in the world.[8] Published results show consistent findings in data from 10 states ($n=53,998$), in which 44.1%, 12.7%, and 2.6% reported 1-3, 4-6 and 7-9 EALs, respectively, and a graded increase in the risk of health conditions including coronary heart disease, diabetes, overall physical and mental health with increasing ACE score.[9]

Knowledge of the negative impact of EALs has led to policy initiatives and law[10] geared toward early intervention and prevention of EALs. Some have questioned whether inquiring about EALs in adults is beneficial. Despite this being a common concern of physicians and researchers, there is little to suggest that asking about EALs is harmful.[11] Studies have demonstrated that IBS patients want to learn about the impact of psychological factors on symptoms,[12] and that psychological treatment such as cognitive behavioral therapy (CBT) reduces IBS symptoms and improves health related quality of life.[13] One goal of CBT is to decrease reliance on negative coping mechanisms,[14] which are common in those with a history of EALs.[15]

In previous studies, we have measured EALs in IBS patients and HCs with the Early Trauma Inventory Self Report- Short Form (ETI-SR),[4, 16] which measures items within the

categories of general trauma, physical punishment, emotional abuse and sexual abuse before the age of 18. Emotional abuse was found to be the strongest predictor of IBS.[4] Similar to the ETI-SR, the ACE questionnaire includes items in the domains of physical, emotional, and sexual abuse, and general trauma occurring before the age of 18. However, unlike the ETI-SR, the ACE can provide dichotomous outcome measures for each domain and for the overall survey indicating the presence or absence of EALs (i.e., prevalence). The ACE questionnaire has not been studied in IBS.

The aims of this study were to: 1) Compare the prevalence of EALs using the ACE score in IBS patients and HCs; 2) Correlate ACE and ETI-SR scores in IBS and HCs to confirm the validity of ACE in IBS, 3) Compare the mean ETI-SR scores in IBS and HCs with and without EALs; and 3) Determine the correlation between ACE with severity of IBS symptoms and abdominal pain.

METHODS

Study Subjects

Male and female participants who were at least 18 years of age were drawn from IBS patients and HCs recruited for studies conducted at our center between June 2010 and April 2015. IBS subjects were predominantly recruited from newspaper or internet community advertisements and from GI clinics who fulfilled Rome III diagnostic criteria. The diagnosis was confirmed by a clinician with expertise in IBS. HC subjects were recruited by advertisement without a history of IBS or other chronic GI or pain conditions, and were not taking psychotropic medication or participating in psychotherapy. Subjects were compensated for completion of a medical history and physical examination and questionnaires.

Questionnaires

Bowel Symptom Questionnaire (BSQ)—This questionnaire measures the presence of IBS and other GI symptoms using Rome III questions and IBS symptom severity and pain severity using a 0 to 20 numeric rating scale over the past week (none to most intense imaginable).

Adverse Childhood Events (ACE) Questionnaire—The ACE questionnaire (Table 1, Supplementary Table 1) assesses the presence of EALs (before age 18) with 18 questions in 8 domains (number of questions) of physical (1), emotional (2), and sexual abuse (4), and includes household substance abuse (2), parental separation or divorce (1), mental illness in household (2), incarcerated household member (1), and parent treated violently (2). ACE score is calculated by assigning 1 point for each domain “Yes”=1 or “No”=0 (ACE score range 0-8= Physical abuse + Emotional Abuse + Sexual Abuse + Household Substance Abuse + Parent Separation/Divorce + Household Mental Illness + Incarcerated Household Member + Parent Treated Violently).[7] ACE can also be scored as presence (ACE total score = 1) or absence (ACE total score = 0) of an EAL.

Early Trauma Inventory Self Report-Short Form (ETI-SR)—The ETI-SR was administered in conjunction with the ACE in order to help confirm the validity of the ACE in IBS. It inventories the occurrence (before the age of 18) of 27 EAL items in the following domains (number of items): general trauma (11), physical (5), emotional (5), and sexual abuse (6). Each of the 27 items is scored as “Yes”=1 or “No”=0 (total score range 0-27). [16]

Other Psychometric Instruments

Current anxiety and depression symptoms were assessed with the Hospital Anxiety and Depression (HAD) Scale.[17] Somatic symptom severity was measured using the Personal Health Questionnaire (PHQ-15) [18] however, it was modified by removal of three GI symptom items (score 0–24) when comparing IBS with HCs. The Visceral Sensitivity Index (VSI)[19] assessed GI-symptom specific anxiety.

The study was approved by the UCLA Institutional Review Board, and all subjects signed a written informed consent prior to start of study.

Statistical Analysis

Multiple logistic regression was used to predict the odds of IBS status from ACE scores while controlling for age, sex, race and education. Spearman's correlation was used to assess the association between pairs of continuous measures. In a secondary analysis, ACE score was analyzed as a categorical variable similar to a recently published large scale study determining if ACE exposure increases odds of having chronic illness.[9] For this analysis, alcoholism and drug abuse were considered as separate ACE categories rather than as one category of substance abuse; thus the ACE score range was 0-9. A p-value threshold of 0.05 was used to define statistical significance, and a range of 0.05 to < 0.1 was interpreted as weak evidence for an effect. Regression analysis p-values reported in the manuscript are adjusted for demographics unless otherwise specified. The p-values in the tables represent comparisons with and without controlling for demographics. Psychological symptoms typically correlate with EAL scores, and thus we considered the analyses not adjusted for these variables to be primary. However, in a secondary analysis, we adjusted for both demographics and psychological symptoms. Bivariate analyses were conducted using both Wilcoxon test and χ^2 tests. All analyses were done using R version 3.1.1 (<http://cran.r-project.org/>).

RESULTS

Subject Characteristics

Subjects included 148 Rome III positive IBS patients (73% women) and 154 HCs (59% women). Compared to HCs, IBS patients were comprised of more women, had a lower BMI, and had higher scores for HAD anxiety and depression symptoms, and somatic symptom severity (Table 2). For HAD anxiety, 75% of IBS patients and 100% of HCs were in the normal range (0-10), and for HAD depression, 96% of IBS patients and 99.4% of HCs were in the normal range.

Prevalence of EALs in IBS using the ACE Questionnaire

As shown in Table 3, the overall prevalence of EALs was higher in IBS compared to HCs. The presence of EALs (i.e., ACE total score ≥ 1) increased the odds of having IBS (odds ratio (OR)=2.05 [95% confidence interval (CI): 1.21-3.48], $p=0.008$). Compared to HCs, IBS subjects had significantly higher ACE total scores (2.07 vs. 1.28, $p<0.001$). Although the relationship between ACE score and IBS was significant after controlling for demographics, there was only a weak association ($p=0.059$) after additionally adjusting for HAD anxiety and depression scores.

In our secondary analysis, where the ACE score range was 0-9, IBS status again correlated with higher ACE scores in the distributions ranges of 0, 1-3, 4-6, and 7-9 (Figure 1). There was a graded relationship between the number of categories of EAL and IBS status. Compared to an ACE score = 0, the odds of having IBS increased with ACE scores of 1-3 (OR=1.77, 95% CI [1.03, 3.06], $p=0.04$), 4-6 (OR=3.83, 95% CI [1.66, 8.89], $p=0.002$), and 7-9 (OR=4.08, 95% CI [0.68, 24.36], $p=0.123$) after adjusting for age, race, sex, and education.

General trauma (71% vs. 57%; $p=0.022$) and emotional abuse (27% vs. 14%; $p=0.004$) were significantly more prevalent in IBS than HCs. Within the general trauma category IBS was associated with household mental illness (41% of IBS patients vs. 18% of HCs; $p<0.001$), and an incarcerated household member (10% in IBS vs. 5% in HCs; $p=0.019$). General trauma was reported in the majority of both IBS patients and HCs, in part due to the substantial rates of parental divorce/separation in both IBS and HCs. While the prevalence of sexual abuse was significantly associated with IBS before adjusting for sex and other demographics (20% vs. 10%, $p=0.022$), there was only a trend after adjusting for sex and demographics ($p=0.079$). Physical abuse was not predictive of IBS (Table 3). Incarcerated household member was the only ACE domain that was significantly associated with IBS after additionally adjusting for HAD anxiety and depression scores ($p=0.045$).

Correlation of ACE score and IBS and non-GI symptoms

In IBS patients, the total ACE score modestly correlated with overall IBS symptom severity ($r=0.17$, $p=0.036$) and abdominal pain ($r=0.20$, $p=0.015$). ACE score also correlated with overall somatic symptom severity as measured by the PHQ-15 within IBS patients ($r=0.27$, $p<0.001$). There was a trend for a positive correlation of ACE score with HAD anxiety ($r=0.15$, $p=0.061$), and no correlation with HAD depression ($r=0.03$, $p=0.73$) or GI symptom specific anxiety (VSI, $r=0.13$, $p=0.11$).

Association of ACE and ETI-SR scores in IBS and HCs

There was a strong positive correlation between the ETI-SR total score and ACE total score in all subjects ($r=0.59$, $p<0.001$) as well as within the IBS subjects ($r=0.65$, $p<0.001$), and HCs ($r=0.51$, $p<0.001$). Using the ACE Questionnaire, participants who were classified as having an EAL in each of the four domains (general trauma, emotional abuse, sexual abuse and physical abuse) had significantly higher ETI-SR scores within that domain (Figure 2, p range: 0.002 - <0.001).

DISCUSSION

EALs have been associated with an increased risk of physical and mental health and behaviors. Large-scale studies have demonstrated a graded relationship between exposure to EALs measured with the ACE questionnaire and prevalence of chronic medical illnesses including coronary artery disease, diabetes, and mental distress; however, the association of ACE scores and GI disorders has not been reported.[9] Here we measured EALs in IBS using the ACE questionnaire and found that ACE score is associated with an increased risk of having IBS. Specific key findings include: 1) IBS status is predicted by a history of emotional abuse and either a mentally ill or incarcerated household member; 2) The advantages of ACE over the ETI-SR include that the ACE provides the prevalence of EALs and the score is positively correlated with overall symptom and abdominal pain severity in IBS, and 3) While ACE and ETI-SR scores were significantly correlated, individuals with an EAL defined by ACE reported a mean of at least 2 items within each ETI-SR domain vs. 0-1 items in those without an ACE defined EAL. The latter finding suggests that using a cutoff score of 1 EAL item in each ETI-SR domain is overly sensitive in determining prevalence of EALs. Even though an association between EALs and IBS prevalence and symptom severity has previously been reported, we believe that the current study provides novel information regarding this relationship: First, the association with IBS was determined among IBS patients with confirmed diagnoses and most IBS patients had normal HAD anxiety and depression symptom scores. Second, we were able to compare the ACE score to another measure of EALs as well as to symptoms.

Others have reported that exposure to EALs in a general population cohort of 53,998 individuals is associated with increased odds of having chronic diseases, including coronary artery disease, myocardial infarction, diabetes, asthma, and frequent mental distress. Our results in a community sample are consistent with these findings, i.e., an increased exposure to EALs is associated with an increased odds of IBS, even after adjusting for demographic variables.[9] In addition, the prevalence of EALs (e.g., any abuse, household substance abuse or mental illness) in our subjects was comparable to that in large community populations of IBS and controls.[20, 21]

The household mental illness EAL significantly differentiated IBS and HCs (41% in IBS vs. 18% in HCs using the ACE). This result is consistent with our findings in a larger sample (28% IBS vs. 13% HCs)[4] and in a recently published population study (37% IBS vs. 22% controls).[20] There are several factors that may explain this association. It is possible that this is due to shared genetic factors as IBS clusters in families[22] and is associated with mental illness.[23] The association may also be due to environmental factors such as the parental response to abdominal pain, which has been suggested as an etiological mechanism in IBS,[24] and may also be affected by mental illness. Instruments measuring EALs in IBS prior to this study have not included questions about incarcerated household members and thus this association with IBS is novel and deserves attention as a topic of future research. The third predictor of IBS, emotional abuse, agrees with findings of studies that used a variety of instruments to assess EALs.[4, 25, 26]

We found that the ACE score positively correlated with severity of overall symptoms and pain in IBS. This association between EALs and symptoms is also consistent with the finding of increased pain to rectal distension among IBS patients with history of abuse in comparison to both IBS patients and HCs without a history of abuse.[27] Results of functional brain imaging studies have shown that abuse in IBS is associated with increased activation of central pain pathways (dorsal cingulate gyrus) and reduced activation of central pain inhibitory pathways,[28] as well as alterations in the salience network,[29] which plays a key role in attention to internal (emotional, cognitive, interoceptive) and external somatosensory stimuli based on personal relevance.[30] Thus, it is not surprising that the relationship between ACE scores and IBS was in part accounted for by current anxiety and depression symptoms. It is possible that EALs are associated with psychological symptoms, which in turn can be associated with a greater risk of developing or reporting IBS symptoms. However, it is also possible that there is a direct relationship of EALs to IBS and the experience of having IBS symptoms is associated with symptom-specific anxiety. To explore this association further, we separately adjusted for VSI and found that the relationship between ACE score and IBS was diminished even more so than with HAD anxiety and depression symptoms. Therefore, the experience of EALs may be associated with an increased risk of having IBS symptoms, which is associated with increased GI symptom-specific anxiety. Based on our previous study assessing the relationship of EALs as measured by ETI-SR and IBS,[4] we believe that there is an association of EALs and IBS independent of current anxiety and depression symptoms. In the current study, the fact that when controlling for anxiety and depression symptoms the effect of ACE and IBS was only weak ($p=0.059$) may have been in part due to the smaller size. Nonetheless, because our study is cross-sectional, we cannot determine causal effects but this should be established by longitudinal studies in the future.

In this study, the prevalence of sexual abuse as measured by ACE was significantly associated with IBS, but it was not significant after adjusting for demographics including sex. This is consistent with previous findings that the association between sexual abuse and IBS is more predominant in women.[3, 31] Our sexual abuse prevalence in IBS of 20% was consistent with other studies which reported rates of 13-54% depending on the method of assessment and definition of abuse used.[3, 27, 31, 32]

In addition to a potential therapeutic effect of the disclosure of EALs themselves and the resulting insight, determining the presence of EALs in IBS may be helpful in guiding therapy and impacting treatment outcomes. In a survey of 1,242 IBS patients, the majority endorsed a desire to learn about the impact of psychological factors on symptoms.[12] While EALs are not psychological factors per se, they can have psychological consequences. IBS patients also desire empathetic providers,[33] and a high quality provider-patient relationship has been shown to improve patient outcomes.[34] IBS patients with a history of abuse respond better to psychological therapy (pharmacotherapy and CBT) than those without abuse. Psychological therapies may not specifically focus on EALs, but they can improve coping of symptoms, global well-being and disease specific quality of life in IBS patients with abuse.[35, 36] Larger studies have shown that psychological therapies improve GI symptoms independent of their effects on psychological distress in IBS.[37]

Limitations of the present study include a study population predominantly from the West Los Angeles area, the possibility of recall bias given our focus on childhood traumatic events, and lack of information on childhood support and psychological counseling. In addition, the ACE used in this study was an older version that did not include the categories of physical and emotional neglect. Also, while the study was powered to detect a relationship between EALs and IBS status, exploratory analyses conducted within subgroups such as sex were likely underpowered.

In summary, this is the first study to evaluate EALs using the ACE questionnaire in GI disease. In IBS, we found that a history of household mental illness, incarcerated household member and emotional abuse were notable predictors of IBS. The ACE questionnaire is a useful instrument to measure EALs in IBS based on its use in large studies, its ability to measure prevalence across different EAL domains, and its correlation with IBS symptom severity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

IBS	irritable bowel syndrome
EALs	early adverse life events
ACE	adverse childhood experiences
ETI-SR	Early Trauma Inventory Self Report-Short Form
VSI	visceral sensitivity index
HAD	Hospital anxiety and depression scale
PHQ	Personal Health Questionnaire
VSI	Visceral Sensitivity Index
CDC	Centers for Disease Control and Prevention
BSQ	Bowel Symptom Questionnaire
OR	odds ratio

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Key Messages

- This is the first study to evaluate early adverse life events (EALs) using the Adverse Childhood Experiences (ACE) questionnaire in gastrointestinal (GI) disease.
- The aims of the study were to estimate the prevalence of EALs in patients with irritable bowel syndrome (IBS) using the ACE questionnaire and determine the correlation of ACE score with GI symptoms.
- Male and female IBS and healthy control subjects completed validated questionnaires measuring GI symptoms, EALs (ACE), and current psychological symptoms.
- The main results of the study were: 1) A history of EALs (i.e., ACE score 1) was associated with significantly higher odds (2-fold) of having IBS, 2) IBS status was predicted by a history of emotional abuse and a mentally ill or incarcerated household member, and 3) ACE score significantly correlates with both overall IBS symptom and abdominal pain severity.

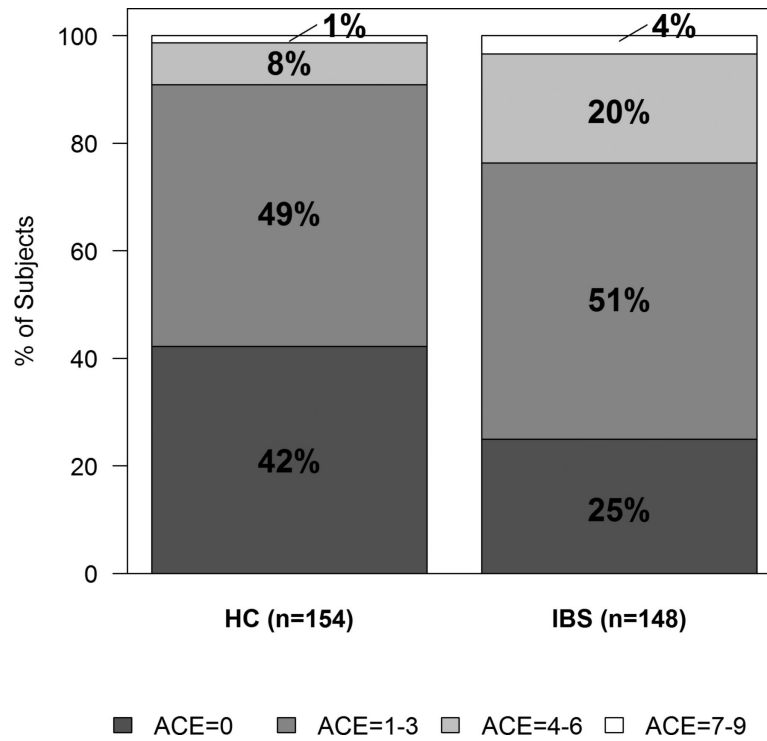


Figure 1. Distribution of ACE Score in IBS vs. HC

Distribution of ACE scores within the ranges of 0, 1-3, 4-6, and 7-9 is shown. There was a significant difference between IBS vs. HCs ($p=0.007$). ACE, adverse childhood experiences; HC, healthy control; IBS, irritable bowel syndrome

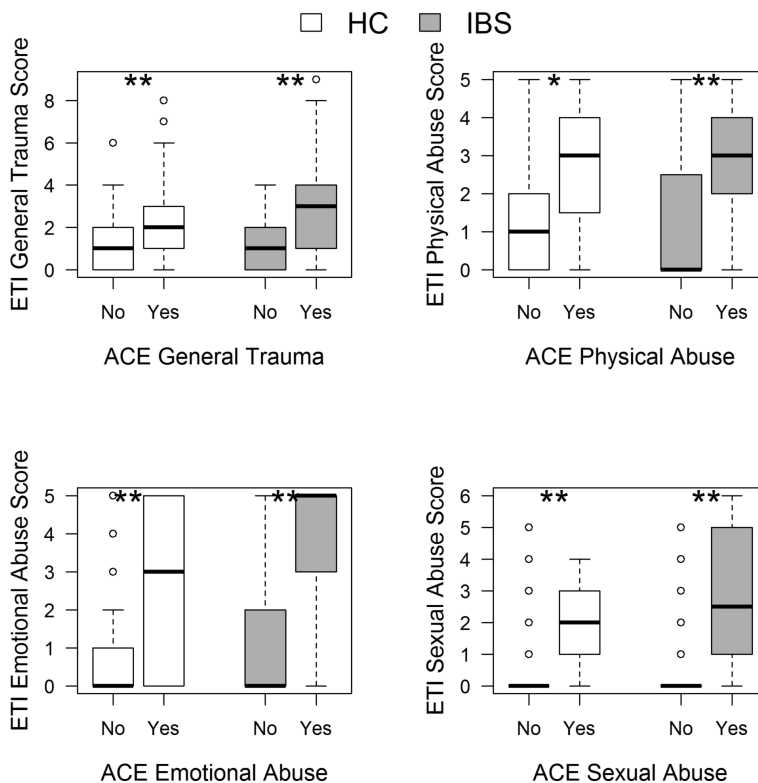


Figure 2. ETI-SR scores according to presence or absence of EALs as defined by the ACE Questionnaire

ETI-SR score distribution among HC and IBS patients with (“Yes”, ACE score = 1) and without (“No”, ACE score = 0) EALs as defined by ACE in each of the four EAL domains. Box plots show median and interquartile ranges. ETI-SR scores were significantly higher in HC and IBS subjects with an EAL compare to those without an EAL (* p<0.01; **p<0.001). ETI-SR, early trauma inventory self report short form; ACE, adverse childhood experiences; IBS, irritable bowel syndrome

Table 1

ACE and ETI-SR Questionnaire Overview

ACE	ETI-SR
<ul style="list-style-type: none"> • 18 question survey for EALs before age 18 • Domains (number of items): Physical abuse (1), Emotional (2), and Sexual abuse (4), General trauma (8). <ul style="list-style-type: none"> a) General Trauma Subcategories: Substance abuse (2), Parental separation or divorce (1), Mental illness in household (2), Incarcerated household member (1), and Parent treated violently (2). b) ACE scoring guide uses specific criteria to assign 1 point for each domain, “Yes”=1 or “No”=0 c) Total ACE Score (range 0-8)=Physical abuse + Emotional abuse + Sexual abuse + Substance abuse + Parental separation or divorce + Mental illness in household + Incarcerated household member + Parent treated violently 	<ul style="list-style-type: none"> • 27 question survey for EALs before age 18 • Domains (number of items): General trauma (11), Physical abuse (5), Emotional (5), and Sexual abuse (6). • Each of the 27 items was scored as “Yes”=1 or “No”=0 (total score range 0-27).

ACE, adverse childhood experiences; EALs, early adverse life events; ETI-SR, Early trauma self report short form

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Table 2

Subject Characteristics

Traits: Mean (SD)	Missing	HC (n=154)	IBS (n=148)	p value
Women (%)	0	91 (59%)	108 (73%)	0.015
Age in years (SD)	0	30.26 (10.92)	31.05 (10.03)	0.235
BMI (SD)	5	26.56 (6.13)	24.64 (5.07)	0.001
Race (%)	15			0.143
<i>Asian</i>		41 (28%)	26 (19%)	
<i>African American</i>		18 (12%)	12 (8%)	
<i>Caucasian</i>		66 (45%)	77 (55%)	
<i>Other/Mixed</i>		22 (15%)	25 (18%)	
Education (%)	9			0.304
<i>High School Graduate or Less</i>		9 (6%)	5 (3%)	
<i>Some College</i>		67 (45%)	57 (40%)	
<i>College Graduate</i>		44 (30%)	42 (29%)	
<i>Any Post Graduate Work</i>		29 (19%)	40 (28%)	
HAD Anxiety (0-21)	0	3.92 (2.86)	7.69 (4.45)	p<0.001
HAD Depression (0-21)	0	1.59 (2.17)	3.44 (3.19)	p<0.001
VSI Score (0-90)	2	4.25 (6.37)	39.23 (17.72)	p<0.001
PHQ-12 Score (0-24)	2	2.16 (2.32)	10.31 (4.64)	p<0.001
GI Symptoms				
<i>Overall Severity (0-20)</i>			9.56 (4.39)	
<i>Abdominal Pain (0-20)</i>			9.26 (4.34)	

SD, standard deviation; HC, healthy control; IBS, irritable bowel syndrome; BMI, body mass index; HAD, hospital anxiety and depression; VSI, visceral sensitivity index; PHQ, personal health questionnaire

Table 3

The Prevalence of EALs by ACE Questionnaire

EAL Domain	HC (%)	IBS (%)	Unadjusted p value	Adjusted p value ¹
Overall Prevalence	59.74	75.68	0.003	0.008
General Trauma	56.49	70.95	0.012	0.022
Household Substance Abuse	23.38	31.76	0.122	0.262
Parental Separation/Divorce	38.96	43.92	0.414	0.414
Household Mental Illness	18.18	41.22	p<0.001	p<0.001
Incarcerated Household Member ^{2*}	4.55	10.14	0.077	0.019
Parents Treated Violently	11.69	20.95	0.042	0.077
Physical Abuse	7.79	12.16	0.249	0.194
Emotional Abuse	13.64	27.03	0.004	0.004
Sexual Abuse	9.74	19.59	0.022	0.079

EAL, early adverse life events; ACE, adverse childhood experiences; HC, healthy control; IBS, irritable bowel syndrome

¹ p-value adjusting for demographic variables (i.e. age, race, sex, and education)

² p-value was significant after adjusting for demographic and psychological (i.e., HAD anxiety and depression scores) variables

* p=0.0449