

Case Control Study

Stressful life events and psychosocial correlates of pediatric inflammatory bowel disease activity

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Abstract

AIM

To investigate the association of psychiatric and psychosocial correlates with inflammatory bowel disease (IBD) activity in children and adolescents.

METHODS

A total of 85 pediatric IBD patients (in remission or active state of the disease) and their parents completed a series of questionnaires and semi-structured interviews measuring life events, depression, anxiety, family dysfunction, and parent mental health. Differences between the remission and the IBD active group and the association of any significant variable with the disease activity state were examined.

RESULTS

Parents of children being in active state of the disease reported more life events ($P = 0.005$) and stressful life events ($P = 0.048$) during the past year and more mental health symptoms ($P < 0.001$), while the children

themselves reported higher levels of anxiety symptoms ($P = 0.017$) compared to the remission group. In the logistic regression multivariate analysis, the only predictor which had a significant positive effect on the probability of the patients being in active state was parent mental health symptoms (OR = 4.8; 95%CI: 1.2-25.8).

CONCLUSION

Life events, child anxiety and parent mental health symptoms may be important correlates of pediatric IBD activity and targets of thorough assessment and treatment.

Key words: Inflammatory bowel disease; Children and adolescents; Stressful events; Anxiety; Depression

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Core tip: The present study examined the associations of several psychosocial factors and outcomes with pediatric inflammatory bowel disease (IBD) activity. Second, it shed some light on the relationship of the disease activity (*i.e.*, IBD remission or active state) with preceding life events. Addressing simultaneously psychosocial needs of both children and parents in the course of pediatric IBD seem to be of importance in any effective preventive and therapeutic intervention. Moreover, the role of stressful events in the course of pediatric IBD although being mediated or moderated by individual factors seem to be a possible target for future research and psychosocial treatment modalities.

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INTRODUCTION

Epidemiological studies indicate that the incidence of pediatric inflammatory bowel disease (IBD), consisting of Crohn's disease (CD), ulcerative colitis (UC) and IBD unclassified (IBDU), has been increasing over time^[1]. Elevated levels of depression, anxiety, low self-esteem, disrupted social functioning, family dysfunction, and parental distress are among the most common findings from studies comparing pediatric IBD patients with other chronic disease patients or healthy controls^[2,3].

However, only few studies have investigated the association of psychiatric and psychosocial correlates with IBD activity in children and adolescents. Specific depressive symptoms (*e.g.*, lack of interest and energy, decreased appetite) have been shown to be related with moderate/severe disease activity^[4]. Higher levels of depressive symptoms have been also related to poorer subjective health in IBD pediatric patients^[5]. A recent

study^[6] found that the disease activity was associated with adolescents' general well-being, emotional functioning, social functioning, and body image. In another sample of young adults with IBD, poor college adjustment and physical quality of life were correlated with increased disease activity^[7]. However, no significant correlations were reported elsewhere^[5,8-11].

Moreover, impaired parent mental health and physical functioning have been correlated significantly with pediatric IBD symptom exacerbation^[12]. Similarly, family general dysfunction has been related with more symptomatic IBD among adolescents, and maternal positive affect (*e.g.*, mothers describing themselves as more active, and interested) has been related with less IBD symptoms^[13]. Finally, although the role of stressful life events has been studied in adult IBD patients with mixed findings^[14], there are no published reports examining the relationship of stressful events with the disease activity in pediatric populations. Only two studies comparing IBD patients to healthy and clinical controls^[15,16] and one study comparing depressed to non-depressed IBD pediatric patients^[17] supported the association of retrospectively reported stressful life events with the onset of pediatric IBD.

The present study investigates the relationship of several psychosocial factors and outcomes with pediatric IBD activity. More specifically, we try to provide a more comprehensive examination than currently available evidence by assessing differences in the often neglected life events among other possibly significant psychosocial problems, such as depressive and anxiety symptoms, family dysfunction, and parent mental health between an IBD remission group and an IBD active group of children and adolescents. It was hypothesized that the active group would show more stressful life events the year prior the present assessment and higher levels of psychosocial problems. Furthermore, we examine the association of any psychosocial variable that is shown to be correlated with the disease activity state by entering these variables in the same model as covariates. The aim of the latter examination is to clarify interactions and the possible moderating role of any of the abovementioned psychosocial correlates in their association with pediatric IBD activity.

MATERIALS AND METHODS

The study was reviewed and approved by the Aghia Sophia Children's Hospital Institutional Review Board. All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Participants

This cross-sectional study was conducted at the Gastroenterology Unit of the First Department of Pediatrics in collaboration with the Department of Child Psychiatry of the National and Kapodistrian University of Athens, School of Medicine, Aghia Sophia Children's Hospital. Eligible for inclusion were all children and their parents,

Table 1 Demographic information by inflammatory bowel disease activity and type of disease

	IBD active group (<i>n</i> = 43)		Remission group (<i>n</i> = 42)	
	CD (<i>n</i> = 30)	UC (<i>n</i> = 13)	CD (<i>n</i> = 27)	UC (<i>n</i> = 15)
Age, mean (yr)	12.8 ± 2.2	12.9 ± 2.0	13.9 ± 2.0	13.1 ± 1.4
Child gender (female), %	56.7	61.5	66.7	46.7
Parent gender (female) ¹ , %	80.8	77.8	86.9	75

¹Gender of the parent who was present during the assessment. IBD: Inflammatory bowel disease; CD: Crohn's disease; UC: Ulcerative colitis.

diagnosed with IBD according to the ESPGHAN Porto-criteria^[18,19] who were either admitted in the First Department of Pediatrics or followed as outpatients. The period of recruitment lasted for 24 mo. Inclusion criteria were age between 8-18 years and the ability to read Greek and complete the questionnaires themselves. Exclusion criteria were diagnosis of developmental pervasive disorder or mental retardation, and a comorbid chronic illness. No patient was on psychiatric medication. One hundred subjects fulfilling the inclusion criteria were asked to participate. A total of 85 children and adolescents (50 females) with a mean age of 13.2 years ± 2.4 years and their parents agreed to participate in the study (85% response rate) and they were included in the analysis. The cases that refused to participate did not differ from the study group according to age, sex and disease activity. The characteristics of the study sample are shown in Table 1. Regarding steroid medication, 44.9% (*n* = 38) of the study population was on steroids at the time of evaluation, 14.7% (*n* = 6) of those in remission and 74.9% (*n* = 32) of those with a relapse. Three participants were of non-Greek ethnicity.

Materials and procedures

All patients were classified at the time of the evaluation, as being in remission or in active state of IBD according to the Pediatric Crohn's Disease Activity Index (PCDAI)^[20] or the Pediatric Ulcerative Colitis Activity Index (PUCAI)^[21] depending on the diagnosis. For both scales, remission is defined by a total score < 10 and active state if the total score was ≥ 10. Disease activity was assessed both as activity index and as disease state (remission or relapse). Both children and their parents completed the questionnaires in the outpatient or inpatient clinics. Socio-demographic details and past medical and psychiatric history were recorded.

The parents completed a semi-structured psychosocial interview evaluating recent life events for their children^[22,23], which is based on Coddington's Life Events Questionnaire^[24]. The onset of each event that had occurred over the previous 12 mo was dated to within 4 wk. Life events that are measured through this interview include: (1) danger to self (child's illness or accidents, involvement in a household or community disaster or being the subject of a personal attack; (2) danger to others (expectation or occurrence of physical threat where the person exposed is a parent, sibling, friend or

significant other; (3) disappointments (e.g., to the self includes breakdown of boyfriend/ girlfriend relationship, examination failure; to another includes loss of job, new financial difficulties, extramarital affair); and (4) loss (includes only death and permanent separations). Life events data were collected only from parents in order not to cause survey fatigue to the patients. Both the stressful events (those carrying a moderate to severe degree of negative impact on the child according to parents' subjective perception) and the total number of events (the objective number of reported events) were computed in the present analysis, so as to take into consideration the possible impact of events that parents may underestimate.

Child and adolescent anxiety symptoms were measured by the Revised Children's Manifest Anxiety Scale (RCMAS)^[25]. The RCMAS is a widely used self-report 37-item questionnaire, with higher values corresponding to higher levels of anxiety. The psychometric properties of the RCMAS have been found acceptable in previous research^[26].

The Children's Depression Inventory (CDI)^[27], a self-report 27-item scale, was used to screen for depressive symptoms. The total score ranges from 0 to 54, with higher values corresponding to higher levels of depression. Previous research has shown that the CDI is adequately reliable and valid with respect to depressive symptoms^[28].

In order to assess parent mental health symptoms, the Symptom Checklist-90-Revised (SCL-90-R) was administered^[29]. The SCL-90-R is a 90-item multidimensional questionnaire designed to screen for a broad range of psychological problems. Each of the 90 items is rated on a five-point Likert scale of distress. The Global Severity Index (GSI), the mean rating across all items, was used for assessing parent mental health symptoms. The psychometric properties of the SCL-90-R GSI have been found acceptable in previous research^[30] and support its use as a self-report measure.

Family dysfunction was assessed through the McMaster Family Assessment Device (FAD)^[31]. It is a 60-item instrument that assesses 6 domains of family functioning as well as general family dysfunction. The 12-item General Functioning scale, which assesses overall family pathology or dysfunction, was analyzed in the present study. Higher mean values indicate greater general dysfunction. The reliability and validity of the FAD General Functioning scale have been demonstrated in clinical and non-clinical samples^[32].

Table 2 Comparisons of self-reported child emotional problems, parent mental health symptoms, family dysfunction and life events by inflammatory bowel disease activity group

Variable	IBD active group (<i>n</i> = 43)	IBD remission group (<i>n</i> = 42)	<i>P</i>
Life events	3.8 ± 2.5	2.4 ± 2.8	0.005 ²
Stressful life events	2.9 ± 2.1	2.0 ± 2.3	0.048 ²
FAD GFS family dysfunction	22.6 ± 5.5	20.1 ± 4.9	0.061 ¹
SCL-90-R parent mental health symptoms	1.11 ± 0.72	0.52 ± 0.39	< 0.001 ¹
RCMAS anxiety symptoms	54.3 ± 12.7	46.9 ± 13.1	0.017 ¹
CDI depression symptoms	8.9 ± 5.6	7.2 ± 5.5	0.2 ¹

¹Student's *t* test; ²Mann-Whitney test. IBD: Inflammatory bowel disease; FAD GFS: Family Assessment Device General Functioning Scale; SCL90-R: Symptom Checklist-90-Revised; RCMAS: Revised Children's Manifest Anxiety Scale; CDI: Children's Depression Inventory.

Statistical analysis

Continuous variables are presented using mean ± standard deviation (SD) while categorical variables are presented by absolute (*n*) and relative (%) frequencies. In order to test our hypothesis, Student's *t*-test was used for comparisons of means between IBD remission group and IBD active group, with the exception of continuous variables with a small number of distinct values in the dataset where the non-parametric Mann-Whitney statistic was used. Categorical variables were compared between the two groups by Fisher's exact test. Exact logistic regression analysis was applied in order to evaluate to what extent the explanatory variables that were already found to be associated with IBD activity in univariate analysis had a multivariate effect on the latter. The estimate of the relative risks of being in IBD active state was performed by calculating the odds ratios (OR) and the corresponding 95%CI. All tests were two-sided and a level of ≤ 0.05 was considered statistically significant. Data were analyzed using STATA 11.0 (Stata Corporation, College Station, TX 77845, United States).

RESULTS

Disease state was not related to age or gender ($P = 0.17$ and $P = 0.55$ respectively).

Comparisons of psychosocial variables by IBD activity group

The results of the univariate analysis, that is the differences in each psychosocial factor tested individually by IBD activity group, are presented in Table 2. Parents of children being in active state of the disease reported more life events ($P = 0.005$) and stressful life events ($P = 0.048$) during the past year, and more mental health symptoms ($P < 0.001$), while the children themselves reported higher levels of anxiety symptoms ($P = 0.017$), compared to the remission group. Similarly, when the disease activity was assessed through activity index, it was positively associated with life events ($P = 0.04$) during the past year, parent mental health symptoms ($P = 0.0081$) and children's anxiety symptoms ($P = 0.0028$). Evaluation of the abovementioned differences

after stratifying according to the diagnosis (CD or UC) had not sufficient statistical power.

Multivariate effects of psychosocial variables on IBD activity in the logistic regression analysis

Since no change in the direction of the observed relations was detected in the stratified analysis, data were combined for all the subsequent analyses. When the factors which were proven to be significant in the univariate analysis (*i.e.*, life events and stressful life events during the past year, self-reported anxiety symptoms, and parent mental health symptoms) were included in the logistic regression multivariate analysis, the only predictor variable which had a significant positive effect on the probability of the patients being in IBD active state was parent mental health symptoms (OR = 4.8; 95%CI: 1.2-25.8). Since steroid medication was related to self-reported anxiety symptoms ($P = 0.006$) and parent gender was related to parent mental health symptoms ($P = 0.038$), were both considered confounding variables and included in the final model. Steroid medication had a significant association with disease state with patients on steroids being more likely to be in relapse (OR = 19.8; 95%CI: 3.2-120.8), whereas parent gender was statistically not significant and therefore removed from the regression equation.

DISCUSSION

This study was an effort to examine differences in the often neglected life events among other possibly significant psychosocial variables, such as depression and anxiety symptoms, family dysfunction, and parent mental health between an IBD remission group and an IBD active group of children and adolescents. Results indicate that parent-reported life events during the past year, self-reported anxiety symptoms, and parent mental health symptoms are related with the disease activity. Moreover, parent mental health symptoms seem to be a strong correlate of IBD activity when all significant variables are entered into a model simultaneously.

Self-reported emotional problems (*i.e.*, depressive and anxiety symptoms) tended to be higher in the IBD active group than in the remission group, with self-reported

anxiety symptoms, in particular, differing significantly between the 2 groups. This finding agrees with previous research showing that internalizing problems are correlated with IBD symptom exacerbations^[4]. Family dysfunction also did not differ between children and adolescents with or without active state of the disease, although the difference was close to statistical significance.

Parents reported significantly more mental health symptoms in the IBD active state than in the remission group, consistent with previous studies^[12,13]. Interestingly, they also reported significantly more life events during the year prior the present assessment. This finding is the first to our knowledge to support the relationship of preceding life stress with IBD activity in pediatric populations, although 2 previous studies have supported the association of stressful life events with the onset of pediatric IBD^[15,16]. Moreover, in the present study, while the parents in the active group compared to the remission group reported significantly more life events in total, this difference between the two groups was not significant regarding the events that the parents perceived as stressful for their children. It could be hypothesized that this discrepancy might suggest that parents could underestimate the potential negative impact of some life events on their children wellbeing and functioning and consequently not report them as stressful. In general, parents could ignore some aspects of the life of the patients, and underestimate or overestimate other known stressors. At the same time, one could argue that young patients couldn't estimate correctly the power of different events when using a questionnaire to detect them. The combination of reports from multiple informants (*i.e.*, parents and children) could possibly yield more reliable estimations.

Parent mental health symptoms were shown to be the only strong independent psychosocial correlate of IBD activity when all significant variables were entered into the same model of regression analysis. It is interesting that the associations of childrens' anxiety symptoms and life events with the disease activity were not significant anymore in the final model. These findings could be interpreted in different ways. With regard to anxiety symptoms, although some of the effect seen at the univariate analysis was probably due to the confounding effect of steroid medication (which was strongly related to the probability of relapse, as most patients experiencing a flare of the disease receive steroids) there is a possibility that anxiety symptoms may have an important impact on disease activity and a larger sample would provide enough power to detect it. With regard to life events, the significant relationship with disease activity that was initially found in the univariate analysis may have been subsequently moderated by the effect of parent mental health symptoms in the model of regression analysis since parents themselves reported the events and this reporting may have been possibly influenced by their mental health state. Alternatively, there may be a mediating factor such as parent coping strategies that was not examined in the present analysis

and was related to parent mental health symptoms on the one hand and the effect of life events on the other hand. This unexamined factor could have weakened the effect of life events on IBD activity in the final model, although it did not manage to weaken the relative effect of parent symptomatology. Moreover, the disease activity is a momentary state that can change within days or weeks, so that it may be difficult to detect any associations with the number of life events. In any case, these preliminary findings deserve further examination in future research.

The present study extends previous research mainly in two ways. First, it examined the associations of several psychosocial factors and outcomes with pediatric IBD activity both in univariate and regression analyses providing a more comprehensive picture of these complex relations; second, it shed some light on the relationship of the disease activity (*i.e.*, IBD remission or active state) with preceding life events, an issue that was missing in pediatric IBD literature. The findings reported here can offer some useful implications. Addressing simultaneously psychosocial needs of both children and parents in the course of pediatric IBD seem to be of importance in any effective preventive and therapeutic intervention; moreover, the role of stressful events in the course of pediatric IBD although being mediated or moderated by individual factors seem to be a possible target for future research and psychosocial treatment modalities.

The present findings should be interpreted in the context of some limitations. First, to diminish the burden of the examination on the patients we did not use adequate diagnostic interviews to screen for comorbid psychiatric disorders; second, the study was based only on parent-reported life events that limit the interpretation of the results; moreover, the study did not examine the effect of socioeconomic status on the reported differences, although this limitation is common in pediatric IBD studies, with high socioeconomic status threatening generalizability of results. Similarly, factors such as hospital stay and parent perceived social support that have been found to be associated with impaired mental health outcomes in children and parents, respectively, were not examined in the present analysis. In addition, the sample size was rather small, leading to a low statistical power. The deviance from normality of the continuous variables of our sample led to the use of non-parametric statistics that had less statistical power than parametric ones if there was a normal distribution. The cross-sectional design of the study did not allow us to examine variations over time or make causal inferences; last, it would be interesting to include a control group not affected by IBD, since even inactive IBD patients may have a higher rate of self-reported psychosocial problems than age-matched controls. Regardless of these limitations, the present study clearly suggests that several psychosocial factors and outcomes (*i.e.*, life events, child anxiety and parent mental health symptoms) may be important correlates of pediatric IBD

activity and they may be targets of thorough assessment and treatment.

COMMENTS

Background

Epidemiological studies indicate that the incidence of pediatric inflammatory bowel disease (IBD) has been increasing over time. Elevated levels of depression, anxiety, low self-esteem, disrupted social functioning, family dysfunction, and parental distress are among the most common findings from studies comparing pediatric IBD patients with other chronic disease patients or healthy controls.

Research frontiers

Only few studies have investigated the association of psychiatric and psychosocial correlates with IBD activity in children and adolescents. Moreover, although the role of stressful life events has been studied in adult IBD patients with mixed findings, there are no published reports examining the relationship of stressful events with the disease activity in pediatric populations.

Innovations and breakthroughs

The authors provide a more comprehensive examination than currently available evidence by assessing differences in the often neglected life events among other possibly significant psychosocial problems, such as depressive and anxiety symptoms, family dysfunction, and parent mental health between an IBD remission group and an IBD active group of children and adolescents. Furthermore, they examine the association of any psychosocial variable that is shown to be correlated with the disease activity state by entering these variables in the same model as covariates.

Applications

Several psychosocial factors and outcomes (*i.e.*, life events, child anxiety and parent mental health symptoms) may be important correlates of pediatric IBD activity and they may be targets of thorough assessment and treatment.

Peer-review

The paper is well-written, easy to read and give some new considerations on the treated issue. The authors indicate correctly all the limitations.

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