

RESEARCH ARTICLE

Daily hassles score associates with the somatic and psychological health of patients with Crohn's disease

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Abstract

Objective To examine the associations of daily hassles with the somatic and psychological health of Crohn's disease (CD) patients.

Method A cross-sectional study of 400 self-selected adult CD patients was performed with completion of demographic, medical, and psychosocial questionnaires: economic status; Patient Harvey-Bradshaw Index of disease activity; Daily Hassles Scale (DHS); Short Inflammatory Bowel Disease Questionnaire (SIBDQ) and Short-Form Health Survey (SF-36 Physical and Mental Health) quality of life measures; Brief Symptom Inventory of psychological stress with summary Global Severity Index (GSI); Family Assessment Device; and List of Threatening Life Experiences. Analyses included correlations, regressions, and Sobel test statistic.

Results The patients were aged 38.7 ± 14.1 years, 61% female and 67% working. The Patient Harvey-Bradshaw Index was 5.52 ± 4.87 . The DHS was 88.0 ± 23.2 , similar in men and women, higher in smokers, and increased with greater disease activity ($p < .001$). The most commonly reported hassles were time, social, and work. DHS had significant negative correlations with age, disease duration, and economic status and positive correlations with GSI, SF-36, and SIBDQ. An increased Daily Hassles score was associated with reduced SIBDQ ($p < .001$) and SF-36 Mental Health ($p < .001$) and increased GSI ($p < .001$) and Patient Harvey-Bradshaw Index ($p < .001$). This effect of DHS on Patient Harvey-Bradshaw Index was mediated by GSI (Sobel $t = 6.09$, $p < 0.001$).

Conclusion Daily hassles in CD patients are shown for the first time to be associated with increased psychological stress and disease activity and reduced quality of life and lower economic status. This has psychotherapeutic implications.

KEYWORDS

Crohn's disease, daily hassles, health-related quality of life, psychological distress

1 | INTRODUCTION

Crohn's disease is a common form of chronic, idiopathic inflammatory bowel disease. The disease affects mostly the small and large bowel and often has extraintestinal complications involving the joints, eye, skin, and liver (Lichtenstein, Hanauer, & Sandborn, 2009). Crohn's disease presents usually in young adults and runs a fluctuating clinical course characterized by exacerbations and remissions. Patients need continuous pharmacological therapy, whether to treat flares or maintain disease remission. There is recourse to surgery in a significant number of patients. Crohn's disease is associated with a reduced ability to work and consequent loss of income, and involves a substantial financial outlay in direct medical costs and a host of indirect expenses (Odes, 2008). Crohn's disease is a condition associated with a great deal of psychological distress. This is quite understandable, given its lifelong course and associated disability, its unpredictable and often unsatisfactory response to treatment, the ever-present possibility of serious adverse effects from biological and immunosuppressive medication, and the risk of malignancy developing (Peyrin-Biroulet et al., 2015).

Several studies examined the association of psychosocial factors with the course of disease among patients with inflammatory bowel disease (Drossman, Patrick, Mitchell, Zagami, & Appelbaum, 1989; Maunder, 2005). We have recently described the disease-modifying role of major threatening life experiences in patients with Crohn's disease and ulcerative colitis (Slonim-Nevo et al., 2016; Slonim-Nevo et al., 2017). Threatening life experiences affecting the patient or close relatives and friends include critical events like death, severe illness, severe injury, divorce, unemployment, and financial crises. In our cohort of patients in Israel, as many as 50% of individuals reported such events occurring in a preceding 6-month period, which was the timeframe reviewed by the relevant self-completed questionnaire. Patients with Crohn's disease and ulcerative colitis experiencing threatening life experiences reported high scores of disease activity and psychological stress and had reduced mental and physical health-related quality of life, by quantile or multiple linear regression analysis. Threatening life experiences impacted negatively on the patients' economic status, as was shown in a path analysis.

The Daily Hassles Scale (DHS), which contained 117 questions, was developed for adults as a research alternative to inventories of major stressful life events (Kanner, Coyne, Schaefer, & Lazarus, 1981). This questionnaire was subsequently shortened and modified to include a response that the individual did not experience the hassle (Kohn et al., 1992). Daily hassles are quite different from serious life events. Daily hassles are the minor, well-known irritating and frustrating adverse events that occur in every individual's daily life during transactions with the environment, and they are interpreted as salient, harmful, or threatening to the individual's well-being (Holm et al., 1992). Examples of such hassles are as follows: time-related pressures as having too little time to accomplish a given task or too much to do at once; workplace stress like conflicts with supervisors or being taken for granted or ignored; social problems like disappointments, rejection, or betrayal of trust; lack of leisure time; financial burdens, cash flow difficulties and trouble raising a loan; conflicts with family or friends or colleagues; and disease-associated stigmas like physical appearance and fitness; and experiencing gossip and isolation.

In the National Study of Daily Experiences carried out in 1,031 healthy men and women, it was found that 50% of reported hassles were the result of interpersonal tensions (Almeida, 2005). Other common stressors occurred in the workplace, school, and home. These stressors were associated with feelings of loss, danger, and frustration. Men were

significantly more exposed to stressors at work than women. Daily hassles were associated with increased symptoms of psychological stress, such as depression (McIntosh, Gillamers, & Rodgers, 2010). Stress is heightened in adolescents and immigrants. A study in 600 healthy adolescent boys and girls in Austria reported more depressive symptoms and more daily hassles in first and second-generation immigrants than native Austrians (Stefanek, Strohmeier, Fandrem, & Spiel, 2012). The hassles in these teens were related to interpersonal relationships, schooling, and leisure. Of three theoretical models describing the relationship between critical life events, depression, and daily hassles, a “fully mediated effects” structural equation model identified daily hassles as the mediator of the path between critical life events and a range of depressive symptoms.

Daily hassles and stressors have long been recognized as impacting several disease states (DeLongis, Coyne, Dakof, Folkman, & Lazarus, 1982). The mechanisms of this process are incompletely understood. In a study of risk factors for cardiovascular disease, daily hassles were correlated with changes in physical activity and smoking habit, but not with alcoholic consumption, blood pressure, or blood lipids, in 166 healthy Dutch men and women (Twisk, Snel, Kemper, & Mechelen, 1999). Stressful life events and daily hassles with a rapid trajectory were related to increased mortality in men in the VA Normative Aging Study (Aldwin, Jeong, Igarashi, Choun, & Spiro, 2014).

The effect of daily hassles on the psychological and somatic health of patients with Crohn's disease is not well understood because very few studies have been performed. One study incorporated 10 Crohn's disease patients followed for 28 days; the patients completed a diary of daily minor stressful events, major life events, and disease symptoms (Garrett, Brantley, Jones, & McKnight, 1991). Daily stress was shown to impact significantly on disease symptoms after controlling for the effect of major life events. However, in a larger cohort of 123 Crohn's disease patients followed prospectively for 6 months, regression analysis revealed that both major life events and daily strains independently contributed to the variance in self-reported and medically verified symptoms of Crohn's disease and ulcerative colitis (Duffy et al., 1991). The major stress events were more strongly correlated with disease activity than were daily events. A third study involved 20 Crohn's disease patients followed up over a period of 84 days. A significant correlation between daily hassles and disease activity was found only in half the subjects (Traue & Kosarz, 1999). These studies thus show inconsistency with regard to the possible effect of daily hassles in Crohn's disease. Based on these and other papers from the literature, it has been suggested that perceived stress in the form of daily hassles could induce increased disease activity, which in turn would lead to more adverse psychological symptoms (Searle & Bennett, 2001). Knowledge in this field, however, remains incomplete.

Given the effect of major life events on morbidity in our cohort of Crohn's disease patients, it was of interest to examine whether common minor daily hassles would also be related to the course of Crohn's disease. We therefore performed a cross-sectional study on a self-selected cohort of adult Crohn's disease patients recruited from major hospitals and over the Internet, and examined disease characteristics, sociodemographic variables, and psychological measures by employing a series of questionnaires. We wished to determine whether daily hassles, like major life events, would have a significant negative association with the course of Crohn's disease patients in terms of increased disease activity, heightened psychological distress, and reduced health-related quality of life. We further sought to determine the path whereby daily hassles could affect disease activity.

2 | METHOD

2.1 | Study population and setting

This study forms part of a broader ongoing socioeconomic study of Crohn's disease in the Israeli adult (aged 18 years and older) patient population aimed at determining the social and psychological stressors of patients and the economic burden of disease. Patients were eligible to participate whatever the duration or severity of their illness, irrespective of their medical treatment and any surgery. Patients were recruited consecutively by two concurrent methods, as follows.

Patients with a confirmed diagnosis of Crohn's disease were informed of the study when presenting for follow-up, or for acute (nonhospitalized) care, at the outpatient gastroenterology departments of five participating

university-affiliated, tertiary-care public hospitals, which were distributed in the north, south, east and west of Israel (Rambam Health Campus, Tel-Aviv Medical Center, Soroka Medical Center, Shaare Zedek Medical Center, Tel-Hashomer Medical Center). Patients were given hardcopy questionnaires to complete once they had read the institutional review board (IRB)-approved description of the study, its aims and methodology, and any possible benefit or risk to the patients, and they signed the consent form.

The coordinator was available to clarify any questions. The questionnaires were to be filled in at home and returned by prepaid mail to the study coordinator, who would not know the identity of the patients filling in the questionnaires. When a consenting patient did not return the questionnaire within a month, a reminder was given by mail or telephone. Of the hospital patients invited to participate in the study, 64% agreed to fill in the questionnaires, but in fact 45% actually completed the questionnaires. Alternatively, the questionnaire could be completed via the Internet, but few hospital patients selected this option.

Additionally, the study was advertised on the The Israel Foundation for Crohn's Disease and Ulcerative Colitis and the CAMONI Patients' Social Network websites. Patients viewing the websites were invited to participate by clicking on a link that took them to a dedicated website at the Ben-Gurion University of the Negev, where they found a description of the study, its aims and methodology, any possible benefit or risk to the patients (as above), and the identical questionnaire itself. Those who wished to participate indicated their consent to do so by completing the Internet questionnaire. Completion via the Internet was deemed to imply informed consent, although no consent form was signed and the patients' identities remained unknown. Because the questionnaire was completed online, there was no need for the use of emails, a further protection of patient privacy.

The university website presented the first name and telephone number of a dedicated, computer-skilled worker available to answer any queries by telephone on a 24-hour basis. This worker was forbidden to request any identifying information and could receive calls but not make calls. Patients with recurrent queries would have had to make multiple calls. This worker in fact did not receive any calls from patients. Of the patients who clicked on the link to the questionnaire, 32% actually filled in the questionnaire. It was further assumed that these participants would have a definite diagnosis of Crohn's disease. Treating physicians were not involved in completing any parts of the questionnaires. The self-administered instruments were all in the public domain and used as published, without being adapted to the particular obstacles encountered by patients with Crohn's disease. The time period of data collection in this cross-sectional study was July 2013 through June 2015.

2.2 | Data collection and measurements

2.2.1 | Demographic and medical questionnaire

Subjects filled in a series of questionnaires that are in the public domain, using the fully validated translations into Hebrew, as described in detail (Slonim-Nevo et al., 2016). Subjects were thus required to have an adequate knowledge of Hebrew because no other translations were used. All these questionnaires have been used previously in patients with Crohn's disease (Slonim-Nevo et al., 2016). Subjects provided information about gender, age, education, marital and family status, and economic status. Patients self-rated their economic status on an arbitrary 5-point scale ranging from 1 (*very poor*) to 5 (*very rich*).

In addition, patients recorded the duration of Crohn's disease since diagnosis and any medical treatments, hospitalizations, and surgery for Crohn's disease. Data about comorbidities were obtained from subjects recruited at the hospitals and confirmed in their records. Such data were unavailable for the patients recruited by Internet.

2.2.2 | Patient Harvey-Bradshaw Index

This measure of Crohn's disease activity was specifically designed for self-completion by the patients (Bennebroek et al., 2013). It comprises four questions pertaining to the past day's symptoms of general well-being, abdominal pain, and diarrheal episodes and complications. Each question has a range of responses (for diarrhea the patient states the number of episodes), and all responses are summed to provide the Patient Harvey-Bradshaw Index. A Patient Harvey-Bradshaw Index < 5 indicates disease remission, 5–7 mild disease, 8–16 moderate disease, and >16 severe

disease. The question about an abdominal mass was part of the original Harvey-Bradshaw Index (Harvey & Bradshaw, 1980) but was omitted from the Patient Harvey-Bradshaw Index, thus making the questionnaire suitable for self-completion by patients without recourse to a physician.

2.2.3 | Daily Hassles Scale (DHS)

This is the modified 51-question instrument (Kohn et al., 1992). Patients rate the questions on a 4-point scale ranging from 1 (*not at all part of my life*) to 4 (*very much part of my life*). It incorporates hassles that are related to work, social relations, finance, time, acceptance, and stigma of disease. The total score is calculated by summation of the responses to all 51 questions; the possible range is 51–204. In addition, subscores for each of the five domains can be calculated: These domains are social hassles, work hassles, time hassles, money hassles, and social acceptance. The range of scoring of each domain depends on the number of questions in each domain. In the total and subscale scores, a higher score means more exposure to daily hassles. There are no norms for this scale in a healthy population.

2.2.4 | MOS Short-Form Survey instrument (SF-36)

This generic health-related quality of life measure (Ware et al., 1992) comprises 36 items in eight domains, which in turn are grouped as Physical Health Summary score (domains of physical functioning, role-physical, bodily pain, general health) and Mental Health Summary score (domains of vitality, role-emotional, social functioning, mental health). Responses refer to the past 4 weeks. The range of responses to each question varies from 2 to 6, and the composite score is expressed as a percentage. The range of each summary score is 0–100; a higher score means a better quality of life. Normal values vary between populations and countries but would be 80 or higher.

2.2.5 | Short Inflammatory Bowel Disease Questionnaire (SIBDQ)

This inflammatory bowel disease-specific health-related quality of life tool (Alrubaiy, Rikaby, Dodds, Hutchings, & Williams, 2015; Irvine, Zhou, & Thompson, 1996) measures the physical, social, and emotional status of patients with Crohn's disease. Its 10 items refer to the last 2 weeks and are rated on a 7-point scale ranging from 1 (*all the time*) to 7 (*never*). The total score is in the range 10–70, and a higher value indicates a better quality of life. A non-Crohn's disease person would score 70.

2.2.6 | Brief Symptom Inventory (BSI)

This instrument (Derogatis et al., 1983) measures psychological distress in the past month. Its 53 questions assess nine symptomatic dimensions (depression, somatization, obsession-compulsive, interpersonal sensitivity, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism). Patients rated the items on a 4-point scale, where a higher score implies more psychological distress. The BSI yields a score for each dimension as well as a useful global summary score called the General Severity Index (GSI), also on a 4-point scale, which is used in the current research. In nonpatient, non-Crohn's disease individuals the GSI was reported as 0.30 ± 0.31 .

2.2.7 | McMaster Family Assessment Device

This instrument (Epstein, Baldwin, & Bishop, 1983) measures the perception of family functioning and communication. It consists of 12 questions that investigate family functioning in terms of relying upon and understanding each other, being able to communicate and share concerns, and finding support in the family. Patients rated the items on a 4-point scale ranging from 1 (*strongly agree*) to 4 (*not agree at all*). Responses to the 12 questions are averaged to yield a total score in the 1–4 range; a higher value indicates a worse family functioning.

2.2.8 | List of Threatening Life Experiences

This questionnaire (Brugha et al., 1990) measures the amount of negative life experiences that the patient had over the last 6 months and incorporates a set of 12 questions, each describing a single life event with long-term contextual

threat such as death, severe injury, separation, loss of employment, financial crises. Each item is answered as “yes, happened to me in the last six months” or “no, did not happen.” The possible range of responses is 0–12; a higher score reveals exposure to more threatening life experiences.

2.3 | Statistical Analysis

All data collected were pooled in a single database. Data analyses were performed using IBM SPSS (version 22). Descriptive statistics were used. Continuous variables are expressed as means and standard deviations for normally distributed variables, or medians and interquartile range for variables with non-normal distribution; categorical variables are expressed as frequencies and percentages. The DHS scores of each disease activity state were compared by analysis of variance (ANOVA) with Bonferroni correction. The demographic, medical, and sociopsychological variables were correlated with the DHS score using the Spearman's rank correlation. The relationship of age, education, gender, economic status, and DHS with quality of life (SIBDQ, SF-36), psychological distress (GSI), and disease activity was examined using multiple linear regression analysis—using the natural logarithm transformations of dependent variables that were not normally distributed. A possible role for GSI as a mediator of the effect of DHS on Patient Harvey-Bradshaw Index was examined by calculation with the Sobel test statistic. P values < 0.05 determined statistical significance for all the analyses.

2.4 | Ethical Considerations

The IRB of all the participating hospitals approved the study and both forms of subject recruitment. IRB regulations require that the patient be given an IRB-approved written description of the study, its aims and methodology, any possible benefit or risk to the patients, and a guarantee of patients' privacy. The patients attending at the various hospitals were required to sign an informed consent form before receiving the questionnaires. Patients completing the questionnaires on the website did not supply identifying information or email addresses and were not required by the IRB to complete an informed consent form. They were deemed to have assented to participate in the study when they sent in the completed questionnaires.

3 | RESULTS

3.1 | Characteristics of Study Participants

The cohort comprised 400 Crohn's disease patients. The patients were of mean age 38.7 ± 14.1 years, 61% female, 60% married or partnered, and 67% working. The mean duration of disease was 11.4 ± 8.8 years. The mean Patient Harvey-Bradshaw Index was 5.5 ± 4.9 ; and 52.5% of patients had a total index <5 and were therefore in clinical remission. Among the patients, 43.3% were on biologic medication and 34.5% were postsurgery. Further demographic and medical details are given in Table 1. Of the total cohort, 278 patients (69.3%) had been recruited at the hospitals and completed hardcopy questionnaires and 122 (30.7%) had been recruited via the Internet and filled in the questionnaires online. These two groups of patients did not differ statistically in terms of age, gender, working status, and medical parameters, except in Patient Harvey-Bradshaw Index (hospital recruits 5.2 ± 4.7 vs. Internet recruits 6.2 ± 5.2 , $p < .04$) and current smoking (22% vs. 13%, respectively, $p < .05$). Disease duration was similar in hospital recruits and Internet recruits, 11.5 ± 8.9 years and 11.1 ± 8.5 years, respectively.

3.2 | Sociopsychological Measures

The DHS mean score was 88.0 ± 23.2 , indicating a low rate of exposure to hassles in the cohort (Table 2). The subscales of DHS indicated that the most common hassles were time hassles, social hassles, and work hassles, while hassles related to money, social acceptance, and stigma of disease were less frequent. The total daily hassles score was similar in men and women, 87.1 ± 2.37 and 88.5 ± 22.9 respectively. It was similar in married or coupled persons

TABLE 1 Sociodemographic and medical characteristics of the cohort (N = 400)

Variable	Median (Min; Max) (IQR) or Mean \pm SD or N (%)
Age (years)	35 (18–79) (28–47); 38.7 ± 14.1
Female gender	243 (60.8%)
Married/coupled	240 (60.0%)
Number of children	1 (0–9) (0–3)
Education (years)	15 (4–30) (12–17)
Working	268 (67.0%)
Economic status	3 (1–5) (3–4)
Past smoker	188 (47.0%)
Current smoker	74 (18.5%)
Patient Harvey-Bradshaw Index	4 (0–29) (2–8); 5.52 ± 4.87
Patient Harvey-Bradshaw Index	
Remission < 5	210 (52.5%)
Mild disease 5–7	87 (21.8%)
Moderate disease 8–16	87 (21.8%)
Severe disease > 16	16 (4.0%)
Disease duration (years)	10 (0–47) (4–16); 11.36 ± 8.75
Medications (ever)	
Mesalamine	121 (30.3%)
Immunomodulators	202 (50.5%)
Biological	173 (43.3%)
Corticosteroids	80 (20.0%)
Surgery (ever)	138 (34.5%)
Hospitalization (last year)	95 (23.8%)

Note. IQR = interquartile range; SD = standard deviation.

versus single or divorced individuals, 86.0 ± 21.9 and 90.8 ± 24.9 , respectively. The DHS score was higher in smokers than nonsmokers, 95.0 ± 24.3 and 86.0 ± 22.2 , respectively. DHS score varied by disease activity: in remission, mild activity, moderate activity and severe activity it was 81.5 ± 19.3 , 88.6 ± 23.9 , 97.9 ± 24.4 and 98.0 ± 27.5 , respectively, $p < .001$ (ANOVA). Applying the Bonferroni correction post hoc, we found that the significant differences were between remission and moderate activity ($p < .001$), remission and severe activity ($p = .006$), and mild activity and moderate activity ($p = .026$).

The scores of the other psychosocial questionnaires also appear in Table 2. In the cohort, there was mild psychological distress (GSI mean 1.19), moderate family dysfunction (Family Assessment Device mean 1.8), and moderate exposure to threatening life experiences (List of Threatening Life Experiences mean 1.85). The cohort had a moderate quality of life by both SF-36 and SIBDQ measures.

Patients who filled in the questionnaires online reported significantly higher scores for total daily hassles and all of its sub-sections, and had reduced SF-36 Mental Health and SIBDQ scores and higher scores for GSI and Family Assessment Device, compared with the patients who had filled in the hardcopy questionnaires at the hospitals (Table A1). Men had higher scores compared to women on SIBDQ and SF-36 Physical Health in the hospital recruits ($p = .011$ and $p = .002$, respectively), and a higher score on SF-36 Physical Health in Internet recruits ($p = .025$). Patients who were working had higher scores for SIBDQ, SF-36 Physical and Mental Health and a lower score for GSI than those not working, in both hospital recruits and Internet recruits (Table A2a). Current smokers had lower scores for SIBDQ, SF-36 Physical Health and SF-36 Mental Health, and a higher GSI score, than nonsmokers in the

TABLE 2 Daily Hassles Scale total and subscale scores and psychological measures

	Median (Min–Max) IQR*	Mean ± SD
Daily Hassles Scale		
Total	84 (51–178)(71–100)	87.97 ± 23.18
Social hassles	15 (10–41)(13–19.5)	16.83 ± 5.28
Work hassles	11 (4–28)(9–15)	12.52 ± 4.82
Time hassles	18 (8–34)(13–22)	17.80 ± 5.70
Money hassles	9 (6–23)(7–12)	10.15 ± 3.61
Social acceptance	8 (5–20)(6–10)	8.57 ± 2.91
Stigmatization vocalization	6 (4–16)(4–8)	6.48 ± 2.68
<i>Psychological measures</i>		
Global severity index	1.19 (0–3.71)(0.43–1.86)	1.19 ± 0.92
Family assessment device	1.75 (1–4)(1.33–2.17)	1.80 ± 0.55
Threatening life experiences	1 (0–12)(0–3)	1.85 ± 1.99
SF-36 Physical Health	43.8 (10.3–62.4)(33.4–50.7)	42.1 ± 11.0
SF-36 Mental Health	42.7 (15.4–64.2)(33.7–51.6)	42.2 ± 11.4
Short Inflammatory Bowel Disease Questionnaire	47 (12–70)(36–59)	46.8 ± 14.1

Note. IQR = interquartile range; SD = standard deviation; SF-36 = Short-Form Health Survey. Range of scores: Daily Hassles Scale 51–204; Global severity index 0–4; Family Assessment Device 1–4; List of Threatening Life Experiences 0–12; SF-36 Physical or Mental Health 0–100; Short Inflammatory Bowel Disease Questionnaire 10–70.

TABLE 3 Correlations between Daily Hassles Scale total score and demographic, medical, and psychological measures

	Correlation Coefficient	p ^a
Age	–.101	<0.05
Economic status	–.399	<0.01
Harvey-Bradshaw Index	.283	<0.01
Disease duration	–.105	<0.05
Global severity index	.689	<0.01
Family assessment device	.456	<0.01
Threatening life experiences	.413	<0.01
SF-36 Physical Health	–.225	<0.01
SF-36 Mental Health	–.568	<0.01
Short Inflammatory Bowel Disease Questionnaire	–.468	<0.01

^aSpearman's rank correlation.

hospital recruits; however, there were no significant differences noted between smokers and nonsmokers in Internet recruits.

3.3 | Correlations

A Spearman's rank correlation analysis between DHS total score and demographic and medical characteristics was carried out (Table 3). There were significant negative associations of DHS with age, disease duration, and particularly economic status. Thus, poorer and younger patients and those having shorter disease duration had a higher score for daily hassles. The correlation of DHS with Patient Harvey-Bradshaw Index was positive, indicating a more active disease state when the DHS score was higher. The DHS was greater when there were more experiences of psychological

TABLE 4 Results of multiple linear regression analysis for log transformed Short Inflammatory Bowel Disease Questionnaire, SF-36 Physical Health and Mental Health, Global Severity Index, and Patient Harvey-Bradshaw Index

Variables	Short Inflammatory Bowel Disease Questionnaire	SF-36 Physical Health	SF-36 Mental Health	Global Severity Index	Patient-Harvey-Bradshaw Index
Standardized regression coefficients					
Age	.029	-.154**	.194***	-.043	.029
Education	.097 [†]	.114 [†]	.091 [†]	-.126***	-.090
Gender (male)	.117**	.164***	.089 [†]	-.064	-.142**
Economic status	.186***	.198***	.140**	-.034	-.120 [†]
Daily hassles	-.365***	-.136**	-.441***	.676***	.237***
Adjusted R ²	.253	.137	.342	.511	.119

* $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$.

distress (GSI), family dysfunction and threatening life experiences. More hassles were related to a reduced quality of life on all measures.

Disease duration correlated positively with a higher score for SF-36 Mental Health for hospital-recruited patients (Spearman's correlation coefficient 0.186, $p = .002$) and Internet recruits (correlation coefficient 0.354, $p < .001$). A higher economic status correlated with reduced disease activity, better quality of life, and diminished psychological distress, irrespective of site of patient recruitment (Table A2b).

3.4 | Regression and Path Analyses

Results of the multiple linear regressions for log transformed quality of life measures (SIBDQ and SF-36), GSI, and Patient Harvey-Bradshaw Index appear in Table 4. Log transformation was required because the data were not normally distributed. Regarding the quality of life measures, age, and daily hassles were negative predictors of SF-36 Physical and Mental Health, whereas education, male gender, and economic status were positive predictors. For SIBDQ, education, male gender, and economic status were positive predictors and daily hassles was a negative predictor; age had no significant effect. Daily hassles positively predicted an increase of mental health symptoms (GSI) and disease activity. Education predicted reduced GSI. Male gender and poorer economic status predicted more disease activity. For the SIBDQ, SF-36 Mental Health, GSI, and Patient Harvey-Bradshaw Index, the greatest beta values were from daily hassles.

The regression analysis was done separately for the hospital- and Internet-recruited patients (Table A3). DHS was the main predictor of the psychological measures and the Patient Harvey-Bradshaw Index in both sets of patients; of note, the beta values of DHS in the Internet recruits were higher than in hospital recruits. In the Internet-recruited patients, the demographic variables had no effect on these measures, with the exception of a minor impact of age on SF-36 measures and Patient Harvey-Bradshaw Index.

A Sobel test analysis was carried out to investigate the way in which the DHS scores affects disease activity measured by Patient Harvey-Bradshaw Index (Figure 1). DHS is shown to be related directly to the Patient Harvey-Bradshaw Index (path C, beta .245, $p < .001$). However, when GSI is added to the model, the paths DHS to GSI (path A) and GSI to Patient Harvey-Bradshaw Index (path B) are highly significant (A: beta .687, $p < .001$; B: beta .347, $p < .001$), whereas the path DHS to Patient Harvey-Bradshaw Index (path C') loses all significance. The effect of daily hassles on disease activity is mediated by the GSI distress measure.

We also did the Sobel test analysis separately for the hospital-recruited and Internet-recruited patients. The Sobel test statistic was 2.69 ($p < 0.05$) for the Internet patients and 7.21 ($p < 0.001$) for the hospital patients. The beta values and significances were similar to the Sobel test for the entire cohort together, indicating again that GSI mediates the effect of DHS on the Patient Harvey-Bradshaw Index.

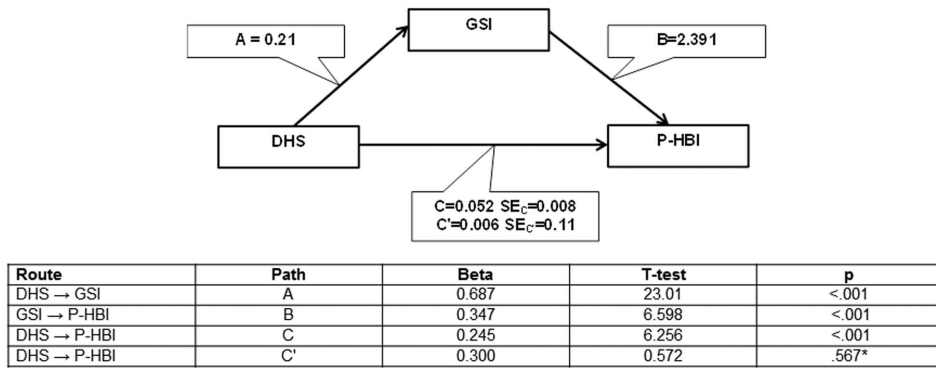


FIGURE 1 Path analysis depicting GSI as the mediator between DHS and Patient Harvey-Bradshaw Index based on Sobel test (Sobel test statistic = 6.09 $p < 0.001$)

Note. DHS = Daily Hassles Scale score; GSI = Global Severity Index; P-HBI = Patient Harvey Bradshaw Index; SE = standard error.

*Full mediation model due to nonsignificant direct effect under mediation conditions

4 | DISCUSSION

This is to our knowledge the first full analysis of the DHS in a nonselected cohort of patients with Crohn's disease. Although there are no norms for DHS in normal populations, it would appear that exposure to hassles was low in the cohort. The most commonly reported hassles concerned the issues of time, social relationships, and work. The cohort had moderate exposure to serious life events and family dysfunction. In this cohort, the economic status was self-reported moderate. Increased daily hassles was correlated most strongly with poor economic status, more active disease, psychological distress, family dysfunction, threatening life experiences, and reduced quality of life. In older persons in our cohort, there was less exposure to daily hassles, although the correlation between age and frequency of hassles was weaker. Men and women had a similar frequency of daily hassles. Therefore, daily hassles were related to a poorer psychological and economic state of the patient, and less to age and not at all to gender.

The regression model emphasized the contribution of both daily hassles and economic status independently with all the measures of quality and satisfaction with life, distress, and disease activity. The daily hassles score was the major predictor of quality of life, psychological distress, and the disease activity score in the Internet recruits, whereas in the hospital recruits demographic variables like education, gender, and economic status also affected several of the outcome measures. The path analysis, in the whole cohort and in the hospital recruits and Internet recruits analyzed separately, showed that the effect of daily hassles is mediated by the psychological distress engendered in the individual subjected to the hassles. While a cross-sectional study is not designed to show cause and effect, the path analysis nevertheless indicates that psychological distress is the mediator between daily hassles and disease activity.

Daily hassles are the challenges of day-to-day living. They are predictable, such as commuting to work, or unpredictable events, such as a car breakdown, that are short-lived and independent of serious life stressors (Serido, Almeida, & Wethington, 2004). According to the transactional model of stress, if the hassle is conceptualized as a threat, the subject will react with heightened stress (Lazarus et al., 1984). Compared with stress-free days, days with hassles are characterized by increased physical health symptoms and exacerbation of chronic health problems (Almeida et al., 2011). Poor control over daily hassles leads to impaired functioning, as in adolescents (Kanner, Feldman, Weinberger, & Ford, 1987). Daily hassles measured in various forms have been used to characterize psychological effects in a variety of conditions and diseases. These include asthma in low-income individuals, where daily hassles predicted anxiety and depression (Carter et al., 2012) and rheumatoid arthritis, where joint pain is increased (Fifield et al., 2004). Other conditions exacerbated by daily hassles were psoriasis (Verhoeven et al., 2009), cardiac disease (Bomhof-Roordink et al., 2015), fibromyalgia (Van Houdenhove et al., 2002), and headache (De Benedittis et al., 1992). Daily hassles affected

binge eating (Crowther, Sanftner, Bonifazi, & Shepherd, 2001), smoking habit (Twisk et al., 1999), and the use of cocaine (Back et al., 2008).

Hassles have been related to physiological changes in humans, such as changes in the immune system and hormonal levels (Piazza, Almeida, Dmitrieva, & Klein, 2010). Regression analysis with partial correlation analysis showed that an increased perception of daily hassles was associated with raised blood levels of sICAM-1 and IL-6, markers of increased inflammation, and D-dimer, associated with hypercoagulability, in relatively healthy adult men and women completing the Combined Hassles and Uplifts Scale (Jain, Mills, von Känel, Hong, & Dimsdale, 2007).

A biopsychosocial model was postulated where stress and anxiety can produce immunologic alterations in the gut mucosa and alter gut permeability (Long et al., 2010). Patients with ulcerative colitis in clinical remission but with symptoms of stress were shown to have abnormal levels of cytokines IL-1 β , IL-8, and IL-13 (Jonefjall, Öhman, Simrén, & Strid, 2016). The irritable bowel syndrome, characterized by abdominal pain and diarrhea as in Crohn's disease and severe psychological distress has no demonstrable pathology in the gut, but there is increased gut permeability and raised levels of IL-1 β , IL-6, IL-8 and TNF α (Ohman et al., 2010; Scully et al., 2010).

While daily hassles do not have the permanent threat of severe life events, such as a death, and are obviously less severe, they do appear to have long-term implications for the health of individuals (Piazza et al., 2013). Identification of persons at such risk may lead to changes in medical and sociopsychological care that will impact favorably on prognosis. This will include modifying how the individual reacts to the stress of daily hassles. Such lifestyle modification may also improve the function of the individual at the workplace.

Crohn's disease is a lifelong condition filled with distress (Garrett et al., 1991). Patients are concerned about diarrhea of sudden onset, disease complications, osteoporosis, lifestyle and quality of life, sexual intimacy and body stigma, diet, depression, and the competence of their physicians (Canavan, Abrams, Hawthorne, Drossman, & Mayberry, 2006). Longitudinal observations indicate that patients do not lose their concerns as the disease progresses, and long-standing disease is not accompanied by a better quality of life. Psychological distress may also impair patients' understanding of physicians' directives (Sewitch et al., 2002).

In our cohort, however, longer disease duration was correlated with an improved mental health state (SF-36 Mental Health and GSI score). A possible explanation for our finding is that about half of our patients were in remission. This association was observed too in a large Crohn's disease cohort entering remission on infliximab and followed for 1 year (Lichtenstein et al., 2004). Anxiety and depression related significantly to a greater frequency of relapses in 18 months of follow-up in patients with Crohn's disease or ulcerative colitis (Mittermaier et al., 2004). It follows that teaching these patients to react to hassles in a nonstressful manner might improve their psychological well-being. Indeed, it is increasingly advocated that a psychology service should be incorporated in all departments handling patients with Crohn's disease (Reiss et al., 2015).

Our cohort was self-selected and community-based and is likely representative of all stages of the disease. Almost half the patients were in remission at the time of the study, and the rates for biologic therapy, hospitalization, and surgery represent current practice. The strong correlation of psychological distress with the total hassles score was an expected observation and emphasizes the need to teach these patients methods of stress reduction. The correlation of daily hassles with disease activity is interesting and agrees with previous reports (Long et al., 2010). People troubled by daily stressors would be expected to have a reduced quality of life (Huppertz-Hauss et al., 2015; Vazquez et al., 2014). There was also a significant relationship of the daily hassles score with the duration of disease, emphasizing that patients do not necessarily improve their ability to manage their chronic disease with the passage of time (McCombie, Mulder, & Gearry, 2013). The regression analysis adds to our understanding of these correlations. Daily hassles were a predictor of poorer quality of life, increased distress, and increased disease activity, emphasizing the important role of these seemingly minor daily events in susceptible persons.

A worse economic status also predicted poorer quality of life and less satisfaction with life in the cohort. Of note, there was an inverse relationship between economic status and daily hassles. This is in line with the fact that poorer individuals are more susceptible to the distress of daily hassles. It is also well known that poorer populations everywhere have greater morbidity and mortality from chronic disease. Our data show a definite association between better

economic status and improved physical and mental well-being in our patients. Male gender predicted better quality of life, and it is known that women with Crohn's disease suffer a worse course compared with men (Wagtmans, Verspaget, Lamers, & Van Hogezaand, 2001). Interestingly, older age was a predictor of better mental health by the SF-36 measure.

4.1 | Limitations

Our study has certain limitations. Almost one third of the patients were recruited via the Internet. While studies of patients recruited from Internet populations have become more common, there is the problem of nonverification of the diagnosis and an inability to access patients' medical records. In our cohort the Internet recruits reported more daily hassles and psychological distress, and lower scores for health-related quality of life. We had no possibility to determine the reasons for this difference between the patients groups, and future studies should address this issue. Such knowledge would also be important when recommending appropriate psychotherapy. The performance of the study in a single population is a further limitation. Although the study sought to recruit all ethnic groups in Israel at the hospitals, fewer than 5% of the subjects were Arabs. Perhaps this is explained by the low prevalence of Crohn's disease in Israeli Arabs, and possibly less access to the Internet; these are subjects for further study. Extension of this study to other countries is required. Finally, our study was cross-sectional and cannot shed light on the downstream effect of daily hassles in Crohn's disease. This should be addressed in longitudinal studies, with an emphasis on newly recruited patient cohorts.

4.2 | Clinical Applications

The findings of our study provide pointers for clinical intervention beyond the use of medications and dietary supplements. Crohn's disease patients do not receive appropriate psychological and social counselling in many hospitals and health care centers. Management of such patients should include the teaching of stress reduction measures by social workers or psychologists, with attention not only to major stressors in life but also to common daily hassles, with extended follow up to gauge the long-term effect of such interventions.

5 | CONCLUSION

In conclusion, our findings show that knowledge of the presence of daily hassles is highly relevant when assessing patients' quality of life, including mental health symptoms, and the activity of the disease. The constant wear and tear distress effect imposed by daily hassles as shown here is associated with measurable deterioration of both psychological and physical health in Crohn's disease patients. Longitudinal studies will show whether appropriate psychological counseling can effectively reduce the stress engendered by daily hassles and so improve the well-being of patients.

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APPENDIX

TABLE A1 Daily hassles scale total and subscale scores and psychological measures by source of questionnaire

	Patients recruited at hospitals (N=278)	Patients recruited via internet (N=122)	
	Mean ± SD	Mean ± SD	
Variable	Median (Min;Max)(IQR ⁺)	Median (Min;Max)(IQR ⁺)	p
Daily Hassles Scale			
Total	85.8±22.8 82.0 (51.0;178.0)(68.0;98.3)	92.9±23.3 90.0 (51.0;168.0)(76.0;105.3)	.002
Social hassles	16.5±5.2 15.0 (10.0;41.0)(13.0;19.0)	17.6±5.3 17.0 (11.0;36.0)(14.0;20.5)	.010
Work hassles	12.1±4.6 11.0 (4.0;28.0)(8.0;15.0)	13.6±5.2 13.0 (7.0;28.0)(9.0;17.0)	.004
Time hassles	17.4±5.7 17.0 (8.0;34.0)(13.0;22.0)	18.7±5.5 18.0 (8.0;31.0)(15.0;23.0)	.036
Money hassles	9.9±3.7 9.0 (6.0;23.0)(7.0;11.8)	10.7±3.4 10.0 (6.0;22.0)(8.0;12.0)	.004
Social acceptance	8.3±2.9 8.0 (5.0;20.0)(6.0;10.0)	9.2±2.9 9.0 (5.0;17.0)(7.0;11.0)	.001
Stigmatization	6.2±2.4 5.0 (4.0;16.0)(4.0;7.0)	7.0±2.8 6.0 (4.0;15.0)(5.0;9.0)	.005
vocalization			
Psychological Measures			
Global severity index	.9±.7 .8 (.0;3.2)(.4;1.3)	1.1±.8 1.0 (.0;3.1)(.5;1.6)	.008
Family Assessment	1.8±.6 1.7 (1.0;4.0)(1.3;2.1)	1.9±.5 1.9 (1.0;3.2)(1.4;2.2)	.018
Device			

(Continues)

TABLE A1 (Continued)

Variable	Patients recruited at hospitals (N=278)	Patients recruited via internet (N=122)	p
	Mean \pm SD Median (Min;Max)(IQR*)	Mean \pm SD Median (Min;Max)(IQR*)	
Threatening life experiences	1.9 \pm 2.1 1.0 (.0;12.0)(.0;3.0)	1.8 \pm 1.7 1.0 (.0;8.0)(.0;3.0)	.563
SF-36 Physical Health	42.3 \pm 11.3 43.8 (10.3;62.4)(33.1;51.1)	41.8 \pm 10.5 43.8 (15.7;61.6)(33.8;49.5)	.549
SF-36 Mental Health	43.3 \pm 11.2 44.4 (15.4;64.2)(34.4;52.6)	39.6 \pm 11.5 39.0 (16.0;61.0)(32.1;49.2)	.003
Short Inflammatory Bowel Disease Questionnaire	48.4 \pm 13.8 49.0 (12.0;70.0)(38.0;61.0)	43.0 \pm 14.1 44.0 (14.0;69.0)(32.0;55.3)	.000

* Interquartile range

Daily hassles: Independent t-test; Psychological Measures: Mann-Whitney test.

Range of scores: Daily Hassles Scale 51–204, Global severity index 0–4, Family Assessment Device 1–4, List of Threatening Life Experiences 0–12, SF-36 Physical or Mental Health 0–100, Short Inflammatory Bowel Disease Questionnaire 10–70.

TABLE A2a Univariate analysis (ANOVA) of psychological measures and disease activity score by gender and source of questionnaire

Independent variable: Gender		Hospital-recruited patients				Internet-recruited patients			
Dependent Variable									
		N	Mean	SD	p	N	Mean	SD	p
Short Inflammatory Bowel Disease Questionnaire	Female	167	46.71	13.23	0.011	76	41.43	13.96	0.110
	Male	111	51.00	14.41		46	45.65	14.12	
SF-36 Physical Health	Female	163	40.55	11.47	0.002	75	40.15	10.75	0.025
	Male	108	44.87	10.43		46	44.53	9.51	
SF-36 Mental Health	Female	163	42.93	11.34	0.467	75	38.94	11.88	0.411
	Male	108	43.94	11.12		46	40.71	10.80	
BSI : Global Severity Index	Female	167	0.93	0.67	0.528	76	1.15	0.75	0.536
	Male	111	0.88	0.76		46	1.06	0.75	
Patient-Harvey-Bradshaw Index (P-HBI)	Female	167	5.74	4.58	0.019	76	6.25	5.07	0.955
	Male	111	4.40	4.81		46	6.20	5.39	

Independent variable: Working									
Dependent Variable		Hospital-recruited patients				Internet-recruited patients			
		N	Mean	SD	<i>p</i>	N	Mean	SD	<i>p</i>
Short Inflammatory Bowel Disease Questionnaire	Female	99	44.60	13.23	0.001	33	37.58	15.30	0.009
	Male	179	50.54	14.41		89	45.04	13.18	
SF-36 Physical Health	Female	96	37.21	11.47	0.000	32	38.67	9.79	0.048
	Male	175	45.05	10.43		89	42.94	10.54	
SF-36 Mental Health	Female	96	41.14	11.34	0.017	32	36.16	11.99	0.046
	Male	175	44.53	11.12		89	40.86	11.09	
BSI : Global Severity Index	Female	99	1.15	0.67	0.000	33	1.37	0.72	0.022
	Male	179	0.78	0.76		89	1.02	0.74	
Patient-Harvey-Bradshaw Index (P-HBI)	Female	99	6.59	4.58	0.000	33	6.76	5.05	0.495
	Male	179	4.44	4.81		89	6.03	5.23	

Independent variable: Smoking									
Dependent Variable		Hospital-recruited patients				Internet-recruited patients			
		N	Mean	SD	<i>p</i>	N	Mean	SD	<i>p</i>
Short Inflammatory Bowel Disease Questionnaire	Female	206	50.05	13.20	0.000	105	43.63	14.30	0.324
	Male	58	42.17	15.15		16	39.88	12.89	
SF-36 Physical Health	Female	200	42.92	11.08	0.032	104	41.56	10.68	0.490
	Male	57	39.31	11.44		16	43.52	9.56	
SF-36 Mental Health	Female	200	44.56	11.13	0.001	104	39.88	11.85	0.550
	Male	57	38.77	11.03		16	38.02	9.23	
BSI : Global Severity Index	Female	206	0.83	0.65	0.001	105	1.08	0.75	0.256
	Male	58	1.17	0.80		16	1.31	0.73	
Patient-Harvey-Bradshaw Index (P-HBI)	Female	206	4.95	4.66	0.031	105	5.89	4.75	0.137
	Male	58	6.48	5.04		16	7.94	7.11	

Independent variable: Family status [*]									
Dependent Variable		Hospital-recruited patients				Internet-recruited patients			
		N	Mean	SD	<i>p</i>	N	Mean	SD	<i>p</i>
Short Inflammatory Bowel Disease Questionnaire	Female	168	49.27	14.00	0.219	72	44.33	13.38	0.180
	Male	109	47.17	13.63		49	40.82	15.02	
SF-36 Physical Health	Female	164	42.88	11.01	0.296	72	42.14	10.76	0.558
	Male	106	41.41	11.64		48	40.99	9.96	
SF-36 Mental Health	Female	164	43.85	11.09	0.349	72	40.58	11.42	0.303
	Male	106	42.54	11.54		48	38.36	11.58	
BSI : Global Severity Index	Female	168	0.85	0.68	0.056	72	0.98	0.73	0.014
	Male	109	1.01	0.72		49	1.32	0.75	
Patient-Harvey-Bradshaw Index (P-HBI)	Female	168	5.14	4.82	0.832	72	6.46	5.06	0.605
	Male	109	5.27	4.58		49	5.96	5.41	

^{*}Coupled/Married vs. Single/Divorced

SD Standard deviation

TABLE A2b Correlation analysis (Spearman's rho) of disease duration or economic status with psychological measures and disease activity score by source of questionnaire

			Hospital-recruited	Internet-recruited
Disease duration	Short Inflammatory Bowel Disease Questionnaire	Correlation Coefficient	0.099	0.169
		<i>p</i>	0.101	0.067
		N	277	119
SF-36 Physical Health		Correlation Coefficient	0.051	0.020
		<i>p</i>	0.408	0.832
		N	270	118
SF-36 Mental Health		Correlation Coefficient	.186**	.354**
		<i>p</i>	0.002	0.000
		N	270	118
BSI : Global Severity Index		Correlation Coefficient	−0.084	−.245**
		<i>p</i>	0.165	0.007
		N	277	119
Patient-Harvey-Bradshaw Index (P-HBI)		Correlation Coefficient	0.021	0.090
		<i>p</i>	0.722	0.330
		N	277	277

(Continues)

TABLE A2b (Continued)

			Hospital-recruited	Internet-recruited
Economic Status	Short Inflammatory Bowel Disease Questionnaire	Correlation Coefficient	.368**	.289**
		<i>p</i>	0.000	0.001
		<i>N</i>	274	121
	SF-36 Physical Health	Correlation Coefficient	.302**	.267**
		<i>p</i>	0.000	0.003
		<i>N</i>	267	120
	SF-36 Mental Health	Correlation Coefficient	.365**	.192*
		<i>p</i>	0.000	0.036
		<i>N</i>	267	120
	BSI : Global Severity Index	Correlation Coefficient	-.348**	-.221*
		<i>p</i>	0.000	0.015
		<i>N</i>	274	121
	Patient-Harvey-Bradshaw Index (P-HBI)	Correlation Coefficient	-.222**	-.314**
		<i>p</i>	0.000	0.000
		<i>N</i>	274	121

*Correlation is significant at the 0.05 level (2-tailed).

**Correlation is significant at the 0.01 level (2-tailed).

TABLE A3 Results of multiple linear regression analysis for log transformed short inflammatory bowel disease questionnaire (SSIBDQ), SF-36 physical health and mental health, global severity index (GSI), and disease activity score (P-HBI), by questionnaire source

a Hospital-recruited patients					
Variables	Short Inflammatory Bowel Disease Questionnaire	SF-36 Physical Health	SF-36 Mental Health	Global Severity Index	Patient-Harvey-Bradshaw Index
Standardized regression coefficients					
Age	0.073	-0.129*	0.167**	-0.017	-0.027
Education	0.094	0.131**	0.087	-0.128**	-0.145*
Gender (male)	0.146**	0.187**	0.095	-0.076	-0.236***
Economic status	0.248***	0.202**	0.202***	-0.057	-0.099
Daily Hassles	-0.261***	-0.098	-0.392***	0.666***	0.183**
Adjusted R ²	0.221	0.124	0.322	0.506	0.123

b Internet-recruited patients

Variables	Short Inflammatory Bowel Disease Questionnaire	SF-36 Physical Health	SF-36 Mental Health	Global Severity Index	Patient-Harvey-Bradshaw Index
Standardized regression coefficients					
Age	−0.082	−0.190 [*]	0.273 ^{**}	−0.102	0.174 [*]
Education	0.141	0.079	0.062	−0.113	−0.057
Gender (male)	0.061	0.117	0.088	−0.039	0.089
Economic status	0.107	0.189	0.021	0.013	−0.217 [*]
Daily Hassles	−0.493 ^{***}	−0.219 [*]	−0.530 ^{***}	0.687 ^{***}	0.293 ^{**}
Adjusted R ²	0.311	0.150	0.358	0.486	0.176

*p<0.05, ** p<0.01, *** p<0.001.