Psychiatric symptom levels and perceived family functioning in adolescents who underwent endoscopy and gastric biopsy for gastrointestinal disease symptoms

Didem Ayyıldız[1], Zeliha Demirtas[2], Yelda Çufalı[3], Hicran Akın[4]
[1]M.D, Department of Child and Adolescent Psychiatry, Private Practise, Bursa, Turkey https://orcid.org/0000-0001-9149-201X
[2]M.D., Department of Child Gastroenterology and Hepatology, Dortcelik Pediatrics Hospital, Bursa, Turkey https://orcid.org/0000-0002-4554-1658
[3]M.D., Department of Anaesthesiology and Reanimation, Dortcelik Pediatrics Hospital, Bursa, Turkey https://orcid.org/0009-0003-9832-5259
[4]M.D., Department of Infectious Diseases and Clinical Microbiology, Dortcelik Pediatrics Hospital, Bursa, Turkey https://orcid.org/0009-0004-9576-4851

SUMMARY

Objective: Our knowledge of the links among gastrointestinal diseases, psychiatric disorders and family environment in adolescents is largely based on very limited data. Thus, this paper aims to examine the psychiatric symptom levels and family function areas in youths, who underwent endoscopy and gastric biopsy because of gastrointestinal complaints and compare their results with healthy controls.

Method: Patients aged 12-18 who were scheduled to undergo diagnostic endoscopy at the Gastroenterology outpatient clinic of a Pediatric Hospital, and age and gender- matched healthy controls from the COVID-19 vaccination outpatient clinic of the same hospital have been referred to Child and Adolescent Psychiatry Unit. Adolescents who were determined to have clinically normal intelligence in the psychiatric evaluation conducted by a Child and Adolescent Psychiatry specialist, were enrolled. Revised-Child Anxiety and Depression Scale (R-CADS) was used to assess depressive and anxiety symptom levels and Family Assessment Device (FAD) to determine family functionality.

Results: Worse general family functioning is positively correlated with higher anxiety levels and total internalizing scores in the study group. Family history of any medical disease was detected to be statistically significantly higher in the "endoscopic findings +" (with abnormal signs) group

Discussion: Contrary to expectations, we did not find a significant difference between patients with gastrointestinal problems and healthy controls in terms of psychiatric symptom levels. However, it's worthwhile noting that higher Protection factor index (PFI) (academic achievement and Socio-economic status) and better family functions predicted lower depression scores of patients with gastrointestinal problems.

Key Words: Gastrointestinal disorders, functional; psychiatry; adolescent; family functions

INTRODUCTION

In recent years, the fact that the interaction between the human gastrointestinal tract and the CNS (Central Nervous System) has a crucial role in the development of varied neuropsychiatric disorders is among the most commonly discussed (1-3). It is generally accepted that the system called the brain-intestinal axis includes the CNS, autonomic nervous system, enteric nervous system, hypothalamus-pituitary-adrenal (HPA) axis and the connections, established between them by neural, immunological, endocrine and metabolic pathways (4-8). One of the several explanations for co-occurrence of both the symptoms of chronic gastrointestinal disorders and psychiatric disorders is that the excessively increased activity of the HPA axis, which regulates the stress response (9, 10). In the literature, there are a few examples of neurophysiological studies in patients with Inflammatory Bowel Disease (IBD), the most prevalent chronic gastrointestinal disorder in which psychological factors are frequently investigated have shown alterations in specific brain regions and task-related networks associated with stress response, cognitive flexibility, and autonomic hyperarousal functions. These alterations, which lead to information processing abnormalities in areas associated with

DOI: 10.5505/kpd.2025.98569

Cite this article as: Ayyildiz D, Demirtas Z, Cufali Y, Akin H. Psychiatric symptom levels and perceived family functioning in adolescents who underwent endoscopy and gastric biopsy for gastrointestinal disease symptoms. Turkish J Clin Psych 2025; 28:

The arrival date of article: 28.11.2024, **Acceptance date publication:** 22.05.2025

Turkish J Clinical Psychiatry 2025;28:

stress hyperresponsiveness, biased threat appraisal, and cognitive inflexibility, have suggested to be similarly demonstrated in also anxiety disorders (11).

Clinical research, as well has been pointing out the fact that gastrointestinal symptoms, such as abdominal pain, burning, nausea-vomiting or bloating could significantly affect quality of life of children and adolescents regardless of the reason (organic or functional) (12,13). Endoscopy has frequently been used for diagnosis in patients feature with gastrointestinal symptoms such as epigastric/abdominal pain, burning, nausea-vomiting, bloating but the endoscopic findings haven't always got explanation for these symptoms. When the structural abnormalities related to the organic diseases cannot be demonstrated, the conditions have been diagnosed as functional gastrointestinal diseases (FGID). Considering the factors related to unnecessary endoscopic procedures such as invasiveness, potential risk of harm and additional financial burden to health system; it would be important to reveal the features children and adolescents with organic/functional gastrointestinal diseases have (14). Therefore, clarifying accompanying psychopathologies and psychosocial factors in children and adolescents with organic/functional gastrointestinal diseases has been attracting considerable interest in recent years in order to reduce unnecessary tests, organize tailored treatments and interventions to improve the course of the disease. It is also well known that healthy/unhealthy family functions are associated with the individual's psychosocial adjustment (15-17). From this point of view, the present study has aimed to assess the relationships among gastrointestinal diseases, psychiatric symptom levels and family functions in adolescents, who underwent endoscopy and gastric biopsy because of gastrointestinal complaints and compare them with healthy controls. This paper is also a preliminary attempt to investigate whether there is a difference in terms of psychiatric problems and family history of medical/gastrointestinal or psychiatric disorders between the youths whose diagnosis of gastritis or ulcer was confirmed by histopathologically and those who did not have abnormal signs.

METHODS

Procedures

Youths aged 12 to 18, who were planned to undergo endoscopy after applying to the Gastroenterology outpatient clinic of a pediatric hospital due to gastrointestinal complaints between May and December 2022 and referred to the Anesthesiology and Reanimation outpatient clinic constituted the study group. After obtaining written consent from the youths, necessary diagnostic endoscopy was performed, and biopsies were taken by a pediatric gastroenterology specialist. Biopsies were analyzed by an experienced pathologist. The healthy control group, on the other hand, was formed by selecting from adolescents in the same age group and matched in terms of gender with study group who applied to the COVID vaccine polyclinic and did not have a chronic medical disease or psychiatric application. Adolescents, who had not previously had diagnoses of chronic GIS (gastrointestinal system) disease/any other chronic disease or psychiatric disorder, were referred to the Child and Adolescent Psychiatry specialist. According to the psychiatric interview, adolescents who had the impression of clinically normal intelligence, and who agreed to participate in the study were included and participants were asked to fill out the Revised Child Anxiety and Depression Scale (RCADS), Family Assessment Device (FAD) and a case report form, which was created by the child and adolescent psychiatrist. The sociodemographic characteristics (age, gender, annual grade point average (1-5) of the patients and age, education level, employment status, monthly income of the parents), medical history and diagnosed medical disease or gastrointestinal complaints presence of their family members were included in the case report form. Necessary permissions for the study were obtained from Uludag University, Faculty of Medicine Clinical Research Ethics Committee (date 13.04.2022 and number 2022-8/3). The present study was conducted in compliance with the Declaration of Helsinki.

Measures

Revised Child Anxiety and Depression Scale-RCADS: RCADS is a self-report scale which was

used to evaluate depression, anxiety disorders and obsessive-compulsive disorder in children and adolescents and it was developed by Chorpita et al. (18). Each item of the 47-item scale is scored between 0 and 3. Although scores are calculated separately for Social Phobia, Panic Disorder, Separation Anxiety Disorder, Generalized Anxiety Disorder and Obsessive-Compulsive Disorder, the "total anxiety score" is calculated by adding these subscales; The "Internalizing Disorder" score can be obtained by adding the total anxiety score and the Depressive Disorder score. The Turkish validity and reliability study of the scale was performed by Görmez et al. (19). The authors emphasized that the evidence that the scale is a valid and reliable tool for Turkish population was satisfactory. In our study the child form was filled by the adolescent herself.

Family Assessment Device: In our study, the "Family Assessment Device" was used to evaluate family functions. The scale developed by adapting the Mc Master family functions model; The model consists of 6 sub-dimensions ("problem solving", "communication", "roles", "affective responsiveness", "affective involvement", "behavior control") and a 7th subscale that includes a general assessment. Each of the 60 items of the scale, which is filled by family members older than 12 years of age, is scored between 1 and 4. High scores indicate ineffective family functions. "2 points" are deemed as the cut-off value for the healthy/unhealthy distinction (20). The Turkish validity-reliability study of the scale was done by Bulut. Psychometric properties of the original scale were satisfactory, and the use of 60-item version was supported in the same study (21). In our study, family functions were assessed based on youth reports.

Statistical analyses

Data were analyzed using the Statistical Program for Social Sciences- SPSS for IBM, 20.0. Descriptive statistics were presented as mean, standard deviation, or frequency (%). Chi-square test was used to determine the gender distribution between study group and controls and in comparisons of endoscopic findings +/- groups. Mann-Whitney U-test was used to evaluate age and socioeconomic status (SES). SES was calculated in SPSS by considering the variables of mother's education level, father's education level, mother's employment status and monthly income level. Although the educational level and working status of the parents were ordinal variables, they were accepted continuous variables and the sum of the scores was expressed as socio economic status (SES). Academic achievement level which was an ordinal variable (1-5) was also considered as a continuous variable. Independent-sample t-test was used for normally distributed data, and Mann-Whitney U-test was used for data that did not show normal distribution in the comparison of RCADS and FAD total score and subscale scores. Pearson correlation test was used to evaluate the correlation among the subscale scores in the study group. Statistical significance value was determined as $p < 0.05$.

RESULTS

The patient group was consisted of 55 adolescents who were planned for diagnostic endoscopy in the gastroenterology outpatient clinic between May and December 2022. However, after completing the researcher form, 2 participants who were found to be under treatment for chronic medical diseases such as Hashimoto's disease (n=1) and asthma (n=1), and 3 participants who were under psychiatric treatment and follow-up were excluded from the study group (n=50). After removing 1 patient who used Levothyron for thyroid dysfunction and one another who was revealed to be under treatment for allergic asthma, 46 people formed the control group.

In 11 of 50 cases, who met inclusion criteria for study group, no pathological sign was observed in endoscopy, and the histopathological results were normal. It has been revealed that of the remaining 39 cases; 1 had Celiac Disease, 3 had peptic ulcer and 35 had gastritis findings. One, whose pathological result was compatible with Celiac Disease, were not included in the statistical analysis in order to obtain more homogeneous sample.

The average age was (M=15.34, SD=1.6) of the participants in the study group and (M=14.86,

Table 1. Group comparisons regarding RCADS and FAD subscale scores.

	Study group	Control group	95% Confidence interval of the difference		Z/t	p
	Mean–SD	Mean–SD	lower	upper		
RCADS						
Social Anxiety Disorder	11.03–6.4	10.93–6.1	-2.43	2.55	.046	.963[a]
Panic Disorder	9.42–6.8	7.46–5.8	-.58	4.50	-1.422	.155
SAD	4.20–3.5	3.25–2.7	-.33	2.23	-1.109	.267
GAD	7.74–3.9	7.63–4.0	-1.49	1.69	.127	.899 [a]
OCD	6.24–4.1	5.97–4.3	-1.41	1.95	-.447	.655
M. depression	11.09–7.4	9.38–6.8	-1.13	4.55	-1.050	.294
Total Anxiety	38.13–21.6	31.10–16.8	-.78	14.83	-1.398	.162
Total Internalizing score	49.25–27.8	40.48–22.1	-1.35	18.87	-1.157	.247
FAD						
Problem Solving	1.80–.6	2.12–.7	-.53	-.006	-2.225	**.026**
Communication	1.86–.5	1.87–.5	-.21	.23	-.052	.959
Roles	1.92–.4	2.00–.4	-.24	.11	-.793	.428
Affective Responsiveness	1.82–.7	1.75–.7	-.19	.39	-.420	.675
Affective Involvement	2.35–.3	2.28–.4	-.09	.22	-1.221	.222
Behavior Control	2.07–.3	2.03–.3	-.10	.17	-.736	.462
General Functioning	1.70–.6	1.73–.6	-.25	.24	-.049	.961

RCADS: Revised Child Anxiety and Depression Scale; FAD: Family Assessment Device; SAD: Separation Anxiety Disorder GAD: Generalized Anxiety Disorder; OCD: Obsessive Compulsive Disorder
Mann Whitney U test [a]Independent samples-t test for social anxiety disorder and GAD variables

SD=1.8) in healthy controls. The majority of participants were girls (43) (87.7%) and only 6 (12.2%) of them were boys in the study group. Of the healthy controls, matched in terms of gender with study group, 41 (89.1%) were girls and of 5 (10.9%) were boys. Study and healthy control groups were similar with regard to age (z=-1.416, p=.157), gender (fisher's exact test=.570) and SES (z= -1.394, p=.163).

The most common gastrointestinal complaint of the patients in the study group was pain (abdominal, gastric) 69.0%, followed by nausea-vomiting 17.2%, burning 10.3%, swallowing difficulties 3.4%.

Except for GAD, all RCADS sub-scores were higher in the patient group. However, none of these differences were statistically significant. Moreover, there was no significant difference between groups with regard to FAD sub-scales except for problem solving. The average score of the problem-solving subscale of the patient group was statistically significantly lower than the healthy controls (z=-2.225, p=.026). (Table 1).

As anticipated, correlation analyses have revealed that there was significant negative relationship between SES and total anxiety score (p=.037, r=-.312) and total internalizing score (p=.025, r=-.334) sub-scales of R-CADS of the study group. In addition, the "general functioning" subscale of FAD was significantly correlated with total anxiety score (p<.001, r=.623) and total internalizing score (p<.001, r=.655) (Table2).

When 11 cases with normal endoscopy and pathology results and 38 cases with abnormal findings were compared regarding familial factors; the rate of having family history of psychiatric illness (X^2=.658) and the rate of having family history of gastrointestinal disease (X^2=.578) were similar in both groups, while family history of any medical disease aspect (X^2=.034) was found to be statistically significantly higher in the positive result group (with abnormal signs). Categorical variables were formed according to the cut-off values with optimum specificity and sensitivity for each subscale, determined in the Turkish validity and reliability study of the RCADS scale and the group with endoscopic finding - and + were compared. There

Table 2: Correlation analyses in the study group

		SES	Total anxiety	Total int.	GF	PS	Com.	Roles	AR	AI	BC
SES	P										
	R										
Total anxiety	P	**.037***									
	R	**-.312**									
Total int.	P	**.025***	**.000****								
	R	**-.334**	**.986**								
GF	P	.631	**.000****	**.000****							
	R	-.072	**.623**	**.655**							
PS	P	.920	**.000****	**.000****	**.000****						
	R	.015	**.489**	**.523**	**.847**						
Com.	P	.698	**.000****	**.000****	**.000****	**.000****					
	R	-.058	**.433**	**.464**	**.762**	**.747**					
Roles	P	.739	**.004****	**.002****	**.000****	**.000****	**.000****				
	R	-.050	**.394**	**.416**	**.741**	**.615**	**.571**				
AR	P	.551	**.000****	**.000****	**.000****	**.000****	**.000****	**.000****			
	R	-.089	**.539**	**.570**	**.769**	**.652**	**.639**	**.661**			
AI	P	.201	.101	.058	**.000****	**.000****	**.008****	**.000****	**.000****		
	R	.190	.230	.265	**.496**	**.425**	**.358**	**.517**	**.577**		
BC	P	.831	.400	.501	**.020***	.075	.294	**.005****	**.004****	**.000****	
	R	.032	.119	.095	**.315**	.244	.146	**.376**	**.386**	**.493**	

were no significant differences in terms of psychiatric symptom levels between the two groups.

Further analyses were performed to detect the effects of risk and protection factors on psychiatric symptom levels and family functionality in the study group. Having a family history of medical disease, having a family history of gastrointestinal disease and having a family history of psychiatric disease, which are dichotomous variables, were added up to the risk factor index (RFI). Academic achievement level and SES variables formed the protection factor index (PFI). Hierarchical linear regression analysis was carried out to examine factors predicting depressive symptom levels in the study group. The general functioning subscale of FAD was entered as the first block and the results indicated that the model was significant ($F=20.250$, $p<.001$), and 34.2 % of the variance was explained by the model in the hierarchical linear regression analysis. After entry of the PFI variable at the second block, the model was still significant ($F= 13.928$, $P < .001$) and total variance explained by the model as a whole was 42.3 % (R squared change = .081). In the model 2; the PFI significantly predicted lower depressive symptom scores in adolescents ($B= -.527$, $p=.026$). The general functioning variable were still statistically significant ($B=6.119$, $p<.001$) (Table 3).

DISCUSSION

The present findings have demonstrated that there was no statistically significant difference between study group and healthy controls regarding psychiatric symptom levels. This was probably as a result of the fact that the data of psychiatric symptoms and family function areas were based on only adolescents' self-reports in the current study. This apparent lack of significant difference between groups can be attributed to the fact that adolescents tend to underrate their own psychiatric problems. Another possible explanation for these results may be that the patients participated in our study were in the process of diagnosis, that is, the duration of their complaints would be relatively short. There was also no significant difference in terms of psychiatric symptom levels between patients with abnormal and normal pathological signs in the present study. However, these results

Table 3: Hierarchical linear regression analysis findings for variables predicting major depression symptom levels in study group.

	Unstandardized Coefficients		Standardized Coefficients Beta	p
	B	Std. Error		
Model 1				
General functioning	6.119	1.431	.535	<.001
Model 2				
PFI	-.527	.228	-.289	.026

Note: PFI (Protection Factor Index) was used as continuous variable

should be carefully evaluated due to the limited number of cases in the endoscopic finding-negative group. A few attempts have been made with the purpose of examining the differences before and after endoscopy in terms of psychiatric symptoms and quality of life (QofL). In a prospectively designed adult study, no significant alterations were found between pre- and post-endoscopy in terms of patients' quality of life, depressive and anxiety levels. Further, they did not find significant difference between those with and without organic abnormalities similar with our findings (22).

Moreover, we found no significant difference between the two groups regarding the subscales of family functionality except for the problem-solving area. It was observed that families in the study group showed better functionality in the problem-solving area. In their study on children with functional abdominal pain syndrome, Ghanizadeh et al. found that family functioning levels were not significantly different from the normal population, like our results (23). Our findings are in contradiction with a previous study of Ozyurt et al. (2019) (24), which found that emotional and peer relationship problems were more common and family functionality was impaired in all areas of youths whose gastritis diagnosis was confirmed histopathologically. In that study without comparison with healthy controls, "2" were determined as cut point for family functionality sub-domains, and it was detected that the average score of the participants in all domains was found to be above 2. According to the results of the review article evaluating the family functioning of children with functional gastrointestinal disorders; the impairment in family functioning was detected to be more than in the healthy controls in the majority of the studies. In addition, it has been suggested that the difficulties may have experienced by children with gastrointestinal disorders and their families were in certain areas according to the consistent findings on worse family functionality in the fields such as roles, communication, and affective involvement. Relationships with individual psychosocial factors such as children's perceived quality of life and self-perception were investigated; a positive relationship was found between psychiatric problems and poor family functioning, while an inverse relationship was found with positive self-concept (25). The lower levels of current psychiatric symptoms of the cases may have led to their better functionality in the problem-solving area, or reversely, the level of psychiatric symptoms may have been lower because their problem-solving skills are good in the present study.

One of the remarkable findings of our study is the fact that the significant portion of the adolescents, who applied to the gastroenterology outpatient clinic during 8-month period and were scheduled for an endoscopy examination, were girls (87.2%). Considering the results in terms of gender in studies investigating the relationship between functional or organic gastrointestinal diseases and psychological problems, female gender was associated with multiple gastrointestinal complaints and high levels of depressive symptoms. In an adult study, the abdominal pain severity of the patients with functional bowel disorders was found to be positively associated with depression for women (26). Although findings on children and adolescents are scarce, epidemiological data of children and adolescents with functional abdominal pain show that girl gender is leading (27,28).

Our results would seem to suggest that worse general family functioning is positively correlated with higher anxiety levels and total internalizing scores, and better "general functioning" level is protective from depression. Although our study did not find a significant difference between those experiencing gastrointestinal symptoms and healthy controls in terms of psychiatric symptom levels, it lends support to the studies suggesting that negative family functionality or less resilient family patterns may be a determinant of psychiatric comorbidity and worse QofL (29, 30). Clinicians who deal with patients with gastroenterological complaints should refer patients to family-centered treatment focusing on general well-being, addressing concerns about treatments, or increasing motivation to comply with diet and medications. This approach would support reduce the incidence of psychiatric symptoms (31, 32).

It's fundamental to note that higher academic achievement level and SES were also found associated with lower depression scores in adolescents with gastrointestinal symptoms according to our

findings. The literature suggests that school absenteeism in children and adolescents with chronic illnesses may be related to academic challenges, but the low socioeconomic status of the family also mediates this link (33,34). Revealing educational and socioeconomical risk factors related to accompanying psychiatric problems in children with chronic diseases would enable developing preventive strategies such as school-based programs (35).

Given that our findings are based on a limited sample (especially number of cases in the histopathology normal group), the results from such analyses should therefore be treated with utmost caution. The fact that unintended bias related to majority of participants who made up the sample of our study was girls should also be taken into consideration. Additionally, only the adolescents themselves filled out the scales in which we evaluated psychiatric problems and family functioning. It is known that parents of children and adolescents with chronic gastrointestinal diseases are also accompanied by psychiatric problems, and they may be a confounding factor on the results regarding family functionality (36). Therefore, the fact that parents' psychiatric symptom levels were not evaluated is another limitation of our study.

Further data collection would be needed to determine whether there are factors vary in those with and without histopathological signs. Since it is well known children and adolescents with a chronic medical or psychiatric illness might be adversely affected by emotional and behavioral attitudes of family members, future works in which psychiatric diagnoses of both youth and their parents are evaluated with structured diagnostic interviews will contribute to the elucidation of psychological factors that predict organic diseases.

Conflict of Interest: None declared by the authors.

Financial Disclosure: None declared by the authors.

Study concept and design: D.A., Z.D., Y.Ç; Acquisition of the subjects and/or data: Z.D, Y.Ç, H.A.; analysis, and interpretation of the data: D.A., Z.D.; preparation of the article: D.A., Z.D. All authors have approved the final version of the article.

Correspondence address: M.D., Didem Ayildiz, Department of Child and Adolescent Psychiatry, Private Practise, Bursa, Turkey
didemayyldz@gmail.com

REFERENCES

1. Hsiao EY, McBride SW, Hsien S, Sharon G, Hyde ER, McCue T, Codelli JA, Chow J, Reisman SE, Petrosino JF, Patterson PH, Mazmanian SK. Microbiota modulate behavioral and physiological abnormalities associated with neurodevelopmental disorders. Cell. 2013 Dec 19;155(7):1451-63. doi: 10.1016/j.cell.2013.11.024. Epub 2013 Dec 5. PMID: 24315484; PMCID: PMC3897394.

2. Dash S, Clarke G, Berk M, Jacka, FN. The gut microbiome and diet in psychiatry: focus on depression. Curr Opin Psychiatry. 2015; 28: 1-6.

3. Dinan TG, Stilling RM, Stanton C, Cryan JF. Collective unconscious: How gut microbes shape human behavior. J Psychiatr Res. 2015; 63: 1-9.

4. Doğan A, Yaşar S, Kayhan S, Kırmızıgöz Ş, Kaplan A. Bağırsak-beyin aksı. Turk J Neurochirurgie. 2018; 28: 377-379.

5. Coelho-Aguiar Jde M, Bon-Frauches AC, Gomes AL, Veríssimo CP, Aguiar DP, Matias D, Thomasi BB, Gomes AS, Brito GA, Moura-Neto V. The enteric glia: identity and functions. Glia. 2015 Jun;63(6):921-35. doi: 10.1002/glia.22795. Epub 2015 Feb 20. PMID: 25703790.

6. Charrier B, Pilon N. Toward a better understanding of enteric gliogenesis. Neurogenesis. 2017; 4: 1283-1293.

7. Forsythe P, Kunze WA, Bienenstock J. On communication between gut microbes and the brain. Curr Opin Gastroenterol. 2012; 28: 557-562.

8. De Palma G, Collins SM, Bercik P. The microbiota-gut-brain axis in functional gastrointestinal disorders. Gut microbes. 2014, 5: 419-429.

9. Sic A, Cvetkovic K, Manchanda E, Knezevic NN. Neurobiological Implications of Chronic Stress and Metabolic Dysregulation in Inflammatory Bowel Diseases. Diseases. 2024; 12(9): 220.

10. Dinan TG, Quigley EM, Ahmed SM, Scully P, O'Brien S, O'Mahony L, Keeling PN. Hypothalamic-pituitary-gut axis dysregulation in irritable bowel syndrome: plasma cytokines as a potential biomarker? Gastroenterology. 2006; 130(2): 304-311.

11. Mayer EA, Ryu HJ, Bhatt RR. The neurobiology of irritable bowel syndrome. Mol Psychiatry. 2023; 1-15.

12. Engelmann G, Erhard D, Petersen M, Parzer P, Schlarb AA,

Resch F, Brunner R, Hoffmann GF, Lenhartz H, Richterich A. Health-related quality of life in adolescents with inflammatory bowel disease depends on disease activity and psychiatric comorbidity. Child Psychiatry Hum Dev. 2015 Apr;46(2):300-7. doi: 10.1007/s10578-014-0471-5. PMID: 24838299.

13. Warschburger P, Hänig J, Friedt M, Posovszky C, Schier M, Calvano C. Health-related quality of life in children with abdominal pain due to functional or organic gastrointestinal disorders. J Pediatr Psychol. 2013; 39: 45-54.

14. Bremner AR, Sandhu BK. Recurrent abdominal pain in childhood: the functional element. Indian Pediatr. 2009 May;46(5):375-9. PMID: 19478350.

15. Qiu Y, Xu L, Pan Y, He C, Huang Y, Xu H, Lu Z, Dong C. Family Resilience, Parenting Styles and Psychosocial Adjustment of Children With Chronic Illness: A Cross-Sectional Study. Front Psychiatry. 2021 May 12;12:646421. doi: 10.3389/fpsyt.2021.646421. PMID: 34054605; PMCID: PMC8149598.

16. Galán-González E, Martínez-Pérez G, Gascón-Catalán A. Family functioning assessment instruments in adults with a non-psychiatric chronic disease: A systematic review. Nurs Rep. 2021; 11(2): 341-355.

17. Shao R, He P, Ling B, Tan L, Xu L, Hou Y, Yang Y. Prevalence of depression and anxiety and correlations between depression, anxiety, family functioning, social support and coping styles among Chinese medical students. BMC Psychol. 2020; 8: 1-19.

18. Chorpita BF, Moffitt CE, Gray J. Psychometric properties of the Revised Child Anxiety and Depression Scale in a clinical sample. Behav Res Ther. 2005; 43: 309-322.

19. Gormez V, Kilincaslan A, Ebesutani C, Orengul AC, Kuvan, Ceri V, Nasiroglu S, Filiz M, Chorpita BF. Psychometric Properties of the Parent Version of the Revised Child Anxiety and Depression Scale in a Clinical Sample of Turkish Children and Adolescents. Child Psychiatry Hum Dev. 2017 Dec;48(6):922-933. doi: 10.1007/s10578-017-0716-1. PMID: 28251450..

20. Epstein NB, Ryan CE, Bishop DS, Miller IW, Keitner GI. The McMaster model: A view of healthy family functioning. The Guilford Press, 2003.

21. Kabacoff RI, Miller IW, Bishop DS, Epstein NB, Keitner, GI. A psychometric study of the McMaster Family Assessment Device in psychiatric, medical, and nonclinical samples. J Fam Psychol. 1990; 3: 431.

22. Van Kerkhoven LA, van Rossum LG, van Oijen MG, Tan ACITL, Laheij RJF, Jansen JB. Upper gastrointestinal endoscopy does not reassure patients with functional dyspepsia. Endoscopy. 2006; 38: 879-885.

23. Ghanizadeh A, Moaiedy F, Imanieh MH, Askani H, Haghighat M, Dehbozorgi G, Dehghani SM. Psychiatric disorders and family functioning in children and adolescents with functional abdominal pain syndrome. Journal of gastroenterology and hepatology. 2008; 23(7pt1): 1132-1136.

24. Özyurt G, Cagan-Appak Y, Karakoyun M, Baran M. Evaluation of emotional, behavioral problems and family functioning in adolescents with chronic gastritis. Arc Argent Pediatr. 2019; 117: 110-114.

25. Garr K, Odar Stough C, Origlio J. Family functioning in pediatric functional gastrointestinal disorders: A systematic review. Journal of Pediatric Psychology. 2021; 46(5), 485-500.

26. Deutsch D, Bouchoucha M, Uzan J, Raynaud JJ, Sabate JM, Benamouzig R. Abdominal pain severity is mainly associated with bloating severity in patients with functional bowel disorders and functional abdominal pain. Dig Dis and Sci. 2022; 67(7): 3026-3035.

27. Korterink JJ, Diederen K, Benninga MA, Tabbers MM. Epidemiology of pediatric functional abdominal pain disorders: a meta-analysis. PloS one. 2015; 10: e0126982.

28. Martins GP, Sandy NS, Alvarenga LR, Lomazi EA, Bellomo-Brandão MA. Functional abdominal pain is the main etiology among children referred to tertiary care level for chronic abdominal pain. Arq Gastroenterol. 2022; 59(01): 97-101.

29. Cushman G, Shih S, Reed B. Parent and family functioning in pediatric inflammatory bowel disease. Children. 2020; 7(10): 188.

30. Dong C, Wu Q, Pan Y, Yan Q, Xu R, Zhang R. Family resilience and its association with psychosocial adjustment of children with chronic illness: A latent profile analysis. Journal of pediatric nursing. 2021; 60: e6-e12.

31. Plevinsky JL, Hommel KA. Psychological Aspects of Inflammatory Bowel Disease in Children and Adolescents. In Pediatric Inflammatory Bowel Disease. (pp. 699-709). Cham: Springer International Publishing. 2023.

32. Agrawal M, Spencer EA, Colombel JF, Ungaro RC. Approach to the management of recently diagnosed inflammatory bowel disease patients: a user's guide for adult and pediatric gastroenterologists. Gastroenterology. 2021; 161(1), 47-65.

33. Wikel K, Markelz AM. Chronic Health Conditions, School Attendance, and Socioeconomic Factors: A Literature Review. The Journal of Special Education Apprenticeship. 2023; 12(2): 9.

34. Pinquart M, Teubert D. Academic, physical, and social functioning of children and adolescents with chronic physical illness: a meta-analysis. Journal of pediatric psychology. 2012; 37(4).

35. Thongseiratch T, Chandeying N. Chronic illnesses and student academic performance. Journal of Health Science and Medical Research. 2020; 38(3): 245-253.

36. Nomura S, Hirano Y, Takeuchi I, Shimizu H, Arai K. Anxiety, Depression, and Quality of Life in Parents of Adolescents with Inflammatory Bowel Disease: A Longitudinal Study. Pediatric Gastroenterology, Hepatology & Nutrition. 2023; 26(5): 239.