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Psychological Functioning of Children and Adolescents With Eosinophil-Associated Gastrointestinal Disorders

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Abstract

This study examined health-related quality of life and adjustment among children with eosinophil-associated gastrointestinal disorders (EGID) compared with an age-matched sample without acute or chronic illness. Participants were youth ages 2 to 18 years. Children and caregivers completed measures of psychological symptoms and health-related quality of life (HRQOL). Significant group differences were found for child report of depressive, as well as anxiety symptoms. Significant group differences were also found for caregiver report of psychological symptoms and social skills. Finally, based on parent and youth report, HRQOL and greater school absenteeism were associated with EGID diagnosis.

Children with chronic gastrointestinal disorders may experience recurrent abdominal pain, fatigue, poor growth, and interference with daily activities (Mackner, Crandall, & Szigethy, 2006). Not surprisingly, social and psychological functioning, as well as physical functioning may be impacted (Mackner et al., 2006; van der Zaag-Loonen, Grootenhuis, Last & Derkx, 2004). While recurrent, functional, abdominal pain is often associated with psychological distress and poorer overall adjustment (Szigethy et al., 2007), youth with organic disease are also vulnerable.

Children and adolescents diagnosed with inflammatory bowel disease (IBD), which includes Crohn's disease, ulcerative colitis, and indeterminate colitis, are at increased risk for mood

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and behavioral difficulties. Previous research suggests internalizing symptoms are common (see reviews by Hommel, Denson, & Crandall, 2008; Mackner, Sisson, & Crandall, 2004), with risk for depression and anxiety particularly high within the first two years of diagnosis (Burke et al., 1989). A subset of IBD patients also evidenced externalizing behavior problems, but it is less clear if these symptoms are significantly different from healthy controls (Engstrom, 1999; Mackner & Crandall, 2005).

Given the risk for adjustment difficulties, the health-related quality of life (HRQOL) of children diagnosed with IBD has received increasing attention. HRQOL encompasses physical, social, and emotional attitudes and behavior related to individuals' health status (Drotar et al., 1998). As such, HRQOL measures describe parent and self-perceptions of child functioning within specific, as well as overall domains of perceived functioning. Recent research indicates that children and adolescents diagnosed with IBD evidence significantly poorer health-related quality of life than medically healthy peers (Cunningham et al., 2007; Hommel et al., 2008), including increased school absenteeism and more days spent sick in bed rather than playing (Varni et al., 2006). While our understanding of IBD has improved significantly, other emerging inflammatory gastrointestinal conditions, such as eosinophil-associated gastrointestinal disorders (EGID), have been neglected in the psychological literature.

EGID represents an increasingly recognized series of inflammatory diseases present in the gastric tract. The diseases are defined by eosinophil-rich inflammation in the esophagus (eosinophilic esophagitis [EE]), stomach (eosinophilic gastritis [EG]), small intestine [eosinophilic enteritis]), large intestine (eosinophilic colitis [EC]), or multiple intestinal segments [eosinophilic gastroenteritis]). Similar to IBD, these conditions typically manifest in sometimes severe symptoms such as vomiting, abdominal pain, diarrhea, dysphagia, failure to thrive, and weight loss (Furuta et al., 2007; Kapel et al., 2008; Rothenburg, 2004; Sant'Anna, Rolland, Fournet, Yazbeck, & Drouin, 2004). Additionally, medical treatment regimens can be complex and burdensome.

EGID has only been recently described in the medical literature (Rothenburg, 2004; Sant'Anna et al., 2004) and little is known about the psychological impact on children and adolescents. Children and adolescents with EGID face significant challenges in coping with the extraordinary burdens of food hypersensitivity and treatments for these disorders. For example, treatment may require an elemental diet (liquid amino acid-based formulas). Such treatment is usually unpalatable and often requires placement of a feeding tube. Similar to IBD, children and adolescents with EGID may have unpredictable and frequent symptom flare-ups including pain and discomfort, which can limit their activities, cause high levels of psychological distress, and lower HRQOL (Engstrom, 1992; Marklund, Ahlstedt, & Nordstrom, 2004).

To our knowledge, no studies have documented the psychological adjustment and HRQOL of children and adolescents with EGID. Data concerning the psychological adjustment and the HRQOL experienced by children and adolescents with EGID are necessary in order to plan for the comprehensive medical and psychological management needs of this complex population. To address these important unmet scientific and clinical needs, we conducted what is to our knowledge the first comprehensive, controlled description of the psychological adjustment and HRQOL of children and adolescents with EGID. The primary hypothesis was that children and adolescents with EGID would demonstrate higher levels of psychological symptoms and lower levels of HRQOL than an age-matched sample of physically healthy children.

Methods

Study Population

This study was approved by the IRB in 2005 and data were collected over the span of one year. The primary recruitment source for participants with EGID was the Cincinnati Center for Eosinophilic Disorders (CCED) within Cincinnati Children's Hospital Medical Center (CCHMC). The study population and eligibility criteria included youth (ages 2.5 to 18 years) with EGID diagnosed by endoscopic biopsy and pathology review. Typically, EE was defined as >24 eosinophils/high power field (hpf). Other forms of EGID were diagnosed by significantly greater levels of normal eosinophils as defined previously (DeBrosse, Case, Putnam, Collins, & Rothenberg, 2006) as well as the presence of abnormal intestinal architecture (e.g. cryptitis; Rothenberg, 2004). Children diagnosed with mental retardation or another developmental disorder were excluded from recruitment. Fifty-three out of a potential eligible sample of 59 youth and their mothers completed the instruments. Six qualified patients were not included in the study as due to the following: 3 declined without stating a reason, 1 was reportedly too ill to participate, 1 was excluded due to having an EGID-related diagnosis ruled out, and 1 was excluded due to invalid responses to questionnaires.

A control group of healthy children was recruited from a CCHMC clinical trials database that included the names of children whose families volunteered to have their name listed to be involved with future research. Exclusionary criteria for controls included a history of a chronic illness or current acute illness. Children with EGID were matched with a control group child of the same gender and within 2 years of age. Age groups were represented as follows: 2-4 years old (EGID N= 11; Control N= 16), 5-7 years old (EGID N= 19; Control N= 14), 8-12 years old (EGID N= 14; Control N= 15), and 13-18 years old (EGID N= 9; Control N= 10). Fifty-five youth and their mothers participated as part of the control group.

Measures

A total of 108 mothers and children participated in this study after providing written informed consent and assent. Mothers completed all parent-report forms, while children and adolescents were administered age-appropriate versions of child-report measures. In some cases, age-appropriate child self-report measures were not available; N's are noted below. Participants completed questionnaires in a private room within CCHMC's Behavioral Medicine and Clinical Psychology division. All measures were selected because they have established reliability and validity in clinically relevant domains of psychological symptoms and HRQOL; all included domains were hypothesized to be affected by EGID and associated treatments:

Behavior Assessment System for Children – Parent and Teacher Report Scales (BASC-PRS/TRS)

—The BASC (Reynolds & Kamphaus, 1992) was used to describe children's psychological symptoms and has adequate reliability, as well as validity for both parent and teacher versions (Reynolds & Kamphaus, 1992). BASC-PRS are available for children between the ages of 2 and 21 (total N= 108). TRS forms are available regarding children ages 2-21 and were administered for participants currently attending school (i.e., not home schooled, on summer break, or too young to attend school; total N= 45).

Children's Depression Inventory (CDI)—Children's depressive symptoms were assessed by the CDI (Kovacs, 1999), a 27 item self-report inventory for children between the ages of 7-18 (EGID N= 31; Control N= 28). The CDI is a widely used self-report with high reliability and validity (Kovacs, 1999).

Multidimensional Anxiety Scale for Children (MASC) (March, Parker, Sullivan, Stallings, & Conners, 1997)—Children's anxiety symptoms were measured by the MASC, a 39 item self-report inventory for children between the ages of 8-19 (EGID N= 23; Control N= 25) that has excellent test-retest reliability and validity (March et al., 1997).

Pediatric Quality of Life Inventory (PEDS-QL)- Parent and Child Report Forms—The PEDS-QL (Varni, Seid, & Rode, 1999) is a widely used multidimensional approach for measuring HRQOL in healthy children and adolescents, as well as those with acute and chronic health conditions. The PEDS-QL has strong reliability and validity to distinguish between healthy children and children with acute or chronic health conditions (Varni et al., 1999). Child report forms are available for youth between the ages of 5 and 18 (EGID N= 42; Control N= 39) while parent report forms are available for youth 2-18 years old (EGID N= 53; Control N=55).

Statistical Analyses

Independent sample *t* tests were used to compare mean levels of psychological symptoms and HRQOL between children and adolescents diagnosed with EGID and controls. Chi-square analyses were used to compare the frequencies of children in the two groups who scored in the clinical range (i.e., T scores above 65) for psychological symptoms. Analyses of covariance were conducted to control for socioeconomic differences (maternal education and income) between the groups. Multivariate analyses of variance followed by post-hoc tests were conducted to identify differences in the frequencies of subgroups of children and adolescents with various EGID diagnoses whose scores were clinically significant.

Results

Description of Sample

Characteristics of participants are presented in Table 1. The majority of participants were male, Caucasian, lived with both parents, and had a mean age of 8.3 years (SD= 4.4 years). Group comparisons indicated that mothers of children and adolescents diagnosed with EGID reported lower levels of income ($p < .05$) and levels of education ($p < .02$) compared with the control group.

Within the EGID sample, the most frequent diagnoses were EE (N=20), EC (N=12) and eosinophilic enteritis (N=12). Patients were prescribed a variety of dietary regimens including an elemental diet (N=20).

Psychological Functioning

Parent and Teacher-reported Adjustment (BASC)—Table 2 summarizes analyses comparing EGID and the controls on measures of psychological symptoms. Parents of children and adolescents diagnosed with EGID reported higher frequencies of internalizing ($p < .001$) and externalizing symptoms ($p < .001$) on the BASC compared with controls. Children and adolescents with EGID were also rated by their parents as having less developed social skills than controls ($p < .001$). Teachers also perceived children and adolescents with a diagnosis of EGID as having more frequent internalizing symptoms ($p < .05$) compared with controls.

Based on parent report, a higher percentage of children and adolescents (45.3%) with EGID than controls (1.9%) demonstrated levels of internalizing symptoms in the clinical range. [χ^2 (1, N=107) = 31.52, $p < .001$]. A similar pattern was found for the Behavioral Symptom Index: Nearly one fourth (22.6%) of children and adolescents with EGID had scores in the clinical range compared with controls (0%) [χ^2 (1, N=108) = 14.01, $p < .001$]. Based on

teacher report, a higher percentage of children and adolescents with EGID had symptoms on the somatization scale in the clinical range (20%) compared with controls (0%) [χ^2 (1, $N=108$) = 7.77, $p < .001$].

Depressive Symptoms (CDI)—As shown in Table 3, children and adolescents with EGID reported greater overall depressive symptoms on the CDI compared to controls ($p < .01$) and more symptoms on three subscales than controls: anhedonia ($p < .001$), negative mood ($p < .01$), and negative self-esteem ($p < .001$).

Anxiety Symptoms (MASC)—Reports of total anxiety symptoms on the MASC were no different between the groups. However, differences were obtained on two MASC subscales: children and adolescents with EGID reported greater physical symptoms of anxiety ($p < .05$) as well as autonomic arousal ($p < .01$) than controls (see Table 3).

HRQOL (PedsQL)—As shown in Table 4, children and adolescents diagnosed with EGID evidenced lower HRQOL than controls based on both parent and youth reports. Parents also reported that children and adolescents with EGID missed significantly more school days in the past month (mean = 4.91 versus 0.5) ($p < .001$), as well as the past year (mean = 23.18 versus 2.83; $p < .001$) than the controls. Finally, children and adolescents diagnosed with EGID were more likely to have received mental health services ($N=25$ versus $N=8$; $p < .001$), as well as medication for mental health needs ($N=13$ versus $N=4$; $p < .05$) than the controls.

Analyses of covariance were conducted to determine whether differences between EGID and control groups remained after statistically controlling for differences in demographic factors (i.e., maternal education and family income). Following analysis, group differences in psychological symptoms and HRQOL did remain after controlling for maternal education and family income. Two exceptions were the BASC teacher report (adaptability scale) and the child and adolescent report of the MASC (tense/restless scale). Differences reported in the tables and text reflect scores adjusted by covariance analyses.

Discussion

To our knowledge, this is the first controlled study of psychological functioning and HRQOL among children and youth diagnosed with EGID. Results indicated poorer psychological adjustment in children and adolescents with EGID compared with a control group of participants without such disorders. In addition, the impact of EGID and associated treatments on children and adolescents extended well beyond psychological symptoms to affect daily functioning. Specifically, children and adolescents with EGID demonstrated significantly poorer adjustment in every domain of HRQOL, including greater school absenteeism in the past year (an average of 23 days missed) than healthy peers (three days). Further, the overall HRQOL scores of this group of children with EGID were lower than those reported by children with a wide range of chronic illnesses in previously published research (Varni, Limbers, & Burwinkle, 2007).

What may account for the observed differences in psychological symptoms and HRQOL? One potential factor is that the clinical course and medical treatment for EGID impose stressors and burden on children and families that may compromise their psychological adjustment and HRQOL. Children and adolescents with EGID and their parents can experience a high level of anxiety related to their current symptoms and uncertainty about whether and when future symptoms will occur (Rothenberg, 2004; Sant'Anna et al., 2004). The salient psychological burdens that are associated with severe food restriction and ongoing medical treatment for EGID may also contribute to the high level of psychological

distress associated with this condition. It is also possible that children with EGID develop physical symptoms because of increased levels of psychological distress, imparting a vicious cycle between physical and psychological symptoms.

Our findings indicate that children and adolescents with EGID are at risk for poor adjustment and may benefit from ongoing psychological support to enhance their HRQOL. While more children and adolescents with EGID in this study received mental health services and medication for mental health needs compared with controls, it should be noted that the majority had never received counseling or psychotropic medication. However, it was not possible to determine whether these community-based mental health services were targeted toward reduction of psychological distress directly associated with EGID-related symptoms and burdens of medical treatment.

Several limitations of the study should be considered in interpreting our findings: Because this was a cross-sectional study, it was not possible to determine the age of onset of psychological symptoms or whether the levels of psychological distress increased as a function of the duration of EGID. Furthermore, our data could not distinguish the impact of the primary disease from the associated medical therapy on psychological symptoms and HRQOL. Finally, our patient population may not be entirely representative of typical EGID (Guajardo et al., 2002). In particular, participants in the present study had a high rate of elemental formula utilization, which may have intensified the level of psychological symptoms experienced by children. Additionally, participants in this particular study reported a lower level of SES compared to their control counterparts, which may have impacted perceived HRQOL. Previous research indicates SES is often associated with health outcomes, including HRQOL, in childhood chronic illness (Hassan, Loar, Anderson, & Heptulla, 2006; Overstreet, Holmes, Dunlap, & Frentz, 1997). To our knowledge however, no information regarding the SES demographics of families coping with EGID has been published. For this reason, additional studies are needed to document the generalizability of the present findings to other samples of children and adolescents with EGID.

Implications for Practice

Children and adolescents with EGID may benefit from specific behavioral interventions that are designed to reduce anxiety about their condition and associated treatments (Varni et al., 2007). In particular, children with EGID may experience physiological arousal and further interpret it as a sign of anxiety. Interventions aimed at reducing cognitive and physiological symptoms of anxiety may be particularly useful to this population. In addition, anticipatory guidance for parents concerning EGID and its treatment may also be helpful in reducing the psychological impact of food hypersensitivity (Marklund, Ahlstedt, & Nordstrom, 2006) and level of illness-related uncertainty experienced by children and adolescents with EGID, which may increase risk for psychological maladjustment. Finally, standardized measures such as those used in the present study could be used to evaluate the impact of EGID on children's psychological well being over the course of their medical treatment (Drotar, 2004).

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Table 1
Participant Demographic Characteristics

	EGID	Control	
	N=53	N=55	<i>p</i> value
Child sex (% male)	76%	76%	.55
Child Ethnicity (% Caucasian)	94%	94%	.64
Child age (in years)	8.5 ± 4.2	8.2 ± 4.6	.70
2-4 years old	11	16	
5-7 years old	19	14	
8-12 years old	14	15	
13-18 years old	9	10	
Married parent status	81%	87%	.27
Parent education (in years)			
Mother	15.5	16.5	.02
Father	15.5	16.1	.26
Family income			
N ≤ \$75,000	21	16	.04
N over \$75,000	29	39	
Disease Type			
EE	20		
EC	12		
Eosinophilic enteritis	12		
EG	10		
Eosinophilic duodenitis	9		
Eosinophilic gastroenteritis	3		

Table 2
General Psychological Symptom Scores: Parent and Teacher Report

	EGID		Control		p value
	M (SD)	N	M (SD)	N	
BASC-Parent report					
Internalizing problems					
Composite	67 (12)	55	44 (8)	53	.00
Externalizing problems					
Composite	54 (10)	54	46 (8)	53	.00
Behavioral symptoms					
Index	58 (14)	55	45 (8)	53	.00
Adaptive skills					
Composite	46 (11)	55	54 (8)	53 19	.00
BASC-Teacher report					
Internalizing problems					
Composite	54 (11)	25	47 (6)		.05
Externalizing problems					
Composite	48 (8)	26	50 (9)	18	.62
Behavioral symptoms					
Index	49 (11)	25	50 (10)	19	.85
Adaptive skills					
Composite	52 (10)	26	51 (10)	18	.71
School problems					
Composite	52 (13)	22	50 (12)	14	.67

* all scores represent standard T scores

Table 3

Symptoms of Anxiety and Depression: Youth Report

	EGID		Control		p value
	M (SD)	N	M (SD)	N	
Depressive Symptoms (CDI)					
Total Score	49 (9)	31	41 (10)	28	.01
Negative Mood	51 (11)	31	45 (8)	28	.01
Interpersonal problems	46 (6)	31	44 (9)	28	.21
Ineffectiveness	47 (8)	31	45 (7)	28	.39
Anhedonia	53 (11)	31	42 (5)	28	.00
Negative self-esteem	46 (6)	31	45 (8)	28	.00
Anxiety Symptoms (MASC)					
Total Score	51 (11)	23	48 (10)	24	.48
Physical symptoms	51 (10)	23	45 (8)	24	.05
Harm avoidance	48 (11)	23	50 (13)	24	.49
Social Anxiety	49 (11)	23	50 (11)	24	.68
Tense/Restless	49 (10)	23	47 (8)	24	.53
Somatic/Autonomic	52 (9)	23	43 (8)	24	.01
Perfectionism	48 (12)	23	50 (12)	24	.74
Anxious coping	47 (12)	23	51 (13)	24	.34
Humiliation/Rejection	48 (11)	23	52 (11)	24	.28
Performing in public	50 (11)	23	48 (10)	24	.63
Separation Panic	55 (12)	23	52 (9)	24	.24

* all scores represent standard T scores

Table 4

HRQOL Scores: Parent and Youth Report

	EGID		Control		p value
	M (SD)	N	M (SD)	N	
PedsQL-Parent report					
Total score	62 (16)	53	87 (11)	55	.00
Physical subscale score	66 (20)	53	90 (15)	55	.00
Emotion subscale score	56 (19)	53	81 (12)	55	.00
Social subscale score	70 (20)	53	89 (13)	55	.00
School subscale score	52 (22)	47	85 (16)	50	.00
Psychosocial subscale score	60 (17)	53	85 (11)	55	.00
PedsQL-Youth report					
Total score	67 (13)	42	81 (10)	39	.00
Physical subscale score	72 (17)	42	87 (10)	39	.00
Emotion subscale score	64 (17)	42	76 (17)	39	.01
Social subscale score	72 (23)	42	81 (17)	39	.05
School subscale score	58 (21)	42	78 (14)	39	.00