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Evaluation of psychiatric symptomatology, quality of life, and caregiver burden in mothers and children with primary immunodeficiency

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KEYWORDS
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Abstract
Background: The present study aimed to evaluate the quality of life, depression, and anxiety scores of children with primary immunodeficiency (PID) and depression, anxiety scores, and the caregiving burden of their mothers.
Methods: A total of 149 children aged 2-18 years and their mothers were included in the present study, along with 125 healthy children and their mothers as a control group. The Pediatric Quality of Life Inventory (PedsQL), Child Depression Inventory (CDI), and Screening for Child Anxiety-Related Emotional Disorders (SCARED) questionnaire were used based on the views of children and their mothers. The Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Temperament Evaluation of Memphis, Pisa, Paris, San Diego Autoquestionnaire (TEMPS-A), and Zarit Caregiver Burden Scale (ZCB) were used for the mothers.
Results: According to children and their mothers, the scores of the PedsQL were lower than that of the control group ($P < 0.05$). In addition, according to the views of children and mothers, we found that PID children had higher depression and anxiety scores than healthy children ($P < 0.05$). The depression and anxiety levels of mothers in the patient group were also significantly higher than those in the control group ($P = 0.05$ and $P = 0.001$).
Conclusion: Statistically, we found significantly lower psychosocial health summary scores and total scale score levels from the subclass of PedsQL in the patient group than in the control group. According to the views of both children and mothers, we observed that PID children had higher depression and anxiety scores than healthy children. It was also found that the BDI and BAI values in case of mothers in the patient group were significantly higher than those in the control group.

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Introduction

Primary immunodeficiencies (PIDs) are rare congenital diseases occurring due to defects in one or more components of the immune system. PIDs are characterized by recurrent and/or severe infections, and cause serious morbidity and mortality.[1] For this reason, PIDs could affect all aspects of lives of children and their families to varying degrees.[2-10] The life expectancy of these children has been prolonged with the early diagnosis of PIDs, the early initiation of treatment, and reduced frequency of infections. Owing to the prolongation of life expectancy, children and their families are exposed to the psychosocial effects of chronic diseases for a longer period.[2,7,8,11] Having a child with a chronic disease disrupts the normal daily routine of the caregiver family, causing interruption in work and social life.[12] Clinical manifestations of anxiety and depression may also occur in children with chronic diseases. Children and adolescents with depression may experience clinical manifestations such as loss of interest in activities they normally enjoy, indecisiveness, attention and concentration problems, difficulty in participating in school and daily activities, and loss of self-care.[8,11]

A family member taking care of a child with a chronic disease is employed to meet the medical, physical, psychological, and developmental needs of the child as well as the family. The burden of caregiving is a multidimensional task and observed in the physical, psychological, financial, and social aspects of live of a caregiver as a process in which positive emotions, such as personal success and development, and negative emotions, such as helplessness, guilt, and anger, are experienced.[13,14]

The present study aimed to evaluate the quality of life, depression, and anxiety of PID children and the depression, anxiety, and caregiving burdens of their mothers.

Materials and Methods

Participants

The study included 149 patients as well as their mothers, aged 2–18 years who were diagnosed with PID and receiving intravenous or subcutaneous immunoglobulin treatment in the Pediatric Allergy Immunology Clinic of the University Medical Faculty Hospital. A control group comprised 125 healthy children of the same age group as that of the above-mentioned patient group as well as their mothers. Children with mental and motor dysfunctions, syndromic changes, autism, and psychotic disorders were not included in the study. Among the patients with PID, 140 were receiving intravenous treatment, and nine were receiving subcutaneous immunoglobulin treatment. In our clinic, patients with suspected immunodeficiency were diagnosed and classified according to the criteria of the International Union of Immunological Societies (IUIS) and the European Society for Immunodeficiencies (ESID).[1,15] The study was approved by the Ethics Committee of Medical School of Fırat University; written informed consent was obtained from the parents of all children enrolled in the study.

Questionnaires

Pediatric Quality of Life (PedsQL) Inventory

The PedsQL Inventory was developed in 1999 by Varni et al.[16] The reliability and validity of the scale was conducted for Turkish studies.[17,18] The PedsQL scores were given as Total Scale Score (TSS), Physical Health Summary Score (PSS), and Psychosocial Health Summary Score (PsychoSS). The higher the subscale scores, the higher the quality of life.

Child Depression Inventory (CDI)

The CDI was developed by Kovacs based on the Beck Depression Inventory (BDI).[19] The reliability and validity of the scale was conducted for Turkish studies.[20] The scale included questions about childhood depression-specific areas, such as school status and friendships. The highest score that could be obtained from the scale is 54, and the cut-off point is 19. The higher the score, the more severe the depression.

Screening for Child Anxiety-Related Emotional Disorders (SCARED) Questionnaire

Birmaher et al. developed this scale to screen for childhood anxiety disorders.[21] The reliability and validity of the scale was conducted for Turkish studies.[22] The scale has two forms: the first for parents and the other for children. A score of 25 or above, which consists of a total of 41 items, is considered a warning for anxiety disorders.

Beck Depression Inventory (BDI)

The BDI scale was developed by Beck et al.[23] It measures emotional, cognitive, and motivational symptoms of depression. The cut-off point of 17 was accepted for Turkish validity and reliability studies.[24]

Beck Anxiety Inventory (BAI)

Beck et al.[25] developed BAI in 1988. It is used to determine the frequency of anxiety symptoms experienced by individuals. The reliability and validity of the scale was conducted for Turkish studies.[26] The scale consists of 21 items and is scored between 0 and 3.

Temperament Evaluation of Memphis, Pisa, Paris, San Diego Autoquestionaire (TEMPS-A)

The TEMPS-A Temperament Scale was developed by Akiskal et al. and was designed to evaluate the dominant affective temperament in an individual.[27] The reliability and validity of the scale was conducted for Turkish studies.[28] The Turkish version of the scale consists of 99 items and aims to determine depressive, hyperthymic, irritable, cyclothymic, and anxious temperaments.

Zarit Caregiver Burden (ZCB) Scale

Zarit et al. developed the scale in 1980 to evaluate the stress experienced by caregivers of individuals in need of care.[29] The reliability and validity of the scale was conducted for Turkish studies.[30] The scale includes mental tension and disruption in private life, limitations and restrictions in social life, deterioration in social relations, economic burden, and dependency.

Statistical Analysis

Statistical analysis was performed using SPSS version 22.0 (IBM, Armonk, NY, USA). Percentage values and frequencies were calculated for qualitative variables, and the data were expressed as median (interquartile range: 25th and 75th percentiles) for quantitative variables. The Independent Group *t*-test was used for comparisons between groups. The Mann - Whitney U Test was used when non-parametric conditions were met; ANOVA was used for comparison between more than two groups. The Kruskal - Wallis test was used when non-parametric conditions were met, and the Chi-square test was used for comparisons of ratios between groups. $P < 0.05$ was considered as statistically significant.

Results

A total of 149 children diagnosed with PID (patient group) and 125 healthy children (control group) were included in the study. No differences were observed between patient and control groups in terms of mean age and gender distribution ($P > 0.05$). When socioeconomic status was evaluated, a statistical difference was observed between patient and control groups in terms of education and income levels, and occupation status of their mothers ($P < 0.05$; Table 1).

The parents of six subjects (4%) in the patient group and three subjects (2.4%) in the control group were divorced. All the children lived with their mothers. Fathers of three patients (2%) in the patient group and one (0.8%) child in the control group had died. Thirteen mothers in the patient group and nine mothers in the control group had chronic diseases such as asthma, eczema, diabetes, hypertension. In addition, six mothers in the patient group and four mothers in the control group had psychiatric illnesses such as depression and panic disorder. However, no statistically significant differences were discovered between the groups in terms of these characteristics ($P > 0.05$). Age at the onset of ailments in children with PID was 18 (8.5–48) months, and the follow-up period was 36 (18–72) months. In addition, 23 (15.4%) patients with PID had additional chronic diseases (e.g., asthma, rhinitis, atopic dermatitis, familial Mediterranean fever, and bronchiectasis; Table 2).

According to the views expressed by children, statistically, PsychoSS and TSS levels were significantly lower in the patient group than in the control group ($P < 0.05$); however, no statistically significant differences were discovered between the control and patient groups in terms of PSS levels ($P > 0.05$; Table 3). In patients with PID, according to the views of children, a positive correlation was noticed between PSS and the follow-up period of patients, and the number of annual hospitalizations (Table 4). According to the views of mothers, statistically lower PSS, PsychoSS, and TSS levels were observed in the patient group, compared to

Table 1 Sociodemographic characteristics of participants and their mothers.

Characteristics	Children with PID (n = 149)	Healthy children (n = 125)	P-value
Children's age (years)	9 (6-13)†	9 (7-10)	0.65
Children's gender, n (%)			
Boys	93 (63.1)	66 (52.8)	0.08
Girls	55 (36.9)	59 (47.2)	
Number of children in the family	2 (2-3)	2 (2-3)	0.01
Number of individuals in family	4 (4-5)	4 (4-5)	0.47
Mother's educational status, n (%)			
Elementary school	62 (41.6)	30 (24.0)	0.0001
Middle school	21 (14.1)	5 (4.0)	
High school	47 (31.5)	38 (30.4)	
University	19 (12.8)	52 (41.6)	
Mother's occupation, n (%)			
Housewife	138 (92.6)	57 (45.6)	0.0001
Self-employment	7 (4.7)	8 (6.4)	
Officer	4 (2.7)	60 (48)	
Family's monthly income, n (%)			
<$300	10 (6.7)	31 (24.8)	0.0001
$ 300 - 450	19 (12.8)	13 (10.4)	
$ 450 - 650	72 (48.3)	17 (13.6)	
$ 650 - 750	24 (16.1)	21 (16.8)	
>$750	24 (16.1)	43 (34.4)	

†Median (interquartile range): 25th and 75th percentiles.

Table 2 Basic clinical characteristics of children with primary immunodeficiency.

Characteristics	Number	Percent (%)
Classification of primary immunodeficiencies		
Unclassified antibody deficiency	56	37.6
Common variable immunodeficiency	44	29.5
Immunoglobulin G subgroup deficiency	14	9.4
Ataxia telangiectasia disease	9	6
Transient hypogammaglobulinemia of infant	5	3.4
Selective IgM deficiency	5	3.4
Combined immunodeficiency	5	3.4
X-Linked Agammaglobulinemia	4	2.7
Severe combined immunodeficiency	4	2.7
Partial DiGeorge syndrome	2	1.3
NFKB1 mutation	1	0.7
Other diseases in children		
Yes	23	15.4
No	126	84.6
Annual number of infections in children	8 (3 - 13.5)†	
Annual number of children hospitalization‡	2 (0 - 3) †	
Child's age at onset of complaints due to immunodeficiency (months)	18 (8.5 - 48)†	
Follow-up period of child due to immunodeficiency (months)	36 (18 - 72)†	

†Median (interquartile range): 25th and 75th percentiles.
‡Hospitalizations for immunoglobulin therapy of patients are not included.

Table 3 Comparison of children's quality of life, depression, and anxiety according to the views expressed by children and their mothers in both groups.

Characteristics	Number	Median (25th and 75th percentiles)	P-value
PSS-C†			
Patient group	130‡	75 (65-80)	0.058
Control group	117	80 (70-85)	
PsychoSS-C†			
Patient group	130‡	75 (68.75-82.03)	0.001
Control group	117	78.12 (71.80-84.37)	
TSS-C†			
Patient group	130‡	75 (68.75-81.25)	0.002
Control group	117	81.25 (73.40-87.50)	
CDI-C			
Patient group	105§	9 (7-12.5)	0.0001
Control group	118	7 (5-11)	
SCARED-C			
Patient group	101*	26 (18-35)	0,001
Control group	109	20 (15-29)	
PSS-M†			
Patient group	149‡	75 (68.75-84.37)	0.001
Control group	125	81.25 (73.40-87.50)	
PsychoSS-M†			
Patient group	149‡	70 (65-80)	0.0001
Control group	125	80 (70-85)	
TSS-M†			
Patient group	149‡	78.12 (68.75-81.25)	0.0001
Control group	125	81.25 (73.40-90.62)	
CDI-M			
Patient group	105§	9 (7-11.5)	0.0001
Control group	118	6 (5-11)	
SCARED-M			
Patient group	101*	25 (20-38)	0.002
Control group	109	21 (16-31)	

Median (25th and 75th percentiles): Median (interquartile range): 25th and 75th percentiles.
†Scores of Pediatric Quality of Life Inventory are given as total scale score (TSS), physical health summary score (PSS), and psychosocial health summary score (PsychoSS).
‡Health-related quality of life-child form was completed for children aged >5 years
§Child depression inventory was completed for children aged ≥7 years
*Screening for child anxiety-related emotional disorders questionnaire was completed for children aged ≥ 8 years
PSS-C: Physical health summary score - child form, **PSS-M:** Physical health summary score - mother form, **PsychoSS-C:** Psychosocial health summary score - child form, **PsychoSS-M:** Psychosocial health summary score - mother form, **TSS-C:** Total scale score of pediatric quality of life inventory - child form, **TSS-M:** Total scale score of pediatric quality of life inventory - mother form. **CDI-C:** Child depression inventory - child form, **CDI-M:** Child depression inventory - mother form, **SCARED-C:** Screening for child anxiety-related emotional disorders questionnaire - child form, **SCARED-M:** Screening for child anxiety-related emotional disorders questionnaire - mother form.

the control group ($P < 0.05$; Table 3). In patients with PID, a positive correlation was discovered between PsychoSS and the number of children in family, the number of individuals in family, and the follow-up period of patients. According to mothers, a negative correlation was discovered between the ages of onset of ailments. However, according to the mothers of PID patients, a positive correlation was observed between PSS and the number of children in the family, the number of individuals in the family, and the number of annual hospitalizations. However, a negative correlation was observed between the age of onset of ailments and the number of children in the family, the number of individuals in the family, and the number of annual hospitalizations. In addition, a positive correlation was observed between TSS and the number of children in family and the number of individuals in family (Table 4).

According to the views of children and their mothers, children with PID had higher depression and anxiety scores than healthy children (Table 3), and no correlation was observed between child depression scores and the number of children in the family, the number of individuals in the family, the age of onset of ailments, patient's follow-up period, and annual number of infections and hospitalizations (Table 4). However, according to the views expressed by mothers of patients with PID, a positive correlation was existed between the child anxiety scores and

Table 4 Correlation between child anxiety and depression, pediatric quality of life inventory, and demographic characteristics according to the views expressed by children and their mothers in the patient group.

Characteristics	CDI-C	SCARED-C	CDI-M	SCARED-M	PSS-C	PsychoSS-C	TSS-C	PSS-M	PsychoSS-M	TSS-M
Child's age at onset of complaints	r = -0.04 P = 0.6	r = -0.3 P = 0.1	r = -0.04 P = 0.6	r = 0.01 P = 0.8	r = -0.01 P = 0.8	r = -0.1 P = 0.2	r = 0.1 P = 0.1	r = -0.4 P = 0.04	r = -0.2 P = 0.01	r = 0.02 P = 0.7
Follow-up period in child clinic	r = -0.05 P = 0.6	r = 0.03 P = 0.4	r = -0.02 P = 0.8	r = 0.1 P = 0.02	r = 0.1 P = 0.04	r = 0.04 P = 0.6	r = 0.05 P = 0.5	r = 0.1 P = 0.1	r = 0.1 P = 0.03	r = 0.07 P = 0.3
Annual number of infections in children	r = 0.04 P = 0.6	r = 0.07 P = 0.3	r = 0.07 P = 0.4	r = 0.2 P = 0.06	r = 0.05 P = 0.5	r = -0.1 P = 0.08	r = -0.04 P = 0.6	r = 0.1 P = 0.1	r = 0.1 P = 0.054	r = -0.03 P = 0.6
Annual number of hospitalizations in children	r = 0.05 P = 0.6	r = 0.04 P = 0.6	r = 0.08 P = 0.3	r = 0.1 P = 0.04	r = 0.1 P = 0.03	r = -0.1 P = 0.2	r = 0.06 P = 0.4	r = 0.2 P = 0.004	r = -0.1 P = 0.07	r = -0.09 P = 0.2
Number of children in the family	r = -0.09 P = 0.3	r = -0.1 P = 0.07	r = 0.03 P = 0.7	r = 0.09 P = 0.2	r = -0.01 P = 0.8	0.005 0.9	r = 0.04 P = 0.6	r = 0.1 P = 0.03	r = 0.2 P = 0.0001	r = 0.1 P = 0.02
Number of individuals in family	r = -0.06 P = 0.4	r = -0.04 P = 0.6	r = 0.02 P = 0.7	r = 0.04 P = 0.6	r = 0.1 P = 0.2	r = -0.006 P = 0.9	r = 0.1 P = 0.1	r = 0.1 P = 0.03	r = 0.2 P = 0.003	r = 0.2 P = 0.0001
PSS-C	r = -0.01 P = 0.8	r = -0.02 P = 0.7	r = -0.01 P = 0.9	r = -0.01 P = 0.9	--	--	--	r = 0.6 P = 0.8	r = -0.1 P = 0.08	r- = 0.07 P = 0.4
PsychoSS-C	r = -0.01 P = 0.8	r = 0.03 P = 0.7	r = 0.001 P = 0.9	r = 0.03 P = 0.6	--	--	--	r = -0.1 P = 0.1	r = -0.1 P = 0.06	r = 0.01 P = 0.8
TSS-C	r = 0.1 P = 0.07	r = 0.1 P = 0.08	r = 0.07 P = 0.4	r = 0.02 P = 0.1	--	--	--	r = -0.01 P = 0.8	r = 0.1 P = 0.03	r = 0.06 P = 0.4
PSS-M	r = 0.1 P = 0.08	r = 0.5 P = 0.06	r = -0.01 P = 0.9	r = 0.1 P = 0.08	r = 0.01 P = 0.8	r = -0.1 P = 0.1	r = -0.01 P = 0.8	--	--	--
PsychoSS-M	r = -0.02 P = 0.7	r = 0.03 P = 0.4	r = 0.001 P = 0.9	r = 0.01 P = 0.8	r = -0.1 P = 0.08	r = -0.1 P = 0.06	r = 0.1 P = 0.03	--	--	--
TSS-M	r = 0.2 P = 0.08	r = 0.02 P = 0.3	r = 0.07 P = 0.4	r = 0.05 P = 0.3	r = -0.07 P = 0.4	r = 0.01 P = 0.8	r = 0.06 P = 0.4	--	--	--

PSS-C: Physical health summary score-child form, **PSS-M:** Physical health summary score - mother form, **PsychoSS-C:** Psychosocial health summary score - child form, **PsychoSS-M:** Psychosocial health summary score - mother form, **TSS-C:** Total scale score of pediatric quality of life inventory - child form, **TSS-M:** Total scale score of pediatric quality of life inventory - mother form. **CDI-C:** Child depression inventory - child form, **CDI-M:** Child depression inventory- mother form, **SCARED-C:** Screening for child anxiety-related emotional disorders questionnaire - child form, **SCARED-M:** Screening for child anxiety-related emotional disorders questionnaire - mother form.

Table 5 Correlation between depression, anxiety, temperament, and caregiving burden of mothers and depression, anxiety, and demographic characteristics of children in the patient group.

Characteristics	BDI	BAI
Child's age of onset of ailments	r = 0.07 P = 0.3	r = 0.07 P = 0.3
Follow-up period of patient in the clinic	r = 0.07 P = 0.3	r = 0.1 P = 0.04
Annual number of infections in children	r = 0.01 P = 0.8	r = 0.1 P = 0.1
Annual number of hospitalization in children	r = 0.1 P = 0.1	r = 0.1 P = 0.01
Number of children in the family	r = -0.02 P = 0.7	r = 0.03 P = 0.7
Number of individuals in family	r = -0.08 P = 0.3	r = -0.06 P = 0.4
CDI-C	r = -0.03 P = 0.7	r = -0.07 P = 0.4
CDI-M	r = 0.1 P = 0.08	r = 0.003 P = 0.9
SCARED-C	r = 0.01 P = 0.6	r = 0.09 P = 0.2
SCARED-M	r = 0.05 P = 0.4	r = 0.02 P = 0.7
Depressive temperament	r = 0.4 P = 0.0001	r = 0.2 P = 0.0001
Cyclothymic temperament	r = 0.5 P = 0.0001	r = 0.4 P = 0.0001
Hyperthymic temperament	r = -0.1 P = 0.03	r = -0.1 P = 0.07
Irritable temperament	r = 0.1 P = 0.04	r = 0.2 P = 0.004
Anxious temperament	r = 0.5 P = 0.0001	r = 0.4 P = 0.0001
Zarit caregiver burden scale	r = -0.05 P = 0.5	r = -0.2 P = 0.08

BDI: Beck depression inventory, **BAI:** Beck anxiety inventory, **CDI-M:** Child depression inventory - mother form, **CDI-C:** Child depression inventory - child form, **SCARED-M:** Screening for child anxiety - related emotional disorders questionnaire - mother form, **SCARED-C:** Screening for child anxiety-related emotional disorders questionnaire - child form.

the patient's follow-up period in the clinic and the number of annual hospitalizations (Table 4).

The BDI and BAI values of mothers in the patient group were also significantly higher than those of the control group (P = 0.05 and P = 0.001). In case of mothers of children with PID, a positive correlation was observed between BAI scores, patient's clinical follow-up, and the number of annual hospitalizations (Table 5). In addition, when the temperament characteristics of mothers in the patient and control groups were compared, a statistical difference observed in terms of depressive temperament, hyperthymic temperament, and anxious temperament. It was also observed that depressive and anxious temperament characteristics were higher in the patient group than in the control group (P < 0.05; Table 6). In addition, a positive correlation was observed between depression and anxiety levels of mothers of the children with PID and depressive, cyclothymic, irritable, and anxious temperament characteristics (Table 5).

No statistical differences were observed between the patient and control groups in terms of caregiving burden scores (P > 0.05; Table 4). However, although 32.2% of mothers in the patient group perceived a moderate - heavy care burden, so did 22.4% of mothers in the control group (Table 5).

Table 6 Comparison of depression, anxiety, temperament types and caregiving burdens of mothers in both groups.

Characteristics	Number	Median (25th and 75th percentiles)	P-value
Beck depression inventory			
Patient group	149	6 (1-12.5)	0.05
Control group	125	4 (2-7)	
Beck anxiety inventory			
Patient group	149	5 (2-12.75)	0.001
Control group	125	3 (0-6)	
Depressive temperament			
Patient group	149	5 (3-7)	0.04
Control group	125	4 (2-7)	
Cyclothymic temperament			
Patient group	149	5 (2.5-7)	0.06
Control group	125	5 (4-10)	
Hyperthymic temperament			
Patient group	149	8 (5-11)	0.009
Control group	125	9 (8-11)	
Irritable temperament			
Patient group	149	2 (0.5-4.5)	0.08
Control group	125	1 (0-4)	
Anxious temperament			
Patient group	149	5 (3-7)	0.01
Control group	125	4 (2-6)	
Zarit caregiver burden scale			
Patient group	149	41 (33.5-49)	0.8
Control group	125	40 (35-49)	

Median (25th and 75th): Median (interquartile range = 25th and 75th percentiles).

Discussion

Primary immunodeficiencies are chronic diseases with an early onset in life and require constant care, treatment, and close monitoring. PIDs affect all aspects of life of children and their families at various levels.[2,3,5,7,9,31] Past studies reported that PID children have significantly lower levels of health-related quality of life, compared to healthy children.[2-10,31] Kuburovic et al. showed that the health-related quality of life of PID children was lower, compared to the control group, according to the views expressed by both children and their parents.[2] It was observed that children with significant anxiety symptoms but not depression had significantly lower quality of life. The authors also found that the health-related quality of life of PID children was significantly lower than that of children with juvenile idiopathic arthritis (JIA). Similarly, a meta-analysis reported that patients with PID had lower health-related quality of life, compared to healthy individuals and patients with other chronic diseases, such as diabetes mellitus and JIA.[3] Berg et al. demonstrated that children with PID had a lower health-related quality of life, compared to healthy children and children with acute lymphoblastic leukemia in remission.[8] Titman et al. reported that according to children and parents, PID children had lower quality of life not only than healthy children but also than children with diabetes.[7] In addition, Zebracki et al. comparing PID children with the control group, reported that PSS and PsychoSS levels were significantly lower, as viewed by parents.[31] However, the authors found no difference in terms of quality of life between patients with PID and children with JIA.

According to the views of mothers in the present study, PSS, PsychoSS, and TSS levels were found to be worse in children with PID than in healthy children. In addition, according to the views of PID children, worse quality of life scores were found in the PsychoSS and TSS subgroups. There was a positive correlation between the PSS according to children's statements and the follow-up period of patients and the number of annual hospitalizations in the patient group. According to mother's statements, a negative correlation was observed between PSS and PsychoSS and the age of onset of ailments in the patient group. In the present study, no relationship was observed between depression and anxiety levels and the quality of life of PID children. However, Kuburovic et al. reported a negative correlation between anxiety levels and the quality of life of PID children, but the same relationship was not observed in depression levels.[2] Our study results established that PID children experienced physical, social, psychological, and environmental problems that negatively affect their quality of life during treatment and follow-up of the disease. We believe that the results obtained in the present study could be used for different purposes, such as choosing appropriate treatments and interventions for patients, planning new health policies for countries, and increasing the productivity of patients and their relatives. Fasshauer et al. reported that a psychosocial training program applied for 6 months in adult PID patients significantly improved their health-related quality of life.[32]

It has been reported that increased proportion of anxiety and depression in children with chronic diseases play a critical role in the emergence of negative consequences

in many areas such as medical, psychosocial, adaptation to disease, quality of life, school performance, and transition to adulthood.[2,7,8,11] Lewis and Vitulano reported that children with chronic diseases are three to four times more at risk of having mental problems than their peers without chronic diseases.[33] Kuburovic et al. determined that according to their parents, PID children demonstrated signs of anxiety (25%) and significant depression (20%).[2] Significant anxiety manifestations in PID children were approximately two to three times more frequent than in children with JIA or their healthy peers. Berg et al. reported that PID children experienced more mental and psychosocial problems, compared to healthy children.[8] Similarly, Titman et al. found that PID children experienced a higher proportion of psychological difficulties, compared to healthy children.[7] Another study reported that according to parents, PID children had a higher range of psychosocial impairments, such as depression, anxiety, somatization, social withdrawal, and inadequacy of social skills, compared to children with asthma.[11]

In the present study, according to both children and their mothers, the depression and anxiety scores of PID children were found to be significantly higher than those of the control group. Unlike adult depression, children might exhibit more restless emotions than sad affection. Children with poor impulse control in particular may exhibit tantrums and aggressive behaviors.[34] Also, according to the mothers of PID children, a positive correlation was observed between the child anxiety scores, patient's follow-up period, and the number of annual hospitalizations. In light of these results, we believe that depressive manifestations in PID children are related to the primary disease. The duration and severity of the disease do not affect their depression levels, but anxiety increases with increase in the duration and severity of the disease. Kuburovic et al. reported that anxiety symptoms are more common than depressive symptoms in children with PID.[2] The authors explained this by hypothesizing that the development of anxiety symptoms, rather than depressive symptoms, in children could be a more common response to a chronic disease, anxiety symptoms may be undesirable adverse reactions of specific treatment, and PID itself might be at greater risk of developing anxiety than depressive psychopathology by its nature.

Many studies have reported that parents of children having chronic diseases are diagnosed with depression and anxiety disorders more frequently than parents of children without chronic diseases.[8,11,12] Berg et al. used the General Health Questionnaire (GHQ-30) to identify minor psychiatric disorders experienced by parents with PID and reported that mothers of PID children had worse mental health than mothers of healthy children.[8] In the present study, the mothers of PID children had higher depression and anxiety levels than the mothers of healthy children. A positive correlation was observed between BAI scores and patient's clinical follow-up and the number of annual hospitalizations in case of mothers of PID children. Parents, especially mothers of PID children, are at risk of developing psychological disorders, such as depression and anxiety, because of having a sick child, caring for a sick child, restriction of social life and daily activities, and economic difficulties. However, we believe that educational and psychological support programs for families during the treatment and follow-up of their PID children would reduce the frequency of depression and anxiety in parents and provide a significant improvement in their quality of life. In the present study, comparison of mothers of PID children to mothers of the control group showed that depressive temperament and anxious temperament characteristics were higher in mothers of PID children. Previous studies have reported that temperamental characteristics are the basis of mood disorders and that dominant temperamental characteristics of an individual predispose to mood disorders.[35,36] Mothers of PID children with certain temperamental characteristics could be used as a precursor of psychological reactions they might show and psychiatric diseases that might develop.

Caring for a sick child brings with it negativities for families, such as restriction of social life and daily activities, difficulties in family and marital relations, economic difficulties, and not being able to spare enough time for other family members.[13,14] Studies on the burden of caregiving in the pediatric population are very limited. In general, mothers are the primary caregivers of children with chronic diseases, and it can be considered that they are the most affected lot. In the present study, no difference was observed in terms of the burden of caregiving between the patient and control groups, and no correlation was discovered between depression and anxiety levels of mothers of PID children and caregiving burden. However, although more mothers in the patient group (32.2%) perceived a moderate to heavy burden of caregiving, 22.4% of mothers in the control group also realized the same burden. In line with these results, we think, it would be beneficial to use measurement tools that define a caregiver and reveal support factors to avert early burnout because of caregiving.

Strengths and Limitations

The effect of psychiatric symptomatology, quality of life, caregiving burden, and associated socio-demographic variables in both PID children and their parents is an area that has not been investigated adequately. We think that the presence of patient and control groups, diversity in the number of scales used, and validity and reliability of these scales in Turkish setup in the present study are the positive aspects of our study. Nevertheless, the Turkish validity and reliability of the Child Depression Inventory and the SCARED Questionnaire was done as a thesis; these studies were not published as a research article. This could be considered as a limitation.

In addition, although reliability of the children's quality of life anxiety and depression scales was increased by having both parents and children fill in the scales, inability to use structured interview techniques, presence of individual perceptions and differences, and lack of data, such as knowledge levels of parents about the disease, could be listed as general limitations of the study. In addition, lack of some objective burden variables (e.g., distance from the treatment center, social support of caregiver, assistant caregivers, and sleep pattern and quality) could be listed as another limitation. Finally, it could be possible that all PID patients were underrepresented in the present

study because most patients were in the humoral immunodeficiency group and consisted of children receiving only immunoglobulin treatment.

Conclusion

According to mothers all subgroups of quality of life in PID children were found to be lower, compared to the control group; according to children other subgroups of quality of life (except for PSS) were lower, compared to the control group. In addition, although not at the level of clinical diagnosis, children and mothers were more depressed and anxious in the patient group. In conclusion, in our opinion, to develop a multidisciplinary approach toward PID children, it would be appropriate to inform the family about the medical aspects of child's disease as well as about difficulties of care and the psychosocial disorders that develop over time.

Author Contributions

The authors confirm their contribution to the paper as follows: study conception and design: NK, SK, MK; data collection: NK, SK; analysis and interpretation of results: NK, SK, GT, FÖ, MK; draft manuscript preparation: NK, SK, GT, FÖ. All authors reviewed the results and approved the final version of the manuscript.

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