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Life quality, depression, and anxiety levels in parents of children with primary immunodeficiency

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Abstract

Background: Primary immune deficiencies (PID) encompasses genetic disorders that result in recurrent infections and immune dysregulation, often increasing the risk of malignancies. The aim of this study is to determine the quality of life, depression, and anxiety in parents of children with PID.

Methods: Various validated assessment tools, including the Beck Depression Inventory (BDI), State and Trait Anxiety Inventory (STAI), the 36-item Short Form Survey (SF-36), and a demographic form, were employed to gather data from 85 parents of 64 PID patients and 85 parents of 75 healthy children.

Results: The findings reveal that parents of PID patients exhibited higher BDI, STAI-S, STAI-T, and fatigue subdomain of SF-36 ($p = .013$, $p = .013$, $p = .027$, $p = .000$). Both parents had lower energy levels than the normal population, but mothers experienced higher levels of anxiety and depression. PID mothers' had higher scores than fathers of PID patients with healthy children in BDI, STAI-S, and STAI-T ($p = .002$, $p = .010$, $p = .001$). Mothers of PID patients reported lower scores in RLEP, E/F, EWB, P, and GH compared to fathers ($p = .009$, $p = .005$, $p = .034$, $p = .001$, $p = .003$). Additionally, the study found that STAI-T influenced all subdimensions of HRQOL. These results highlight the substantial emotional and psychological burden placed on parents caring for children with PID.

Conclusion: The study underscores the importance of supporting caregivers to enhance the overall well-being of both parents and children with PID. Such support can potentially alleviate depression and anxiety levels among parents, ultimately improving their quality of life and aiding in the management of children with PID.

KEYWORDS
anxiety, depression, parental mental health, primary immune deficiency, quality of life, SF-36

Abbreviations: BDI, the Turkish Forms of Beck Depression Inventory; E/F, energy/fatigue; EWB, emotional well-being; GH, general health; HC, health change; HRQOL, health-related quality of life; IUIS, the International Union of Immunological Societies; P, pain; PF, physical functioning; PID, primary immune deficiencies; RLEP, role limitations due to emotional problems; RLPH, role limitations due to physical health; SCID, severe combined immunodeficiency; SF, social functioning; SF-36, short form-36; STAI-S, State Anxiety Inventory; STAI-T, Trait Anxiety Inventory.

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1 | INTRODUCTION

Primary immune deficiencies (PID) represent a collection of chronic genetic disorders known for causing recurrent infections, immune dysregulation, and an increased risk of malignancy. The global prevalence of PID varies, ranging from 1 case per 8500 to 1 case per 100,000 individuals based on diagnosed symptomatic patients.[1] The International Association of Immunological Societies (IUIS) currently recognizes a total of 485 different innate immune defects.[2] The life expectancy of individuals with PID has increased thanks to advancements in treatment options and the continual development of new drugs. However, despite these improvements, patients experience morbidity, impacting their quality of life (HRQOL). PID, like other chronic diseases, not only affects the patients themselves but also profoundly impacts their siblings and parents. All family members' physical, social, and psychological well-being can be affected. The need for isolation to prevent frequent infections, rigorous hospital follow-ups for immunocompromised patients, and intravenous immunoglobulin (IVIG) treatments administered in hospital settings add to the challenges faced by patients. These disruptions, coupled with the substantial medication load for both immunodeficiency and comorbid conditions, impact their HRQOL. Moreover, not all patients can easily obtain an accurate genetic diagnosis, further complicating their journey in dealing with PID. Fatigue, low mood, and anxiety are commonly reported in both children and adults with PID.[3–5] The aim of this study is to determine the quality of life, depression, and anxiety levels in parents of children with PID.

Key message

In our study, we demonstrated that parents of primary immune deficiencies (PID) patients experience high levels of depression and anxiety, and their health-related quality of life (HRQOL) is diminished. This can be explained by both immunodeficient children need more effort to care for and avoid infections and diseases than healthy ones. A low energy/fatigue score can confirm this effort. Our research represents the most extensive study conducted to date, examining and contrasting mothers and fathers of patients with PID. The findings unveil a noteworthy discrepancy, as mothers exhibited significantly higher levels of anxiety, depression, fatigue, and pain scores. Mothers reported lower scores in terms of role limitations due to emotional problems, emotional well-being, and general health. Furthermore, our paper is valuable because it provides detailed information on which areas the quality of life for families deteriorates. We believe that assisting families in this regard based on these insights will contribute to the literature. We expect that by promoting the well-being of caregivers, we can contribute to the children's follow-up and treatment process, potentially reducing their depression and anxiety levels and improving their quality of life. We hope that the publication of our study on this family group, measuring anxiety, depression, and quality of life with scales, in a respected journal like PAI, will attract more attention to this issue and contribute to awareness. In line with the literature, considering the high levels of anxiety we found and their impact on HRQOL, a psychodrama intervention is planned for mothers of children with PID to enhance their coping strategies and resilience in dealing with anxiety.

2 | METHODS

This study was conducted in the Pediatric Allergy and Immunology Department of Basaksehir Cam and Sakura City Hospital, University of Health Sciences. IUIS criteria were used for PID classifications.[2] The parents of children with PID who applied to the Department of Pediatric Allergy and Immunology are included in the study. Parents with chronic illnesses were not included in the study. Families were invited to participate during their child's routine medical visit. We obtained written consent from all caregivers. Caregivers completed a demographic form, The Turkish Forms of Beck Depression Inventory (21 multiple-choice questions), State Anxiety Inventory (STAI-S) (20 multiple-choice questions on a 4-point scale—how a person feels at a specific moment in time), Trait Anxiety Inventory (STAI-T) (20 multiple-choice questions on a 4-point scale—how a person feels anxiety over time), and short form-36 (SF-36) (36 multiple-choice questions). Parents with healthy children and no chronic diseases were included in the study as a control group. Approval for the study was received from the local ethics committee of Basaksehir Cam and Sakura City Hospital (KAEK/2023.07.305).

2.1 | Statistical analyze

The data analyzed in the study were processed using SPSS 23. Group comparisons were conducted using an independent samples *t*-test for continuous data and chi-squared analysis for categorical data. Given the extensive number of analyses, Pearson product-moment correlation coefficients were employed to assess the strength of the relationship.

For categorical variables, proportions and percentages were generated to explore their distribution. One-way analysis of variance (ANOVA) was used to identify group differences in normally distributed continuous variables. At the same time, the Kruskal–Wallis *H* test was utilized to identify group differences on skewed continuous variables. Pearson's chi-squared test was utilized to identify group

differences in categorical variables. Fisher's exact test was used for categorical values with some cell values <5.

In this study, we employed a stepwise regression approach to analyze the relationship between SF-36 subscales and a set of predictor variables, such as characteristics of both children with PID and parents.

3 | RESULTS

3.1 | Demographics of patients

The study involved 64 patients with PID and 75 healthy children. The mean age of PID patients was 99.98 ± 56.56 months while healthy children's mean age was 66.09 ± 53.96 months. Regarding gender distribution, 41.5% ($n = 22$) of the PID patients were female, and 58.5% ($n = 31$) of the healthy children were female (Table 1). The patient's mean age of diagnosis of 43.38 ± 43.35 months. The mean duration of follow-up and treatment was 55.06 ± 41.794 months (Table 2).

3.2 | Demographics of parents

The study involved 85 parents of PID patients and 85 parents of healthy children. Among the parents, the mean age was 37.35 ± 7.26 years for the study group and 34.31 ± 6.85 years for the control group (Table 1). In the study group, 60.0% ($n = 51$) were female, while 72.9% ($n = 62$) of the control group were female. The income level of the study group was observed to be lower compared to the control ($p = .020$). There was no difference in the unemployment rate, and educational level between the groups ($p = .537$, $p = .194$) (Table 1).

3.3 | Characteristics of primary immunodeficiency diseases

Patients were classified according to the IUIS, and the most frequent groups observed were combined immunodeficiencies with associated or syndromic features ($n = 20$, 31.3%) and predominantly antibody deficiencies ($n = 12$, 18.7%), respectively. Patients with IgA deficiency were not included in the study. The other groups were as follows: Immunodeficiencies affecting cellular and humoral immunity ($n = 8$, 12.5%), diseases of immune dysregulation ($n = 3$, 4.7%), congenital defects of phagocyte number or function ($n = 3$, 4.7%), autoinflammatory disorders ($n = 3$, 4.7%), defects in intrinsic and innate immunity ($n = 2$, 3.1%), and bone marrow failure ($n = 1$, 1.6%). Twelve patient's deficiencies ($n = 12$, 18.7%), although not yet classified according to IUIS, were still being monitored for PID. The diagnoses of 20 (33.3%) patients were supported by genetic results. When patients were grouped according to their IUIS classification, there were no significant differences in the scores for BDI, STAI-S, STAI-T, physical functioning (PF), role limitations due to physical health (LRPH), role limitations due to emotional problems (RLEP), energy/fatigue, emotional well-being (EWB), social functioning (SF), pain (P), general health (GH), and health change (HC) ($p = .937$, $p = .449$, $p = .501$, $p = .561$, $p = .425$, $p = .876$, $p = .197$, $p = .215$, $p = .566$). There was a family history of PID in 16 cases (25%). Consanguinity was observed to be common among parents with PID, with a prevalence of 51.5% (33) in the patient group and 12.0% (9) in the control group ($p = .000$) (Table 2).

TABLE 1 Demographic data of primary immune deficiencies patients, parents, and control groups.

	Patient ($n = 85$)	Control ($n = 85$)	p-Value
Age of parents (years)	37.35 ± 7.262	34.31 ± 6.850	.276
Gender of parents (male)	34 (40.0%)	23 (26.1%)	.074
Parental employment	36 (42.3%)	40 (47.0)	.537
Parental education level			
Literacy	3 (3.6%)	2 (2.4%)	.194
Elementary education	36 (42.4%)	30 (35.2%)	
High school	26 (30.5%)	20 (23.5%)	
University	20 (23.5%)	33 (38.9%)	
	Patient ($n = 64$)	**Control ($n = 75$)**	**p-Value**
Age of children (months)	99.98 ± 56.56	66.09 ± 53.96	**.035**
Gender of children (male)	42 (%48.8)	44 (%51.2)	.400
Consanguinity	33 (51.5%)	9 (12.0%)	**.000**
Income level			
<1000 USD	40 (55.6%)	32 (44.4%)	**.020**
>1000 USD	24 (35.8%)	43 (64.2%)	

Note: Statistical significance ($p < .05$) is indicated by bold.

TABLE 2 The characteristics of PID patients.

	N = 64
Classification of patients from the International Union of Immunological Societies	
Immunodeficiencies affecting cellular and humoral immunity SCID (RAG2 = 1, DNA-Ligase-4 = 2, T-B-NK+ SCID = 2) = 5 CID (CD40 = 1, CD40L = 1, MHC2 = 1) = 3	8 (12.5%)
Combined immunodeficiencies with associated or syndromic features Ataxia-telengiectasia (ATM) = 9 Kabuki syndrome (KMT2D) = 3 Hyper Ig-E syndrome (PGM-3, STAT-3) = 2 Hepatic veno-occlusive disease with immunodeficiency (VODI) = 1 DiGeorge syndrome = 4 MOPD1 Deficiency (Roifman syndrome) = 1	20 (31.3%)
Predominantly antibody deficiencies X linked agammaglobulinemia (Bruton tyrosine kinase) = 6 Autosomal recessive agammaglobulinemia (IGLL1) = 1 CVID = 4 Hyper IGM syndrome(AID) = 1	12 (18.7%)
Diseases of immune dysregulation LRBA deficiency = 2 CTLA-4 deficiency = 1	3 (4.7%)
Congenital defects of phagocyte number or function Chronic granulomatous disease = 3	3 (4.7%)
Defects in intrinsic and innate immunity Acute liver failure due to NBAS deficiency = 1 MSMD (IL-12/IL-23 receptor 1 chain deficiency) = 1	2 (3.1%)
Autoinflammatory disorders PLAID (PLC 2 associated antibody deficiency and immune dysregulation) = 1 ADA2 deficiency = 2	3 (4.7%)
Complement deficiencies	–
Bone marrow failure Dyskeratosis Congenita = 1	1 (1.6%)
Phenocopies of inborn errors of immunity	–
Unclassified	12 (18.7%)
Age at diagnosis, months	43.38 ± 43.35
Follow-up duration, months	55.06 ± 41.79
Family history of PID	16 (25.0%)
Confirmed genetic diagnosis	20 (33.3%)

3.4 | Comparison of parents of the patients and control groups according to life quality, depression, and anxiety levels

The scores of parents with PID patients were higher than those of parents with healthy children in BDI, STAI-S, STAI-T, and fatigue subdomain of SF-36 ($p = .013$, $p = .013$, $p = .027$, $p = .000$). Additionally, our examination extended to the assessment of the HRQOL through the SF-36 survey, encompassing analysis of other subdomains. The scores corresponding to PF, LRPH, RLEP, EWB, SF, P, GH, and HC unveiled no substantial differences between parents of PID patients and parents of healthy children ($p = .266$, $p = .462$, $p = .576$, $p = .605$, $p = .487$, $p = .676$, $p = .210$, $p = .193$) (Tables 3 and 4).

TABLE 3 Comparison of beck depression, STAI-A, and STAI-T scores.

	Mean ± SD		
	Study group	**Control group**	***p*-Value**
Beck depression			
Parents	15.48 ± 10.16	11.78 ± 9.04	**.013**
Mothers	18.25 ± 9.96	13.35 ± 8.74	**.006**
Fathers	11.32 ± 9.09	7.52 ± 8.61	.116
State anxiety			
Parents	42.58 ± 8.67	39.11 ± 9.36	**.013**
Mothers	44.63 ± 7.59	40.10 ± 8.91	**.004**
Fathers	39.50 ± 9.38	36.43 ± 10.22	.257
Trait anxiety			
Parents	47.14 ± 7.96	44.47 ± 7.60	**.027**
Mothers	49.35 ± 7.84	45.23 ± 7.62	**.006**
Fathers	4.82 ± 7.03	42.43 ± 7.32	.479
	Mothers of the study group	**Fathers of the study group**	***p*-Value**
Beck depression	18.25 ± 9.96	11.32 ± 9.09	**.002**
State anxiety	44.63 ± 7.59	39.50 ± 9.38	**.010**
Trait anxiety	49.35 ± 7.84	43.82 ± 7.03	**.001**

Note: Statistical significance ($p < .05$) is indicated by bold.

3.5 | Comparison of mothers of the patients and control groups according to life quality, depression, and anxiety levels

The scores of mothers with PID patients were higher than those of mothers with healthy children in BDI, STAI-S, STAI-T, and the fatigue subdomain of SF-36 ($p = .006$, $p = .004$, $p = .006$, $p = .000$) (Tables 3 and 4).

3.6 | Comparison of fathers of the patients and control groups according to life quality, depression, and anxiety levels

BDI, STAI-S, and STAI-T did not show differences between fathers of PID patients and the control group ($p = .116$, $p = .257$, $p = .479$). Fathers of PID patients also reported higher fatigue scores when compared to the control group ($p = .000$) (Tables 3 and 4).

TABLE 4 Comparison of short form-36 scores.

	Mean ± SD		
Comparison SF-36 subdimensions of study and control groups	**Study group**	**Control group**	***p*-Value**
Physical functioning			
Parents	79.24 ± 9.96	82.65 ± 19.93	.266
Mothers	76.27 ± 17.46	80.24 ± 21.00	.275
Fathers	83.68 ± 22.77	89.13 ± 15.27	.284
Role limitations due to physical health			
Parents	64.71 ± 38.05	60.29 ± 39.95	.462
Mothers	59.80 ± 38.10	56.05 ± 39.64	.610
Fathers	72.06 ± 37.3	71.74 ± 39.38	.976
Role limitations due to emotional problems			
Parents	63.91 ± 33.82	60.78 ± 38.89	.576
Mothers	56.21 ± 32.32	58.60 ± 38.50	.720
Fathers	75.49 ± 33.14	66.67 ± 40.20	.389
Energy/fatigue			
Parents	46.35 ± 19.24	57.35 ± 20.00	**.000**
Mothers	41.47 ± 17.41	54.60 ± 20.08	**.000**
Fathers	53.68 ± 19.78	64.78 ± 18.18	**.034**
Emotional well-being			
Parents	61.65 ± 18.46	63.11 ± 18.22	.605
Mothers	58.20 ± 18.26	61.16 ± 17.82	.387
Fathers	66.82 ± 17.79	68.35 ± 18.64	.759
Social functioning			
Parents	66.17 ± 24.83	68.67 ± 21.87	.487
Mothers	62.25 ± 23.25	67.94 ± 22.59	.193
Fathers	72.06 ± 26.30	70.65±/20.15	.820
Pain			
Parents	69.44 ± 27.50	71.14 ± 25.56	.676
Mothers	61.83 ± 27.93	68.31 ± 26.08	.212
Fathers	80.81 ± 22.84	78.80 ± 22.89	.747
General health			
Parents	57.17 ± 19.73	60.88 ± 18.66	.210
Mothers	52.06 ± 18.30	58.39 ± 18.68	.073
Fathers	64.85 ± 19.55	67.61 ± 17.24	.578
Health change			
Parents	51.47 ± 25.10	56.47 ± 24.74	.193
Mothers	50.98 ± 27.36	54.84 ± 25.54	.444
Fathers	52.21 ± 21.64	60.87 ± 22.39	.153
Comparison of mother and father of study group	**Mothers**	**Fathers**	***p*-Value**
Physical functioning	76.27 ± 17.46	83.68 ± 22.77	.114
Role limitations due to physical health	59.80 ± 38.10	72.06 ± 37.31	.146
Role limitations due to emotional problems	56.21 ± 32.32	75.49 ± 33.14	**.009**
Energy/fatigue	41.47 ± 17.41	53.68 ± 19.78	**.005**
Emotional well-being	58.20 ± 18.26	66.82 ± 17.79	**.034**
Social functioning	62.25 ± 23.25	72.06 ± 26.30	.074
Pain	61.86 ± 27.93	80.81 ± 22.84	**.001**
General health	52.06 + 18.30	64.85 ± 19.55	**.003**
Health change	50.98 ± 27.36	52.21 ± 21.64	.819

Note: Statistical significance ($p < .05$) is indicated by bold.

3.7 | Comparison of mothers and fathers of the patients according to life quality, depression, and anxiety levels

The scores of mothers with PID patients were higher than those of fathers of PID patients with healthy children in BDI, STAI-S, and STAI-T ($p = .002$, $p = .010$, $p = .001$). Mothers of PID patients reported lower scores in RLEP, E/F, EWB, P, and GH compared to fathers ($p = .009$, $p = .005$, $p = .034$, $p = .001$, $p = .003$) (Tables 3 and 4).

3.8 | Other Results

The STAI-S showed a strong correlation with both the BDI and the STAI-T ($r = .711$, $p = .000$; $r = .722$, $p = .000$), and STAI-T was strongly associated with decreased emotional well-being ($r = -.729$, $p = .000$) (Table 5).

In our study investigating the subdomains of HRQOL, we observed the following relationships: PF; Parents' age, and STAI-S collectively explained 9.8% of the variance. RLPH; Parents' age and STAI-T collectively accounted for 25% of the variance. RLEP; gender and depression score jointly explained 12% of the variance. E/F; depression and STAI-T together accounted for 49.2% of the variance. EWB; sibling order, STAI-T, and STAI-S jointly explained 58.2% of the variance. SF; having a genetic diagnosis, and STAI-T collectively explained 29.6% of the variance. P; Parents' age, Number of Children, and STAI-T together accounted for 34.9% of the variance. GH; working status (Employed), and STAI-T collectively explained 30.5% of the variance. HC; STAI-T alone explained 15.3% of the variance. All coefficients' VIF values are smaller than 1.5[6] and have no multicollinearity problems (Table 6).

4 | DISCUSSION

PID is a chronic group of diseases that leads to morbidity and mortality, and early diagnosis holds vital importance. Children with PID faced notable limitations in terms of their physical functioning and psychological well-being when compared to their healthy peers.[7–10] They experience impaired psychosocial, emotional, and academic functioning.[4,5,11] Previous research consistently indicates that elevated levels of anxiety and depression are consistently associated with a decrease in mental health and overall HRQOL in PID patients.[3–5,12,13]

There are numerous studies assessing the child's psychology from the parent's perspective.[9,14,15] It is demonstrated that children with PID had anxiety and depressive symptoms and notably reduced pediatric HRQOL both from the perspectives of the child and the parent.[4,8,14] Meelad et al. reported that children often rated themselves as physically and socially active, while their parents had concerns in these areas.[14] Kuburovic found that children with PID reported similar school functioning to controls, as their self-reports. However, parents of children with PID reported lower school functioning compared to both the JIA group and healthy children.[4,9] Piazza-Waggoner found that children with mild illnesses exhibited less adaptive coping, and their caregivers demonstrated more maladaptive coping compared to other groups.[4,14] Children often self-assessed more positively than their parents with the same medical condition, implying better self-evaluation skills[4,10,11] or distressed caregivers may view their child's behavioral functioning more negatively.[11] However, this difference could also imply that children consistently underestimate the severity of their illness.[4,10] Caregivers' reports on family roles and emotional responsiveness, as well as children's reports on family communication, were shown to contribute to predicting child behavioral functioning.[16] Depressive symptoms in parents are found to be correlated with depressive symptoms in

TABLE 5 The correlations between the Beck Depression Inventory (BDI), state anxiety, and trait anxiety.

		BDI	STAI-S	STAI-T
Beck Depression Inventory	*r* coefficient	1	**0.711**[a]	**0.644**
State anxiety	*r* coefficient	**0.711**[a]	1	**0.722**[a]
Trait anxiety	*r* coefficient	**0.644**	**0.722**	1
Physical functioning	*r* coefficient	**−0.233**	**−0.314**	**−0.267**
Role limitations due to physical health	*r* coefficient	**−0.336**	**−0.411**	**−0.457**
Role limitations due to emotional problems	*r* coefficient	**−0.317**	**−0.254**	**−0.289**
Energy-fatigue	*r* coefficient	**−0.584**	**−0.588**	**−0.662**
Emotional well-being	*r* coefficient	**−0.567**	**−0.632**	**−0.729**[a]
Social functioning	*r* coefficient	**−0.471**	**−0.484**	**−0.428**
Pain	*r* coefficient	**−0.477**	**−0.378**	**−0.542**
General health	*r* coefficient	**−0.377**	**−0.377**	**−0.476**
Health change	*r* coefficient	−0.131	**-0.304**	**-0.391**

Note: Statistical significance ($p < .05$) is indicated by bold.

[a]Strong correlations.

TABLE 6 Regression analysis of SF-36 subdimensions.

	Role limitations due to								
	PF	**PH**	**EP**	**EF**	**EWB**	**SF**	**P**	**GH**	**HC**
Parental characteristics									
R-square (adj.)	.098	.253	.120	.492	.582	.296	.349	.305	.153
Age	0.191*	0.188*					0.209*		
Gender (female)			−0.194*						
Education									
Working status (employed)								−0.202*	
Income									
Number of children							−0.205*		
People in family									
Consanguinity (yes)									
Characteristics of PID children									
Age									
Gender (female)									
Sibling order					0.211**				
Genetic diagnosis (yes)						0.255**			
Age of diagnosis									
IV Ig treatment (yes)									
Outpatient inf.						0.186*			
Inpatient inf.								−0.193*	
Duration of treatment									
Depression & anxiety levels									
Total BDI score			−0.268**	−0.246**					
STAI – trait		−0.466*		−0.520**	−0.580**	−0.457**	−0.209**	−0.469**	−0.404**
STAI – state	−0.26*				−0.233*				

Abbreviations: EF, energy/fatigue; EP, emotional problems; EWB, emotional well-being; GH, general health; P, pain; PF, physical functioning; PH, physical health; SF, social functioning.
Statistical significance is indicated by $^{*}p < .05$; $^{**}p < .01$.

their children.[17] In families affected by HIV, where isolation, frequent infections, and guilt are common like PID, improvements in caregiver supervision are associated with reductions in anxiety among children.[18] Therefore, the well-being of parents and their caregiving capacity have an important impact on the health of children and monitoring their illnesses. Interventions designed to address modifiable psychosocial factors, such as cognitive-behavioral exercises to alter illness perceptions, enhance coping effectiveness, or boost self-esteem, should be examined.[19]

Research on parents of patients with PID remains limited, despite numerous studies conducted on pediatric and adult PID patients themselves.[20–22] In our study, PID parents showed higher depression, state anxiety, and trait anxiety scores, along with increased fatigue. Untreated depression and anxiety can impair economic productivity, work and social functioning, relationships, physical health, and caregivers' problem-solving abilities, ultimately impacting their HRQOL negatively.[23] Previous research focusing on parents of children with SCID,[9,22,24] and CGD[10] has demonstrated that HRQOL is inferior compared to the general population. Parents indicated that their foremost concerns about their children's PID were the enduring nature of the illness, its manageability, and the potential side effects of treatment.[25] Prolonged protective isolation prompted parents to navigate difficult situations and offer strategies for managing the hospital environment, practicing self-care, handling social interactions, and time management.[26] Even 1 year after their child's hematopoietic stem cell transplant (HSCT), mothers continued to experience traumatic experiences.[27] Even though caregivers might report increased life stress, this does not necessarily hinder them from expressing overall high life satisfaction. A study on DiGeorge syndrome caregivers revealed that mothers experienced higher stress levels compared to the general population while maintaining normal life satisfaction.[28] In other words, despite the challenges posed by the illness, or perhaps because of them, patients and their families have been found to exhibit higher satisfaction with their mental/emotional well-being.[19,28] Contrary to some studies on specific PID types, our research included various PID types and revealed no differences in anxiety, depression, and HRQOL scores based on the IUIS classification, aligning with previous research in diverse patient groups.[2,14,20]

In our study investigating the subdomains of HRQOL, we observed some remarkable relationships. Trait anxiety has negative effects on all of the subdimensions of HRQOL except physical functioning and role limitations due to emotional problems. Previous studies have reported similar results, indicating that trait anxiety influences overall life functioning. This underscores the importance of implementing interventions for these families.[20] Parents' age positively affects physical subdimensions such as physical functioning, general health, and pain. This may be associated with the increase in life experiences and anxiety management skills that come with age. Another striking result was observed in emotional well-being. An explanatory factor of 58% was determined, and it was found that the child's position among siblings is positively related to parental emotional well-being. This could be related to the experience in raising children, but unfortunately, it might also be because as the number of children with PID increases, they can be more easily overlooked. The absence of a specific diagnosis may hinder patients and their caregivers from addressing crucial inquiries concerning the illness's long-term presence, potential repercussions, and prognosis.[20] We showed that providing an accurate genetic diagnosis helps to resolve uncertainty and enhances social functioning. Female gender is a risk for role limitations due to emotional problems, as seen in previous comparisons of the study and control groups.[12,29] This could be related to both societal gender roles of mothers as caregivers and the need for care due to the early onset of the disease, which in turn may hinder the completion of separation-individuation processes.

In studies involving parents, it was noted that mothers outnumbered fathers in terms of participation.[14,28,30,31] Abolhassani conducted a study on fathers due to the typically pronounced and extended parental over-concern observed in mothers as mentioned above.[20] In a study investigating the anxiety among parents with PID during the COVID-19 pandemic, the anxiety and post-traumatic stress scores of mothers and fathers in the study group showed no difference.[31] On the other hand, HRQOL of patients who underwent HSCT was studied, and mothers reported lower physical functioning compared to both the child and fathers.[30] Our study is the largest study to date that compares mothers and fathers in PID patients and contributes original insights, revealing that mothers had notably higher depression, state anxiety, and trait anxiety, and they reported a lower HRQOL in domains related to role limitations due to emotional problems, energy/fatigue, emotional well-being, pain, and general health.

AUTHOR CONTRIBUTIONS

Sibel Kaplan Sarıkavak: Writing – original draft; data curation; visualization; validation; investigation; formal analysis; resources. **Talat Sarıkavak:** Investigation; writing – original draft; validation; visualization; formal analysis; data curation; resources. **Özge Türkyılmaz Uçar:** Investigation; resources; data curation; validation. **Çiğdem Aydoğmuş:** Investigation; resources; data curation; validation. **Mehmet Halil Celiksoy:** Writing – review and editing; writing – original draft; conceptualization; investigation; methodology; formal analysis; project administration; validation; visualization; supervision; data curation; resources.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

ETHICS STATEMENT

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