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Original article

Health-related quality of life among a group of Egyptian children with inborn errors of immunity: a cross-sectional study

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Background: *Inborn Errors of Immunity (IEI) significantly impact the patients' life, limiting their physical and social activities. Health-related quality of life (HRQOL) can also be adversely influenced by the delay in diagnosis and treatment of infections .*

Methods: *We sought to assess HRQOL of IEI patients at a major tertiary care hospital in Egypt by using the Arabic version of pediatric quality of life inventory generic core scale (PedQl 4.0) questionnaire answered by the patient or his/her parents .*

Results: *We enrolled 50 IEI patients, 34 of them (68%) were males and 16 (32%) were females. Their mean ± SD age was 86.8 ± 36.9 months. The lowest HRQOL score was for school functioning with a mean score of 33.23 (SD=14.06). Social functioning score was significantly lower in older children (p=0.034). The rate and duration of hospitalization negatively affected social functioning. Pulmonary involvement in the form of bronchiectasis and interstitial lung disease caused a significant decline in quality of life. The procedures of receiving intravenous immunoglobulin (IVIG) therapy had no effect on the QOL .*

Conclusion: *IEI patients suffer from a decreased quality of life in terms of school and physical functioning. Healthcare providers managing IEI pediatric patients should pay attention to their quality of life to improve their optimal academic achievement and emotional wellbeing.*

Keywords: HRQOL, health-related quality of life, IEI, inborn errors of immunity, QOL, quality of life.

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INTRODUCTION

Inborn errors of Immunity (IEI) are a heterogeneous group of inherited disorders affecting the immune system. So far, more than 300 causative genetically defined single-gene mutation have been detected.[1] The prevalence of IEI is much higher than generally thought, with around 6 million people living worldwide. Patients with IEI are generally more prone to develop respiratory and gastrointestinal recurrent infections and/or autoimmune diseases.[2]

The Quality of life (QOL) is a multidimensional concept that encompasses physical, psychological, and social aspects of well-being.[3] IEI significantly influences patients' lives, limiting their working ability and physical and social activities.[4] Health-related quality of life (HRQOL) in patients with IEI can be also adversely impacted by delays in diagnosis and in treatment of infections. HRQOL is not assessed as often as it should be, despite the concept being widely used in research.[5]

A recently published bibliometric analysis focusing on the HRQOL in IEI patients was done utilizing data from the Science Citation Index Expanded (SCIE) and Social Sciences Citation Index (SSCI) within the Web of

Science core datasets up to January 1, 2024. It noted that despite the importance of HRQOL in IEI, the volume of publications in this field was still consistently low. It also concluded that the improvement in survival rate following hematopoietic stem cell transplants and gene therapy, did not significantly the impact on HRQOL owing to the adverse effects of interventions.[6]

We aimed to assess the HRQOL in children with IEI in face of the challenges in our middle-low-income community with limited health facilities.

METHODS

This comparative cross-sectional study was conducted in the Pediatric Allergy, Immunology and Rheumatology Unit, Children's Hospital, Ain Shams University from August 2020 to April 2021. It included 50 patients diagnosed with IEI based on the International Union of Immunological Societies (IUIS) criteria.[7] We also enrolled 25 age and sex matched healthy control group from the outpatient clinic of the Children's Hospital, Ain Shams University. Both groups underwent evaluation by the Arabic version of Pediatric Quality of Life Inventory Generic Core Scale (PedQl 4.0) questionnaire. The validity and reliability of PedsQL for healthy children and children with chronic diseases have been established for the Arabic version.[8,9] The Mapi Research Trust has granted permission for its use (10-2-2020). The questionnaire was filled by the parent and/or the patient.

The PedsQL is a self-rated and proxy-rated questionnaire, and both versions include 23 items in the following scales: physical functioning (eight items), emotional functioning (five items), social functioning (five items), and school functioning (five items).Within the scales, all items are in a 5-point response-scale format (0= never a problem, 1= almost never a problem, 2= sometimes a problem, 3= often a problem, 4= almost always a problem), and all are reverse scored and linearly transformed to a 0–100 scale. Higher scores indicate better HRQOL. Data about patients' demographic data, frequency and duration of infections and treatment modalities were collected from our records.

Consent and Ethical Considerations: An oral informed consent was obtained from parents or legal guardians of patients before enrolment in the study. This study protocol was approved by local ethical committee of the pediatrics Department, Faculty of Medicine, Ain Shams University Number: M S 284/ 2020.

Statistical Analysis

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS 25). Data was presented and suitable analysis was done according to the type of data obtained for each parameter. For analytical analysis we used ANOVA test, Kruskal-Wallis test and correlation analysis using Pearson's and Spearman's rho methods.

RESULTS

The 50 patients comprised 34 (68%) males and 16 (32%) females with a male to female ratio of 2:1. Their mean ± SD age was 86.8 ± 36.9 months. Their mean age ± SD at time of diagnosis and a diagnosis lag were 62.58 ± 38.27 months and 25.78 ± 22.7 months, respectively.

The patients had the following diagnoses: 23 (46%) had combined immunodeficiency (CID), 7 (14%) had neutrophil dysfunction, 13 (26%) had predominant antibody deficiency (PAD) and 7 (14%) had Inborn error of innate immunity. Twenty-two (44%) of our patients were living in rural area and 28 (56%) patients in urban area. Eighteen (36%) of the studied patients had family history of sibling affected with the same disease and 15 (30%) had history of previous sib death. Among the patients, 30 (60%) go to schools. Our control group comprised 18 (72%) males and 7 (28%) females with a male and female ratio of 2.5:1. Their mean ± SD age was 89.56 ± 30.33 month.

The HRQOL total score and each item of its questionnaire were significantly lower in patients with IEI than controls indicating worse

QOL 173±48.3 and 389.9±21.66, respectively (p=<0.001); Table (1). Current patients' age was negatively affecting the social function of QOL (p=0.034), whereas age at diagnosis or diagnostic lag did not affect the QOL (p=0.508, p=0.594). The presence of complications such as bronchiectasis, interstitial lung disease caused a decline in quality of life as indicated by lower scores (p> 0.001); Table (2). The HRQOL score was not significantly different among different types of IEI (whether CID, neutrophil dysfunction, PAD, or defects in innate immunity) being161±49.7, 189±39.9, 190±47.3, and 163±48.04, respectively (p=0.25).

Thirty-three (66%) patients were receiving IVIG; however, the process of visiting the hospital for the monthly dose of intravenous immunoglobulin (IVIG) did not affect patients' QOL (p> 0.901); Table (3). There was no statistically significant difference in the HRQOL between males and females (p> 0.336). (Table 4). The rate and duration of hospitalization did not affect the scores of the HRQOL (p>0.081), except in the social function component, which showed a negative correlation with a value of -0.29 and -0.423 respectively (p< 0.002). (Table 5).

Table 1. Quality-of-life scores in the studied sample

HRQOL Scores	Controls (N=25) Mean ± SD	Cases (N= 50) Mean ± SD	p-Value
Physical functioning	96.28 ± 4.61	49.42 ± 15.57	<0.00*
Emotional functioning	99.4 ± 1.66	51.7 ± 14.8	<0.00*
Social functioning	100 ± 0	51.7 ± 18.34	<0.001*
School functioning	98.17 ± 2.76	33.23 ± 14.06	<0.001*
Total Score	389.92 ± 21.66	173.41 ± 48.31	<0.001*

N: number; *: significant

Table 2. PID complications and quality of life scores in the IEI patients

HRQOL Scores	IVIG		Student t-test	
	No (N= 17)	Yes (N= 33)	t	p-Value
Physical functioning	48.44 ± 13.52	49.93 ± 16.7	-0.317	0.752
Emotional functioning	54.12 ± 16.7	50.45 ± 13.83	0.826	0.413
Social functioning	54.12 ± 17.87	50.45 ± 18.72	0.665	0.509
School functioning	38.13 ± 13.87	31.52 ± 14.02	1.151	0.259
Total Score	174.62 ± 48.16	172.8 ± 49.12	0.125	0.901

N: number; *: significant

Table 3. Relation between IVIG treatment and quality of life scores in the IEI patients

HRQOL Scores	IVIG		Student t-test	
	No (N= 17)	Yes (N= 33)	t	p-Value
Physical functioning	48.44 ± 13.52	49.93 ± 16.7	-0.317	0.752
Emotional functioning	54.12 ± 16.7	50.45 ± 13.83	0.826	0.413
Social functioning	54.12 ± 17.87	50.45 ± 18.72	0.665	0.509
School functioning	38.13 ± 13.87	31.52 ± 14.02	1.151	0.259
Total Score	174.62 ± 48.16	172.8 ± 49.12	0.125	0.901

Table 4. Variation of HRQOL according to gender in the IEI patients

HRQOL Scores	Male (N=34) Mean ± SD	Female (N=16) Mean ± SD	t	p-Value
Physical functioning	51.96 ± 16.09	44.04 ± 13.29	1.709	0.094
Emotional functioning	52.79 ± 13.33	49.38 ± 17.78	0.759	0.452
Social functioning	53.68 ± 18.52	47.5 ± 17.8	1.114	0.271
School functioning	35 ± 15.63	30.42 ± 11.17	0.881	0.386
Total Score	177.97 ± 48.62	163.73 ± 47.71	0.972	0.336

Table 5. Variation of HRQOL with rate and duration of hospitalization in the IEI patient

Cases group N= 50		Physical functioning	Emotional functioning	Social functioning	School functioning	Total Score
Rate of hospitalization	Pearson Correlation	-0.130	-0.237	-0.298	-0.319	-0.249
	p-Value	0.370	0.097	0.035*	0.080	0.081
Duration of hospitalization	Pearson Correlation	-0.197	-0.225	-0.423	-0.325	-0.344
	p-Value	0.170	0.116	0.002*	0.075	0.014*

N: number; *: significant

DISCUSSION

Patients with IEI suffer from recurrent infections and other symptoms of Immune dysregulation. This usually necessitates frequent and recurrent hospitalization and intake of long-term medications. Such policy makes IEI a major factor impacting patients' quality of life.

Among our series of IEI patients, there was a significant affection of HRQOL scores. Such affection was acknowledged and reported in numerous studies [9-15] in spite being conducted on different age groups and different countries with different health care facilities. This signifies the major effect induced by chronic illness on patients' lives, especially in those with IEI.

The impact of gender on QOL was controversial in different studies. In our study there was no difference, and this was acknowledged in studies done on some adult patients[12,16] and pediatrics patients with IEI.[17] However, a study on adults with common variable immunodeficiency (CVID) who were taking regular IVIG noted negative association between females and QOL in terms of both

physical and social activity. This might be explained by some female activities in terms of pregnancy and nursing children. Our study did not include adults in the child-bearing age.

In our study the length of diagnostic lag did not statistically correlate with HRQOL. However, the opposite was found in some pediatric[17] studies and adult studies.[15,18-20] The authors explained this observation by the relation between delayed diagnosis and repeated hospitalization, infections and liability for the occurrence of more complications, and morbidity. Our findings are indeed limited by the sample size.

The presence of complication such as bronchiectasis and interstitial lung disease did not impact the HRQOL score contrary to what was expected and cited in literature.[12,15,21] Its consequences of recurrent and prolonged hospitalization is supposed to have a major impact on patients' QOL.[15,17] Again, this may reflect a milder extent of pulmonary complications and may need further investigation in comparison to other relevant studies.

Interestingly, the adherence to hospital visits for monthly IVIG had no adverse effect on patients' QOL in our study. The positive effect of IVIG on improvement of the HRQOL score was acknowledge by a study done by Routes J et al.[24] after one year of regular therapy. This indicates that controlling infection and hence the decreased the rate of admission to health care facilities improves patients' QOL. Some other studies noted that there was no difference between QOL in patients on regular IVIG in comparison to those on subcutaneous immunoglobulin (SCIG). Both therapies should be adhered to in IEI.

Limitations of the study: The conclusions are limited by the studied sample size which is due to the rarity of IEI. The cross-sectional design and variation of diseases did not allow for accurate assessment of the impact of IVIG therapy on the QOL.

In conclusion, despite advancements in medical treatments for IEI, more focus on HRQOL is needed to enhance patient satisfaction and overall wellbeing. This would advocate for more personalized treatment plans improve their quality of life.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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