



Impact of Early Diagnosis and Intravenous Immunoglobulin on the Health-Related Quality of Life of Primary Immune Deficiency Children

Salim Zridi^{1*}, Islam Mansouri¹, Fatima Ailal^{1,2}, Ibtihal Benhsaiene^{1,2}, Jalila El Bakkouri³, Ahmed Aziz Bousfiha^{1,2}

¹Laboratory of Clinical Immunology, Inflammation and Allergy (LICIA), Faculty of Medicine and Pharmacy, Hassan II University, Casablanca, Morocco.

²Department of pediatric infectious and immunological diseases, Abderrahim El Harouchi Children Hospital, University Hospital Center Ibn Rochd, Casablanca, Morocco.

³Immunology Laboratory, IBN Rochd University Hospital, Casablanca, Morocco.

ABSTRACT

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Background: Inborn errors of immunity (IEI) are rare hereditary genetic, with around 485 rare immune system defects. Health-Related Quality of life (HRQOL) of children and adolescents with IEI is influenced by the early diagnosis of the disease, Immunoglobulin replacement, type of IEI, socio-economic status, family, social support, medical et social environment. Little attention is given to the HRQOL of patients, health professionals and stakeholders tend to focus on medical treatment more than the other aspect of the quality of life. The objective of this study is to measure the improvement of the HRQOL after the diagnosis and the Immunoglobulin treatment of IEI patients in Morocco.

Results: Total HRQOL was improved after diagnosis and treatment administration (Ig therapy) for the two groups of IEI patients using the generic EQ-5D-Y instrument ($p = 0.0009$). The improvement was most significant in the physical domain, financial, and schooling domains using the KIDSCREEN-52 instrument.

Conclusions: Health-Related Quality of Life plays a major role in health care; it gives insights into the factors that may improve the provision of health services.

KEYWORDS:

PID, IEI, QOL, HRQOL of children.

INTRODUCTION

Inborn errors of immunity (IEID) are a group of over 485 diseases characterized by defects within the immune system [1, 2]. Immunoglobulin (Ig) replacement is a mainstay of therapy for most patients with antibody deficiencies to return immunoglobulin levels to physiologic levels. Ig replacement therapy is a lifesaving treatment for a majority of IEI patients. It consists of regular administration of Ig therapies derived from human plasma, providing antibodies that protect individuals against infections and reduce autoimmune symptoms, which decreases the frequency of infections, improves the prognosis of individuals living with

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an IEI disease and eventually improves their health-related quality of life. Early diagnosis and adequate implementation of appropriate treatment including Ig therapies are life-enhancing for individuals, cost-saving for the health system, preventing comorbidities and infections, and improving the health-related quality of life.[3].

We hypothesized that the early diagnosis and the administration of Ig therapy would increase the health-related quality of life of Moroccan IEI patients.

The health-related quality of life is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity [4]. Numerous HRQOL instruments emerged, including generic measures that focus primarily on aspects of physical, psychological, and social functioning. To capture the burden of disease from the perspective of an individual, HRQOL measures for children should focus on how their illness affects their daily life and how they feel [5].

In this article, we measure the health-related quality of life of our patients before and after the diagnosis and Ig

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replacement therapy to assess the impact of the early diagnosis and the Ig therapy on patients with IEI using two HRQOL instruments: Kidscreen-32 and EQ-5D-Y.

Methods:

In order to measure the health-related QOL of our patients with IEI, we recruited from the reference center for primary immunodeficiencies, ABDERRAHIM EL HAROUCHI hospital in Casablanca, 54 patients (aged 4-18) and their parents, who consented to the study. The questioning of patients and their families took place in the period from November 2019 to November 2021, using 2 questionnaires: KIDSCREEN-52 and EQ-5D-Y. In our study, we first retrospectively measured HRQOL before diagnosis, using the two questionnaires (KIDSCREEN-52 and EQ-5D-Y). Each patient took up to 15 minutes of interviews to obtain their HRQOL before diagnosis. Then, we measured the HRQOL after the diagnosis in a prospective interview of 15 minutes, using the same questionnaires. In each questionnaire, we use the proxy version and the self-administered version taking into account the age of each patient. Inclusion criteria: Patients with IEIs, aged from 4 to 18 Years old, Getting IGIV in Casablanca children's hospital Abderrahim El Harouchi – University Hospital of Casablanca.

EQ-5D-Y: European Quality of life questionnaire 5 Dimensions; child-friendly self-complete instrument measuring HRQOL in children and adolescents aged **from 4 to 15 years old**. The EuroQol EQ-5D is a preference-based measure used to determine utility values, consisting of five

dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and five levels (no problems, slight problems, moderate problems, severe problems, and extreme problems) [6].

KIDSCREEN-32: The Kidscreen-52 was used to assess QoL in children and adolescents aged from 8 to 18 years old [7]. The Kidscreen-52 is divided into ten dimensions: Physical well-being, psychological well-being, Mood and emotions, Self-perception, Autonomy, Parent relations and home life, Social support and peers, School environment, Social acceptance, and Financial resources. All questions are answered on a 5-point scale (1. No problem to 5. A lot of problems). Higher scores reflect better QoL. In a large European study, the Kidscreen-52 was shown to be reliable, valid, and sensitive [7].

The results in the present series of KIDSCREEN were compared first to the T score mean of 50 established in the general population used for the KIDSCREEN validation and second to the weighted mean for controls from different studies in which the KIDSCREEN-52 was used to evaluate children with the disease [8]. All the statistical analysis was performed using SPSS for both questionnaires.

Results:

Our patients have been diagnosed and received their treatment in the Moroccan national reference center of primary immune deficiency in Casablanca Children's Hospital. 54 IEI patients were included in our study, 28% are female and 72% are male.

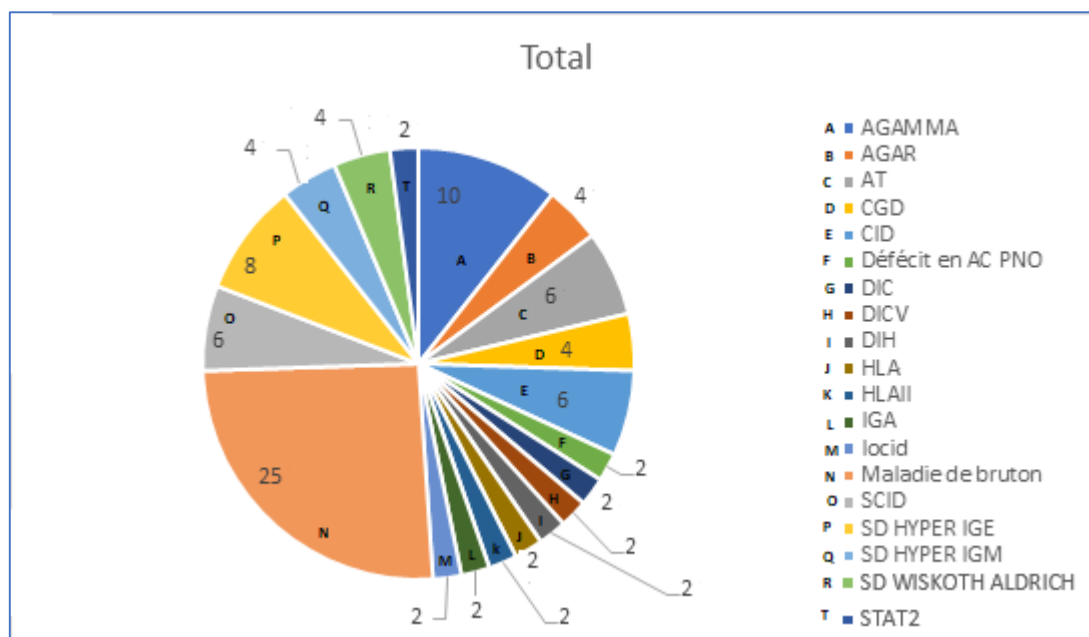


Figure 1. Diagnosis of our IEI patients

The most common IEI disease in the Bruton disease, it represents more than 25% of our patient, 8,51% of Sd hyper IgE, 6,38 (SCID, AT, and CID) the agammaglobulinemia

represent more than 10% of our IEI patients following the other IEI diseases in small percentages.

Health-Related Quality of life measurement using EQ 5D Y questionnaire :

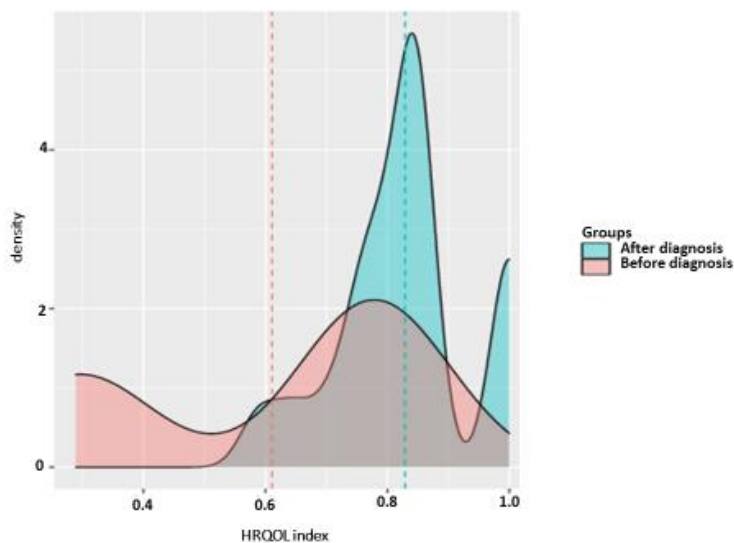


Figure 2. HRQOL-EQ-5D-Y index of Children Group 1 (4 to 7 years old)
W = 321 p value = 0.00094

The HRQOL index mean before the diagnosis is significantly lower than the HRQOL index after the diagnosis, which means a significant improvement of the

HRQOL of children aged from 4 to 7 years old after the diagnosis (p-value < 0.05)

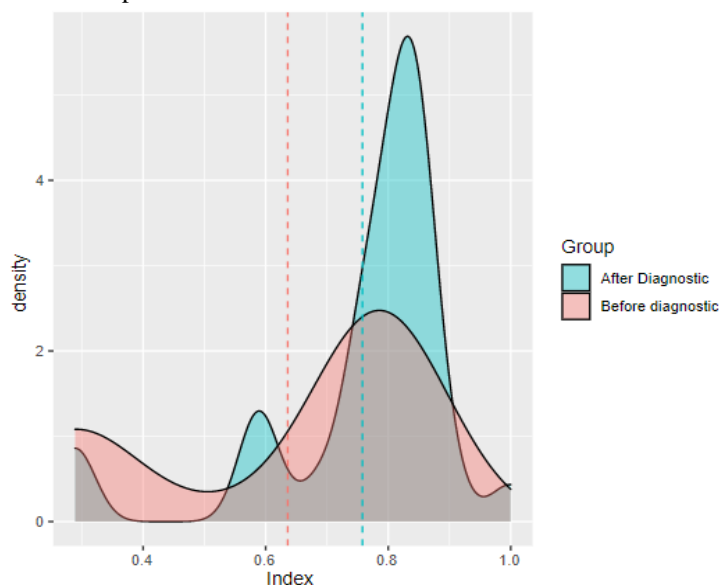


Figure 3. HRQOL - EQ-5D-Y index of Children Group 1: (8 to 15 years old)
W = 552 p value = 0.00806

The HRQOL index mean before the diagnosis is significantly lower than the HRQOL index after the diagnosis, which means a significant improvement of the HRQOL of children

aged from 8 to 15 years old after the diagnosis (P-value < 0.05)

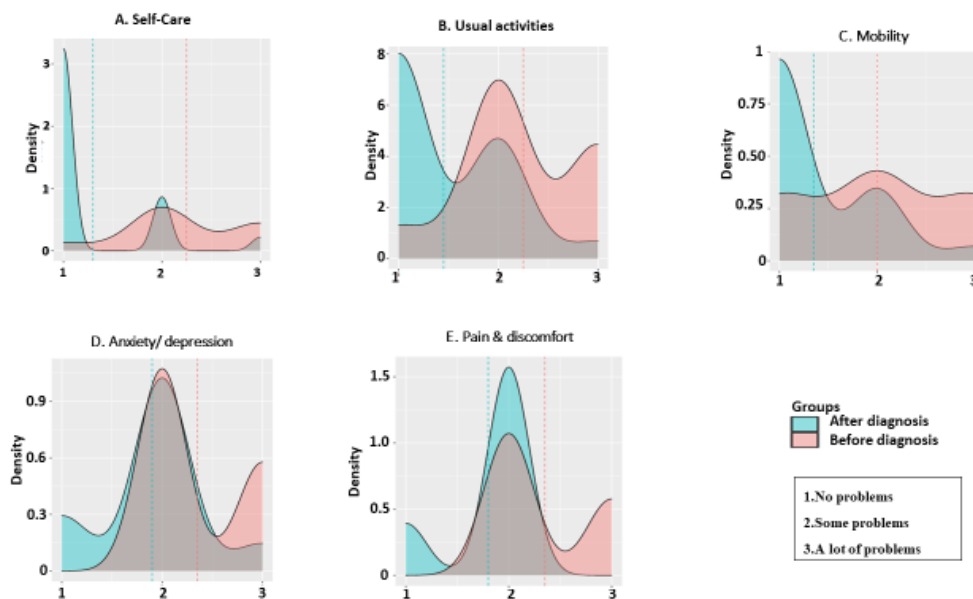


Figure 4. HRQOL using EQ 5D Y of IEI Group 1 (4 to 7 Years old)

The HRQOL Domains covered by the EQ 5D Y questionnaire are Mobility, Anxiety/ depression, pain/ discomfort, usual activities and self-care. after measuring the HRQOL domains of our patients before and after the

diagnosis, we remarque the improvement in all domains (P-value<0.05) except the Anxiety/ depression with insignificant p-value >0.00.

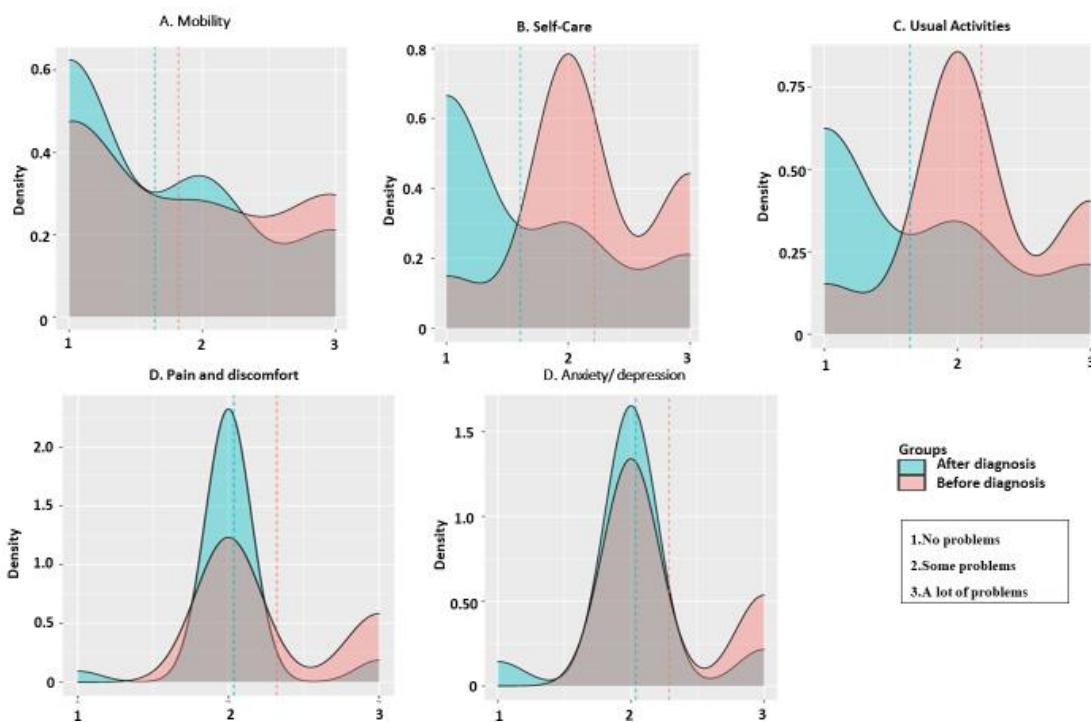


Figure 5.HRQOL using EQ 5D Y of IEI Group 2 (8 to 15 Years old)

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Table 1. HRQOL KIDSCREEN difference between early and late diagnosed groups of IEI children

		Group 1: 8 to 11 Years old			Group 2: 12 to 18 Years old		
		Before Diagnostic	After Diagnostic and IGIV	P-Value	Before Diagnostic	After Diagnostic and IGIV	P-Value
Physical Well-being	Mean (SD)	21,25	36,62	<0,005**	24,3	33,65	<0,005**
	Median (range)	20,7	38,47		30,56	39,47	
Psychological Well-being	Mean (SD)	25,45	35,49	<0,005**	26,93	34,55	<0,005**
	Median (range)	28,62	36,9		28,62	36,9	
Moods & Emotions	Mean (SD)	38,32	38,19	>0,005	35,47	39,76	<0,005**
	Median (range)	36,69	36,69		36,69	36,69	
Self-Perception	Mean (SD)	43,49	43,92	>0,005	42,86	42,16	>0,005
	Median (range)	42,5	42,5		41,83	40,51	
Autonomy	Mean (SD)	29,31	38,21	<0,005**	30,64	38,18	<0,005*
	Median (range)	31,56	40,53		31,56	40,53	
Parent Relation & Home Life	Mean (SD)	44,63	45,3	>0,005	44,38	44,8	>0,005
	Median (range)	45,72	45,72		45,72	45,72	
Financial Resources	Mean (SD)	20,21	34,74	<0,005**	22,21	36,34	<0,005**
	Median (range)	21,24	34,2		21,25	35,4	
Social Support & Peers	Mean (SD)	17,68	36,11	<0,005**	25,06	33,62	<0,005**
	Median (range)	9,39	39,48		30,94	39,48	
School Environment	Mean (SD)	25,72	45,02	<0,005**	27,04	41,16	<0,005**
	Median (range)	23,93	46,35		33,85	46,93	
Social Acceptance (Bullying)	Mean (SD)	30,02	33,01	>0,005	32,02	35,01	>0,005
	Median (range)	31,12	35,31		33,12	32,31	

The HRQOL Domains covered by the EQ 5D Y questionnaire are A). Mobility, B). Self-care, C). Usual Activities, D). pain and discomfort and E). Anxiety/depression. after measuring the HRQOL domains of our patients before (pink) and after the diagnosis (blue), we observe an improvement in all domains (P-value<0.05) except the Anxiety/ depression and pain and discomfort and mobility with insignificant p-value >0.005.

For group 1 (children aged from 8 to 11 years old), after the diagnosis and Ig treatment, we observe an improvement in the physical well-being, psychological well-being, autonomy, financial resources, social support & peers and school environment HRQOL dimensions of KIDSCREEN-52. For group 2 (children aged from 12 to 18 years old), after the diagnosis and Ig treatment, we observe an improvement in physical well-being, psychological well-being, autonomy, financial resources, social support & peers, school environment, and mood & emotions HRQOL dimensions of KIDSCREEN-52.

The results of the KIDSCREEN questionnaire suggested that our patients had a low generic QoL. The KIDSCREEN results can only be considered dimension by dimension. For both parametric and non-parametric analyses, all the scores are significantly lower than the instrument reference score of 50.

DISCUSSION

In this study, we measure the health-related quality of life of IEI patients before and after the diagnostic (n=54). The HRQOL scores of our patients before the diagnosis is lower than the HRQOL Scores after the diagnosis and IGIV using the two generic instruments KIDSCREEN and EQ 5D Y. Health Related quality of life of IEI patients KIDSCREEN -52 mean score is lower than the reference general population KIDSCREEN mean score of 50 for all of the HRQOL KIDSCREEN domains. Significant improvements were also observed in all the HRQOL domains (physical, psychological, financial, Social Support, Social Acceptance and Autonomy after the diagnosis except mood and emotions and parent relations and home.

The general HRQOL index scores of EQ 5D Y for children aged from 4 to 7 and from 8 to 15 years old after the diagnosis are better than the HRQOL scores before the diagnosis (P-values < 0.05).

The HRQOL Domains covered by the EQ 5D Y questionnaire are Mobility, Anxiety/ depression, pain/ discomfort, usual activities and self-care. After measuring the HRQOL domains of our patients before and after the diagnosis, we remarque the improvement of the HRQOL after diagnosis in all domains (P-value<0.05) except the Anxiety/ depression with insignificant p-value >0.005 for patients aged

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from 4 to 7 years and except Anxiety/ depression and pain and discomfort with insignificant p-value >0.005 for children aged from 8 to 15 years.

Table 2. Discussion of the findings about HRQOL of children with IEI and Mucoviscidosis

	Study/number of patients/year/countries	IEI/PID	HRQOL tools	Findings
Primary Immune deficiency	Hamid et al. 2018 [3]	SCID patients	PedsQL	The SCID patients have a lower quality of life scores using PedsQL due to delays in diagnostics.
	2011, Iran, 36 patients [5]	CVID, HIgM, XLA	SF-36	IEI patients had lower quality of life before the diagnosis and the delays in diagnosis affect the HRQOL of patients Patients with long delay diagnosis showed significantly lower SF36 scores (p = 0.003)
	[9](Iran, 70 patients)	CVID, XLA, HIgM, SIgAD	PedsQL, SF-36	Iranian IEI patients have significantly lower scores in both mental and physical components compared to the normal population
	[10], UK, 85 patients	XLA, CVID, HIgM	PedsQL, SDQ	CVID patients experienced more complications and had lower Qol scores
Mucoviscidosis	Anne Marie Nathan et Al, UK, 2010, 78 patients	Mucoviscidosis	SF-36, SGRQ	Patients with the highest treatment burden had worse QOL Positive correlation between time since diagnosis and improvement in perceived QOL

None of the IEI quality of life studies used the KIDSCREEN and EQ-5D-Y questionnaires but in table 2, all the HRQOL affirm that the diagnosis and treatment improve the HRQOL of IEI patients also the Mucoviscidosis patient's quality of life.

CONCLUSIONS

For the first time, we use the KIDSCEEN and EQ-5D-Y HRQOL questionnaires with the Moroccan patient, which has proved that the quality of life of our patients is low compared to the general population. This is an improvement of the HRQOL of IEI patients after the diagnosis and Ig treatment. After using the KIDSCREEN-52 HRQOL questionnaire, we got insights into all the factors that affect the quality of life of our patients such as lack of financial resources, access to schooling, social acceptance, and mood and emotions, these insights consist of a call to actions for the community to support the IEI patients. The measurement of the HRQOL is very important for the health care service providers and for the patients and their families.

More studies should be conducted after our study to know what are the main factors that affect the HRQOL of IEI patients except the diagnostic delay and the lack of IgIV treatment.

Ethics approval and consent to participate

Consent for publication

Availability of data and materials

Competing interests

The authors declare no competing interests.

Authors' contributions

All the authors wrote the drafts of the manuscript, prepared the tables, and revised the original manuscripts for resubmission. All co-authors contributed to and edited drafts of the original and revised manuscripts and tables and approved the final submitted version.

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