



Quality of Life among Children with Osteogenesis Imperfecta Receiving Bisphosphonate Therapy Before and during the 1st Year of the COVID-19 Pandemic in Dr. Soetomo Hospital, Surabaya

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Abstract

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BACKGROUND: Osteogenesis imperfecta (OI) is a chronic illness caused by a connective tissue disorder that may lead to frequent fractures. Therefore, it may influence the quality of life (QoL). The study on QoL among children with OI during the coronavirus disease-19 (COVID-19) pandemic is still limited.

AIM: This study aims to evaluate QoL before and during the COVID-19 pandemic in children with OI.

METHODS: This cross-sectional study took place in the Pediatric Endocrinology Outpatient Clinic at Dr. Soetomo General Hospital, Surabaya, in 2020. The pre-pandemic data came from 2019 medical records. The questionnaire used was the Pediatric Quality of Life Inventory (PedsQL) 4.0 generic core. Twenty-two patients joined the study; 11/22 of them were girls.

RESULTS: The mean age, fracture, and frequency of zoledronic acid treatment were 6.9 years old, 2.5×/year, and 7.1×/year, respectively. The PedsQL comparisons before and during the first year of the COVID-19 pandemic in each dimension were: Physical (49.57 vs. 42.76; $p = 0.001$), emotional (63.41 vs. 54.54; $p = 0.001$), social (58.86 vs. 53.86; $p = 0.015$), and school functioning (66.13 vs. 56.74; $p = 0.001$), respectively. The most affected dimension was school functioning (mean difference (minimum–maximum): (–9.39) (–14.28–[–4.49])), whereas the physical, emotional, and social functioning were 6.81 (3.43–10.19), 8.86 (5.06–12.67), and –5.00 (–8.93–[–1.07]), respectively.

CONCLUSION: The QoL in children with OI during the COVID-19 pandemic was worst, especially in the school functioning dimension. Online consultation options may be beneficial to improving the QoL.

Introduction

The coronavirus disease-19 (COVID-19) pandemic is wreaking havoc on a variety of industries, including the healthcare system [1]. Chronic disease patients have found it difficult to visit hospitals and obtain medicines due to mass quarantine. Travel restrictions were enacted to overcome the viral spread and spike in deaths, putting them at risk of worsening their condition [2], [3]. People with chronic diseases are the vulnerable populations with lower quality of life (QoL) during this COVID-19 pandemic [4].

Osteogenesis imperfecta (OI) is a congenital abnormality autosomal dominant connective tissue disorder caused by mutations in COL1A1 and COL1A2 [5]. The OI incidence increases from year to year. The estimated OI incidence is approximately around one per 15,000 or 20,000 globally. The case occurrence ranges from 6 to 7 per 100,000 births [6], [7]. The Indonesian Pediatric Endocrine Working Group showed that 118 children suffered from OI in Indonesia.

OI children require multidisciplinary management and bisphosphonate treatment for a long time to reduce bone loss. This management and

treatment have a major impact on the patient's QoL: sleep quality, pain in daily activities, medical care needs, enthusiasm in living daily life, ability to walk around, and satisfaction with performance [8]. The COVID-19 pandemic burdens the health-care system throughout the world. Medical services such as bisphosphonate treatment and rehabilitation in individuals with OI, which have long-term goals to optimize the health and well-being of bone fragility and deformity, will be disrupted due to a non-routine control at the hospital.

QoL analysis on OI is essential for evaluating patient outcomes and well-being. Research related to the QoL of children with OI in the COVID-19 pandemic is still limited. This study aimed to compare QoL before and during the 1st year of the COVID-19 pandemic in children with OI.

Materials and Methods

Sample

This study consisted of children and adolescents diagnosed with OI Types I–VII. The

types are according to OI's Sillence *et al.* and Glorieux classification [9]. The patients with OI are registered at the Pediatric Endocrinology Outpatient Clinic of Dr. Soetomo General Hospital, Surabaya, Indonesia.

The inclusion criteria for the subjects were as follows: Children aged 2–18 years old diagnosed with OI, parents, or caregivers who could communicate with researchers and fill out questionnaires, and children whose caregivers consented to participate in this study. The exclusion criteria were critically ill and required pediatric intensive care unit care. This study was conducted based on the Declaration of Helsinki and approved by Ethical Board Committee at Dr. Soetomo General Hospital (No. 2026/KEPK/VII/2020).

Data collection

This descriptive and observational study was conducted with a cross-sectional design from July 16, 2020, to July 15, 2021. Subjects were interviewed over the phone to collect basic data, and the pediatric quality of life inventory (PedsQL) questionnaires were distributed online to participants. The researcher obtained informed consent from the parents or caregivers about this study before they completed the questionnaires. The same team compiled all the procedures throughout the study.

Characteristic form

The demographics form consisted of questions about gender, age, and disease related to the topics such as OI, number of fractures, sites of fracture, number of zoledronic acids administered, and parents or caregiver's educational background.

Pediatric quality of life inventory

The PedsQL™ 4.0 generic core was used to assess the QoL. It was translated into Bahasa Indonesia by the Mapi Research team. This self-report instrument consists of 23 items in four domains: Physical functioning (eight items), emotional functioning (five items), social functioning (five items), and school functioning (five items). Responses are used to calculate the total psychosocial health and physical summary scores. The scores were summarized according to a statistical model established by the authors of the PedsQL™ 4.0 generic core. Fourteen parent proxy-report includes ages 2–4 (toddler), 5–7 (young child), 8–12 (child), and 13–18 (adolescent). Moreover, it assesses parents' perceptions of their child's PedsQL [10], [11].

They were expressed as transformed scores on a 0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0), with higher scores indicating better QoL. If

more than 50% of the items on the scale are missing, the scale score is not computed. In numerous PedsQL studies published since 2001, items on the PedsQL had minimal missing responses, suggesting that children and parents are willing and able to provide good quality data regarding the child's QoL [11].

The validity and reliability of this PedsQL were demonstrated in a study by Varni *et al.* [10] and indicated a good result. Validity is also determined by predicting the patients' and their parents' morbidity and disease burden. As a result, reliability is defined as the consistency of results across multiple tests. Furthermore, statistics from Universitas Airlangga tested the validity and reliability of the PedsQL questionnaire, which were valid.

Statistical analysis

The data analysis was done using the SPSS 17.0 software (IBM SPSS; Armonk, NY, USA). Element's mean and standard deviation (SD) were used to calculate the baseline and clinical characteristics data. The Shapiro–Wilk test was used to determine normality because the subject was <50. The social, school, and total scores data were analyzed using a paired *t*-test because they are normally distributed. Meanwhile, physical and emotional dimensions were analyzed using Wilcoxon signed-rank test because they were not normally distributed.

Results

Clinical characteristics

This study comprised 22 OI children with the same number of males and females, with the mean age as 6.96 years old. The education level of 13 caregivers was mainly high school graduates. The mean total AZ therapy that was administered to OI children was 7.14 (SD 4.32) times. The mean number of fractures in the past year was 2.50 (SD 6.51) times, with the femur being the most common fracture site in 17 children with OI. Table 1 shows the study participants' characteristics.

Table 2 presents the comparison of the PedsQL before and during the 1st year of the COVID-19 pandemic. The comparisons in each dimension were: Physical (49.57 vs. 42.76; $p = 0.001$), emotional (63.41 vs. 54.54; $p = 0.001$), social (58.86 vs. 53.86; $p = 0.015$), and school functioning (66.13 vs. 56.74; $p = 0.001$), respectively. The most affected dimension among PedsQL was school functioning with a mean difference of -9.39 (-14.28 – $[-4.49]$); whereas, the physical, emotional, and social functioning were 6.81 (3.43–10.19), 8.86 (5.06–12.67), and -5.00 (-8.93 – $[-1.07]$), respectively.

Table 1: Characteristic of study participants

Parameters (n = 22)	Frequency, n (%)
Sex	
Male	11 (50)
Female	11 (50)
Age group (years old), mean (± SD)	6.96 (± 4.56)
2-< 5	9 (40.91)
5-< 8	6 (27.27)
8-< 13	3 (13.64)
13-18	4 (18.18)
Education level of caregiver	
Elementary school	0
Junior high school	5 (22.73)
Senior high school	13 (59.09)
University	4 (18.18)
Fracture site	
Upper arm	2 (9.09)
Lower arm	2 (9.09)
Femur	17 (77.27)
Leg/ankle	1 (4.55)
Frequency of ZA administered, mean (± SD)	7.14 (± 4.32)
≤ 6	12 (54.55)
≥ 6	10 (45.45)
Number of fractures last 1 year, mean (± SD)	2.5 (± 6.51)
< 3	18 (81.82)
≥ 3	4 (18.18)

ZA: Zoledronic acid, n: Number, SD: Standard deviation

Discussion

This study showed that QoL was significantly worse during the 1st year of the COVID-19 pandemic than before the pandemic in every dimension. School functioning became the most affected dimension compared to others, with a mean difference of -9.39 before and during the COVID-19 pandemic. School functioning includes difficulty concentrating in class, forgetting, doing/completing schoolwork, and not attending school. They are not feeling well and do not go to school because they have to go to the doctor or the hospital. A previous study in 2019 stated that patients with type IV OI had a significantly lower QoL score both in social functioning and school functioning domains [12].

During the 1st year of the COVID-19 pandemic, the physical functioning domain was significantly decreased compared to before the COVID-19 pandemic (49.57 vs. 42.76). A similar study from Vanz *et al.* [13] stated that the lowest score on the QoL questionnaire

Table 2: Comparison of the quality of life in children with osteogenesis imperfecta before and during the first year of the coronavirus disease-19 pandemic based on caregiver's or parent's perspectives

Domains (functioning) (before/during the 1 st year of the COVID-19 pandemic)	Mean (± SD)/median (minimum-maximum)	Mean difference (95% CI)	p
Physical			
Before	49.57 (3.12-100.0)	6.81 (3.43-10.19)	0.001 ^a
During	42.76 (3.10-75.0)		
Emotional			
Before	63.41 (0-100.0)	8.86 (5.06-12.67)	0.001 ^a
During	54.54 (0-75.0)		
Social			
Before	58.86 (± 23.14)	-5.00 (-8.93--1.07)	0.015 ^b
During	53.86 (± 17.25)		
School			
Before	66.14 (± 28.06)	-9.39 (-14.28--4.49)	0.001 ^b
During	56.74 (± 20.83)		
Total score			
Before	59.49 (± 21.39)	-7.52 (-10.49--4.54)	<0.001 ^b
During	51.98 (± 16.06)		

a: Wilcoxon signed-rank test, b: paired t-test, significant (p < 0.05), COVID-19: Coronavirus disease-19, CI: Confidence interval, SD: Standard deviation.

during the COVID-19 pandemic was in the physical functioning domain. Limited physical activity during the COVID-19 pandemic negatively impacts QoL in children with OI. They quickly got tired, which increased pain or discomfort.

High body Z-score, bone mineral density (BMD) Z-score lumbosacral, BMD Z-score femoral neck, the severity of OI, and fracture frequency correlated with QoL scores of children with OI. Patients with physical disabilities can have higher well-being and life satisfaction [12].

The social functioning domain includes difficulty getting along with peer groups, inability to do the things that other children can do at their age, or trouble keeping up with friends. The social functioning domain was poorer during the COVID-19 pandemic than before the COVID-19 pandemic. Limited social activities may cause this condition during the COVID-19 pandemic, and children cannot play with their peer groups. A review conducted by Thompson in 2016 [14] stated that adults with bone dysplasia describe varying degrees of social isolation and its effect on educational achievement. Celin and Fano (2016) [15] showed that 22% of children with OI had never participated in social activities.

The emotional functioning domain during the COVID-19 pandemic also significantly decreases compared to before the COVID-19 pandemic. The PedsQL questionnaire on the emotional functioning domain includes items like feeling afraid of anything to do with the child, sad or moody, irritable, sleep problems, and worrying about what will happen to the child. Adolescents diagnosed with OI and their parents have described challenges in daily life that include psychosocial and emotional stressors that extend to all family members. A study in the United States found that parents of children with functional limitations were more depressed than parents whose children experience others circumstances. The study of Vanz *et al.* [16] stated that a decrease in QoL of caregivers of children with OI was due to the disease itself.

Children with other chronic diseases during the COVID-19 pandemic reported the same QoL. Anxiety due to procedure and treatment issues increased during this period. Rochmah *et al.* [17] and Önal *et al.* [18] have shown that the QoL parameters, including cognitive condition, physical appearance perceived, and communication skills showed a significant decrease (p < 0.05). Meanwhile, a study from Van Gorp *et al.* (2021) [19] in the Netherlands stated no significant difference in the QoL of children with cancer in the outpatient clinics before and after the COVID-19 pandemic. The country's health-care system can explain these controversies. The psychosocial needs of children and families with cancer continued without interruption because they had telehealth services during the COVID-19 pandemic.

This study included 22 children with OI, with the same proportion of males and females and a mean age

of 6.96 (SD 4.56) years. Newacheck *et al.* [20] revealed that OI has no gender preference between males and females, and the prevalence was equal across races. Most patients had a mean age distribution of 8.67 years, implying that the most affected patients were under 10. In the past year, the mean number of fractures was 2.50 (SD 6.51) times, with the femur being the most common fracture site in 17 children with OI [21].

The study's limitation is that because the interview was conducted online, the signal was occasionally poor, causing the interview process to be disrupted. The interview could not be too long because the patient was fussy when left alone for too long by the caregiver.

Conclusion

The COVID-19 pandemic affected the QoL of children with OI, particularly in the school functioning dimension. The possibility of telehealth consultation could help to improve their QoL.

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