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April 22, 2022



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Determinant Factors of the Quality of Life in Children with Osteogenesis Imperfecta during the COVID-19 Pandemic

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Abstract

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BACKGROUND: Osteogenesis imperfecta (OI) is a common chronic illness with increasing prevalence. Coronavirus disease 2019 (COVID-19) and large society restriction policies in Indonesia cause problems and might affect the quality of life (QoL) of children with OI.

AIM: The objective of the study was to evaluate determinant factors (such as number of hospital visits per year, calcium and/or Vitamin D consumption, fear and obstacles of visiting the hospital, and parent's layoff) of OI children's QoL pre and during the 1st year of the COVID-19 pandemic.

METHODS: This was a cross-sectional study design conducted in the Pediatric Endocrinology Outpatient Clinic, Dr. Soetomo Hospital, Surabaya, Indonesia, during the 1st year of COVID-19 pandemic to assess the patient's QoL. This study used a diagnostic group with questionnaires. The instrument included the Pediatric Quality of Life Inventory 4.0 Generic Score, a standardized interview questionnaire comprising questions on the participant characteristics and determinant factors pre and during the COVID-19 pandemic. Analysis of determinant factors pre and during the pandemic used McNemar. Correlation between determinant factors and QoL used linear regression for physical and emotional dimensions and logistic regression for social, school, and total score.

RESULTS: Of the 22 children with OI, 19 had fear of visiting the hospital ($p < 0.001$), and 16 had obstacles to visiting the hospital ($p < 0.01$). Taking calcium and/or Vitamin D supplementation pre and during the COVID-19 pandemic affected school functioning ($p = 0.015$) and the total score ($p = 0.027$).

CONCLUSION: The significant risk factors pre and during COVID-19 were fear of and obstacles to visiting the hospital. Supplementation of calcium and/or Vitamin D pre and during the COVID-19 pandemic significantly impacted school functioning and the total score.

Introduction

The WHO has declared coronavirus disease 2019 (COVID-19) a public health emergency of international concern. The first COVID-19 case occurred in a group of people in Wuhan, China, who were diagnosed with unknown pneumonia in December 2019, and COVID-19 has since spread worldwide. To prevent the spread of the disease, the government has implemented several strategies, including policies involving large-scale social restrictions [1], [2].

On the other hand, this policy disturbs daily activities and could have significant health and well-being implications [3]. In patients with chronic illnesses such as osteogenesis imperfecta (OI) who require follow-up visits, examinations, medication refills, and access to health facilities, travel restrictions can be a significant issue; therefore, the patients cannot be routinely checked by the doctors [4], [5], [6]. Chronic disease patients may find it difficult to visit hospitals during COVID-19, placing them in danger and worsening the condition [7]. Children with chronic

conditions feel afraid when attending the hospital since it is a high-risk location for developing COVID-19 and dread complications [8].

OI is a congenital connective tissue disorder caused by COL1A1 and COL1A2 gene mutations. OI is becoming more common by the year, with an estimated 1:15,000–20,000 people suffering from it worldwide [9], [10]. The prevalence of OI is 4.0–6.7 per 100,000 newborns, according to research from the United States and Finland [10], [11]. According to the data from the Pediatric Endocrine Working Group for pediatric endocrinology, 118 patients in Indonesia are members of the Indonesian OI Forum (FOSTEO).

Bone fragility, osteopenia, skin diseases, blue sclera, OI, and hearing loss are symptoms of this condition that require comprehensive care that significantly impacts the patient's quality of life (QoL) [3], [10], [11]. Research on the determinant factors impacting the QoL of children with OI in the COVID-19 pandemic era is still limited. The purpose of the present study was to evaluate the determinant factors such as number of hospital visit per year, calcium and/or Vitamin D consumption, fear and obstacles of

visiting the hospital, and also parent's lay off of the QoL in children with OI pre and during the 1st year of the COVID-19 pandemic.

Methods

Children and adolescents with OI types I–IV, as defined by the Silience classification [12], participated in this study. The patients were registered at Surabaya's Dr. Soetomo General Hospital's Pediatric Endocrinology Outpatient Clinic.

The inclusion criteria for the subjects were children aged 2–18 years with OI, parents/caregivers who could communicate with researchers and fill out questionnaires, and children whose caregivers agreed to participate in this study. Patients who were critically ill and required PICU care were excluded. The Dr. Soetomo General Hospital Ethics Board Committee approved this study (No. 2026/KEPK/VII/2020).

Data gathering

This study design was cross-sectional and conducted from July 16, 2020 to July 15, 2021. The pediatric quality of life inventory (PedsQL) questionnaires was distributed online to participants, and subjects were interviewed over the phone to collect basic data. The researcher informed the parents or caregivers about the study and asked for their consent before completing the questionnaires. When the parents or caregivers decided to participate, the family signed the informed consent. It was then given back to the researcher. Throughout the study, the same team compiled all of the procedures.

Socio-demographic form

The socio-demographic form consisted of gender, age, disease related to OI, parent's/caregiver's educational background, and type of OI.

Pediatric quality of life inventory

Varni *et al.* developed the PedsQL™ 4.0 Generic Core to assess QoL. It was translated into Bahasa Indonesia by the Mapi Research Team. This self-report instrument covers four domains: physical functioning (eight items), emotional functioning (five items), social functioning (five items), and school functioning (five items). The responses are used to calculate the total, psychosocial health, and physical summary scores. To summarize the results, the authors of PedsQL™ 4.0.14 created a statistical model. Parent proxy - the report assesses parents' perceptions of their child's PedsQL

and includes ages 2–4 (toddler), 5–7 (young child), 8–12 (child), and 13–18 (adolescent) and evaluates parents' views on their child's PedsQoL [13], [14].

They were converted to a 0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0), with higher scores indicating better QoL. The scale score is not computed if more than half of the items on the scale are missing. Items on the PedsQL had minimal missing responses in several PedsQL studies published since 2001, implying that children and parents are willing and able to provide good quality data regarding the child's QoL [14].

The validity and reliability of this PedsQL study were demonstrated by Varni *et al.* and determined to be a good result. Predicting the subjects' and parents' morbidity and disease burden also determines validity. As a result, reliability refers to the consistency of results over time and across different tests. Universitas Airlangga tested the validity and reliability of the PedsQL questionnaire, and it was found to be valid [14].

Determinant factors

The determinant factors in this study were compiled based on several previous studies. The number of hospital visits extracted from Alshahrani *et al.* stated that access changes to health services and the economic burden during the COVID-19 pandemic impact young people's mental and physical well-being worldwide, especially those with chronic diseases [8]. Calcium and/or Vitamin D supplementation was compiled by Otaify *et al.*, Palomo *et al.*, and Vuorimies *et al.* They found that those supplementations were necessary while receiving Zoledronic Acid treatment in OI children to avoid and correct hypocalcemia and Vitamin D deficiency [15], [16], [17].

Anxiety and parents' layoff during a pandemic were based on what Adibelli and Sümen stated: That there is an increase in parental layoff and anxiety during a pandemic [18]. The obstacles to visiting the hospital were from Sutthisompohn and Kusol stated that conditions in which caregivers have obstacles to control have a significant and negative impact on the quality of life of children with chronic diseases [19].

Data analysis

A Descriptive analysis was performed to explain the subject's characteristics. If data are normally distributed, the mean and standard deviation will be visible. McNemar employed determinant factors analysis both before and during the pandemic. Linear regression was used to identify determinants of QoL in the physical and emotional dimensions. For the social, school, and total score dimensions, logistic regression was used. The significant level ($p < 0.05$) is set at 5%. The data were analyzed using the SPSS 17.0 program (IBM SPSS, Armonk, NY, USA).

Results

The results showed that the total sample consisted of 22 children with OI, with a mean age of 6.96 years old. The caregivers' academic level was primarily high school graduates, and type 3 became the most common OI type based on the silence classification [12]. The clinical characteristic is described in Table 1.

Table 1: Characteristic of the study participants

Parameters (n = 22)	Frequency n (%)	Mean (± SD)
Sex		
Male	11 (50)	
Female	11 (50)	
Age group (years)		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		
Junior high school	5 (22.73)	
Senior high school	13 (59.09)	
University	4 (18.18)	
Type of OI		
1	2 (9.1)	
3	17 (77.3)	
4	3 (13.6)	

n = number.

The frequency of anxiety or fear and obstacles to visiting the hospital during the COVID-19 pandemic increased significantly compared to before ($p < 0.001$; $p < 0.002$). The frequency of hospital visits per year, the proportion of habitual factors taking calcium and/or Vitamin D supplementation, and the impact of layoffs on caregivers/parents are described in Table 2.

This study found that the mean difference in physical, emotional, social, and school functioning before and during the 1st year of the COVID-19 pandemic for each determinant factor was decreased, which was

Table 2: Determinant factors in patients with OI before and during the COVID-19 pandemic

Determinant factors	Pre/during the COVID-19 pandemic	Frequency n (%)	P
No. of hospital visit per year	Pre		
	< 3	(50)	0.065*
	≥ 3	11 (50)	
	During		
< 3	18 (81.8)		
Calcium and/or vitamin D supplementation consumption	Pre		
	Yes	19 (86.4)	0.063*
	No	3 (13.6)	
	During		
Yes	14 (63.6)		
Anxiety/fear of visiting the hospital	Pre		
	Yes	2 (9.1)	< 0.001**
	No	20 (90.9)	
	During		
Yes	19 (86.4)		
Obstacles for visiting the hospital	Pre		
	Yes	4 (18.2)	0.002**
	No	18 (81.8)	
	During		
Yes	16 (72.7)		
Parent's layoff	Pre		
	Yes	2 (9.1)	0.087*
	No	20 (90.9)	
	During		
Yes	6 (27.3)		
	No	16 (72.7)	

*McNemar, **significant ($p < 0.05$).

represented by a number <0. However, there was an increase in social functioning by 2.50 (±5.0) from the number of hospital visits. The decrease in the greatest mean difference in school functioning for children who did not take calcium and/or vitamin D supplementation was -16.66 (±9.04). Determinant factors affecting QoL of OI children pre and during COVID-19 pandemic are described in Table 3.

In statistical analysis, it was found that the mean difference of physical and emotional functioning was normally distributed data, so a logistic regression test was performed. A linear regression test was performed on the mean difference between social functioning, school functioning, total score, and normally distributed data. No determinant factors are significantly affected in physical, emotional, or social functioning. Taking calcium and/or Vitamin D supplementation before and during the COVID-19 pandemic significantly affected school functioning and the total score with p-values of 0.015 and 0.027, respectively.

Discussion

Calcium and/or Vitamin D supplementation pre and during the COVID-19 pandemic affected school functioning and the total score significantly with p-values of 0.015 and 0.027, respectively. Calcium and/or Vitamin D supplementation during the 1st year of the COVID-19 pandemic and a greater decrease occurred in children with OI who did not regularly take supplementation. A study by Otaify *et al.* on OI children, all patients were on continuous calcium supplementation before and during intravenous zoledronic acid treatment. The patient took an additional dose of calcium carbonate (50 mg/kg/day) to avoid hypocalcemia, and the dose was continuously adjusted according to laboratory follow-up serum calcium results [15]. Vuorimies *et al.* reported a transient decrease in serum calcium during infusion with zoledronate and two patients developed symptoms of severe hypocalcemia require intravenous calcium treatment [17].

During the 1st year of the COVID-19 pandemic, 19 out of 20 caregivers or parents admitted to having a fear of visiting the hospital ($p < 0.001$). However, it did not have a significant impact on the decreased QoL of children with OI. According to a study conducted by Alshahrani *et al.* in children with chronic diseases such as cancer, 55.3% of patients did not feel safe visiting the hospital during an outbreak, primarily due to apprehension about contracting viruses in high-risk environments such as hospitals. Approximately 94.8% of patients were concerned about contracting the virus or infecting family members. By 53.5% of patients 8, patients with cancer appear to be more concerned about complications from contracting the virus than

Table 3: The determinant factors affecting the quality of life (QoL) of children with OI during the 1st year of the COVID-19 pandemic

Determinant factors (during the 1 st year of the COVID-19 pandemic)	Mean (± SD) of mean difference of the functioning in QoL pre and during the 1 st year of the COVID-19 pandemic				
	Physical	Emotional	Social	School	Total score
No. of hospital visit per year					
< 3	-8.16 (± 7.81)	-9.44 (± 8.89)	-6.67 (± 8.74)	-10.36 (± 11.79)	-8.66 (± 6.84)
≥ 3	-0.77 (± 1.58)	-6.25 (± 7.50)	2.50 (± 5.0)	-5.01 (± 5.76)	-2.39 (± 2.75)
Consumption of calcium and/or vitamin D					
Yes	-5.13 (± 6.89)	-7.86 (± 8.25)	-2.50 (± 8.49)	-5.23 (± 10.07)	-5.18 (± 5.67)
No	-9.75 (± 8.42)	-10.62 (± 9.42)	-9.37 (± 8.21)	-16.66 (± 9.04)	-11.61 (± 6.74)
Having fear of visiting the hospital					
Yes	-7.23 (± 8.0)	-8.16 (± 8.20)	-4.74 (± 9.35)	-7.80 (± 10.59)	-6.98 (± 6.91)
No	-4.15 (± 4.75)	-13.33 (± 11.55)	-6.67 (± 5.77)	-19.43 (± 9.64)	-10.91 (± 4.91)
Obstacles of visiting the hospital					
Yes	-8.19 (± 8.38)	-8.75 (± 8.27)	-5.62 (± 9.29)	-8.12 (± 11.41)	-7.67 (± 7.27)
No	-3.12 (± 3.40)	-9.17 (± 10.21)	-3.33 (± 8.16)	-12.77 (± 10.09)	-7.10 (± 5.52)
Parents loss their jobs					
Yes	-7.81 (± 9.22)	-10.83 (± 10.21)	-5.83 (± 7.36)	-2.49 (± 11.36)	-6.76 (± 6.67)
No	-6.81 (± 7.63)	-8.12 (± 8.14)	-4.69 (± 9.57)	-11.98 (± 10.06)	-7.80 (± 6.93)

the general population. The study looked at the quality. Despite their fear of visiting the hospital, the patients' lives were unaffected. This study differs from Adıbelli and Sümen, who demonstrated that QoL was self-reported, as well as children's sub-dimensional scores from prospective parents who stated that isolation negatively impacted their mental well-being. Parents' fear of becoming infected can lead to a cycle of infection [18].

This study found that the obstacles to visiting the hospital were significantly different before and during the COVID-19 pandemic but did not statistically affect the decrease in the QoL of patients with OI. Based on interviews, the researchers found that of the 16 caregivers or parents who had difficulties bringing their children to the hospital, most were due to difficulties in accessing public services, either because of the difficulty of finding public transportation or related to the number of roads that were closed or the need for a permit, especially when the government launched the large society restriction program to reduce the number of COVID-19 cases. Sutthisompohn and Kusol stated that conditions in which caregivers have obstacles to control have a significant and negative impact on the QoL of children with chronic diseases. Children may require continuous hospital visits for treatment but have limited physical movement. They cannot follow daily routines and experience fatigue, pain, anxiety, and fear that result in behavioral regression [19]. Children and families experiencing increased anxiety during the pandemic are supported by more frequent telemedicine conferences with treating physicians and referrals to psychiatric and psychological services [8].

During the COVID-19 pandemic, there were an increase in parent's layoffs and a decrease in QoL, but the differences were not statistically significant. This study found that the decline in QoL was greater in working parents. Non-working parents may spend more time at home to ensure that their children are happy. School functions experienced the smallest decline when compared to other functions. It is also possible that when the COVID-19 pandemic was declared in Indonesia, online schools were put in place, giving caregivers more time to accompany their children to class. Parents who lose their jobs will face financial

difficulties. According to Sutthisompohn and Kusol's research, some parents or caregivers need to quit their jobs because their children require hospitalization and need regular care, which means reduced income [19].

There was a decrease in hospital visits during the pandemic compared to the pre-pandemic. Subjects who visited <3 times per year had a decreased QoL, and subjects who visited more than three times per year had increased social function. QoL was not significantly different compared to the number of hospital visits. The study by Alshahrani *et al.* found that changes in access to health services and the economic burden during the COVID-19 pandemic have impacted the mental and physical well-being of young people worldwide, especially among those with chronic diseases [8].

There were 22 subjects enrolled in this study with the same proportion among gender. Similarly, Newacheck stated that there was no difference in gender preference in children with OI [20]. In contrast, Kabengo *et al.* found that female prevalence was more profound than male [21]. The mean age of the present study was 6.96 years. A study from Kabengo *et al.* found that most of the patients diagnosed with OI were under 10 years old [21]. Type III OI was the most common type in this study. This finding is in line with the study of Rothschild *et al.* that 37.1% of subjects had type III OI compared to other types [22].

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

Taking calcium and/or Vitamin D supplements pre and during COVID-19 had a significantly affecting on OI children's school and total score. Fear and barriers to visiting the hospital during the pandemic were significantly different from before.

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Author Contributions

Nur Rochmah and Rahma Ira Mustikasari, designed the study and statistical analysis; Muhamamd Faizi and Irwanto Irwanto supervisor on data assessment and publication process. All authors contributed to the literature search and final approval of the version to be submitted. The literature search and final approval of the version to be submitted were done by all authors.

Disclosure

The authors declare that there are no conflicts of interest in this work.

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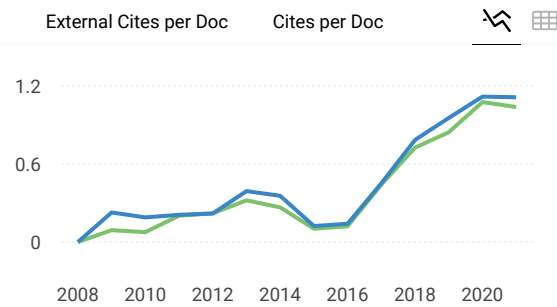
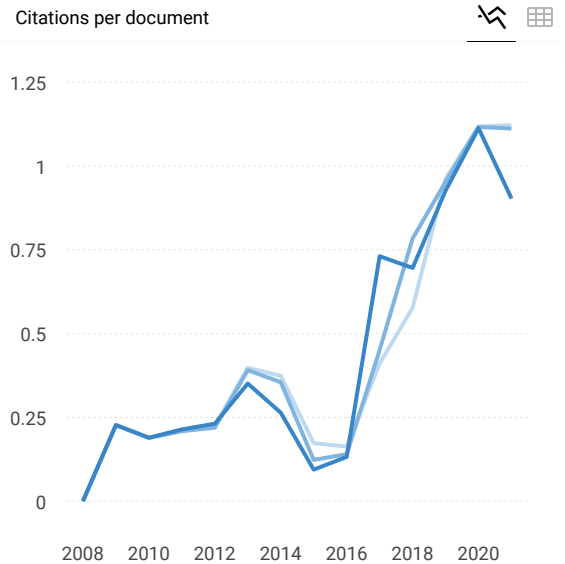
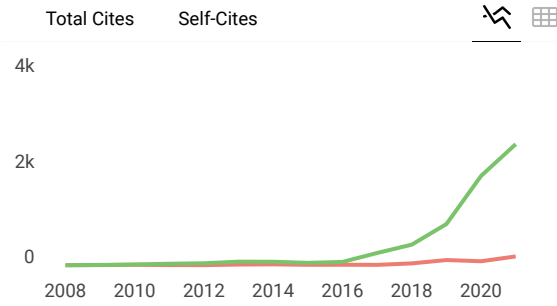
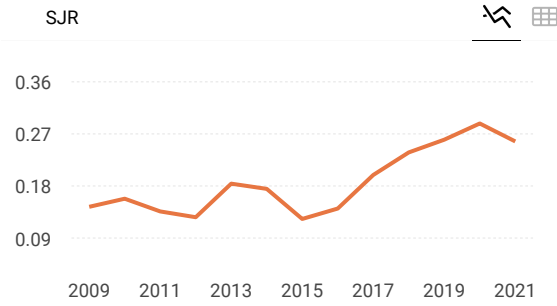
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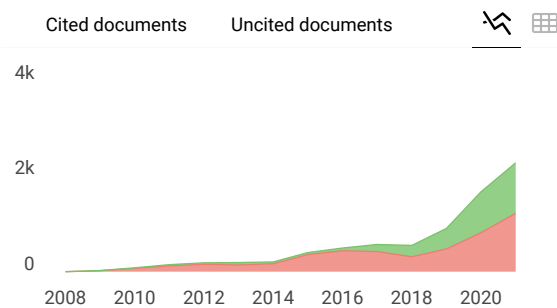
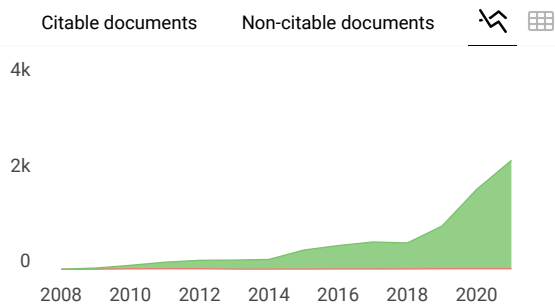
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