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Original Article

HRQoL Evaluation of Pediatric Osteogenesis Imperfecta with Zoledronic Acid Therapy

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ABSTRACT

Background: Zoledronic acid, a bisphosphonate, increases bone mineral density (BMD), which can reduce clinical manifestations in osteogenesis imperfecta. This study investigates the impact of zoledronic acid therapy on the quality of life of pediatric patients with osteogenesis imperfecta.
Methods: A retrospective analytical study was conducted on 16 pediatric patients with osteogenesis imperfecta who received intravenous zoledronic acid. Quality of life was assessed before and after therapy using the PedsQL 4.0 questionnaire. A paired t-test was used to analyze changes in each domain of the PedsQL 4.0. The results were expressed as an adjusted odds ratio with a 95% confidence interval. A p <0.05 was considered statistically significant.
Results: A significant increase was found in the children's self-reported social performance (+12.083, p = 0.023) and proxy-reported physical performance, social performance, and total score (+14.844, p = 0.006; +10.625, p = 0.010; +10.364, p = 0.006, respectively). An insignificant increase was found in child-reported physical performance, school performance, and total score (+8.833, p = 0.148; +5.000, p = 0.359; +7.065, p = 0.115, respectively), and proxy-reported emotional and school performance (+2.500, p = 0.669; +6.250, p = 0.167, respectively). An insignificant decrease was found in child-reported emotional performance (-2.500, p = 0.669).
Conclusion: After receiving bisphosphonate therapy, pediatric patients with osteogenesis imperfecta experienced an increased quality of life. Physical and social aspects showed the greatest improvement. Emotional well-being showed the lowest increase in the child's perception, with a decrease in parent perception after therapy.

Keywords: Bisphosphonate treatment; Human and medicine; Osteogenesis imperfecta; Pediatric; Quality of life

INTRODUCTION

Osteogenesis imperfecta (OI), often called brittle bone disease, is a group of dysplastic bone diseases inherited phenotypically and genetically. Bone deformity and fragility are the main characteristics when detecting osteogenesis imperfecta. Although not a common disease, estimates for the incidence of osteogenesis imperfecta are around 1 per 20,000 to 1 per 10,000 live births worldwide. Osteogenesis imperfecta is usually caused by an autosomal dominant mutation in genes encoding type I collagen (COL1A1 and COL1A2), affecting the quantity or structure of collagen.[1] Patients with osteogenesis imperfecta tend to have a low areal bone mineral density,[2] associated with lower mechanical strength.[3] Fractures involve the spine, ribs, and upper and lower extremities, and the rate varies significantly from less than one to seve ral per year. Other clinical manifestations often encountered are dentinogenesis imperfecta,[4,5] hearing disorders,[6] and joint hypermobility.[7]

Due to the clinical condition experienced by children with osteogenesis imperfecta, they of-

ten have a worse quality of life than normal children. All clinical manifestations are usually associated with a lower quality of life.[8,9] Because of that, zoledronic acid as a bisphosphonate is expected to improve their quality of life. Bisphosphonates are considered to reduce pain, improve deformities, and increase bone mineral density to reduce the frequency of fractures, which is expected to improve quality of life by increasing the patient's confidence and improving the patient's physical condition and function.[10,11] However, the effect of this treatment on quality of life is considered unclear because controlled trials to date have used different definitions and measures from several journals.[12–14] This study focused on quality of life in general. It did not focus on other symptoms as, in a systematic review by Dwan et al.[11], it was mentioned that more research is needed that focuses on general quality of life so then definite conclusions can be drawn. Measurements of quality of life are quite difficult to do. In addition to the various measurement scales and definitions, exact measurements and measuring instruments are also obstacles due to the many factors that need considering. Existing research on quality of life is still lacking and not broad enough because of these differences.

PedsQL 4.0, as a quality-of-life measurement tool, has been widely used in many chronic conditions of children so then comparisons can be made in various conditions.[15] Because there were language differences between the original form of the questionnaire and the place where it was used in this study, a validated translation was needed, and fortunately, the Indonesian translation of this questionnaire has been validated by Mapi™ Research Group.[16] On this basis, PedsQL 4.0 was used as a valid measure of quality of life. PedsQL 4.0 has been used several times to measure the quality of life in osteogenesis imperfecta because, in osteogenesis imperfecta, the condition of patients with bone fragility greatly affects their physical and social abilities. Therefore, this questionnaire was chosen for this study.[17]

In line with what was previously mentioned, pediatric patients with osteogenesis imperfecta will show an increased quality of life in all perceptions and aspects after receiving zoledronic acid as a bisphosphonate therapy compared to before the treatment.[11] Research has been conducted extensively on the quality of life of pediatric patients with osteogenesis imperfecta after receiving zoledronic acid therapy. However, studies on this topic have rarely been conducted in Indonesia. Only case reports were found on this topic at the time of writing this study. On this basis, research was conducted on the quality of life of pediatric patients with osteogenesis imperfecta undergoing bisphosphonate therapy, especially intravenous zoledronic acid. Later, this research can be the basis for clinical implementation and more detailed research to be carried out in the future.

METHODS

Study Design

This study is a descriptive retrospective study consisting of a pre-post comparison with the bivariate analysis method using PedsQL 4.0 questionnaire data from patients with osteogenesis imperfecta. The population studied was pediatric osteogenesis imperfecta patients. The sampling technique of this research was purposive sampling. The variables observed were the population's quality of life before and after receiving zoledronic acid therapy. The data was obtained by conducting interviews via video calls with the respondents (children and parents). Then, the data was processed according to PedsQL 4.0, entered into a statistical computer program, and analyzed using the paired t-test method.

The inclusion criteria used in this study were as follows: Patients and parents/caregivers of patients with osteogenesis imperfecta who underwent outpatient treatment; Pediatric patients 2-18 years old accompanied by their parents/caregivers; Patients must have undergone zoledronic acid therapy; and Willing to be a research subject. The exclusion criteria included: Patients

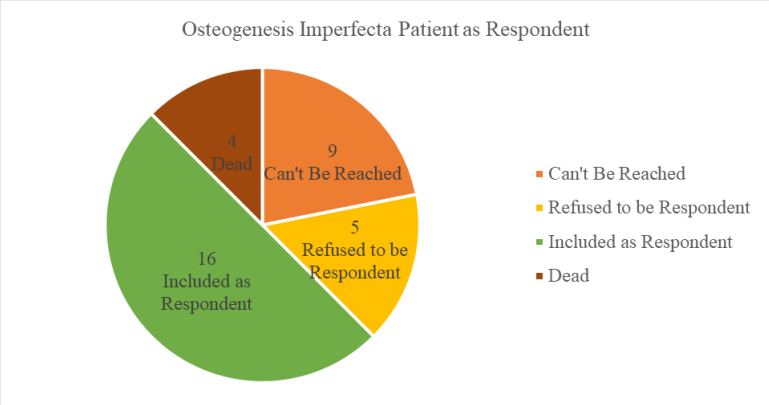

Figure 1. Distribution of Respondent.

with other diseases that are not complications of osteogenesis imperfecta; Patients in a condition that could not allow interviews; Patients experiencing conditions or illnesses that interfere with their quality of life besides osteogenesis imperfecta (undergoing fractures, COVID-19, etc.); and Receiving another form of therapy beside Zoledronic Acid.

In this study, the total initial sample obtained of patients with osteogenesis imperfecta was 34. According to the inclusion and exclusion criteria, there were 16 patients as the final willing participants (Figure 1).

Ethical Clearance

Before collecting the data directly from patients, this research obtained permission and approval from the Research Ethics Committee of Dr. Soetomo General Academic Hospital, with ethical clearance number 0283/KEPK/2021.

Data Collection

The data collection process was carried out using a PedsQL 4.0 questionnaire form. The questionnaire contained 23 question items, consisting of physical, emotional performance, social performance, and school performance. The physical performance score was defined by 8 question items related to how the children's physical abilities work in their daily activities to assess their quality of life. Emotional performance was defined by 5 question items related to the emotional stability of the respondent's children's daily lives, such as whether they often feel sad, afraid, worried, and angry, and questions related to the respondent's sleep quality. The social performance score was defined by 5 question items related to how the child respondents interact and relate to their friends and people around them. The school performance score was defined by 5 question items. In assessing the school performance scores, the PedsQL 4.0 form had different questions according to the age range of the child respondents. For respondents aged 5-18 years, there were 5 questions for the children and parent proxies, while for the respondents aged 2-4 years, there were 3 questions for the parent proxies. Scale reversal was carried out and changed each point of choice to a value of 0-100, namely 0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0. totaled according to each category. In this study, a form for each age was used, and the interviews with the children and parent's proxies were conducted twice to assess the variables needed for the data collection.[15]

Video calls between the parents and pediatric patients and researchers were used as a data collection method because of COVID-19 restrictions. The COVID-19 restrictions had to be considered when conducting the quality-of-life assessment. To reduce bias, all respondents were interviewed by the same researcher. The questions asked were those listed in PedsQL 4.0, accompanied by additional explanations (paraphrases) from the researcher as the interviewer. Interviews with the patients and their parents were conducted separately, and when an interview was conducted on one subject, another subject was not allowed

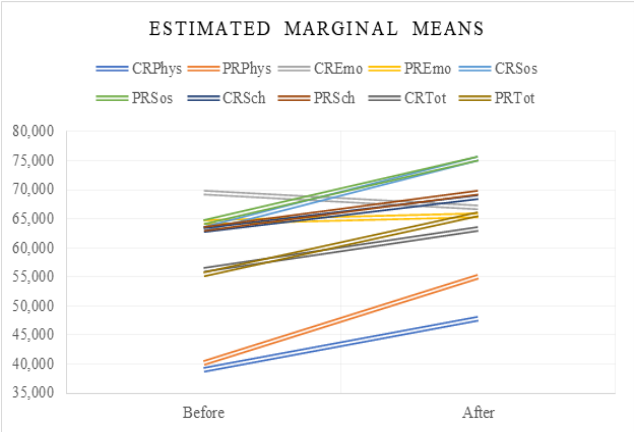

Figure 2. Estimated marginal means.

to be near the subject being interviewed. The interviews had two stages: a retrospective interview regarding the patient's quality of life condition before receiving zoledronic acid therapy and an interview about the patient's quality of life condition after receiving the therapy. In both stages of the interview, a 30-minute lag was given so that the interview's focus was not disturbed, so then the data obtained became more consistent and less biased.[18]

Data Processing

The analysis was carried out using the paired t-test method with two dependent sets of data, namely the data from before and after therapy, to find the significance of the increase or decreases in said data. The first condition for the paired t-test was the conducting of a normality test on the standardized residual of each data because, in this analysis, the data used was parametric data with a normal distribution. If the results obtained from the normality test involved data distributions that were not normal, then it was preferable to use a non-parametric statistical test. In the Shapiro-Wilk normality test, the residuals were standardized for each data on the basis of $p = 0.05$ and the general assumption that $p > 0.05$ was normal and $p < 0.05$ was abnormal. The Shapiro-Wilk method was chosen because the total number of data items was less than 30. All data was normally distributed and so the paired t-test analysis was continued with. The paired t-test was conducted 10 times, consisting of four aspects of the questionnaire and one total score, each consisting of two categories of content, namely the children's reports and proxy reports, which had to be analyzed separately.

Table 1. Respondent's demographic.

		Frequency	Percentage
Sex	Male	10	62,5
	Female	6	37,5
Age	2 - 4 y.o	4	25,0
	5 - 7 y.o	8	50,0
	8 - 12 y.o	1	6,25
	13 – 18 y.o	3	18,75
Duration of Therapy	≤ 2 Years	2	12,5
	> 2 Years	14	87,5

RESULTS

Participant

Table 1 shows the results of the demographic statistics of 16 respondents with osteogenesis imperfecta who participated in this study. The demographic data taken was gender, age, duration of use of zoledronic acid therapy, and age at the start of taking zoledronic acid therapy. The number of patients is shown as a percentage of 16 patients. Most of the respondents were male (62.5%). For the age distribution, most were in the age range of 5 - 7 years (50%). For most patients, zoledronic acid therapy was undertaken for more than two years.

In this study, the respondent patients were divided according to age grouping and respondent type (proxy and children) based on the PedsQL 4.0 questionnaire method of grouping. Some of the data was unobtainable, either because of the form (forms aged 2 - 4 years did not contain reports by the children) or the unavailability of the data (school performance scores for children aged 2 - 4 years).[15]

In the physical performance aspect, the highest increase in score was found in the child's report on respondent B06, with an increase of 50.000 points on average. The lowest decrease was obtained in the report of the child of respondent D10, at -25.000 (Figure 2). In the emotional performance aspect, the highest increase in score was obtained in the parent proxy report

Table 2. PedsQL 4.0 Result

	Respondent	Code	A09	A13	A21	A23	B01	B03	B05	B06	B08	B14	B22	B31	C12	D10	D20	D34
Physical	Child	Before	-	-	-	-	25.000	31.250	25.000	18.750	31.250	25.000	68.750	31.250	46.875	65.625	50.000	50.000
Performance	Report	After	-	-	-	-	37.500	68.750	31.250	68.750	31.250	31.250	56.250	37.250	59.375	40.625	56.250	56.250
		Diff	-	-	-	-	12.500	37.500	6.250	50.000	0	6.250	-12.500	6.000	12.500	-25.000	6.250	6.250
	Proxy	Before	68.750	43.750	18.750	43.750	34.375	28.125	18.750	18.750	40.625	18.750	71.875	28.125	46.875	65.625	46.875	50.000
	Report	After	87.500	62.500	40.625	84.375	53.125	56.250	31.250	56.250	81.250	31.250	50.000	40.625	56.250	43.750	50.000	56.250
		Diff	18.750	18.750	21.875	40.625	18.750	28.125	12.500	37.500	40.625	12.500	-21.875	12.500	9.375	-21.875	3.125	6.250
Emotional	Child	Before	-	-	-	-	40.000	70.000	60.000	90.000	40.000	60.000	90.000	80.000	100.000	85.000	65.000	55.000
Performance	Report	After	-	-	-	-	80.000	90.000	50.000	70.000	70.000	50.000	60.000	70.000	100.000	40.000	60.000	65.000
		Diff	-	-	-	-	40.000	20.000	-10.000	-20.000	30.000	-10.000	-30.000	-10.000	0	-45.000	-5.000	10.000
	Proxy	Before	80.000	70.000	40.000	50.000	50.000	80.000	65.000	85.000	35.000	45.000	80.000	75.000	75.000	90.000	65.000	45.000
	Report	After	80.000	65.000	70.000	70.000	80.000	75.000	50.000	65.000	70.000	65.000	45.000	75.000	80.000	50.000	60.000	70.000
		Diff	0	-5.000	30.000	20.000	30.000	-5.000	-15.000	-20.000	35.000	20.000	-35.000	0	5.000	-40.000	-5.000	25.000
Social	Child	Before	-	-	-	-	70.000	20.000	50.000	60.000	60.000	60.000	70.000	70.000	95.000	75.000	75.000	55.000
Performance	Report	After	-	-	-	-	80.000	60.000	60.000	90.000	70.000	60.000	50.000	80.000	95.000	90.000	85.000	85.000
		Diff	-	-	-	-	10.000	40.000	10.000	30.000	10.000	0	-20.000	10.000	0	15.000	10.000	30.000
	Proxy	Before	90.000	50.000	60.000	55.000	65.000	55.000	55.000	55.000	45.000	55.000	65.000	80.000	85.000	85.000	75.000	60.000
	Report	After		65.000	80.000	85.000	65.000	55.000	75.000	85.000	65.000	75.000	50.000	85.000	80.000	70.000	85.000	85.000
		Diff	10.000	15.000	20.000	30.000	0	0	20.000	30.000	20.000	20.000	-15.000	5.000	-5.000	-15.000	10.000	25.000
School	Child	Before	-	-	-	-	70.000	30.000	60.000	40.000	50.000	60.000	90.000	60.000	75.000	85.000	70.000	80.000
Performance	Report	After	-	-	-	-	70.000	70.000	50.000	80.000	55.000	50.000	90.000	50.000	80.000	70.000	80.000	85.000
		Diff	-	-	-	-	0	40.000	-10.000	40.000	0	-10.000	0	-10.000	5.000	-15.000	10.000	5.000
	Proxy	Before	-	-	-	-	60.000	40.000	60.000	40.000	50.000	60.000	80.000	70.000	80.000	90.000	70.000	60.000
	Report	After	-	-	-	-	60.000	60.000	65.000	75.000	55.000	65.000	80.000	70.000	80.000	65.000	80.000	80.000
		Diff	-	-	-	-	0	20.000	5.000	35.000	5.000	5.000	0	0	0	-25.000	10.000	20.000
Total Score	Child	Before	-	-	-	-	45.652	36.956	45.652	47.826	43.478	47.826	78.261	56.522	75.000	58.695	63.043	76.087
	Report	After	-	-	-	-	63.043	69.565	45.652	73.913	65.217	45.652	63.043	56.522	80.435	57.609	68.478	70.652
		Diff	-	-	-	-	17.391	32.609	0	26.087	21.739	-2.174	-15.218	0	5.435	-1.086	5.435	-5.435
	Proxy	Before	77.778	52.778	36.111	48.611	50.000	47.826	45.652	45.652	42.391	45.652	73.913	58.695	68.478	52.173	61.956	80.435
	Report	After	88.889	63.889	59.722	80.556	63.043	60.869	57.608	68.478	69.565	57.608	55.435	68.478	71.739	51.087	66.304	70.652
		Diff	9.524	13.096	20.238	28.571	13.043	13.043	11.956	22.826	27.174	11.956	-18.478	9.783	3.261	-1.086	4.348	-9.783

on respondent B08 with an increase of 35.000 points on average, and the lowest decrease was obtained in the report of the child respondent D10, at -45.00. In the social performance aspect, the highest score increase was found in the child proxy report for respondent B03, with an increase of 40.000 points on average, and the lowest decrease was obtained in the parent proxy report for respondent B22, which was -20.000. For the average total score of the two aspects (children's reports and proxy reports), there was an increase in scores for both. The highest increase in score was found in the results of the children's reports on respondents B03 and B04, with an increase

Table 3. Data analysis results.

	Mean	SD	Shaphiro-Wilk Test (α=0.05)	Two-tailed Sig.	Mean Difference	Std. Error	95% Confidence	
							Lower Bound	Upper Bound
Physical Performance								
Children Report (n:12)				Sig .148	8.833	5.678	**-3.664**	**21.331**
Before	39.063	16.723	Sig .100					
After	47.896	14.511	Sig .006					
Proxy Report (n: 16)				Sig .006	14.844	4.595	**5.049**	**24.639**
Before	40.234	17,965	Sig .119					
After	55.078	17.112	Sig .123					
Emotional Performance								
Children Report (n:12)				Sig .730	-2.500	7.058	-18.034	13.034
Before	69.583	19.709	Sig .612					
After	67.083	17.117	Sig .887					
Proxy Report (n: 16)				Sig .669	2.500	5.737	-9.729	14.729
Before	64.375	17,689	Sig .180					
After	65.625	3.770	Sig .095					
Social Performance								
Children Report (n:12)				Sig .023	12.083	4.583	**1.995**	**22.171**
Before	63.333	18.006	Sig .196					
After	75.417	14.841	Sig .226					
Proxy Report (n: 16)				Sig .010	10.625	3.619	**2.911**	**18.339**
Before	64.375	14.127	Sig .068					
After	75.313	12.970	Sig .436					
School Performance								
Children Report (n:12)				Sig .359	5.000	5.222	-6.494	16.494
Before	63.167	17.943	Sig .851					
After	68.750	15.094	Sig .095					
Proxy Report (n: 12)				Sig .167	6.250	4.225	-3.049	15.549
Before	63.333	15.570	Sig .578					
After	69.583	9.159	Sig .086					
Total Score								
Children Report (n:12)				Sig .115	7.065	4.125	-2.014	16.144
Before	56.250	14.089	Sig .166					
After	63.315	10.580	Sig .153					
Proxy Report (n: 16)				Sig .006	10.364	3.263	**3.409**	**17.319**
Before	55.506	13.344	Sig .123					
After	65.870	9.553	Sig .465					

of 40.000 points on average, and the lowest decrease was obtained in the proxy report of the respondents' parents D10, which was -25.000. In addition to assessing each aspect of the PedsQL 4.0 questionnaire, the results of the overall average score for each respondent will also be shown here. The highest increase in overall average score was found in the child's report on respondent B03, with an increase of 32.609 points on average, and the lowest decrease was obtained in the proxy report on the respondent's parents D34, which was -9.783 (Table 2).

Analysis was carried out for each aspect with the following results. In the physical performance aspect, the analysis of the children's reports assumed that the differences are less significant than the proxy reports. In the physical aspect of the child's report, an increase of 8.833 was obtained, and in the proxy report, we obtained an increase of 14.844. The analysis results of the children's and proxy reports on emotional performance assumed that the difference was not statistically significant. In the emotional aspect of the child's report, a decrease of -2.500 was found and in the proxy report, there was an increase of 2.500 (Table 3). This contradictory data may be caused by excluding child reports in the 2 - 4 years age range, which only has proxy reports. In analyzing the social performance of the children's and proxy's reports, both result differences were assumed to be significant. In the child's report, an increase of 12.083 was obtained and in the proxy report, there was an increase of 10.625. In the school performance aspect, the child and proxy reports showed an insignificant difference. The school aspect of the children's reports showed an increase of 5.000 and in the proxy report, there was an increase of 6.250. The analysis of each respondent's average total PedsQL 4.0 score with a paired t-test was done to determine the overall trend. For the result analysis of the children's reports, the score difference was not significant, and the result of the proxy reports difference was statistically significant. The total score for the children's reports shows an increase of 7.065, while there was an increase of 10.364 for the proxy reports score.

DISCUSSION

This study aims to determine how zoledronic acid administration in pediatric osteogenesis imperfecta affects their quality of life. We can conclude that what we found in this research doesn't align with our hypothesis; most of the aspects improved significantly and not significantly, especially in the physical and social aspects, which showed the highest increase compared to the others, while there were also some decreases in score.

According to similar studies, an increase in the scores on the physical aspect is the expected outcome of the zoledronic acid therapy.[10,12,14] Regarding significance, this study obtained two different results in the child's report and the parent's report, possibly caused by the differences in both perspectives.[19] This is because how parents regard their child's performance may differ from their child's experiences. This is why there is some difference in the scores between the children and proxy's perspectives, even though both experience an increase. Another reason why there are variations between each score is that in the physical aspect, which is directly related to the zoledronic acid efficacy in a patient's bones, said efficacy might vary. This also depends on each patient's severity, which was not discussed in this research.[11] In a similar study, the significant increases in scores for the physical aspects of quality of life are quite diverse. Some have increased significantly, and some have not. This can be caused by the condition and perception of patients in other studies that are being used as a comparison being quite diverse in how they assess quality of life. It is true that, in general, the physical aspect has improved but there is a difference in scoring. [12,14,20]

The analysis of the social aspects of this study showed a significant increase in both child reports and parent proxy reports. According to the results in similar studies, an increase in scores in this aspect is expected.[10,12,14] Statistically significant results were found in both groups of results,

while the significance of other similar prospective studies tends to vary. This can be influenced by the increasing age of the research respondents, as we conducted our sampling using therapy duration that should align with the increasing age of the respondent. Increasing age is said to affect the children's maturity when socializing. They can adapt to their conditions, environment, and the people around them as they age and mature.[12,20]

In the analysis of school performance, the results of this study showed an insignificant increase in the mean score in two reporting groups (children's report and proxy report). The cause of this can also be the academic ability of each patient, where the effect of quality of life enhanced by zoledronic acid therapy does not show a significant increase. It should also be noted that the data collection was carried out during the transition period of the COVID-19 pandemic, so the scores for the school aspect were also affected in this regard.[21] The mean scores obtained in the school aspect were almost similar to those of children with osteogenesis imperfecta from a larger sample study comparing the quality of life of patients with osteogenesis imperfecta with controls of normal children. Similar studies using the prospective system also showed an improvement in this aspect but the significance of the study was higher than that of this study, which had a larger sample.[20]

In terms of the total score, the results in this study showed an increase in the scores for both parts, child reports and proxy reports. Although the significance was different, the child report increases were not statistically significant, while for the proxy reports, the increase was statistically significant. As mentioned earlier, this can be influenced by the different perspectives of what is experienced by the children and their parents.[19] This also showed that intravenous administration of zoledronic acid in osteogenesis imperfecta improved the patients' overall quality of life. However, the level of efficacy for each patient may differ as indicated by the different statistical significances. Other factors that may cause statistically significant differences are external factors (environment, family, caregivers, etc.) and internal factors (children's mental and academic abilities, etc.) that usually affect the patients' emotional, social, and school aspects. An increase in total QoL score was the expected result, in line with the results of similar studies.[10,12,14]

Following the analysis of all aspects, it can be concluded that almost all aspects of the PedsQL 4.0 questionnaire experienced increased scores. Except for the emotional aspect, the children's reports of the aspects show a decrease, while there is an increase in the results of the parental proxy reports, although both were not statistically significant. When referring to the patient's answers in our interviews, the insignificant increases and decreases in the emotional aspect possibly have a similar cause, specifically the trauma experienced by the patient when experiencing a bone fracture either spontaneously or not while in the time range of the therapy, resulting in a decrease in the result. The psychological trauma experienced made some patients unable to carry out certain physical activities such as walking, running, and lifting moderate to heavy objects. Therefore, the limitations and trauma felt after experiencing these fractures caused a decrease in the quality of life of some respondents.[11] There were also internal (children's mental development) and external factors (environment, family, caregivers, etc.) that took effect. As the age of the respondents increases, the better their PedsQL emotional score should be. This is in line with the high correlation between the respondent's age dimension and the PedsQL emotional score dimension, which does not follow this research result.[22] This study did not follow the results of a case-control conducted at the same hospital using the measurements of DASH and SF-36, which stated that patients became more confident to move and were not afraid of the possibility of re-fracture. In this study, some patients did not show an increase in the emotional aspect, as indicated by the paired t-test results with a slight in-

crease or even decrease.[13] Prospective studies carried out with similar assessments and smaller samples also showed a significant increase, in contrast to the results of this study, which were retrospective.[20]

This research has some areas for improvement. The first is the limited number of samples. This study covered all patients in the main referral hospital in Eastern Indonesia. We would have had more respondents if we followed the epidemiological theory of osteogenesis imperfecta being present in 1 in 10,000-20,000 live births.[1] Patients with osteogenesis imperfecta may also have parents choosing to undergo outpatient treatment at their regional hospitals after receiving initial therapy. The second is the data collection method. As previously mentioned, the condition data before receiving zoledronic acid therapy was taken according to the patient's memory and the respondent's proxy. This was done because of the urgency and time constraints of this study. The third is the data collection; for some patients aged 2 - 4 years old, their school performance results couldn't be obtained because the patients had yet to go to any school activities. For other patients who had started therapy under the age of two years, the condition "before therapy" is considered the condition at the age of three years, based on the end of the age of two years and the beginning of the age of three years, also able to be referred to as 1000 days. The first stage in life is the peak of early development in children, in which is assumed that the quality of life of children can be measured and compared with the quality of life conditions at the age above.[20]

CONCLUSION

Osteogenesis imperfecta pediatric patients experienced an increased quality of life in most aspects from every perception after receiving zoledronic acid therapy. Physical and social performance were the aspects that experienced the greatest improvement. Emotional performance was the aspect that experienced the lowest increase according to the children's perceptions and there were decreased proxy perceptions in the quality of life score based on the PedsQL 4.0 questionnaire before and after zoledronic acid therapy.

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CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

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