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Original Article

HRQoL Evaluation of Pediatric Osteogenesis Imperfecta with Zoledronic Acid Therapy

Tri Wahyu Martanto[1], Hamzah Rafly Rahman[2], Patricia Maria Kurniawati[3]

[1]Department of Orthopedic and Traumatology, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, Indonesia
[2]Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
[3]Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

Correspondence should be addressed to Tri Wahyu Martanto, Department of Orthopedic and Traumatology, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Mayjend Prof. Dr. Moestopo No. 6-8 Surabaya 60286, Indonesia. e-mail: tri-wahyu-m@fk.unair.ac.id

ABSTRACT

Background: Zoledronic acid as bisphosphonates could increase bone mineral density (BMD), which in osteogenesis imperfecta will reduce clinical manifestations. Pediatric patients with osteogenesis imperfecta given zoledronic acid therapy should improve their quality of life.
Methods: A retrospective analytic study was conducted on 16 pediatric osteogenesis imperfecta patients who had received intravenous zoledronic acid. Interview using PedsQL 4.0 regarding the condition before and after therapy assessed the quality of life. A paired t-test was used to assess the contrast in each aspect of PedsQL 4.0. Results were expressed as an adjusted odds ratio with a 95% confidence interval. P-value <0.05 is considered statistically significant.
Results: A significant increase was found in the child report of social performance (+12.083, p=0.023), and proxy report of physical performance, social performance, and total score of the proxy report (+14.844, p=0.006; +10.625, p=0.010; +10.364, p=0.006). An insignificant increase was found in the child report of physical performance, school performance, and total score of the child report (+8.833, p=0.148; +5.000, p=0.359; +7.065, p=0.115), and proxy report of emotional performance and school performance (+2.500, p=0.669; +6.250, p=0.167). An insignificant decrease was found in child reports of emotional performance (-2.500, p=0.669).
Conclusion: After receiving bisphosphonate therapy, pediatric patients with osteogenesis imperfecta experienced an increased quality of life in most aspects within every perception. Physical and social aspects experienced the greatest improvement. Emotional is the aspect that experienced the lowest increase in the child's perception and decreased parent perception of the value of quality of life after bisphosphonate therapy.

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

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 of 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) by 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 several per year. Other clinical manifestations often encountered are dentinogenesis imperfect,[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 bisphosphonate was 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 the 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 use 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 mentioned in a systematic review by Dwan [11], that more research is needed that focuses on the quality of life in this case so that 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 many factors that need reconsidering. Existing research on the 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 that comparisons can be made in various conditions.[15] Also, because there are language differences between the original form of the questionnaire and the place where it will be used in this study, a validated translation is needed, and fortunately, the Indonesian translation of this questionnaire has been validated by Mapi™ Research Group.[16] On this basis, PedsQL 4.0 is used as a valid measure of the quality of life in this quality. 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 ability. 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 bisphosphonate therapy compared to before 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 are rarely 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 with 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 of pre-post comparison with bivariate analysis method using PedsQL 4.0 questionnaire data from patients with osteogenesis imperfecta. The population studied included pediatric osteogenesis imperfecta patients. The sampling technique of this research is purposive sampling. The variables observed were the population's quality of life before and after receiving zoledronic acid therapy. Data were obtained by conducting interviews via video calls with respondents (children and parents). Then, data were processed according to PedsQL 4.0 data, entered into a statistical computer program, and analyzed using the paired t-test method.

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

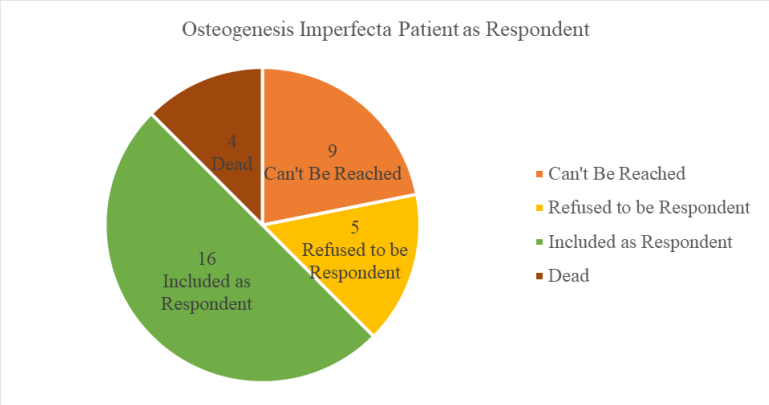

Figure 1. Distribution of Respondent.

teria included Patients with other diseases that are not complications of osteogenesis imperfecta; Patients in conditions 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.); Receiving another form of therapy beside Zoledronic Acid.

In this study, the total initial sample obtained as patients with osteogenesis imperfecta was 34. Data were obtained from the data available at the pediatric clinic with ethical clearance certificate number 0283/KEPK/X/2021 under permission and approval from the Research Ethics Committee of RSUD, Dr. Soetomo. With the final number of willing patients and according to inclusion and exclusion criteria, there were 16 patients (Figure 1).

Data Collection

The data collection process was carried out using a PedsQL 4.0 questionnaire form. The questionnaire contains 23 question items, which consist of physical, emotional performance, social performance, and school performance. The physical performance score was defined by 8 question items related to how children's physical abilities work in 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 child respondents interact and relate to friends and people around them. And the school performance score was defined by 5 question items. In assessing school performance scores, the PedsQL 4.0 form has different questions according to the age range of the child respondents. For respondents aged 5-18 years, there are five questions for children and parent proxies, while for respondents aged 2-4 years, there are three questions for parent proxies. A 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 interviews with children and parent's proxies were conducted twice to assess the variables needed for data collection.[15]

Video calls between parents and pediatric patients and researchers were used as a method of data collecting because of COVID-19 restrictions. Therefore, COVID-19 restrictions must be considered while conducting a quality-of-life assessment. To reduce bias, all respondents must be interviewed by the same researcher. The questions asked are those listed in PedsQL 4.0, accompanied by additional explanations (paraphrases) from the researcher as the interviewer. Interviews of patients and their parents were conducted separately, and when an interview was conducted on one subject, another subject was not allowed to be near the subject being interviewed. The interview has 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 therapy. In both stages of the interview, a 30-minute lag was given so that the interview's focus was not disturbed so that the data obtained became more consistent and less biased.[18]

Data Processing

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

RESULTS

Participant

Table 1 shows the results of demographic statistics on 16 respondents of patients with osteogenesis imperfecta who participated in this study. Demographic data taken were 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%). In the age distribution, most are in the age range of 5-7 years (50%). For most patients, zoledronic acid therapy was more than two years (87.5%).

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

In this study, respondent patients were divided according to the grouping of age and respondent type (proxy and children) based on the PedsQL 4.0 questionnaire ways of grouping. Some data were unobtainable, either because of the form (forms aged 2-4 years did not contain reports of children) or the unavailability of 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, and 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 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 at -20.000. And on the average total score of the two aspects (children's reports & proxy reports), there is an increase in scores for both. The highest increase in score was found in the

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

results of children's reports on respondents B03 and B04, with an increase of 40.000 points on average, and the lowest decrease was obtained in the proxy report of respondents' parents D10, which was at -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 of the respondent's parents D34, which was at -9.783 (Table. 2).

Table 3. Data Analyst Result

	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					

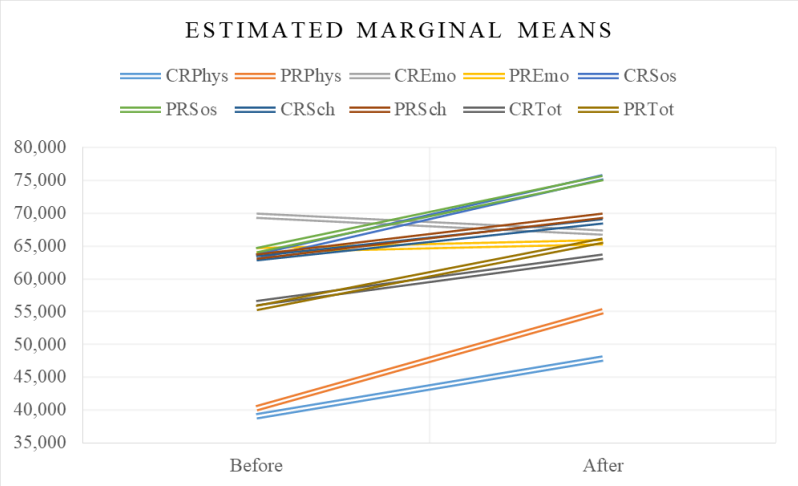

Figure 2. Estimated Marginal Means

Analysis was carried out on each aspect with the following results. In the physical performance aspect, analysis of 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 children's and proxy reports in 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, an increase of 2.500. This contradictory data in this aspect analysis 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 children's and proxy's reports, both result differences were assumed significant. In the child's report, an increase of 12.083 is obtained; in the proxy report, there is an increase of 10.625. In the school performance aspect, the child's and the proxy's reports show an insignificant difference. The school aspect of children's reports shows an increase of 5.000, and in the proxy report, an increase of 6.250. Analysis of each respondent's average total PedsQL 4.0 score with a paired t-test was done to determine the overall trend. With the result analysis of children's reports, the score difference was not significant, and the result of proxy reports difference was statistically significant. The total score for children's reports shows an increase of 7.065 and an increase of 10.364 in proxy's 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 physical and social aspects, which showed the highest increase compared to the others, but some have decreased in the score.

According to similar studies, an increase in scores on the physical aspect is the expected outcome of zoledronic acid therapy.[10,12,14] About significance, this study obtained two different results in the child's report and the parent's report, possibly caused by differences in both perspectives.[19] The way parents see how their child's performance may differ from their child's experiences. That's why there is some difference in score between children and proxy's perspective, even though both experience an increase in score. Another reason there's variation between each score was that in the physical aspect, which is directly related to zoledronic acid efficacy in a patient's bone, the efficacy of zoledronic acid in each patient might vary, and that also depends on each patient's severity which was not discussed in this research.[11] In a similar study, the significant

increase in scores on the physical aspects of quality of life is quite diverse. Some have increased significantly, and some have not increased statistically significantly. This can be caused by the condition and perception of patients in each other study that is used as a comparison is quite diverse in assessing their quality of life. So it is true that, in general, the physical aspect has improved, but there is a difference in scoring. [12,14,20]

Analysis of the social aspects of this study showed a significant increase in both child reports and parent proxy reports. According to results in similar studies, an increase in scores in this aspect is expected.[10,12,14] Statistically significant result was 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 this research respondent, as we have done our sampling using therapy duration that should align with the increasing age of the respondent. Increasing age is said to affect children's maturity in socializing. They can adapt to their conditions, environment, and 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 so that the effect of quality of life enhanced by zoledronic acid therapy does not show a significant increase. It should also be noted that data collection was carried out during the transition period of the COVID-19 pandemic, so scores on 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 in 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 improvement in this aspect, but the significance of that 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 score of both parts, child reports and proxy reports. Although the significance was different, the child reports increase was not statistically significant, while in proxy reports, the increase was statistically significant. As mentioned earlier, this can be influenced by different perspectives on what is experienced by children and parents.[19] This also showed that intravenous administration of zoledronic acid in osteogenesis imperfecta improved patients' overall quality of life. However, the level of efficacy in each patient may differ as indicated by different statistical significance. 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 patients' emotional, social, and school aspects. An increase in total QoL score was indeed the expected result, in line with the results of similar studies.[10,12,14]

From 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, children's reports of emotional aspects show decreased and an increase in the results of parental proxy reports, although both were not statistically significant. When referring to the patient's answers in our interview, the insignificant increase and decrease in emotional aspect possibly have one similar cause, the trauma experienced by the patient when experiencing a bone fracture either spontaneously or not while in the time range of therapy, thus showing a decrease in the result. The psychological trauma experienced made some respondent 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 are also in-

ternal (children's mental development) and external factors (environment, family, caregivers, etc.) that took effect. And as the increasing age of the respondent increases, the better the 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 with 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 emotional aspect, as indicated by the paired t-test results with a slight increase 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 indeed retrospective.[20]

This research also has some areas for improvement. The first is the limited number of samples. However, this study has covered all patients in the main referral hospital in Eastern Indonesia. We would have more respondents if we followed the epidemiological theory of osteogenesis imperfecta in 1 in 10,000-20,000 live births.[1] Patients with osteogenesis imperfecta may also cause this limitation with a wide spread of areas 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. It was done because of the urgency and time constraints of this study. The third is data collection; for some patients aged 2-4, the school performance results couldn't be obtained because those patients have yet to go to any school activity. For some other patients who 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, or can be referred to as 1000 days. The first stage in life is the peak in early development in children, which is assumed that age 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 of 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 in children's perceptions and decreased proxy's perceptions in the quality of life score based on the PedsQL 4.0 questionnaire from before and after zoledronic acid therapy.

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