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Correlation of Lumbosacral Radiography, Calcium, Phosphate, and Vitamin D Levels with Bone Mass Density (BMD) in Pediatric Patient

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Abstract

Background: *Dual X-ray absorptiometry (DXA) still represents the "gold standard" for the diagnosis of osteoporosis, meanwhile the availability of DXA has not been widely distributed, especially in minute areas. This study compares bone mass density (BMD) with a lumbosacral radiograph and laboratory parameters, that may help the early detection of osteoporosis.*

Purpose of Research: *This study analyzes the lumbosacral radiographs and the correlation between calcium, phosphate, and vitamin D levels with bone density in pediatric patients at Saiful Anwar Hospital, Malang, East Java.*

Research Method and Sample: *This is an analytical observational retrospective study that examines pediatric patients undergoing BMD, lumbosacral radiography, and laboratory tests on their calcium, phosphate, and vitamin D levels at Saiful Anwar Hospital, Malang, over the past year.*

Result and Discussion: *Based on the findings of this study, there is a significant correlation between lumbosacral radiograph and BMD with a p-value of <0.005, sensitivity of 90%, and specificity of 96%; and a significant correlation between vitamin D and bone density, with a p-value <0.005. The availability of vitamin D is more sensitive to detected osteoporosis rather than calcium dan phosphate blood level.*

Conclusion: *Excellent sensitivity and specificity of lumbosacral radiographs may become a modality for the early detection of osteoporosis in children in minute health facilities. In addition to lumbosacral radiographs, vitamin D can also act as a parameter for the early detection of osteoporosis in pediatric patients and is more accurate if the examination is combined.*

Keywords: Pediatric BMD, Lumbosacral Radiograph, Calcium, Phosphate, Vitamin D

Introduction

Osteoporosis is a significant health problem in children, with approximately 50% of children experiencing fractures at least once prior to entering adulthood [1]. A decrease in bone density in children before reaching peak bone mass will increase the risk of fractures and reduce the individual quality of life in adulthood [2]. The diagnosis of osteoporosis in children is based on the presence of spinal fractures or decreased bone density accompanied with multiple fractures [3, 4]. Spanish Society of Pediatric Rheumatology (SERPE) recommends that patients with a chronic disease, especially those with endocrinal, nutritional, rheumatological, and gastrointestinal disorders, are highly advised to undergo monitoring of their bone density levels, and assessed through bone mineral densitometry, as a gold standard [5]. Spinal frecture bgmana asesment nya.

In Indonesia, the availability of BMD equipment as a modality for the early detection of osteoporosis has not been widely distributed, especially in minute areas [6-8]. In this study, the author compares BMD with several parameters: the radiological parameter, lumbosacral radiography, and the laboratory parameters such as calcium, phosphate, and vitamin D levels, aiming for the early detection of osteoporosis can be made possible in remote areas of Indonesia.

Research Method

This study utilized an analytical observational analytic approach with a cross-sectional study design. The exclusion criteria encompassed patients with bone malignancies and pediatric individuals who had experienced a fracture in the preceding six months. The Medilink Densitometry device and its software (Figure 1) were employed for BMD analysis, while the PACS system was utilized for the semi-quantitative measurement of corpus vertebrae in the lumbosacral radiographs (Figure 2). A pediatric radiologist, muskuloskleletal radiologist, a resident with over three years of experience reviewed the results of the BMD and lumbosacral radiograph assessments. The correlation of the collected data was analyzed using linear regression and analytical correlation on the numerical data and chi-square analysis on the nominal data, presented in diagrams and tables using the SPSS 26 software.

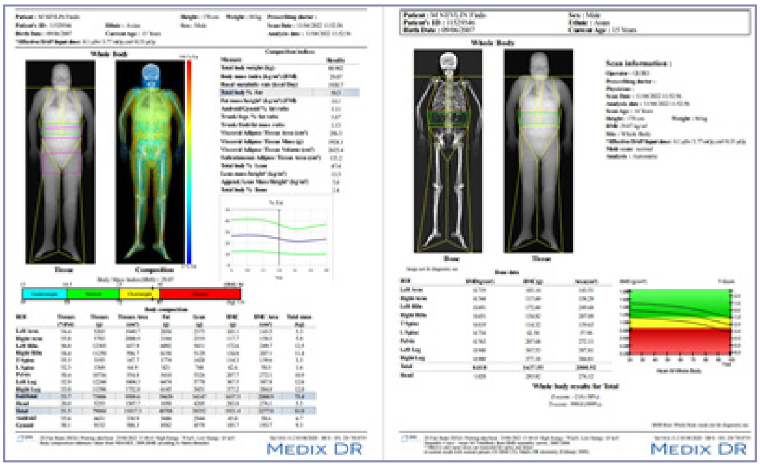

Figure 1: The Result of the BMD Examination

The figure above presents the result of the analysis of BMD data from the Medilink device. Aside from identity, there are also body weight, body height, body fat composition, and bone density as depicted in Z-score.

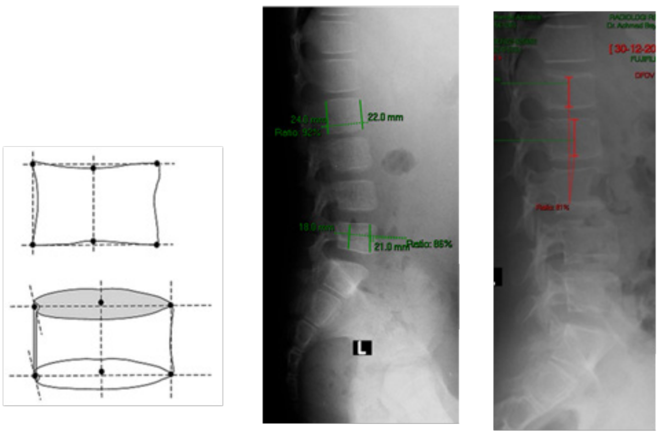

Figure 2: The Measurement of Decrease in Corpus Vertebrae Height

The figure above illustrates the principle of corpus vertebrae height decrease measurement based on the six points at the anterior-media-posterior superior dan inferior endplate sides. The measurement can be done by comparing the difference in the height of the corpus vertebrae on the anterior-medial-posterior side as shown in the middle photo, or by comparing the height of the surrounding corpus vertebrae, on the left photo as an example, the height of the L1 corpus vertebrae is compared with that of the L2 corpus vertebrae.

Result

The majority of research subjects in this study are female, within the age range of 5-11 years. On average, the subjects are classified as underweight. Among the comorbidities observed in this study, the most prevalent are systemic lupus erythematosus (SLE) accounting for 19.5%, nephrotic syndrome at 14.6%, and type I diabetes mellitus (DM) also at 14.6% (Table 1). The average bone mineral density (BMD) value, represented by the Z-score, is 0.827 ± 2.89. Furthermore, the average calcium level among the children in this study is 9.33 ± 0.850 mg/dL, the average phosphate level is 4.65 ± 0.967 mg/dL, and the average vitamin D level is 23.24 ± 9.91 ng/mL.

Table 1: The Characteristics of the Research Subjects

		n	%
Sex	Female	25	61.00
	Male	16	39.00
Age Group	5–11 years old	25	61.00
	12–18 years old	16	39.00
BMI Group	Underweight	22	53.6
	Normal	11	26.8
	Overweight	3	7.3
	Have Obesity	5	12.2
BMD	Normal	30	73.2
	Low Bone Mass	11	26.8
LS Radiograph	Normal Radiograph	27	65.9
	Osteoporosis	14	34.1
Comorbidity	Asthma	2	4.8
	SLE	8	19.5
	Nephrotic Syndrome	6	14.6
	Blood Disorder	4	9.7
	Type I DM	6	14.6
	CAH	2	4.8
	Precocious Puberty	4	9.7
	Delayed Puberty	1	2.4
	Down’s Syndrome	1	2.4
	Hyperthyroidism	1	2.4
	Hypothyroidism	3	7.3
	Paraparese Inferior	1	2.4
	Marasmus	2	4.8

Correlation analyses were conducted based on the collected data, and the results are presented in Table 2. The correlation between vitamin D and BMD (Z-score) was found to be statistically significant (p-value < 0.05), with a correlation coefficient value (r) of 0.356. This indicates that there is a positive relationship between vitamin D levels and bone density, suggesting that higher vitamin D levels are associated with better bone density.

Table 2: The Correlation Test between Calcium, Phosphate, and Vitamin D with BMD

	r	p	Description
Vitamin D – BMD	0.356sp	0.022*	Significant
Calcium – BMD	0.220sp	0.166	Not Significant
Phosphate – BMD	0.093sp	0.570	Not Significant

Description: * : Significant at alpha 5% sp: Spearman’s Correlation

However, the relationship between calcium and phosphate levels and BMD (Z-score) was not statistically significant. In the case of calcium levels, although the correlation coefficient value (r) was 0.220, indicating a positive direction, the correlation did not reach a significant level of significance (p-value > 0.05). Similarly, the correlation between phosphate levels and BMD (Z-score) had a very low correlation coefficient value of 0.093 and did not achieve a significant level of significance (p-value > 0.05). These findings suggest that there is no substantial relationship between calcium or phosphate levels and bone density in this study population.

The results of the correlation data of the lumbosacral radiograph with the results of the BMD (Z-Score) are presented in a 2x2 table with the condition that the Z-Score less than or equal to (-2) is grouped in the "low bone mass" category, and the Z-Score higher than (-2) is grouped in the "normal" category (Table 3). The evaluation of the lumbosacral radiograph was grouped into two categories, namely (1) osteoporosis, where there is a > 5% decrease in the corpus vertebrae height according to the operational definition, and (2) normal, where there is no fracture nor decrease in the corpus vertebrae height.

Table 3: The Result of Correlation Data between Lumbosacral Radiograph and BMD

	BMD	Osteoporosis	Normal	Total
Foto Lumbosakral		(Low Bone Mass)		
Osteoporosis		9	5	14
Normal		1	26	27
Total		10	31	41

Source: Primary data, 2023

The result of the correlation analysis between lumbosacral radiographs and BMD is significant with a p-value of 0.000, which is < 0.05, with a sensitivity 90%, specificity of 86%, a positive predictive value of 64.2%, and a negative predictive value of 96%.

Discussion

In cases of malnutrition, where individuals are underweight, there is a lack of nutritional intake which can disrupt the balance of bone formation. On the other hand, in cases of overweight and obesity, hyperinsulinemia occurs, which can lead to increased osteocalcin activity. This increased activity may result in reduced osteoblast and osteoclast function, ultimately leading to decreased bone turnover [6-8]. In situations where there is a lack of physical activity, the availability of calcium can decrease due to the RANK/RANKL mechanism and the osteoprotegerin (OPG) pathway [3, 10-13]. Additionally, an increase in adipose cells can lead to elevated levels of pro-inflammatory cytokines, which in turn can stimulate osteoclast activity and increase bone resorption by osteoclasts, resulting in decreased bone formation. [14, 15].

There is a significant acceleration of bone growth primarily driven by anabolic hormones such as growth hormone (GH) and insulin-like growth factor 1 (IGF-1), in pubertal stage, may contribute to osteoblast differentiation, muscle development, and myogenesis [10, 16, 17]. In male, typically exhibit increased bone width and size compared to girls due to the influence of testosterone on periosteal apposition [10, 18]. Estrogen plays a role in bone development in both sexes, promoting osteoblast differentiation and reducing osteoclast activity [2, 19].

Children with chronic diseases often experience impaired growth and delayed sexual maturation [10, 20, 21]. Estrogen deficiency can lead to various effects such as osteoblast apoptosis, oxidative stress, increased activation of the light chain activator NF-κB (nuclear factor kappa B), and the RANKL (receptor activator of nuclear factor kappa B ligand)/osteoprotegerin (OPG) ratio, ultimately activating bone resorption [11]. In this study, it is noteworthy that all subjects have chronic diseases, which increases their risk of experiencing reduced bone mass. Chronic diseases have been linked to various factors that contribute to decreased bone density, emphasizing the importance of managing bone health in this population (1, 19-21). (masuk metabolik dx)

The Correlation between Calcium, Phosphat, Vitamin D Level with BMD

Calcium exists in intracellular and extracellular forms in the body, primarily stored in bones [16, 22, 23]. Calcium absorption depends on the small intestine, and its concentration in plasma is tightly regulated by factors like kidney reabsorption and intestinal exchange [16, 22]. Parathyroid hormone (PTH) and 1,25-dihydroxyvitamin D (1, 25(OH) 2D) play key roles in calcium homeostasis [19, 24]. Studies suggest that blood calcium levels have limited correlation with bone density since the level in plasma is regulated by homeostatic mechanisms [20, 22, 25, 26].

Phosphate abnormalities such as hyperphosphatemia nor hypophosphatemia, did not necessarily indicate low bone mass, as result of regulation of homeostatic mechanism. Other studies have also found a lack of correlation between phosphate and bone density [16, 23].

Vitamin D plays a distinct role in bone formation compared to calcium and phosphorus. It acts as a hormone and prohormone in bone metabolism [13, 16]. Vitamin D can be synthesized in the skin through exposure to sunlight or obtained from certain foods. It undergoes enzymatic conversion to its active form, 1, 25(OH)2D, which increases intestinal calcium absorption and promotes bone resorption [11, 13, 16, 23]. The balance of calcium and phosphate is essential for bone mineralization, with excess minerals stored in the bones, meanwhile vitamin D level only available in blood plasma, that feasible detected for screening of osteoporosis [13, 16, 25].

The Correlation between Lumbosacral Radiograph and BMD

Based on the correlation between lumbosacral radiographs and BMD (Table 3), there are 5 false positive cases, that may happen because of counting callus formation densities. However, these cases do not have a clinical impact as per the definition of osteoporosis provided by the International Society for Clinical Densitometry (ISCD) in 2018, which considers spinal fractures independent of BMD results [27-29]. The presence of spinal fractures can still be useful for clinicians in providing therapy and fall prevention management for patients and retrospectively plain radiograph may have role beside BMD to diagnose pediatric osteoporosis [9, 20, 29].

Among the five patients with false positive results, four are children (5-11 years old) and one is a teenager. All of these patients are malnourished, with 60% being underweight and 40% being obese. Underlying conditions include malnutrition (Marasmus), thalassemia, long-term steroid use (> 2 years), SLE, and Cushing's syndrome. These clinical findings align with the existing literature, which suggests that being underweight or malnourished can lead to malabsorption, resulting in reduced intake of calcium, phosphate, and vitamin D, thereby impacting overall bone metabolism [9-11].

The patient's comorbidities play a significant role in the quality of bone density. Long-term steroid use increases bone resorption, inhibits osteoclast apoptosis, and reduces osteoblast activity [9, 12]. Glucocorticoids also impact muscle, the IGF-I axis, and gonadotropin levels, leading to increased bone resorption [1, 15]. Cushing's syndrome, characterized by endocrine disorders, negatively affects bone growth [18, 30]. Chronic diseases contribute to chronic inflammation and bone destruction, stimulating osteoclastogenesis and inhibiting osteoblast differentiation and collagen synthesis, resulting in osteoporosis [1, 31-34]. Thalassemia-related osteoporosis is multifactorial, involving chronic anemia, expansion of the bone marrow, and excess iron deposition [31]. In borderline cases with normal BMD results (Z-score above -2) and normal calcium, phosphate, and vitamin D levels, lumbosacral radiographs serve as a screening tool to identify trabecular bone fractures caused by compromised bone support.

Asymptomatic spinal fractures may occur during the ongoing process of decreased bone density [21, 35]. The spine, being the main weight-bearing structure, experiences constant pressure. Therefore, decreased vertebral body height can occur earlier in cases of declining bone density before being detected by BMD [27]. The International Society for Clinical Densitometry (ISCD) defines osteoporosis in children as a decrease in vertebral body height or the presence of vertebral fragility fractures, regardless of BMD results [36-39].

Research Limitations

This study has limitations regarding the assessment of factors that can affect bone density, such as nutrition, sun exposure, physical activity, disease progression, and medication history, and the presence of multiple diseases in some patients makes it challenging to determine the individual impact of each variable in the study.

Conclusion

In pediatric patients with risk factors for osteoporosis, it is recommended to conduct initial assessments including lumbosacral radiography, bone mineral density (BMD) assesment, and vitamin D levels. Lumbosacral radiography can be a useful tool for early detection in settings where BMD devices are not readily available, particularly in developing countries.

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