Alkaline Phosphatase (ALP) Activity as a marker for Vitamin D deficiency

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Abstract

Background: Osteomalacia or rickets is a known metabolic bone disorder, resulting from Vitamin D deficiency, or its active metabolites, leading to defective mineralization of bone.

Design and Setting: A retrospective hospital-based study, conducted at King Khalid University Hospital, Riyadh, Saudi Arabia in the period, January 1990 and December 2014.

Materials and Methods: Medical records of patients diagnosed with rickets or osteomalacia were reviewed. The diagnosis was based on clinical, biochemical and radiological evidence.

Results: Hundred and eighty-seven patients' 123 females (65.8%) and 64 male (34.2%) patient were diagnosed with osteomalacia or rickets based on clinical, radiological, and biochemical

data, and supported with low concentration of 25-hydroxy Vitamin D of less than 50 nmol/L. Serum alkaline phosphatase was universally high.

Conclusion: Raised serum alkaline phosphatase (ALP) activity is a sensitive marker, which could be used as a screening test to detect rickets or osteomalacia. It is cheap and readily available.

Keywords: Adolescent, children, osteomalacia, rickets, screening, serum alkaline phosphatase (ALP) activity.

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Introduction

Osteomalacia, or rickets is known metabolic bone disorder, resulting from Vitamin D deficiency or its active metabolite, leading to defective mineralization of bone.[1] In developing countries like Saudi Arabia, is still seen in children and adolescents,[2-4] and also with increasing frequency in developed world.[5] The diagnosis can be determined by several methods[6,7] either by biochemical i.e bone profile and radiological or Vitamin D assay. Peach et al[8] in, 1982, suggested that plasma alkaline phosphatase (ALP) activity could be used as a single routine biochemical test. It is cheap and readily available. Vitamin D assay though specific and

diagnostic, is expensive and not universally available, as well as, serum parathyroid hormone (PTH).

This study was conducted to determine the suitability of serum alkaline phosphatase (ALP) activity as a screening tool in the diagnosis of rickets or osteomalacia.

Materials and Methods

This is a retrospective, hospital based study, conducted at the Pediatric Endocrine Clinic, King Khalid University Hospital, Riyadh, Saudi Arabia in the period, January 1990 and December 2014, on patient with, the diagnosis of rickets and osteomalacia. The diagnosis was based on clinical, biochemical and radiological [9,10] changes. This was supported by low Vitamin D concentrations, as well as, raised levels of parathyroid hormone (PTH). In order to ascertain if the value of serum alkaline phosphatase (ALP) activity is suitable as a screening test, the values of concentration of serum alkaline phosphatase (ALP) activity were correlated to the other laboratory, and radiological findings. Patients with hepato-biliary, haematological disorders and other bone disorders, such as, metaphyseal dysplasia, hypophosphatasia and hypoparathyroidism, were excluded.[11-13]

Results

Two hundred and nine children and adolescents presented with rickets and osteomalacia during the period under review. Patients were excluded from the study; hepatobiliary disorder (9), hypoparathyroidism (4), metaphyseal dysplasia (3), various haematological disease (3), infantile

hypophosphotamia (2), and pseudo-hypo-hyperparathyroidism (1) patient. Therefore, a total of 187 patients included, 123 females (65.8%), and 64 males (34.2%) patients, aged 3 months to 16.5 years with a mean age of 13.6 years. All were Saudis from the central region of Saudi Arabia. Serum concentrations of 25-hydroxy Vitamin D were low, ranging between <10 to 45 nmol/L (normal; >50) and mean serum concentration of parathyroid hormone which was done in 56 patients was 185 pg/ml with a range 0f 20-460 (normal; 5-15).

Table 1 shows the biochemical characteristics in patients with osteomalacia and rickets. Serum concentrations of alkaline phosphatase (ALP) activity was universally high.

Table 1: Biochemical data in 187 patients with osteomalacia or rickets, mean (range)

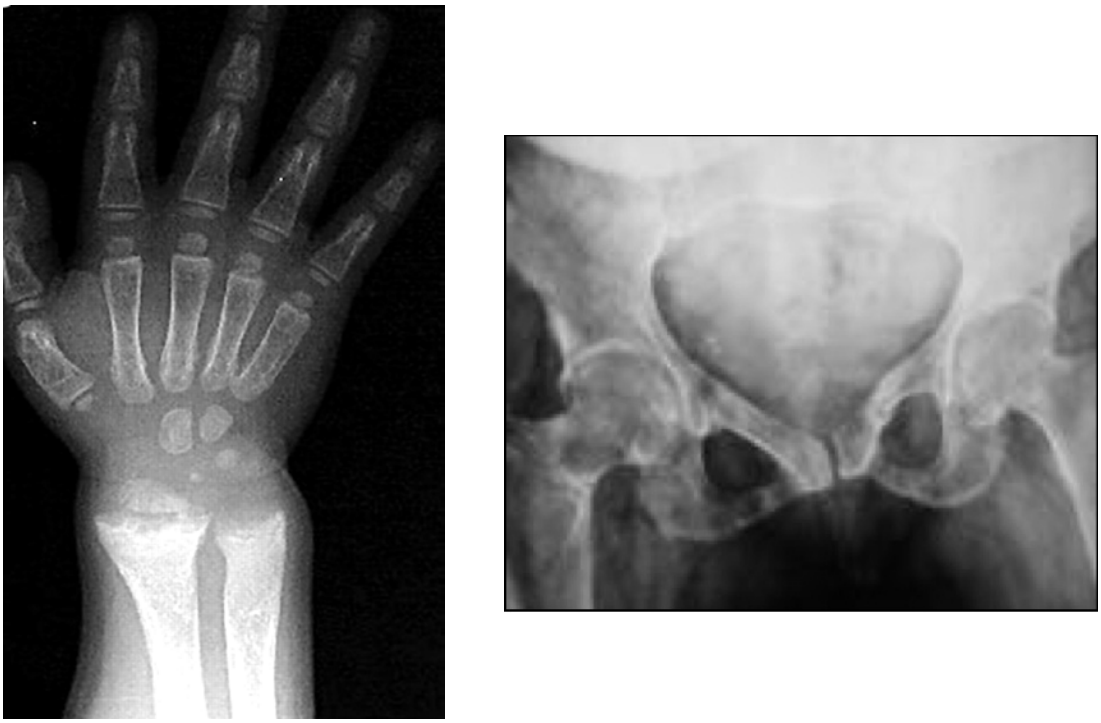
Serum Ca **Normal 2.2 – 2.6 mmol/L** **Mean (range)**	**Serum P** **1.4 – 2.1 mmol/L** **Mean (range)**	**ALP** **<600 U/L** **Mean (range)**	**PTH** **5-15 pg/ml** **Mean (range)**
2.1 (1.4 – 2.3) mmol/L	1.2 (0.8 – 2.6) mmol/L	1480 (650 – 2950)	185 (20-460) pg/ml

Ca - Calcium
P - Phosphate,
ALP - Alkaline phosphatase activity
PTH - Parathyroid hormone

Discussion

Rickets and osteomalacia are disorders characterized by defective bone and cartilage mineralization in children and bone mineralization in adults. The abnormal calcification of cartilage occurs at epiphyseal growth plates. Delayed maturation of the cartilage cellular

sequences and disorganization of cell arrangement are also present. The resultant profusion of disorganized, non-mineralized, degenerating cartilage causes widening of the epiphyseal plates with flaring or cupping and irregularity of the epiphyseal-metaphyseal junctions. The abnormal calcification of bone is restricted to the organic matrix at the bone-osteoid interfaces of remodeling tissue. The insufficient mineralization of newly formal matrix paradoxically results in enhanced bone volume and increased susceptibility to fractures or bone deformities (Figure 1 and 2). Many of the disorders of mineralization occur as a result of various Vitamin D deficiency. As a result, hypocalcemia leads to secondary hyperparathyroidism[14] with its biochemical abnormalities.



A **B**

Figure 1:Antero-posterior radiograph of the wrist (A) showing the typical cupping and fraying of the radius, and (B) anterio-posterior radiograph of the pelvis showing loozer's zone "pseudofracture".

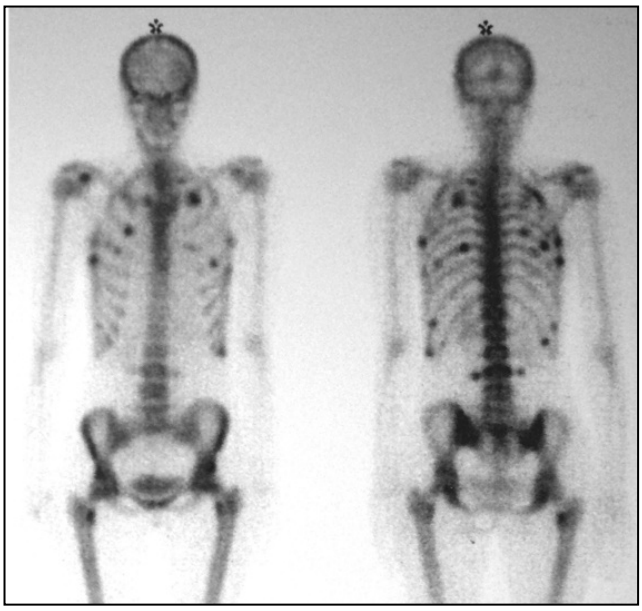


Figure 2: (A) Anterior, (B) posterior view of Tc^{99m} bone scan, demonstrating a high uptake of trace throughout the skeleton "super scan". "Multiple stress fractures".

Biochemical abnormalities in patients with rickets and osteomalacia vary with the duration of the disease. However, the rachitic and osteomalacic syndromes may be divided into calcipenic and phosphopenic forms, as well as those in which mineral availability is apparently normal. In general, patients with the calcipenic diseases exhibit a low or marginally normal serum calcium level, a decreased serum phosphorus concentration, and secondary hyperparathyroidism. In the other hand, however, some patients have normal serum calcium and phosphorus concentrations. Nevertheless, alkaline phosphatase activity in plasma is generally elevated in all forms of rickets and osteomalacia.

In our study, both forms were present, with elevated serum alkaline phosphatase activity, as a constant finding, table 1. The non-invasive gold standard test for the diagnosis of osteomalacia

or rickets is the serum concentration of 25-hydroxy-Vitamin D, however, this is not available to everybody and it is rather expensive. Serum concentrations of alkaline phosphatase activity could be used as a screening test, considering other causes of false positive and negative test.[6,8,14]

Since the report by Peach et al,[8] who suggested plasma alkaline phosphatase (ALP) activity as a single routine biochemical test to detect rickets or osteomalacia, many reports in the medical literature also who suggested that.[16-19] However, other reports contradicting that,[20] as normal alkaline phosphatase activity can be normal in early stages. Our result, favor the use of serum concentration of alkaline phosphatase activity as a screening test.

In conclusion, raised serum alkaline phosphatase (ALP) activity, is a sensitive marker which could be used as a screening test to detect rickets or osteomalacia. It is cheap and readily available everywhere.

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References

1. Holick MF. Vitamin D deficiency. N Engl J Med 2007;357:261-81.

2. Karrar ZA. Vitamin D deficiency rickets in developing countries. Ann Trop Paediatr 1998;(185):89-92.

3. Al Jurayyan NA, El Desouki ME, Al Herbish AS, Al Mazyad AS, Al Qahtani MM. Nutritional rickets and osteomalacia in school children and adolescent. Saudi Med J 2002;23(2):182-185.

4. Sedrani SH. Low 25-hydroxy-Vitamin D and normal serum calcium concentration in Saudi Arabia, Riyadh region. Ann Nutr Metab 1984;28:181-5.

5. Weisburg P, Scanion KS, Li R, Cogswell ME. Nutritional rickets among children in the United States : Review of cases reported between 1986 and 2003. Am J Clin Nutr 2004;8016 (6 Supplement):1697-705 S.

6. Bingham CT, Fitzpatrick LA. Non-invasive testing in the diagnosis of osteomalacia. Ann J Med 1993;95:519-522.

7. Cooke WT, Swan CHJ, Asquith P, Melikian V, Mc Feely WE. Serum alkaline phosphatase and rickets in urban school children. Br Med J 1973;1(5849):324-27.

8. Peach H, Composton JE, Vedi S, Horton LWL. Value of plasma calcium, phosphatase, and alkaline phosphatase measurements in the diagnosis of histological osteomalacia. J Clin Pathol 1982;35(6):625-630.

9. Moon RJ, Harvey NC, Davies JH, Cooper C. Vitamin D and skeletal health in infancy and children. Osteoporosis Int 2014;25(12):2673-84.

10. El Desouki M, al Jurayyan N. Bone mineral density and bone scintigraphy in children and adolescents with osteomalacia. Eur J Nucl Med 1997;24(2):202-205.

11. Temsah MH, Al Jurayyan NA. Infantile hypophosphatasia. Middle East Pediatrics 2003;8:134-35.

12. Al Jurayyan NA, Mohamed S, Saad Uddin MF, Al Jurayyan AN. Pseudohypoparahtyroidism type 1B: a rare cause of femoral fracture. J Taibah University Med Sci 2011;6(1):42-46.

13. Al Jurayyan NA, Al Omran HIO, Al Jurayyan AZN, Al Issa SDA, Babiker AMI. Concomitant hypoparathyroidism can mask Vitamin D deficiency. SAJMS 2015;3(1) in press.

14. Kruse K. Pathophysiology of calcium metabolism in children with vitamin D deficiency rickets. J Pediatr 1995;126:736-41.

15. Stamp TC, Round JM. Serum alkaline phosphatase and rickets. Br Med J 1973;2(5858):113.

16. Belfield A, Goldberg DM. Normal ranges and diagnostic value of serum 5 nucleotidase and alkaline phosphatase activity in infancy. Arch Dis Child 1971;46(250):482-86.

17. Klasmer R. Serum phosphatase activity and clinical rickets in children in Jerusalem. Am J Dis Child 1944;67(5): 348-354.

18. Chinoy MA, JAved MI, Khan A, Sadruddin N. Alkaline phosphatase as a screening test for osteomalacia. J Ayub Med Coll Abbottabad 2011;23(1):23-5.

19. Kover I, Mayne P, Barltrop D. Plasma alkaline phosphatase activity in screening test for rickets in preterm neonates. The Lancet 1982;319(8267):308-310.

20. Vasude Van J, Jenifer A, Reddy GM, Thayumanaran S. Serum alkaline phosphatase for screening of hypo-Vitaminosis D. Indian Pediatr 2014;51:60-61.