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Serum Alkaline Phosphatase for Screening of Hypovitaminosis D

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This study assessed the utility of serum alkaline phosphatase as a screening test to identify vitamin D deficiency and documented that it was not a useful screening tool.

Keywords: *Rickets, Vitamin D deficiency.*

Assessment of levels of serum 25-hydroxy vitamin D [25(OH)D], the major circulating form of vitamin D, is the best available indicator of vitamin D status. However, the assays are costly and not widely available. In view of the high prevalence of subclinical vitamin D deficiency, a simple and cost effective method of detecting hypovitaminosis D is required. Raised levels of serum alkaline phosphatase (SAP) indicate a state of increased bone turnover as it is a product of osteoblasts [1]. Osteomalacia causes high levels of SAP, thereby leading to the hypothesis that raised SAP levels can predict hypovitaminosis D. The present study aimed to evaluate the utility of SAP as a screening tool to detect hypovitaminosis D. This study was conducted in a tertiary care teaching hospital in Chennai, South India, between June 2012 and January 2013. Institutional human ethics committee approval was obtained. Children aged between 6 months and 18 years who were either normal or suffering from minor illness were eligible for inclusion in the study. Children with serious illness requiring ICU admission and patients with other skeletal diseases (renal rickets, osteogenesis imperfecta) were excluded. After obtaining informed consent from parents/guardians, clinical examination and blood sampling was done. Serum alkaline phosphatase was estimated by the para-nitro phenyl phosphate (PNPP) method. Serum was separated in a centrifuge and stored at -20°C until analyzed. 25 (OH)D levels were measured by an immunochemiluminometric assay in ADVIA Centaur auto analyzer with a assay range of 3.7-150 ng/mL.

A total of 230 children were included in the final analysis. Out of the total study subjects, 49.6% were below five years, 30.9% were between 5 to 9 years, and 16.5% were between 10 to 14 years. There were 112 (48.7%) females. Sixty (26.1%) children were healthy; infections (18.7%), undernutrition (13.9%), recurrent abdominal pain (16 %), asthma/wheeze (6.5%) and allergies (4.8%) were the most common morbidities. Clinical vitamin D deficiency was present only in 7 (3%) of the study participants. Neuro-developmental problems, seizures,and skin and soft tissue infections contributed to the remaining morbidity.

Based on 25(OH) D levels, participants were classified as either normal (>20 ng/mL) or insufficient/deficient (<20 ng/mL). The utility of SAP to predict vitamin D deficiency/ insufficiency was assessed by sensitivity, specificity and predictive values for different cut-off levels of SAP.

Out of 230, only 87 (37.8%) children were having normal and the remaining 143 (62.2%) were having insufficient/deficient 25(OH) D levels. For no cut-off value of SAP the combination of sensitivity and specificity was high enough to make SAP a good screening test. The predictive values were also very poor for all the cut-off levels **(*Table* I).**

In a study by Baig, *et al*. [2], only 19% of vitamin D deficient patients had raised SAP levels. Kovar, *et al*. [3] were the first to establish the role of SAP as a marker of vitamin D deficiency in premature infants. Several others [4-6] hypothesized that SAP could be the earliest marker of vitamin D deficiency. In contrast, current study documents that SAP is not a useful parameter for the screening of hypovitaminosis D, which is consistent with the studies done by other authors [7,8].

Rise in SAP has been well documented with rickets or

TABLE I PERFORMANCE OF SERUM ALKALINE PHOSPHATASE IN PREDICTING VITAMIN D INSUFFICIENCY/DEFICIENCY (*N*=230)

Serum alkaline Phosphatase (U/L)	*N (%)*	*Sensitivity*	*Specificity*	*Positive predictive value*	*Negative predictive value*
Above 100	227 (98.7)	98.0%	0%	62.0%	0%
Above 150	219 (95.2)	93.0%	1.1%	60.7%	9.1%
Above 200	167 (72.6)	74.1%	29.9%	63.5%	41.3%
Above 250	98 (42.6)	44.8%	60.9%	65.3%	40.2%
Above 300	43 (18.7)	18.2%	80.5%	60.5%	37.4%
Above 350	12 (5.2)	4.9%	94.3%	58.3%	37.6%
Above 400	6 (2.6)	3.5%	98.9%	83.3%	38.4%

osteomalacia. However, rickets is only a fraction of the total prevalence of vitamin D deficiency. Most of the children with vitamin D insufficiency or deficiency in the present study did not have overt signs of rickets. We conclude that SAP levels are not useful as a screening test to predict hypovitaminosis D.

Contributors: JV and AJ: conceptualized the study and contributed to manuscript editing; GMMR: data collection data analysis and preparation of the manuscript; ST: Overall guidance, protocol finalization and manuscript writing.
Funding: None; *Competing interests*: None stated.

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