



Review Article

Serum and salivary alkaline phosphatase levels in oral health and disease: A brief review

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ABSTRACT

Alkaline phosphatase is an intracellular hydrolase enzyme participating in the metabolic processes of cells. The enzyme alkaline phosphatase (AP) occurs in many organisms ranging from bacteria to man. Alkaline phosphatase levels were increased in various disease processes like periodontitis, gingivitis, and bone disorders. The alkaline phosphatase enzyme released in secretions like the serum, saliva, and gingival crevicular fluid. The serum and salivary levels were used as a diagnostic aid in oral diseases.¹ The below was a brief review of the alkaline phosphatase levels both in serum and saliva.

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1. Introduction

Alkaline phosphatase (AP, EC3.1.3.1 orthophosphoric-monoesterase, alkaline optimum) is a membrane-bound enzyme that occurs in almost all living organisms.² The enzyme alkaline phosphatase (AP) occurs in many organisms ranging from bacteria to man. The basic function was catalyzing the hydrolysis of monoesters of phosphoric acid and also catalyzes the trans-phosphorylation reaction with the presence of large concentrations of phosphate acceptors. These intracellular enzymes are increasingly released from the damaged cells into the gingival crevicular fluid (GCF), serum, and saliva. The rise in salivary ALP levels reflects inflammation and the destruction of healthy tissues suggesting it as a biomarker. Specimens like Whole saliva, gingival crevicular fluid, plaque, and serum can be used as a source of sample for these markers.³ The normal level of alkaline phosphatase is 20-140IU/L (international unit per liter) in adults. ALP levels are significantly higher in children and pregnant women.

Saliva is an oral fluid and has been used as a diagnostic fluid in medicine and dentistry. Salivary components

for diagnosis include enzymes and immunoglobulins, hormones of host origin, bacteria and bacterial products, ions, and volatile compounds. A specimen like the whole saliva can be collected with ease as compared to GCF in large amounts with less discomfort. Alkaline phosphatase plays a prime interest among the salivary biomarkers, especially from the dental aspect.⁴

An increase in ALP levels in the serum is frequently associated with a variety of diseases like dental caries, malignant, and potentially malignant disorders and also in some bone diseases like Paget's disease. Untreated Celiac Disease patients also showed elevated levels. Lowered levels of ALP are less common than elevated levels. Some conditions or diseases such as hypophosphatasia, postmenopausal women receiving estrogen therapy because of osteoporosis, men with recent heart surgery, malnutrition, magnesium deficiency, hypothyroidism, severe anemia, children with achondroplasias and cretinism,

2. Salivary Alkaline Phosphate in Periodontitis, Gingivitis

Salivary ALP takes part in the normal turnover of the periodontal ligament, alveolar bone, and root cementum

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formation, and also maintenance. Neutrophils, fibroblasts, osteoblasts, and osteoclasts produce alkaline phosphatase. ALP levels were higher in active periodontal disease sites in Gingival Crevicular fluid (GCF), according to a few longitudinal studies reported.³ Gao J et al. (1999) found that ALP activity was highest in osteoblasts, moderate in periodontal ligament PDL fibroblasts, and lowest in gingival fibroblasts.⁵ The level of the enzyme may vary depending upon factors such as age, gender, blood type, etc. Constant growth in children shows has higher values of alkaline phosphatase in their serum, especially during the growth spurt.

Within the area of the periodontium and gingival crevice, the cells such as polymorphonuclear leukocytes, macrophages, osteoblasts, and fibroblasts produce membrane-bound glycoproteins.⁶ The levels of alkaline phosphatase were increased during the acute phase of periodontal disease that was restored to normal after periodontal therapy according to few studies.³

3. Salivary Alkaline Phosphate and Alveolar Bone

Alkaline phosphatase creates a pH favourable for hydroxyapatite crystal formation in the bone matrix. Their increased activities might be a consequence of destructive processes in alveolar bone in advanced stages of the development of the periodontal disease.³ The membranes of mineralizing tissue cells (e.g., osteoblasts) are enriched with ALP and are also present in polymorphonuclear leukocytes (PMN) granules. The saliva constitutes mineral contents like calcium and phosphorous along with which Alkaline Phosphatase of bone. Analysis of saliva for alkaline phosphatase will detect any underlying bone disease or a disease that affects blood calcium level (hyperparathyroidism), vitamin D deficiency, or damaged liver cells.⁴ ALP is also produced by some oral bacteria, including gram-negative microorganisms found in subgingival plaque.⁵ Alkaline phosphatase also seems to be one of the key markers in the identification of pluripotent embryonic stem as well as related cells.³ No activity was detected in cementoblasts.

4. Alkaline Phosphatase Level in Dental Pulp

High levels of ALP also have been demonstrated in dental pulp cells. In the previous studies, ALP activity was analyzed in normal healthy human dental pulps, in reversible pulpitis, and in irreversible pulpitis. In the reversible pulpitis specimens, the ALP activity increased almost eight times. In the irreversible pulpitis specimens, the values decreased sharply and were roughly equivalent to those seen in typical healthy pulps. They also suggested the role of alkaline phosphatase levels were increased immediately after injury.⁵

5. Alkaline Phosphatase Level in Malignancy and Potentially Malignant Disorders

Cancer is the most common disease in India, responsible for maximum mortality. A biopsy is an invasive procedure, and not many patients will be willing to get it done if the lesions are not symptomatic. Several studies have found that there is an increased level of alkaline phosphatase in Oral leukoplakia and other premalignant lesions. Various biochemical changes occur in the body during carcinogenesis, and also biochemical parameter such as ALP evaluation is an inexpensive and potential marker for early detection of cancer that helps diagnosis.^{7,8}

The use of saliva in evaluating the biomarkers for early diagnosis of cancer risk potential may be more appropriate in oral cancer, as saliva reflects most of the oral diseases & effects of oral mucosa in cancer and can be better reflected in saliva as it bathes the entire oral cavity.⁶ Cellular Alkaline phosphatase is considered a marker of the induction of tumor cell differentiation. Dhivyalakshmi et al. studies showed that lactate dehydrogenase could be more reliable than alkaline phosphatase in the diagnosis of oral carcinoma. Merza et al. found that alkaline phosphatase level is more striking in case of local malignancy.⁹

Elevated Serum ALP levels are noted in patients with metastatic and primary tumors of the liver and bone, like hepatic metastasis of colorectal cancer and bone and liver involvement in breast cancer. Patients with malignancies, therefore, have an elevated serum ALP and may be an indicator of metastatic disease.¹⁰ ALP levels also exhibit variation concerning parameters such as tumor extension, size, stage, LNM, and BI status, thus confirming its role as a tumor marker.

6. Salivary Alkaline Phosphatase and Dental Caries

Salivary alkaline phosphatase (ALP) can balance remineralization processes of enamel, and there is no evidence regarding its effects on the concentrations of calcium and phosphate in saliva.¹¹

Dental caries, as a common chronic infectious disease of the oral cavity, is a complex, multi-factorial phenomenon involved with saliva characteristics. Different biochemical aspects of saliva, such as buffering capacity and inorganic components, may affect the development of dental caries. The typical structure of enamel consists of hydroxyapatite, which contains a high amount of calcium and phosphate; thus, saliva may be adequate on enamel maturation and remineralization for its calcium and phosphate content. According to Vahedi et al., although buffering ALP is not related to the severity of dental caries, the ion activity product for hydroxyapatite (IPHA) index which indicates the amount of salivary calcium and phosphate levels is related to dental caries prevalence. Shahrabi et al. in their study have found no relationship between salivary ALP and

dental caries in children.¹¹

7. Alkaline Phosphatase and Dental Implants

Dental implant surgery depends on the interdental papilla of the teeth adjacent to the edentulous site and the crestal bone. Two methods can predict Crestal bone loss. One was the radiographic examination by using the standardized paralleling radiographic technique, and the second one was biochemical test by using Alkaline phosphatase (ALP) in saliva as marker by which it may be useful as possible bone turnover marker to establish the diagnosis and prognosis of periodontal disease.¹² Thus ALP considered a valid biomarker for bone remodeling process around dental implants.

8. Conclusion

From the literature studies, it can be stated that the alkaline phosphatase levels were increased in the various pathologic conditions as well as in the physiological process and also helps in the maintenance of the bone homeostasis. Evaluating the standards will help as a diagnostic aid in the disease process. Both the serum as well as salivary ALP levels may be used as biomarkers for many oral disease processes and in malignancy.

9. Source of Funding

None.

10. Conflict of Interest

None.

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