Salivary alkaline phosphatase and oral health: A review

Shishir Ram Shetty1, Sura Ali Ahmed Fuoad Al-Bayati2, Mohammed Said Hamed3, Hossam Abdelatty Eid Abdemagyd4

College of Dentistry, Gulf Medical University, Ajman, United Arab Emirates
1 Assistant Professor in Oral Medicine & Radiology
2 Associate Dean (Academics), and Associate Professor in Oral Medicine
3 Dean and Head of Oral and Maxillofacial Surgery
4 PhD, Associate Dean (Clinical) and Associate Professor in Periodontics - Oral Medicine and Periodontology Department, Faculty of Dentistry, Suez Canal University, Egypt

KEYWORDS ABSTRACT
Alkaline phosphatase, Caries, Jaw growth, Oral cancer, Periodontics, Saliva.

Aim The aim of this paper was to analyze the literature published on the research related to salivary alkaline phosphatase and oral health.
Materials and methods An Internet search using Google search engine and key words salivary alkaline phosphatase oral cavity and dental health was carried out to obtain details of the published literature in this research area from 1975 to 2016. The data available in the articles were analyzed and presented under broad headings of salivary alkaline phosphatase in periodontitis, dental caries, jaw growth and oral malignancy.
Conclusion Monitoring of Salivary Alkaline Phosphatase levels could be used as an additional diagnostic tool for many oral and dental diseases.

Introduction
Detection of disease in its early stages is a key to its prognostic outcome. Early detection tools need to be easy to obtain and non-invasive, which makes salivary diagnostics as one of the suitable alternatives to blood. There are multiple advantages when saliva is used as a diagnostic tool compared to serum or tissues. In fact, its non-invasive method of collection, smaller sample fraction, good patient compliance, cost effectiveness, easy storage and transportation, greater sensitivity, and correlation with levels in blood are the advantages of salivary diagnostics (1). Moreover, owing to emerging new technologies, salivary biomarkers have been developed for a wide range of medical conditions such as malignancies, autoimmune disorders, infections and metabolic diseases (2). Among the salivary biomarkers alkaline phosphatases have been of prime interest especially from the dental aspects.

The enzyme alkaline phosphatase (AP), which occurs in many organisms ranging from bacteria to man, basically functions by catalyzing the hydrolysis of monoesters of phosphoric acid and also catalyze a trans-phosphorylation reaction in the presence of large concentrations of phosphate acceptors (3). AP activity in human serum is widely used as a biomarker for a variety of disease states involving particularly the liver and bone (4).

The function of AP in the bone matrix is to generate the pH at which a molecule has a net neutral charge, thus leading to hydroxyapatite crystallization (5, 6). The earliest published works about structure and function of AP date back to the 1907-1912 period, mainly by research work carried out by Suzuki et al., Grosser and Husler, and von Euler (4). The normal laboratory range for AP is 20 to 140 IU/L (international units per liter). Because of constant bone growth, children have higher levels of AP in their serum especially during growth spurt, when levels can be as high as 500 IU/L (7). Bone-related conditions such as fracture, acromegaly, osteogenic sarcoma, bone metastases, leukemia, myelofibrosis, and myeloma on rare occasions can cause elevation in serum AP levels (8).

Salivary alkaline phosphatase and periodontitis
It has been observed in several recent studies that in patients with untreated chronic periodontitis the level of AP in whole saliva was higher when compared to healthy individuals (9). Researchers have also discovered that a positive correlation exists between pocket depth and AP in periodontitis patients (10). Researchers have stated that AP is released by secondary granules of neutrophils and its concentration increases considerably with increase in inflammation and plaque accumulation (10).

The majority of researchers are of the opinion that
AP levels can be considered as potential markers for periodontal disease and also state that the quantitative analysis of salivary AP would help us distinguish between different periodontal conditions (11, 12). Some studies reported increased activity of AP in the acute phase of periodontal disease, and also observed that the enzyme level was restored to its normal range after periodontal therapy (13).

In a study by Todorovic et al. in 2006, it was observed that the increased activity of some of the salivary enzymes, like creatine Kinase, lactate dehydrogenase, aspartate aminotransferase, alanine and gama glutamyl transferase, indicates that the pathological destructive process has affected the alveolar bone, thus suggesting advanced levels of periodontal disease (14).

Dabra et al. in 2012 examined the activities of salivary ALP and acid phosphatase (ACP) in patients with periodontal disease, before and after periodontal treatment (15). The results obtained in their study showed statistically significant increased activities of ALP and ACP in saliva from patients with periodontal disease in relation to controls. It was also observed that significant reduction in the enzyme levels was seen after conventional periodontal therapy (15).

Ramesh et al. in 2013 conducted a study which included 40 female subjects, aged 50-60 years (16), divided in two groups: the first included 20 postmenopausal women without chronic periodontitis and the second 20 postmenopausal women with chronic periodontitis. When the salivary ALP levels were recorded, they found a significant increase in postmenopausal women with periodontitis. Based on these results, they concluded that salivary ALP levels could be used as additional diagnostic aid in diagnosing periodontitis in post-menopausal women (16).

Kishore et al. in 2014 examined the activities of salivary ALP and other salivary markers in pre and post-periodontal therapy patients (17) and found that these were significantly higher in patients with periodontal disease in relation to controls. However the authors also noticed that there was a significant reduction in the enzyme levels after conventional periodontal therapy (17).

Salivary alkaline phosphatase and dental caries

Few studies have been reported linking salivary AP levels to dental caries. Shahrabi et al. in 2008 carried out a study to recognize the components of saliva which are protective factors in children to evaluate and predict caries susceptible and caries resistant individuals (18). They collected unstimulated whole saliva from 75 children aged 3-5 years and determined salivary calcium, inorganic phosphate, and alkaline phosphatase. They found that there were no significant changes in salivary calcium, alkaline to phosphate and AP activity and their relation with progress of caries (18).

Hedge et al. in 2014 evaluated salivary AP levels and calcium ion levels in gender and age matched (25-50 years) caries active subjects (DMFT index greater than 10) with type II diabetes mellitus (60 subjects) and non-diabetic controls (60 subjects) (19). They found that AP (ALP) activity in saliva was higher in diabetic patients when compared to controls, with salivary calcium ions significantly higher in non-diabetic subjects (19).

Jazeri et al. conducted in 2015 a study to determine the relationship between salivary ALP activity and the concentrations of calcium and phosphate in saliva (20). They evaluated salivary markers including ALP in 120 males, aged 19 to 44 years and found that no significant relationship existed between ALP activity and calcium and phosphate concentrations in saliva and recommended further research in this area (20).

Salivary alkaline phosphatase and jaw growth predilection

Some researchers evaluated salivary ALP changes as an additional diagnostic tool to optimize the timing in orthodontic treatment.

Tarvade et al. in 2015 evaluated the salivary AP (ALP) activity in growing subjects in relation to the stages of individual skeletal maturation assessed using the middle phalanx of the third finger (21). The study was conducted on 60 girls and 60 boys aged 10 to 15 years selected using simple random sampling technique. The results of the study revealed highly significant differences between levels of salivary ALP and radiographic maturation stages of middle phalanx of third finger (21).

Ameer et al. in 2015 conducted a study to evaluate the activity of AP in saliva during orthodontic tooth movement using different magnitude of continuous orthodontic forces in thirty orthodontic patients aged 17-23 years with Class II division 1 malocclusion all requiring bilateral maxillary first premolar extractions (22). The study subjects were randomly divided into three groups according to the magnitude of the force application (40, 60 and 80 g). The results of their study revealed that ALP enzyme level increased with increasing magnitude of orthodontic force (from 40 to 80 g). The ALP level significantly increased from baseline after 7 days of force application and peaked at 21 days for all the three force levels. From the results of their study they concluded that the ALP level reflects the biological activity that takes place in the periodontium during orthodontic tooth movement, and therefore this can be used as a diagnostic tool for monitoring of correct orthodontic tooth movement (22).
Salivary alkaline phosphatase in oral potentially malignant disorders

Prakash et al. in 2016 conducted a study where they observed that the S-ALP enzyme was significantly greater in diabetes mellitus, smokers and subjects with potentially malignant disorders without any periodontitis compared to systemically healthy individuals (23). Based on the findings of their study, they emphasized that the screening of premalignancies and malignant lesions can be made by measuring salivary AP levels (23).

In a study conducted Dhiyalalakshmi et al. in 2014, salivary AP and lactate dehydrogenase resulted to be equally sensitive markers for the early detection of oral carcinoma (24). However they also found that on statistical analysis salivary lactate dehydrogenase could be a more reliable marker than salivary AP in the detection of oral carcinoma (24).

Merza et al. in 2010 conducted a study on serum and salivary AP in hematologic as well in acute leukemia and oral squamous cell carcinoma patients (25). Based on the results of their study, they concluded that the alterations in AP levels are more striking in saliva in case of local malignancy, such as oral squamous cell carcinoma, whereas the changes are more prominent in serum than saliva in the case of disseminated malignancy, like leukemia (25).

Conclusion

Based on the results of many studies, salivary alkaline phosphatase changes could be used as an additional diagnostic tool for many oral and dental diseases as well as in monitoring patient’s response to different treatments.

References

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