

# Salivary Alkaline Phosphatase as an Accurate Biomarker in Oral Health: A Review

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## Abstract

**Background:** Alkaline phosphatase, a phospho-hydrolytic enzyme, is released from cells during bone formation. This is a protein that binds calcium and phosphate. It was secreted by several cells during bone formation such as neutrophils, fibroblasts and osteocytes. A biomarker is substances in biologic samples that may predict a disease state in patient. Saliva, a unique diagnostic fluid, has gained interest as a biomarker due to its immediate reactivity with oral cavity changes. The main goal research was to investigate the role of ALP in oral health. **Methodology:** In order to perform this study, relevant publications were searched for using keywords such as " Alkaline phosphatase, saliva, oral disease " in the academic databases, Web of Science, PubMed, Scopus and Google Scholar. **Conclusions:** The study found that ALP enzyme is a suitable biomarker for oral disease screening and oral health monitoring.

**Keywords:** Alkaline Phosphatase, saliva, oral health, oral disease

## 1. INTRODUCTION

Oral health can be described as a standard condition for the health of oral and related tissues that allow a person to do daily activities as eating, drinking and other social activities without active disease, or annoyance or confusion which contribute to overall wellbeing.<sup>1</sup> Saliva is a bodily fluid that is non-invasively and safely collected from the oral cavity. In addition, saliva contains many biomarkers that can accurately reflecting oral health/disease.<sup>2</sup> Alkaline phosphatase (ALP) is a membrane-bound enzyme that occurs in almost all living organisms.<sup>3</sup> The enzyme ALP, found in bacteria and humans, catalyzes phosphoric acid hydrolysis and trans-phosphorylation reactions. Its release into GCF, serum, and saliva indicates inflammation and tissue destruction, potentially serving as a biomarker.<sup>4,5</sup>

## 2. METHODS

In order to perform this study, relevant publications were searched for using keywords such as " Alkaline phosphatase, saliva, oral disease " in the academic databases, Web of Science, PubMed, Scopus and Google Scholar.

### 2.1. Biomarkers

A biomarker in clinical settings must be reproducible, changeable, and accessible for

recognition and quantification using available biological test methods.<sup>6,7</sup> Biomarkers aid in disease diagnosis, treatment monitoring, and prognosis by recognizing disease stages from early clinical expression.<sup>8</sup> Periodontics studies aim to identify a reliable biomarker for diagnosing periodontitis in the present and future conditions.<sup>9</sup>

### 2.2. Oral Health

Oral health has the most important aspect in our life time. Oral health integrity is a key aspect of overall health, wellness and quality standard of life. The mouth is considered the window of the body health in general. It can show signs and symptoms of nutrition deficiencies or general infection such as dental plaque, dental decays, periodontal tissue disease, tooth loss, and oral cancer. Teeth are the hardest structures of the human body whose main function is chewing. Bacteria settle in plaque and can cause tooth decay and gum disease, which are worldwide oral diseases in the oral cavity.<sup>10</sup>

### 2.3. Saliva

Saliva is a unique, complex, and vital bodily bio fluid with several systems that serve a wide range of physiological demands, including protection from infection for the mouth, mucosa and the entire body.<sup>11</sup> It is released by major

salivary glands, as well 200-400 tiny salivary glands located throughout the oral cavity.<sup>12</sup> Saliva has a role in food digestion, cleansing, protection, maintaining the integrity of the oral mucosa, and keeping the oral cavity in a state of homeostasis.<sup>13</sup>

Damage to the mucosa and the teeth can result from local and systemic illnesses that disrupt and interrupt saliva's complex, balanced activities. Other times, systemic diseases cause changes in saliva without having a substantial regional impact.<sup>14</sup>

### 2.4. Saliva as Diagnostic Fluid

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.<sup>15</sup> 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.<sup>16</sup>

### 2.5. Alkaline Phosphatase

Alkaline phosphatase is a hydrolase enzyme and its activity has been evident in bone-forming cells, and any change in the enzyme seen in serum and bone have been used as indicator for assessing metabolism of bone in a number of diseases.<sup>17, 18</sup> ALP is detected in GCF collected from inflamed periodontium as well as from osteoblasts during bone formation.<sup>19,20</sup> It is produced by many cells such as polymorphonuclear leukocytes (PMNLs), osteoblasts, macrophages, and fibroblasts within the area of the periodontium and gingival crevice.<sup>21</sup> ALP is detected in the parotid, submandibular, and minor salivary glands, as well as in desquamated epithelial cells, leukocytes, and bacteria from dental plaque. The presence of this enzyme in the saliva is usually indicative of inflammation and destruction of the periodontal tissues.<sup>22</sup> 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.<sup>23</sup>

### 2.6. ALP and Oral Health

ALP is a phosphor-hydrolytic enzyme balancing the remineralization–demineralization cycle as it is primarily involved in calcium and phosphate binding. It seems that the function of this protein relatively depends on the salivary pH and

buffering capacity.<sup>24</sup> The presence of ALP in the saliva is generally indicative of inflammation and/or destruction of the periodontal tissues.<sup>25</sup> Neutrophils store ALP in particular granules and secretory vesicles, from which it is primarily released during the neutrophils' migration to the infection site. The pocket epithelium is predominantly composed of neutrophils, and it has been suggested that neutrophils are the main source of ALP during inflammation.<sup>26</sup>

### 2.7. Periodontal Disease

Periodontitis are the most frequent diseases that impair appearance, social life, and tooth retention. This complex, long-term inflammatory disease causes pocket formation, gingival bleeding, bone resorption, and attachment loss.<sup>27</sup> Periodontal disease is caused by a localized buildup of pathogenic bacteria in tooth plaque and their toxic metabolic products, which damages epithelial function, promotes its growth, and produces tissue-destructive proteinases.<sup>28,29</sup> Many of the biomarkers produced by inflammatory and immunological cells during the illness penetrate the gingival fluid, blood, and saliva, making them easy to measure.<sup>30, 31</sup> Abdulkareem and Akram found that the ALP enzyme had the lowest mean value in the control group compared to the patients' groups (periodontitis and reduced periodontium).<sup>32</sup> Salman and Ghudhaib found higher ALP levels in diabetic and diabetic periodontitis patients than in controls, possibly due to ALP's role as a marker for bone and liver problems.<sup>33</sup>

Previous research found that hypothyroidism patients with periodontitis had higher salivary ALP levels.<sup>34</sup>

ALP rose considerably with inflammation and plaque buildup, indicating further cellular damage. ALP in serum is linked to bone disease, while salivary spikes may indicate soft and hard tissue changes in active periodontal disease.

### 2.8. Dental Caries

Dental caries is a prevalent, long-term infectious illness of the oral cavity that is a complicated, multifaceted process influenced by the properties of saliva. Dental caries may develop differently depending on various salivary biochemical characteristics, including its ability to act as a buffer and its inorganic content.<sup>23</sup> Vahedi et al. state that whereas buffering ALP has no bearing on the severity of dental caries, the ion activity product for hydroxyapatite index—which measures the levels of calcium

and phosphate in saliva—has a correlation with the prevalence of dental caries.<sup>35</sup> However, Shahrabi et al. discovered no connection between salivary ALP and dental caries in children.<sup>36</sup>

### 2.9. Dental Implants

Dental implant surgery is dependent upon the crestal bone. Crestal bone loss can be predicted using two different techniques. First, a standardized parallel radiography technique was used for the radiographic examination. Secondly, a biochemical test was performed to determine the diagnosis and prognosis of periodontal disease. ALP in saliva was used as a marker for potential bone turnover.<sup>37</sup> Paknegad et al. (2003) found that the level of ALP was higher in implants than in teeth<sup>38</sup>, this could be due to that elevated ALP level in the periodontal ligament may due to renewal of the tissue or presence of a pathological condition.<sup>39</sup> Therefore, it has a dual function in the periodontal inflammation process and in the regeneration process; this may explain the higher level of ALP around dental implants.

### 2.10. Orthodontic Tooth Movement

Orthodontic tooth movement involves applying a force to a tooth, typically using light continuous force from an arch wire-bracket combination, to align teeth without root resorption or bone resorption, enhancing ALP and lactate dehydrogenase activities.<sup>40, 41</sup> In order to assess the activity of ALP in saliva during orthodontic tooth movement, Ameer et al. studied thirty orthodontic patients with Class II division 1 malocclusion who were between the ages of 17 and 23. All of the patients required bilateral maxillary first premolar extractions. Three groups of study participants were randomly assigned based on the force application magnitude (40, 60, and 80 g). According to their study's findings, the amount of ALP enzyme rose as orthodontic force increased (from 40 to 80 g). After applying force for seven days, the ALP level rose considerably from baseline and peaked for all three force levels at twenty-one days. They deduced from their study's findings that the ALP level.<sup>42</sup>

### 2.11. Oral Potentially Malignant Disorders

Oral potentially malignant disorders (OPMDs), a terminology suggested by the World Health Organization in 2007 for premalignant lesions and conditions, has been reported with a high-risk percentage of malignant transformation to

oral squamous cell carcinoma (OSCC).<sup>43</sup> Prakash et al. in 2016 conducted a study where they observed that the salivary ALP enzyme was significantly greater in diabetes mellitus, smokers and subjects with OPMDs. Based on the findings of their study, they emphasized that the screening of premalignancies and malignant lesions can be made by measuring salivary ALP levels.<sup>44</sup>

### 3. CONCLUSION

The current study indicated that ALP enzyme is a good biomarker for screening oral diseases, and can be used as a monitor of oral health.

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