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## Short Communication

# Lactate Dehydrogenase: The Beacon of Hope?

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### ABSTRACT

Lactate dehydrogenase enzyme (LDH) helps in the conversion of glucose into pyruvic acid during aerobic glycolysis and is found in the cytoplasm of most cells in the human body. When oxidative stress occurs in the body, LDH may be released extracellularly and its level is usually indicative of the severity of tissue damage. LDH has proved to be an inestimably resourceful marker in early prediction of serious diseases involving extensive tissue or cellular damage. This short communication explores the potential of LDH as a salivary biomarker of cell injury and death.

**KEYWORDS:** LDH, saliva, smokers, vapers, enzyme

Lactate dehydrogenase (LDH) is a ubiquitous enzyme found in most living cells, with peak concentrations evidently found in cells of the kidneys, liver, lungs, blood, and the like. This enzyme catalyzes the conversion of glucose into pyruvic acid during aerobic glycolysis. It is found in the cytoplasm of most cells in the human body and is released, and thereby discovered extracellularly upon cell death. When oxidative stress or oxidative damage occurs in the body, LDH may be released, thus raising its level in serum and saliva. Therefore, its extracellular presence is always affiliated with cellular death and tissue breakdown or injury.<sup>[1]</sup>

The role of saliva as a potential diagnostic tool in the detection of manifold oral diseases has been duly established by numerous studies.<sup>[2-4]</sup> This has encouraged studies on LDH activity to be conducted on salivary samples.<sup>[5]</sup> In a recent study, LDH levels in both active and passive smokers were gleaned and compared for the first time along with control individuals. The aim of

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the study was to compare the levels of LDH in active and passive smokers. The results revealed statistically significant differences in salivary LDH levels among passive and active smokers as well as normal controls, thereby affirming the study's hypothesis. It was concluded that LDH levels can potentially be an effective biomarker for oral cancer using saliva as the diagnostic tool.<sup>[6]</sup>

Since tobacco smoking has significant deleterious effects on human health, other alternatives have been sought, especially in recent times. The most popular alternative that is currently in vogue is smoking electronic cigarettes (e-cigarettes). This is actually an electronic device that simulates tobacco smoking where instead of smoke, the user inhales vapor. Thus, using an e-cigarette is referred to as "vaping". In a recently published study by our group in this prestigious journal, salivary LDH levels in cigarette smokers and e-cigarette vapers were examined and documented for the first time along with healthy control individuals with intriguing results.<sup>[7]</sup> The *raison d'être* of e-cigarettes is that in comparison to conventional cigarettes, they release fewer toxins and carcinogens, as attested by contemporary scientific evidence. However, our results imparted some interesting results. They indicated heightened levels of salivary LDH amongst vapers, thus warranting further study and analysis in this regard, especially in light of the fact that serum LDH levels amongst vapers have not been documented and compared with the levels amongst smokers and non-smokers. As the vaping habit is seen as a burgeoning trend in the young adult population globally, it is crucial to question the preconception that vaping is a safer option when compared to conventional cigarette smoking. The palpable increase in salivary LDH levels among smokers as compared to non-smokers could presumably be an effect of the breakdown of oral epithelial cells due to the presence of reactive oxidative substances (ROS) which are produced by smoking.<sup>[8]</sup> ROS are known to instigate damage to the epithelial cells lining the mouth and the airways, initiate oxidative-sensitive cellular pathways, and precipitate DNA damage.<sup>[9]</sup>

The significance of LDH levels in the body tissues are accentuated by the fact that higher levels of LDH enzyme are expressly released during tissue injury or damage. Thus, LDH can potentially be an invaluable biomarker of cell injury and death. It follows then that LDH levels in potentially malignant conditions and malignancies can play a vital role in early diagnosis, thereby patently improving prognosis and treatment outcomes. Notwithstanding the fact that the benefits of using saliva as a liquid biopsy medium to study levels

of biomarkers in the body are considerable (they are non-invasive, inexpensive, relatively painless, and easy to use), it is puzzling that only a handful of studies have investigated LDH enzyme levels in saliva.

Some studies have been conducted to evaluate whether salivary LDH levels are increased in patients with oral cancer (OC) or oral potentially malignant disorders (OPMD) when compared to a healthy control group (CG). The results demonstrated that increased levels of LDH-2, -3, -4 were detected in OPMD, and the levels rose further in oral cancer patients.<sup>[4,10]</sup> Another study assessed LDH levels in saliva and serum of patients afflicted with oral submucous fibrosis (OSMF) and leukoplakia. The results indicated a good correlation between serum and salivary LDH levels in OSMF patients, whereas a strong positive correlation was established in leukoplakia patients, thereby corroborating saliva as a propitious tool for early detection of OPMD.<sup>[11]</sup> Another study estimated salivary and serum LDH levels in OSMF cases and the results alluded to serum LDH as the more effective biological marker of OSMF than salivary LDH, whereby serum LDH correlated positively with mouth opening, and frequency and duration of habit amongst OSMF patients.<sup>[12]</sup>

In the oral cavity, LDH levels in the saliva play an indispensable role in preliminary or early detection of oral squamous cell carcinoma (OSCC). In a study done a few years ago, a critical difference in salivary LDH values was ascertained between the control group and cases of OSCC.<sup>[13]</sup> It was also deduced that there was a significant correlation of the enzyme levels with the differentiation of the tumor, thus portending the prognosis and the overall treatment outcome with reasonable accuracy.<sup>[13]</sup> Another study examined the role of salivary LDH as a biomarker in habitual tobacco chewers with no oral lesions, and OSMF and OSCC patients. It was revealed that LDH levels were significantly higher in OSCC, OSMF, and also healthy individuals who were habitual tobacco chewers, as compared to normal controls without tobacco habit.<sup>[14]</sup>

Numerous other studies have affirmed similar results where elevated levels of LDH were demonstrated on manifold patients stricken by an assortment of diseases (sickle cell disease, idiopathic arterial pulmonary hypertension, etc.).<sup>[15,16]</sup> Thus, it can be safely said that the more extensive the tissue/cellular damage, the higher will be the LDH levels in the human body.

Despite the monumental scientific strides that we have made in the recent past, histopathological examination continues to remain the gold standard for definitive diagnosis, especially for oral cancer. However, further

rigorous research and data analysis may pave the way for identification of less invasive procedures as major tools for diagnosis in the future. LDH has proved to be an inestimably resourceful marker in early prediction of serious diseases involving extensive tissue or cellular damage. Thus, harnessing the mighty potential of LDH to recognize both conspicuous and hitherto obscure health risks, improve prognosis and ameliorate treatment outcomes is the need of the hour.

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### Conflicts of interest

There are no conflicts of interest.

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