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Assessment of lactate dehydrogenase status in oral submucosa fibrosis patients

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ABSTRACT

Oral submucous fibrosis (OSMF or OSF) is a chronic, premalignant, complex, (1% transformation risk) condition of the oral cavity. This is generally featured by juxta-epithelial inflammation and progressive fibrosis of the submucosal tissue which includes the lamina propria and deeper connective tissues. With the progression of this disease, the jaws become rigid to that extent that the person will find it difficult to open his mouth. The condition is remotely linked to oral cancers and is associated with areca nut or betel quid chewing, a habit similar to tobacco chewing. 25 OSMF patients and 25 healthy individuals from the OP of Saveetha Dental College. Serum samples were it is analyzed for serum Lactate Dehydrogenase (LDH) by Pyruvate Method using ERBA CHEM 5 plus analyzer**.** A significant rise in LDH ($p<0.005$) levels in OSMF patients when compared with healthy controls, by the influence of OSMF on LDH metabolism. Our findings suggest that assessment of LDH can be used as an effective biochemical diagnostic tool for the manifestation of OSMF and other types of malignancy in patients.

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INTRODUCTION

Cancer is the second commonest disease in India with the maximum mortality rate of about 0.3 million deaths per year. The Oral Cancer is a significant global concern accounting for estimated cases of 2, 75, 000 and 1, 28, 000 deaths annually (Sri Vasari Kadiyali., 2015, T.N. Umamaheshwari). The main reason is attributed by the usage of tobacco yet 1.93% is not due to tobacco and genetic factors constitute 5-10% (Aliu L *et al.,* 2008, Prassan Kumar Rao. J., 2012)

Oral submucous fibrosis (OSMF) has been cited as "an insidious chronic disease affecting any part of the oral cavity and sometimes the pharynx. Oral cancer is often preceded by potentially malignant disorders (PMD) (Swamy KM., 2016). Rarely, it is preceded by and/or associated with vesicle formation and is always associated with juxta-epithelial inflammatory reaction followed by progressive hyalinization of lamina propria (Pinborg. J.J *et al.,* 1967, Sirsat S.M *et al.,* 1967)

The later subendothelial and submucosal myofibrosis results in the stiffness of the oral mucosa and deeper tissues that marks the limitation of opening of the mouth and protrusion of the tongue thus cause disturbances in swallowing and phonation. There may be significant epithelial atrophy. (Wahi P.N *et al.,* 1966)

Therefore, early detection is well emphasized, since diagnosis at an early stage is comparatively easier and plays a key role in reducing mortality and morbidity (Bhamal A.M *et al.,* 2016) Nowadays, the role of tumour markers in handling head and neck cancer has thus become significant (Patel. S *et al.,* 2015). Several tumour markers in both serum and saliva have been discovered. Lactate dehydrogenase (LDH) is one among them, which is a ubiquitous enzyme that proves important in

recognition of pathologic processes (Kallalli B.N *et al.,* 2016).

Lactate dehydrogenase (LDH) among many biochemical parameters represents a very vital enzyme in patients with cancer that has an easy routine measurement in many clinical laboratories (Homsi. J *et al.,* 2005). LDH catalyzes anaerobic glycolysis in which there is a production of lactate via pyruvate reduction. Lactate dehydrogenase activity in serum heightened up as an indication of necrosis of the cells.

LDH is found in almost all body tissues but mainly concentrated in kidneys, heart, red blood cells, liver, lungs, brains and muscles (Lingen. M. W *et al.,* 2008). Increased LDH levels are due to raised mitotic index and heightened production of lactic acid by tumour cells due to the breakdown of glycoprotein (Joshi. P. S *et al.,* 2012). Tissue breakdown releases Lactate dehydrogenase (LDH) and thus LDH can be measured as a surrogate for tissue breakdown (Anuradha. C. D *et al.,* 1998).

This work is focused in evaluating the level of serum LDH in OSMF patients and to correlate the LDH levels in these selected cases using the relatively minimally invasive, readily available serum as the diagnostic tool.

MATERIALS AND METHODS

Patients for this study were selected from those attending the outpatient department of Saveetha Dental College, and hospitals and divided into two groups as follows Group I – Normal healthy individuals – 25 individuals Group II - Patients with OSMF – 25 individuals

Inclusive criteria: Individuals with the age group of thirty-five to Sixty-five years OSMF Patients

Exclusive criteria: Individuals with other systemic illness like cardiovascular disease, Renal failure, Stroke, endocrine illness. Immunocompromised individuals

Sample collection and procedure: Informed consent was obtained from the patient before sample collection. 3 ml of venous blood was collected and distributed in plain collection tubes and centrifuged in 3000rpm for 10 minutes. Then the serum was separated and then it is analyzed for serum Lactate Dehydrogenase (LDH) by Pyruvate Method using ERBA CHEM 5 plus analyzer.

RESULTS AND DISCUSSION

Lactate dehydrogenase is an enzyme for transferring hydrogen and is also involved in the metabolic chain of anaerobic glycolysis during its final step. LDH is involved in catalyzing the oxidation of L- lactate to pyruvate with nicotinamide-adenine dinucleotide (NAD) as a hydrogen acceptor. The enzyme consists of four peptide chains of two types: M (muscle) and H (heart), each under separate genetic control. LDH which is a cytoplasmic enzyme is present mandatorily in all major organ systems. The LDH has an extracellular appearance that is used in detecting cell damage or cell death. Due to its vast distribution in the body, serum LDH is abnormal in a host of disorders. It is discharged into the peripheral blood after cell death caused by, e.g., ischemia, excess heat or cold, starvation, dehydration, injury, exposure to bacterial toxins, after ingestion of certain drugs, and from chemical poisonings.

Table 1: Mean, SD and p value of Control and Study groups

parameters	control	OSMF patients	significance
LDH	117.52 ± 16.98	170.28 ± 25.31	<0.005

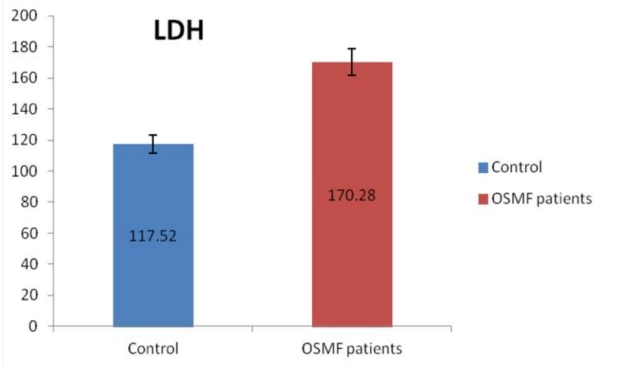

Figure 1: Influence in increasing LDH activity

Carcinogenic changes have enormous influence in increasing LDH activity. These carcinogenic change can result in decreased lactate to pyruvate conversion resulting in an abnormality in the regeneration of NAD which can interfere with glycolysis part of carbohydrate metabolism. Virulent tumour tissue or contiguous tissue damaged by a tumour discharges enzymes into circulation that contributes towards an unusual increase in enzyme levels. Elevation in LDH levels is due to increased mitotic index and more lactic acid production by tumour cells due to a breakdown of glycoprotein (K. Mallikarjuna Swamy). In our study, there is a significant increase in LDH levels 170.28 ± 25.31 in SMF patients when compared with healthy controls 117.52 ± 16.98, and the significance value is $p<0.005$.

The diagnosis of the wide variety of lesions that occur in the oral cavity is the vital section in dental practice (Saraswathi.T. R *et al.,* 2006).

Using different molecular analyses, the intracellular LDH activity in different cell line and tumour tissues acquired from patients can be analyzed (Markopoulos. A. K *et al.,* 2010). This is not only to

understand the complication is n cancer biochemistry but also helps in the early clinical recognition of tumours. (Sudhakar. S *et al.,* 2011). The salivary LDH level has been regarded as a reliable molecular marker for oral cancer in most of the studies (Jahanbani. J *et al.,* 2009).

Thus, the increase in their LDH level could be considered as a sign for OSMF. Since the p-value is less than 0.005, it can be taken that the values are statistically significant. Thus, the serum LDH level in OSMF patients increases relatively in comparison with control cases.

CONCLUSION

Lactate dehydrogenase has extensive potential benefits as a screening aid in the diagnosis of oral cancers. Our findings suggest that the assessment of LDH can be utilized as an effective biochemical diagnostic tool for the manifestation of OSMF. Diagnosis of OSMF at an early stage is comparatively easier and plays a key role in reducing mortality and morbidity.

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