Journal of Advanced Medical and Dental Sciences Research

@Society of Scientific Research and Studies ***NLM ID:*** *101716117*

Journal home page: www.jamdsr.com doi: 10.21276/jamdsr Index Copernicus value = 85.10

(e) ISSN Online: 2321-9599; (p) ISSN Print: 2348-6805

Original Research

Estimation of serum Lactate Dehydrogenase in oral leukoplakia and oral submucous fibrosis

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ABSTRACT:
Introduction: Lactate dehydrogenase (LDH) is an enzyme which is found in the cytoplasm of almost all body tissues and its main purpose is to catalyze the oxidation of lactate to pyruvate. Lactate dehydrogenase is always confined within cell cytoplasm and becomes extracellular when a cell dies, however its extracellular presence is always related to cell necrosis and tissue breakdown. **Aims and objective**: To evaluate the serum LDH levels in patients with normal oral mucosa, oral leukoplakia and oral submucous fibrosis and to correlate the LDH levels in these cases. Materials and method: A study comprised of 10 cases of normal healthy individuals (Group 1), 10 cases of oral leukoplakia (Group 2) and 10 cases of oral submucous fibrosis (Group 3). Venous blood was collected from each of these evaluated for LDH levels using the standard kit method. **Results**: Mean LDH levels of oral leukoplakia subjects were significantly higher than OSMF group and normal healthy subjects. **Conclusion**: Serum LDH might be used as a biochemical marker, as it is simple and easily accepted by the patient. These findings can also be used as valuable aid in monitoring treatment outcomes in potentially malignant disorders.
Key words: Lactate dehydrogenase, Serum, Oral potentially malignant disorders, Leukoplakia

Received: 26/07/2020 **Modified:** 26/09/2020 **Accepted:** 28/09/2020

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This article may be cited as: Anthwal N, Gupta S, Begum S. Estimation of serum Lactate Dehydrogenase in oral leukoplakia and oral submucous fibrosis. J Adv Med Dent Scie Res 2020;8(10):162-164.

INTRODUCTION:
Oral submucous fibrosis (OSMF) is a chronic insidious scarring disease affecting any part of oral mucosa and/or pharynx, sometimes preceded by vesicle formation, always associated with juxtaepithelial inflammation followed by fibroelastic changes in the lamina propria and epithelial atrophy, leading to stiffness of the oral mucosa with progressive inability to open the mouth and inability to eat.[1] It was first reported by Schwartz in 1952, that titled the term "atropica idiopathica mucosae oris" to this condition. In 1953, Joshi termed this condition as "submucous fibrosis."[2]
The term "Leukoplakia" was first proposed in the year 1877 by the Hungarian dermatologist Erno Schwimmer. Literally; the word leukoplakia means a 'white patch' which was derived from Greek word leukos- white, plakia- patch.[3] Warnakulasuriya et al in 2007 defined leukoplakia as "A plaque of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer".[4]
Lactate dehydrogenase (LDH) is an enzyme which is found in the cytoplasm of almost all body tissues and its main purpose is to catalyze the oxidation of lactate to pyruvate. Lactate dehydrogenase is always confined within cell cytoplasm and becomes extracellular when a cell dies, however its extracellular presence is always related to cell necrosis and tissue breakdown.[5] Lactate dehydrogenase levels in the tissue are very high (500 times) as compared with serum levels.[6] This enzyme is found mostly in all body tissues but mainly concentrated in heart, liver, red blood cells, kidneys, muscles, brains and lungs. The level of LDH varies according to the metabolic requirement of each tissue and alternation in LDH levels have been observed during development, biological conditions, and

pathological processes. Lactate dehydrogenase activity is mainly due to genomic changes during malignant transformation. Leakage of enzyme from even small amount of damaged tissue can increase the level of LDH to a significant level substantiating its value as a biomarker in tissue damage.[7-8] Serum LDH levels have been used as a biochemical marker in diagnosis in various cancers like oral, laryngeal and breast cancer. It is a ubiquitous enzyme that plays a significant role in the clinical diagnosis of pathologic processes. The aim of the present study was to evaluate the serum LDH levels in patients with normal oral mucosa, oral leukoplakia and oral submucous fibrosis and to correlate the LDH levels in these cases using the relatively minimally invasive, easily available serum as the diagnostic tool.

MATERIALS AND METHOD:

A study was conducted on 30 subjects in IDST College, Modinagar in the year 2017 and the study was approved by the ethical committee. The study group comprised of 10 cases of normal healthy individuals (Group 1), 10 cases of oral leukoplakia (Group 2) and 10 cases of oral submucous fibrosis (Group 3). Treated cases of oral leukoplakia and oral submucous fibrosis along with patients suffering from malignancy, hepatitis, hypothyroidism, anemia (hemolytic or pernicious anemia), lung disease, liver disease, kidney disease, pancreatitis, muscle trauma, muscular dystrophy, arrhythmia, pulmonary infarction and stroke were excluded from the study.

The patients' arm was relaxed on the working table comfortably and the tourniquet was applied about 1.5 to 2 inches above the antecubital fossa. The area was rendered aseptic with 70% alcohol, and 5 ml of venous blood was drawn from median cubital vein under aseptic technique. The tourniquet was released and the needle was removed; simultaneously, alcohol-soaked cotton was placed on the needle puncture sites and instructions were given to apply finger pressure for 5 minutes and then dispose the cotton. Collected blood sample was kept in test tubes at room temperature for 30-60 minutes to allow sedimentation of cellular fraction of blood. Later, the sedimented blood sample was centrifuged at 3000 rpm for 10-15 minutes. Supernatant serum was separated out with the help of a micro-pipette. The estimation was done within 3 hours of collected samples using a commercially available LDH assay kit (Crest Biosystems) and a UV visible spectrophotometer. It works on the principle that LDH catalyzes the oxidation of lactate to pyruvate accompanied by the simultaneous reduction of NAD to NADH. LDH activity in serum is proportional to the increase in absorbance due to the reduction of NAD.

All the data was collected and statistically analysed with the help of SPSS software (statistical package for social sciences) version 19.0 using mean, standard deviation, analysis of variance (ANOVA) and Post hoc Bonferroni test. A probability value of ≤ 0.05 was considered to be statistically significant.

RESULTS:

In all the study groups included in the present study, majority of the patients were males (84.5%) and rest were females (15.5%). The age of the patients in the present study ranged from 22-55 years with a mean of 38.5 years.

In the present study, mean LDH level in normal healthy individuals, oral leukoplakia and oral submucous fibrosis was 160.49±34.14 IU/L, 270.84±31.89 IU/L and 241.40±42.08 IU/L respectively. The p-value was found to be statistically significant. Individual group comparison using Bonferroni post hoc tests showed a significantly very high mean LDH levels with oral leukoplakia subjects and very low levels in normal healthy individuals. Mean LDH levels of oral leukoplakia subjects were significantly higher than OSMF group and normal healthy subjects (Table 1).

Table 1: Mean LDH level in normal healthy individuals, oral leukoplakia and oral submucous fibrosis

Group	**LDH (IU/L)**	
	Mean	**SD**
Group 1	160.49	34.14
Group 2	270.84	31.89
Group 3	241.40	42.08
ANOVA (F)	84.026	
p – value	**< 0.001**	
Group	**LDH [Post hoc Bonferroni (p – value)]**	
Group 1 vs Group 2	0.0001	
Group 1 vs Group 3	< 0.001	
Group 2 vs Group 3	0.0001	

Group 1- Normal healthy individuals, Group 2- Oral leukoplakia, Group 3- Oral submucous fibrosis, SD-standard deviation

DISCUSSION:

LDH is an enzyme noticeable in the cytoplasm of almost every cell in the human body, which becomes extracellular upon cell death. Transformation of normal tissue to potentially malignant disorders and further to oral cancer results in variation in glycolytic pathway that manifests as a shift from aerobic to anaerobic glycolysis; with the increase in the glycolytic activity and concomitant increase in LDH enzyme may be reflected in certain tissues.[9, 10] The present study was done to determine the serum LDH levels in patients with normal oral mucosa, oral leukoplakia and oral submucous fibrosis and to correlate the LDH levels in these cases.

In the present study, mean LDH levels of oral leukoplakia subjects were significantly higher than that of OSMF group and normal healthy subjects. These results were in accordance with the study done by Sciubba, Narang et al and Rathore et al.[11-13] In oral potentially malignant disorders, increased mitotic index and more lactic acid production by dysplastic cells takes place due to breakdown of glycoproteins. Thus, increase in serum LDH level occurs as a result of alteration in the glycolytic pathway from aerobic to anaerobic in dysplastic cells.[9] The LDH activity in OSMF cases can be linked to the muscle fatigue as a result of chewing that might eventually increase the glycolytic activity. Muscle fatigue causes accumulation of pyruvate due to hypoxia which has to be converted to lactate, resulting in high glycolytic activity in OSMF. Another reason is the hypoxic state related to OSMF and hypoxia elicits glycolytic pathways. In hypoxic state or in absence of oxygen, the pyruvate, the end product of glycolysis, is converted to lactate and this reaction is mediated by LDH.[14] Tilakarathne et al showed that increased hypoxia plays an important role in malignant transformation and progression of OSMF.[15]

CONCLUSION:

In the present study, serum LDH level was significantly increased in potentially malignant disorders (like OL, OSMF) as compared to healthy patients. Hence, quantification of serum LDH might be used as a biochemical marker, as it is simple and easily accepted by the patient. These findings can also be used as valuable aid in monitoring treatment outcomes in potentially malignant disorders.

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