

Study on Serum Lactate Dehydrogenase Level in Precancerous, Cancerous and Normal Subjects in Bihar

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ABSTRACT

Background: Present study was carried out to evaluate the serum level of lactate hydrogenase enzyme in normal, precancerous and cancerous subjects independently, to probe into the possible interrelationship among them, by utilizing biochemical parameter as an adjunct or solely to diagnose malignant condition.

Material and Method: The study was carried out to evaluate the role of serum LDH as a biochemical parameter in the oral premalignant and malignant and normal subjects. Estimation of LDH was carried out by spectrophotometric method of Wroblewski and LaDue. Statistical analysis was done using student t Test.

Result: Increased level of LDH was found in serum in patients with oral premalignant and malignant lesions. And the raised level of LDH had a positive correlation with the histologic grading.

Conclusion: Though LDL as an enzyme does not satisfy all the criteria necessary for it to be labeled as an ideal tumor marker yet its use in the detection and diagnosis of cancer.

Keywords: Lactate dehydrogenase, Leukoplakia, oral cancer.

INTRODUCTION

One of the most challenging and unresolved problem of today is the prevalence of incidence of oral cancers especially in the high risk zone like our country India. Out of all types of cancers, alone 3 to 4 % proportion¹ is of oral cancers as here in India is due to habit of chewing tobacco, beetle nuts, and alcohol intake are very popular. Taking into consideration the incidences of oral cancers worldwide there is stern need of detecting and standardizing easier methods for screening and diagnostic as purposes. Studies on enzymes in cancers were started by Warburg and his associates since 1930. Of the various enzymes studied, the most remarkable enzyme seems to be LDH and its isoenzymes. Malignant tissues have high glycolytic activity². This makes the major difference between normal and malignant tissues. LDH is a major

enzyme of glycolysis, reversibly catalyzes pyruvate to lactate. With increased glycolytic activity, increase in LDH activity has been marked out, which is reflected in certain tissue fluids and sera. There seems to be the direct relationship between malignant transformation of tissues and glycolytic pathway and in turn to LDH³. So its level in the serum might give us idea about the malignant potential and activity of the clinically innocuous lesions.

So far a number of studies conducted in order to correlate LDH with malignancy and most of them being localized to various organs other than oral cavity.^{3,4,5}. Even those studies pertaining to carcinomas of oral cavity mostly involved estimation of tissue level rather than serum. The drawback of these investigations is that, a

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systematic picture of the condition is rarely obtained from localized tissue studies. Mali KL⁶ *et al* carried out estimation of serum LDH in different types of malignancies. Authors have reported significantly raised level of LDH in all types of malignancies. Treville Pereira *et al*⁷ in 2015 estimated the serum lactate level in oral premalignant lesion and squamous cell carcinoma. He found raised level of serum LDH and also had a positive correlation with oral premalignant lesions. Present study was thus carried out to evaluate the serum level of LDH in normal, precancerous, and cancerous independently to probe into the possible interrelationship among them so as to utilize the biochemical parameter as an adjunct or solely to diagnose malignant condition well before they are clinically or histologically apparent and to monitor the progress of the disease at every step.

MATERIAL AND METHODS

Present study was carried out in the Department of Oral Pathology at Sarjug Dental College and hospital. The subjects were divided in 3 groups. Group I comprised of 15 healthy individuals who exhibited no sign of any systemic disease and pathological oral lesion. Second group consisted of 11 patients who had clinically diagnosed premalignant lesions which were confirmed subsequently by histopathology. Group III consisted of 29 patients with various types of malignancies affecting oral cavity and related facial structures. All the patients were clinically staged according to TNM status as per norms laid down by international union against cancer (IUCC). All the lesions were subjected to histopathological evaluation and after the confirmation of malignancy, the degree of differentiation was noted and graded according to broader's classification. A special questionnaire was also prepared for a detailed evaluation of premalignant and malignant lesions. Patient suffering from myocardial infarction or any other chronic diseases or pregnant women were excluded from the study.

Table 1 depicts the total number of precancerous and cancerous patients and mean value of LDH in all 3 groups.

S.NO	SUBJECT	TOTAL NO. OF SUBJECTS	P VALUE	SERUM LDH LEVEL (WL UNITS/ML) MEAN ± STANDARD DEVIATION
1	Normal	15	<0.005	338.82±75.24
2	Premalignant	11	0.005	485.66±123.98

5cc blood was collected from median cubital vein, serum was separated and subjected to biochemical analysis in the department of biochemistry santosh hospital central laboratory. Spectrophotometric method of Wroble and Ladue as modified by Henry *et al* (1960)⁸ was used for lactate dehydrogenase analysis.

Statistical Analysis:

The data were analysed with student independent t-test using SPSS statistics Base 17.0 software value P<0.05 was accepted as statistically significant.

RESULT

In the present study totally 55 subjects were assessed for serum LDH. In control group which consisted of 4 females and 11 males showed the average value of LDH as 338.88±75.24 units per ml. The age variance in group I was from 21 to 35 years. In group II, 11 subjects including 6 females and 5 males. The age variance was from 38-70 (mean age 54.724). There were 5 cases of clinically discernible leukoplakia, 2 cases of clinically discernible leukoplakia (with moderate epithelial dysplasia), 2 of candidal leukoplakia, another 2 of erythroplakia, one of oral submucous fibrosis. 6 premalignancies were there in buccal mucosa, 8 were in tongue, 2 in retromolar region.

Serum LDH value of group II was 485.66±123.98. Clinical and histopathological evidence of carcinoma was established unequivocally in 29 of the patients which comprised group III. 9 females and 20 males were present in this group. Age variance in this group was 30-70 years (mean 54.27 years). On observing the histopathological differentiation of lesions, it was found that poorly differentiated lesions (5 cases) recorded highest values of 1380±169.46 followed by moderately and well differentiated lesions. Cases having 6 and 16 subjects with value of 776.83±274.50 units and 194.53 units/ml respectively.

3	Malignant	29	0.001	706.72±388.01
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Table 2: Clinical and histopathological evidence of carcinoma was established unequivocally in 29 of the patients of III group. Age variance was 30-40 years.

Site	Number of lesions
Buccal mucosa	7
Hard palate	1
Mandible	3
Parotid region	1
Retromolar region	4
Floor of mouth	5
Lower lip	1
Vestibule of mouth	2
Tongue	1
Maxillary antrum	3

Apart from diagnosis TNM staging was done according to UICC and histopathological grading was done according to Broader's classification.

Table 3: TNM Staging

S.NO	DEGREE OF DIFFERENTIATION	NO. OF SUBJECTS	MEAN LDH VALUE ± STANDARD DEVIATION (WL UNITS/ML)
1	Well differentiated	16	479.35±194.53
2	Moderately differentiated	6	776.83±274.5
3	Poorly differentiated	5	1380±169.46

Table 4: TNM Staging in subjects with mean LDH value.

TNM STAGING	NO. OF SUBJECTS	MEAN LDH VALUE ± STANDARD DEVIATION (WL
Stage II	8	441.13±131.01
Stage III	14	883.59±387.23
Stage IV	7	706.72±388.01

DISCUSSION

The control group in the present study was comprised of 15 cases. Mean LDH value was 338.82 WL units/ml (SD±75.24). Mean LDH value of premalignant II showed the LDH value 485.66±123.98. LDH values were found to be elevated in most of the cases. Using student t-test P value was found to be <0.005 which is indicated highly significant finding in comparison to control.

Mean LDH value of the malignant group was 762.72 WL units/ml (SD±388.01). A total of 29 patients

comprised this group of the 29 cases, 1 patient had a well differentiated Squamous Cell Carcinoma with a coexistent pleomorphic adenoma, while the other had an adenocarcinoma. The rest of the patients had Squamous Cell Carcinoma with a coexistent pleomorphic adenoma, while the other had an adenocarcinoma. The control group in the present study was comprised of 15 cases. Mean LDH value was 338.82 WL units/ml (SD±75.24). Mean LDH value of premalignant II showed the LDH value 485.66±123.98. LDH values were found to be elevated in most of the cases. Using student t-test P

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Mean LDH value of the malignant group was 762.72 WL units/ml ($SD \pm 388.01$). A total of 29 patients comprised this group of the 29 cases, 1 patient had a well differentiated Squamous Cell Carcinoma with a coexistent pleomorphic adenoma, while the other had an adenocarcinoma. The rest of the patients had Squamous Cell Carcinoma with a coexistent pleomorphic adenoma, while the other had an adenocarcinoma.

The rest of the patients had squamous cell carcinomas of varying degrees of differentiation. A relation between the TNM classification (clinical staging) of the lesion and their degree of differentiation was histopathologically attempted.

No significant rise in the LDH value from premalignant to malignant group was formed with P value found to be <0.05 . At the same time LDH value showed a definite increase from control to the malignant group which was statistically significant with $P < 0.001$.

Raised level of LDH is in total agreement with other studies done in this direction. Though, most of these studies have been carried out in systemic malignant lesion, yet the very few studies on oral cancer show a similar trend. It has been reported by Hariharan et al that a definite correlation exist between the stage of the disease and the total LDH value. However finding of our study did not concerned with the above results. We could not find significant correlation between LDH and the clinical staging of the disease.

In our study, we could find a significant correlation between the degree of differentiation of tumor and the LDH level also. Khan N et al 1984 carried out one such study. While their results showed a significant changes of serum LDH in relation to the tumor size and metastasis, and found no relation to the degree of differentiation of tumor

Release of LDH from deranged malignant cells is expounded by Wroblewski as a source of body fluid, LDH elevation in patients with leukemia, solid malignant tumor and lymphomas cancer cells have a distinct metabolic path. The rate of oxygen consumption of cancer cells is somewhat below the value given by the normal cells. However cells tend

to use nearly 5-10 times more glucose as compared to normal tissues and converts the most of it into lactate, even though they have nearly rate of respiration. The phenomenon is called "AEROBIC GLYCOLYSIS".

Our finding also showed a definite correlation between poorly differentiated lesions and elevated serum LDH level. Though very rare studies done regarding oral carcinomas and LDH levels substantiate our findings.

Increased LDH level has been found in mice with transplanted carcinoma⁹ when the malignant growth itself seemed too small to account for the rise, indicating that serum elevation in malignant tumor could be due to induction process initiated by the tumor and involving normal tissues as well.

From the various hypothesis proposed by various workers, it is seen that 3 mechanisms may be responsible for the rise in the level of serum LDH¹⁰. They can be necrosis and cellular degeneration, induction process initiated by the tumor and involving normal tissues and muscle degeneration caused by protein deficit.

For oral carcinoma the initial 2 mechanism seems to be the most plausible. An ideal tumor marker should have high disease specificity to the tumor being studied and should be associated only with the tumor. A tumor marker should reflect the disease status, and it should prognosticate a lower or higher risk for possible development of recurrence and should correlate with the cure rate.

CONCLUSION

Though LDH as an enzyme does not satisfy all the criteria necessary for it to be labeled as an ideal tumor marker yet its use in the detection and diagnosis of cancer is justified based on the fact that a majority of the above are fulfilled. With new advancements of techniques and methods of evaluation of enzyme, we can better understand the rate of LDH as a marker of carcinogenesis.

CONFLICTS OF INTEREST

The authors declare they have no potential conflict of interests regarding this article.

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