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Research Article

STUDY ON SERUM LACTATE DEHYDROGENASE LEVEL IN PRECANCEROUS, CANCEROUS, AND HEALTHY SUBJECTS

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ABSTRACT

Objective: 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 the malignant condition.

Methods: The study was carried out to evaluate the role of serum lactate dehydrogenase (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's t-test.

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

Conclusion: Serum LDH in normal subject is 338.82 WL unit /ml. However the mean LDH value increases to 485.66 in premalignant lesion and to 762.72 WL unit /ml in malignancy. Thus we conclude that serum LDH level increases in premalignant lesion and malignancy.

Keywords: Lactate dehydrogenase, Leukoplakia, Oral cancer.

INTRODUCTION

One of the most challenging and unresolved problems 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 3-4% proportion [1] is of oral cancers as here in India is due to the habit of chewing tobacco, beetle nuts, and alcohol intake is 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 lactate dehydrogenase (LDH) and its isoenzymes. Malignant tissues have high glycolytic activity [2]. 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, an 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 the malignant transformation of tissues and glycolytic pathway and in turn to LDH [3]. 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 to correlate LDH with malignancy and most of them being localized to various organs other than oral cavity [3-5]. 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 systematic picture of the condition is rarely obtained from localized tissue studies. Mali *et al.* [4] carried out estimation of serum LDH in different types of malignancies. Authors have reported significantly raised the level of LDH in all types of malignancies. Pereira and Shetty [5], in 2015, estimated the serum lactate level in the oral premalignant lesion and squamous cell carcinoma. He found raised level of serum LDH and also had a positive correlation with oral premalignant lesions. This 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.

METHODS

This study was carried out in the Department of Oral Pathology at Sarjug Dental College, Darbhanga. The subjects were divided into 3 groups. Group I comprised 15 healthy individuals who exhibited no sign of any systemic disease and pathological oral lesion. The 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 tumor node metastasis (TNM) status as per norms laid down by International Union Against Cancer. All the lesions were subjected to histopathological evaluation and after the confirmation of malignancy; the degree of differentiation was noted and graded according to Broder's classification. A special questionnaire was also prepared for a detailed evaluation of premalignant and malignant lesions. The patient suffering from myocardial infarction or any other chronic diseases or pregnant women were excluded from the study.

About 5 cc blood was collected from a median cubital vein; serum was separated and subjected to biochemical analysis in the Department of Biochemistry, Santosh Hospital central laboratory. The spectrophotometric method of Wroble and Ladue as modified by Henry *et al*. (1960) [3] was used for lactate dehydrogenase analysis.

Statistical analysis

The data were analyzed with Student independent t-test using SPSS Statistics Base 17.0 software value $p<0.05$ was accepted as statistically significant.

RESULTS

In this study, totally 55 subjects were assessed for serum LDH. In the control group, which consisted of 4 females and 11 males showed the average value of LDH as 338.88±75.24 WL 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 to 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, and 1 of oral submucous fibrosis. 6 premalignancies were there in buccal mucosa, 8 were in tongue, and 2 in the retromolar region.

Serum LDH value of Group II was 485.66±123.98. Clinical and histopathological evidence of carcinoma were established unequivocally in 29 of the patients who 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.

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

Clinical and histopathological evidence of carcinoma were established unequivocally in 29 of the patients of III group. Age variance was 30-40 years.

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

DISCUSSION

The control group, in the present study, was comprised 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's t-test, p value was found to be <0.005 which is indicated highly significant finding in comparison to control (Table 1).

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 serum LDH level in malignancy are taken from different site and location of Head and Neck region (Table 2).

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. Although most of these studies have been carried out in the systemic malignant lesion, the very few studies on oral cancer show a similar trend. It has been reported by Hariharan *et al.,* that a definite correlation exists between the stage of the disease and the total LDH value. However, the finding of our study did not concern with the above results. We could not find a significant correlation between LDH and the clinical staging of the disease.

Table 1: Mean LDH values in healthy control, premalignant and malignant groups

Serial number	Subject	Total number 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
3	Malignant	29	0.001	706.72±388.01

LDH: Lactate dehydrogenase

Table 2: The distribution of sites of the malignant lesions in this group were as follows

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

Table 3: Mean LDH value according to differentiation

Serial number	Degree of differentiation	Number 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

LDH: Lactate dehydrogenase

Table 4: LDH value according to different clinical staging in oral cancer

TNM staging	Number 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

LDH: Lactate dehydrogenase, TNM: Tumor node metastasis

In our study, we could find a significant correlation between the degree of differentiation of tumor and the LDH level also. Khan *et al.,* 1984 carried out one such study. While their results showed significant changes of serum LDH in relation to the tumor size and metastasis and found no relation to the degree of differentiation of the tumor (Table 3).

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 convert the most of it into lactate, even though they have nearly the 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. Although very rare studies done regarding oral carcinomas and LDH levels substantiate our findings (Table 4).

Increased LDH level had been found in mice with transplanted carcinoma [9] when the malignant growth itself seemed too small to account for the rise, indicating that serum elevation in a 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 LDH [10]. 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

Although LDL as an enzyme does not satisfy all the criteria necessary for it to be labeled as an ideal tumor marker, 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.

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