Original Research Article

Serum Lactate Dehydrogenase: A Possible Metastatic Indicator of Lung Carcinoma

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ABSTRACT

Aim: This study was aimed to quantify serum lactate dehydrogenase (LDH) level in lung cancer patients and correlate with metastasis of the lung cancer.

Materials and methods: 150 patients with histological confirmed lung cancer including non small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) and 150 age & sex matched control subjects were included in this study. Serum LDH levels were quantified in lung cancer and control subjects by IFCC method. The independent sample *t*-test was used to assess the association between serum LDH level and metastasis of lung cancer.

Results: Lung cancer patients with metastatic stage group showed a statistical significant elevated serum LDH level than non-metastatic stage group.

Conclusion: Our study results suggest a significant association between elevated LDH level and metastasis of lung cancer in both NSCLC and SCLC patients. The pretreatment LDH level can be helpful in early detection of metastasis and to direct better treatment strategy.

Key words: Lactate dehydrogenase (LDH), Metastasis, Lung cancer

INTRODUCTION

Metastasis is a leading cause of morbidity and mortality among cancer patients and lung cancer patients mostly appear with early metastasis and poor prognosis at the time of findings. [1] So, early detection of metastasis is necessary before treatment to provide better intervention and treatment strategy. The molecular transformation of tumor cells lead to the synthesis and shedding of distinct molecular species that can be detected in biofluids like plasma, serum and circulating cells. These serum biomarkers can be used as tumor markers if they are related to tumor formation or growth. [2] Increasing evidences suggest that serum markers present with early detection of diagnosis, prognosis and treatment response. In recent years, among serum biomarkers serum LDH has been gaining an important attention as a prognostic marker owing to consisting reports regarding poor survival among multiple malignancies [3-5] including lung cancer [6] are associated with increased level of LDH, suggesting LDH as a more informational and potential biomarker of metastasis. Therefore, this study is designed to quantify serum LDH level in patients with lung carcinoma and to provide more valuable information of LDH as a metastatic indicator.

MATERIALS AND METHODS

Newly diagnosed 150 patients attending cancer OPD at SMS hospital,

Jaipur, were included in this study. The diagnosis was confirmed by histopatho-logical examination. The cases were classified as 113 with non-small-cell lung cancer (NSCLC) and 37 with small-cell lung cancer (SCLC). Staging was done according to the 7th edition of AJCC cancer staging manual. [7] According to staging, cases were classified into two groups: 77 patients with non-metastatic group and 73 patients with metastatic group. Patients presented with myocardial infarction, liver disease and any other infection were excluded from the study. Similar age and sex matched 150 healthy controls were included in the study. Serum LDH levels were measured on Beckmann Coulter AU680 based on Spectrophotometric method by IFCC method followed by statistical analysis. Data was analysed by SPSS (version 15, Chicago, IL, USA). Independent sample t-test was used to compare between two groups and results were presented as mean ± standard deviation. The diagnostic cut-off range of LDH was 450 IU/L.

RESULTS

Table 1: Serum LDH level in Lung Cancer Patients v/s Control Subjects

Character	Patient	Control	P-value
Number	150	150	
LDH(IU/L)	370.04±60.76	432.77±179.65	0.001

Table 2. Serum LDH level in Lung Cancer Patients non-metastatic v/s metastatic stage

Character	Non-metastatic	Metastatic	P-value
Number	77	73	
LDH (IU/L)	350.73±80.40	520.49±210.92	0.001

Table 3. Serum LDH level in Lung Cancer Patients NSCLC v/s SCLC

Character	NSCLC	SCLC	P-value
Number	113	37	
LDH (IU/L)	420.87±175.56	469.08±186.98	0.17

Table 1 presents the serum LDH concentration in lung cancer patients v/s control group .The mean value of serum LDH in patients v/s control groups was (83.27±44.35 v/s 41.81±20.92) IU/L. Serum LDH concentration was found significantly elevated in lung cancer group compared to those in control group (p<0.001).

Table 2 describes serum LDH concentration between non-metastatic and metastatic stages of lung cancer patients. The mean value of serum LDH in non-metastatic stage v/s metastatic stage was (350.73±80.40 v/s 520.49±210.92) IU/L. Metastatic lung cancer patients showed significantly higher level of LDH as compare to non-metastatic lung cancer patients, suggesting the role of serum LDH in metastasis of lung cancer.

Table 3 describes serum LDH concentration in different histology of lung cancer patients. The mean value of serum LDH in NSCLC v/s SCLC was (420.87±175.56 v/s 469.08±186.98) IU/L. No significant difference was observed between NSCLC and SCLC subjects.

DISCUSSION

Our study explored a significant association between LDH level and lung carcinoma as lung cancer patients exhibited an increased serum LDH level compared to control subjects. Patients with metastatic stage were observed with significantly higher level of LDH than non-metastatic stage. Out of 150 patients 27.33%(41) patients had abnormal serum LDH level, out of which 46.58%(34) presented in metastatic group and 9%(7) in non-metastatic group. Furthermore, patients with higher metastatic score presented with more LDH level than lower metastatic score suggesting a prominent role of LDH as a metastatic indicator. On further exploration of LDH level in different histology 24.77% NSCLC patients and 35.13% SCLC patients exhibited abnormal LDH level. Our study did not reveal any statistical significant difference of LDH level between NSCLC and SCLC, though, SCLC patients showed more aggression and metastasis. It may be due to lower number of SCLC patients in our study.

Our study results are supported by a meta-analysis, [8] stating that higher level of LDH might be correlate with poor prognosis in both NSCLC and SCLC patients. Lee DS et al.,(2016) [9] also proposed an

independent role of serum LDH associated with stage IV NSCLC patients and correlated with modestly prognostic overall survival in lung cancer patients.

Tumor cells primarily depend on glycolysis for their expedite growth (Warburg effect) [10,11] and hypoxia is another characteristic feature of growing tumor cells. Hypoxia has been shown a favorable environment to invase and migration of cancer cells to metastasize. [12] Moreover, previous reports have suggested that hypoxia inducible factor-1 α (HIF-1α) are overexpressed in malignant cells which accelerate the cancer cell progression and lead to metastasis through upregulation of LDH level in tumor cells. [13] LDH is a metabolic enzyme that catalyzes the conversion of pyruvate to lactate and LDH activity is accelerated in hypoxic tumor microenvironment. [14] Lactate is a substrate for anaerobic glycolysis which provides nutrition to cancer cells for proliferation. Beside this, lactate itself also promotes higher expression of HIF-1 α. Thus HIF-1 α and LDH interact simultaneously with each other in malignant cells and cell proliferation occurs. [13] In addition, LDH induces tumor angiogenesis, another essential feature of tumor metastasis. These results suggest that increased LDH level play a pivotal role in severe tumor burden and metastasis of cancer.

LDH level can also be increased in other disorders like myocardial infarction, liver disease, hypothyroidism and infectious diseases. [15,16] As these all factors are excluded in our study and LDH levels were measured only for lung carcinoma. This increases the strength of our study demonstrating that LDH might be a potentially useful marker to assist in early intervention of severe tumor burden and metastasis of disease. However, LDH isoenzymes are not quantified in our study which might be more beneficial to understand the site specific metastasis of lung cancer.

CONCLUSION

In conclusion, our study suggest that elevated LDH level is independently associated with metastasis of lung cancer. Due to more feasible and economical to routine clinical work LDH can be used as a useful serum marker in early detection of metastasis of lung cancer. Even though, due to lack of specificity and sensitivity of serum markers, additional markers should be done in clinical practice to assess the metastasis of lung cancer.

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