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Original Research Article

CORRELATION BETWEEN SERUM LDH(LACTATE DEHYDROGENASE) AND GGT(GAMMA GLUTAMYL TRANSFERASE) LEVELS WITH CERVICAL CANCER PROGRESSION: A RADIANT INSIGHT

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Abstract

Background: Cervical cancer remains a pressing global health concern, especially affecting women in underserved regions. The study aims to estimate the levels of serum LDH and GGT levels in cervical cancer. Specifically, it seeks to determine the relationship between correlations of LDH with GGT of Cervical cancer patients. **Materials and Methods:** The research enrolled 60 women undergoing radiation therapy for confirmed cervical cancer diagnoses. An additional 60 healthy women served as age-matched controls. Patients were categorized into stages I, II, and III based on the FIGO classification. Serum LDH and GGT levels were quantified using established methods. **Result:** The study uncovered a significant elevation in LDH and GGT levels corresponding to advanced cervical cancer stages. Analysis revealed a positive correlation between LDH and GGT levels in cervical cancer patients. Conversely, no significant correlation was noted in the control group, indicating specificity cancer-related alterations. **Conclusion:** The findings underscore the importance of monitoring LDH and GGT levels in cervical cancer patients as potential indicators of disease severity and progression. Further research is warranted to validate these findings and explore the mechanistic links between LDH, GGT, and cervical cancer pathogenesis, with the ultimate goal of improving diagnostic and prognostic strategies for this disease.

INTRODUCTION

Cervical cancer is a serious type of cancer that starts in the cells of the cervix, which is the lower part of the uterus It is one of the most common cancers affecting women around the world, with more than half a million new cases and over a quarter of a million deaths every year.[1] Most of these cases and deaths happen in developing countries, where women have less access to screening and treatment .In India, cervical cancer is the most common cancer among women of all ages, and the most common cause of cancer death among women between 15 and 44 years old.[2] Because there is no regular screening program in India, many women with cervical cancer are diagnosed when the cancer is already advanced and hard to treat. This leads to very low survival rates for these women.[3] To improve survival rates, it is important to detect cervical cancer early, before it spreads to other parts of the body. However, many women do not know the signs and symptoms of cervical cancer, or they do not have enough health care services to get tested and treated.[4] One way to help diagnose cervical cancer early is to use a blood test that measures a protein called lactate dehydrogenase (LDH). LDH is an enzyme that helps break down sugar for energy in cells.[5] When cells are damaged or dying, they release LDH into the blood. High levels of LDH in the blood can indicate that there is a lot of cell damage or death happening in the body, which could be caused by cancer or other diseases.[6] By measuring LDH levels in women with cervical cancer, doctors can get an idea of how much the cancer has grown and spread, and how well the treatment is working. LDH can also help predict if the cancer is likely to come back after treatment.[7] Warburg reported that tumor cells use glucose at a higher rate and produce more lactate. LDH is an enzyme that has been found to be increased in many cancers. It also correlates with the clinical stage of the disease.[8] Gamma-glutamyltransferase (GGT) is another enzyme that has clinical significance. It is mainly used as a marker of liver disease and alcohol intake.[8,9] However, several studies have shown that

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GGT is associated with increased risk, spread, relapse, and poor outcomes of various cancers, such as digestive, respiratory, female genital, genitourinary, breast, lymphoid, and hematopoietic cancers.[10-12] GGT is an enzyme that participates in glutathione (GSH) metabolism, which is responsible for transferring gamma-glutamyl groups. GSH metabolism is essential for cellular protection against oxidative stress, which occurs as a result of normal metabolic processes. GSH and GGT influence the equilibrium between cell growth and death, and have a role in tumor development, invasion and resistance to anticancer drugs. Elevated GGT levels have been correlated with advanced tumor stages in cervical cancer patients.[13] Cervical cancer is a major health problem in India, but there is limited data on the role of serum enzymes such as GGT and LDH in its diagnosis and prognosis. This study aimed to evaluate the serum levels of GGT and LDH in cervical cancer patients and compare them with age-matched healthy controls. The main objective of this study is to assess the correlation of serum GGT and LDH levels with cervical cancer.

MATERIALS AND METHODS

This study measured the serum levels of two enzymes, LDH and GGT, in patients with cervical cancer. The study was carried out in the Biochemistry Department of Government Medical College and Superspeciality Hospital, Nagpur, between January 2012 and April 2013. The research adhered to a predefined protocol and received the consent of the institutional ethics board. All the participants gave their written consent before taking part in the study.

We enrolled 60 women with cervical cancer who had a confirmed diagnosis by clinical and histopathological examination. The cervical cancer cases were classified into stages I, II and III according to the FIGO classification. We also recruited 60 healthy and normal women as controls who were matched with the cases by age. The cases and controls were women aged between 35 and 75 years.

We divided all the cases and controls into two groups:

1. Group A: 60 women with cervical cancer
2. Group B: 60 healthy women as controls

The study included cervical cancer patients who were 35-75 years old and had clinical and histopathological confirmation of their diagnosis. The control group consisted of healthy females in the same age range who did not have any family history of cervical cancer. Both groups excluded patients who had any of the following conditions or factors: myocardial infarction, thyroid dysfunction, liver diseases, pancreatic disease, chronic renal diseases, diabetes mellitus, hypertension, other malignancies, alcoholics and smokers, pulmonary diseases, hemolytic anemia, sickle cell anemia, or patients on anti-epileptics and anti-psychotics and pregnancy. We did not include any stage IV cases in our research. A sterile, disposable syringe and needle were used to draw 2 ml of venous blood from the anti-cubital vein of each participant. The blood samples were aseptically transferred to a clean dry sterile plain bulb. After clotting, serum was separated by centrifugation. Serum parameters were estimated without delay. The following methods were used to measure serum parameters on a Semi autoanalyser: Serum LDH was determined by the Modified IFCC Method .Serum GGT was assessed by the Carboxy substrate method which involves the hydrolysis of gamma-glutamyl-p-nitroanilide by GGT and the formation of a yellow product.

Statistics: To analyze the data, we employed GraphPad Prism (United States) as our statistical software. We conducted an unpaired t test to evaluate the difference in the means of the two groups. We also performed simple linear regression to investigate the association between two variables in each group. We adopted a significance level of 0.05 and considered any p-values below this level as statistically significant.

RESULTS

The [Table 1]. Shows the mean and standard deviation of age, serum LDH and serum gamma glutamyl transferase for patients with different stages of cervical cancer and a control group. The findings suggest a notable statistical significance difference in serum LDH and serum gamma glutamyl transferase levels among the groups, with higher values in more advanced stages of the disease. The p values for these two variables are less than 0.001, indicating a high statistical significance. However, there is no significant difference in age among the groups, as the p value is 0.05, which is above the commonly used threshold of 0.05.

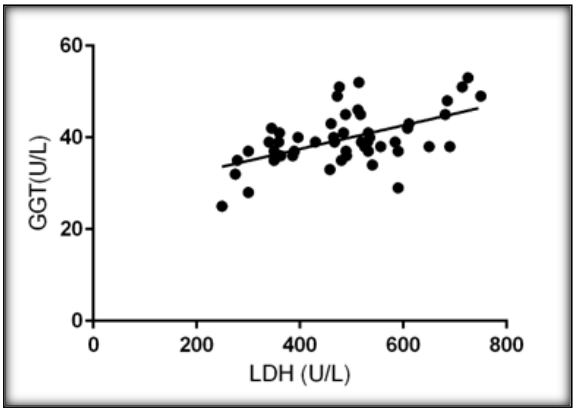

Figure 1 A. The Correlation of LDH with GGT of Cervical cancer patients

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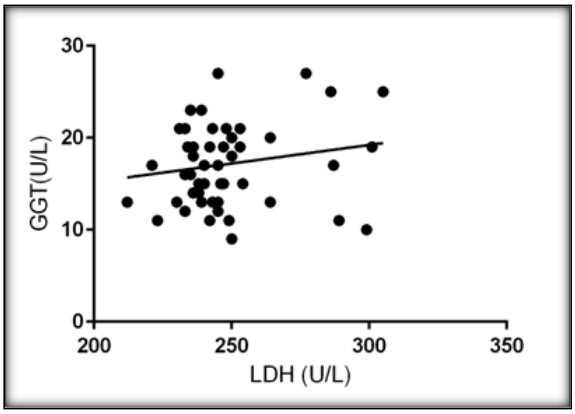

Figure 1 B. The Correlation of LDH with GGT of Controls

The LDH level had a significant positive correlation with the GGT level in cervical cancer patients (P <0.001) Y = 0.02569*X + 27.23 [Figure 1]

The results showed that there was a significant positive correlation between LDH and GGT levels in cervical cancer patients (P <0.001), meaning that higher LDH levels were associated with higher GGT levels. The linear regression equation for this relationship was Y = 0.02569*X + 27.23, where Y is the GGT level and X is the LDH level. This equation can be used to estimate the GGT level from the LDH level in cervical cancer patients.

The LDH level had a no correlation with the GGT level in controls (P= 0.2229) Y = 0.04021*X + 7.167. [Figure 2]

The results showed that there was no significant relationship between the levels of LDH and GGT in the control group, as indicated by the P-value of 0.2229. The linear regression equation for the control group was Y = 0.04021*X + 7.167, where Y is the LDH level and X is the GGT level.

Table 1: Serum LDH and GGT level among cases and controls

	Stage 1,2 and 3 of Cervical cancer patients (n=60)	Control (n=60)	P Value
Age	49.50± 6.56	50.4 ± 7.51	0.05.
Serum LDH (U/L)	427.28.0 ± 52.71	245.3 ± 4.34	< 0.001
Serum gamma glutamyl transferase	37.34± 1.17	19.04 ± 1.46	<0.001

DISCUSSION

The results of this study suggest that serum LDH and GGT levels are useful biomarkers for the diagnosis and prognosis of cervical cancer. Previous studies have reported that elevated LDH and GGT levels are associated with poor survival and increased risk of recurrence in cervical cancer patients.[8,12] LDH is an enzyme that catalyzes the conversion of lactate to pyruvate, and its elevation reflects increased glycolysis and hypoxia in tumor cells.[13] GGT is an enzyme that transfers gamma-glutamyl groups from glutathione to other amino acids, and its elevation indicates increased oxidative stress and glutathione depletion in tumor cells.[14] Both LDH and GGT are involved in the metabolic reprogramming of cancer cells, which is a hallmark of malignant transformation.[15] LDH and GGT are two enzymes that have been found to be positively correlated in cervical cancer patients. This means that higher levels of one enzyme are associated with higher levels of the other. One possible explanation for this correlation is that LDH and GGT are both regulated by the same factors, such as HIF-1. HIF-1 is a transcription factor that activates genes that help tumor cells survive in low oxygen environments. Therefore, LDH and GGT may be part of the tumor's adaptation to hypoxia.[16] The lack of correlation between LDH and GGT levels in the control group suggests that these enzymes are not affected by physiological factors, such as age, sex, or liver function, in healthy individuals. The linear regression equation for the control group shows that the LDH level increases slightly with the GGT level, but the slope is very low and the intercept is close to the normal range of LDH. This indicates that there is no significant relationship between these two variables in the absence of cancer.

Routine blood tests can assess the levels of serum LDH and GGT, which are important indicators of the disease stage and course. These tests are simple and convenient, and they can help clinicians monitor the disease status and response to treatment. Moreover, these biomarkers can be used to monitor the response to treatment and to detect early signs of recurrence or metastasis. However, there are some limitations to this study that should be acknowledged. First, the sample size was relatively small, and the study was conducted in a single center. Therefore, the results may not be generalizable to other populations or settings. Second, the study did not include other potential confounding factors, such as tumor size, histological type, or treatment modalities, which may affect the LDH and GGT levels in cervical cancer patients. Third, the study did not investigate the molecular mechanisms underlying the regulation of LDH and GGT expression and activity in cervical cancer cells. More research is required to clarify how they affect the disease process and outcome.

CONCLUSION

This study demonstrated that serum LDH and GGT levels are significantly elevated in cervical cancer patients compared to healthy controls, and that they correlate positively with each other and with the stage of the disease. These findings suggest that serum LDH and GGT levels are potential biomarkers for the diagnosis and prognosis of cervical cancer.

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