

Lactate Dehydrogenase as an Independent Prognostic Marker of Chemotherapy Response in Patients with Germ Cell Tumors: A Study from a Tertiary Care Hospital, Rawalpindi

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ABSTRACT

Objective: To determine the association of raised Lactate Dehydrogenase (LDH) levels with response to chemotherapy in germ cell tumor patients managed at a tertiary care oncology unit

Study Design: Prospective observational study

Place and Duration of Study: Medical Oncology Department, Combined Military Hospital Rawalpindi, Pakistan, from Sep to Dec 2024

Methodology: This study was conducted on patients of germ cell tumors managed with chemotherapy. Serum LDH levels and other relevant biochemical assessments were done along with physical examination at the time of diagnosis. Standard chemotherapy was provided to all the patients, and response was assessed at the end of the cycle in all the patients by the treating team. Association of raised LDH levels at the time of diagnosis and other factors was observed with response to treatment in all the study participants.

Results: Seventy patients of germ cell tumors were recruited in this study after application of inclusion/exclusion criteria. Mean age of the germ cell tumor patients included in the study was 39.07 ± 10.55 years. All the patients were male in this study. At the end of the chemotherapy session, patients who had raised LDH at the time of diagnosis and those who were classed as poor risk did not have a good response to treatment ($p\text{-value} < 0.05$).

Conclusion: Raised serum LDH levels at the time of diagnosis and being classified as poor risk at the time of diagnosis were the factors significantly associated with a poor response to chemotherapy in patients of germ cell tumors included in our study.

Keywords Chemotherapy; Germ cell; LDH; Response

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INTRODUCTION

Cancerous conditions can occur in almost all tissues of the body, and the prevalence of these conditions is on the rise in both developed and lower-and middle-income countries.¹ High prevalence rates in lower- and middle-income countries are alarming because health budgets and facilities are limited and cannot cater for a large number of patients suffering from these potentially lethal conditions.² Timely diagnosis and staging of patients may help the treating teams to pick up the cases with good response to treatment and manage them aggressively to minimize the mortality and morbidity.³

Chemotherapeutic agents for management of various neoplastic conditions have been under constant evolution in the last three decades.⁴ Response to chemotherapy in patients of different cancers depends upon several patient-related and illness

factors.⁵ A lot of tumor markers and biochemical markers have been used for predicting response to treatment in patients with germ-cell tumors.⁶ Biochemical markers are usually non-invasive and cost-effective investigations; therefore, widely used for clinical and research purposes.

The role of biochemical markers in diagnosis and predicting the prognosis has been evolving with time, and both clinicians and researchers are trying to make the best use of them. There could be multiple markers that could be incorporated in clinical practice to look for patients who could have a better prognosis. Neutrophil-lymphocyte ratio, C-reactive protein, and lactate dehydrogenase have been in practice for this purpose for various malignant conditions.⁷ A recent study included patients with various cancers and measured their LDH levels at baseline. It was found that LDH levels of more than 1000IU/L were associated with poor treatment outcome.⁸ Dieckmann et al., in 2019, studied patients suffering from testicular germ cell tumours and tried to evaluate the relationship of various tumour markers with response

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to treatment. Raised LDH levels at the time of start of treatment were associated with poor treatment outcome in their study participants.⁹

The burden of neoplastic conditions is no less in our country. Limited health care budgets make things difficult both for patients and treating teams. Expensive investigations are difficult to carry out specially to look for response to treatment. These facts increase the importance of cost-effective investigations like biochemical markers in our clinical settings. Saeed et al. published a study from Shaukat Khanum Memorial Hospital which showed that out of total patients with germ cell tumours, 42% had dysgerminoma, 25% had mixed germ cell tumours, 18% had yolk sac tumour, 13% had teratoma and 2% had embryonal carcinoma.¹⁰ Keeping in view these figures and availability of limited local data, we planned this study with the rationale to look for association of raised LDH levels and other factors with response to chemotherapy in germ cell tumor patients managed at tertiary care oncology unit.

METHODOLOGY

This Prospective observational study was conducted at the Medical Oncology Department, Combined Military Hospital from September 2024 to December 2024. Non-probability consecutive sampling technique was used to recruit the patients of germ cell tumors for this study. Sample size was calculated using the WHO sample size calculator by using the population prevalence proportion of germ cell tumors as 0.1%.¹¹

Inclusion Criteria: Patients of both genders between the age of 18 and 65 years diagnosed with any type of germ cell tumor, consenting for treatment and recruitment in this study, were included.

Exclusion Criteria: Patients with malignancies other than germ cell tumors, autoimmune disorders, and uncontrolled systemic illnesses were excluded. Patients who had any contraindication to medications included in chemotherapy or those who did not opt for chemotherapy were excluded. Patients who were lost to follow-up during treatment were also not included. Those who could not undergo clinical assessment at the time of completion of chemotherapy were excluded as well.

After ethical approval from the ethical review board committee (letter no. 715) and written informed consent from the patients and/or their caregivers, patients with germ cell tumors who met the criteria

were enrolled. Diagnosis of germ cell tumor and classification into subgroups were made by the consultant oncologist, incorporating clinical and histopathological findings as per the study protocols. The tumor type according to risk was classified by the treating team based on relevant clinical and laboratory findings. All baseline investigations, including relevant tumor markers, were carried out for all patients before the start of chemotherapy. Study participants underwent chemotherapy cycles as per guidelines and were regularly assessed for their clinical condition. At the end of each cycle, they were classified as having a good or poor response based on residual disease and tumor marker levels. The association of raised LDH (2.5 times or more than the upper limit of normal), alpha-fetoprotein (AFP), and β -hCG levels with the poor-risk group and poor response to treatment in our study participants was assessed.

Characteristics of patients and the distribution of response types to treatment were described using descriptive statistics. Chi-square and Fisher's exact tests were used to assess associations between elevated LDH, alpha-fetoprotein (AFP) and β -hCG levels and the poor-risk group with poor response to treatment. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 24.0 (SPSS-24.0). Associations were considered significant if p-values were less than or equal to 0.05.

RESULTS

Seventy patients with germ cell tumors were recruited in this study after application of inclusion/exclusion criteria. Mean age of the germ cell tumor patients included in the study was 39.07 ± 10.55 years. Table-I summarizes the general characteristics of study participants. All the patients included in this study were male. 35(50.0%) patients had seminomatous tumors while 35(50.0%) patients had non-seminomatous tumors. Out of the total patients, 39(55.7%) had Stage-I tumors, 20(28.6%) had stage-II tumors, while 11(15.7%) had stage-III tumors. Among our study participants, 39(55.7%) were classed as good risk while 31(44.3%) were classed as poor risk.

Results of statistical analysis have been summarized in Table-II. It was observed that at the end of the chemotherapy session, patients who had elevated LDH at the time of diagnosis (p -value > 0.001) and those who were classified as poor risk (p -value = 0.003) had a higher likelihood of a good response to

treatment. Serum AFP levels (p -value-0.499) and β -hCG levels (p -value-0.063) were not significantly associated with the response to treatment in our study participants.

Table-I: Characteristics of patients of germ cell tumors included in this study (n=70)

Parameters	Values
Mean Age of patients (years) Mean + SD	39.07 $\pm$ 10.55 years
Gender	
Male	70(62.9%)
Female	00 (0.0%)
LDH levels	
Less than 2.5 times the upper limit of Normal	44(62.9%)
2.5 times or more of upper limit of Normal	26(37.1%)
Risk classification	
Good Risk	39(55.7%)
Poor Risk	31(44.3%)
Response to Chemotherapy	
Good	24(34.3%)
Poor	46(65.7%)
Stage	
I	39(55.7%)
II	20(28.6%)
III	11(15.7%)
Type of tumor	
Seminomatous	35(50.0%)
Non-Seminomatous	35(50.0%)

*LDH - Lactate Dehydrogenase, SD - Standard Deviation

Table-II: Association of various factors with response to chemotherapy in patients with germ cell tumors (n=70)

Parameters	Good response	Poor response	p -value
Risk classification			
Good	19(79.2%)	20(43.4%)	0.003
Poor	05 (20.8%)	26(56.6%)	
Serum LDH levels			
Less than 2.5 times the normal	22(91.6%)	22(47.8%)	<0.001
2.5 times or more	02(8.4%)	24(52.2%)	
Serum AFP levels			
Less than 1000 times	11(45.8%)	25(54.3%)	0.499
1000 times or more	13(54.2%)	21(45.7%)	
β -hCG levels			
Less than 5000 times	16(66.6%)	20(43.4%)	0.063
5000 times or more	08(33.4%)	26(56.6%)	

*LDH - Lactate Dehydrogenase, AFP - Alpha-Fetoprotein, β -hCG - Beta-Human Chorionic Gonadotropin

DISCUSSION

Our study findings revealed that elevated serum LDH levels at the time of diagnosis were significantly associated with poor response to chemotherapy in patients with germ cell tumors. Malignancies across different systems are responsible for high mortality and morbidity among patients of all age groups globally. Germ cell tumors also contribute considerably to these mortality and morbidity figures.¹² Targeting patients with an aggressive approach who could benefit most from treatment

usually benefits both the patient and the health care system, as resources are directed more toward eligible patients.¹³ Various tumor markers and other clinical parameters have been used to predict response to treatment and identify patients who could benefit more from treatment.¹⁴ This study was conducted to examine the association of elevated LDH levels and other factors with response to chemotherapy in patients with germ cell tumors managed at tertiary care oncology units.

Patel et al., performed a study to look for elevated serum LDH levels in patients diagnosed with germ cell tumors. They revealed that levels were significantly higher in patients who had metastatic disease. Results of their study also revealed that levels of LDH significantly declined in patients who responded to chemotherapy.¹⁵ Our study design was slightly different, and results of our study showed that high levels of LDH at the time of diagnosis were associated with poor treatment response. Response to chemotherapy and LDH levels in blood have a multidimensional relationship which needs to be explored in detail from various angles.

Global Germ Cell Tumor Collaborative Group (G3) analyzed patients of seminoma and looked for prognostic significance of raised LDH levels in these patients. They found that raised LDH levels had prognostic significance and could be used in routine clinical practise.¹⁶ Our results supported their findings, as raised serum LDH levels at the time of diagnosis and being classified as poor risk at the time of diagnosis were the factors significantly associated with a bad response to chemotherapy in patients of germ cell tumours included in our study.

Nair et al., published a study from India regarding outcomes and factors determining outcome in patients managed for seminomatous tumors. Multiple factors, especially having non-pulmonary metastatic disease, were significantly related to poor outcome.¹⁷ We only studied the relationship of biochemical markers with poor outcome and found that serum LDH at the time of diagnosis was associated with poor outcome in our patients. Outcome of cancer after standard chemotherapeutic management depends on several factors, and if a simple marker could predict the outcome at the time of diagnosis, this could be incorporated in guidelines.

Poor-risk patients of testicular germ cell tumors were assessed by Lakshmi et al., in 2022 regarding the role of tumor markers in predicting outcome.¹⁸ It was

revealed that patients with elevated LDH and β -hCG levels had poor outcomes. Our results supported their results in this regard.

Another similar study published in India studied the relationship of raised LDH with poor prognosis of patients of breast cancer.¹⁹ It was found that a positive association existed between poor prognosis in patients and raised LDH. Vasanth *et al.*, reported similar results in a study published in 2023 in the population of western India.²⁰ Therefore, our results remain in accordance with recent existing literature of our region.

LIMITATION OF STUDY

Patients with malignancies may have multiple cancer-related or other conditions which may cause a rise in LDH and interfere with the results. Moreover, treatment outcome depends upon the number of patients and treatment-related factors which could interfere with the study results. Control of confounding factors and a sophisticated study design may generate better results and demonstrate the association of raised LDH with poor response to treatment in a more accurate way.

CONCLUSION

Raised serum LDH levels at the time of diagnosis and being classified as poor risk at the time of diagnosis were the factors significantly associated with bad response to chemotherapy in patients of germ cell tumors included in our study.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

R & MHB: Data acquisition, data analysis, critical review, approval of the final version to be published.

MN & SMS: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

HMD: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

- Hao T, Li-Talley M, Buck A, Chen W. An emerging trend of rapid increase of leukemia but not all cancers in the aging population in the United States. *Sci Rep* 2019; 9(1): 12070. <https://doi.org/10.1038/s41598-019-48445-1>
- Miranda-Filho A, Piñeros M, Ferlay J, Soerjomataram I, Monnereau A, Bray F. Epidemiological patterns of leukaemia in 184 countries: a population-based study. *Lancet Haematol* 2018; 5(1): e14-e24. [https://doi.org/10.1016/S2352-3026\(17\)30232-6](https://doi.org/10.1016/S2352-3026(17)30232-6)
- Yang J, Nittala MR, Velazquez AE, Buddala V, Vijayakumar S. An Overview of the Use of Precision Population Medicine in Cancer Care: First of a Series. *Cureus* 2023; 15(4): e37889. <https://doi.org/10.7759/cureus.37889>
- Tilsed CM, Fisher SA, Nowak AK, Lake RA, Lesterhuis WJ. Cancer chemotherapy: insights into cellular and tumor microenvironmental mechanisms of action. *Front Oncol* 2022; 12(3): 960317. <https://doi.org/10.3389/fonc.2022.960317>
- Pathak S, Zajac KK, Annaji M, Govindarajulu M, Nadar RM, Bowen D, et al. Clinical outcomes of chemotherapy in cancer patients with different ethnicities. *Cancer Rep* 2023; 6(Suppl 1): e1830. <https://doi.org/10.1002/cnr2.1830>
- Janicic A, Petrovic M, Zekovic M, Vasilic N, Coric V, Milojevic B, et al. Prognostic Significance of Systemic Inflammation Markers in Testicular and Penile Cancer: A Narrative Review of Current Literature. *Life* 2023; 13(3): 600. <https://doi.org/10.3390/life13030600>
- Sung M, Jang WS, Kim HR, Park JA, Lim SM, Kim HR, et al. Prognostic value of baseline and early treatment response of neutrophil-lymphocyte ratio, C-reactive protein, and lactate dehydrogenase in non-small cell lung cancer patients undergoing immunotherapy. *Transl Lung Cancer Res* 2023; 12(7): 1506-1516. <https://doi.org/10.21037/tlcr-23-7>
- Liu R, Cao J, Gao X, Zhang J, Wang L, Guo L et al. Overall survival of cancer patients with serum lactate dehydrogenase greater than 1000 IU/L. *Tumor Biol* 2016; 37(3): 14083-14088. <https://doi.org/10.1007/s13277-016-5228-2>
- Dieckmann KP, Simonsen-Richter H, Kulejewski M, Anheuser P, Zecha H, Isbarn H, et al. Serum Tumour Markers in Testicular Germ Cell Tumours: Frequencies of Elevated Levels and Extents of Marker Elevation Are Significantly Associated with Clinical Parameters and with Response to Treatment. *Biomed Res Int* 2019; 2019(3): 5030349. <https://doi.org/10.1155/2019/5030349>
- Saeed K, Sadaf T, Siddiqui N, Syed AA, Jamshed A. Malignant ovarian germ cell tumors-Survival outcomes from a single institution in Pakistan. *J Cancer Allied Spec* 2015; 1(2): 4-8. <https://doi.org/10.37029/jcas.v1i2.32>
- Ozaki Y, Narita T, Hatakeyama S, Tanaka T, Togashi K, Hamaya T, et al. Trends of incidence and age in adults with testicular germ cell tumors: a two-decade multicenter retrospective study. *Transl Androl Urol* 2023; 12(2): 161-167. <https://doi.org/10.21037/tau-22-521>
- Lobo J, Leão R. Editorial: Diagnostic and predictive biomarkers in testicular germ cell tumors. *Front Oncol* 2022; 12(3): 1027363. <https://doi.org/10.3389/fonc.2022.1027363>
- Adra N, Althouse SK, Liu H, Brames MJ, Hanna NH, Einhorn LH, et al. Prognostic factors in patients with poor-risk germ-cell tumors: a retrospective analysis of the Indiana University experience from 1990 to 2014. *Ann Oncol* 2016; 27(5): 875-879. <https://doi.org/10.1093/annonc/mdw045>
- King JM, Althouse S, Cary C, Masterson T, Foster RS, Ashkar R, et al. Surveillance after Complete Response to First-Line Chemotherapy in Patients with Metastatic Nonseminomatous Germ Cell Tumor. *J Urol* 2022; 208(3): 641-649. <https://doi.org/10.1097/JU.0000000000002751>

15. Patel P, Sharma V, Raval G, Rawal RM, Patel MM, Balar DB et al. Serum lactate dehydrogenase levels in malignant germ cell tumors of ovary. *Int J Gynecol Cancer* 1996; 6(3): 328-332.
<https://doi.org/10.1046/J.1525-1438.1996.06040328.X>
 16. Seidel C, Daugaard G, Nestler T, Tryakin A, Fedyanin M, Fankhauser CD, et al. The prognostic significance of lactate dehydrogenase levels in seminoma patients with advanced disease: an analysis by the Global Germ Cell Tumor Collaborative Group (G3). *World J Urol* 2021; 39(9): 3407-3414.
<https://doi.org/10.1007/s00345-021-03635-3>
 17. Nair LM, Krishna KMJ, Kumar A, Mathews S, Joseph J, James FV. Prognostic factors and outcomes of nonseminomatous germ cell tumours of testis-experience from a tertiary cancer centre in India. *Ecancermedalscience* 2020; 14(3): 1145.
<https://doi.org/doi:10.3332/ecancer.2020.1145>
 18. Lakshmi KH, James FV, Kumar A, Joseph J, Km JK. Tumor Marker Decline in Predicting Treatment Outcome among Poor-Risk Testicular Germ Cell Tumors-A Tertiary Cancer Center Data. *South Asian J Cancer* 2022; 11(3): 218-222.
<https://doi.org/doi:10.1055/s-0042-1743423>
 19. Malhotra G, Gattani RG, Shinde RK, Gianchandani SG, Nayak K, Salwan A. Significance of Serum Lactate Dehydrogenase as a Prognostic Marker and Outcome Predictor in Patients With Breast Cancer. *Cureus* 2024; 16(3): e55932.
<https://doi.org/doi:10.7759/cureus.55932>
 20. Vasanth A, Patel SM, Arora R, Parekh CD, Dave P, Patel BM, et al. Study of neoadjuvant chemotherapy in advanced malignant ovarian germ cell tumors at a tertiary center in western India. *J Gynecol Oncol* 2024; 35(2): e19.
<https://doi.org/doi:10.3802/jgo.2024.35.e19>
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