

Comparison of Response Rate of RCHOP Chemotherapy in Germinal Center B-cell like vs non-Germinal Center B-cell like Diffuse Large B cell non-Hodgkin Lymphoma

Irfan Ali, Nadeem Paracha, Sobia Latif, Syed Saif ul Hassan, Sajid Hussain

Department of Medical Oncology, Combined Military Hospital/National University of Medical Sciences (NUMS), Rawalpindi Pakistan

ABSTRACT

Objective: To compare response rate of RCHOP chemotherapy in patients of germinal center B-cell like vs non-germinal center B-cell like diffuse large B cell non-Hodgkin lymphoma.

Study Design: Prospective comparative study.

Place and Duration of Study: Oncology Department, Combined Military Hospital Rawalpindi, Pakistan Aug 2021 to Jul 2023.

Methodology: This study was conducted on patients who were diagnosed with diffuse large B cell non Hodgkin lymphoma at out oncology unit. Patients were divided into two Groups for the sake of comparison. Group-I had patients with germinal center B-cell like lymphoma while Group-II had patients with non-germinal center B-cell like lymphoma. Both the Groups were administered standard R-CHOP chemotherapy for six cycles after every twenty-one days. At the end of six cycles, response via Deauville score (PET scan), presence of neutropenia and mortality were compared in both the Groups.

Results: A total of ninety patients diagnosed as diffuse large B cell lymphoma were recruited for this study. Median age of the lymphoma patients included in the study was 43 (41) years. Out of total patients, 55(61.1%) were male while 35(38.9%) were female. At the end of six cycles of RCHOP chemotherapy, response was statistically significantly better in GCB patients as compared to non-GCB patients (p -value<0.001).

Conclusion: Patients suffering from germinal center B-cell like had better response on PET scan at the end of six cycles of R-CHOP chemotherapy as compared to patients managed for non-germinal center B-cell like lymphoma. Neutropenia and deaths were seen more in patients who suffered from non-germinal center B-cell like lymphoma.

Keywords: Germinal Center B-Cell Like; Non-Hodgkin Lymphoma; Response; R-CHOP.

How to Cite This Article: Ali I, Paracha N, Latif S, Hassan SS, Hussain S. Comparison of Response Rate of RCHOP Chemotherapy in Germinal Center B-cell like vs non-Germinal Center B-cell like Diffuse Large B cell non-Hodgkin Lymphoma. Pak Armed Forces Med J 2026; 76(Suppl-9): S1544-S1547.

DOI: <https://doi.org/10.51253/pafmj.v76iSUPPL-9.11663>

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Hematological malignancies have been diagnosed at an alarming rate in patients of all age Groups in recent past in almost all parts of the world.¹ Situation is not different in developing countries where health budget is limited and public sector facilities are insufficient to cater for huge burden of these malignancies.² Non-Hodgkin lymphoma has similar epidemiological profile and diffuse large B cell lymphoma is a fairly common diagnosis in hematology and oncology units.³ Timely diagnosis, categorization of sub-type and start of appropriate treatment may reduce mortality and morbidity associated with this cancer.

Chemotherapeutic agents have been under constant evolution in last three decades.⁴ Though surgery, chemotherapy, radiation therapy, immunotherapy and multiple other modalities may be used for management of malignant conditions but still

chemotherapy usually remains the main type of treatment in most of the patients especially with hematological malignancies.⁵ In patients with non-Hodgkin lymphomas, exact categorization of sub-type of lymphoma may be of utmost importance before starting the chemotherapeutic regimen.⁶

Literature has been published from all across the world regarding response of patients with DLBCL with RCHOP chemotherapy. A phase 3 comparison of dose intensification at 14th and 21st day was conducted by Cuunningham et al. on patients newly diagnosed with DLBCL. It was concluded that there was no difference on dose intensification at 14th or 21st day and molecular subtype also did not make any difference on response of patients to chemotherapy.⁷ Predictive role of 18F-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography/computed tomography (PET/CT) was studied for patients managed for germinal centre like and non-germinal centre like diffuse large B-cell lymphoma. This scanning technique had a predictive value for disease progression in patients with the GCB subtype of DLBCL treated with R-CHOP but not for non-GCB

Correspondence: Dr Irfan Ali, Department of Medical Oncology, Combined Military Hospital, Rawalpindi Pakistan

Received: 18 Feb 2024; revision received: 26 May 2024; accepted: 29 May 2024

subtype treated with same chemotherapeutic regimen.⁸ He *et al.*, published a study from China and revealed that R-CHOP regimen can improve the prognosis of patients managed for non-GCB subtype DLBCL.⁹

Oncology is a continuously evolving medical specialty in our part of the world. Hematological malignancies are dealt by both hematologist and oncologist in Pakistan. A recent local study published in BMC research notes summarized the whole clinico-pathological profile of patients managed with Diffuse Large B Cell Lymphoma (DLBCL) in Pakistan.¹⁰ Still there is a lot of gap in local data regarding treatment response to set chemotherapeutic regimens used for treating these conditions in our population especially with regards to sub-types of lymphomas. We therefore planned this study with the rationale to compare response rate of R-CHOP chemotherapy in patients of germinal center B-cell like vs non-germinal center B-cell like diffuse large B cell non-Hodgkin lymphoma.

METHODOLOGY

This Prospective comparative study was conducted at the Oncology Department, Combined Military Hospital from August 2021 to July 2023. Non-probability consecutive sampling technique was used to recruit the patients of DLBCL for this study. Sample size was calculated by WHO sample size calculator by using the two Groups. Group-I had patients of germinal centre B-cell like 78.8% while Group-II had patients of non-germinal centre B-cell like diffuse large B cell lymphoma 43.3%.¹¹

Inclusion Criteria: Patients of both genders between the age of 18 and 65 years diagnosed with DLBCL undergoing RCHOP chemotherapy were included in the study.

Exclusion Criteria: Patients with malignancies other than DLBCL, autoimmune disorders and uncontrolled systemic illnesses were not recruited in this study. Patients who had any contraindication to medications included in R-CHOP chemotherapy or those who did not opt for RCHOP chemotherapy were excluded. Patients who lost to follow up during the course of treatment were also not included. Those who could not undergo PET scan due to any reason at the end of six cycles of R-CHOP chemotherapy treatment were excluded as well.

After ethical approval from the ethical review board committee (letter no 475) and written informed consent from the patients and/or their care-givers,

patients of DLBCL fulfilling the criteria were enrolled. Diagnosis of DLBCL was made by consultant oncologist by incorporating clinical and histopathology findings.¹² Type of DLBCL (GCB and non-GCB) was determined by immunohistochemistry¹³ in histopathology department of Armed Forces Institute of pathology. Patients after the typing were divided into two Groups as GCB and non-GCB. Both the Groups were administered standard RCHOP therapy by consultant oncologist of our department for six cycle repeated every twenty one days.¹⁴ After six cycles of treatment (six weeks post last chemotherapy) all the study participants underwent PET scan to look for the response to treatment. Response was based on Deauville scale score which was calculated by assessing the residual uptake on PET scan. The score could be from 1 to 5. Score from 1-3 was taken as good response while score of 4-5 was taken as poor response.¹⁵

All statistical analysis was performed using Statistics Package for Social Sciences version 24.0 (SPSS-24.0). Characteristics of patients and the distribution of the type of DLBCL were described by using the descriptive statistics. Chi-square and Fischer exact tests were used to determine the comparison of response, neutropenia and mortality among the two study Groups. Differences between Groups were considered significant if *p*-values were less than or equal to 0.05.

RESULTS

A total of ninety patients diagnosed as diffuse large B cell lymphoma were recruited for this study. Median age of the lymphoma patients included in the study was 43 (41) years. Table-I summarized the clinical and demographic characteristics of patients of DLBCL recruited in this study. Out of total patients, 55(61.1%) were male while 35(38.9%) were female. After six cycles of treatment, 61(67.7%) had good (Deauville scale score 1-3) response while 29(32.3%) had poor (Deauville scale score 4-5) response. With regards to adverse effects 72(80%) did not have neutropenia while 18(20%) patients had neutropenia during the course of treatment. Out of 90 patients 3(3.3%) died during the treatment.

Table-II summarized the results of comparison. Patients were divided into two Groups for the purpose of comparison. Group-I had patients with GCB while Group-II had patients which were non-GCB. At the end of six cycles' of R-CHOP chemotherapy, response was statistically significantly better in GCB patients as

compared to non-GCB patients (p -value<0.001). Patients with non-GCB tumors also had more chances of having neutropenia as compared to patients with GCB (p -value=0.001). Mortality was also seen significantly more in non-GCB patients (p -value=0.005).

Table-I: Characteristics of Patients of Diffuse Large B cell Lymphoma recruited in this Study (n=90)

Parameters	Values
Mean Age of patients (years)	
Median (IQR)	43.0(41.0)
Gender	
Male	55(61.1%)
Female	35(38.9%)
Neutropenia	
No	72(80%)
Yes	18(20%)
Mortality	
No	87(96.7%)
Yes	03(3.3%)
Response to R-CHOP	
Good (Deauville scale score 1-3)	61(67.7%)
Poor (Deauville scale score 4-5)	29(32.3%)
Type of tumor	
GCB Type (Germinal Center B-Cell-like)	65(72.2%)
Non-GCB type (Germinal Center B-Cell-like)	25(27.8%)
Site of tumor	
Nodal	67(74.4%)
Extra-Nodal	23(25.6%)

Table-II: Comparison of Response and other Factors in both the Groups after 6 Weeks of R-CHOP treatment (n=90)

Parameters	Germinal center B-like (n=65)	Non-Germinal center B-like (n=25)	p-value
Response to R-CHOP			
Good	53(81.5%)	08(32%)	<0.001
Poor	12(18.6%)	17(78%)	
Neutropenia			
No	58(89.2%)	14(56%)	0.001
Yes	07(10.8%)	11(44%)	
Mortality			
No	65(100%)	22(88%)	0.005
Yes	0(0%)	03(12%)	

DISCUSSION

Hematological malignancies are responsible for high mortality and morbidity among patients of all age Groups in all parts of the world. Lymphomas make big chunk of these potentially lethal cancerous conditions. With advancement in immuno-histochemistry and other diagnostic modalities researchers and clinicians have been able to categorize and sub categorize these lymphomas so that targeted treatment could be offered to the affected individuals and increase the chances of remission with limited adverse effects. Non-Hodgkin lymphomas is an umbrella term which covers multiple sub types. We for this study targeted patients of diffuse large B cell lymphoma and compared the response rate of R-CHOP chemotherapy in patients of germinal center B-

cell like vs non-germinal center B-cell like tumors managed at our oncology unit of a tertiary care military hospital of Pakistan.

Huang *et al.*, published a study on Chinese patients suffering from DLBCL and assessed repose of different types of tumors to CHOP and R-CHOP treatment. It was revealed that patients managed with RCHOP had better survival as compared to patients managed with CHOP. Moreover, GCB patients showed better response as compared to non-GCB patients.¹⁶ We administered RCHOP to all patients and observed that GCB patients had a better response on PET scan after six cycles of treatment as compared to non-GCB patients. Xia *et al.*, published a similar study and concluded that most of the patients suffering from DLBCL were in GCB Group and when chemotherapy treatment was given RCHOP turned out to be an effective option in both GCB and non-GCB patients but it was clear from their data set that GCB patients had better treatment outcome as compared to non GCB patients.¹⁷ Our results supported the findings generated by Xia *et al.*, as GCB patients had statistically significant better response to R-CHOP chemotherapy when compared to non-GCB patients. Another similar study targeted patients of DLBCL and looked for response of RCOP chemotherapy in non GCB patients. They found out that R-CHOP is beneficial for patients suffering from non GCB DLBCL and improved the survival.¹⁸ We included both GCB and non-GCB patients and concluded that patients suffering from germinal center B-cell like had better response on PET scan at the end of six cycles of R-CHOP chemotherapy as compared to patients managed for non-germinal center B-cell like lymphoma. Neutropenia and deaths were seen more in patients who suffered from non-germinal center B-cell like lymphoma. Tyagi *et al.*, in 2022 published a study from India and studied positron emission tomography scan-based response assessment to chemotherapy in patients managed for DLBCL. They revealed that response was better in GCB patients as compared to non-GCB patients.¹⁹ Our results were similar as that results of population of our neighbouring country.

LIMITATION OF STUDY

Response to treatment could be affected by multiple disease related and overall health related factors therefore with this study design it cannot be concluded that response was actually because of germinal center type of tumor. Response was only recorded with the help of PET scan and clinical factors were not taken into account. Researchers in

future can overcome these limitations by better study design and incorporating clinical response parameters as well and can generate better results.

CONCLUSION

Patients suffering from germinal center B-cell like had better response on PET scan at the end of six cycles of RCHOP chemotherapy as compared to patients managed for non-germinal center B-cell like lymphoma. Neutropenia and deaths were seen more in patients who suffered from non-germinal center B-cell like lymphoma.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

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

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

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

SH: 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. <http://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*; 5(1): e14-e24. [http://doi.org/10.1016/S2352-3026\(17\)30232-6](http://doi.org/10.1016/S2352-3026(17)30232-6)
- Thandra KC, Barsouk A, Saginala K, Padala SA, Barsouk A, Rawla P. Epidemiology of Non-Hodgkin's Lymphoma. *Med Sci* 2021; 9(1): 5. <http://doi.org/10.3390/medsci9010005>
- 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. <http://doi.org/10.3389/fonc.2022.960317>
- Sheikh IN, Elgehiny A, Ragoonanan D, Mahadeo KM, Nieto Y, Khazal S. Management of Aggressive Non-Hodgkin Lymphomas in the Pediatric, Adolescent, and Young Adult Population: An Adult vs. Pediatric Perspective. *Cancers* 2022; 14(12): 2912. <http://doi.org/10.3390/cancers14122912>
- Hübel K. Lymphoma: New Diagnosis and Current Treatment Strategies. *J Clin Med* 2022; 11(6): 1701. <http://doi.org/10.3390/jcm11061701>
- Cunningham D, Hawkes EA, Jack A, Qian W, Smith P, Mouncey P et al. Rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisolone in patients with newly diagnosed diffuse large B-cell non-Hodgkin lymphoma: a phase 3 comparison of dose intensification with 14-day versus 21-day cycles. *Lancet* 2013; 381(9880): 1817-1826. [http://doi.org/10.1016/S0140-6736\(13\)60313-X](http://doi.org/10.1016/S0140-6736(13)60313-X)
- Kim J, Lee JO, Paik JH, Lee WW, Kim SE, Song YS. Different predictive values of interim 18F-FDG PET/CT in germinal center like and non-germinal center like diffuse large B-cell lymphoma. *Ann Nucl Med* 2017; 31(1): 1-11. <http://doi.org/10.1007/s12149-016-1123-6>
- He XH, Li B, Yang S, Lu N, Zhang X, Zou SM, et al. R-CHOP regimen can significantly decrease the risk of disease relapse and progression in patients with non-germinal center B-cell subtype diffuse large B-cell lymphoma. *Chin J Cancer* 2012; 31(6): 306-314. <http://doi.org/10.5732/cjc.011.10420>
- Mahmood H, Habib M, Aslam W, et al. Clinicopathological spectrum of Diffuse Large B Cell lymphoma: a study targeting population yet unexplored in Pakistan. *BMC Res Notes* 2021; 14(1): 354. <http://doi.org/10.1186/s13104-021-05768-5>
- Cho MC, Chung Y, Jang S, Park CJ, Chi HS, Huh J et al. Prognostic impact of germinal center B-cell-like and non-germinal center B-cell-like subtypes of bone marrow involvement in patients with diffuse large B-cell lymphoma treated with R-CHOP. *Medicine* 2018; 97(45): e13046. <http://doi.org/10.1097/MD.00000000000013046>
- Vodicka P, Klener P, Trneny M. Diffuse Large B-Cell Lymphoma (DLBCL): Early Patient Management and Emerging Treatment Options. *Oncotargets Ther* 2022; 15(3): 1481-1501. <http://doi.org/10.2147/OTT.S326632>
- Shen R, Fu D, Dong L, Zhang MC, Shi Q, Shi ZY, et al. Simplified algorithm for genetic subtyping in diffuse large B-cell lymphoma. *Signal Transduct Target Ther* 2023; 8(1): 145. <http://doi.org/10.1038/s41392-023-01358-y>
- Susanibar-Adaniya S, Barta SK. 2021 Update on Diffuse large B cell lymphoma: A review of current data and potential applications on risk stratification and management. *Am J Hematol* 2021; 96(5): 617-629. <http://doi.org/10.1002/ajh.26151>
- Kurch L, Hüttmann A, Georgi TW. Interim PET in Diffuse Large B-Cell Lymphoma. *J Nucl Med* 2021; 62(8): 1068-1074. <http://doi.org/10.2967/jnumed.120.255034>
- Huang Y, Ye S, Cao Y, Li Z, Huang J, Huang H, et al. Outcome of R-CHOP or CHOP regimen for germinal center and nongerminal center subtypes of diffuse large B-cell lymphoma of Chinese patients. *Sci World J* 2012; 2012(1): 897178. <http://doi.org/10.1100/2012/897178>
- Xia Y, Li ZM, Shi YX, Xia ZJ, Jiang WQ, Huang HQ. Short-term efficacy of rituximab-CHOP and CHOP regimens on two subtypes of diffuse large B-cell lymphoma. *Ai Zheng* 2009; 28(2): 146-149.
- He XH, Li B, Yang S. R-CHOP regimen can significantly decrease the risk of disease relapse and progression in patients with non-germinal center B-cell subtype diffuse large B-cell lymphoma. *Chin J Cancer* 2012; 31(6): 306-314. <http://doi.org/10.5732/cjc.011.10420>
- Tyagi A, Abrari A, Khurana A, Tyagi S. Immunohistochemical subtyping of diffuse large B-cell lymphoma into germinal center B-cell and activated B-cell subtype, along with correlation of the subtypes with extranodal involvement, serum lactate dehydrogenase, and positron emission tomography scan-based response assessment to chemotherapy. *J Cancer Res Ther* 2022; 18(4): 1129-1136. http://doi.org/10.4103/jcrt.ICRT_842_20