

CD30 expression and its association with clinicopathological features in diffuse large B-cell lymphoma: A retrospective analysis

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Abstract

Objective: To determine the frequency of CD30 (cluster of differentiation 30) expression in diffuse large B-cell lymphoma (DLBCL), and its association with clinicopathological features.

Method: A retrospective study was conducted between March 2023 and December 2024 at the Department of Histopathology, Shifa International Hospital, Islamabad, Pakistan. The study included cases of diffuse large B-cell lymphoma diagnosed between 5 March 2022 and 5 March 2023. CD30 immunostaining was evaluated using proportional scoring and intensity scoring, and a combined score of ≥ 3 was considered CD30 positive. Its association with age, gender, tumour site and immunophenotype was explored. Data were analysed using SPSS version 25.

Results: Of the 91 patients, 64 (70.3%) were male and 27 (29.7%) were females, while 50 (54.9%) were aged ≥ 50 years and 41 (45.1%) were < 50 years. CD30 expression was noted in 28 (30.8%) cases. No significant association was found for CD30 expression with age ($p=0.276$, $\phi=0.12$), gender ($p=0.878$, $\phi=0.02$) and tumour location ($p=0.507$, $\phi=0.07$). A trend towards association was observed between immunophenotype and CD30 expression ($p=0.072$, Cramér's $V=0.24$).

Conclusion: CD30 expression was observed in less than one-third of cases of diffuse large B-cell lymphoma, indicating its potential relevance in disease classification and therapeutic targeting.

Keywords: CD30 expression, Clinicopathological features, Diffuse large B-cell lymphoma, Gene expression profiling, Hans algorithm. (JPMA 76: 1856; 2026) DOI: <https://doi.org/10.47391/JPMA.30999>

Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma, characterised by its heterogeneous clinical presentation and varied prognosis. The World Health Organisation (WHO) has categorised DLBCL into various subtypes and distinct disease entities. However, a significant proportion of DLBCL cases remain unclassified, demonstrating biological heterogeneity and lacking clear diagnostic criteria. Efforts have been made to develop molecular and immunophenotypic subgroups that could indicate prognosis and give clues about therapy. Gene expression profiling (GEP) has identified two major biologically distinct subgroups: germinal centre B-cell-like (GCB) DLBCL and activated B-cell-like (ABC) DLBCL.¹ While GEP is a valuable tool for research, its complexity and cost limit its clinical application. Immunohistochemical (IHC) algorithms, such as the Hans, Choi, Tally and Visco-Young, have been proposed as more practical alternatives for predicting GEP subtypes.^{2,3}

The complexity of DLBCL's pathogenesis and its diverse outcomes necessitate the identification of reliable biomarkers to aid in diagnosis, prognosis, and therapeutic decisions. Many specialised cell-surface markers, such as CD99, CD23 and CD5, have been employed to predict the prognosis of DLBCL.⁴⁻⁶ One such biomarker, CD30, has recently gained attention for its potential role in the pathophysiology of lymphomas.

CD30 is a member of the tumour necrosis factor (TNF) receptor superfamily and is typically associated with classical Hodgkin lymphoma (CHL), anaplastic large cell lymphoma (ALCL), primary mediastinal large B-cell lymphoma (PMBCL) and primary effusion lymphoma.⁷ Its expression in DLBCL has been studied with varying results, raising questions about its consistency and significance across different clinical contexts. Understanding the frequency of CD30 expression in DLBCL and its association with clinicopathological features could provide valuable insights into its role in this malignancy. To our knowledge, few studies are available on the clinicopathological features of CD30-positive DLBCL, particularly in Asian patients. The current study was planned to address this gap in literature by evaluating the frequency of CD30 expression in DLBCL patients, and to analyse its association with various clinicopathological features.

Materials and Methods

The retrospective study was conducted at the Department

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of Histopathology, Shifa International Hospital, Islamabad, Pakistan, from March 2023 to December 2024. Clinicopathological data of patients diagnosed with diffuse large B-cell lymphoma (DLBCL) between 5 March 2022 and 5 March 2023 were retrieved from the Pathology Information System. All eligible cases were included using a consecutive non-probability sampling technique. Approval was obtained from the Institutional Ethics Review Board, which also granted an exemption from informed consent.

All patients with de novo DLBCL were included regardless of age, gender, or anatomical site. Cases with prior chemotherapy, primary mediastinal large B-cell lymphoma, unclassifiable lymphoma, or insufficient tissue for IHC evaluation were excluded.

DLBCL diagnosis was established through histopathological examination of haematoxylin and eosin (H&E)-stained sections, revealing diffuse sheets of large atypical lymphoid cells with vesicular chromatin and prominent nucleoli (Figures 1-3). The diagnosis was confirmed using IHC with a panel of markers, including CD20, CD10, B-cell lymphoma 6 (BCL6), and multiple

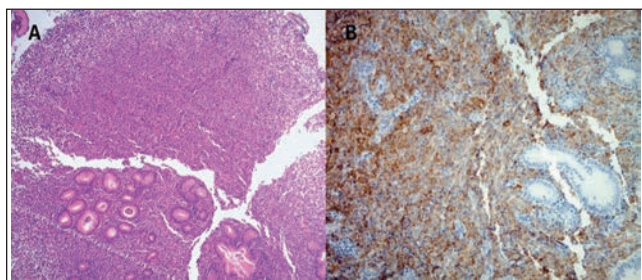


Figure-1: Colon biopsy showing CD30 positive diffuse large B-cell lymphoma (DLBCL). (A) Haematoxylin and eosin (H&E) stained section (20X magnification) displaying diffuse infiltration by atypical lymphoid cells. (B) CD30 immunohistochemical (IHC) staining (40X magnification) showing strong membranous and cytoplasmic positivity. CD30 Proportion Score (PS) = 5 and Intensity Score (IS) = 3, yielding a total score of 8, consistent with CD30 positivity.

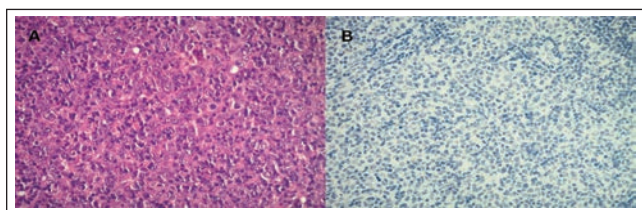


Figure-2: Lymph node biopsy showing CD30 negativity in diffuse large B-cell lymphoma (DLBCL). (A) Haematoxylin and eosin (H&E) stained section (40X magnification) showing diffuse infiltration by atypical lymphoid cells. (B) CD30 immunohistochemical (IHC) staining (40X magnification) of the same tissue demonstrated no significant membranous or cytoplasmic staining. CD30 Proportion Score (PS) = 0 and Intensity Score (IS) = 0 resulted in an interpretation of CD30 negativity.

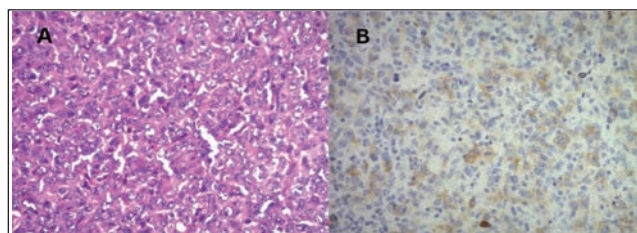


Figure-3: Abdominal mass biopsy showing CD30 positivity in diffuse large B-cell lymphoma (DLBCL). (A) Haematoxylin and eosin (H&E) stained section (40X magnification) showing diffuse infiltration by atypical lymphoid cells. (B) CD30 immunohistochemical (IHC) staining (40X magnification) demonstrating membranous and cytoplasmic positivity. CD30 Proportion Score (PS) = 3 and Intensity Score (IS) = 2 yielding a combined score of 5, indicating CD30 positivity.

myeloma oncogene-1 (MUM1), following the WHO classification.¹ The cases were further subtyped using the Hans algorithm.^{2,3}

H&E and CD30 immunostaining were performed on formalin-fixed, paraffin-embedded tissue blocks using the Ventana BenchMark XT automated immunostainer (Roche Diagnostics, Tucson, Arizona, USA) with an anti-CD30 mouse monoclonal antibody (clone Ber-H2; Roche, USA). The stained slides were reviewed by two experienced histopathologists. Photomicrographs were captured using a digital microscope camera (Leica Microsystems, Wetzlar, Germany) at $\times 20$ and $\times 40$ magnifications. CD30 expression was scored using the semiquantitative Proportion Score (PS) and Intensity Score (IS) criteria described by Malysz et al.⁸ PS represented the percentage of CD30-positive tumour cells and was graded on a 0–5 scale, with 0 = no positive cells, 1 = $<1\%$, 2 = 1–10%, 3 = 11–33%, 4 = 34–66%, and 5 = $>67\%$. IS reflected the strength of CD30 staining, with 0 = no staining, 1 = weak, 2 = intermediate, and 3 = strong. A combined score of PS + IS ≥ 3 was considered CD30-positive DLBCL, whereas a score of 0–2 was considered CD30-negative.⁸

Tumour stratification was performed using the Hans algorithm,^{2,3} which classifies DLBCL into germinal centre B-cell-like (GCB) and non-germinal centre B-cell-like (non-GCB) subtypes based on the expression of CD10, BCL6 and MUM1. Cases expressing CD10 or BCL6 with MUM1 negativity were classified as GCB, whereas all other cases were classified as non-GCB. Cases lacking sufficient marker expression were labelled unclassified. This method serves as a surrogate for gene expression profiling and is widely used in clinical pathology practice.

Data were analysed using SPSS version 25. The association of CD30 expression with clinicopathological variables, including age, gender, tumour site and immunophenotype, was evaluated using the chi-square test. Effect sizes were measured using the Phi coefficient for 2 $\times$ 2 comparisons

and Cramér's V for variables with more than two categories. A p-value <0.05 was considered statistically significant.

Results

Of the 91 patients, 64 (70.3%) were male and 27 (29.7%) were females, while 50 (54.9%) were aged ≥ 50 years and 41 (45.1%) were aged <50 years. The site of involvement was nodal in 47 (51.6%) cases and extranodal in 44 (48.4%). The largest proportion of patients, 38 (41.8%) exhibited a germinal centre B-cell-like (GCB) phenotype while 26 (28.6%) displayed a non-germinal centre B-cell-like (non-GCB) phenotype. Additionally, 27 (29.7%) patients had no definitive immunophenotype classification (Table 1).

CD30 expression was noted in 28 (30.8%) cases. No significant association was found for CD30 expression with age ($p=0.276$, $\phi=0.12$), gender ($p=0.878$, $\phi=0.02$) and tumour location ($p=0.507$, $\phi=0.07$). A trend towards association was observed between immunophenotype

Table-1: Clinical characteristics of the subjects (n=91).

Clinical Characteristics	n (%)
Gender	
Male	64 (70.3)
Female	27 (29.7)
Age (years)	
<50	41 (45.1)
≥ 50	50 (54.9)
Site of involvement	
Nodal	47 (51.6)
Extranodal	44 (48.4)
Immunophenotype	
GCB	38 (41.8)
Non-GCB	26 (28.6)
Unclassified	27 (29.7)
CD30 expression	
Positive	28 (30.8)
Negative	63 (69.2)

Table-2: Association of CD30 expression with clinicopathological features.

Variable	CD30+ [n (%)]	CD30-[n (%)]	χ^2 (df)	Effect Size	p-value
Age (years)					
<50	15/41 (36.6%)	26/41 (63.4%)	$\chi^2(1) = 1.18$	$\phi = 0.12$	0.276
≥ 50	13/50 (26.0%)	37/50 (74.0%)			
Gender					
Female	8/27 (29.6%)	19/27 (70.4%)	$\chi^2(1) = 0.02$	$\phi = 0.02$	0.878
Male	20/64 (31.3%)	44/64 (68.8%)			
Tumour Location					
Nodal	13/47 (27.7%)	34/47 (72.3%)	$\chi^2(1) = 0.44$	$\phi = 0.07$	0.507
Extranodal	15/44 (34.1%)	29/44 (65.9%)			
Immunophenotype					
GCB	7/38 (18.4%)	31/38 (81.6%)	$\chi^2(2) = 5.27$	Cramér's V = 0.24	0.072
Non-GCB	9/26 (34.6%)	17/26 (65.4%)			
Unclassified	12/27 (44.4%)	15/27 (55.6%)			

CD30: Cluster of differentiation 30, χ^2 : Chi-square, df: Degree of freedom, GCB: Germinal centre B-cell-like, Non-GCB: Non-germinal centre B-cell-like.

and CD30 expression ($p=0.072$; Cramér's V =0.24), with higher frequency of CD30 expression in the non-GCB and unclassified DLBCL subtypes (Table 2).

Discussion

The current study found that CD30 expression was present in 30.8% of DLBCL cases, with no significant association between CD30 expression and clinicopathological variables including age, gender, or tumour site. A trend towards association between immunophenotype and CD30 expression was observed ($p=0.072$, Cramér's V=0.24). Although this association was not statistically significant, CD30 expression was more frequent in non-GCB (34.6%) and unclassified (44.4%) DLBCL subtypes, suggesting possible biological relevance.

Previous studies have reported highly variable CD30 expression in DLBCL, ranging from 3.9% to 75%,^{9,10} largely due to differences in scoring criteria, antibody clones, sample sizes and population characteristics. The current finding of 30.8% is consistent with reports from other Asian cohorts, such as the one in Indonesia.¹¹ The lack of statistically significant associations in the current cohort may be due to sample size limitations, biological heterogeneity of DLBCL, and overlapping clinicopathological features across subgroups. The observed trend with immunophenotype aligns with prior work showing more frequent CD30 positivity in non-GCB DLBCL¹² and may reach statistical significance in larger, multicentre studies.

Although the tumour site did not show a significant association with CD30 expression, 34.1% of extranodal cases were CD30 positive. This finding contrasts with a previous meta-analysis, which reported that CD30 expression was associated with a lower number of extranodal sites involved.¹³ Extranodal disease in DLBCL has been linked to distinct clinical behaviours and variable prognosis, depending on the involved organ. CD30 positivity in extranodal sites could represent a biological subset with potential responsiveness to targeted therapy. Immunophenotypically, non-GCB DLBCL is generally associated with poorer survival compared to the GCB subtype.¹⁴ The higher rate of CD30 positivity in non-GCB and unclassified subtypes in the current cohort suggests a possible therapeutic niche for CD30-targeted agents in these higher-risk groups. Unclassified cases, which comprised 29.7% of the current cohort, may reflect

technical or biological complexity, and their prognostic implications remain uncertain, emphasising the need for further molecular characterisation. A population-based study in British Columbia concluded that CD30 immunohistochemistry may be useful as a prognostic marker in R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone) treated GCB-DLBCL, as it is associated with a trend towards a better outcome.¹⁵

Brentuximab vedotin, a CD30-directed antibody-drug conjugate, has shown significant efficacy in classical Hodgkin's lymphoma and systemic anaplastic large cell lymphoma, and emerging data have supported its role in CD30-positive DLBCL.¹⁶ When combined with chemotherapy backbones, such as R-CHOP or R-ICE (rituximab, ifosfamide, carboplatin and etoposide), it can improve outcomes in selected patients. In Pakistani settings, where novel agents may be limited by cost and accessibility, IHC-based CD30 testing provides a practical and cost-effective tool for identifying eligible patients. Integrating brentuximab vedotin with existing modalities, such as autologous stem cell transplantation in relapsed cases, or exploring combinations with other novel agents, like polatuzumab vedotin, or checkpoint inhibitors, could enhance disease control.¹⁷ This biomarker-driven, multimodal strategy offers a holistic approach to improving prognosis in DLBCL.

The current study has limitations of a small sample size. Also, survival data were not taken into consideration. Incorporating overall survival (OS) and progression-free survival (PFS) analysis in future research would allow direct evaluation of the prognostic value of CD30 expression. Establishing a pathology-oncology data linkage could facilitate Kaplan-Meier survival analysis and multivariate modelling, helping in determining whether or not CD30-positive cases, especially in non-GCB or extranodal presentations, have distinct clinical outcomes. Such evidence would support the tailored use of CD30-targeted therapy in the local population.

Conclusion

CD30 expression was observed in less than one-third of cases of DLBCL, indicating its potential relevance in disease classification and therapeutic targeting.

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References

1. Menon MP, Pittaluga S, Jaffe ES. The histological and biological spectrum of diffuse large B-cell lymphoma in the World Health Organization classification. *Cancer J*. 2012;18:411-20. doi:10.1097/PPO.0b013e31826aee97.
2. Hwang HS, Park CS, Yoon DH, Suh C, Huh J. High concordance of gene expression profiling-correlated immunohistochemistry algorithms in diffuse large B-cell lymphoma, not otherwise specified. *Am J Surg Pathol*. 2014;38:1046-57. doi:10.1097/PAS.0000000000000211.
3. Culpin RE, Sieniawski M, Angus B, Menon GK, Proctor SJ, Milne P, et al. Prognostic significance of immunohistochemistry-based markers and algorithms in immunochemotherapy-treated diffuse large B cell lymphoma patients. *Histopathology*. 2013;63:788-801. doi:10.1111/his.12223.
4. Hong J, Park S, Park J, Jang SJ, Ahn HK, Sym SJ, et al. CD99 expression and newly diagnosed diffuse large B-cell lymphoma treated with rituximab-CHOP immunochemotherapy. *Ann Hematol*. 2012;91:1897-906. doi:10.1007/s00277-012-1533-z.
5. Linderth J, Jerkeman M, Cavallin-Ståhl E, Kvaløy S, Torlakovic E. Immunohistochemical expression of CD23 and CD40 may identify prognostically favorable subgroups of diffuse large B-cell lymphoma: a Nordic Lymphoma Group Study. *Clin Cancer Res*. 2003;9:722-8.
6. Niitsu N, Okamoto M, Tamaru JI, Yoshino T, Nakamura N, Nakamura S, et al. Clinicopathologic characteristics and treatment outcome of the addition of rituximab to chemotherapy for CD5-positive in comparison with CD5-negative diffuse large B-cell lymphoma. *Ann Oncol*. 2010;21:2069-74. doi:10.1093/annonc/mdq057.
7. Schneider C, Hübinger G. Pleiotropic signal transduction mediated by human CD30: a member of the tumor necrosis factor receptor (TNFR) family. *Leuk Lymphoma*. 2002;43:1355-66. doi:10.1080/10428190290033288.
8. Malysz J, Erdman P, Klapper J, Zhu J, Creer M, Bayerl MG. Clinical implications of CD30 expression in aggressive B-cell lymphomas. *Clin Lymphoma Myeloma Leuk*. 2016;16:429-33. doi:10.1016/j.clml.2016.04.011.
9. Pallesen G. The diagnostic significance of the CD30 (Ki-1) antigen. *Histopathology*. 1990;16:409-13. doi:10.1111/j.1365-2559.1990.tb01151.x.
10. Noorduin LA, de Bruin PC, van Heerde P, van de Sandt MM, Ossenkoppele GJ, Meijer CJ. Relation of CD30 expression to survival and morphology in large cell B cell lymphomas. *J Clin Pathol*. 1994;47:33-7. doi:10.1136/jcp.47.1.33.
11. Santoso MR, Hardianti MS, Indrawati I, Anggorowati N. CD30 expression and its correlation with clinicopathologic features in Indonesian diffuse large B-cell lymphoma. *Asian Pac J Cancer Biol*. 2020;5:107-13.
12. Salas MQ, Climent F, Domenech ED, Mercadal S, Paredes V, Oliveira AC, et al. CD30 expression in diffuse large B-cell lymphoma (DLBCL) correlates with non-GCB subtype but does not have prognostic impact in patients treated with first line R-CHOP/R-CHOP-like. *Blood*. 2016;128:4209.
13. Rodrigues-Fernandes CI, Abreu LG, Radhakrishnan R, Perez DE, Amaral-Silva GK, Gondak RD, et al. Prognostic significance of CD30 expression in diffuse large B-cell lymphoma: a systematic review with meta-analysis. *J Oral Pathol Med*. 2021;50:587-93.
14. Meyer PN, Fu K, Greiner TC, Smith LM, Delabie J, Gascoyne RD, et al. Immunohistochemical methods for predicting cell of origin and survival in patients with diffuse large B-cell lymphoma treated with

- rituximab. *J Clin Oncol*. 2011;29:200-7.
15. Slack GW, Steidl C, Sehn LH, Gascoyne RD. CD30 expression in de novo diffuse large B-cell lymphoma: a population-based study from British Columbia. *Br J Haematol*. 2014;167:608-17.
 16. Francisco JA, Cervený CG, Meyer DL, Mixan BJ, Klussman K, Chace DF, et al. cAC10-vcMMAE, an anti-CD30-monomethyl auristatin E conjugate with potent and selective antitumor activity. *Blood*. 2003;102:1458-65.
 17. Herrera AF, Chen L, Nieto Y, Holmberg L, Johnston P, Mei M, et al. Brentuximab vedotin plus nivolumab after autologous haematopoietic stem-cell transplantation for adult patients with high-risk classic Hodgkin lymphoma: a multicentre, phase 2 trial. *Lancet Haematol*. 2023;10(1):e14-23.
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Author Contribution:

AZ: Data acquisition, analysis, interpretation, drafting, final approval and agreement to be accountable for all aspects of the work.

ZA: Concept, revision, final approval and agreement to be accountable for all aspects of the work.

SB: Revision, final approval and agreement to be accountable for all aspects of the work.