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Frequency of New Onset Diabetes Mellitus in Patients Receiving Treatment for Diffuse Large B Cell Lymphoma

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ABSTRACT

Objectives: To determine the frequency of new-onset diabetes mellitus in patients receiving treatment for diffuse large B-cell lymphoma. **Methodology:** This study was done at Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore after Six months following approval of the study synopsis from 7th February to 7th May. We enrolled 150 patients aged 18–40 years with newly diagnosed DLBCL were enrolled using non-probability consecutive sampling. Patients with prior diabetes or central nervous system lymphoma were excluded. Glycemic status was assessed post-chemotherapy using fasting blood glucose and HbA1c. Associations with demographic and clinical variables were analyzed. **Results:** New-onset diabetes mellitus was observed in 32.0% (n = 48) of patients. A significant association was found with family history of diabetes (p = 0.009) whereas age, BMI, gender, smoking, alcohol use, lymphoma stage, or type of therapy had no significant association. **Conclusion:** The frequency of new-onset diabetes among DLBCL patients undergoing chemotherapy is substantial. Family history of diabetes emerged as a significant risk factor. Routine screening for hyperglycemia should be incorporated into oncology care to ensure early diagnosis and management of diabetes during cancer treatment.

INTRODUCTION

Lymphoma represents a malignant neoplasm originating within the immune system, primarily affecting lymph nodes and lymphoid tissues.[1-2] It is broadly classified, based on histopathological features, into Hodgkin lymphoma and non-Hodgkin lymphoma. Among the latter, diffuse large B-cell lymphoma (DLBCL) is the most common subtype, comprising around 24% of non-Hodgkin lymphoma cases annually.[3] Diabetes mellitus is a chronic metabolic syndrome characterized by sustained elevations in blood glucose levels, stemming from both genetic susceptibility and environmental contributors. According to recent data from the International Diabetes Federation, an estimated 537 million individuals aged 20–79 were living with diabetes in 2021. This number is projected to increase to 643 million by 2030 and 783 million by 2045.[4]

Epidemiological studies consistently demonstrate an association between diabetes mellitus and elevated risks of malignancies in organs such as the liver, pancreas, endometrium, colon, breast, and bladder.[5] It is also linked to a heightened risk of hematologic cancers and is recognized as an independent predictor of both overall and disease-specific mortality.[6] Studies further suggest an elevated risk of non-Hodgkin lymphoma in individuals with diabetes.[7-8] First-line lymphoma treatment regimens often include high doses of prednisolone. However, the impact of such cyclic steroid administration on the development of new-onset diabetes or worsening of preexisting diabetes is not clearly established.[9] Common steroid-based immunochemotherapy protocols include rituximab with cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP), as well as cyclophosphamide, rituximab, vincristine, and prednisolone (R-CVP).[10-11] A clinical study reported a 32.5% incidence of diabetes mellitus in DLBCL patients treated with the CHOP chemotherapy regimen.[12] In comparison, a retrospective study found that nearly 47% of patients developed steroid-induced hyperglycemia after receiving R-CHOP therapy.[13]

Rationale of this study is to determine the frequency of new onset diabetes mellitus in patients receiving

treatment for diffuse large B cell lymphoma. Literature has shown that incidence of diabetes mellitus is not ignorable in patients with malignant lymphoma. Diabetes mellitus is a lifelong complication and no study had been done before in local population. Therefore, it's important to confirm the extent of problem for the local population. In order to early recognize the problem in such sensitive patients by doing routine blood sugar charting at each medical encounter or before/during chemotherapy treatment may help in early diabetes mellitus treatment and prevention of Diabetes associated complications.

METHODOLOGY

This cross-sectional study was conducted at Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore, over a period of six months following approval of the study synopsis. A sample size of 150 cases was calculated using the WHO sample size calculator with a 95% confidence level, 7.5% margin of error, and an anticipated prevalence of diabetes mellitus of 32.5% among patients with DLBCL. A non-probability consecutive sampling technique was employed. Patients aged between 18 to 40 years, of either gender, with a newly diagnosed case of DLBCL and accepted through the walk-in clinic of the hospital were included. Patients with a prior diagnosis of diabetes mellitus or central nervous system DLBCL were excluded based on the medical records.

After informed consent, eligible patients were enrolled in the study. Demographic and clinical variables including BMI, age, gender, duration and size of lymphoma, history of smoking (more than 5 pack-years), alcohol intake (more than 20 ml/day), family history of lymphoma or diabetes, stage of lymphoma, and type of treatment received (chemotherapy, radiotherapy, or both) were recorded on a structured proforma. Glycemic status was assessed either by fasting blood glucose levels (≥126 mg/dL) or HbA1c (>6.5%) measured after initiation of chemotherapy. Patients found to have diabetes mellitus were managed according to standard institutional protocols.

Data were analyzed using SPSS version 25. Normality of quantitative variables was assessed using the Shapiro–Wilk test. Continuous variables such as age, BMI, duration of lymphoma, and size of lymphoma were reported as mean and standard deviation. Categorical variables including gender, smoking status, alcohol consumption, family history of lymphoma or diabetes, stage of lymphoma, type of therapy, and presence of diabetes mellitus were presented as frequencies and percentages. Stratification was performed for potential effect modifiers such as age, gender, BMI, duration and size of lymphoma, smoking, alcohol use, family history, disease stage, and treatment modality. The chi-square test was applied to assess the association of these factors with the frequency of new onset diabetes mellitus.

RESULTS

The demographic distribution showed that a slight majority of participants (54.7%) were aged between 18 and 30 years, while the remaining 45.3% were aged between 31 and 40 years. The study sample consisted of 56.0% males and 44.0% females. Most patients (71.3%) had a normal BMI ranging from 18 to 25 kg/m^2, whereas 28.7% had a BMI greater than 25 kg/m^2. Regarding lifestyle factors, 26.7% of the patients had a history of smoking, and 13.3% reported alcohol use. A positive family history of diabetes was observed in 20.7% of participants, while 12.0% reported a family history of lymphoma. In terms of lymphoma staging, stage II was the most frequent (38.0%), followed by stage III (23.3%), stage IV (21.3%), and stage I (17.3%). Chemotherapy was the most commonly administered therapy (61.3%), followed by radiotherapy (32.7%) and immunotherapy (6.0%). (Table 1)

Table 1

Demographic and clinical information of participants (n=150)

Variables	Group	Count	Percent
Age(Years)	18–30	82	54.7%
	31–40	68	45.3%
Gender	Male	84	56.0%
	Female	66	44.0%
BMI	18–25	107	71.3%
	>25	43	28.7%
History of Smoking	Yes	40	26.7%
	No	110	73.3%
Alcoholism	Yes	20	13.3%
	No	130	86.7%
Family History of Diabetes	Yes	31	20.7%
	No	119	79.3%
Family History of Lymphoma	Yes	18	12.0%
	No	132	88.0%
Stage of Lymphoma	I	26	17.3%
	II	57	38.0%
	III	35	23.3%
	IV	32	21.3%
Type of Therapy	Chemotherapy	92	61.3%
	Immunotherapy	9	6.0%
	Radiotherapy	49	32.7%

Descriptive statistics of continuous variables revealed that the mean age of participants was 29.36 ± 6.34 years, and the mean BMI was 23.97 ± 2.95 kg/m^2. The average duration of lymphoma since diagnosis was 13.27 ± 6.60 months. The mean lymphoma size was 4.94 ± 2.09 cm. Regarding metabolic parameters, the mean HbA1c was 5.78 ± 0.65%, while the mean fasting blood sugar level was 101.91 ± 19.83 mg/dL (Table 2)

Table 2

Descriptive Statistics of Continuous Variables of participants (n=150)

Variable	Mean	Standard Deviation
Age(years)	29.360	6.341
BMI (kg/m^2)	23.971	2.951
Duration of Lymphoma (months)	13.270	6.600
Lymphoma Size (cm)	4.943	2.093
HbA1c (%)	5.783	0.647
Fasting Blood Sugar (mg/dL)	101.905	19.825

The frequency of new onset diabetes mellitus in the cohort was 32.0% (n = 48), while 68.0% (n = 102) of the participants remained non-diabetic during the course of treatment. (Table 3)

To assess the association of new onset diabetes mellitus with various demographic and clinical factors, cross-tabulation with chi-square tests was performed. No statistically significant association was found between

diabetes status and age group (p = 0.536), gender (p = 0.507), BMI (p = 0.631), history of smoking (p = 0.752), alcoholism (p = 0.217), family history of lymphoma (p = 0.137), stage of lymphoma (p = 0.953), or type of therapy (p = 0.062). However, a significant association was observed with family history of diabetes (p = 0.009), suggesting that patients with a family history of diabetes were more likely to develop new onset diabetes mellitus during lymphoma treatment. (Table 4)

These findings indicate that while most demographic and clinical variables did not significantly affect the risk of treatment-induced diabetes, familial predisposition to diabetes emerged as a notable factor warranting further attention in clinical practice.

Table 3

Frequency of New Onset Diabetes Mellitus in Patients Receiving Treatment for Diffuse Large B Cell Lymphoma

New Onset Diabetes Mellitus	Count	%
Yes	48	32.0%
No	102	68.0%

Table 4

Frequency of New Onset Diabetes Mellitus in Patients Receiving Treatment for Diffuse Large B Cell Lymphoma According to Various Effect Modifiers

Variable	Group	Group-A (Count %)	Group-B (Count %)	Total	Chi-Square p-value
Age	18–30	28 (58.3%)	54 (52.9%)	82	0.536
	31–40	20 (41.7%)	48 (47.1%)	68	
Gender	Male	25 (52.1%)	59 (57.8%)	84	0.507
	Female	23 (47.9%)	43 (42.2%)	66	
BMI	18–25	33 (68.8%)	74 (72.5%)	107	0.631
	>25	15 (31.3%)	28 (27.5%)	43	
History of Smoking	Yes	12 (25.0%)	28 (27.5%)	40	0.752
	No	36 (75.0%)	74 (72.5%)	110	
Alcoholism	Yes	4 (8.3%)	16 (15.7%)	20	0.217
	No	44 (91.7%)	86 (84.3%)	130	
Family History of Diabetes	Yes	16 (33.3%)	15 (14.7%)	31	0.009
	No	32 (66.7%)	87 (85.3%)	119	
Family History of Lymphoma	Yes	3 (6.3%)	15 (14.7%)	18	0.137
	No	45 (93.8%)	87 (85.3%)	132	
Stage of Lymphoma	I	8 (16.7%)	18 (17.6%)	26	0.953
	II	19 (39.6%)	38 (37.3%)	57	
	III	10 (20.8%)	25 (24.5%)	35	
	IV	11 (22.9%)	21 (20.6%)	32	
Type of Therapy	Chemotherapy	36 (75.0%)	56 (54.9%)	92	0.062
	Immunotherapy	2 (4.2%)	7 (6.9%)	9	
	Radiotherapy	10 (20.8%)	39 (38.2%)	49	

DISCUSSION

The current study revealed a 32% frequency of new-onset diabetes mellitus (DM) among patients with diffuse large B-cell lymphoma (DLBCL) undergoing chemotherapy, consistent with findings from international literature. This figure is particularly aligned with the study by Lee SY et al[13] who documented a 32.5% incidence of glucocorticoid-induced diabetes mellitus in lymphoma patients receiving CHOP chemotherapy. Their study identified age ≥60 years, baseline HbA1c >6.1%, and BMI >30 kg/m^2 as independent predictors of diabetes, highlighting the role of metabolic predisposition. Although our study focused on a younger cohort (18–40 years), we observed a significant association with family history of diabetes, suggesting that genetic susceptibility remains a key factor regardless of age.

Further support for the metabolic complications of chemotherapy is provided by Moore-Vasram S et al[14] who analyzed over 19,000 patients with hematologic malignancies in a population-based cohort study from Ontario. They found that glucocorticoid exposure significantly increased the risk of new-onset diabetes (HR 1.29, p = 0.04) and hyperglycemia (HR 1.28, p = 0.003). Their data emphasized that hyperglycemia, particularly in patients with leukemia and NHL, was associated with increased all-cause mortality. Although our study did not assess mortality, the substantial prevalence of new-onset DM observed mirrors the risks emphasized in their work and validates the importance of proactive glycemic monitoring during chemotherapy.

Interestingly, Kristjanson M et al[15] examined steroid-induced hyperglycemia in patients with DLBCL treated with R-CHOP and reported that while hyperglycemia developed early in treatment, it did not significantly affect overall survival or infection rates. This contrasts with findings by Moore-Vasram S et al[14] indicating that the impact of treatment-induced hyperglycemia may vary across populations or healthcare systems. However, the early manifestation of hyperglycemia, as noted in both studies, reinforces the need for routine glucose monitoring from the very first chemotherapy cycle, which is consistent with our clinical recommendations. In our study, most demographic and treatment-related variables, such as age group, gender, BMI, smoking, alcohol use, and lymphoma stage, did not show a statistically significant association with new-onset DM. However, family history of diabetes was significantly associated (p = 0.009), supporting the findings by Lee SY et al[12] and Marić A et al[166] who found that prior metabolic vulnerabilities or insulin resistance can amplify the risk when glucocorticoids are administered. Marić A et al[16] further illustrated that even non-diabetic DLBCL patients experienced postprandial hyperglycemia and persistent elevation in HbA1c levels after R-CHOP therapy, due to corticosteroid-induced insulin resistance. These findings suggest that glycemic disturbances may extend beyond the treatment window, an area that our cross-sectional design could not assess but should be addressed in future research.

The study by Saputri JH et al[17] also supports our findings. They conducted a prospective analysis in non-diabetic NHL patients undergoing their first CHOP cycle and found a statistically significant rise in blood glucose levels by day six post-treatment. These results confirm that even a single chemotherapy cycle can trigger acute hyperglycemia, underscoring the necessity of early screening and intervention to prevent complications. Beyond DLBCL, the broader implications of diabetes during cancer therapy have been explored in other malignancies. For instance, Mellor R et al[18] assessed the effect of chemoradiotherapy in head and neck cancer patients with diabetes and found that those requiring insulin were at a markedly higher risk for ICU admission and chemotherapy omission due to diabetes-related complications. Their findings suggest that pre-existing diabetes or diabetes developed during therapy can lead to serious interruptions in cancer treatment, emphasizing

the clinical relevance of our findings even outside the DLBCL context.

Although not directly studying diabetes incidence, DeBoer RJ et al[19] highlighted systemic challenges in delivering effective chemotherapy in low-resource settings through their cohort of Hodgkin lymphoma patients in rural Rwanda. Their study demonstrated that early treatment abandonment and advanced disease stages impacted outcomes significantly. These factors could also influence diabetes risk indirectly, as malnutrition, inconsistent care, or stress hyperglycemia may confound glycemic status. While our setting offered consistent access to treatment, the comparison highlights the importance of contextual healthcare infrastructure when assessing outcomes like steroid-induced DM.

Additionally, Cheng JX and Yu K[20] explored adipokines involved in the pathogenesis of obesity and type 2 diabetes, emphasizing the molecular links between inflammation, fat metabolism, and insulin resistance. Their findings support the hypothesis that certain cytokine pathways activated during malignancy and steroid therapy may predispose patients to metabolic dysregulation, further justifying why lymphoma patients—particularly those genetically or metabolically predisposed—are at increased risk for developing diabetes during treatment.

The current study has several strengths. It is the first known local investigation into the frequency of new-onset diabetes among DLBCL patients undergoing chemotherapy, offering context-specific insights for clinicians in Pakistan. The study utilized both fasting blood glucose and HbA1c criteria for diagnosis, enhancing reliability. A sample size of 150 patients allowed for effective subgroup analysis and statistical testing. Furthermore, a structured data collection method minimized recall bias and improved the robustness of the results.

However, the study is not without limitations. The cross-sectional design restricts our ability to establish causality or assess the long-term persistence of diabetes beyond chemotherapy. Unlike Marić A et al[16] and Saputri JH et al[17] who measured serial glucose changes during and after treatment, our study captured glycemic status at a single point post-therapy, which may under-diagnose transient or fluctuating hyperglycemia. The exclusion of older adults (>40 years), who are more vulnerable to steroid-induced diabetes as noted by Lee SY et al.[12], limits the generalizability of our findings to the broader lymphoma population. Additionally, our study lacked postprandial glucose or continuous glucose monitoring, tools that would have provided a more nuanced picture of glycemic variation, as shown in Marić A et al.'s study.[16]

CONCLUSION

This study confirms that steroid-containing chemotherapy regimens carry a substantial risk of new-onset diabetes mellitus, even in young, non-diabetic patients. The significant association with family history of diabetes highlights the importance of pre-treatment risk profiling. Based on evidence from our study and supported international literature, it is strongly recommended that routine glycemic screening and early intervention protocols be integrated into standard lymphoma treatment regimens. Future research should focus on prospective, longitudinal studies to assess long-term outcomes and refine predictive models for identifying high-risk patients.

REFERENCES

1. Nielsen C, Jerkeman M, Jöud AS. Tattoos as a risk factor for malignant lymphoma: a population-based case–control study. EClinicalMedicine 2024 Jun 1;72. https://doi.org/10.1016/j.eclinm.2024.102649
2. Lee DN, Lee DH, Koo JY, Lim SC. Solitary large malignant lymphoma in the head and neck region. Molecular and Clinical Oncology 2024;20(6):39. https://doi.org/10.3892/mco.2024.2737
3. Liu Y, Barta SK. Diffuse large B-cell lymphoma: 2019 update on diagnosis, risk stratification, and treatment. Am J Hematol 2019;94(5):604-16. https://doi.org/10.1002/ajh.25460
4. Atlas D. International diabetes federation. 7th ed. Brussels, Belgium: International Diabetes Federation; 2015.
5. Gong IY, Cheung MC, Read S, Na Y, Lega IC, Lipscombe LL. Association between diabetes and haematological malignancies: a population-based study. Diabetologia. 2021;64:540-51. https://doi.org/10.1007/s00125-020-05338-7
6. Zhou W, Li W, He C, Ma R, Gao Q, Wang Y, et al. Influence of Hyperglycemia on the Prognosis of Patients with Diffuse Large B-Cell Lymphoma. Diab Metab Synd Obesity 2022;15(null):2039-49. https://doi.org/10.2147/dmso.s370017
7. Wang Y, Liu X, Yan P, Bi Y, Liu Y, Zhang Z-J. Association between type 1 and type 2 diabetes and risk of non-Hodgkin's lymphoma: a meta-analysis of cohort studies. Diab Metab 2020;46(1):8-19. https://doi.org/10.1016/j.diabet.2019.04.006
8. Xu J, Wang T. Association of diabetes mellitus with non-Hodgkin lymphoma risk: a meta-analysis of cohort studies. Hematology 2019;24(1):527-32. https://doi.org/10.1080/16078454.2019.1636485
9. Baech J, Severinsen MT, Øvlisen AK, Frederiksen H, Vestergaard P, Torp-Pedersen C, et al. Risk of diabetes and the impact on preexisting diabetes in patients with lymphoma treated with steroid-containing immunochemotherapy. Blood Adv 2022;6(15):4427-35. https://doi.org/10.1182/bloodadvances.2021006859
10. Yang F, Zhang J, Abraham A, Yan JT, Hammer RD, Prime MS. Adherence to guidelines-recommended diagnostic testing was associated with overall survival in patients with diffuse large B-cell lymphoma after rituximab-based treatment: an observational cohort study. J Canc Res Clin Oncol 2023;149(7):3691-700. https://doi.org/10.1007/s00432-022-04179-8
11. Wright CM, Dreyfuss AD, Baron JA, Maxwell R, Mendes A, Barsky AR, et al. Radiation Therapy for Relapsed or Refractory Diffuse Large B-Cell Lymphoma: What Is the Right Regimen for Palliation? Adv Radiat Oncol 2022;7(6):101016. https://doi.org/10.1016/j.adro.2022.101016
12. Lee SY, Kurita N, Yokoyama Y, Seki M, Hasegawa Y, Okoshi Y, Chiba S. Glucocorticoid-induced diabetes mellitus in patients with lymphoma treated with CHOP chemotherapy. Support Care Cancer 2014 May;22(5):1385-90. Epub 2013 Dec 21. PMID: 24362844.

https://doi.org/10.1007/s00520-013-2097-8.
13. Lamar ZS, Dothard A, Kennedy L, Isom S, Robinson M, Vaidya R, Hurd D, McClain D, Lesser G. Hyperglycemia during first-line R-CHOP or dose adjusted R-EPOCH chemotherapy for non-Hodgkin lymphoma is prevalent and associated with chemotherapy alteration – a retrospective study. Leuk Lymphoma. 2018;59(8):1871-1877. https://doi.org/10.1080/10428194.2017.1410889
14. Moore-Vasram S, Sawhney M, Houlden RL, Groome PA, Goldie C, Li W, et al. Determining the Associations Between Glucocorticoid Use During Hematologic Chemotherapy Treatment and New-onset Diabetes and Hyperglycemia and Mortality: A Population-based Cohort Study. Can J Diabetes 2024;48:195-203.e1. https://doi.org/10.1016/j.jcjd.2024.01.001
15. Kristjanson M, Lambert P, Decker KM, Bruin S, Tingey E, Skrabek P. Steroid-Induced Hyperglycemia and Its Effect on Outcomes of R-CHOP Chemotherapy for Diffuse Large B Cell Lymphoma. Curr Oncol 2023;30:10142-51 https://doi.org/10.3390/curroncol30120738
16. Marić A, Miličević T, Vučak Lončar J, Galušić D, Radman M. Patterns of Glucose Fluctuation are Challenging in Patients Treated for Non-Hodgkin's Lymphoma. Int J Gen Med 2020;13:131-40. https://doi.org/10.2147/ijgm.s245779
17. Saputri J, Novida H, Ashariati A. Glycemic Control of NHL Non DM patient in the First CHOP Chemotherapy. Medico-Legal Update 2021;21:393-400. https://doi.org/10.37506/mlu.v21i1.2341
18. Mellor R, Girgis CM, Rodrigues A, Chen C, Cuan S, Gambhir P, et al. Acute Diabetes Related Complications in Patients Receiving Chemoradiotherapy for Head and Neck Cancer. Current Oncology 2024;31:828-38. https://doi.org/10.3390/curroncol31020061
19. DeBoer RJ, Shyirambere C, Driscoll CD, Butera Y, Paciorek A, Ruhangaza D, et al. Treatment of Hodgkin Lymphoma With ABVD Chemotherapy in Rural Rwanda: A Model for Cancer Care Delivery Implementation. JCO Glob Oncol 2020;6:1093-102. https://doi.org/10.1200/go.20.00088
20. Cheng JX, Yu K. New Discovered Adipokines Associated with the Pathogenesis of Obesity and Type 2 Diabetes. Diabetes Metab Syndr Obes 2022;15:2381-9. https://doi.org/10.2147/dmso.s376163