Effect of Lymphoma Treatment on Development of New Onset Diabetes

Abstract

Background: Lymphoma, a heterogeneous malignancy of lymphocytes, is commonly treated with chemotherapy regimens like R-CHOP, which include glucocorticoids known to induce hyperglycemia and potentially cause new-onset diabetes or worsen existing diabetes. This study aimed to evaluate the effect of lymphoma treatment on the development of new-onset diabetes and related complications.

Methods: This observational cohort study included 61 lymphoma patients: 39 non-diabetic and 22 diabetic. Detailed history, physical exams, and lab investigations (FBS, 2-hour postprandial blood sugar, and HbA1c) were conducted before and after treatment.

Results: In the non-diabetic group, 23.1% developed new-onset diabetes. These patients had higher mean weight (85 ± 8 kg vs. 79 ± 7 kg, $P = 0.046$) and BMI (28.5 ± 3.2 vs. 23.4 ± 1.7, $P < 0.001$). Post-treatment, fasting blood sugar increased (123 ± 20 mg/dL vs. 90 ± 10 mg/dL, $P < 0.001$), as did 2-hour postprandial blood sugar (179 ± 31 mg/dL vs. 138 ± 16 mg/dL, $P = 0.003$) and HbA1c (5.9 ± 0.4% vs. 5.1 ± 0.3%, $P < 0.001$). BMI increase significantly predicted new-onset diabetes (OR = 1.984, 95% CI = 1.205–3.267, $P = 0.007$). In the diabetic group, 72.7% experienced complications, with higher post-treatment HbA1c levels (8.4 ± 0.7% vs. 7.5 ± 1%, $P = 0.033$) and more complications in those treated with R-CHOP (87.5% vs. 33.3%, $P = 0.025$).

Conclusions: Lymphoma treatments, especially those with steroids like R-CHOP, significantly increase the risk of new-onset diabetes and related complications, necessitating careful glucose monitoring and management.

Keywords: Lymphoma, Chemotherapy, R-CHOP, New-onset diabetes.

Introduction

Lymphoma refers to a wide range of tumors that develop from the abnormal growth of lymphocytes, making up around 5% of all cancer cases. The current overall survival rate is roughly 72% [1].

Lymphomas are categorized into two main categories: non-Hodgkin (90%) and Hodgkin (10%). The majority (90%) of lymphomas originate from B cells, although T cell and natural killer cell types are also detected. Lymphoma is the fourth most prevalent malignancy in adults in Egypt, with non-Hodgkin lymphoma (NHL) accounting for 76.6% and Hodgkin lymphoma accounting for 23.4% [2].

The main therapeutic approaches for Hodgkin lymphoma consist of chemotherapy as a standalone treatment, chemotherapy accompanied by radiotherapy, or radioimmunotherapy. In the treatment of NHL, commonly utilized regimens include R-CHOP or dose-adjusted R-EPOCH. These regimens combine high-dose glucocorticoids such as prednisone with cytotoxic chemotherapy [3].

Patients diagnosed with NHL who receive high cumulative doses of steroids as part of their first treatment may have a higher likelihood of acquiring new-onset steroid-induced diabetes mellitus (DM) or experiencing worsening of preexisting DM. In addition, individuals with preexisting diabetes mellitus (DM) that has problems such as atherosclerosis are at an increased risk of developing cardiac difficulties connected with anthracycline treatment [4].

Glucocorticoid-induced hyperglycemia is caused by decreased insulin sensitivity in peripheral tissues, increased hepatic gluconeogenesis, and heightened proteolysis and lipolysis [5].

The risk of new-onset diabetes in lymphoma patients is linked to the diabetogenic effects of steroids used in treatment protocols like R-CHOP. Steroids cause hyperglycemia by boosting gluconeogenesis and decreasing peripheral glucose uptake, resulting in a temporary spike in

blood glucose levels. This aligns with observed significant increases in fasting blood sugar, 2-hour postprandial blood sugar, and HbA1c levels post-treatment [9].

The significant link between increased BMI and new-onset diabetes in lymphoma patients can be explained by mechanisms such as increased adiposity leading to insulin resistance, exacerbated by steroid-containing chemotherapy. This regimen induces hyperglycemia through enhanced gluconeogenesis and impaired glucose uptake. Additionally, obesity-related chronic inflammation, hormonal dysregulation, and metabolic stress from cancer treatments further contribute to glucose intolerance [13].

Glucocorticoid-induced hyperglycemia was observed in patients who fulfilled at least one of the following conditions: being elderly, having a family history of diabetes mellitus (DM), having obese first- or second-degree relatives, or having a body mass index (BMI) above the 95th percentile [5].

In this study, we aimed to detect the effect of lymphoma treatment about development new onset diabetes and diabetic patient.

Patients and methods

Study design and population:

This observational cohort study was carried at Internal Medicine Department - Benha University Hospitals on 61 patients diagnosed with lymphoma and receiving its protocol of treatment over a period of one year from May 2023 to May 2024. The study was done after being approved by the ethical committee of the Faculty of Medicine, Benha University (MS 19-5-2023). Informed written consent was obtained from the patients included.

Inclusion criteria were patients aged ≥ 18 years of both genders, lymphoma and receiving protocol of lymphoma treatment such as R-CHOP, ABVD, BU/CY, or CVP. For the diabetic group, patients needed to have a documented diagnosis of diabetes mellitus (DM) according to the American Diabetes Association [6], defined as a fasting plasma glucose (FPG) level of ≥ 126 mg/dL (7.0 mmol/L) [6].

Fasting is characterized by the complete absence of caloric intake for at least 8 hours. A blood glucose level of 200 mg/dL (11.1 mmol/L) or higher, measured after an oral glucose tolerance test (OGTT), is significant. This test must adhere to World Health Organization (WHO) guidelines, involving a glucose load of 75 grams of anhydrous glucose dissolved in water. Additionally, an HbA1C level of 6.5% (48 mmol/mol) or higher is indicative. A random plasma glucose value of 200 mg/dL (11.1 mmol/L) is considered the minimum threshold.

Exclusion criteria were patient refusal, any malignancy other than lymphoma (such as solid tumors), tumors of dual origin (mixed tumors).

Patients were further divided into two groups as follows: Non – Diabetic Group: included 39 patients with lymphoma and currently receiving its treatment without diabetes. Diabetic Group: included 22 patients with lymphoma and currently receiving its treatment with concomitant DM.

All studied cases were subjected to A) Detailed history taking: This included collecting socio-demographic data (name, age, gender, marital status), medical history (comorbidities, medication adherence), and details on the type of lymphoma (Hodgkin or Non-Hodgkin). Additionally, the specific lymphoma treatment protocols used, such as R-CHOP, ABVD, BU/CY, or CVP, were documented. **B) Full physical general and local examination:** This involved taking anthropometric measurements (weight, height, and Body Mass Index [BMI]). Vital signs recorded included heart rate, respiratory rate and systolic blood pressure (mmHg).

C) Laboratory investigations: Laboratory investigations were conducted by collecting five milliliters of venous blood from each patient under strict aseptic conditions. Tests included a Complete Blood Count (CBC), Fasting Blood Sugar (FBS) measured before and after lymphoma treatment, HbA1C levels before and after treatment, and 2-hour postprandial blood sugar levels before and after treatment.

Outcome measurement: In non-diabetic group: incidence of new-onset DM in the group was recorded during the study period. In diabetic group: incidence of diabetes-related complications was recorded during the study period.

Statistical methods

Data management and statistical analysis were conducted using SPSS version 28 (IBM, Armonk, New York, USA). The normality of the quantitative data was evaluated using the Shapiro-Wilk test and direct data visualization methods. Based on the normality assessment, quantitative data were summarized using means and standard deviations. Categorical data were converted into numerical values and proportions. The paired t-test was used to compare fasting blood sugar, 2-hour postprandial blood sugar, and HbA1c levels before and after treatment. The independent t-test analyzed quantitative data related to the incidence of new-onset diabetes or complications, while the Chi-square or Fisher's exact test was employed for categorical data analysis. Multivariate logistic regression analysis was performed to predict the occurrence of new-onset diabetes, with odds ratios and their 95% confidence intervals calculated. All statistical tests were two-sided, and P values less than 0.05 were considered significant.

Results

The non-diabetic group consisted of 39 cases with a mean age of 43 ± 13 years, predominantly male (61.5% male, 38.5% female). Their mean weight was 81 ± 8 kg, and the mean BMI was 24.6 ± 3. Fasting blood sugar levels increased significantly from 84 ± 7 mg/dL before treatment to 98 ± 19 mg/dL after treatment ($p < 0.001$). Similarly, 2-hour postprandial blood sugar levels rose from 125 ± 11 mg/dL to 147 ± 27 mg/dL post-treatment ($p < 0.001$). The mean HbA1c level also increased from 5.0 ± 0.3% to 5.3 ± 0.5% after treatment ($p < 0.001$). Treatment protocols were distributed as follows: 66.7% received R-CHOP, 15.4% ABVD, 5.1% BU/CY, and 12.8% CVP. Regarding pathology, 25.6% were diagnosed with Hodgkin Lymphoma (HL), and 74.4% had NHL. **Table 1**

Table 1: General characteristics, fasting, 2hpp blood sugar, HBA1C before and after treatment, pathology and treatment protocol of the non-diabetic patients.

General characteristics	Mean ±SD or n (%)	P value
Age (years)	43 ±13	
Sex		
Males	24 (61.5)	
Females	15 (38.5)	
Weight (kg)	81 ±8	
BMI	24.6 ±3	
Fasting blood sugar		
Before	84 ±7	**<0.001***
After	98 ±19	
2hpp blood sugar		
Before	125 ±11	**<0.001***
After	147 ±27	
HBA1C		
Before	5 ±0.3	**<0.001***
After	5.3 ±0.5	
Protocol		
R-CHOP	26 (66.7)	
ABVD	6 (15.4)	
BU/CY	2 (5.1)	
CVP	5 (12.8)	
Pathology		
HL	10 (25.6)	
NHL	29 (74.4)	

SD: Standard deviation; n: number; kg: kilograms; BMI: Body Mass Index; *Significant P-value; n (%): number (percentage); HL: Hodgkin Lymphoma; NHL: Non-Hodgkin Lymphoma; ABVD: Adriamycin (Doxorubicin), Bleomycin, Vinblastine, Dacarbazine; R-CHOP: Rituximab, Cyclophosphamide, Hydroxydaunorubicin, Oncovin (Vincristine), Prednisone; BU/CY: Busulfan, Cyclophosphamide; CVP: Cyclophosphamide, Vincristine, Prednisone.

The study observed that 9 participants (23.1%) developed new-onset diabetes during the study. Participants with new-onset diabetes had a significantly higher mean weight (85 ± 8 kg vs. 79 ± 7 kg, P = 0.046) and BMI (28.5 ± 3.2 vs. 23.4 ± 1.7, P < 0.001) than those without diabetes. Age (P = 0.150) and sex (P = 0.226) were not significant. Before treatment, the new-onset diabetes group had higher fasting blood sugar (90 ± 7 mg/dL vs. 82 ± 6 mg/dL, P < 0.001), 2-hour postprandial blood sugar (136 ± 12 mg/dL vs. 121 ± 9 mg/dL, P < 0.001), and HbA1c (5.1 ± 0.2% vs. 4.9 ± 0.3%, P = 0.014). Post-treatment, these values were even higher (fasting blood sugar: 123 ± 20 mg/dL vs. 90 ± 10 mg/dL, P < 0.001; 2-hour postprandial blood sugar: 179 ± 31 mg/dL vs. 138 ± 16 mg/dL, P = 0.003; HbA1c: 5.9 ± 0.4% vs. 5.1 ± 0.3%, P < 0.001). Study protocol (P = 0.695) and pathology (P = 0.547) showed no significant differences. **Table 2**

Table 2: General characteristics, fasting, 2hpp blood sugar, HBA1C before and after treatment, pathology and treatment protocol according to new-onset diabetes in non-diabetic patients.

		New onset diabetes		
		Yes (n = 9)	No (n = 30)	P-value
Age (years)	Mean ±SD	48 ±13	41 ±13	0.150
Sex				
Males	n (%)	4 (44.4)	20 (66.7)	0.226
Females	n (%)	5 (55.6)	10 (33.3)	
Weight (kg)	Mean ±SD	85 ±8	79 ±7	**0.046***
BMI	Mean ±SD	28.5 ±3.2	23.4 ±1.7	**<0.001***
Before treatment				
Fasting blood sugar	Mean ±SD	90 ±7	82 ±6	**<0.001***
2hpp blood sugar	Mean ±SD	136 ±12	121 ±9	**<0.001***
HbA1C	Mean ±SD	5.1 ±0.2	4.9 ±0.3	**0.014***
After treatment				
Fasting blood sugar	Mean ±SD	123 ±20	90 ±10	**<0.001***
2hpp blood sugar	Mean ±SD	179 ±31	138 ±16	**0.003***
HbA1C	Mean ±SD	5.9 ±0.4	5.1 ±0.3	**<0.001***
Protocol				
R-CHOP	n (%)	7 (77.8)	19 (63.3)	0.695
ABVD	n (%)	2 (22.2)	4 (13.3)	
BU/CY	n (%)	0 (0)	2 (6.7)	
CVP	n (%)	0 (0)	5 (16.7)	
Pathology				
HL	n (%)	3 (33.3)	7 (23.3)	0.547
NHL	n (%)	6 (66.7)	23 (76.7)	

n (%): number (percentage); SD: Standard Deviation; kg: kilograms; BMI: Body Mass Index; HL: Hodgkin Lymphoma; NHL: Non-Hodgkin Lymphoma; R-CHOP: Rituximab, Cyclophosphamide, Hydroxydaunorubicin, Oncovin (Vincristine), Prednisone; ABVD: Adriamycin (Doxorubicin), Bleomycin, Vinblastine, Dacarbazine; BU/CY: Busulfan, Cyclophosphamide; CVP: Cyclophosphamide, Vincristine, Prednisone, *Significant P-value.

A multivariate logistic regression analysis was conducted to predict the onset of new diabetes. The model indicated that a one-unit increase in BMI was associated with a 98% higher risk of developing new-onset diabetes (OR = 1.984, 95% CI = 1.205 – 3.267, P = 0.007). **Table 3**

Table 3: Multivariate logistic regression analysis to predict the occurrence of new-onset diabetes.

	B	S.E.	Wald	OR (95% CI)	P-value
BMI	0.685	0.255	7.243	1.984 (1.205 - 3.267)	**0.007***
Fasting blood sugar	0.121	0.104	1.335	1.128 (0.919 - 1.385)	0.248
HbA1C	0.766	2.813	0.074	2.151 (0.009 - 533.136)	0.785

*Significant P-value; BMI: Body mass index; B: Regression coefficient; SE: Standard error; OR: Odds ratio; 95% CI: 95% Confidence interval

The diabetic group included 22 cases with a mean age of 43 ± 11 years, equally divided between males and females (50% each). Their average mean was 83 ± 5 kg, and the mean BMI was 25.9

± 1.2. Fasting blood sugar increased from 176 ± 36 mg/dL to 198 ± 37 mg/dL (P < 0.001), and 2-hour postprandial blood sugar rose from 251 ± 53 mg/dL to 283 ± 51 mg/dL (P < 0.001). HbA1c levels also went up from 7.8 ± 0.8% to 8.2 ± 0.9% (P = 0.006). Regarding treatment protocols, 72.7% received R-CHOP, 18.2% ABVD, and 9.1% CVP, with no participants on BU/CY. Pathological diagnoses included 22.7% with Hodgkin Lymphoma and 77.3% with NHL. **Table 4**

Table 4: General characteristics, fasting, 2hpp blood sugar, HBA1C before and after treatment, pathology and treatment protocol in diabetic patients.

General characteristics	Mean±SD or n (%)	P-value
Age (years)	43 ±11	
Sex		
Males	11 (50)	
Females	11 (50)	
Weight (kg)	83 ±5	
BMI	25.9 ±1.2	
Fasting blood sugar		
Before	176 ±36	**<0.001***
After	198 ±37	
2h postprandial blood sugar		
Before	251 ±53	**<0.001***
After	283 ±51	
HBA1C		
Before	7.8 ±0.8	**0.006***
After	8.2 ±0.9	
Treatment protocol		
R-CHOP	16 (72.7)	
ABVD	4 (18.2)	
BU/CY	0 (0)	
CVP	2 (9.1)	
Pathology		
HL	5 (22.7)	
NHL	17 (77.3)	

SD: Standard deviation; n: number; kg: kilograms; BMI: Body Mass Index, HL: Hodgkin Lymphoma; NHL: Non-Hodgkin Lymphoma; R-CHOP: Rituximab, Cyclophosphamide, Hydroxydaunorubicin, Oncovin (Vincristine), Prednisone; ABVD: Adriamycin (Doxorubicin), Bleomycin, Vinblastine, Dacarbazine; BU/CY: Busulfan, Cyclophosphamide; CVP: Cyclophosphamide, Vincristine, Prednisone, *Significant P-value.

The study observed that 16 participants (72.7%) experienced diabetes-related complications during the study period. No significant differences were found between participants who developed complications and those who did not regarding age (P = 0.588), sex (P = 1.0), weight (P = 0.567), and BMI (P = 0.083). Before treatment, mean fasting blood sugar (P = 0.650), 2-hour postprandial blood sugar (P = 0.893), and HbA1c levels (P = 0.356) were similar between

the groups. Post-treatment, mean fasting blood sugar (P = 0.323) and 2-hour postprandial blood sugar (P = 0.209) remained comparable, but HbA1c levels were considerably higher in those with complications (8.4 ± 0.7% vs. 7.5 ± 1%, P = 0.033). The distribution of treatment protocols differed significantly: 87.5% of participants with complications received R-CHOP compared to 33.3% without complications (P = 0.025). A higher proportion of participants without complications received ABVD (50%) compared to those with complications (6.3%). No participants received BU/CY, and a small percentage received CVP. Although not statistically significant (P = 0.1), more participants with complications had NHL (87.5% vs. 50%). **Table 5**

Table 5: General characteristics, fasting, 2hpp blood sugar, HBA1C before and after treatment, pathology and treatment protocol according to complications in diabetic patients.

		Complications		
		Yes (n = 16)	**No (n = 6)**	**P-value**
Age (years)	Mean ±SD	44 ±13	41 ±8	0.588
Sex				
Males	n (%)	8 (50)	3 (50.0)	1.0
Females	n (%)	8 (50)	3 (50.0)	
Weight (kg)	Mean ±SD	84 ±6	82 ±4	0.567
BMI	Mean ±SD	26.2 ±1	25.2 ±1.5	0.083
Before treatment				
Fasting blood sugar	Mean ±SD	173 ±32	183 ±49	0.650
2hpp blood sugar	Mean ±SD	252 ±51	248 ±64	0.893
HbA1C	Mean ±SD	7.9 ±0.8	7.6 ±0.9	0.356
After treatment				
Fasting blood sugar	Mean ±SD	203 ±37	185 ±38	0.323
2hpp blood sugar	Mean ±SD	291 ±50	260 ±52	0.209
HbA1C	Mean ±SD	8.4 ±0.7	7.5 ±1	**0.033***
Protocol				
R-CHOP	n (%)	14 (87.5)	2 (33.3)	**0.025***
ABVD	n (%)	1 (6.3)	3 (50)	
BU/CY	n (%)	0 (0)	0 (0)	
CVP	n (%)	1 (6.3)	1 (16.7)	
Pathology				
HL	n (%)	2 (12.5)	3 (50)	0.1
NHL	n (%)	14 (87.5)	3 (50)	

n (%): number (percentage); SD: Standard Deviation; kg: kilograms; BMI: Body Mass Index, *Significant P-value; HL: Hodgkin Lymphoma; NHL: Non-Hodgkin Lymphoma; R-CHOP: Rituximab, Cyclophosphamide, Hydroxydaunorubicin, Oncovin (Vincristine), Prednisone; ABVD: Adriamycin (Doxorubicin), Bleomycin, Vinblastine, Dacarbazine; BU/CY: Busulfan, Cyclophosphamide; CVP: Cyclophosphamide, Vincristine, Prednisone.

Discussion

Our observational cohort study was conducted on 61 lymphoma patients, divided into 39 non-diabetic and 22 diabetic patients. Detailed history taking, physical examinations, and laboratory investigations monitored blood sugar levels and HbA1C before and after treatment. The study aimed to record the incidence of new-onset diabetes in non-diabetic patients and diabetes-related complications in diabetic patients.

In the non-diabetic group, 23.1% of lymphoma patients developed new-onset diabetes, highlighting the significant diabetogenic potential of lymphoma treatment regimens. This suggests that chemotherapy protocols, especially those involving corticosteroids and alkylating agents, can substantially increase the diabetes risk.

A study by Moore-Vasram et al. involving 19,530 leukemia patients found that 4.6% (n=723) developed new-onset diabetes. Among these patients, the highest incidence of new-onset diabetes was observed in those with leukemia at 7.1% (n=279), followed by NHL at 4.0% (n=385), and Hodgkin lymphoma (HL) at 2.8% (n=59) [7].

Additionally, research by Saputri et al. reported a 9.53% (n=2) incidence of new diabetes mellitus (DM) cases following the initial CHOP chemotherapy regimen [8].

Our study reported a higher incidence rate of new-onset diabetes compared to the Danish study. This discrepancy may be attributed to differences in study design, population demographics, and follow-up duration.

Our study found that non-diabetic participants who developed new-onset diabetes had significantly higher mean weight and BMI, indicating that obesity and higher BMI are crucial risk factors for diabetes during lymphoma treatment. This aligns with the established link between obesity and increased insulin resistance, which can be exacerbated by chemotherapy agents that induce hyperglycemia.

In the study by Saputri et al., it was observed that individuals who developed new-onset diabetes often had other health conditions, including being overweight, having a high BMI, dyslipidemia, hypertension, and pre-diabetes [8].

Certain chemotherapeutic drugs impact insulin resistance and β-cell function, with this effect being more pronounced in individuals with comorbidities like obesity, hypertension, and metabolic syndrome. Additionally, Lamar et al. noted that these medications can induce hyperglycemia by damaging pancreatic β-cells, resulting in reduced insulin production and lower insulin sensitivity [10].

Lee et al. consistently found that several clinical factors were significantly linked to the development of DM during CHOP chemotherapy. These factors included a BMI over 30 kg/m² ($p < 0.05$), a history of hypertension or current hypertension, including isolated systolic hypertension ($p < 0.05$) at the start of chemotherapy, metabolic syndrome ($p < 0.05$), and HbA1c levels above 6.1% ($p < 0.05$) [11].

Participants who developed new-onset diabetes had higher mean FBS, 2-HPP blood sugar, and HbA1c levels even before treatment, indicating a predisposition to impaired glucose metabolism. Lymphoma treatment exacerbated this condition, resulting in significantly higher post-treatment blood glucose and HbA1c levels. Patients with borderline or slightly elevated blood sugar levels prior to treatment are at heightened risk of developing diabetes when exposed to chemotherapy.

In their study, Saputri et al. identified a statistically significant impact of chemotherapy on FBG and PPBG levels ($p = 0.032$ and $p = 0.002$, respectively). They observed an increase in FBG and PPBG levels in non-DM patients with NHL before and on the sixth day of their initial chemotherapy session [8].

Steroid-containing chemotherapy regimens like R-CHOP induce hyperglycemia by increasing hepatic gluconeogenesis, decreasing peripheral glucose uptake, and impairing insulin

secretion. This effect is especially pronounced in individuals with pre-existing insulin resistance or borderline glucose intolerance, as indicated by their pre-treatment blood sugar levels in our cohort [12].

However, longer follow-up duration is mandatory to confirm the results of the study as contrasting literature suggests the effect of incident DM and high levels of blood sugar labs are just temporary and are declining in the long-term [5].

In the non-diabetic group, our study's multivariate logistic regression analysis revealed that an increase in body mass index (BMI) significantly raises the risk of developing new-onset diabetes among lymphoma patients undergoing treatment, indicating a strong relationship between higher BMI and diabetes onset in this population.

Similarly, multivariate analysis in the study by **Lee et al.** revealed that age ≥60 years, HbA1c levels >6.1%, and BMI >30 kg/m² were independently significant factors associated with DM development after chemotherapy [11].

Our study revealed that a majority of participants with pre-existing diabetes experienced diabetes-related complications during the study period, demonstrating the significant impact of lymphoma treatment on the progression of diabetes.

This finding aligns with the study by **Baech et al.** which reported that NHL patients with pre-existing non–insulin-dependent DM had a significantly higher risk of requiring insulin prescriptions following treatment [5].

Furthermore, Mellor et al. conducted a study to assess the incidence of acute diabetes-related complications in patients undergoing chemoradiotherapy. The findings indicated that patients with pre-existing type 2 diabetes who were already on insulin therapy at the start of the study had a significantly higher likelihood of encountering severe diabetes-related complications during chemotherapy. Although the study population was relatively small, 80% of these

patients required admission to a high-dependency ward, and 60% had to miss at least one cycle of chemotherapy [14].

In our study, mean FBS, 2-HPP blood sugar, and HbA1c levels before treatment were similar between participants with and without complications. Post-treatment, while FBS and 2-HPP levels remained similar, those with complications had significantly higher HbA1c levels, indicating prolonged hyperglycemia and poor diabetes control, contributing to complications. Chemotherapy, particularly steroid-containing regimens, can exacerbate glucose dysregulation. While short-term measures (FBS and 2-HPP) might remain within similar ranges due to acute fluctuations, HbA1c captures sustained hyperglycemia, which is more closely linked to diabetes-related complications [9].

In our study, most participants with complications were treated with the R-CHOP protocol, whereas fewer without complications received it. Conversely, half of those without complications were treated with the ABVD protocol, indicating that the chemotherapy type affects the likelihood of developing complications.

In a study by Lamar et al., it was discovered that diabetic individuals undergoing R-CHOP or EPOCH-R treatment had a 12-fold higher risk of developing hyperglycemia compared to non-diabetic patients. Additionally, patients with an FBG level of 100 mg/dL or higher had about four times the likelihood of experiencing hyperglycemia [10].

Patients with NHL often require aggressive treatments like the R-CHOP protocol, which includes steroids. These regimens exacerbate hyperglycemia and can lead to beta-cell dysfunction, reducing insulin secretion and worsening hyperglycemia, especially in those with pre-existing diabetes. The significant increase in diabetes-related complications observed in our study likely stems from this exacerbation of underlying glucose dysregulation [15].

In contrast, The ABVD protocol, used primarily for Hodgkin lymphoma, does not include steroids, which reduces the risk of hyperglycemia and subsequent complications. This explains

why a higher proportion of participants without complications were Hodgkin lymphoma patients and treated with the ABVD protocol [16].

Our study had some limitations including the single-center design which may limit generalizability, and the absence of a control group that hinders attributing changes in blood glucose solely to treatment. Additionally, the one-year follow-up may not capture the long-term impact on diabetes development and complications.

Conclusions

Lymphoma treatments, especially those involving steroid-containing regimens like R-CHOP, significantly elevate the risk of new-onset diabetes and diabetes-related complications. This underscores the necessity for proactive glucose monitoring and management strategies in lymphoma patients to mitigate the adverse effects on metabolic health.

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