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FREQUENCY OF PULMONARY TOXICITY IN PATIENTS TREATED FOR HODGKIN LYMPHOMA

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Abstract

Background: *Pulmonary toxicity is an important concern in the treatment of Hodgkin lymphoma (HL), exceptionally among patients getting chemotherapeutic agents such as bleomycin. This research aimed to assess the frequency and severity of pulmonary toxicity in patients treated for Hodgkin lymphoma and to explore factors impact and its occurrence.*

Methods *The study looked at 133 patients in which 94 males and 29 females diagnosed with Hodgkin lymphoma and received anti-cancer treatment including ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine). During treatment periods Lung function was monitored during and after treatment measures of oxygen saturation (SpO2), Diffusing Capacity of the Lung for Carbon Monoxide (DLCO), and Forced Vital Capacity (FVC). Pulmonary toxicity was categorized based on the degree of decline in these measures. Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 22.*

Result: *This study included 133 patients. The majority of patients (93%) kept their oxygen level well maintain spo2 during treatment while 4.5% experienced mild and 2.4% moderate drops in SpO2, suggesting mild to moderate lung toxicity. About DLCO result shows (90%) of the patients did not experience any decline in their DLCO values during treatment, indicating that their lung function remained stable while 13.5% of patients experienced a moderate decrease in their DLCO values and small portion of patients 1.5% severe decrease in DLCO. This study result shows 88.7% of patients, FVC (Forced Vital Capacity) remained stable while 3% of patients had severe drops in their lung capacity. Patients who received treatments containing bleomycin experienced a higher rate of lung problems.*

Conclusion: *The frequency of pulmonary toxicity in patients treated for Hodgkin lymphoma was relatively low but remarkable specially among those encounter bleomycin-containing regimens. Although the majority of patients maintained stable lung function a small number of patients experienced varying degrees of lung toxicity. These findings underscore the importance of monitoring lung*

function in HL patients and suggest that future research should focus on reducing pulmonary side effects to improve long-term health outcomes.

INTRODUCTION

Hodgkin lymphoma (HL) is a type of cancer that affects the lymphatic system, which is a key part of the body's immune system. Unlike other lymphomas, HL is distinguished by the presence of Reed-Sternberg cells, which are large, abnormal lymphocytes found in the lymph nodes. These cells are crucial for diagnosing HL and serve as a hallmark of the disease. While HL is relatively rare, accounting for about 12–18% of all lymphoma cases worldwide, it is regarded as one of the most treatable types of cancer, particularly with advances in treatment over the past few decades[1.] HL is divided into two categories by biological and clinical studies such as classical Hodgkin lymphoma and nodular lymphocyte-predominant Hodgkin lymphoma (NLP-HL)[2]. In 2015, around 9,050 fresh cases of Hodgkin lymphoma are expected to be identified in the United States [3]. Hodgkin lymphoma has a bimodal disorder distribution, with an become greater rate in patients in their teenage years or early 20s and a similar grater incidence in patients older than 55 years [4.] The integrate modality therapy with chemotherapy and radiation come up with best disease control among patients with Hodgkin lymphoma (HL). However, the early and chronic toxicities from chemotherapy, targeted therapy, and radiation therapy (RT) can cause notable morbidity among survivors, including pulmonary dysfunction [5-6]. Abnormalities in PFTs have been correlate with decreased overall survival in huge studies of the general population [7]. The principal therapy for HL has been chemotherapy primarily using the ABVD regimen (doxorubicin, bleomycin, vinblastine, dacarbazine). ABVD regimen can be generally accepted to be absolutely the best treatment for patients with classical HL since it provides high chances to achieve remission and long-term survival [8]. Hodgkin lymphoma (HL) is a type of cancer and it is one of the most curable forms of cancer mainly when diagnosed early. The treatment for HL has advance significantly over the years, with the use of chemotherapy, radiation therapy, and in some cases, stem cell transplantation. The treatment protocol is typically based on the stage of the disease, the patient's overall health. Chemotherapy ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) is commonly used for Hodgkin lymphoma treatment protocol. ABVD has been highly positive effective in early-stage of HL and also good effect in advanced-stage cases. It targets rapidly dividing cells, including cancer cells, to slow or stop their growth. Despite its effectiveness, certain chemotherapy agents (bleomycin) can cause side effects like pulmonary toxicity (lung damage)[9]. Radiation therapy is important component to treat the Hodgkin lymphoma early stages cases. Radiation therapy used to target and remove the remaining cancer cells after receiving chemotherapy. Advances in radiation techniques, such as involved-field radiation therapy (IFRT) have helped reduced damage to surrounding healthy tissue mainly in children and young adults, who are more sensitive to radiation [10.] Immunotherapy and stem cell transplantation are crucial treatment options for Hodgkin lymphoma (HL), especially in cases where the disease is resistant to standard therapies. Both therapies represent important advances in improving outcomes for patients with challenging HL cases.[11-12]

To observe the pulmonary functions during treatment tenure by the help of different diagnostic methods such as Pulmonary Function Test. PFT is remains the mainstay for detecting and monitoring lungs functions parameters like DLCO, FVC, SPO2. It provides numerical parameters of lungs functions. This is the first study from Peshawar to our knowledge, to assess pulmonary impairment in patients treating for Hodgkin lymphoma. The objective of this study was to determine the pulmonary functions parameter changes detected by diagnostic methods and focusing on the drop in the DLCO, FVC and SPO2.

Material and Methods

Study Design:

This retrospective cross-sectional study was undertaken at Shaukat Khanum Memorial Cancer Hospital Peshawar, spanning from January 2021 to December 2021, subsequent to obtaining approval

from the Institutional Review Board (IRB). Data were acquired retrospectively from the institutions' computerized database.

Study Population:
Enrollees comprised patients who underwent treatment for Hodgkin lymphoma. Exclusion criteria encompassed individuals with a medical history indicative of lungs problems or pre-existing abnormal PFT findings before the initiation of Hodgkin lymphoma treatment.

Data Collection:
Patient data were systemically gathered via a dedicated data collection tool. PFT assessments were conducted at baseline, before the initiation treatment for Hodgkin lymphoma and at regular intervals throughout the treatment course. Parameters assessed included DLCO FVC SPO2 function, and any pertinent findings discernible from pulmonary function test. Lungs functions parameters (DLCO, FVC, SPO2) was operationally characterized as mild (80-90%) moderate (79-70%) and severe (less than 70%).

Statistical Analysis:
Data pertaining to all patients receiving Hodgkin lymphoma therapy who underwent Pulmonary function test at Shaukat Khanum Memorial Cancer Hospital and Research Center Peshawar were meticulously reviewed chronologically, spanning from January 1st, 2022, to December 31st, 2023. Instances of lungs functional abnormalities were diligently documented and electronically archived using a standardized data sheet. Statistical analyses were performed utilizing IBM Statistical Package for the Social Sciences (SPSS) Version 25. Variables, such as the duration of Chemotherapy and radiotherapy and the incidence of pulmonary dysfunctions, were expressed as frequencies and percentages. Cumulative incidence was calculated to ascertain the total number of patients manifesting pulmonary functions over the course of two year, while the incidence rate, represented in "individual years," was computed to delineate the duration until the manifestation of adverse effect of Hodgkin lymphoma treatment. Data were further elucidated via graphical representations.

Ethical Considerations:
Ethical approval was taken from the Institutional Review Board (IRB). Throughout the duration of the research endeavor, strict adherence to ethical guidelines ensured the preservation of patient privacy with no unauthorized dissemination of patient information beyond the research team.

Data Analysis Software:
Data analysis was conducted employing IBM SPSS V25 statistical software. Parameters, including the duration of Hodgkin lymphoma treatment and the incidence of pulmonary dysfunctions were analyzed descriptively and presented as frequencies and percentages. Cumulative incidence and incidence rates were calculated to offer insights into the occurrence and temporal manifestation of treatment adverse events with data visualization facilitated through graphical representations.

Results:
The study aimed to investigate the effects of Hodgkin lymphoma therapy on lungs functions in patients. The results are summarized below;
In this study, 133 patients with Hodgkin lymphoma (HL) were included, and the primary focus was on assessing the effect of treatment on pulmonary function, particularly the occurrence of pulmonary toxicity. The findings reveal interesting patterns regarding oxygen saturation (SpO2), Diffusing Capacity of the Lung for Carbon Monoxide (DLCO), and Forced Vital Capacity (FVC) in patients undergoing chemotherapy and radiotherapy. Results showed that 93% of patients well tolerant treatment and maintain oxygen saturation (SpO2) during treatment tenure while 4.5% experienced mild and 2.4% moderate decrease indicating mild to moderate lung toxicity. For Diffusing Capacity of the Lung for Carbon Monoxide (DLCO), 90% of patients had stable values, while 13.5% showed moderate and 1.5% severe reduce suggesting some lung impairment. Regarding Forced Vital Capacity (FVC), 88.7% of patients maintained stable lung capacity, though 3% had severe drops. Particularly patients treated with bleomycin-based regimens exhibited a higher rate of pulmonary toxicity. These findings emphasize the importance of monitoring lung function during treatment.

4.1 Gender Distribution

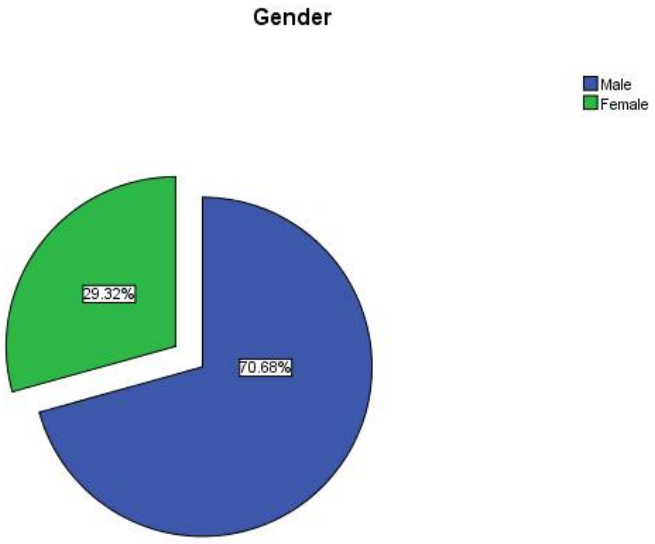

Fig 01: This Pie-chart shows a significant difference in the gender distribution of the participants in this study, with 94 (70.7%) males and 39 (29.3%) females included.

4.2 Age Distribution

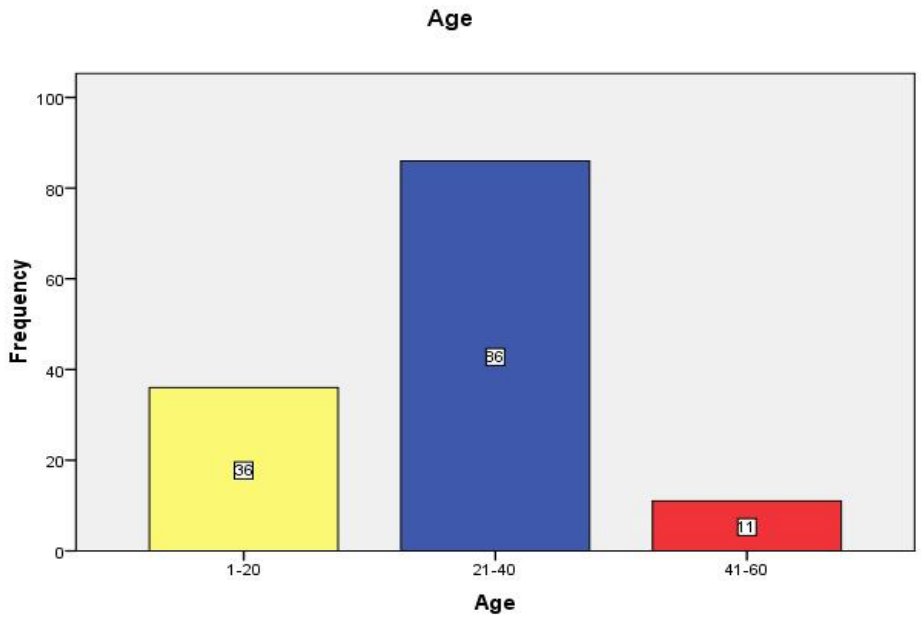

Figure 02: This bar graph shows the age distribution of our patient. In which 86% of the patient fall in age 21-40 years, while other age groups include 36% and 11% respectively.

4.3. Co-morbidity

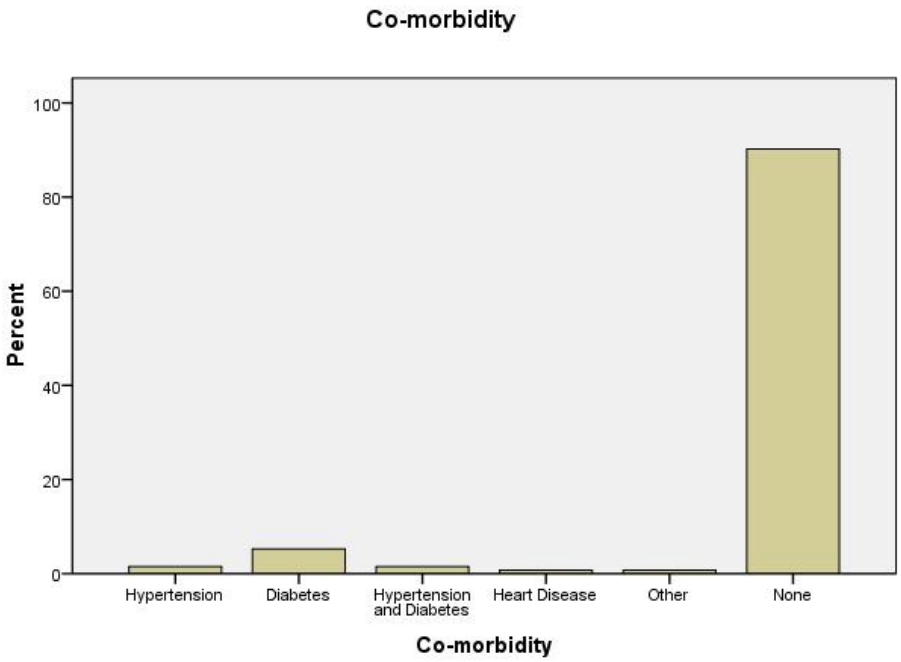

Fig 03: The bar chart illustrates the distribution of comorbidities among 133 patients in the study. Out of the total 133 patients, 13 patients were identified as having different comorbid conditions. The chart visually represents the number of patients with specific comorbidities, highlighting the diversity in the patients' health conditions. The x-axis categorizes the types of comorbidities, while the y-axis shows the number of patients within each category. The chart provides a clear visual representation of diabetes, hypertension, heart disease and patient with no comorbidities.

4.4. Chemotherapy Treatment

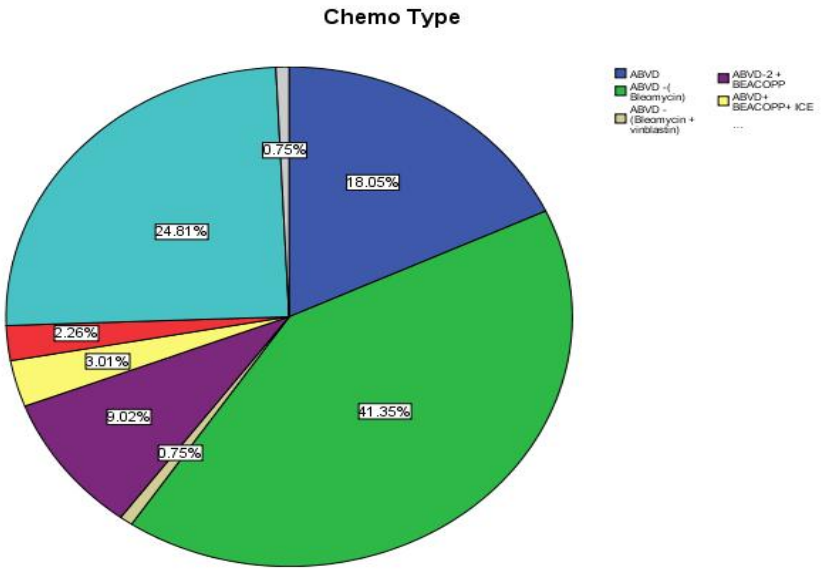

Fig 04: This Pie-chart shows the chemotherapy sessions given to treat Hodgkin's Lymphoma Patients.

4.5. Radiation Treatment for Hodgkin lymphoma

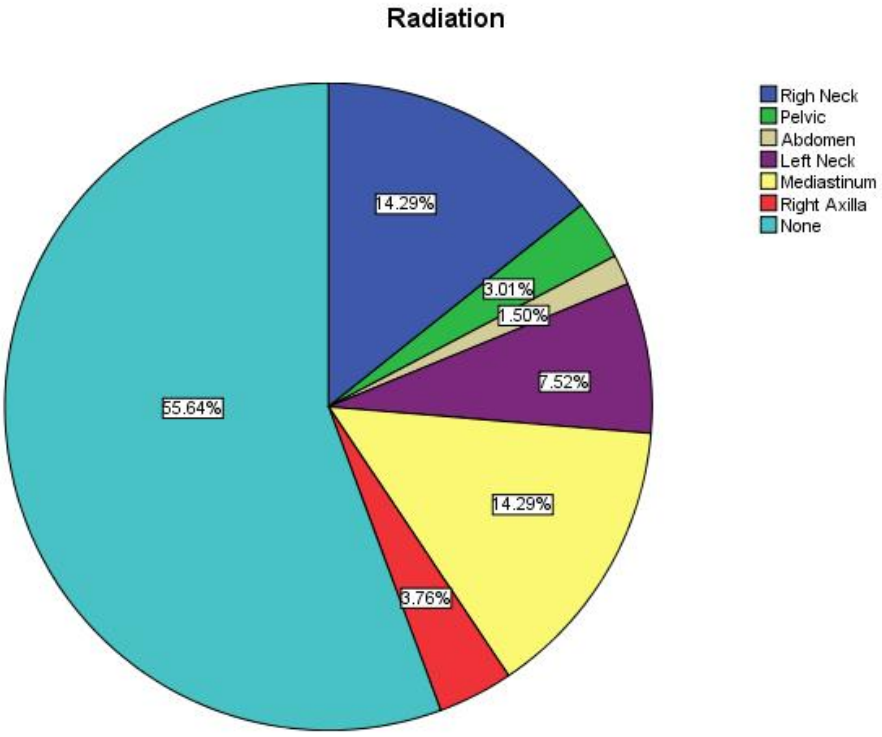

Fig: 05: This Pie-chart shows the different site radiation treatment in Hodgkin's Lymphoma patients.

4.6. Assessment of Pulmonary toxicity: In this study we measure the level of lung toxicity by recording SPO2, DLCO and FVC as following.

Treatment impact on SPO2

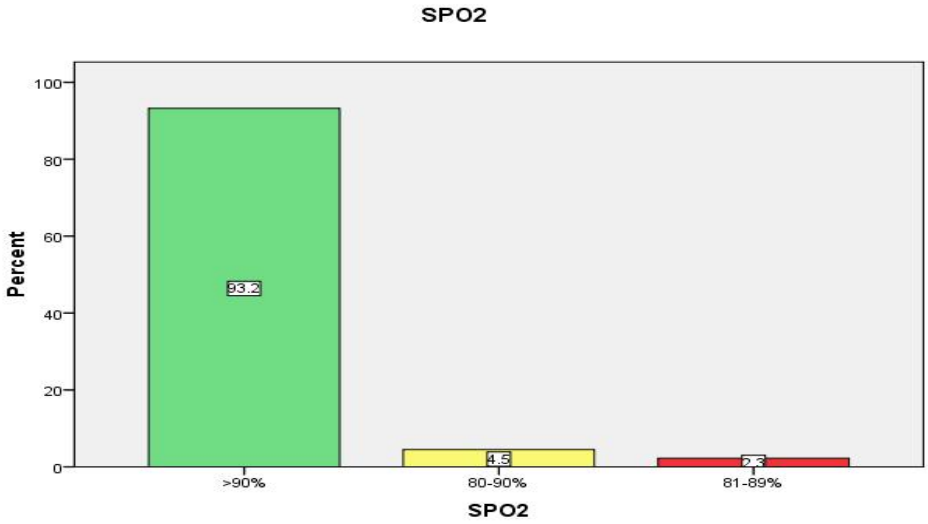

Fig:06: This Bar graph shows that 93% of our patient completed treatment without dropping SPO2, while 4.5% shows mild drop and 2.4 % showed moderate drop in oxygen saturation witnessing lung toxicity.

Diffusion Lung Capacity of carbon monoxide DLCO

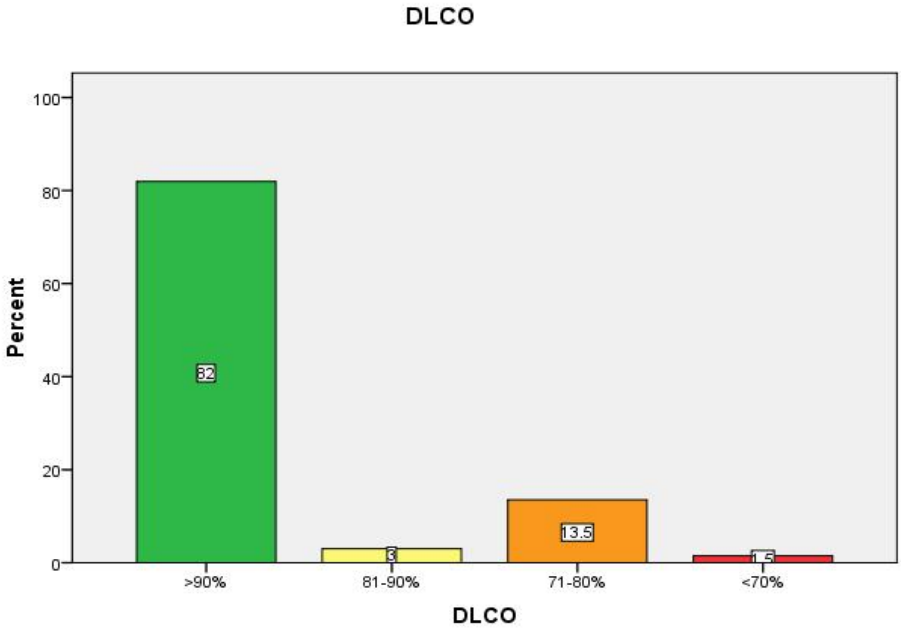

Fig: 07: This bar graph shows that 90% of our patient completed treatment without dropping DLCO while 3% showed mild drop, 13.5% showed moderate drop and 1.5% showed severe drop in DLCO value witnessing the level of lung toxicity.

FVC response to treatment

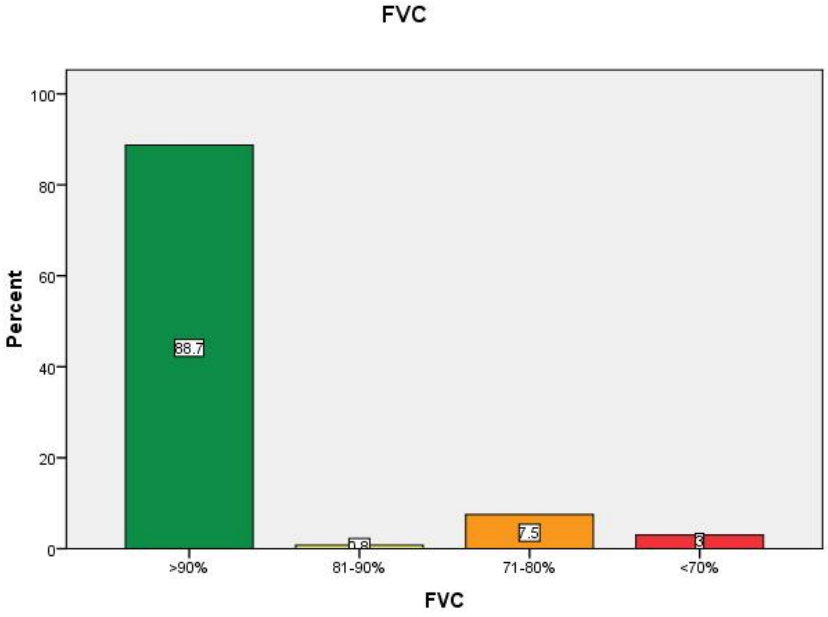

Fig: 08: This bar graph shows that 88.7% of our patient completed treatment without dropping FVC while 0.8% showed mild drop, 7.5% showed moderate drop and 3% showed severe drop in FVC value witnessing the level of lung toxicity.

Discussion

This study investigated the effects of chemotherapy and radiotherapy on lungs parameter in patients treated for Hodgkin lymphoma. The results showed in this study, 133 patients with Hodgkin lymphoma (HL) were included, and the primary focus was on assessing the effect of treatment on pulmonary function, particularly the occurrence of pulmonary toxicity. The findings reveal interesting patterns regarding oxygen saturation (SpO2), Diffusing Capacity of the Lung for Carbon Monoxide (DLCO), and Forced Vital Capacity (FVC) in patients undergoing chemotherapy and radiotherapy. Results showed that 93% of patients well tolerant treatment and maintain oxygen saturation (SpO2) during treatment tenure while 4.5% experienced mild and 2.4% moderate decrease indicating mild to moderate lung toxicity. For Diffusing Capacity of the Lung for Carbon Monoxide (DLCO), 90% of patients had stable values, while 13.5% showed moderate and 1.5% severe reduce suggesting some lung impairment. Regarding Forced Vital Capacity (FVC), 88.7% of patients maintained stable lung capacity, though 3% had severe drops. Particularly patients treated with bleomycin-based regimens exhibited a higher rate of pulmonary toxicity. These findings emphasize the importance of monitoring lung function during treatment Oxygen Saturation (SpO2).

In one study of 59 patients who received chemotherapy and radiotherapy for Hodgkin Lymphoma, those patients who received radiotherapy had constant decreased %DLCO at 12 months following completion of RT .[13]

In a prospective study conducted by the Dana-Farber Cancer Institute, 52 patients diagnosed with Hodgkin disease were enrolled. Of these, 29 patients received chemotherapy, while 23 patients underwent combined modality therapy, which included chemotherapy and radiation. The baseline median Diffusing Capacity of the Lung for Carbon Monoxide (DLCO) was 94%, with a range from 53% to 121%. Following chemotherapy, the median DLCO showed a decrease of 12% on average at one month ($p<0.001$), 2% at six months ($p=0.09$), and 3% at one year ($p=1$) compared to baseline. For those treated with combined modality therapy, the median DLCO decreased by 13% on average at one month ($p=0.0002$), 18% at six months ($p=0.005$), and 10% at one year ($p=0.0005$) from baseline. Additionally, six patients (12%) experienced symptomatic Bleomycin toxicity, leading to the discontinuation of the drug.[14]

In Our retrospective study however, we conduct 2 years patients' data from January 2021 to December 2023. The result of study points out the impact of treatment on lung function in Hodgkin lymphoma (HL) patients, emphasizing pulmonary toxicity risks. While most patients (93%) maintained stable oxygen saturation (SpO2), 6.9% experienced mild to moderate decrease indicating potential lung toxicity. Similarly, 90% of patients had stable Diffusing Capacity of the Lung for Carbon Monoxide (DLCO), though 15% showed reductions, with 13.5% having moderate and 1.5% severe decreases. Most patients (88.7%) had stable Forced Vital Capacity (FVC), but 3% experienced severe drops, suggesting significant lung damage in some cases. Mostly bleomycin-based regimens were associated with an increase rate of pulmonary toxicity, supporting the need for careful lung monitoring, especially in that receiving bleomycin, to prevent long-term respiratory complications. These findings underscore the importance of individualized lung function management during HL treatment.

Conclusion

All findings from this study highlight the most patients with Hodgkin lymphoma (93%) maintain stable oxygen levels and lung function, a littles numbers percentage experience varying degrees of lung toxicity. DLCO and FVC values were generally stable for most patients, though a minority experienced moderate to severe declines, particularly those treated with bleomycin-containing regimens. These findings underscore the need for ongoing monitoring and early intervention strategies to mitigate the risk of long-term pulmonary complications in HL patients undergoing chemotherapy and radiotherapy.

Conflict of Interest:
The authors have disclosed no other conflicts of interest.

Study limitation:
This study is not without limitations some patients missed their PFT appointment due to different reasons, which is affecting this research results all these are not included in this study.

Authors contributions:
Sohail Ali Collection of data, preliminary analysis, organization of data and writing of manuscript and Data collection and literature search. Interpretation of data, writing and editing of manuscript by Dr Fattah Ullah khan.

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