An-Najah National University

Faculty of Graduate Studies

HEMATOLOGICAL AND BIOCHEMICAL PREDICTORS OF COMPLICATIONS AND OUTCOMES AMONG PATIENTS WITH LYMPHOMA TREATED IN THE PALESTINIAN HEALTHCARE SYSTEM

By

Baraa Aiman Sbaihat

Supervisor

Prof. Ramzi Shwahneh

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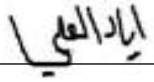
This Thesis was Defended Successfully on 24/11/2024 and approved by

Prof. Ramzi Shwahneh	
Supervisor	Signature
Dr. Mohannad Jazzar	
External Examiner	Signature
Prof. Iyad Al-ali	
Internal Examiner	Signature

Dedication

To those who died and left us due to this terrible disease, to my dear uncle's wife, who was only prevented by death from offering me congratulations on this achievement, may God have mercy on her and make her dwell in Paradise as a reward for her patience with the disease**.** To my heaven on earth who held my hand as I reached these higher degrees today...to my parents, my father and mother, may God bless them.

To those who love goodness and success for me more than themselves. To my dear brothers, we will be happy with your university graduation soon, God willing. To my husband who supported me whenever I was tired and despaired...who spoke to me with words of encouragement and hope. May God bless you.

Acknowledgements

In the beginning and in conclusion, praise be to God. Many thanks. Blessed be God Almighty, thanks to whom I learned that I succeeded. All the times I fell and became despondent and tired, God was always by my side. I prayed and supplicated and saw the answer in front of me. Praise be to God always.

My parents are the light that guides me to the safe path that reassures me in this world, may God protect you. My father is my eyes through which I see this universe. My father, my friend, and my lover. My father did not leave anything for others to give me. He gave me everything I love, everything I need, everything I want. My mother is my moon that lights up the darkness of the night. You stayed up long nights above my head so that I would not feel lonely while studying, and here you are today, getting the results of the nights. My caring mother, beautiful hearted, beloved soul. Escape from the world in your embrace. May God protect you, my dear mother.

My brothers, Mohammad and Maisara, my refuge, my hopes in the world. We grew up together. We played, learned, and studied. We shared every day, every conversation, all the feelings, all the wishes. We grew up and began to graduate from universities while we were together, and I pray to God to keep us together forever. My husband, my happiness came with my parents praying for me to do well. Every time depression took over, you held me to hope and work, helping me and making it easy for me. May God protect you for my days.

All thanks, appreciation and respect to all teachers around the world, to all researchers, to all those working in scientific research, especially to the supervisor Dr. Ramzi Shwahneh, who supervised and helped in the completion of this research. He was very cooperative and answered all questions at all times. He helped me in how to obtain information. Many thanks.

Supportive friends, thank you very much…

The staff of the Oncology Department at Jenin Governmental Hospital extends all thanks and appreciation

Declaration

I, the undersigned, declare that I submitted the thesis entitled:

HEMATOLOGICAL AND BIOCHEMICAL PREDICTORS OF COMPLICATIONS AND OUTCOMES AMONG PATIENTS WITH LYMPHOMA TREATED IN THE PALESTINIAN HEALTHCARE SYSTEM

I declare that the work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

Student's Name: _____

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HEMATOLOGICAL AND BIOCHEMICAL PREDICTORS OF COMPLICATIONS AND OUTCOMES AMONG PATIENTS WITH LYMPHOMA TREATED IN THE PALESTINIAN HEALTHCARE SYSTEM

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Abstract

Background: Lymphomas are a group of malignant neoplasms caused by uncontrolled proliferation of lymphocytes (B cells, T cells, or NK cells) during maturation. They are classified into Hodgkin and non-Hodgkin lymphoma, with nearly 90 subtypes. Risk factors include infections, immunodeficiency, autoimmune diseases, genetics, obesity, drugs, and environmental exposure. Diagnosis starts with clinical examination, followed by CT scan and biopsy. Treatment depends on disease stage and usually involves chemotherapy and radiotherapy, with patient monitoring via clinical and lab assessments. In Palestine, lymphoma patients receive treatment and are monitored throughout the disease. This study aims to assess the relationship between biochemical and hematological parameters and disease progression, complications, and outcomes in lymphoma patients under treatment in Palestinian hospitals. Methods: Data were collected from lymphoma patients of various ages and regions, including: age, gender, diagnosis date, lymphoma type, CBC, liver/kidney function, electrolytes, and treatment details. The data were categorized into two stages: initial diagnosis and last follow-up during treatment, then analyzed. Results: The study involved 150 patients, median age 40.0 (29.0, 59.3) years, mean 43.9 ± 18.2 years; 52.7% were male, and 78.7% had Hodgkin lymphoma. Median time since diagnosis was 5.5 ± 2.6 years. Cancer staging was available for 26 patients; 65.4% of them (11.3% of total) were at stage II. Common symptoms: weakness (71.3%), neck pain (18.0%), dizziness (15.3%), cough (8.7%), and fever (10.0%). Comorbidities included hypertension (9.3%), diabetes (9.3%), and hypothyroidism (1.3%). Most patients (92.0%) received cyclophosphamide; 40.7% ondansetron, 60.0 dexamethasone. In stage I, Hodgkin patients were younger with higher WBC, neutrophils, platelets, and chloride than non-Hodgkin. In stage II, only ferritin was significantly higher in non-Hodgkin patients.

Conclusion: The study reveals associations between disease progression and several lab parameters and risk factors. These findings may aid in improving early detection and developing more effective treatment strategies.

Keywords: lymphoma, Hodgkin lymphoma, non –Hodgkin lymphoma.

Chapter One
Introduction

1.1 background

Lymphoma is considered one of the types of cancers spread globally with a rate of 5%., as it is in the form of a heterogeneous malignant tumor in the lymphocytes. There are a very large number of types of lymphoma that reach 90 types, Hodgkin and Non-Hodgkin lymphoma are the major types [1, 2]. Lymphoma arises as a result of the unprogrammed proliferation that may occur during the process of cell division and cell development of lymphoblast, B, T, and killer cells [2].

The number of survivors of Hodgkin and Non-Hodgkin lymphoma has been increasing recently, due to advances in treatment [3, 4]. However, many lymphoma patients either during the treatment period or at the beginning of the disease, or who have been recovered and received treatment for a long period of time may develop several complications in various body systems [5]. These complications include the risk of developing another malignant tumor, cardiovascular disease, endocrine disorder, pulmonary disease and infection [4]. The nervous system can be greatly affected by lymphoma, whether the central or peripheral nervous system, through the production of extra-axial, intra-axial lesions or by meningeal metastases [6]. Lymphoma may also cause blockage of blood vessels by cancer cells [6].

Cancer in occupied Palestine is the second cause of death after cardiovascular diseases, as the number of deaths due to cancer for the year 2016-2020 was 14% of the total population, which is about 5.35. In 2015, the incidence of Hodgkin's lymphoma in females was 4%, and 4% in non-Hodgkin's lymphoma for both males and females. On the other hand, the incidence of non-Hodgkin's lymphoma in females increased by 4.2% in 2020, while the rate was 2.1% in Hodgkin lymphoma for each of the males and females [7].

symptoms of lymphoma are almost the same for both Hodgkin and non-Hodgkin types, including the presence of a painless tumor in the lymph nodes [8], as they are concentrated in fever, severe sweating during the night, sudden weight loss without reasons, lack of activity and energy and the presence of swollen lymph nodes in different parts of the body, especially in the neck area [2,9]. Cancer is initially

diagnosed by taking a biopsy from the patient, then medical imaging of all kinds (x-ray, CT, MRI), according to the need of the case, to know the extent of spread and the staging of lymphoma [8].

Lymphomas encompass a diverse collection of cancer types originating from the uncontrolled growth of various subsets of lymphocytes, including B-cells, T-cells, and natural killer (NK) cells, each at distinct stages of development. These lymphocyte-related malignancies exhibit considerable heterogeneity. Collectively, lymphomas constitute about 5% of all cancer cases, with an estimated overall survival rate of around 72% [2.

In this study, we recruited 250 patients to participate in the study, However, 100 of them did not complete their required examinations and were therefore excluded from the study.we collected a sample consisting of 150 patients with both types of lymphoma, Hodgkin's and non-Hodgkin's who are undergoing treatment in hospitals and health centers in the Palestinian territories. The study findings showed that the mean age was (43.9 ± 18.2) years with 79 (52.7%) were male in gender. The majority of the patients had Hodgkin lymphoma 118 (78.7%).The cancer stage was monitored for only 26 patients, and the majority of them were in the second stage of the disease17 (65.4%, 11.3% of all patients) were in stage II. At the same time, the highest percentage of symptoms that patients showed was general weakness 107 (71.3%), 13 (8.7%) reported cough, 27 (18.0%) reported neck pain, 23 (15.3%) reported dizziness, and 15 (10.0%) reported fever. Cambodian was not indicated for all patients, while the largest percentage was for hypertension and diabetes mellitus 14 (9.3%) had hypertension, 14 (9.3%) had diabetes mellitus, and 2 (1.3%) had hypothyroidism. Given at the treatment that patients take, we note that a large number of them take cyclophosphamide, then other treatments in a lesser order (92.0%), 90 (60.0%) received dexamethasone and 61 (40.7%) received ondansetron. This study presented a set of results after analyzing the data to examine the presence of a relationship between biochemical and hematological factors with the outcomes and complications for these patients.

This marks the first study in Palestine that focuses on researching lymphoma patients and identifying links or relationships that connect complications and outcomes with the results of regular laboratory and medical examinations conducted to monitor the progression of the disease and its treatment. Through this study, the medical condition

can be tracked more precisely, with a specific emphasis on the biochemical and hematological factors associated with the outcomes and complications. Additionally, this study has enabled contributions towards treatment, ultimately reducing mortality rates and enhancing the therapeutic progress for the disease.

Due to the progress in medical treatments, there is an increasing number of individuals who have survived Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL). A comprehensive comprehension of the delayed consequences of cancer and its therapies, encompassing the potential for developing subsequent malignancies as well as non-cancerous complications, especially cardiovascular conditions, is crucial for the appropriate, extended-term monitoring and care of these patients [4].

The study examined about 64 variables collected from Palestinian hospitals for lymphoma patients, including laboratory tests (CBC, liver function...), clinical examinations, symptoms, commodities (general weakness, medical history...), and the treatments administered (Cyclophosphamide, Ondansetron...). Where these data were taken from 150 lymphoma patients of both sexes (males and females) of different ages, which ranged between (18_45) with both types of Hodgkin and Non-Hodgkin lymphoma.These data were analyzed and the relationships between the variables were determined using the SPSS program.

1.2 Etiology

There are several factors that can increase the incidence of lymphoma, which are environmental factors: such as exposure to pesticides and herbicides, genetic factors: including mutations, cellular modifications, and family history, infection factors: including viral and bacterial infection(Helicobacter pylori, hepatitis C, Epstein Barr virus) and autoimmune system diseases: such as rheumatoid arthritis and Sjögren’s syndrome [2, 10, 11].

1.3 Pathogenesis

T and B lymphocytes are among the most important parts of the immune system, which in turn limit infection. The principle of action of these cells is integration, whereby B cells produce antibodies that bind to infected cells (antigens), while T cells recognize previous antigens. The process lead to activated T cells to secrete proteins and cytokines, which in turn enhance the local immune response. Mostly cancer occurs due

to a defect in the cells, whether in terms of cell growth, cellular signals, or programmed cell death (apoptosis), which results in the formation of a solid tumor. Oncogenic transformation of B and T cells takes place in several steps, resulting in a solid and leukemic tumor [12].

1.4 Hodgkin lymphoma

Hodgkin lymphoma or Hodgkin disease is a rare cancerous tumor that has been classified into two categories based on the causative factors and clinical manifestations, namely: Classical Hodgkin and nodular lymphocyte-predominant Hodgkin lymphoma. The incidence of Hodgkin lymphoma is more in young ages (20-34) and male more than female [1, 13, 14]. Epstein-Barr virus is one of the most important causes that may cause Hodgkin's lymphoma, in addition to autoimmune system diseases and immunosuppressants that the body can be exposed to, such as drugs that suppress the immune system for a long time [1, 13].

1.5 Non-Hodgkin lymphoma

Non-Hodgkin lymphoma arises from lymphoid tissues of B, T cells and is a malignant tumor. As a type of lymphoma, these factors may increase the risk of incidence non-Hodgkin lymphoma, genetic mutations, toxic substances, and viral and bacterial infections [15]. Non-Hodgkin lymphoma is divided into several types, depending on the cells from which the tumor originates, symptoms and clinical manifestations on patients, and the extent of therapeutic response. It is classified into “aggressive non-Hodgkin’s” and “indolent non-Hodgkin's”[15, 16]. Based on the type of cells of origin of the tumor, they are classified into mature B cells, including Mantle cell lymphoma, marginal zone lymphoma, and primary CNS lymphoma, Follicular lymphoma, Burkitt lymphoma, diffuse large B cell lymphoma. And mature T cells include Adult T cell lymphoma and mycosis fungoides [15].

1.6 Diagnosis

Lymphoma is an uncommon and non-specific diagnosis, and there is no single clinical or laboratory test or examination to diagnose or deny lymphoma. The set of symptoms that may appear on patients with lymphoma may not be specific to lymphoma, as it may accompany other diseases, as is the case in extra nodule lymphoma that may It also appears in disease related to the digestive system, nervous system, and skin disorder

[17]. It is possible to detect lymphoma through an apparent defect in the lymph nodes, lymphadenopathy, but not all patients who present for treatment in health care centers and hospitals because of lymphadenopathy, the cause of the defect is a malignant tumor, but only 1.1%, either the majority of cases are other disorder or a different diagnosis. However, diagnosis is associated with several other factors that should be considered related to lymphatic disease, for example, focusing on the location of the disease, its duration, and the extent of spread or localization, so that the diagnosis can be made more accurately [18].

1.7 Stages

Cancer staging is the method through which the disease is described and helps doctors predict progress. It also helps them determine the appropriate treatment plan for each case, then follow up on the patient and study the results. Through elaborate anatomy of the tumor and studying its nature, the stage of the cancer is determined [19]. Determining the stage of cancer is a prerequisite for evaluating cancer and determining the appropriate treatment plan. Although doctors realize the necessity of determining the stage of cancer before dealing with the patient, entering it into clinical records, and following up on his medical cases, many of them neglect this part. Accurate documentation of the stage of cancer is not only important for patients, but also contributes to the evaluation of the disease among the population of the region to facilitate the development of detection, diagnosis, examination and treatment plans. Cancer control programs depend on whether the tumor is localized, early stage, advanced stage, or late stage. The early stage of the disease requires surgical operations, chemotherapy, or radiation as needed. However, if the tumor has spread, the need is psychological palliative support [20]. Lymphoma, as a metastatic type of cancer, also requires staging. Hodgkin lymphoma is based on the Ann Arbor staging system. While in non-Hodgkin patients the disease is advanced and metastatic (Fig 1, Fig 2), the Ann Arbor system in some cases may be inappropriate. In contrast, lactate dehydrogenase enhances use Ann Arbor as prognostic factor [21]. Hodgkin lymphoma is also based on the Ann Arbor staging system, where the treatment plan is based on it. The staging of Hodgkin lymphoma is depend on the location of the tumor in relation to the lymph node, its number and size, as well as the location of the tumor, whether it is local or systemic.

The stage of the disease is the most important prognostic factor in the survival rate. In both stages 1 and 2, the 5-year survival rate is 90%, while in stage 4, the 5-year survival rate is lower and reaches 60%. The stages are divided in the Ann Arbor system as shown in the table below:

Table 1

Ann arbor system

stage	explanation
Stage I	The tumor is in one confined area or forms in only one lymph node, (I-E).
Stage II	The tumor is in two or more area or form in one lymph node or more (II-E).
Stage III	The tumor is in more than one location and also outside the lymph nodes (III-E)
Stage IV	The tumor has spread widely and extends to other parts of the body

Ann arbor system A system followed in dividing lymphoma of both types, Hodgkin and non-Hodgkin, into stages. In the table above, there are divisions of lymphoma stages with an illustrative definition for each stage. In addition to the basic stages, there are also sub-classifications.E (It expresses the presence of the tumor in a limited area and also outside the lymph nodes), A(It expresses the presence of a tumor, but without clear clinical symptoms and manifestations) and B(It expresses the presence of a tumor with obvious symptoms such as unexplained weight loss and fever).

Figure 1

Staging of Non-Hodgkin Lymphoma

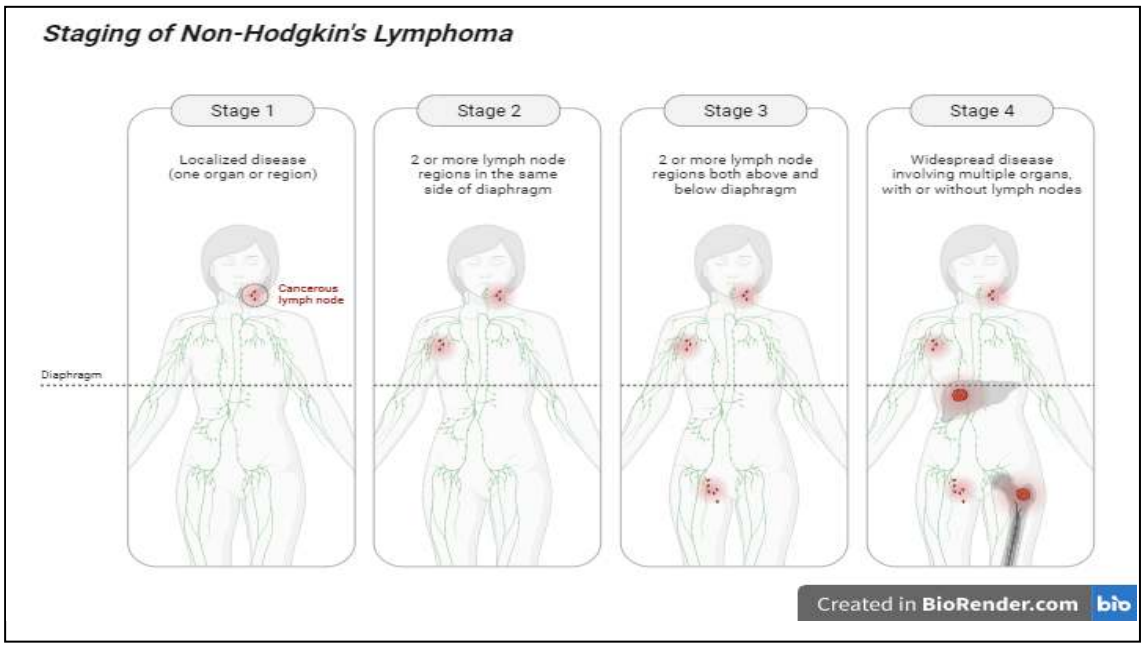
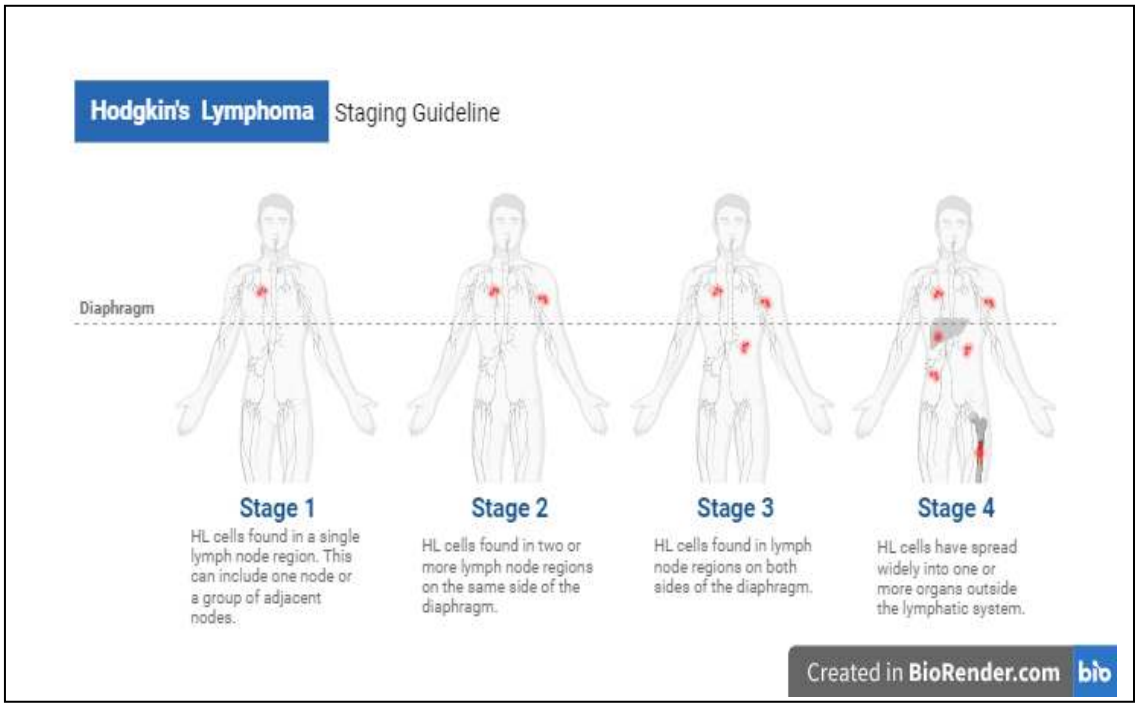


Figure 2

Staging of Hodgkin Lymphoma



1.8 Lymphoma in Palestine

Cancer treatment in Palestine represents the basis of the Palestinian health care system, as cancer care is considered a national service. The Palestinian National Authority pays the costs of treatment for cancer patients who receive treatment in government and private hospitals. Despite the challenges facing the Palestinian health system due to the Israeli occupation, it is trying to do its utmost to diagnose and treat cancer with the best existing capabilities, while neglecting the nature of the lives that patients live. The State of Palestine currently consists of the West Bank, East Jerusalem, and the Gaza Strip, with a population of about 5.1 million people, 3.05 million living in the West Bank and 2.05 living in the Gaza Strip, according to the Palestinian Central Bureau of Statistics for the year 2022. The Palestinian Cancer Registry has been in existence for about 25 years, but it lacks complete data on cancer, as it is limited to the following information, which is the incidence rate and the percentage of cancer in the specific location according to the age and gender of the patient. As for survival statistics, death rates, and the ages of patients when the disease was diagnosed or When recovering from it, all information is not available in the previous record [22].

Despite all the political and economic challenges and difficulties facing the Palestinian health care system, it is considered one of the best health systems compared to other Arab countries in terms of survival rates, life expectancy, and mortality rates for mothers, infants, and children [23].

The Palestinian health care system provides treatment for cancer patients in its governmental and non-governmental branches. There are four governmental hospitals in the West Bank and three in the Gaza Strip. They provide health care for cancer patients, including limited small oncology departments and also provide chemotherapy, but they do not contain a specialized and advanced pathology department and does not provide radiation therapy. Radiation therapy is only provided at Augusta Victoria Hospital (Al-Mutalaa Hospital) in East Jerusalem. Recently, two non-governmental hospitals were added to the service of providing chemotherapy for patients with cancer and hematological diseases, namely Al-Najah National Hospital in Nablus and the Arab Istishari Hospital in Ramallah, with limited capabilities as well [24].

In 2019, the number of cancer cases was 117.8 per 100,000 population. Compared to the infection rate in 2013, which was 79.5 per 100,000 population, the increase was not significant [24]. While n 2016, the death rate due to cancer was 14%, as it is considered the second cause of death after cardiovascular diseases, which is the first cause of death in occupied Palestine, with a rate of 30.6%. Between 2000-2016, Palestine witnessed A significant increase in the death rate from cancer, 136%. From 2016-2020, 14% constituted the increase in deaths due to cancer. Lung cancer is the most common (especially in males), breast cancer (in women more), colon and rectum (for both sexes), leukemia, which is most common among children, and breast cancer. Lymphoma of both Hodgkin and non-Hodgkin's lymphoma. Cancers that are non-Hodgkin's lymphoma (NHL) and Hodgkin's lymphoma (HL): Compared to men, women saw a 4% increase in Hodgkin's lymphoma (HL) cancer cases in 2015.Males and females had the same prevalence of non-Hodgkin's lymphoma (NHL) cancer development at the period, which was 4% [22]. This study is focused on researching the existence of a relationship between hematological and biochemical factors with lymphoma patients receiving treatment in Palestine. Patient data will be researched and analyzed for the two main types: Hodgkin and non-Hodgkin.

- **Brief Introduction:**

1. Theoretical basis.
2. Problem statement.
3. Study hypothesis.
4. Importance of the study.
5. Objectives.

1.9 Theoretical basis

Malignant lymphoma arises from abnormal and unprogrammed proliferation of lymphocytes. In Palestine, the prevalence of lymphoma was estimated at about 15.4%. The estimated survival rate in lymphomas was 72% [25]. Lymphomas are of many types (more than 30). This might explain the differences in terms of symptoms, diagnosis, nature of the disease, and tracking of the pathological condition [26]. Non-Hodgkin's and Hodgkin's lymphomas are the most common types [25]. Lymphomas affect patients from both genders and have devastating consequences on the life and wellbeing of the patients [25].

In clinical practice, laboratory tests are often used to monitor patients including those with lymphomas to track their health status, evaluate their response to treatment, and monitor the regression or progression of lymphoma disease. These tests include liver function tests (AST, ALT, bilirubin, albumin, and transferrin), kidney function tests (uric acid, creatinine, bun, sodium, potassium, chloride, and calcium), and complete blood count (CBC).

Patients with lymphoma, especially Hodgkin's lymphoma, after undergoing chemotherapy and radiotherapy make good progress and a clear response to treatment, but there are patients with a rate of 10-15% who have bad complications and their health deteriorates. It has been proposed that level of albumin in the body can be used to evaluate and prior treatment of patients who have lymphoma type diffuse large B-cell lymphoma DLBCL. Additionally, albumin level can be used as an indicator of the expectations of the risk and complications that may occur to the patient [27]. On the other hand, albumin was also shown to contribute to the medical diagnosis of DLBCL [27]. It has been observed that albumin is at low levels in patients with lymphoma and is also significantly affected in the progression of the tumor. The focus of previous studies

was on the relationship of albumin to lymphoma progression and diagnosis as well. In our current study, biochemical factors will be followed up and linked to lymphoma.

1.10 Problem statement

Previous studies did not address the relationship between hematological indices, biochemical variables, and clinical characteristics of the patients with the complications that can occur in lymphoma patients who receive treatment in the Palestinian hospitals. Therefore, little is known on how the different hematological indices, biochemical variables, and clinical characteristics of the patients can be used to predict prognosis and response to treatment in the Palestinian healthcare system.

1.11 Study hypothesis

1.11.1 Research question

1. Is there a relationship between chemical and hematological factors with the complications that may occur for lymphoma patients who are treated in Palestinian centers and hospitals?
2. If there is a relationship between chemical and hematological factors with the complications that may occur for lymphoma patients who are treated in Palestinian centers and hospitals what is it?
3. If there is a relationship, how can it affect later on the treatment of patients or the follow-up of disease progress?

1.11.2 Hypothesis

- Alternative non directional Hypothesis: There is a relationship between at least one of the biochemical or hematological factors with the complications that may occur for lymphoma patients in Palestine.
- Null hypothesis: There is no relationship between any of the biochemical or hematological factors with the complications of lymphoma patients in Palestine

1.12 Importance of the study

The findings of this study may contribute to the progress of treatment, thus shortening the duration of treatment by focusing on the factors associated with complications by doctors and oncologists, which helps reduce the risks of the disease including the risk of death.

1.13 Objectives

This study will be conducted to:

- Investigate associations between hematological indices and biochemical biomarkers with complications and outcomes among patients with lymphoma treated in the Palestinian healthcare system
- Identify significant predictors of outcomes and complications among patients with lymphoma treated in the Palestinian healthcare system

1.14 Literature review

In Palestine, the prevalence of lymphoma is 15.4%, which is considered a not small percentage.. There are complications associated with HL, including primary CNS angiitis, cerebellar degeneration, and POEMS syndrome, which affects five different areas of the body (polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, and skin changes)(Jamil and Mukkamalla, 2022) In NHL, indolent lymphoma, such as follicular lymphoma, marginal zone lymphoma, can transform into a more aggressive and invasive NHL, like diffuse large B-cell lymphoma.(Jamil and Mukkamalla, 2022) The effect of lymphoma can reach the peripheral organs represented by the central and peripheral nervous system, and its effect is direct through the production of intraparenchymal or extra-axial mass lesions or by meningeal infiltration Or the circulatory system, which is the blockage of blood vessels due to the presence of cancer cells.(Glass, 2006) Patients with lymphoma, especially HL, after undergoing chemotherapy and radiotherapy make good progress and a clear response to treatment, but there are patients with a rate of 10-15% who have bad complications and their health deteriorates [28]. A study that can benefit from the level of albumin in the body to evaluate and prior treatment of patients who have lymphoma type diffuse large B-cell lymphoma DLBCL and also use it as an indicator of the expectations of the risk and complications that may occur to the patient. Serum albumin level at diagnosis of diffuse large B-cell lymphoma: an important simple prognostic factor. On the other hand, albumin also contributed to the medical diagnosis of DLBCL [27]. It has been observed that albumin is at low levels in patients with lymphoma and is also significantly affected in the progression of the tumor. Albumin metabolism in patients with lymphoma the focus of previous studies was on the relationship of albumin to lymphoma progression and diagnosis as well. In our current study, biochemical factors will be followed up and linked to lymph.

Chapter Two

Methods

2.1 Methodology

2.1.1 Study context

This study will be conducted on lymphoma patients of all types who receive treatment in West Bank hospitals and medical centers.

2.1.2 Study design

This descriptive cross-sectional study was conducted on lymphoma patients who receive treatment in Palestinian health care centers and hospitals in different locations. The patients were from different governorates, both male and female, of all ages, and the patients' ages ranged between 15-65 years. This study included the two main types of Hodgkin's and non-Hodgkin's lymphoma.

2.1.3 Population

The study will be conducted on all lymphoma patients, regardless of their age, sex, place of residence, and the region in which they receive treatment.

2.1.4 Inclusion criteria

The following group of patients will be included from the study sample:

- Lymphoma patients receiving treatment in the Palestinian hospitals, males and females, old and young
- Lymphoma patients whose disease was discovered, dealt with and started treatment more than 40 days ago

2.1.5 Exclusion criteria

The following group of patients will be excluded from the study sample:

Lymphoma patients who have recently discovered the disease so that it is difficult to track the condition and notice changes or obtain research results

2.1.6 Sample size

Through the Ministry of Health, the number of lymphoma cancer patients in the West Bank is counted, and this research will be studied on at least 250 patients from different regions of the West Bank. The sample is collected by visiting hospitals and centers to view patient records.

2.1.7 Study variable

2.1.7.1 Complete blood count

1. White blood cells
2. Neutrophil granules
3. Lymphocytes
4. Red blood cell
5. Hemoglobin
6. Hematocrit
7. Mean corpuscular volume
8. Mean corpuscular hemoglobin
9. Mean corpuscular hemoglobin concentration
10. Red cell distribution width
11. Platelets
12. Mean platelet volume

2.1.7.2 Liver function test

1. Ferritin
2. Albumin
3. Bilirubin
4. Aspartate aminotransferase
5. Alanine aminotransferase

2.1.7.3 Kidney function test

1. Creatinine
2. Uric acid
3. Blood urea nitrogen

2.1.7.4 Electrolytes

1. Sodium
2. Potassium
3. Chloride
4. Calcium

2.2 Sampling method

2.2.1 Recruitment

The study sample will be taken from Palestinian hospitals, from the Oncology Department, and the files of lymphoma patients will be reviewed and data will be collected in a data collection form.

2.2.2 Study tools

A data collection form will be specifically created for this study. The data collection form will collect: age, gender, co-morbidities, time since diagnosis, type of treatment, chemotherapeutic agents, lab findings like liver function tests (AST, ALT, bilirubin, albumin, and transferrin), kidney function tests (uric acid, creatinine, bun, sodium, potassium, chloride, and calcium), and complete blood count (CBC).

2.2.3 Sample time

The sample collection began after facilitating the task from the Palestinian Ministry of Health in December 2022, but due to the time specified for the blood clinic in Palestinian hospitals and the low number of lymphoma patients that can be monitored during one day of the week during the clinic's working hours, the information technology unit of the Palestinian Ministry of Health was approached. The main branch in Ramallah to obtain approval to collect a larger number of samples through the information technology branch in the hospital. The approval was granted two months after submitting the application (March 2023). The sample continued to be collected until the month of June, then it was transferred to Excel.

2.2.4 Data Collection

Initially, patient data from the hospitals receiving treatment in Palestine will be collected and uploaded to a data collection form on the Excel program to follow the changes that occur to the patient during the treatment period and focus on the results to examine the existence of a relationship between biochemical and hematological factors through medical and laboratory tests.

2.2.5 Statistical Analysis Methods

To test for normal distribution of the data, the Kolmogorov–Smirnov test will be used. Parametric tests like Student's t-test, ANOVA, and Pearson's correlations or nonparametric tests like Mann-Whitney U test, Kruskal-Wallis test and Spearman's rank correlations will be used to compare differences and assess correlations between groups, as appropriate. Multiple linear regression will be performed to identify predictors.

2.2.6 Working Plan

We will conduct this study on the follow-up of the treatment of lymphoma patients in Palestine through the examinations that are conducted for them to investigate the existence of a relationship between at least one of the biochemical and hematological factors with the complications that may occur to lymphoma patients during the period. The study will be carried out in the field through Palestinian hospitals after obtaining the approval of the Ministry of Health to take the data, then the unloading process will be done through the Data Collection Form tables on the Excel program, monitoring the results of patients during the study period, and then determining the existence of the relationship, if any.

Chapter Three

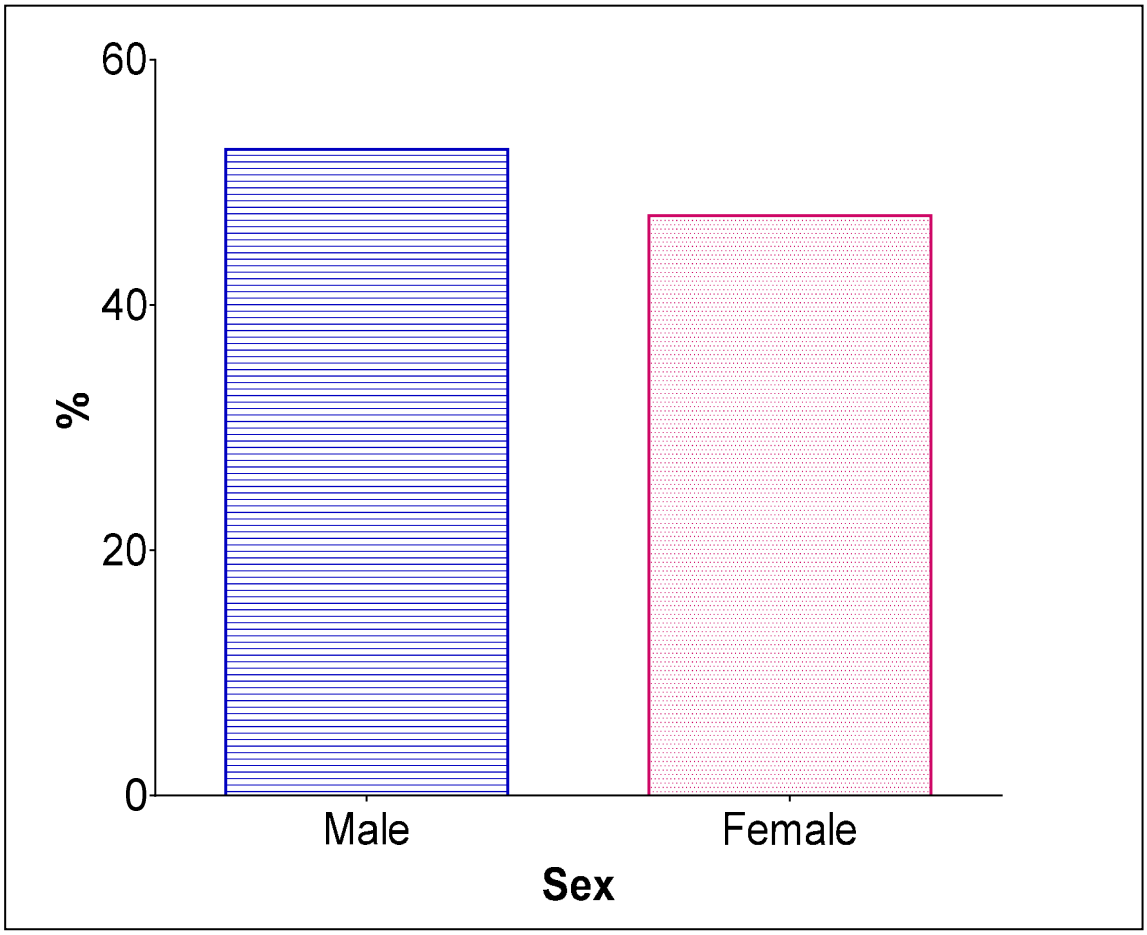
Result

3.1 Characteristics of the patients

In this study, a total of 150 patients with lymphomas were included. The median age of the patients was 40.0 (29.0, 59.3) years and the mean age was 43.9 ± 18.2 years. The median time since diagnosis was 5.0 (4.0, 7.0) years and the median time was 5.5 ± 2.6 years. Of the patients, 79 (52.7%) were male in gender. The stratification of the patients by sex is shown in Figure 3.

Figure 3

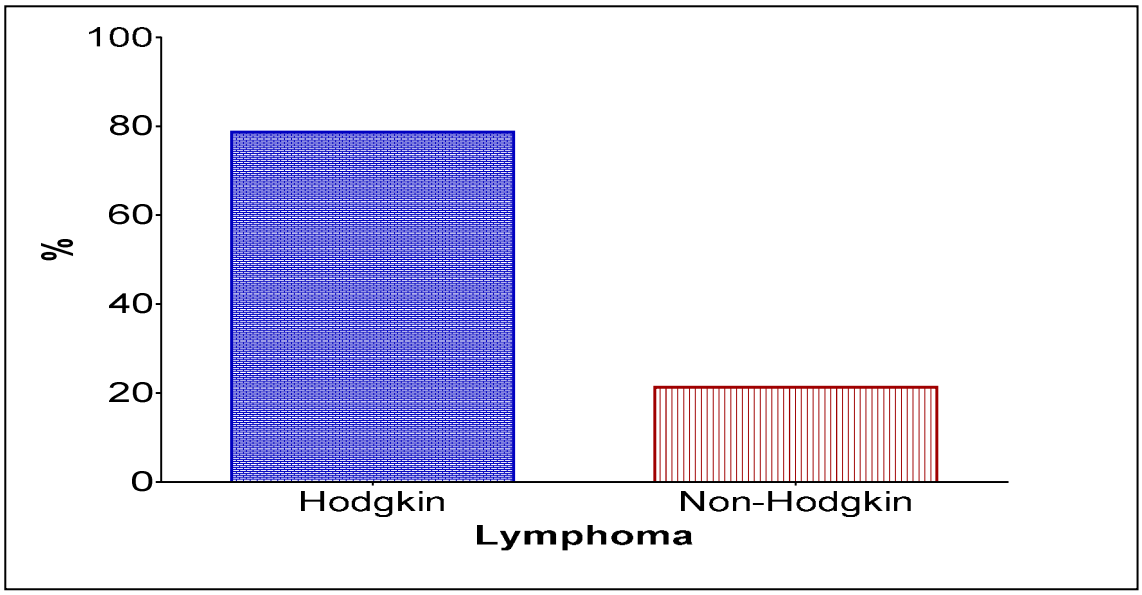
Patients stratified by sex



The majority of the patients had Hodgkin lymphoma 118 (78.7%). Stratification of the patients into types of lymphomas is shown in Figure 4.

Figure 4

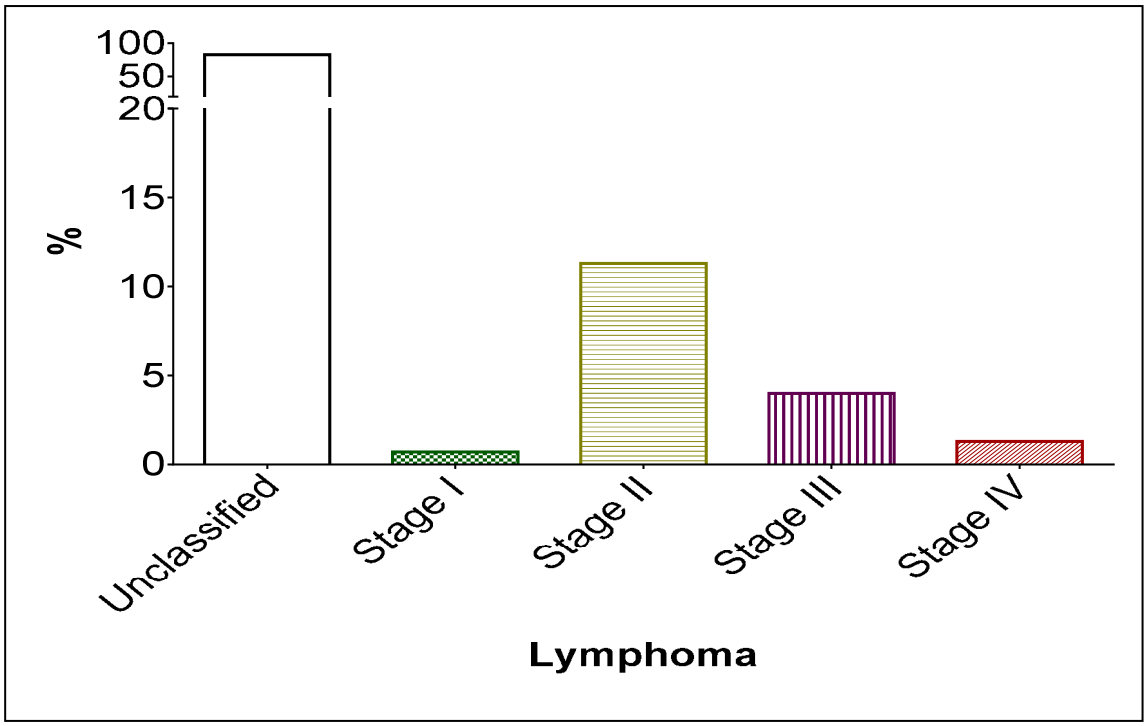
Patients stratified by lymphoma type



Information on the stage of cancer was available for 26 patients only. Of those, 17 (65.4%, 11.3% of all patients) were in stage II. Stratification of the patients into the different cancer stages is shown in Figure 5.

Figure 5

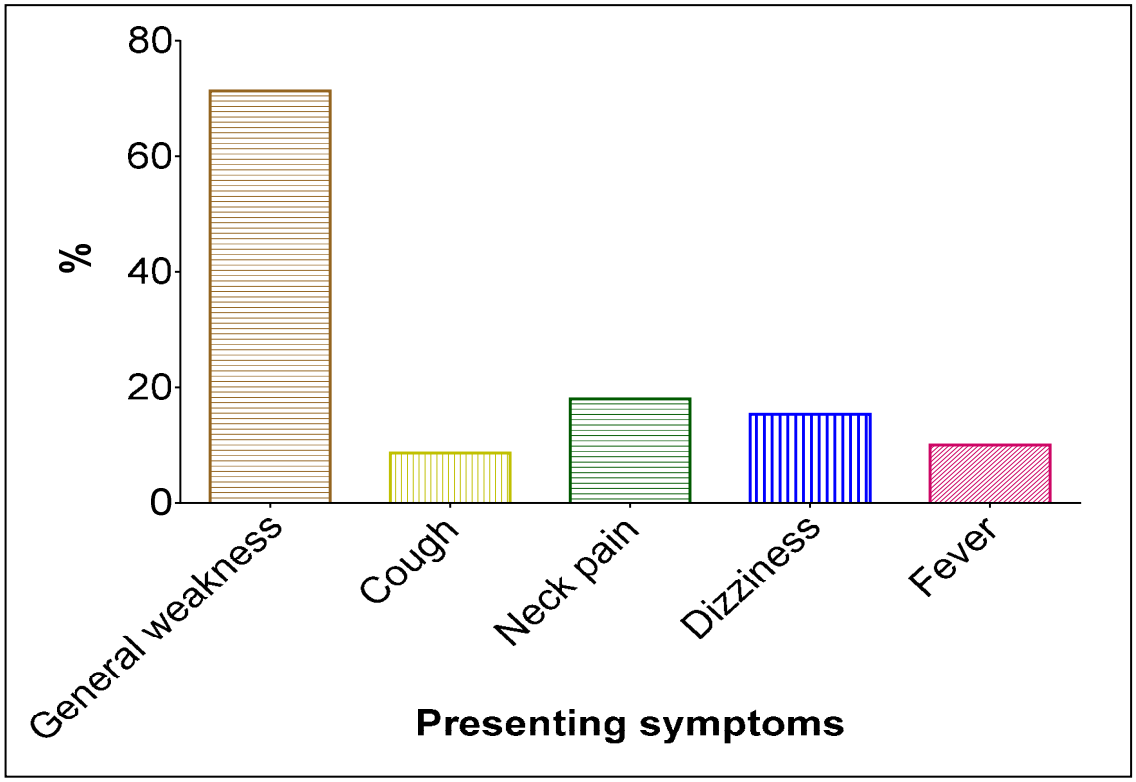
Stratification of the patients into different cancer stages



Of the patients, 107 (71.3%) reported general weakness, 13 (8.7%) reported cough, 27 (18.0%) reported neck pain, 23 (15.3%) reported dizziness, and 15 (10.0%) reported fever. The presenting symptoms are shown in Figure 6.

Figure 6

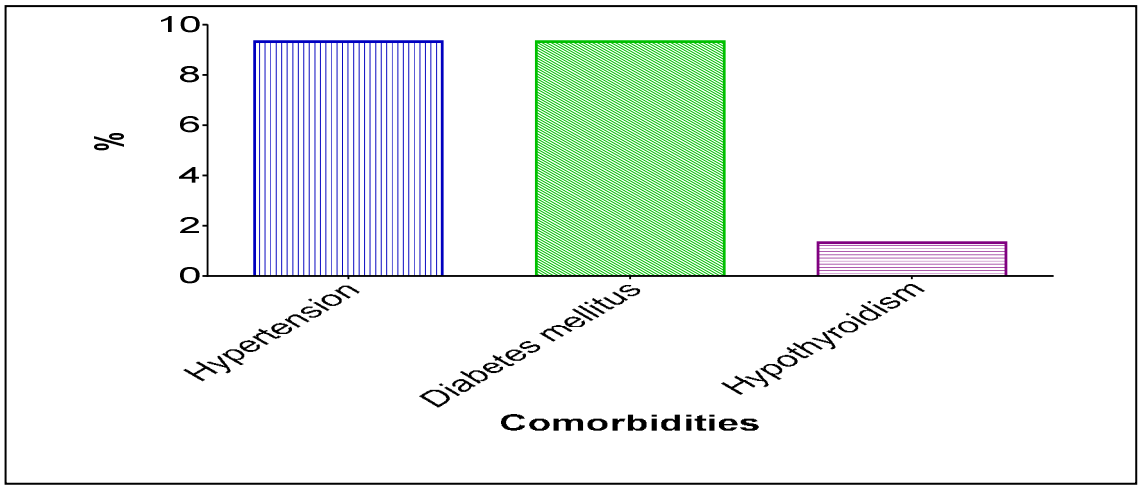
The presenting symptoms reported by the patients



Of the patients, 14 (9.3%) had hypertension, 14 (9.3%) had diabetes mellitus, and 2 (1.3%) had hypothyroidism. The past medical history of the patients is shown in Figure 7.

Figure 7

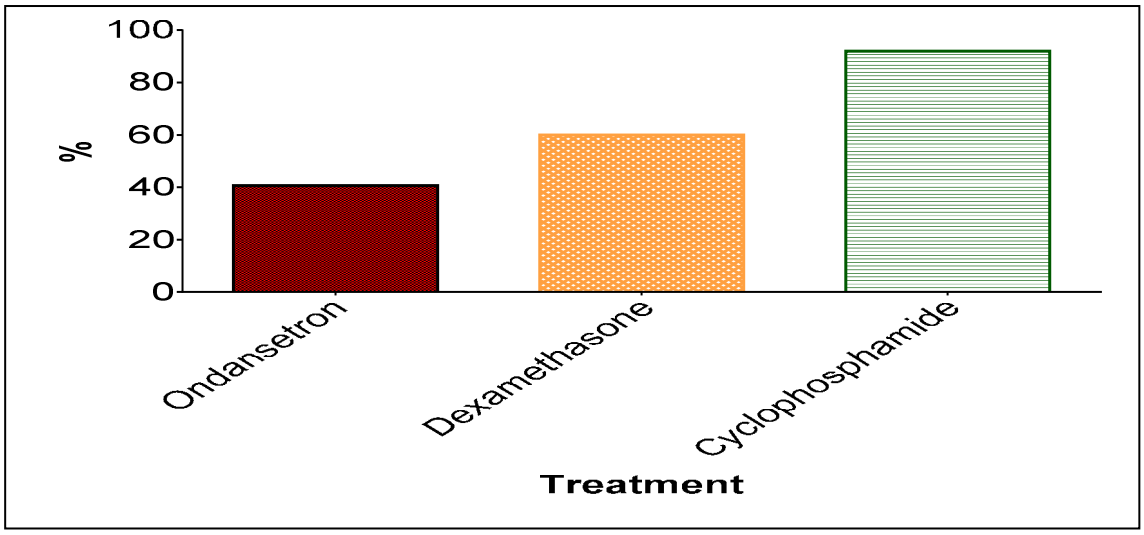
The past medical history of the patients



The vast majority (92.0%) of the patients received cyclophosphamide as a part of their chemotherapy, 61 (40.7%) received ondansetron and 90 (60.0%) received dexamethasone. The treatments used for the patients who participated in this study are shown in Figure 8.

Figure 8

Treatments used for the patients



3.1.1 Hematological and biochemical variables of the patients

The hematological and biochemical variables of the patients were collected in two stages. The mean, SD, and median (Q1, Q3) of the hematological and biochemical parameters are shown in Table 2.

Table 2

Hematological and biochemical parameters of the patients

	Phase 1					Phase 2				
Variable	Mean	SD	Q1	Q2	Q3	Mean	SD	Q1	Q2	Q3
Complete blood count (CBC)										
White blood cells (10^9/L)	10.3	8.8	6.5	8.6	12.3	7.8	4.7	5.3	6.7	8.8
Neutrophil granules (%)	70.0	13.9	62.4	72.1	80.7	65.8	16.5	56.6	67.8	77.8
Lymphocytes (%)	24.2	17.4	14.4	20.2	30.1	25.2	13.0	15.3	24.6	33.9
Red blood cells (10^{12}/L)	4.8	0.7	4.5	4.8	5.2	8.4	45.4	4.4	4.9	5.3
Hemoglobin (g/dL)	13.5	11.9	11.2	12.6	14.3	13.0	2.5	11.6	13.1	14.9
Hematocrit (%)	38.3	6.2	34.6	38.3	42.4	43.7	56.6	35.8	39.8	44.9
Mean corpuscular volume (fL)	80.1	7.9	74.2	80.9	85.9	83.6	7.9	79.8	84.8	88.6
Mean corpuscular hemoglobin (pg)	26.5	3.3	24.3	26.6	29.1	27.9	3.1	26.0	28.3	30.1
Mean corpuscular hemoglobin concentration (%)	32.6	2.8	31.9	32.8	33.7	33.0	1.2	32.2	33.1	33.7
Red cell distribution width (%)	13.7	2.0	12.3	13.4	14.7	13.7	2.4	12.1	13.2	14.9
Platelets (10^3 cells/μL)	296.8	118.5	213.0	283.5	359.3	227.4	107.1	161.3	219.5	280.0
Mean platelet volume (fL)	9.4	7.4	8.0	8.6	9.6	8.8	1.0	8.0	8.5	9.4
Liver function test										
Ferritin (ng/mL)	301.5	1331.6	47.1	98.8	183.2	258.0	914.7	45.2	88.4	153.2
Albumin (g/dL)	4.1	0.8	3.8	4.3	4.7	10.7	55.5	3.8	4.3	4.6
Bilirubin (mg/dL)	2.0	16.1	0.3	0.4	0.6	0.7	1.1	0.3	0.4	0.7
Aspartate aminotransferase (units/L)	26.8	45.6	14.3	18.0	25.8	23.2	21.0	16.0	19.0	25.0
Alanine aminotransferase (units/L)	25.3	54.7	10.0	15.0	22.8	23.4	24.6	12.0	16.0	25.7
Kidney function test										
Creatinine (mg/dL)	0.8	0.3	0.6	0.7	0.8	0.8	0.3	0.6	0.8	0.9
Uric acid (mg/dL)	4.9	2.1	3.8	4.5	5.6	5.4	6.0	3.5	4.8	5.9
Blood urea nitrogen (mg/dL)	12.5	11.6	8.0	11.0	14.0	14.1	13.0	9.0	12.0	14.9
Electrolytes										
Sodium (mEq/L)	137.7	11.5	136.0	139.0	141.0	137.9	4.1	136.0	139.0	140.0
Potassium (mEq/L)	4.3	0.5	4.0	4.3	4.5	4.3	0.5	4.0	4.3	4.6
Chloride (mEq/L)	101.5	9.0	101.0	103.0	104.0	102.9	9.3	101.2	103.3	106.0
Calcium (mg/L)	1.4	1.2	1.2	1.2	1.3	3.0	15.0	1.2	1.2	1.3

SD: Standard deviation, Q1: first quartile, Q2: median, Q3: third quartile

3.1.2 Association between type of lymphoma with the hematological and biochemical variables of the patients

1. Stage 1

As shown in Table 2, the patients who had Hodgkin lymphoma were significantly younger than the patients who had non-Hodgkin lymphoma. Similarly, the patients who had Hodgkin lymphoma were diagnosed since significantly shorter time compared to the patients who had non-Hodgkin lymphoma. On the other hand, the patients who had Hodgkin lymphoma had significantly higher white blood cell count, neutrophil granules, and platelets compared to the patients who had non-Hodgkin lymphoma. Contrarily, the patients who had non-Hodgkin lymphoma had significantly larger mean corpuscular volume compared to the patients who had Hodgkin lymphoma.

The patients who had non-Hodgkin lymphoma had significantly higher bilirubin and creatinine compared to the patients who had Hodgkin lymphoma. On the other hand, the patients who had Hodgkin lymphoma had significantly higher chloride compared to the patients who had non-Hodgkin lymphoma (Table 3). The other variables were not significantly different between patients who had Hodgkin and non-Hodgkin lymphomas.

Table 3

Association between type of lymphoma with the hematological and biochemical variables of the patients in stage 1

	Hodgkin lymphoma			Non-Hodgkin lymphoma			
Variable	Q1	Q2	Q3	Q1	Q2	Q3	p-value
Age (years)	28.0	38.0	56.3	45.0	56.5	68.0	< 0.001
Time since diagnosis (years)	0.0	2.5	5.0	1.0	6.0	7.3	< 0.001
Complete blood count (CBC)							
White blood cells (10^9/L)	6.6	9.1	12.6	5.5	6.9	9.9	0.020
Neutrophil granules (%)	63.4	72.6	80.8	51.9	64.1	79.4	0.022
Lymphocytes (%)	14.8	20.2	28.6	13.0	21.2	39.9	0.464
Red blood cells (10^{12}/L)	4.5	4.8	5.1	4.2	4.7	5.3	0.551
Hemoglobin (g/dL)	11.0	12.3	13.7	11.4	12.7	14.6	0.366
Hematocrit (%)	34.0	37.4	41.6	35.8	39.4	43.8	0.243
Mean corpuscular volume (fL)	72.6	79.7	85.4	79.1	81.8	88.2	0.021
Mean corpuscular hemoglobin (pg)	23.8	26.5	28.9	25.4	26.7	29.4	0.170
Mean corpuscular hemoglobin concentration (%)	31.8	32.9	33.7	32.0	32.7	33.7	0.745
Red cell distribution width (%)	12.5	13.5	14.8	12.4	13.2	15.0	0.512
Platelets (10^3 cells/μL)	248.5	293.0	372.3	168.5	220.0	288.0	< 0.001
Mean platelet volume (fL)	8.0	8.6	9.6	8.2	9.2	10.2	0.072
Liver function test							
Ferritin (ng/mL)	54.3	104.2	197.5	39.8	89.4	183.0	0.352
Albumin (g/dL)	3.8	4.3	4.7	3.8	4.3	4.8	0.868
Bilirubin (mg/dL)	0.3	0.4	0.5	0.4	0.5	0.6	0.011
Aspartate aminotransferase (units/L)	13.9	17.6	25.2	15.8	19.0	26.9	0.280
Alanine aminotransferase (units/L)	10.0	15.0	22.8	10.0	15.7	22.6	0.797
Kidney function test							
Creatinine (mg/dL)	0.6	0.7	0.8	0.7	0.8	0.9	0.011
Uric acid (mg/dL)	3.8	4.5	5.8	3.9	4.5	5.7	0.636
Blood urea nitrogen (mg/dL)	8.0	11.0	13.9	9.1	12.7	15.3	0.072
Electrolytes							
Sodium (mEq/L)	136.0	138.0	140.1	138.0	140.0	142.0	0.077
Potassium (mEq/L)	4.0	4.3	4.6	3.8	4.1	4.5	0.077
Chloride (mEq/L)	101.0	103.0	105.0	99.0	102.0	103.3	0.020
Calcium (mg/L)	1.2	1.2	1.3	1.2	1.2	1.3	0.597

2. Stage 2

Contrary to stage 1, only ferritin levels were significantly higher for the patients who had non-Hodgkin lymphoma in stage 2 as shown in Table 4. The other variables were not significantly different between patients who had Hodgkin and non-Hodgkin lymphomas.

Table 4

Association between type of lymphoma with the hematological and biochemical variables of the patients in stage 2

	Hodgkin lymphoma			Non-Hodgkin lymphoma			
Variable	Q1	Q2	Q3	Q1	Q2	Q3	p-value
Complete blood count (CBC)							
White blood cells (10^9/L)	5.3	6.6	8.7	5.5	6.9	9.6	0.748
Neutrophil granules (%)	59.4	70.2	77.9	49.7	60.7	76.3	0.075
Lymphocytes (%)	16.3	23.5	31.1	14.6	29.4	35.5	0.433
Red blood cells (10^{12}/L)	4.5	4.9	5.2	3.9	4.7	5.2	0.148
Hemoglobin (g/dL)	11.8	13.1	14.5	11.0	12.7	14.9	0.456
Hematocrit (%)	36.6	39.8	43.7	33.1	39.6	44.6	0.469
Mean corpuscular volume (fL)	78.5	84.6	88.0	82.7	87.0	91.5	0.058
Mean corpuscular hemoglobin (pg)	26.0	28.0	29.8	26.6	28.6	30.1	0.278
Mean corpuscular hemoglobin concentration (%)	32.1	33.1	33.7	32.3	32.8	34.0	0.940
Red cell distribution width (%)	12.1	13.0	14.5	12.0	13.7	15.1	0.186
Platelets (10^3 cells/μL)	162.0	219.5	280.0	136.0	194.5	237.5	0.071
Mean platelet volume (fL)	8.0	8.5	9.3	8.0	8.7	9.5	0.538
Liver function test							
Ferritin (ng/mL)	30.2	82.2	150.2	66.7	120.9	192.3	0.017
Albumin (g/dL)	3.9	4.2	4.6	3.7	4.3	4.6	0.948
Bilirubin (mg/dL)	0.3	0.4	0.6	0.3	0.5	0.8	0.085
Aspartate aminotransferase (units/L)	15.8	18.6	25.5	15.8	20.0	23.5	0.688
Alanine aminotransferase (units/L)	12.0	15.1	24.1	10.7	18.3	29.7	0.517
Kidney function test							
Creatinine (mg/dL)	0.6	0.7	0.9	0.6	0.8	0.9	0.372
Uric acid (mg/dL)	3.6	4.9	6.0	3.6	4.8	6.1	0.757
Blood urea nitrogen (mg/dL)	9.0	11.5	14.1	9.3	12.8	16.7	0.111
Electrolytes							
Sodium (mEq/L)	136.0	138.0	140.0	135.0	139.0	140.3	0.750
Potassium (mEq/L)	4.0	4.3	4.6	4.1	4.3	4.6	0.934
Chloride (mEq/L)	101.0	104.0	106.0	98.8	102.5	106.3	0.129
Calcium (mg/L)	1.2	1.2	1.3	1.2	1.3	1.3	0.715

3.1.3 Change in parameters between stage 1 and stage 2

Table 5 shows that there was a significantly greater change in white blood cells count for patients who had Hodgkin lymphoma compared to the patients who had non-Hodgkin lymphoma. On the other hand, there was a greater significant change in ferritin and alanine aminotransferase for the patients who had non-Hodgkin lymphoma compared to the patients who had Hodgkin lymphoma.

Table 5

Change in parameters between stage 1 and stage 2

	Hodgkin lymphoma			Non-Hodgkin lymphoma			
Variable	Q1	Q2	Q3	Q1	Q2	Q3	p-value
Complete blood count (CBC)							
White blood cells (10^9/L)	-5.8	-1.9	1.0	-2.0	-0.3	1.8	0.050
Neutrophil granules (%)	-13.7	-2.3	5.2	-13.4	1.1	7.5	0.397
Lymphocytes (%)	-7.1	0.9	11.7	-10.9	-0.8	10.8	0.385
Red blood cells (10^{12}/L)	-0.3	0.0	0.4	-0.7	-0.3	0.3	0.090
Hemoglobin (g/dL)	-0.8	0.4	1.9	-1.8	-0.1	1.5	0.138
Hematocrit (%)	-2.0	1.9	5.2	-5.0	-1.3	4.4	0.065
Mean corpuscular volume (fL)	-1.0	3.2	8.1	-1.9	3.6	6.1	0.342
Mean corpuscular hemoglobin (pg)	-0.6	1.0	3.0	-0.7	1.2	2.5	0.792
Mean corpuscular hemoglobin concentration (%)	-0.9	0.2	1.2	-0.5	0.4	1.1	0.568
Red cell distribution width (%)	-1.6	-0.3	1.1	-1.2	0.2	1.6	0.187
Platelets (10^3 cells/μL)	-148.8	-67.0	-1.5	-104.0	-21.5	22.8	0.087
Mean platelet volume (fL)	-0.6	-0.2	0.6	-1.4	-0.3	0.3	0.167
Liver function test							
Ferritin (ng/mL)	-95.5	-11.6	23.9	-16.2	13.3	112.8	0.008
Albumin (g/dL)	-0.4	-0.1	0.2	-0.6	-0.2	0.2	0.477
Bilirubin (mg/dL)	-0.1	0.0	0.2	-0.1	0.1	0.3	0.685
Aspartate aminotransferase (units/L)	-5.5	0.9	6.0	-4.4	-0.1	8.3	0.858
Alanine aminotransferase (units/L)	-4.7	1.5	6.6	-0.5	3.5	11.1	0.046
Kidney function test							
Creatinine (mg/dL)	-0.1	0.0	0.2	-0.2	-0.1	0.1	0.070
Uric acid (mg/dL)	-0.6	0.3	1.0	-0.4	0.6	1.3	0.480
Blood urea nitrogen (mg/dL)	-1.5	0.6	3.8	-1.9	0.5	4.2	0.766
Electrolytes							
Sodium (mEq/L)	-3.0	0.0	3.0	-6.0	-0.5	1.8	0.230
Potassium (mEq/L)	-0.3	0.0	0.4	-0.3	0.2	0.7	0.327
Chloride (mEq/L)	-1.1	0.9	4.0	-2.0	1.5	4.0	0.952
Calcium (mg/L)	-0.1	0.0	0.1	-0.1	0.0	0.1	0.771

The patients were stratified based on the hematological or biochemical parameters into 3 categories: low, normal, or high. The normal ranges of the parameters are shown in Table 6.

Table 6

Normal ranges of the hematological and biochemical parameters

Parameter	Normal range
White blood cells	4,500 to 11,000 cells per microliter (μL)
Neutrophil granules	50% to 70%
Lymphocytes	20% to 40%
Red blood cells	4.5 to 5.5 million cells per microliter (μL) of blood for men and 4.0 to 5.0 million cells/μL for women
Hemoglobin	13.8 to 17.2 grams per deciliter (g/dL) for men and 12.1 to 15.1 g/dL for women
Hematocrit	38.8% to 50.0% for men and 34.9% to 44.5% for women
Mean corpuscular volume	80 to 100 femtoliters (fL)
Mean corpuscular hemoglobin	27 to 33 picograms (pg)
Mean corpuscular hemoglobin concentration	32% to 36%
Red cell distribution width	11.5% to 14.5%
Platelets	150,000 to 450,000 platelets per microliter (μL)
Mean platelet volume	7.4 to 10.4 femtoliters (fL)
Liver function test	
Ferritin	2 to 300 nanograms per milliliter (ng/mL) for men and 12 to 150 ng/mL for women
Albumin	3.4 to 5.4 grams per deciliter (g/dL)
Bilirubin	0.2 to 1.2 milligrams per deciliter (mg/dL)
Aspartate aminotransferase	8 to 48 units per liter (U/L)
Alanine aminotransferase	7 to 56 units per liter (U/L)
Kidney function test	
Creatinine	0.6 to 1.2 milligrams per deciliter (mg/dL)
Uric acid	3.4 to 7.0 milligrams per deciliter (mg/dL) of blood for men and 2.4 to 6.0 mg/dL for women
Blood urea nitrogen	7 to 20 milligrams per deciliter (mg/dL)
Electrolytes	
Sodium	135 to 145 milliequivalents per liter (mEq/L)
Potassium	3.5 to 5.0 milliequivalents per liter (mEq/L)
Chloride	96 to 106 milliequivalents per liter (mEq/L)
Calcium	8.5 to 10.5 milligrams per deciliter (mg/dL)

In this study, there were significant differences in the distribution of the patients who had Hodgkin or non-Hodgkin lymphomas into low, normal, and high categories in relation to neutrophil granules, lymphocytes, red blood cell count, mean corpuscular volume, and creatinine in stage 1 as shown in Table 6.

In stage 2, there were significant differences in the distribution of the patients who had Hodgkin or non-Hodgkin lymphomas into low, normal, and high categories in relation to hemoglobin, bilirubin, and calcium as shown in Appendix A.

Chapter Four

Discussion

4.1 Gender and Lymphoma

In this study, patients were categorized by gender into male and female groups, and the analysis revealed that the number of male patients 118 out of 150 patients (78.7%) with lymphoma was greater than the number of female patients. Males are more likely to develop cancer in general. Lymphoma is one of the most common types of cancer in the world, and the incidence of males is higher than that of females [29-31]. In a study conducted on lymphoma patients in Sweden with a sample size of 36,553, the incidence rate of lymphoma was found to be 56.4% among males, approximately 20,738 cases, while among females, it was 43.6%, around 16,057 cases. This indicates a noticeable difference in the proportions, with a higher occurrence rate among males compared to females [31, 32]. The precise and comprehensive reasons for the higher incidence of lymphoma among males compared to females remain unclear. However, several potential factors have been hypothesized and suggested to contribute to the occurrence of lymphoma in males. One such factor is the larger body size of males compared to females, leading to increased cellular division and subsequently a higher likelihood of genetic mutations associated with cancer. Hormonal influences might also play a role, as the male body experiences a greater amount of growth hormone during early life stages than females. Moreover, the mechanisms through which cancer cells form in males may also differ from those in females [29, 33-35].

With regard to non-Hodgkin's lymphoma, the incidence of the disease is lower in women than in men, by less than 30% [35]. The survival rate of males with lymphoma is lower than that of females, and this can be attributed to the female hormonal role, as the childhood age in males is better than in females, then it begins to develop into a menopause that begins to descend again [35, 36].

The majority of lymphoma types show a higher incidence rate in males compared to females, with the exception of two specific types marginal zone and follicular lymphoma. The cause behind this trend could potentially be linked to males' exposure to carcinogenic factors in various work environments. These factors, in turn, might contribute to the development of lymphatic tumors [37, 38]. Males are more than twice

as likely as females to develop NHL during the course of their lifetimes. Men are 60% more likely to die from the disease and 39% more likely to be diagnosed in countries with high HDI scores. The greater risk may be explained by a higher prevalence of specific risk factors in males, such as obesity, HIV, and chemical exposure [39]. Previous studies agreed with our current study in terms of a higher incidence of lymphoma in males than in females. and based on the factors mentioned previously (obesity, exposure to carcinogenic environmental factors at work, hormonal factors...), this could explain the increased incidence of lymphoma in males. In many different regions, the incidence of obesity in males is higher than in females, as men have more overweight [40]. Adipose tissue is formed in males at an earlier age compared to females [41]. A high body mass index BMI is positively associated with a higher incidence of cancer, specifically hematological cancers, including leukemia and lymphoma [42]. While obesity is considered a risk factor for lymphoma, and its prevalence rates are higher among males than females, this explains the reason for the higher incidence of lymphoma in our study among males than among females. Due to the nature of men's work outside the home in different work environments, the possibility of exposure to carcinogenic environmental factors is great. Since carcinogenic factors are considered a risk factor for the occurrence of lymphoma, men's exposure to them during work increases the chance of cancer occurring, and this explains the high rates of lymphoma infection in men. More than women. As we mentioned earlier, hormones also play primary or secondary role in the incidence of cancer and the formation of lymphoma, as is the case in each of the sex hormones, estrogen, progesterone and androgen. They have a strong role in the immune system, the division and renewal of stem cells and formation of tumors. Lymphoma is affected by the immune system, and immune defect may be part of the Causes of lymphoma, This, in turn, may lead to the formation of lymphoma in different proportions between males and females [43, 44].

4.2 Types of Lymphoma

This study included the two main types of lymphoma: Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL). The findings revealed a significantly higher incidence rate of Hodgkin's lymphoma118 (78.7%) compared to non-Hodgkin's lymphoma 32 (21.3)%.Many studies have researched types of lymphoma. In contrast to

the outputs in this study, there is a recent study stated that the prevalence of non-Hodgkin's lymphoma in previous decades increased in a clear and large manner, and at a high speed and with ranked 11th among the types of cancer globally in terms of prevalence and cause of death also in 2020 [45, 46]. Several causes and factors that may have an effect on increasing the incidence of non-Hodgkin's lymphoma have been identified, such as viruses (specifically HIV), environmental factors and some types of medical drugs, but the certain causes are still unclear and incomplete [47, 48]. In 2018, non-Hodgkin lymphoma was the fifth to ninth most common cancer in the world [32]. While HL death rates have consistently decreased from 1.3 cases per 100,000 in 1975 to 0.3 cases per 100,000 in 2014, HL incidence rates have remained stable since the mid-1970s. The relative 5-year survival of individuals with HL has increased across all stages of diagnosis from 70% to 85% during the same time frame [49]. Previous researches examining the descriptive epidemiology of Hodgkin's lymphoma (HL) have documented a persistent global rise in its incidence among young adults [50]. Compared to other western nations, Israel's reported incidence level of HL in young adult Jews who were born in Israel has climbed in recent years to high levels [51].

The incidence of Hodgkin lymphoma is low compared to other types of lymphoma, at 15%.while this type of lymphoma is rare and not widely spread [52]. A recent study was conducted in the United States of America HL accounts for around 10% of newly diagnosed lymphoma cases each year (2.6 cases per 100,000 people), or 2% to 2.5% of all cancer diagnoses [52]. The American Cancer Society stated that in 2022 the number of people with lymphoma will be 89,010, while 8,540 of them will be diagnosed with Hodgkin lymphoma [53].

Hodgkin lymphoma has been associated with several factors that can increase the risk of developing it, such as obesity, smoking, hypertension. The prevalence of hypertension has significantly increased in the twenty-first century., also in young people. In both industrialized and emerging nations, including Palestine, the prevalence of obesity and overweight is growing quickly [54]. Fast foods and incorrect daily behaviors have also increased the prevalence of obesity, and this in turn enhances the incidence of Hodgkin lymphoma because they are considered risk factors for causing Hodgkin lymphoma. This is what supports the prevalence of Hodgkin lymphoma in greater proportions than non-Hodgkin lymphoma Since Palestine is located on the continent of Asia, this is also

considered an enhancement of the incidence of Hodgkin's lymphoma, as it is widespread among the Asian population at high levels [55].

While non-Hodgkin's lymphoma can be caused by causative factors different from Hodgkin's, such as viral infections and infections, as Epstein virus(which infect lymphatic cell type B), Human T-cell leukemia virus type 1 and hepatitis C virus can increase the incidence of non-Hodgkin's lymphoma and immune diseases as well. The prevalence of these viruses in Palestine is not considered to be large compared to the causative factors of Hodgkin's lymphoma. Therefore, this is an explanation for the high prevalence of Hodgkin lymphoma compared to non-Hodgkin lymphoma [15, 56].

4.3 Lymphoma stages

In this study, the stage of lymphoma was not recorded for all patients due to lack of information from the source. The stage was recorded for only 26 patients out of 150, and the majority of them were in stage II the of the disease 17 (65.4%, 11.3% of all patients). Determining the stage of cancer helps in accurate diagnosis of the disease in terms of location and spread, disease progression, treatment plan and therapeutic response [57]. According to the St. Jude system, non-Hodgkin lymphoma is classified into different stages, while the Ann Arbor system, which is based on imaging, classifies Hodgkin lymphoma into several stages [58].

Although general practice treats patients according to restricted (stages I and II, nonbulky) or advanced (stages III or IV) illness, stage II bulky disease is regarded limited or progressed as assessed by histology and a number of prognostic variables [57]. The original staging criteria were primarily formulated for Hodgkin lymphoma (HL). These criteria were later replaced by the Ann Arbor classification, which categorized HL patients into four stages, along with sub classifications A and B. These subcategories were determined based on factors like the occurrence of fevers surpassing 101°F (38.3°C), weight loss, and night sweats. This classification has remained the most extensively employed system since its inception [59, 60]. The selection of therapy and risk stratification prior to treatment are now increasingly done using prognostic indicators, of which stage is merely one element. Stages (I-IIA) of Hodgkin lymphoma are the early stages of the disease. Where the treatment plan for these patients was initially through radiotherapy, but due to disease progression and complications that

patients were exposed to during the treatment period, radiation therapy is no longer used.As for patients in the advanced stages of the disease (stages IIB-IV), the treatment plan focuses on chemotherapy for a long period of time without the use of radiotherapy, The focus is on avoiding serious complications and keeping patients in a stable condition [61, 62]. But in general patient who diagnosed with stage I and II disease, and exhibit unfavorable risk factors, should undergo a treatment regimen involving a combination of chemotherapy and radiation therapy [61].

In our study, we were not able to obtain the stages of lymphoma for all patients. This is because the stages of the disease were not documented for each patient in the Palestinian hospitals from which the sample was collected. The focus must be on writing the stage of the cancer in the patient's record in order to follow the treatment and progress of the disease more accurately and to also benefit scientific research in Palestine.

4.4 Symptoms of Lymphoma

In this study, the symptoms that may appear in lymphoma patients were collected, through which the diagnosis of the disease could be directed.The largest percentage was for general weakness 107 (71.3%), Then followed by neck pain 27 (18.0%), dizziness 23 (15.3%),fever 15 (10.0%) and 13 (8.7%) reported cough. Although there are several symptoms that may appear on patients, lymphoma is painless [1]. Fatigue is considered one of the most common symptoms in cancer patients, including lymphoma patients, as patients lose energy to perform daily tasks with a constant feeling of laziness and inability to be physically active. Their mood changes negatively, and their social relationships are also affected and they no longer enjoy life. Fatigue is considered one of the most common symptoms in cancer patients, including lymphoma patients, as patients lose energy to perform daily tasks with a constant feeling of laziness and inability to be physically active. Their mood changes negatively, and their social relationships are also affected and they no longer enjoy life. Fatigue is also considered a side effect. Which accompanies chemotherapy for patients, as it can occur as a result of blood transfusions or a decrease in hemoglobin levels. Diseases associated with lymphoma, such as diabetes, cardiovascular disease, and anemia, can also contribute to increased fatigue severity for patients at the beginning of treatment [63, 64]. This is

what our study confirmed, that the most common symptom among patients is general weakness.

In the advanced stages of the disease, several symptoms may occur, including unexplained weight loss (>10% during the past 6 months), night sweats, and fever (>38°C For no apparent reason for a month or more) [65]. These previous symptoms are called B symptoms based on Ann arbor system, in which the B substage is characterized by the appearance of these symptoms [17, 59]. If B symptoms appear on the patient, it is necessary to conduct a careful physical examination of the lymph nodes, to take action and to develop an appropriate plan [65]. Symptoms of Hodgkin lymphoma and non-Hodgkin lymphoma are similar and include painless swollen lymph nodes, unexplained weight loss, fever and night sweats [8]. The presence of a tumor in the lymph nodes facilitates the diagnosis of lymphoma. In cases where lymphoma does not appear, the diagnosis is more difficult and complicated, as it is also possible for patients with lymphoma to show unclear and unknown symptoms [66, 67]. Symptoms can be similar to other diseases, so the condition must be diagnosed with the help of more than one specialist [67, 68]. More than two-thirds of patients suffer from lymphadenopathy. The following symptoms are less common in lymphoma patients, which are allergies, itching, and unexplained fever [15]. There is a case report in 2019 that was studied on a patient with hearing loss who suffers from dizziness. Where after conducting the necessary tests, the case was diagnosed with Intravascular large B-cell lymphoma [69]. On the other hand, in a recent study in 2022 that was conducted on 50 lymphoma patients (which includes Hodgkin and non-Hodgkin lymphoma), the symptoms that appeared in the patients were monitored, and the largest percentage was cough (37, 74%), (7, 14%) reported fever, weight loss and night sweats with the same percentage (1, 2%) [70]. One of the common symptoms in patients with both types of Hodgkin and non-Hodgkin lymphoma is fever, and it can occur in many types of malignant tumors. The rise in body temperature occurs as a result of the secretion by macrophages or tumor cells of cytokines (interleukin-1 and interleukin-6)and tumor necrosis factor alpha (TNF-α), that enhance to the activation of Prostaglandins which works and activate the hypothalamus, which is considered the center of thermal balance in the body [71].

In some cases of lymphoma, obstruction of the bronchial tubes may occur due to the presence of a tumor inside the bronchus, and this may lead to the patient suffering from coughing and this is a rare occurrence. On the other hand, patients with Hodgkin lymphoma can develop masses in one or both lungs, in a 15-40% ratio. This explains the occurrence of cough in some lymphoma patients [72].

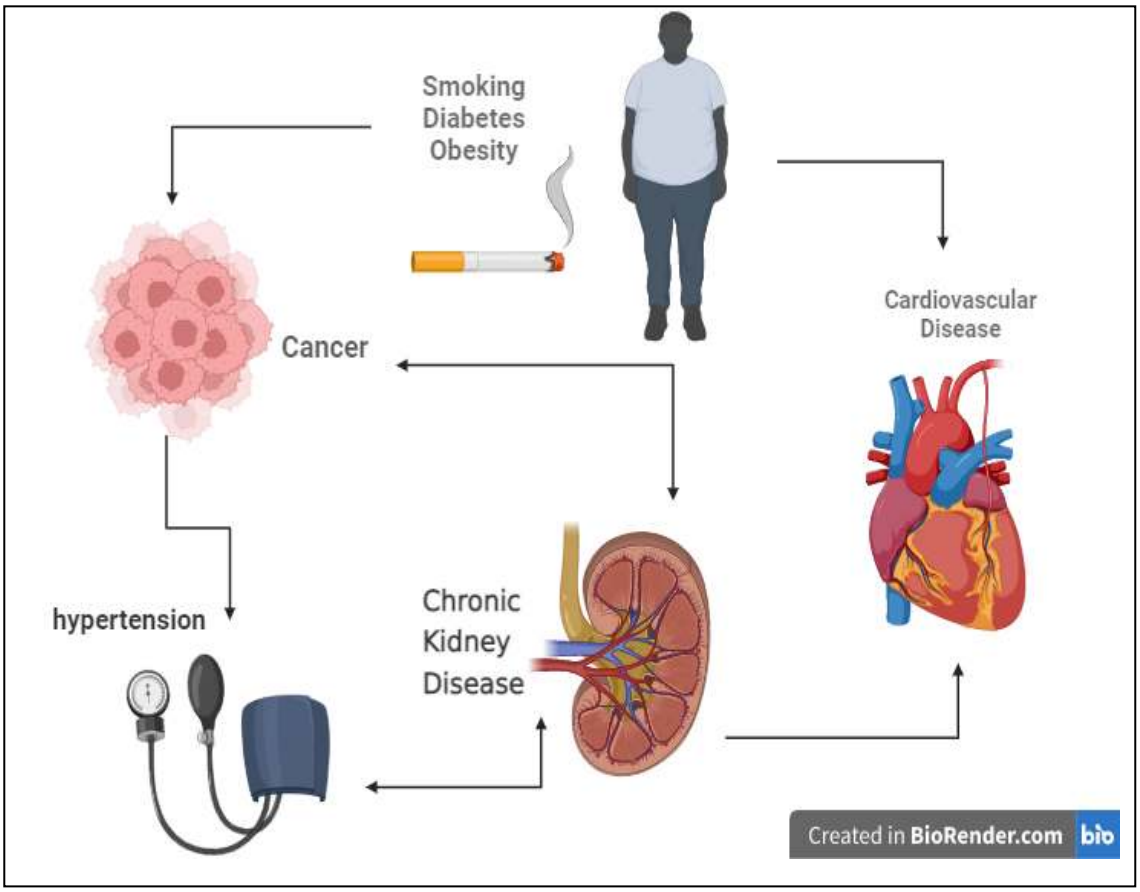
From the above, the studies agreed with the results of our study, where unexplained fever was a symptom of lymphoma (B symptoms), and another study showed that dizziness is highly associated with a type of lymphoma, which is Intravascular large B-cell lymphoma as type of Hodgkin and non-Hodgkin lymphoma. While night sweating was not an obvious symptom. Lymph nodes tumor are also a clear symptom that helps in diagnosing lymphoma. Cough has a significant proportion in the symptoms associated with both Hodgkin and non-Hodgkin lymphomas.

4.5 Comorbidities of lymphoma

Cancer is closely related to cardiovascular diseases, as cancer patients and survivors also suffer from cardiovascular diseases more than others. In particular, a high percentage of cancer patients are at risk of developing Hypertension.[73] Studies have shown a strong link between hypertension and an increase in the incidence of cancer and an increase in the number of deaths from it as well.[74]Cancer and hypertension are multidimensionality related (Figure 9).

Figure 9

Comorbidities and lymphoma risk factor



Diabetes, smoking and obesity are a group of factors that have a major role in affecting the heart and its disease. On the other hand, they also constitute risk factors for both kidney diseases. Cancer and Hypertension, which also, in turn, can cause kidney disease, so it is one of the risk factors for cancer [73].

Hypertension, smoking and obesity are among the risk factors for developing Hodgkin's lymphoma, according to a recent study in 2022 with ($\beta = 0.013$, CI 0.001 to 0.026, $p = 0.048$) reported Hypertension [55]. The increased incidence of cancer and the high number of deaths from various types of cancer are linked to Hypertension [75]. Hypertension accounts for 37% of the diseases associated with cancer [76, 77]. Because of the toxicity from chemotherapy, hypertension is frequently seen in individuals with hematologic malignancies. Despite the fact that innovative anticancer drugs' demonstrated efficiency has significantly altered the therapeutic landscape, cardiovascular adverse effects of chemotherapy, also known as cardiotoxicity, have become a serious issue [78]. Blood pressure is frequently raised by additional cancer

therapies such glucocorticoids and erythropoiesis stimulating drugs (ESA). Traditional treatments for cancer, such as platinum compounds, taxanes and radiotherapy of head and neck are also considered factors that cause hypertension. In recent years, new treatments for cancer have been found, including tyrosine kinase inhibitors (TKI), vascular endothelial growth factor (VEGF) inhibitors, and proteasome inhibitors (PI), which have a significant effect in causing hypertension in patients

A group of therapeutic drugs also cause hypertension including paclitaxel, docetaxel, cabazitaxel which are classified as anti- microtubule agents. cisplatin, cyclophosphamide and ifosfamide derivatives,It is a group of alkylating agents and vinca alkaloids like (vincristine) [79]. Diabetes is one of the most important risk factors that may lead to cancer, such as live, breast, pancreatic and colon cancer [80-82]. In two previous studies on the relationship between diabetes and lymphoma, these studies demonstrated an increased risk of developing non-Hodgkin's lymphoma in patients with diabetes [82-84]. Type 1 and 2 diabetes contribute to the development of non-Hodgkin lymphoma through the defect in the immune system that it causes, which in turn suppresses the immune system, which also contributes to the formation of non-Hodgkin lymphoma. Additionally, there is an increasing body of evidence establishing a connection between insulin, IGF-I, cell proliferation, inhibited apoptosis in cells, and cellular metastasis. These phenomena are implicated in the initiation and advancement of malignancies [82]. Epidemiological research has demonstrated that insulin resistance, marked by elevated insulin levels, is linked to a heightened risk of various malignancies. These include breast, prostate, colon, and kidney carcinomas Recent findings have shed light on certain molecular mechanisms through which insulin receptor (IR) plays a role in cancer. IR is found to be up regulated in several types of human malignancies. Intriguingly, one of the two isoforms of insulin receptor (IR-A), which resembles the fetal isoform of insulin receptor, is particularly overexpressed in cancer. IR-A possesses the unique ability to bind not only insulin but also insulin-like growth factor II (IGF-II) [85].

Carcinogenesis may be impacted by thyroid disorders. Through their effects on cell surface receptors, estrogen pathways, accelerated angiogenesis, and gene expression control, thyroid hormones and TSH can directly promote tumor growth.Additionally,

obesity and diabetes mellitus are connected to thyroid dysfunction and have common risk factors for cancer [86].

In a recent study 2023 to examine the risk factors that may lead to the occurrence of non-Hodgkin lymphoma, the study demonstrated that there is a positive relationship between diabetes and Hypertension with the incidence of non-Hodgkin lymphoma.[45] In a recent 2021 case study an instance of a patient who had hyperthyroidism prior to developing thyroid non-Hodgkin's lymphoma [87]. Hypothyroidism occurs if the TSH level in the body is high (more than 10 mIU/l), in this context, patients with lymphoma are more at risk of developing hypothyroidism as a result of radiation therapy [88]. 20-30% of lymphoma patients who received radiotherapy, especially in the neck area, were diagnosed with hypothyroidism within two to five years after receiving treatment [89, 90]. From the previous studies on diseases associated with lymphoma, there is agreement between our current study and previous studies on hypertension and diabetes, as these diseases are associated with and constitute risk factors for developing lymphoma. As for hypothyroidism, studies tended to indicate a relationship between radiation therapy for lymphoma patients thyroid lymphoma and the occurrence of hypothyroidism.

4.6 Treatment of lymphoma

This study showed that a large number of lymphoma patients receive cyclophosphamide chemotherapy (92.0%), (40.7%) received ondansetron and 90 (60.0%) received dexamethasone.

Cyclophosphamide is a drug that works by the mechanism of anti-tumor effects for the treatment of malignant tumors, specifically lymphomas of both Hodgkin and Non-Hodgkin lymphomas in advanced stages (stage III, stage IV) with approval from the American Food and Drug Administration [91, 92]. Cyclophosphamide is one of the CHOP drug groups that includes 4 treatments (cyclophosphamide, doxorubicin, vincristine, and prednisone), which are chemotherapy for cancer and malignant tumors [93]. CHOP drugs contributed to the recovery of about 30% of patients with non-Hodgkin lymphoma in stages (III, IV), while other studies reported that 55-65% of these patients through the third generation group that includes the following group of drugs (bleomycin, doxorubicin, cyclophosphamide, vincristine, and dexamethason).[93] A

recent study showed that dexamethasone clearly contributes to stimulating programmed cell death and limiting the division, growth and spread of cancer cells, by causing a defect in the cell's DNA [94]. It is a strong glucocorticoid, dexamethasone. The body is affected by dexamethasone in a number of different ways. It functions by preventing neutrophil migration and reducing lymphocyte colony growth Side effects may occur for cancer patients when receiving chemotherapy, such as nausea and vomiting. These patients are given dexamethasone to reduce the severity of these previous symptoms [95]. Ondansetron is an antiemetic drug that helps relieve vomiting and nausea. Cancer patients who receive chemotherapy and radiation may suffer from some unpleasant side effects such as vomiting and nausea, so they are given ondansetron to reduce their severity.Tablets of ondansetron should be taken one to two hours before to radiation, 30 minutes prior to chemotherapy [96]. The results in our current study are consistent with previous studies, as the aforementioned drugs, whether they are antitumor or to reduce the side effects of chemotherapy and radiotherapy, are given to patients with lymphoma as a treatment or as analgesics and side pain relievers.

4.7 Stage 1 \ Stage 2 data collection

In this study, tests were monitored for lymphoma patients receiving treatment in Palestinian hospitals (CBC, liver function, kidney function and electrolytes) in two stages. The first stage was the results of the tests when they entered the hospital and diagnosed the disease. The second stage was the last results that were monitored for patients after periods Different treatment for each patient. Lymphoma, like other types of cancer, when diagnosed, the stage of the disease is determined, by helping to determine the extent of the spread of the malignant tumor, as this silent disease can spread to most organs and parts of the body without being felt except in the advanced stages. The stage of the cancer also has a major role in the therapy plan for each patient in terms of the type of treatment (chemotherapy, radiotherapy, and biological therapy), its concentration, the intensity and number of doses, and surgical operations to remove the tumor if necessary. The importance of determining the stage at the beginning of the disease is not limited to it, but it also contributes to monitoring the disease condition and the progress or decline of the cancer in a specific area. Stage I lymphoma is defined as the presence of the tumor in only one lymph node or site. Stage II is the spread of the lymphoma to another tissue or lymph node. Stage III is when the lymphoma has spread

to both sides of the diaphragm into the lymph nodes in the area. The IV stage is when the tumor has spread widely into tissues and organs outside the lymphatic system [97]. Staging of Hodgkin's lymphoma is based on the Ann Arbor system with the help of CT scans, X-rays of the chest and abdomen, physical examination of the patient, a bone marrow biopsy in addition to accurate detailed of the symptoms that appear on the various systems in the body, while fluordeoxyglucose positron emission tomography plays an important role in accurate diagnosis, staging, and therapeutic response. As in Hodgkin's lymphoma, the Ann Arbor system is also used in staging patients with non-Hodgkin's lymphoma by determining the number of sites where the tumor has spread and the involvement of extracellular lymph nodes [98]. Patients in the I and II stages receive chemotherapy, and cases of recovery from the disease occur in these stages, and this increases their survival rates compared to patients in the advanced stages, III and IV, as chemotherapy often does not cause a regression of the cancer [99]. In our current study, we found a lack of staging for lymphoma patients in the medical records in Palestinian hospitals where they receive treatment and periodic examinations. Therefore, data on the stage of the disease was collected for only 26 patients out of 150, most of them in stage II of lymphoma and this is not sufficient for research.

4.8 Age with Hodgkin and Non-Hodgkin lymphoma

This study showed that there is a relationship between age and type of lymphoma (Hodgkin and non-Hodgkin), where the ages of patients with Hodgkin's lymphoma (Q2 =38) were younger than the ages of patients with non-Hodgkin's lymphoma (Q2 =56.5) with(p-value < 0.001). When the p- value is more than 0.05, it means that there is no relationship, but when the p- value is less than 0.05, it means that there is a relationship and a clear difference. The average age of non-Hodgkin lymphoma patients, according to a study conducted on lymphoma patients, showed the prevalence of lymphoma types between different ages among the population was (67 years), while the average age of Hodgkin lymphoma was between (20-34), so that patients with Hodgkin lymphoma live longer because of their young ages [1]. Non-Hodgkin lymphoma affects people mostly between the ages of 65 and 74, with a median age of 67 [15]. The average age of patients with Hodgkin lymphoma is between 20-40 years. On the other hand, it can affect people aged 55 and over [13]. With aging, the immune system gradually begins to decline in function with chronic inflammation as it begins

the process of remodeling. This process is associated with many risk factors, including chronic inflammatory infections and cancers. One of the most important causes of non-Hodgkin lymphoma is suppression of the immune and chronic inflammation system. This is what can explain the prevalence of non-Hodgkin lymphoma among the elderly [100]. A recent study showed an increase in the number of people infected with hepatitis C virus in the elderly, that is, those over the age of 60 years. Hepatitis C is also considered an infection that causes non-Hodgkin's lymphoma. This supports the spread of non-Hodgkin's disease among the elderly [101]. In the context of infection, Helicobacter pylori also considered a risk factor for increasing the chance of contracting non-Hodgkin's lymphoma and stomach cancer as well, and since the infection of this bacteria spreads among all age groups, it increases among the elderly group. This also supports what was mentioned about the increase in cases of non-Hodgkin's lymphoma in Older age group [102]. One of the most common autoimmune diseases is rheumatoid arthritis, which is also considered a risk factor for developing Hodgkin lymphoma. Rheumatoid arthritis is more common among the elderly, as with increasing age the chance of incidence the disease increases [103].

The age factor is one of the most important factors that increase the survival rate, as confirmed by many studies, as the survival rate of women is more than that of men.All lymphoma types show a substantial unfavorable predictive relationship with age. With age, the severity of the disease and associated diseases increase, and although the comorbidities are not associated with the survival rate, age is associated with them Because of the physiological changes that occur in the body due to age and the problems and disorders that occur in the various organs such as reducing kidney efficiency and a decrease in the rate of filtration and elimination of toxicity, the provision of chemotherapy to elderly patients faces great risks and challenges. This explains why elderly cancer patients are not given high and regularly doses of chemotherapy while it is given to a young lymphoma patient [35]. Bimodal Hodgkin's lymphoma occurs in young people between the ages of 20 and 24, and it also occurs in older people between the ages of 75 and 79, but most cases occur under 40 years of age. This disease has several pathogenesis that increase the chance of its occurrence, such as genetic factors, immune deficiency, and exposure to environmental factors. While the abnormal response of the immune system to the causes of infection promotes the

occurrence of carcinogenic processes that may lead to Hodgkin's lymphoma. In this context, exposure to infections at young stages of life enhances cellular immunity and potentially protects the incidence of HL. It has been shown that many infectious diseases, such as measles, mumps, chicken pox, and smallpox, help reduce the incidence of Hodgkin lymphoma, as the body enhance its immunity during the infection. In contrast, a history of infectious mononucleosis (MI) increases the risk of developing Hodgkin lymphoma in young adulthood [104].

Through the above, the results are consistent with previous studies, as Hodgkin lymphoma has a greater prevalence rate among young people compared to non-Hodgkin lymphoma, in which the average age of incidence is more than 67 years.

4.9 Time of diagnosis

The study showed that there is a clear difference in the time of diagnosis between patients with Hodgkin and non-Hodgkin lymphoma, where the p- value (< 0.001) was the median time of diagnosis in Hodgkin lymphoma (Q2=2.5) while non-Hodgkin lymphoma with median (Q2=6). The term survival rate is used to evaluate the progress of treatment, its effectiveness, and to reduce the incidence of cancer deaths. Survival rates for non-Hodgkin lymphoma patients have made significant progress due to improve in the treatment being provided to patients.

A recent study conducted on non-Hodgkin lymphoma patients in the United States of America confirmed an increase in survival rates for these patients between the years 2014-2018, as this increase indicates progress in treatment. As the noticeable change is the insertion of chemotherapy (rituximab) into the group CHOP. Survival rates increased when rituximab was added to the chemotherapy group for both DLBCL and FL lymphoma by 54.1% to 63.4%, 80.7% to 91.6% respectively. The development of stem cell transplantation and cell toxicity technology also contributed to treating the disease for most stages. On the other hand, obesity had a significant effect on reducing survival rates and vitamin D deficiency also in patients with non-Hodgkin lymphoma, especially DLBCL and T-cell lymphoma [39]. The mortality rate for Hodgkin's lymphoma patients is linked to several factors, including obesity, smoking, and hypertension, as they increase mortality case and thus a decrease in survival rates. a recent global study showed an increase in survival rates overall. This is also due to the

development of treatment and the introduction of improved techniques such as antibody therapy in addition to vaccine therapy. On contrast, the study showed higher rates of mortality from Hodgkin lymphoma in low-income countries. Increased incidence of mortality due to smoking in males, obesity, and increased body mass index(BMI) in both males and females [55].

4.10 The relationship between hematological and biochemical parameters and the type of lymphoma Hodgkin and Non-Hodgkin in the first stage

Data were taken for patients in the first and second stages. The standard deviation, mean and median were calculated for each of the variables as in Table 1 for each stage (stage 1, stage 2).

In type one of lymphoma, Hodgkin lymphoma, the values were significantly higher (Q2) for the following variables (WBC, Neutrophils, Platelets, Chloride and Ferritin). However, the following variables had higher values for (Q2) in type two of lymphoma, non-Hodgkin's lymphoma,(Age, Time of diagnosis, Hematocrit, AST, Creatinine, BUN, Sodium and Bilirubin). As for the rest of the variables, the values were close and the differences were few and not noticeable (Lymphocytes (%), Potassium, RBC, Calcium, HB, RDW, MCH, MCHC, MCV, MPV, ALT, Albumin and Uric acid) In both types of Hodgkin and non-Hodgkin lymphoma.

4.10.1 Complete Blood Count (CBC) and types of lymphoma in stage 1

There is a statistically significant association between number of variables and Hodgkin and non-Hodgkin lymphoma which mention as follows, White Blood Cell (p-value 0.020), Neutrophil granules (%) (p-value 0.022), Mean corpuscular volume (p-value 0.021), Platelets (p-value < 0.001) because of the p-value is less than 0.05. As for the rest of the variables within CBC, there is no statistically significant association because of the p-value is more than 0.05.The study also showed that the number of white blood cells in Hodgkin lymphoma type (Q2=9.1) is more than that of non-Hodgkin lymphoma(Q2=6.9). With Neutrophil granules (%) the number in Hodgkin's lymphoma (Q2=293) was more than in non-Hodgkin's lymphoma type (Q2=220). Also the platelets, the number of platelets was more in Hodgkin's type (Q2=293) than in non-Hodgkin's lymphoma type (Q2=220). In contrast, mean corpuscular volume was higher in non-Hodgkin lymphoma (Q2=81.8) than in Hodgkin lymphoma (Q2=79.7).

Laboratory tests contribute to the diagnosis of lymphoma, through which it is possible to expected complications that may occur for patients. However, complete blood counts can be normal in lymphoma patients, and this does not cancel their diagnosis of the disease [9, 17]. The presence of inflammation in the body is associated with the presence of cancer and its progression, as cancerous stromal tissue contains a large number of white blood cells, as their number and the cytokines they secrete help in the diagnosis and stages of disease progression. These cytokines secreted by WBC promote cell growth and inhibit programmed cell death, which it leads to the formation and progression of cancerous tumors [105-107]. Platelets are considered one of the most important elements of immunity against inflammation associated with cancer. They are directly or indirectly linked to leukocytes and interact together. Platelets manage the inflammatory area in tumors and stimulate leukocytes to the tumor sites and activate them. Thus, cancer patients have changes in the number and activity of platelets and white blood cells Platelets are activated by ADP, which is secreted by tumor cells. Various immune cells are activated in cooperation with platelets to perform their function as needed in the tumor environment. This is in response to the continuous interaction between immune cells and tumor cells [108-110].

In a study that confirmed the significance of platelets in predicting survival for diffuse large B-cell lymphoma patients despite being a minor prognostic factor [111]. A decrease in the number of lymphocytes(lymphopenia) is considered a warning sign for the occurrence of non-Hodgkin's lymphoma This decrease could be due to the secretion of cytokines by the cancerous lymphoma cells, which in turn attacks the lymphocytes [112]. A recent study also reported that a decrease in the number of platelets while a rise in the width of red blood cell distribution is an indicator of the presence of cancer. The study also confirmed that the previous variables are considered strong predictors of diffuse large B-cell lymphoma patients (DLBCL). In this context, the study also showed a decrease in the levels of hemoglobin and albumin with DLBCL patients [113]. In contrast a study of 221 patients with lymphoma, hemoglobin was examined to show that it was in the normal range in patients with lymphoma [9].

A study was conducted on 140 patients with lymphoma, and the results of a complete blood count were taken at the time of diagnosis of the disease. The results were abnormal for leukocytes, platelets, and hemoglobin in 57% of the patients. And 46% of

patients suffer from lymphocytopenia. Decrease in neutrophils (neutropenia) and platelets (thrombocytopenia) was present in all patients. 69% of patients had leucopenia and 63% suffered from a deficiency in red blood cells (anemia) [114]. Some studies showed a relationship between lymphoma and low hemoglobin level <12 [115].

Previously, we note that there is a study that agreed with the results of our study and another that was contrary. Some studies have shown a relationship between low platelet count (thrombocytopenia) and the progression of lymphoma.

4.11 Complete Blood Count (CBC) and types of lymphoma in stage 2

After chemotherapy, a significant decrease in the number of red blood cells (leading to anemia), platelets (thrombocytopenia) and lymphocytes (lymphopenia) can occur [112, 116, 117]. In a study conducted on 317 patients with non-Hodgkin's lymphoma, 54 of them were in the early stages, 180 in the intermediate stages, 76 in the advanced stages, and the rest of the patients were not classified. The patients received chemotherapy, then the results of their blood tests were taken, and they were as follows 42% of them had anemia, 6% decrease in leukocytes, thrombocytopenia in 13% of patients, leukocytosis increased in 26% of patients and platelet count increased in 14% of them [118]. Whereas, a high ferritin level could be an indication of a malignant tumor [115, 119].

4.12 Liver function test with lymphoma

In the first stage, albumin and bilirubin were almost the same in Hodgkin and non-Hodgkin, while the level of ferritin was higher in Hodgkin lymphoma. On the other hand, the levels of AST and ALT were higher in Hodgkin than in non-Hodgkin. The levels of these variables in the second stage were higher in non-Hodgkin lymphoma for ferritin ALT and ALT without differences for albumin and bilirubin. A previous study confirmed the existence of a relationship between the progression of Hodgkin lymphoma and the high level of ferritin in the blood (ferritinemia). In the same context, a Spanish study confirmed that survival rates for more than 5 years were in an inverse relationship with the level of ferritin, where the survival rate was without progression. The risk of disease was 89% when the ferritin level was low and 69% when the ferritin level was above 300 microgram/L [120, 121]. Studies have confirmed the relationship of ferritin levels and lymphoma cancer [122]. In a study conducted on 267 newly

diagnosed non-Hodgkin's lymphoma patients, the possibility of a relationship between a high ferritin level of more than 500 ng/mL was shown with the survival rate for these patients with malignancy. The 5-year progression-free survival rate was 57% when the rate was Ferritin (<500 ng/mL), by 11.6% when the ferritin level was (≥ 500 ng/mL) [115]. Several studies have documented the existence of a relationship between high ferritin levels and lymphoma of Hodgkin and non-Hodgkin lymphoma, where the level of ferritin is considered a factor of the risk of non-Hodgkin lymphoma, while a study confirmed that the cancerous tissues of Hodgkin lymphoma contain a high level of ferritin It has similar properties to ferritin secreted from the liver [115, 120, 121, 123]. Ferritin is characterized by its increase in cases of stress in the body, such as fever and hematological cancer such as lymphoma and leukemia. Ferritin is strongly linked to iron levels (which is stored in the form of ferritin). The increase in ferritin levels occurs as a result of an increase in iron stores when the heme group is destroyed in repeated blood transfusions. In the advanced stages of Hodgkin's lymphoma requires continuous blood transfusions, which in turn raises iron levels in the blood and thus ferritin levels. In hematological cancer, lymphoma and leukemia, disturbances occur in the formation of red blood cells (erythropoiesis) and iron metabolism, and this also leads to disturbances in the levels of ferritin in the circulation A recent study confirmed the use of ferritin levels to predict the presence or regression of Hodgkin lymphoma based on the existing ferritin levels [120, 121, 123].

Albumin is one of the most important predictors of survival and disease progression in lymphoma patients in study conducted on 157 DLCBL patients [124].

Diffuse large B-cell lymphoma (DLBCL) and many other hematological malignancies have demonstrated serum albumin to be a predictive predictor [125]. Another study also confirmed that albumin is an important prognostic factor for the presence of hematological malignancies, including lymphomas, specifically DLBCL. Where the study proved that the level of albumin is ≥4.0 g/dL, this is a risk factor for developing lymphoma type DLBCL [126].

Some studies mentioned the possibility of a relationship between obstructive jaundice and non-Hodgkin's lymphoma, but it is rare,so when diagnosing obstructive jaundice, it is important to regard that the cause of its occurrence is a tumor and often non-

Hodgkin's lymphoma is associated with it. At this point, it is possible to refer to the level of bilirubin, as the conjugated bilirubin was high [127]. In a recent study examining the relationship between bilirubin levels and some types of cancer, a relationship was observed between genetically elevated bilirubin levels and the risk of incidence non-Hodgkin lymphoma [128]. In a previous study that dealt with a case report of a man in his fifties who was suffering from symptoms of obstructive jaundice, then it was revealed that he had lymphoma in the bile duct with significant disturbances in the results of liver function tests ALT, AST and bilirubin which were significantly elevated in the level. The study concluded that Early treatment of obstructive jaundice contributes to the advancement of chemotherapy in the event of lymphoma in the region [129]. In this context, other studies confirmed that obstructive jaundice could be due to the presence of Non-Hodgkin lymphoma, or that biliary obstruction is an important symptom of lymphoma, but it is rare [130, 131]. With regard to aspartate aminotransferase AST, which is one of the most important liver function tests, a study conducted on 179 patients with Diffuse large B-cell lymphoma DLBCL revealed a relationship between AST level and survival rates for those patients who were treated by the R-CHOP protocol. It is a prognostic factor for the risk of DLBCL progression as elevated AST has been associated with advanced stages of the disease [132].

4.13 Kidney function test and lymphoma

In our study, the results of kidney function tests showed that in both stage 1 and stage 2, the creatine level of the two types of Hodgkin lymphoma and non-Hodgkin lymphoma were similar, and this also applies to the uric acid test. As for the Blood urea nitrogen BUN test, the values were higher in the two stages in the non-Hodgkin lymphoma type. The kidneys are the most common organs of the abdominal cavity at risk of developing lymphoma, with a rate of 30%-60% [133]. The kidneys are the most vulnerable organs of the abdominal cavity to lymphoma, with a rate of 30%-60%. Kidney function tests are not significantly affected by lymphoma, as creatine levels can rise between 26% to 56% of patients. In terms of elevated BUN and creatine levels, it may be due to bilateral ureteral obstruction because of Lymphoma or as a side effect of chemotherapy [134]. Kidney problems and diseases are very common in patients with blood tumors (leukemia / lymphoma), as they are considered a risk factor for increasing the death rate [135].

4.14 Electrolytes and lymphoma

A study to investigate the relationship between the kidneys and hematologic malignancies, conducted on 349 patients, confirmed the occurrence of disturbances and abnormal levels of electrolytes, including sodium, magnesium, phosphate, calcium and potassium. These problems and disorders are represented by low levels of potassium" Hypokalemia "by (43-64%) of patients, magnesium "hypomagnesaemia" (25-32%), phosphate "hypophosphatemia"(16-30%) but high level of calcium "Hypercalcemia" About 13% of patients with non-Hodgkin's lymphoma and in 5.4% of patients with Hodgkin lymphoma. An increase in the level of calcium, hypercalcemia, occurred by 30% in patients with malignant tumors [136]. Hypercalcemia is associated with a greater degree of NHL. Many cancer patients, including lymphoma patients, suffer from excessive levels of calcium (hypercalcemia), and this may lead to death. Therefore, attention must be paid to its causes in order to avoid and deal with them. A significant increase in the level of calcium in the blood has been observed in both Hodgkin and non-Hodgkin lymphoma, although the exact cause is not determined. Some researchers suggest that excessive levels of the compound 1,25 (OH)2D are the reason. On the other hand, some studies have shown that the compound PTHrP produced by lymphoma cancer cells can be linked to patients' levels of vitamin D. Studies have indicated the presence of PT in neoplastic hemopoietic cells, which makes them act like paracrine, causing destruction of bone tissue, thus increasing calcium in the blood [137-139]. Our study showed the results of electrolyte examinations as follows. For both the first and second stages, there was an increase in the electrolyte values in non-Hodgkin lymphoma for both sodium and potassium. On the contrary, the study showed an increase in chlorine values in the first stage of Hodgkin lymphoma and the second stage in non-Hodgkin lymphoma. On the other hand, the values of calcium in each of the two stages in the two species were similar. For all the previously mentioned electrolytes, the (p-value >.005), then this indicates that there is no significantly statistical association.

In this context, the results showed an increase in calcium levels (hypercalcemia) in Hodgkin and non-Hodgkin patients for both stage 1 and stage 2. This is consistent with previous studies that confirmed higher calcium levels in patients with blood tumors, specifically in Hodgkin's lymphoma than in non-Hodgkin's lymphoma.

4.15 Limitation

We initially obtained a lot of lymphoma patients in order to analyze the data of as many patients as possible, but due to the lack of documented data in their records, a large number of them were excluded.

There are laboratory tests, such as lactic dehydrogenase (LDH) and transferrin, which were not performed because they are not available to all lymphoma patients on a regular basis. The examination may be performed for the patient only once during the treatment period, but our study based on to analyze the results in two stages. Lack of research and studies on lymphoma in Palestine and focus on other types of cancer in Palestine, such as breast cancer and lung cancer. Many cancer patients are transferred to complete treatment in hospitals in Jerusalem and the occupied Palestinian territories, which makes it difficult to access their data and track their disease status and examinations.

4.16 Recommendations and conclusion

4.16.1 Recommendations

1. Highlighting research in Palestine, especially research related to lymphoma
2. Increased research on the relationship of lymphoma with hematological factors such as platelets and white blood cells
3. It is necessary to record patient data, especially the stage of cancer for each patient
4. Research into the relationship of hypercalcemia with lymphoma, which in turn can help in treatment or early detection of cancer
5. Follow up on albumin and ferritin tests for lymphoma patients and research their relationship to the disease

4.16.2 Conclusion

Lymphoma is a malignant tumor resulting from clonal proliferation, with both types: Hodgkin and non-Hodgkin lymphoma. Lymphoma has many relationships with biochemical and hematological variables in patients. There is a group of relationships that link the occurrence of lymphoma in the beginning, then the progression of the cancer or the improvement of the patient's health status with age, gender, comorbidities, laboratory tests, and the treatment that the patient takes.Lymphoma is clearly linked to gender, as the incidence rate is higher in males than in females, due to physiological and

environmental reasons that enhance the overall incidence of cancer in males more than females. On the other hand, the study showed that patients who suffer from diabetes, hypertension, and hypothyroidism have a greater chance of developing lymphoma. As for the context of treatment,majority of patients receiving treatment in Palestinian hospitals share the same type of treatment. The incidence of Hodgkin and non-Hodgkin lymphoma is related and varies according to age group Lymphoma is a malignant tumor that causes physiological changes in the body and causes various immune and systemic responses. Laboratory test readings change as a result of the presence of the tumor. This can help in detecting the tumor or monitoring it in terms of its progress or decline in the body.

List of Abbreviations

Abbreviation	Meaning
HL	Hodgkin lymphoma
NHL	Non-Hodgkin lymphoma
CBC	complete blood count
CT	computed tomography
MRI	Magnetic resonance imaging
HIV	human immunodeficiency virus
BMI	Body mass index
ESA	erythropoiesis stimulating drugs
TKI	tyrosine kinase inhibitors
VEGF	vascular endothelial growth factor
PI	proteasome inhibitors
IR	insulin receptor
IGF-II	insulin-like growth factor II
TSH	Thyroid-stimulating hormone
DLBCL	Diffuse large B cell lymphoma
FL	Follicular lymphoma
LDH	lactic dehydrogenase
WBC	White blood cells
RBC	Red blood cells
MCV	Mean corpuscular volume
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
RDW	Red cell distribution width
MPV	Mean platelet volume
AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
BUN	Blood urea nitrogen

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Appendices

Appendix A

Stratification of the patients into low, normal, or high categories based on the normal ranges of the hematological and biochemical parameters

Variable	Stage 1					Stage 2				
	Hodgkin lymphoma		Non-Hodgkin lymphoma			Hodgkin lymphoma		Non-Hodgkin lymphoma		
	n	%	n	%	p-value	n	%	n	%	p-value
Complete blood count										
White blood cells										
Low	4	3.4	3	9.4		10	8.5	5	15.6	
Normal	76	64.4	22	68.8	0.264	92	78.0	21	65.6	0.348
High	38	32.2	7	21.9		16	13.6	6	18.8	
Neutrophil granules										
Low	4	3.4	7	21.9		14	11.9	9	28.1	
Normal	47	39.8	11	34.4	0.012	48	40.7	11	34.4	0.106
High	67	56.8	14	43.8		55	46.6	12	37.5	
Lymphocytes										
Low	55	46.6	15	46.9		43	36.4	14	43.8	
Normal	56	47.5	10	31.3	0.027	66	55.9	13	40.6	0.217
High	7	5.9	7	21.9		9	7.6	5	15.6	
Red blood cell										
Low	4	3.4	5	15.6		20	16.9	9	28.1	
Normal	99	83.9	22	68.8	0.028	76	64.4	19	59.4	0.337
High	15	12.7	5	15.6		22	18.6	4	12.5	
Hemoglobin										
Low	51	43.2	11	34.4		30	25.4	15	46.9	
Normal	64	54.2	21	65.6	0.287	87	73.7	16	50.0	0.039
High	3	2.5	0	0.0		1	0.8	1	3.1	
Hematocrit										
Low	34	28.8	6	18.8		23	19.5	10	31.3	
Normal	83	70.3	24	75.0	0.138	90	76.3	21	65.6	0.381
High	1	0.8	2	6.3		5	4.2	1	3.1	
Mean corpuscular volume										
Low	59	50.0	8	25.0		33	28.0	5	15.6	
Normal	59	50.0	24	75.0	0.016	84	71.2	27	84.4	0.253
High	0	0.0	0	0.0		1	0.8	0	0.0	
Mean corpuscular hemoglobin										

Variable	Stage 1					Stage 2				
	Hodgkin lymphoma		Non-Hodgkin lymphoma			Hodgkin lymphoma		Non-Hodgkin lymphoma		
	n	%	n	%	p-value	n	%	n	%	p-value
Low	68	57.6	17	53.1		43	36.4	10	31.3	
Normal	49	41.5	15	46.9	0.692	71	60.2	21	65.6	0.851
High	1	0.8	0	0.0		4	3.4	1	3.1	
Mean corpuscular hemoglobin concentration										
Low	31	26.3	7	21.9		26	22.0	3	9.4	
Normal	86	72.9	25	78.1	0.680	90	76.3	29	90.6	0.132
High	1	0.8	0	0.0		2	1.7	0	0.0	
Red cell distribution width										
Low	4	3.4	1	3.1		5	4.2	0	0.0	
Normal	84	71.2	21	65.6	0.808	83	70.3	19	59.4	0.083
High	30	25.4	10	31.3		29	24.6	13	40.6	
Platelets										
Low	5	4.2	5	15.6		20	16.9	8	25.0	
Normal	103	87.3	24	75.0	0.107	92	78.0	24	75.0	0.156
High	10	8.5	3	9.4		6	5.1	0	0.0	
Mean platelet volume										
Low	10	8.5	1	3.1		3	2.5	1	3.1	
Normal	92	78.0	24	75.0	0.324	104	88.1	29	90.6	0.842
High	16	13.6	7	21.9		11	9.3	2	6.3	
Liver function test										
Ferritin										
Low	0	0.0	0	0.0		1	0.8	0	0.0	
Normal	98	83.1	27	84.4	0.568	106	89.8	26	81.3	0.239
High	19	16.1	3	9.4		10	8.5	6	18.8	
Albumin										
Low	12	10.2	2	6.3		15	12.7	4	12.5	
Normal	104	88.1	29	90.6	0.625	98	83.1	26	81.3	0.668
High	1	0.8	0	0.0		1	0.8	1	3.1	
Bilirubin										
Low	10	8.5	1	3.1		6	5.1	0	0.0	
Normal	101	85.6	27	84.4	0.167	106	89.8	28	87.5	0.048
High	5	4.2	4	12.5		4	3.4	4	12.5	
Aspartate aminotransferase										
Low	0	0.0	0	0.0		3	2.5	0	0.0	
Normal	108	91.5	30	93.8	1.000	110	93.2	30	93.8	0.387
High	10	8.5	2	6.3		4	3.4	2	6.3	
Alanine aminotransferase										

Variable	Stage 1					Stage 2				
	Hodgkin lymphoma		Non-Hodgkin lymphoma			Hodgkin lymphoma		Non-Hodgkin lymphoma		
	n	%	n	%	p-value	n	%	n	%	p-value
Low	4	3.4	2	6.3		4	3.4	2	6.3	
Normal	106	89.8	29	90.6	0.573	110	93.2	27	84.4	0.215
High	8	6.8	1	3.1		3	2.5	3	9.4	
Kidney function test										
Creatinine										
Low	34	28.8	1	3.1		21	17.8	6	18.8	
Normal	81	68.6	29	90.6	0.002	89	75.4	25	78.1	0.709
High	3	2.5	2	6.3		8	6.8	1	3.1	
Uric acid										
Low	2	1.7	0	0.0		5	4.2	1	3.1	
Normal	108	91.5	29	90.6	0.554	97	82.2	27	84.4	0.943
High	8	6.8	3	9.4		16	13.6	4	12.5	
Blood urea nitrogen										
Low	16	13.6	1	3.1		10	8.5	2	6.3	
Normal	93	78.8	28	87.5	0.150	94	79.7	24	75.0	0.519
High	7	5.9	3	9.4		13	11.0	6	18.8	
Electrolytes										
Sodium										
Low	13	11.0	3	9.4		21	17.8	6	18.8	
Normal	99	83.9	28	87.5	0.912	92	78.0	25	78.1	0.953
High	5	4.2	1	3.1		5	4.2	1	3.1	
Potassium										
Low	3	2.5	1	3.1		5	4.2	2	6.3	
Normal	103	87.3	26	81.3	0.833	98	83.1	28	87.5	0.516
High	11	9.3	4	12.5		15	12.7	2	6.3	
Chloride										
Low	7	5.9	1	3.1		2	1.7	2	6.3	
Normal	92	78.0	29	90.6	0.224	76	64.4	21	65.6	0.393
High	19	16.1	2	6.3		40	33.9	9	28.1	
Calcium										
Low	1	0.8	0	0.0		0	0.0	0	0.0	
Normal	1	0.8	0	0.0	0.610	0	0.0	2	6.3	0.044
High	113	95.8	32	100.0		118	100.0	30	93.8	

جامعة النجاح الوطنية
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الملخص

اللمفوما هي أورام خبيثة غير متجانسة تنشأ نتيجة التكاثر غير المنضبط للخلايا اللمفاوية (B، T، أو الخلايا القاتلة الطبيعية (NKخلال مراحل نضجها. تُقسم إلى نوعين رئيسيين: لمفوما هودجكن واللمفوما اللاهودجكن، ويُصنّف منها حوالي 90 نوعًا فرعيًا. تشمل عوامل الخطورة: العدوى، نقص المناعة، أمراض المناعة الذاتية، العوامل الوراثية، السمنة، الأدوية، والعوامل البيئية. يبدأ التشخيص بالفحص السريري، ويُؤكَّد باستخدام التصوير الطبقي المحوري والخزعة. يُحدَّد العلاج وفقًا لمرحلة المرض، ويتضمن عادة العلاج الكيميائي والإشعاعي، مع متابعة الحالة عبر الفحوصات الدورية السريرية والمخبرية.

في فلسطين، يتلقى مرضى اللمفوما العلاج والمتابعة الدورية لحالتهم وتطور المرض. يهدف هذا البحث إلى دراسة العلاقة بين التحاليل الكيميائية الحيوية والدموية وبين المضاعفات، نتائج العلاج، وتطور المرض لدى المرضى الذين يتلقون العلاج في المستشفيات الفلسطينية.

المنهجية: شملت الدراسة جمع بيانات من مرضى لمفوما من مختلف الفئات العمرية والمناطق الجغرافية، ذكورًا وإناثًا، تضمنت: العمر، تاريخ التشخيص، الجنس، نوع اللمفوما، اختبارات الدم ((CBC، وظائف الكبد والكلى، المعادن والاملاح وخطة العلاج. قُسمت البيانات إلى مرحلتين: المرحلة الأولى وهي بداية التشخيص، والمرحلة الثانية هي اخر فحوصات أُجريت للمريض خلال فترة العلاج، وتم تحليلها إحصائيًا.

النتائج: شملت الدراسة 150 مريضًا، بمتوسط عمر 43.9 ± 18.2 سنة، ووسيط 40.0 (29.0، 59.3) سنة؛ 52.7% منهم ذكور، و78.7% مصابون ب لمفوما هودجكن. بلغ متوسط مدة الإصابة 5.5 ± 2.6 سنوات. توفرت بيانات مرحلة المرض لـ 26 مريضًا فقط، وكان 65.4% منهم (11.3% من إجمالي العينة) في المرحلة الثانية.

الأعراض الأكثر شيوعًا كانت: الضعف العام (71.3%)، ألم الرقبة (18.0%)، الدوخة (15.3%)، السعال (8.7%)، والحمى (10.0%). الأمراض المرافقة شملت: ارتفاع ضغط الدم (9.3%)، داء السكري (9.3%)، وقصور الغدة الدرقية (1.3%). تلقى معظم المرضى (92.0%) العلاج ب سيكلوفوسفاميد، و40.7% أوندانسيترون، و60.0% ديكساميثازون.

في المرحلة الأولى، كان مرضى هودجكن أصغر سنًا ولديهم ارتفاع في عدد الكريات البيضاء، العدلات، الصفائح الدموية، ومستوى الكلوريد مقارنة بمرضى اللاهودجكن. أما في المرحلة الثانية، فلوحظ ارتفاع بمستوى الفيريتين لدى مرضى اللاهودجكن دون فروق أخرى ذات دلالة إحصائية.

الاستنتاج: أظهرت الدراسة وجود ارتباطات بين تطور مرض اللمفوما وبعض المؤشرات الحيوية والدموية، مما قد يُسهم في تحسين خطط التشخيص والعلاج المبكر للحد من انتشار المرض وتطور مضاعفاته.

الكلمات المفتاحية: الليمفوما، الليمفوما هودجكين، الليمفوما غير هودجكين.