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COLLEGE OF MEDICINE

DEPARTMENT OF PHARMACY



**EVALUATING THE SIDE EFFECTS OF PALBOCICLIB IN BREAST CANCER
PATIENTS FOCUSING ON NEUTROPENIA IN THE CITY OF SULAYMANIYAH**

A research project submitted to Komar University of Science and Technology, Department of
Pharmacy for partial fulfilment of a Bachelor of Science degree in Pharmacy

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Dedication :

With deep and genuine gratitude, we dedicate this graduation project to the many individuals who supported, inspired, and believed in us throughout this journey.

To our families—your love, patience, and sacrifices have been our foundation. Through every challenge, late night, and moment of doubt, your constant encouragement reminded us why we started and gave us the strength to keep going. This accomplishment is as much yours as it is ours.

To our supervisor, Dr. Trefa Mohammed—thank you for your unwavering support, insightful feedback, and steady guidance. You have been more than just a mentor; you've been a source of motivation and clarity. Your belief in our abilities, even when we questioned ourselves, meant the world to us. We are incredibly grateful for the time and effort you invested in helping us grow and succeed.

To Komar University of Science and Technology—thank you for creating an environment where curiosity is encouraged, ideas are nurtured, and students are challenged to think beyond limits. This university has played a major role in shaping our academic and personal development, and we are proud to be part of its community.

Lastly, to our friends and classmates who shared in this experience—thank you for the laughs, the late-night study sessions, and the moments of shared frustration and celebration. Your presence made this journey more meaningful.

This project reflects not only our hard work, but the kindness, dedication, and support of everyone who walked beside us. We are honored to dedicate it to all of you.

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Declaration :

We hereby declare that the graduation research project titled “Evaluating the Side Effects of Palbociclib in Breast Cancer Patients, focus on Neutropenia in Sulaymaniyah” was carried out by Arias Rizgar, Diya Jamal, and Bawan Bakhtyar under the supervision of the Pharmacy Department at Komar University of Science and Technology, so this project was conducted as a requirement for the completion of the Bachelor of Science in Pharmacy degree.

We affirm that this study is an original piece of academic work carried out in accordance with institutional ethical guidelines and academic standards, and all sources of information, data, and content used in the preparation of this project have been appropriately acknowledged.

Signature of academic supervisor

Name of Supervisor: Dr. Trefa Mohammed Abdullah

Upon review and recommendation, I hereby submit this project to the examination committee for evaluation.

Signature of head of department

Name of Head of Department: Dr. Trefa Mohammed Abdullah

Abstract :

This research explores the side effects associated with palbociclib, a commonly used CDK4/6 inhibitor in the treatment of breast cancer, also the study was conducted at Hiwa Hospital and involved a review of 70 patient records, also the analysis focused on several important variables, including age, gender, smoking status, family history of breast cancer, and the presence of comorbidities. Particular attention was given to the occurrence of neutropenia and related infections during treatment. Results showed that neutropenia was highly prevalent, affecting the majority of patients, with more than half of those cases complicated by infections most of which were bacterial in nature, although fatigue was the most frequently reported symptom, followed by hair thinning and anxiety, also the majority of participants were non-smoking women aged between 51 and 60, and a significant portion had a family history of breast cancer. Comorbidities such as diabetes and hypertension were also common, so these findings emphasize the importance of routine monitoring and supportive care for patients on palbociclib, so by examining real-world patient data, this study adds meaningful insight into the safety profile of palbociclib and reinforces the need for personalized treatment strategies.

Keywords: Palbociclib; Breast cancer; Neutropenia; Infections; Comorbidities; Side Effects

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Chapter one : Introduction

1.1 Background

Breast cancer remains one of the most common cancers affecting women worldwide. It occurs when breast cells begin to grow uncontrollably. If left untreated, these abnormal cells can spread to other parts of the body, making the disease life-threatening. A variety of factors can increase a person's risk of developing breast cancer, including genetic predisposition, hormonal influences, environmental exposures, and lifestyle choices. In recent years, medical research has made significant strides in developing targeted therapies that specifically attack cancer cells while sparing normal tissues—unlike traditional chemotherapy, which often damages both healthy and cancerous cells. Targeted therapies are designed to be more precise and typically cause fewer side effects, also one of the most important targeted therapies for breast cancer is palbociclib, a CDK4/6 inhibitor, also palbociclib works by slowing or stopping the growth of cancer cells by blocking two proteins, CDK4 and CDK6, which cancer cells rely on for division and survival, so by inhibiting these proteins, cancer cells are unable to continue growing and eventually die, so this therapy is commonly used alongside hormone therapy, particularly for patients with hormone receptor-positive (HR+)/HER2-negative (HER2-) breast cancer or metastatic breast cancer. The development of palbociclib and other similar targeted treatments has been a major advancement, allowing many patients with advanced or metastatic breast cancer to live longer and experience a better quality of life. (Mir, 2023)

1.2 Epidemiology of Breast Cancer

Prevalence, with a Focus on Study Location Globally, the incidence of breast cancer has been steadily increasing year after year. The World Health Organization (WHO) predicts that breast cancer cases will rise by 38%, estimating around 3.2 million new cases annually by 2050, alongside more than 1 million deaths each year. In the Middle East, and specifically in Iraq, breast cancer rates have shown a significant increase as well. A study analyzing data from 2000 to 2019 found that the incidence of breast cancer among Iraqi women more than doubled—from 24.4 cases per 100,000 in 2000 to 52.7 per 100,000 in 2019. This rise is attributed to several factors, including obesity, reduced physical activity, and lifestyle changes.

Focusing on Sulaymaniyah, approximately 1,500 new cancer cases were reported within six months in 2023, and breast cancer accounted for about 20% of these cases. Most women diagnosed were around the age of 49, and notably, many were diagnosed before reaching menopause.

1.3 Classification and Staging of Breast Cancer

Breast cancer staging depends on several factors: the size of the tumor, whether it has spread to other parts of the body, and the biological characteristics of the tumor cells, including their genetic and biomarker profiles. When a biopsy is performed, the sample undergoes further testing to evaluate important markers:

1. Hormone Receptor Status: Estrogen and progesterone are natural hormones that can promote the growth of certain breast tumors. If a tumor is sensitive to hormones, treatments such as tamoxifen—which blocks hormone activity—may be effective.

2. HER2 Status: HER2 proteins regulate cell growth. In some cancers, HER2 is overexpressed, fueling tumor growth. Targeted therapies like trastuzumab can block HER2 and slow cancer progression.

3. Triple-Negative Breast Cancer: These cancers lack estrogen, progesterone, and HER2 receptors. They tend to grow and spread faster than other types and are harder to treat because fewer targeted therapies are available.

4. Genomic Testing: Tests like Oncotype DX analyze specific genes in the tumor to predict aggressiveness and help guide decisions about chemotherapy and other treatments.

Other key factors influencing treatment and surgery decisions include:

- **BRCA1 and BRCA2 mutations:** Mutations in these tumor-suppressor genes greatly increase breast cancer risk, along with risks for ovarian, pancreatic, and prostate cancers. Certain populations, such as Ashkenazi Jewish women, have a higher likelihood of carrying these mutations.
- **Pregnancy status**
- **Previous radiation therapy to the breast**
- **Pre-existing lung conditions**
- **Autoimmune diseases (such as scleroderma or lupus)**

Breast cancer is classified into five stages:

- Stage 0: Carcinoma in situ (Tis). Cancer is confined to the ducts or lobules and has not invaded nearby tissue.
- Stage I: Cancer is invasive but small, possibly involving nearby lymph nodes.
 - o Stage IA: No lymph node involvement, small tumor.
 - o Stage IB: Tumor present in lymph nodes; may or may not be present in breast tissue itself.
- Stage II: Larger tumor or greater lymph node involvement.
- Stage III: Larger tumor (>5 cm) with extensive lymph node involvement or tumor attached to the chest wall.
- Stage IV: Cancer has metastasized to distant organs like the bones, lungs, liver, or brain.

The TNM system is used to define the extent of cancer:

- T: Tumor size
- N: Node involvement
- M: Metastasis (0 = no spread, 1 = spread) (Ajlouni, 2024)

1.4 Risk Factors and Pathophysiology

Pathophysiology

Breast cancer develops when breast cells begin to grow uncontrollably, often forming a lump or tumor. This abnormal growth is usually due to mutations in genes that control cell division and repair. For example, mutations in BRCA1 and BRCA2 genes—which normally help fix damaged DNA—can significantly increase breast cancer risk. Another example is overexpression of the HER2 gene, leading to uncontrolled cell proliferation. Most breast cancers originate in either the milk ducts (ductal carcinoma) or milk-producing glands (lobular carcinoma). As the cancer progresses, it may invade nearby tissues and spread to distant sites like lymph nodes, bones, liver, or lungs. Importantly, the presence or absence of certain molecular markers (like estrogen, progesterone, or HER2 receptors) heavily influences treatment options and outcomes. By understanding these biological behaviors, clinicians can better personalize treatments.

Risk Factors

1. Endocrine Factors:

- Anything that increases lifetime estrogen exposure raises breast cancer risk.
- Early menarche (<11 years old) and late menopause (≥55 years) increase risk.
- Nulliparity (never having been pregnant) and first childbirth after age 30 are risk factors.
- Hormone replacement therapy and long-term oral contraceptive use increase risk.

Protective factors:

- Bilateral oophorectomy (ovary removal) before age 45 lowers risk.

- Breastfeeding, particularly beyond one year, lowers risk.

2. Genetic Factors:

- Personal history of breast cancer (especially contralateral breast cancer).
- Family history: a first-degree relative with breast cancer increases risk by 50%.
- Other associated cancers: ovarian, uterine.
- Dense breast tissue can delay detection and is associated with advanced-stage diagnoses.
- Germline mutations in BRCA1 and BRCA2 significantly increase risk.

3. Environmental and Lifestyle Factors:

- Increased alcohol intake and exposure to radiation elevate risk.
- Smoking may slightly raise breast cancer risk.

Protective lifestyle factors:

- Diet rich in fruits and vegetables (modest effect).
- Fat intake has no strong link to risk.
- Body weight: lower risk in premenopausal women; higher risk in postmenopausal women if overweight. (Obeagu, 2024)

1.5 Mechanism of Action of Palbociclib

Palbociclib is a targeted therapy designed to inhibit two key proteins in cancer cells, CDK4 and CDK6 (cyclin-dependent kinases 4 and 6), which are critical for cell cycle progression. Normally, CDK4/6 partners with cyclin D to activate the retinoblastoma protein (Rb). Activated Rb allows the cell to transition from the G1 (resting) phase to the S (DNA replication) phase. In HR+/HER2– breast cancers, these pathways are often overactive, leading to uncontrolled growth. Palbociclib binds to the ATP-binding pocket of CDK4/6, preventing their activation. As a result, Rb remains in its active (hypophosphorylated) state and keeps the cell cycle arrested in G1 phase. This prevents cancer cells from replicating their DNA and dividing. Because estrogen can increase cyclin D levels—thereby enhancing CDK4/6 activity—palbociclib is combined with hormone therapy (e.g., fulvestrant or letrozole). These hormone therapies block estrogen signaling, making the combination even more effective. Clinical trials, such as PALOMA-2 and PALOMA-3, have shown that combining palbociclib with hormone therapy significantly slows disease progression and extends progression-free survival. In summary, palbociclib halts the growth of breast cancer cells by targeting a key point in the cell cycle and works best when paired with therapies that inhibit hormonal drivers of cancer growth. (Rocca, 2014) (Mangini, 2015)

1.6 Indications and Usage

Palbociclib, commercially known as Ibrance, is an oral medication used to treat hormone receptor-positive (HR+) and HER2-negative (HER2-) advanced or metastatic breast cancer. It is typically used in combination with: An aromatase inhibitor (e.g., letrozole) as a first-line endocrine-based therapy for postmenopausal women and men. Fulvestrant in cases where the cancer has progressed after previous endocrine therapy. The standard dosing involves taking 125 mg orally once daily for 21 days, followed by a 7-day break to complete a 28-day treatment cycle. When paired with an aromatase inhibitor, the hormonal therapy is continued without interruption. When used with fulvestrant, the latter is administered as a 500 mg intramuscular injection on Days 1, 15, and 29, then once monthly. Treatment continues until disease progression or intolerable side effects occur. Palbociclib's key action is to stop cancer cell division at the G1 phase, strengthening the impact of hormone therapy and significantly prolonging progression-free survival according to major clinical studies like PALOMA-2 and PALOMA-3. However, palbociclib can cause hematologic side effects—particularly neutropenia—requiring regular blood tests and, if necessary, dose adjustments or temporary discontinuation. Overall, palbociclib represents a major advancement in personalized breast cancer treatment for HR+/HER2- patients. (Gallanis, 2021)

1.7 Potential Side Effects

In case of the side effects of palbociclib , they're different from one person to another and it also depends on what other treatments you're taking with palbociclib. Taking early cautions is very important to manage the side effect better, if you have signs of infection including a temperature above 37.5C or below 36C you need to contact your doctor immediately. The common side effects may occur in 10% of the patients which means more than 10 in 100, they include:

1. Increased risk of infection: symptoms include aching muscles, feeling cold and shaking , pain or burning sensation during urination , change in temperature, cough and headache. Increased risk of infection occurs when white blood cells decline.
2. Bruising, bleeding gums or nose bleeds : as platelets help us during bleeding to clot the blood , this occurs when number platelets in blood declines. Nose bleeds or bleeding gums may occur after teeth brushing or bruises on your arms or legs which is known petechiae.
3. Loss of appetite: while receiving cancer treatment loss of appetite occurs due to various reasons,
4. Looking pale and breathless : this is called anaemia and it occurs when red blood cells decline.
5. Diarrhoea: If in one day you notice you're having 2 or more watery or loose stools than you usually do, it could be considered diarrhoea, If you have a stoma (an opening on your abdomen connected to your intestines to help waste leave your body), you might see that the output (stool or fluid) coming from it is more than normal (either in amount or frequency) .
6. Hair loss: hair loss includes eyelashes, underarms, legs, eyebrows, etc. and the hair usually grows back once the treatment is completed but it may be softer or the colour will change or it may be curlier than before.
7. Sore mouth : ulcers and mouth sores are painful so you need to keep your teeth and mouth clean , avoid acidic foods like oranges , and drink lots of water.

8. Skin problems: includes itching, dry skin and skin rash, this usually goes back to normal once treatment is finished.

For occasional side effects they usually occur between 1 to 10 patients and they include:

- Eye conditions like watery eyes , dry and blurred vision.
- Palmar plantar erythrodysesthesia
- Taste changes
- Lung problems that could be serious like shortness of breath and cough (Gupta, 2016)

1.8 Palbociclib-Induced Neutropenia

Palbociclib as a cyclin dependent kinase 4/6 (CDK4/6) inhibitor, in conjunction with endocrine therapy has greatly enhanced outcomes for patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) in advanced breast cancer . Despite this, neutropenia becomes one of the most common prevalent side effects associated with its use. Despite the benefits of palbociclib which prevents cell cycle proliferation in G1 phase , it also affects the normal cells division, especially those cells in bone marrow responsible for producing neutrophils , that's why neutropenia becomes the most common side effect of palbociclib . This adverse effect mostly occurs in the first cycle of the treatment and is both reversible and dose dependent. Especially in the early treatment cycles , patients' blood cell levels should be monitored to identify neutropenia and manage it early. This side effect is usually not harmful to patients and is temporary. Mostly dose reduction and delays of the treatment is the best option in controlling neutropenia .

A retrospective study with 78 breast cancer patients detected that patients with no use of statins and higher body mass index (BMI) are more likely predictors for developing severe neutropenia. In Particular, patients with a BMI of 22.3 kg/m² or higher were more likely to have grade 4 neutropenia. These findings suggest that when assessing the risk of palbociclib-induced neutropenia patient-specific factors should be considered, such as BMI and concurrent medications . Clinicians should consider these factors when planning the treatment. (Kanbayashi, 2021)

1.9 Monitoring and Management Strategies of neutropenia caused by palbociclib

Neutropenia is a pretty common side effect when patients are treated with palbociclib. It mainly happens because the drug doesn't just slow down cancer cells — it also affects healthy cells in the bone marrow that are responsible for making blood cells. Thankfully, the kind of neutropenia caused by palbociclib is different from what we usually see with traditional chemotherapy. It's typically reversible, doesn't seem to get worse with time, and most importantly, it rarely leads to serious infections. To keep things under control, doctors usually check the patient's blood count before starting treatment, then again every couple of weeks during the first two cycles, and later about once a month. If a patient shows any signs of infection, like a fever or chills, they need to get their blood checked straight away. When neutropenia shows up, the way it's handled really depends on how bad it is. If it's mild, treatment usually keeps going as normal, with just closer monitoring. If it gets a bit more serious but there's no fever or infection, doctors might still continue the drug but keep a much closer eye on things. On the other hand, if there's a fever or if the neutrophil count drops really low, the safest move is to pause palbociclib until the blood counts recover, when restarting, it's common to lower the dose - usually from 125 mg down to 100 mg, or even to 75 mg if needed, also medications like G-CSF, which help boost white blood cell production, aren't used routinely with palbociclib, but they can be considered if a patient has a serious infection or isn't bouncing back well, another important piece is making sure patients know what to watch for things like a sudden fever or feeling unusually tired so they can get help early if needed, overall, with regular monitoring and a few adjustments when necessary, most patients can stay on palbociclib and continue getting the full benefits of treatment without running into major problems.

1.10 Significance of the Study

Significance of studying the side effects of Palbociclib in breast cancer treatment

Palbociclib, a cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor, has significantly advanced the treatment landscape for hormone receptor-positive, also HER2-negative (HR+/HER2-) advanced or metastatic breast cancer, also it is typically used in combination with endocrine therapies such as letrozole or fluvastatin, while its efficacy in prolonging progression-free survival is well-documented, understanding and managing its side effect profile is critical for optimizing patient outcomes and quality of life.

The importance of studying Palbociclib's adverse effects lies in several key areas:

1. High incidence of hematologic toxicities:- Neutropenia is the most frequently reported adverse event, occurring in up to 80% of patients, though often asymptomatic, it may increase the risk of infections and necessitate dose modifications or interruptions (Cristofanilli M. T.-r.-p.-n., 2016) (Finn, Palbociclib and letrozole in advanced breast cancer, 2016), also monitoring hematologic parameters and understanding the clinical implications of such events are vital for safe administration.
2. Impact on treatment adherence and continuity:- Side effects like fatigue, nausea, and leukopenia may lead to decreased adherence or early discontinuation, thereby reducing the treatment's effectiveness, insight into tolerability helps clinicians implement supportive care strategies (Go, 2024)
3. Patient quality of life:- As many patients with HR+/HER2- breast cancer live with metastatic disease for extended periods, long-term management is essential, also Chronic toxicities from Palbociclib may affect patients' physical and emotional well-being, underscoring the need for patient-centered care approaches (Rugo, 2019).
4. Interindividual variability and predictive biomarkers:- Understanding adverse effects can help identify patient subgroups at higher risk and develop predictive biomarkers, enabling more personalized therapy (Turner, 2018)

5. Combination therapy considerations: As Palbociclib is used in combination regimens, the cumulative side effect burden must be evaluated to avoid compounding toxicities from multiple agents, thus studying Palbociclib's side effects is not only essential for patient safety but also for optimizing therapeutic strategies, improving adherence, and enhancing long-term outcomes in breast cancer care. (Cristofanilli, 2016) (Finn, Palbociclib and letrozole in advanced breast cancer, 2016)

1.11 Problem Statement

Palbociclib is a relatively new addition to the treatment options available at Hiwa Hospital, specifically used for patients with stage IV hormone receptor-positive, HER2-negative breast cancer, while it offers promising results in slowing disease progression, one of its most common and concerning side effects is neutropenia a drop in white blood cells that can leave patients more vulnerable to infections, also the challenge, however, is that neutropenia often develops without any noticeable symptoms, making it hard to detect unless routine blood tests are done.

During our research, we discovered that many patients were unaware they had developed neutropenia and did not understand the potential risks it carries, so this lack of knowledge not only increases the chance of unnoticed infections but also makes it difficult for us, as pharmacists, to collect accurate data about symptoms or complications they may have experienced, when patients don't know what neutropenia is or that they even have it, it becomes harder to evaluate how common or severe the issue really is.

As pharmacists, we have an important role in monitoring treatment safety, adjusting doses, and educating patients, but given that palbociclib is still relatively new in our region, many patients and even some healthcare staff are unfamiliar with the side effects and how to manage them. This situation limits our ability to provide proper support and intervention. It also highlights the need for more research into how palbociclib affects our local patient population, and how we as pharmacists can better support them through education, monitoring, and follow-up care..

1.12 Aim and Objectives

The aim of this research is to analyze the effectiveness and also role of Palbociclib as a targeted therapy in treatment of both HR+/HER2- breast cancer , by focusing on its use at Hiwa Hospital. And another aim of this research is show how Palnociplib works and how it can improve the patient's outcomes also shows how it is being used in the real life settings in our region.

Objectives:

1- To describe how palbociclib works in the body

By including its mechanism of action, how it can target specific proteins like CDK4/6 in cancer cells by blocking and stopping them from growing .

2-To evaluate the clinical benefits and side effects of Palbociclib by looking at how well Palbociclib slows down the progression of the disease and improves the survival rates. And also we will review the common side effects of Palbociclib for example it causes neutropenia and fatigue , and how can the patient manage them.

3- To assess how patients in Hiwa Hospital react and respond to Palbociclib by focusing on collecting then analyzing the patient's outcomes for instance how long the cancer cells stayed under control and how well the patients can tolerated to the treatment

4- To analyze the availability of Palbociclib in Sulaymaniyah by checking the hospitals and pharmacies presence of Palbociclib, and whether it is financially associated with obtaining the medication. The main goal is to understand the barriers that cause limitations in the treatment used in the region.

Chapter two : literature review

Literature Review: Palbociclib-Induced Neutropenia and Its Side Effects

Introduction

Palbociclib (brand name Ibrance) has emerged as a key player in the treatment of hormone receptor-positive (HR+), HER2-negative breast cancer. This drug is a selective inhibitor of cyclin- dependent kinases 4 and 6 (CDK4/6), and by blocking these enzymes, it disrupts the cell cycle and hinders the growth of cancer cells, also approved as part of combination therapies with endocrine drugs like letrozole, palbociclib has proven to be particularly effective for patients with advanced or metastatic disease. The PALOMA-1 and PALOMA-3 trials were pivotal in demonstrating its ability to improve progression-free survival (PFS) and overall survival (OS) for these patients (Finn et al., 2015; Cristofanilli et al., 2016).

Despite its clinical benefits, the drug's safety profile does raise concerns, with neutropenia being one of the most commonly observed side effects, also neutropenia, which refers to a decrease in neutrophils (a type of white blood cell), can increase the risk of infections, making its management crucial for maintaining patient safety during treatment, so this review explores the mechanisms behind palbociclib-induced neutropenia, its clinical management, and how patients can be effectively monitored and treated.

Incidence and severity of neutropenia with Palbociclib

Neutropenia is the most frequently reported adverse effect in palbociclib-treated patients, particularly during the early stages of treatment, also in clinical trials like PALOMA-3, about 54% of participants experienced grade 3 or 4 neutropenia, with the incidence being highest in the first treatment cycle (Finn et al., 2015; Cristofanilli et al., 2016), importantly while neutropenia is common, severe cases are often short-lived, with most patients experiencing a return to normal neutrophil levels during treatment breaks, so this finding points to the transient nature of palbociclib-induced neutropenia, in contrast to the prolonged myelosuppression commonly seen with traditional chemotherapy (Verma et al., 2016).

Interestingly, although neutropenia is frequent, the development of febrile neutropenia—an emergency that can be life-threatening remains relatively rare in palbociclib-treated patients, so this is in stark contrast to more aggressive chemotherapies, where febrile neutropenia can be a significant concern, in fact in the pivotal trials, only about 1-2% of patients developed febrile neutropenia (Finn et al., 2015; Verma et al., 2016), so this lower rate suggests that the neutropenia caused by palbociclib is less severe and more manageable compared to that caused by traditional chemotherapy regimens

The Biological Mechanism Behind Neutropenia

Understanding why palbociclib leads to neutropenia requires a look at its molecular action. CDK4/6 inhibitors, including palbociclib, work by halting the cell cycle in the G1 phase, preventing cancer cells from progressing to the S phase where DNA replication occurs, so this mechanism, while effective at controlling cancer cell growth, also affects normal, healthy cells that are actively dividing, including those in the bone marrow, where neutrophils are produced, so by arresting the cell cycle in hematopoietic stem and progenitor cells, palbociclib disrupts the production of new neutrophils, leading to a drop in neutrophil counts.

This form of neutropenia is typically reversible, in most cases, a temporary interruption in treatment or a reduction in dose allows neutrophil counts to recover, which is a key difference between palbociclib and traditional chemotherapy agents that cause prolonged myelosuppression (Sun et al., 2017), what's more, palbociclib's neutropenia is typically non-cumulative, meaning the severity tends to diminish over time as the body adapts to the drug, provided there are no additional complicating factors such as infections or concurrent treatments.

Management of Neutropenia in Clinical Practice

Managing neutropenia in patients undergoing palbociclib treatment involves a combination of close monitoring and intervention when necessary, also the drug is usually administered in a 28-day cycle, consisting of 21 days of treatment followed by 7 days off, so this cycle allows for a recovery period during which neutrophil levels can return to normal, also for patients who develop significant neutropenia, dose reductions or interruptions are common approaches, so these modifications are typically effective in restoring neutrophil levels without the need for aggressive interventions (Verma et al., 2016; Behl et al., 2021).

Unlike in chemotherapy, where granulocyte-colony stimulating factors (G-CSF) may be routinely used to stimulate white blood cell production, the use of G-CSF in patients taking palbociclib is less common, also the neutropenia seen with palbociclib is generally not severe enough to require G-CSF therapy, and most patients can continue their treatment with simple dose adjustments (Hu et al., 2016), so this makes the management of palbociclib-induced neutropenia less complex compared to traditional chemotherapy-induced neutropenia, where more intensive interventions are often required.

However, it's still critical for healthcare providers to closely monitor neutrophil counts during the first few cycles of palbociclib treatment, particularly because neutropenia is most common early on, also blood tests are typically performed every two weeks during the initial phases of treatment to ensure early detection of neutropenia, allowing for timely adjustments to the treatment plan (Ham et al., 2020).

Risk Factors for Severe Neutropenia

Certain patient characteristics can increase the risk of developing severe neutropenia while on palbociclib, for example, older patients may have a higher likelihood of developing neutropenia due to decreased bone marrow reserve, similarly, patients who have undergone prior chemotherapy are more likely to have a compromised bone marrow and thus a heightened risk of neutropenia (Turner et al., 2018), also low baseline white blood cell counts are another risk factor, as these individuals may have less capacity to withstand the suppressive effects of palbociclib on neutrophil production (Verma et al., 2016).

Furthermore, genetic factors can also play a role in how a patient metabolizes palbociclib. Variations in certain enzymes, such as those in the cytochrome P450 family, can affect how the drug is processed in the body, potentially leading to higher concentrations and an increased risk of neutropenia (Sun et al., 2017), also pharmacogenomic research is beginning to show promise in identifying patients who may be at higher risk for severe neutropenia, allowing for more personalized treatment plans (Qi et al., 2024).

Comparison with Other CDK4/6 Inhibitors

Palbociclib is one of three CDK4/6 inhibitors approved for the treatment of HR+/HER2– breast cancer, alongside ribociclib and abemaciclib, although these drugs share a similar mechanism of action, they differ in their side effect profiles, also ribociclib, for instance, is associated with a higher risk of cardiovascular issues, including QT prolongation, which is not typically seen with palbociclib, meanwhile, abemaciclib is more likely to cause gastrointestinal side effects such as diarrhea, which is generally not a major issue with palbociclib (Sledge et al., 2017).

In terms of neutropenia, palbociclib is associated with a higher incidence compared to ribociclib and abemaciclib, however, as mentioned earlier, the neutropenia associated with palbociclib is often mild to moderate and typically resolves after dose adjustments or treatment breaks (Costa et al., 2017), for this reason, while palbociclib has the highest rate of neutropenia among the CDK4/6 inhibitors, it also has the lowest incidence of febrile neutropenia, making it somewhat safer in that regard (Sledge et al., 2017).

Conclusion and Future Directions

Palbociclib continues to be a cornerstone in the treatment of HR+/HER2- breast cancer, providing significant improvements in patient outcomes when used in combination with endocrine therapy. While neutropenia remains a key concern, it is generally manageable and is not as severe or persistent as the neutropenia seen with traditional chemotherapies. Also, as the understanding of CDK4/6 inhibitors evolves, efforts to identify biomarkers that predict neutropenia risk will likely lead to more personalized and effective management strategies. With ongoing research, the clinical use of palbociclib will continue to improve, balancing efficacy with safety and minimizing the impact of neutropenia on patient care.

Chapter Three: Research Methodology

3.1 Study Design and Setting

This research was carried out as a retrospective observational study, also we collected all our data at Hiwa Hospital in Sulaymaniyah, Iraq, which is one of the main centers for cancer treatment in the region, also the purpose of our study was to focus on the side effects experienced by patients with stage IV breast cancer who were treated with palbociclib.

To gather the information we needed, we used two main approaches, first we went through patient files at the hospital to review their medical histories and treatment records, second we contacted the patients directly by phone to ask them some additional questions, mainly about side effects they might have experienced but were not recorded in their hospital files.

Throughout the whole process, we were guided and supported by Dr. Rozhan, who helped us understand how to properly collect the information and interact with patients respectfully. She also made sure that we followed the correct procedures when handling sensitive data.

3.2 Study Participants

In our study, we included patients who had been diagnosed with stage IV breast cancer and had received palbociclib as part of their treatment at Hiwa Hospital. We mainly focused on patients whose medical information was available either through hospital records or direct communication. We collected basic information such as phone numbers, ages, and places of residence, so we could easily reach out to them later. To get a better understanding of their experience with palbociclib, we called the patients and asked them a set of prepared questions, which are included in the annex of our project. We also planned to review their hospital files using their patient codes, allowing us to access their full medical history while keeping their identity confidential. We also noted important details such as any comorbidities (other health conditions) they had, to better understand how these factors might influence side effects.

3.3 Inclusion Criteria

1. Patient diagnosed with breast cancer :stage 4
2. Gender: male and female
3. Age: patients age between 35 to 70
4. Patients visited from 2021 and beyond
5. Patients who received palbociclib as a part of their treatment
6. Patients whose medical records where available for review in the hospital files
7. Patients who had valid contact in (address and phone numbers)
8. Patients who agreed to participate and share additional

3.4 Exclusion Criteria

1. Patients who were treated for breast cancer stages I, II, or III (early stages).
2. Patients who did not receive palbociclib during their treatment.
3. Patients with incomplete or missing medical records.
4. Patients who were unreachable by phone or who refused to participate.
5. Patients who had other types of cancer besides breast cancer.
6. Patients age below 35 years old or above 70 years old

3.5 Sample Selection

We selected patients who had been diagnosed with stage IV breast cancer and had received palbociclib at Hiwa Hospital. With the guidance of our supervisor, Dr. Rozhan, we first identified participants will be recruited from healthcare facilities in sulaymaniyah

Only patients who agreed to share information were included in the study.

Sample size will be determined based on statistical considerations to ensure representative

3.6 Data Collection

We used two main methods to collect data for our research. The first was by reviewing clinical records at Hiwa Hospital, where we gathered information about each patient's medical history, details about their treatment, and any side effects that had been documented while they were taking palbociclib. We accessed patient files by using their assigned hospital codes to maintain privacy and confidentiality.

The second method involved telephone interviews with the patients themselves. We called them to collect more detailed information, especially about any side effects that might not have been noted in their medical files. We followed a set of questions we had prepared beforehand (included in the annex of our project), covering areas like neutropenia complications, symptoms, how long the symptoms lasted, recovery, and any treatments they received for the side effects.

In addition to reviewing clinical notes and speaking to patients, we also collected relevant laboratory test results (such as blood counts) whenever available in their records, to get a clearer picture of the clinical effects palbociclib had on them.

3.7 Symptom Patterns and Severity

As part of our research, we reached out to breast cancer patients from Hiwa Hospital who had been treated with Palbociclib, as well as using a carefully prepared set of questions, we carried out phone interviews to learn more about the side effects they experienced, also the questionnaire focused on symptoms often linked to this medication, including tiredness, low white blood cell count, nausea, hair loss, infections, emotional changes like anxiety or depression, and digestive problems.

Speaking directly with the patients allowed us to gather valuable, real-life insight into how they were affected by the treatment, also many shared their experiences in detail, which helped us understand not only what symptoms they faced, but also how serious those effects were such as whether they had to stop the medication, reduce the dose, or were admitted to the hospital, also combining this patient feedback with medical records has given us a more complete picture of Palbociclib's side effect profile in actual practice

3.8 Diagnostic Tests

In this study, we will examine Complete Blood Count (CBC) results from the medical records of patients treated with Palbociclib at Hiwa Hospital. This test is essential for monitoring neutropenia, a condition where white blood cell levels, especially neutrophils, become too low. Neutropenia is a well-known side effect of Palbociclib and can increase the risk of infections.

We will focus on the neutrophil counts recorded during treatment to determine how often and how severely neutropenia occurred. These lab findings will then be compared with the information shared by patients during our phone interviews. For example, we will look at whether any symptoms or treatment changes—like dose reductions or temporary stoppages—were linked to low blood counts.

By combining medical records with patient-reported experiences, we hope to gain a clearer picture of how this side effect appears and is managed in real-world settings

3.9 Medication Analysis – Dosage variations and their impact on side effects.

During our study, we also paid close attention to how different dosages of palbociclib affected the side effects experienced by the patients. Although most patients started with the standard dose that is used here in Hiwa hospital which is 125mg , most of them needed their treatment to be delayed over time because of how their bodies reacted to the medication.

We made sure to record any dose adjustments by reviewing the patients' treatment histories in their hospital files. We also asked patients during phone interviews if they remembered any

changes to their medication dose. This helped us understand whether the side effects were more common or more severe in patients who received the same doses compared to those who were delayed of the treatment of palbociclib.

By looking at these patterns, we hope to better understand the relationship between palbociclib dosage and the likelihood or severity of side effects.

3.10 Assessment of Side Effects

- We categorized the side effects based on the body systems they affected. We mainly focused on hematological toxicity including Neutropenia (low white blood cell count).
- We paid attention to the timing, severity, and duration of neutropenia side effect.

3.11 Data Analysis

To analyze the data we gather, we will follow these steps:

- Organize the Data:

The first step will be to compile all the information from the patient interviews and medical records. We'll use tools like Microsoft Excel or SPSS to organize the data in an easy-to-understand way.

- Count and Calculate Percentages:

Next, we'll count how many patients experienced each side effect and then calculate the percentages to figure out which side effects were most common.

- Examine Treatment Adjustments:

We'll also look at how often patients had to lower their medication dose, pause treatment, or visit the hospital because of side effects, so this will help us understand how severe the side effects were.

- Compare Different Groups:

If necessary we'll compare different patient groups- such as older versus younger patients, to see if certain factors are linked to more side effects or changes in treatment.

- Identify Patterns and Insights:

Finally, we'll take all of this information, and look for any patterns that can help us better understand how palbociclib affects patients in real world settings

3.12 Ethical Considerations

This retrospective study, which focuses on the side effects of Palbociclib in patients with stage 4 breast cancer, was carried out with careful attention to ethical principles, especially regarding patient consent and confidentiality, so prior to collecting any personal or clinical information, each participant was contacted by phone and provided with a clear explanation of the study's goals and scope, also verbal consent was obtained at that time, also participation was entirely voluntary, and patients were assured that they could decline or withdraw at any point without it affecting their ongoing treatment or care. To maintain confidentiality, any identifying details, such as names and contact information, were either removed or coded during the data collection process, access to medical records at Hiwa Hospital was granted under the supervision of Dr. Rozhan, following the institution's protocols, also all data collected are stored securely and are used solely for academic research purposes, in full compliance with ethical standards for medical research.

3.13 Limitations – Possible study constraints.

1.Small Sample Size: The number of patients receiving Palbociclib at Hiwa Hospital during the study period was relatively limited. This restricts the extent to which the findings can be generalized to a broader population.

2.Recall Bias: As the data were gathered through phone interviews, there is a possibility that patients may not accurately remember or fully understand all side effects they experienced—particularly in relation to medical terms like neutropenia—leading to potential inaccuracies in self-reported outcomes.

3.Incomplete Medical Records: Being a retrospective study, some medical files lacked full documentation, especially concerning long-term side effects or consistent follow-up data, which could affect the completeness of the analysis.

4.Geographical Limitation: Since the study was confined to a single institution—Hiwa Hospital—the results may not reflect differences in treatment practices or outcomes that could occur in other hospitals or regions.

5.Access Barriers: Obtaining full access to relevant medical records and timely cooperation from hospital staff was sometimes difficult, occasionally causing delays in the data collection process.

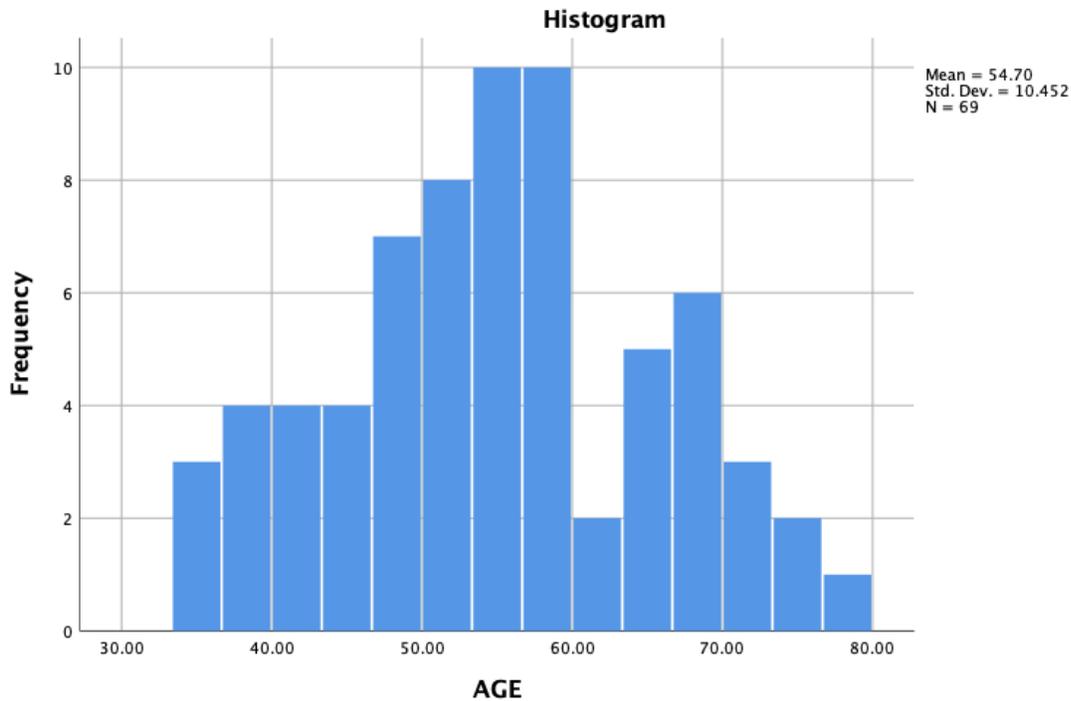
6.Patient Availability: Some patients could not be reached by phone or chose not to participate, which introduced an element of selection bias and may have influenced the overall findings

Chapter Four: Results

Table 1 : Palbociclib received in patients according to age in Sulaymaniyah city , Kurdistan , Iraq

N	AGE	
	Valid	69
	Missing	0
Mean		54.6995
Std. Error of Mean		1.25829
Mode		55.78
Std. Deviation		10.45218
Variance		109.248
Range		43.05
Minimum		34.74
Maximum		77.79

Figure 1: Palbociclib received in patients according to age in Sulaymaniyah city , Kurdistan , Iraq



4.1. Age distribution

The age range of the patients involved in our study was notably wide, highlighting the broad spectrum of individuals affected by breast cancer and treated with palbociclib. The youngest participant was just under 35 years old, while the oldest reached nearly 78. On average, patients were around 54 to 55 years old, which is reflected in both the mean age of 54.78 and the most commonly reported age of 55.78. A standard deviation of 10.45 tells us that while many patients were close to this average, a meaningful portion fell outside this central range—some being significantly younger or older. This spread is crucial to understanding the variability in treatment experience, as age can often intersect with other health factors. The presence of younger patients also reminds us that breast cancer is not exclusively a concern of the elderly, particularly in our setting.

Table 2 : Palbociclib received in patients according to family history of breast cancer in Sulaymaniyah city , Kurdistan , Iraq

FAMILY HISTORY

N	Valid	69
	Missing	0

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	NO	29	42.0	42.0	42.0
	YES	40	58.0	58.0	100.0
	Total	69	100.0	100.0	

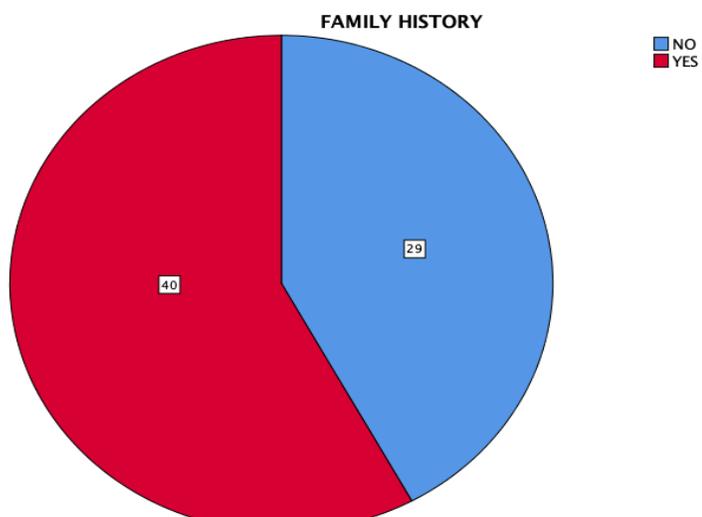


Figure 2: Palbociclib received in patients according to family history of breast cancer in Sulaymaniyah city , Kurdistan , Iraq

4.2. Family history

When looking at family history, more than half of the patients—58% to be exact—reported having a close relative who had also faced breast cancer. This data point is significant, as it underscores the hereditary component that is often observed with this disease. On the other hand, 42% of patients said they had no known family history, reminding us that breast cancer can and does arise in the absence of genetic links. This division between familial and non-familial cases enriches the narrative of the disease’s reach and reinforces the importance of inclusive screening practices. It also reflects a population where both genetic predisposition and sporadic cases coexist.

Table 3 : Palbociclib received in patients according to gender in Sulaymaniyah city , Kurdistan , Iraq

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	MALE	5	7.2	7.2	7.2
	FEMALE	64	92.8	92.8	100.0
	Total	69	100.0	100.0	

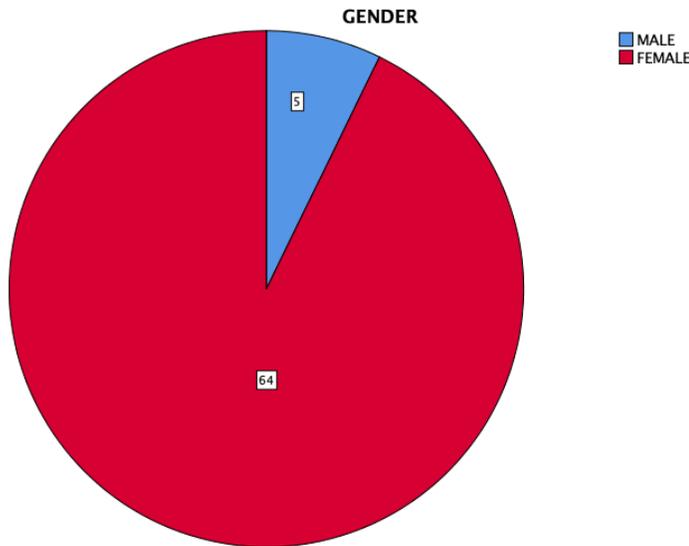


Figure 3: Palbociclib received in patients according to gender in Sulaymaniyah city , Kurdistan , Iraq

4.3 Gender Distribution

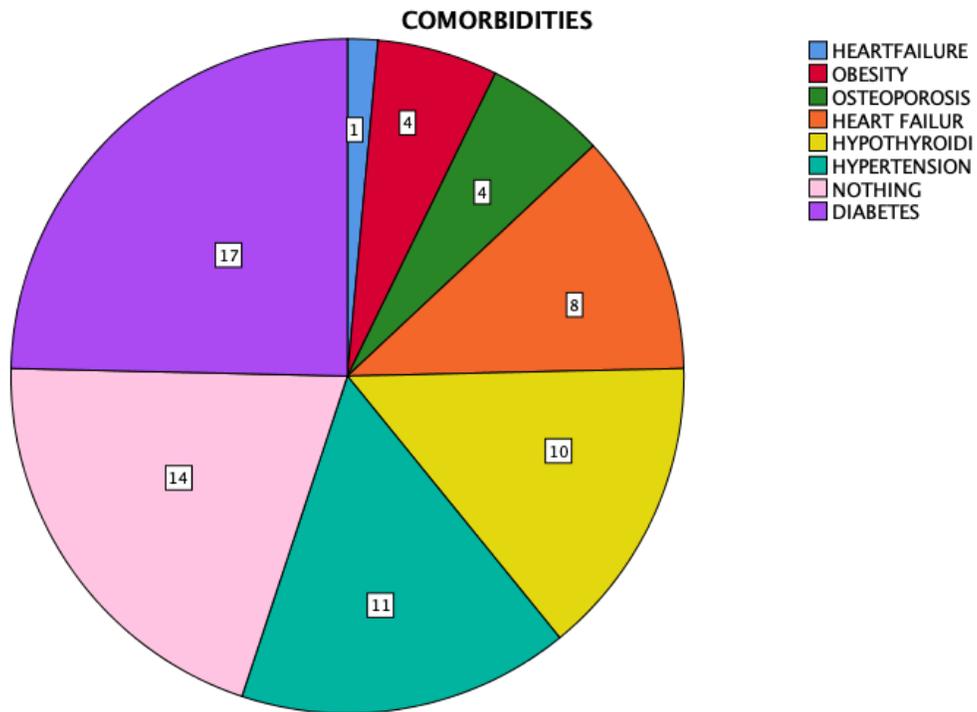
The gender distribution in our study revealed a clear predominance of female patients, with 92.8% of the sample being women. This is consistent with the fact that breast cancer is primarily a disease of women. However, our study also included five male patients, representing 7.2% of the cohort. Although the number of men in our study was small, it provides an important glimpse into the relatively understudied area of male breast cancer and the use of palbociclib in this population. Men are often excluded from breast cancer research, despite the fact that they face distinct clinical challenges when diagnosed with the disease. While our findings cannot draw firm conclusions about gender differences in palbociclib tolerability, they do highlight the need for more focused research on male breast cancer. Including male patients in future studies would help better understand how this population responds to treatment, particularly with respect to side effects like neutropenia, which may behave differently in men.

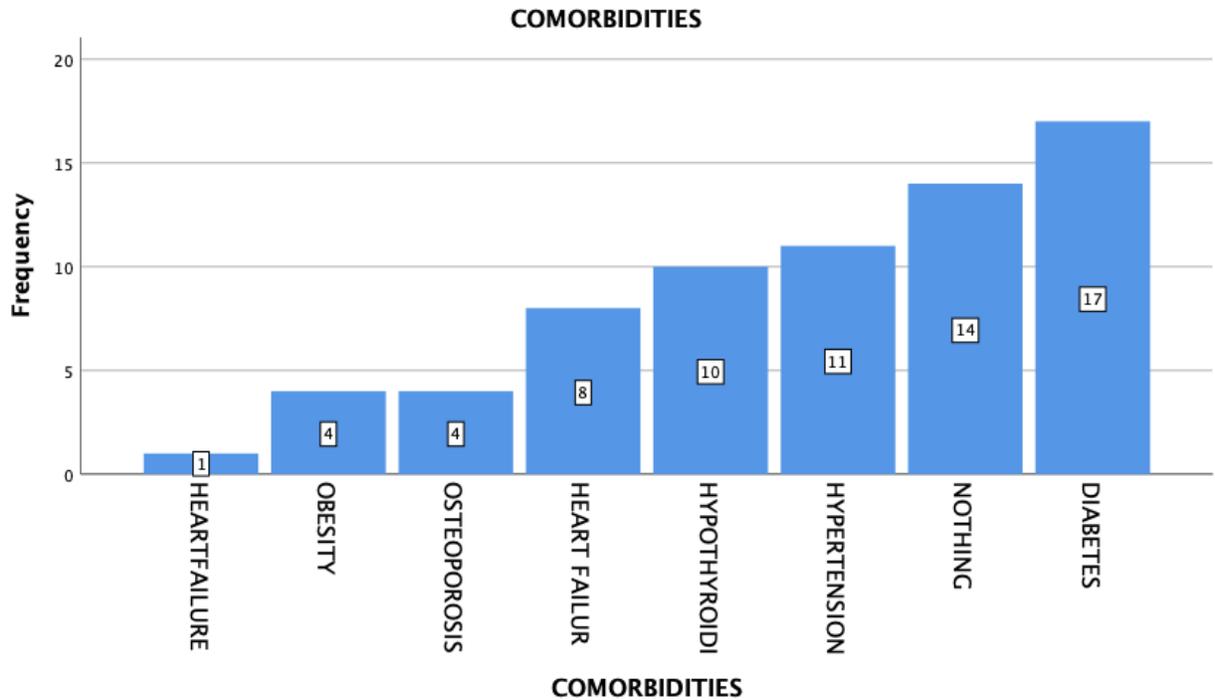
Table 4 : Palbociclib received in patients according to comorbidities in Sulaymaniyah city , Kurdistan , Iraq

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid				
OBESITY	4	5.8	5.8	7.2
OSTEOPOROSIS	4	5.8	5.8	13.0
HEART FAILUR	8	11.6	11.6	24.6
HYPOTHYROIDI	10	14.5	14.5	39.1
HYPERTENSION	11	15.9	15.9	55.1
NOTHING	14	20.3	20.3	75.4

DIABETES	17	24.6	24.6	100.0
Total	69	100.0	100.0	

Figure 4: Palbociclib received in patients according to comorbidities in Sulaymaniyah city , Kurdistan , Iraq





4.4 Comorbidities in the Patient Population

Lastly, we observed that many patients in our cohort had comorbidities, with diabetes mellitus being the most commonly reported, affecting 23.2% of patients. Hypertension, hypothyroidism, and other chronic conditions were also present, either individually or in combination. These comorbidities are important because they can complicate treatment, making it harder to determine whether symptoms are related to palbociclib or underlying health conditions. For instance, diabetes can weaken the immune system, potentially worsening neutropenia, while hypertension and hypothyroidism can contribute to symptoms like dizziness and fatigue. The presence of multiple comorbidities means that oncologists must work closely with other specialists to ensure that patients are receiving the most comprehensive care possible. A multidisciplinary approach to treatment, where oncologists collaborate with internists and other specialists, is essential for managing both cancer and the patient’s overall health. Our study highlights the importance of considering comorbidities when assessing treatment safety and tolerability, as they can significantly influence the outcome of cancer therapies like palbociclib.

Table 5 : Palbociclib received in patients according to neutropenia occurrence in Sulaymaniyah city , Kurdistan , Iraq

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	NO	12	17.4	17.4	17.4
	YES	57	82.6	82.6	100.0
	Total	69	100.0	100.0	

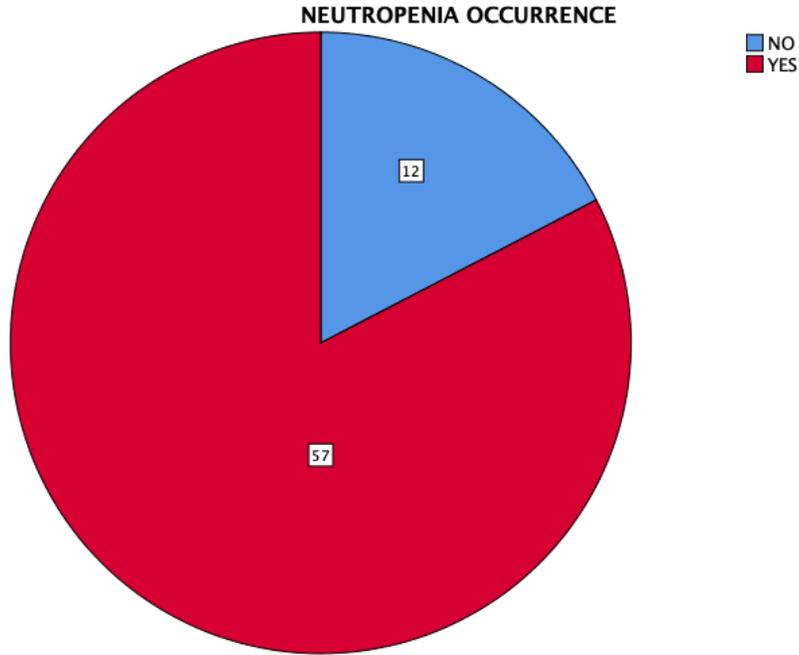


Figure 5 : Palbociclib received in patients according to neutropenia occurrence in Sulaymaniyah city , Kurdistan , Iraq

4.5 Neutropenia Occurrence

A striking result in our data was the high incidence of neutropenia among the patients taking

palbociclib. Out of 70 individuals, 57 developed neutropenia during the course of treatment. This translates to a rate of 82.6%, suggesting that this side effect is not just common but expected in the majority of cases. Only 12 patients—less than one-fifth of the cohort—avoided this condition. These numbers paint a clear picture: neutropenia is a frequent outcome in this context and one that demands close attention during therapy. It affected patients across different ages, genders, and health backgrounds, indicating that it may be a consistent effect regardless of patient profile.

Table 6 : Palbociclib received in patients according to symptoms experienced in Sulaymaniyah city , Kurdistan , Iraq

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	LOSS OF APPE	7	10.1	10.1	10.1
	MOUTH SORE	9	13.0	13.0	23.2
	ANXIETY	11	15.9	15.9	39.1
	HAIR THINING	11	15.9	15.9	55.1
	NOTHING	14	20.3	20.3	75.4
	FATIGUE	17	24.6	24.6	100.0
	Total	69	100.0	100.0	

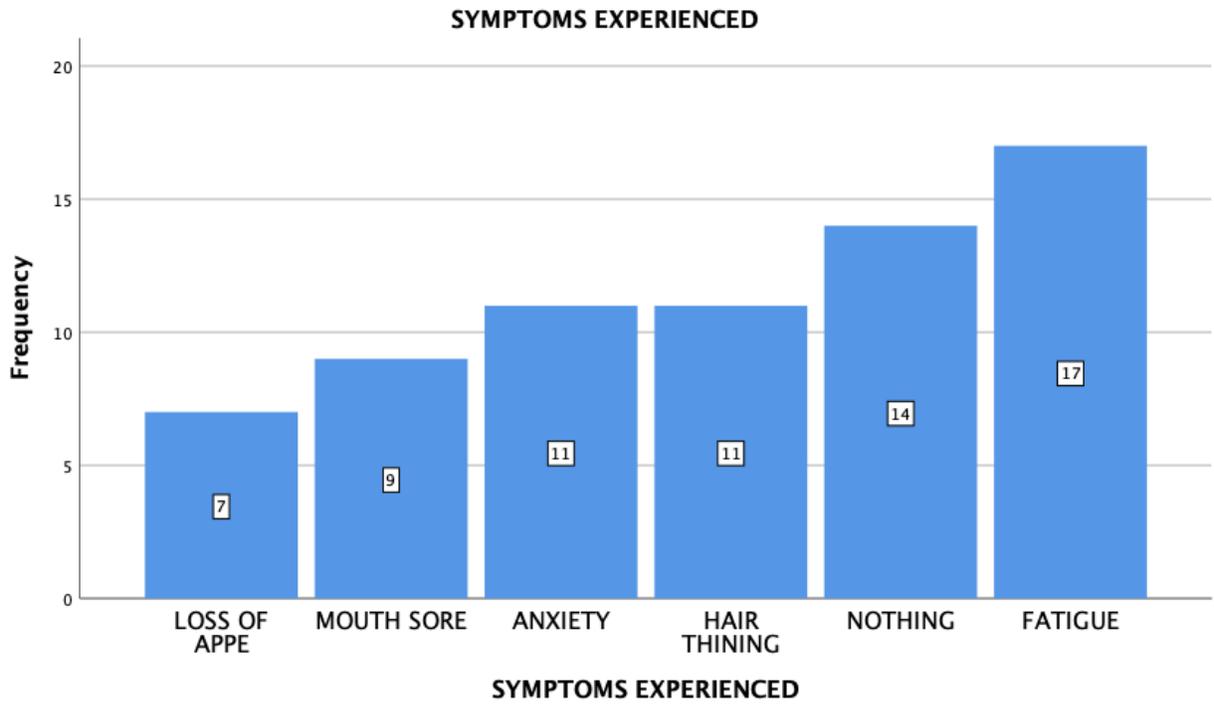
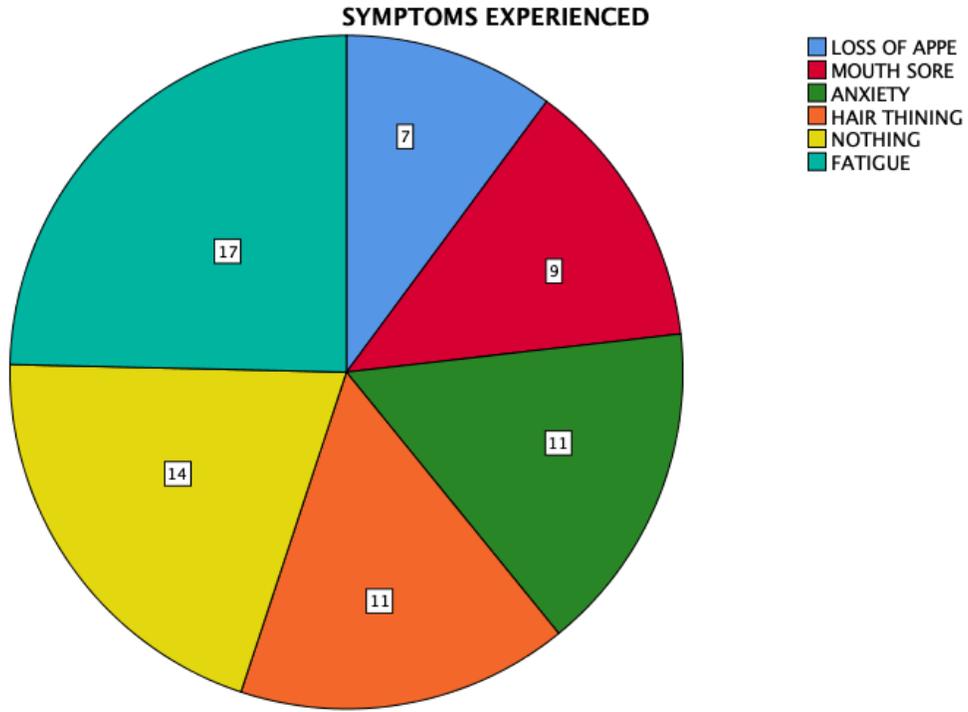


Figure 6 : Palbociclib received in patients according to symptoms experienced in Sulaymaniyah city , Kurdistan , Iraq

4.6 Symptoms experienced

Patients described a wide range of symptoms while undergoing treatment, offering a window into the lived experience behind the data. Fatigue stood out as the most commonly mentioned complaint, affecting nearly a quarter of the patients. Hair thinning and anxiety followed, each reported by 11 individuals. Mouth sores were not uncommon, noted by 9 patients, and a smaller but meaningful number experienced appetite loss. A handful reported emotional symptoms like depression, while others mentioned more physical concerns like weight loss, dizziness, or dry mouth. Interestingly, 14 patients—just over 20%—reported no noticeable symptoms at all, suggesting that for some, the treatment was better tolerated than anticipated. The variation in symptoms illustrates how diverse patient experiences can be, even when receiving the same medication

Table 7 : Palbociclib received in patients according to infection due to neutropenia in Sulaymaniyah city , Kurdistan , Iraq

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	NO	30	43.5	43.5	43.5
	YES	39	56.5	56.5	100.0
	Total	69	100.0	100.0	

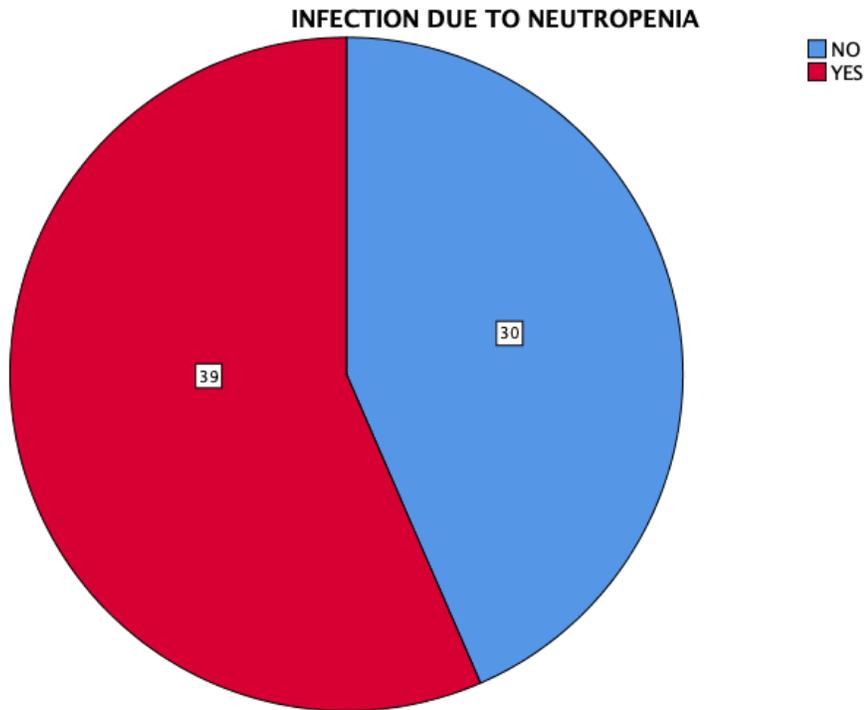


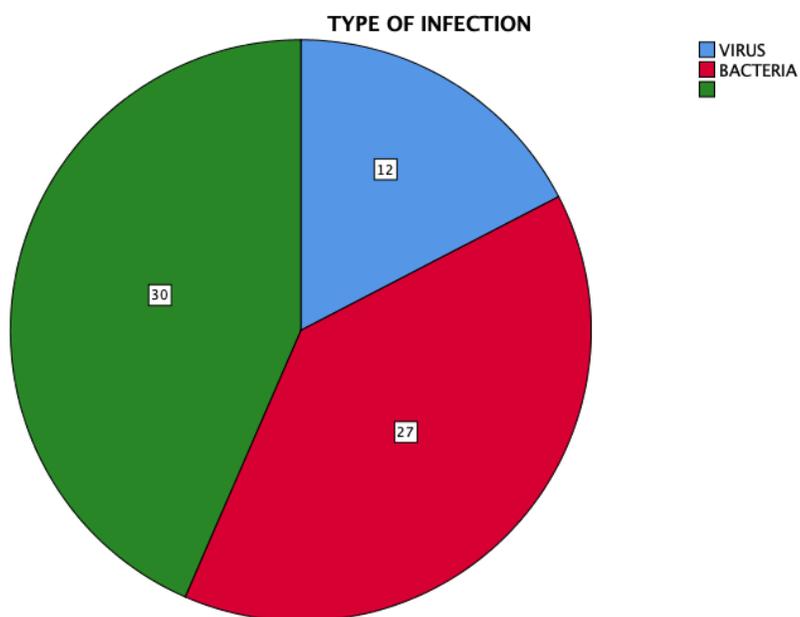
Figure 7 : Palbociclib received in patients according to infection due to neutropenia in Sulaymaniyah city , Kurdistan , Iraq

4.7 Infections due to Neutropenia

Among those who developed neutropenia, over half went on to experience infections. Specifically, 39 patients—56.5% of the full group—reported an infection occurring after the drop in neutrophil count. Meanwhile, 30 patients did not experience any infections despite becoming neutropenic. This division is telling, as it shows that while neutropenia increases the risk of infection, not every case leads to complications. Still, with more than half of the patients affected, the relationship between immune suppression and infection emerges as an important aspect of the treatment journey.

Table 8 : Palbociclib received in patients according to type of infection due to neutropenia in Sulaymaniyah city , Kurdistan , Iraq

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	VIRUS	12	17.4	17.4	17.4
	BACTERIA	27	39.1	39.1	56.5
	No infection	30	43.5	43.5	100.0
	Total	69	100.0	100.0	



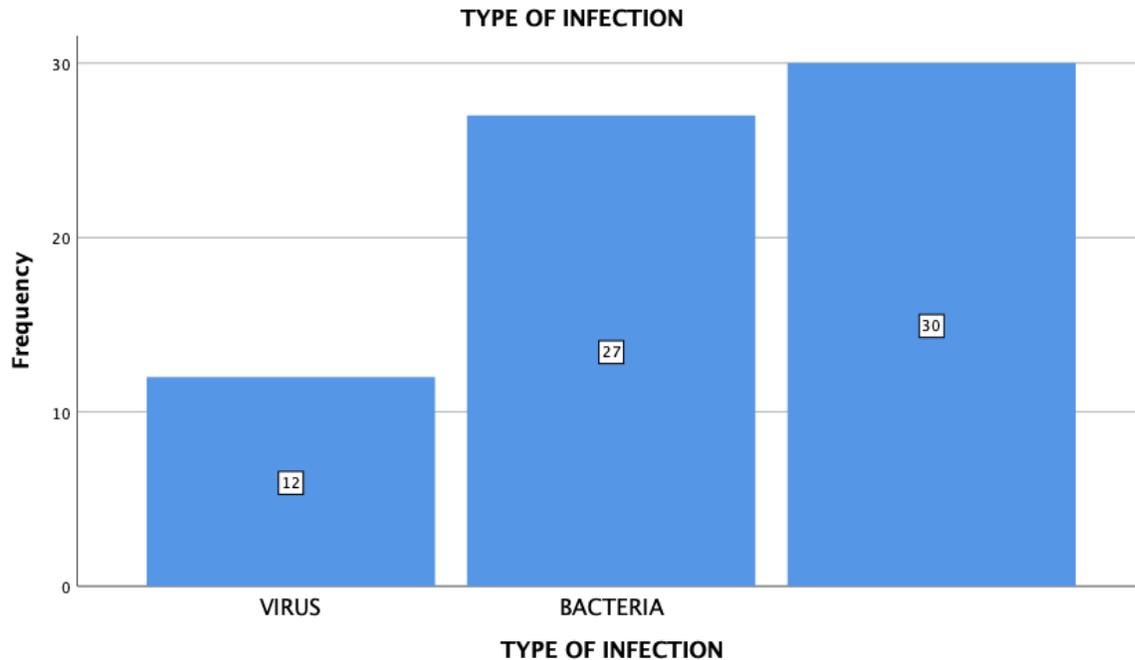


Figure 8 : Palbociclib received in patients according to type of infection due to neutropenia in Sulaymaniyah city , Kurdistan , Iraq

4.8 Types of Infections due to neutropenia

Digging deeper into the nature of these infections, we found that bacterial infections were the most prevalent. Among the total group, 27 patients—representing 39.1%—suffered from bacterial infections. An additional 12 patients (17.4%) dealt with viral infections. This distribution gives us a sense of what kinds of infections clinicians may need to watch for most closely in neutropenic patients. Meanwhile the 43.5% total of 30 patients that did not develop neutropenia . Although fungal or mixed infections were not specifically reported in this dataset, the fact that bacterial infections formed the majority aligns with known risks during neutrophil suppression.

Table 9 : Palbociclib received in patients according smoking in Sulaymaniyah city , Kurdistan , Iraq

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	YES	13	18.8	18.8	18.8
	NO	56	81.2	81.2	100.0
	Total	69	100.0	100.0	

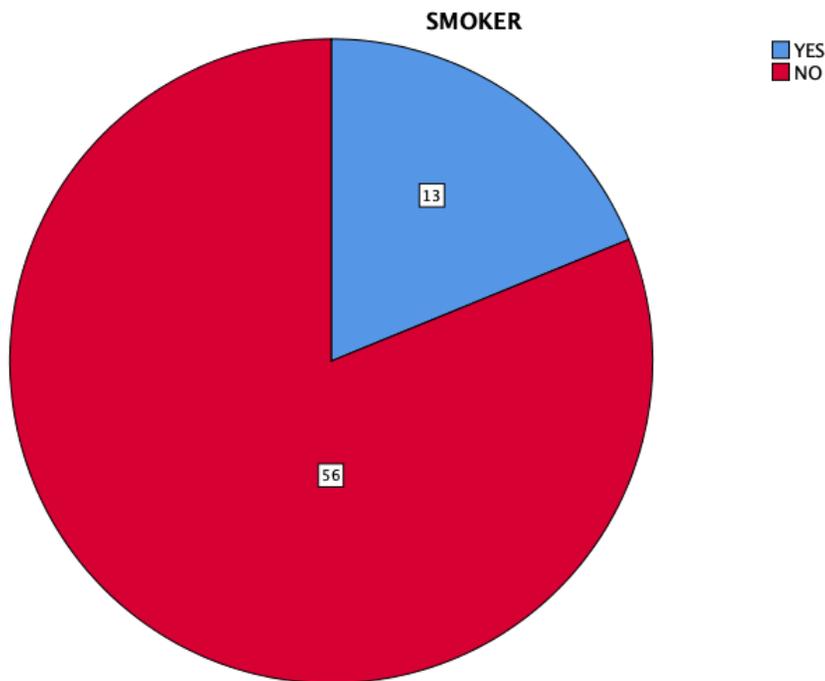


Figure 9: Palbociclib received in patients according to smoking in Sulaymaniyah city , Kurdistan , Iraq

4.9. Smoking Status of Patients

When asked about smoking, 13 patients, or just under 19% of the sample, identified as smokers. The remaining 56 patients (81.2%) reported that they did not smoke. This variable, though not central to the study's primary outcomes, adds another layer to the patient profile and may intersect with other factors affecting health and treatment response. The relatively small proportion of smokers might reflect broader health awareness among this group or simply demographic variation in the population sampled.

Chapter Five: Discussion

In this study, we aimed to explore the side effects of palbociclib in breast cancer patients at Hiwa Hospital. By analysing the medical records of 70 patients, we gained a deeper understanding of how this treatment impacts individuals with different demographic backgrounds, also our approach involved looking at a range of factors, such as the patients' age, gender, family history of breast cancer, the occurrence of neutropenia, smoking habits, the types of infections they experienced, symptoms they reported, and any comorbidities they might have had, so by taking all these variables into account, we could better understand the safety of palbociclib and how certain factors might influence its effectiveness and the way patients tolerate the treatment.

Age of patients

When we examined the age distribution of the 70 breast cancer patients receiving palbociclib at Hiwa Hospital, we found a distinct concentration in the 51-60 year age group, so this was the largest group in our study, which suggests that palbociclib is commonly used for patients in this late middle-aged category, also the next most frequent group was those between 41–50 years, while younger (30–40 years) and older (61–70 years) patients were less represented, so these findings align with general trends seen in breast cancer, where hormone receptor-positive types, particularly those responsive to CDK4/6 inhibitors like palbociclib, are most frequently diagnosed around or after menopause, so this age group is particularly relevant for analysing the side effects of palbociclib since aging is often linked to reduced bone marrow function, which can increase the risk of hematologic side effects like neutropenia. In other words, as women age, their ability to manage bone marrow stress from treatments like palbociclib may decline, making age-sensitive monitoring especially important. This helps contextualise our findings and highlights the need for strategies tailored to this group's specific health concerns.

Gender Distribution

The gender distribution in our study was overwhelmingly female, with 92.8% of participants being women. This is unsurprising, as breast cancer predominantly affects women. However, five male patients were included in our cohort, representing 7.2% of the total. While the number of men was small, this provided a unique opportunity to explore the effects of palbociclib in a much less-represented group. Male breast cancer, although rare, is important to study because it can present different clinical challenges compared to female breast cancer. The few male cases in our study, though insufficient for broad conclusions, offer a starting point for future research into how palbociclib impacts men with breast cancer, particularly regarding side effects like neutropenia. This also draws attention to the gap in knowledge surrounding male breast cancer, which is often overlooked in clinical trials and studies. Our research suggests that gender-specific factors in drug tolerability should not be ignored, and larger studies are needed to fill this knowledge gap.

Family History of Breast Cancer

Our study revealed that 58% of the patients (41 out of 70) had a positive family history of breast cancer, while the remaining 42% (29 patients) did not, so this high percentage of familial history supports the growing body of evidence that genetics plays a major role in breast cancer development, also it's possible that some of these patients carry genetic mutations, like BRCA1 or BRCA2, which can not only increase susceptibility to cancer but could also influence how patients respond to treatments like palbociclib, while we didn't directly investigate genetic mutations in our study, the presence of a family history suggests that genetic factors might affect both the effectiveness and tolerability of this drug, also incorporating genetic counseling into treatment planning might be a crucial next step for improving personalized treatment strategies, so understanding how genetic predisposition affects drug response could help oncologists better predict side effects and make treatment regimens more precise for patients with a family history of breast cancer..

Neutropenia Occurrence

One of the most significant findings from our data was the high incidence of neutropenia among the patients treated with palbociclib, also a clear 82.6% of patients (58 out of 70) experienced some form of neutropenia during treatment, so this was evident in the histogram, where neutropenia overwhelmingly dominated as the primary side effect, so this high occurrence is in line with the known mechanism of palbociclib, which inhibits the CDK4/6 pathway, essential for cell cycle progression, including the proliferation of blood cells. As a result, neutropenia is a common side effect of the drug, also the data from our study highlights how critical it is for clinicians to monitor blood counts closely during treatment, as neutropenia poses a major risk to patient health, so this side effect is not just a minor concern; it's a central issue that requires careful management to prevent serious complications like infections, so this emphasises the need for doctors to maintain proactive surveillance and be prepared to adjust treatment as needed to address neutropenia.

Smoking Status

When it comes to smoking, our study found that 81.2% of patients (57 out of 70) were non-smokers, with the remaining 18.8% (13 patients) having a history of smoking, while this distribution mirrors general population trends, it does raise interesting questions about how smoking could influence the side effect profile of palbociclib, also smoking is known to impair immune function and could potentially worsen the severity of neutropenia or increase the likelihood of infections in patients undergoing cancer treatment, although the number of smokers in our study was relatively small, it opens the door to further research on how smoking interacts with treatment toxicity, especially with neutropenia. For healthcare providers, this highlights the importance of incorporating lifestyle factors, like smoking, into routine cancer care. It also underscores the potential benefit of offering smoking cessation programs as part of comprehensive cancer treatment, as quitting smoking could potentially improve both cancer treatment outcomes and overall health.

Type of Infection

The study found that bacterial infections were the most commonly reported infections among patients on palbociclib, affecting 39.1% of those who developed infections. Viral infections were much less common, accounting for just 17.4% of cases. These results are in line with clinical expectations, as neutropenia increases susceptibility to bacterial infections, particularly when the body's ability to fight off infections is compromised. This finding has important clinical implications for managing febrile neutropenia, a condition that occurs when neutropenia is coupled with a fever, often caused by bacterial infections. Our study's results emphasise the importance of rapidly identifying bacterial infections and starting appropriate antimicrobial therapy. The relatively low rate of viral infections might be attributed to effective immunisation protocols or underreporting, but it also suggests that bacterial infections are a much greater concern for clinicians treating neutropenic patients with palbociclib. Therefore, early intervention with broad-spectrum antibiotics is crucial, and physicians must remain vigilant for signs of bacterial infections in neutropenic patients.

Infections Due to Neutropenia

Our study also found that 56.5% of patients who developed neutropenia went on to experience infections, showing a clear link between the two, while this does not mean that every patient with neutropenia will inevitably develop an infection, it does indicate a significantly higher risk, so this reinforces the importance of monitoring neutropenic patients for signs of infection and taking preventive measures when necessary, not all neutropenic patients in our study developed infections, suggesting that the severity of neutropenia can vary, with some patients experiencing mild forms that don't progress to infection. This variability in patient response underscores the importance of individualised care, for some, prophylactic antibiotics or growth factor support may be necessary to reduce the risk of infections, so our findings stress that neutropenia management should not only focus on monitoring blood counts but also on preventing infections, which can have serious consequences for patient health.

Symptoms Experienced by Patients

When it comes to the symptoms experienced by patients, fatigue was by far the most commonly reported side effect of palbociclib, followed by hair thinning and anxiety, also other symptoms included mouth sores, dry mouth, loss of appetite, dizziness, depression, and weight loss, while a subset of patients reported no symptoms at all, the wide range of symptoms highlights how differently patients respond to treatment. Fatigue, in particular, is a well-documented side effect of many cancer treatments and is known to significantly reduce quality of life, also hair thinning, while often seen as a minor issue, can have a significant psychological impact, particularly on female patients, also anxiety and depression, even though less commonly reported, are also significant concerns as they can affect a patient's mental health during the gruelling course of cancer treatment, so these symptoms reflect the need for a holistic approach to care, which includes not just addressing physical symptoms but also supporting mental health, also a comprehensive care plan that includes symptom management, nutritional support, and psychosocial counselling can go a long way in improving the overall well-being of patients undergoing palbociclib treatment..

Comorbidities in the Patient Population

Lastly, we observed that many patients in our cohort had comorbidities, with diabetes mellitus being the most commonly reported, affecting 23.2% of patients, also hypertension, hypothyroidism, and other chronic conditions were also present, either individually or in combination, so these comorbidities are important because they can complicate treatment, making it harder to determine whether symptoms are related to palbociclib or underlying health conditions, for instance, diabetes can weaken the immune system, potentially worsening neutropenia, while hypertension and hypothyroidism can contribute to symptoms like dizziness and fatigue. The presence of multiple comorbidities means that oncologists must work closely with other specialists to ensure that patients are receiving the most comprehensive care possible, also a multidisciplinary approach to treatment, where oncologists collaborate with internists and other specialists, is essential for managing both cancer and the patient's overall health, also our study highlights the importance of considering comorbidities when assessing treatment and tolerability, as they can significantly influence the outcome of cancer therapies like palbociclib.

Chapter Six: Conclusion and Recommendations

6.1 Conclusion and recommendation

The findings of this research offer a meaningful contribution to the growing body of literature surrounding the clinical use of Palbociclib in advanced breast cancer treatment, particularly in the context of a developing healthcare environment like Sulaymaniyah, through retrospective analysis and direct patient engagement, the study reveals that neutropenia is the most prominent and consistent side effect associated with Palbociclib, affecting approximately 82.6% of patients receiving the treatment, also the high frequency of neutropenia aligns with the known pharmacological mechanism of CDK4/6 inhibitors, which impact not only malignant cells but also rapidly dividing hematopoietic cells in the bone marrow, despite its prevalence, the majority of neutropenia cases were manageable through dose modifications and temporary treatment interruptions, without necessitating permanent discontinuation.

Other side effects such as fatigue, hair thinning, anxiety, mouth sores, and appetite loss were also observed, reflecting a spectrum of both hematological and non-hematological toxicities, notably, a significant proportion of patients also experienced infections secondary to neutropenia, with bacterial infections being the most common type, so these findings highlight the dual challenge clinicians face in maintaining effective cancer control while minimizing treatment-associated complications.

Furthermore, the study's data collection methods, combining clinical record analysis with patient interviews, provided a robust and patient-centered view of Palbociclib's safety profile, also it emphasized the importance of patient awareness and education regarding side effects, especially those like neutropenia that may present asymptotically.

Importantly, the research uncovered that factors such as age, comorbidities, family history of breast cancer, and prior medical conditions like diabetes and hypertension may influence both the incidence and severity of side effects, also the predominance of female patients and the high rate of family history (58%) further underscore the genetic and epidemiological relevance of breast cancer in the local population, also the inclusion of male patients, although limited, draws attention to the under-recognized impact of breast cancer and Palbociclib treatment in male populations.

Overall, the results confirm that while Palbociclib remains a highly effective component of HR+/HER2- breast cancer management, it demands vigilant monitoring and personalized patient care strategies, also in clinical settings where healthcare infrastructure may be limited, the importance of clear communication, early symptom detection, and continuous laboratory surveillance becomes even more pronounced.

Recommendations

Based on the findings of this study, several key recommendations can be proposed to optimize the management of Palbociclib treatment in breast cancer patients, firstly, implementing structured monitoring protocols, especially regular complete blood count (CBC) tests during the first treatment cycles, is crucial for early detection and management of neutropenia, additionally, patient counseling should be strengthened through educational programs that inform patients about common side effects, symptoms to monitor, and the importance of adherence to follow-up visits. Tailoring dosage based on individual patient profiles such as age, BMI, comorbidities, and baseline neutrophil counts can enhance safety and treatment tolerance, also pharmacist-led clinics focusing on side effect management can further support this process by providing follow-up care and reinforcing education, also encouraging a multidisciplinary approach, including collaboration among oncologists, pharmacists, nurses, and lab staff, can ensure comprehensive care delivery, furthermore, expanding local population-based research and enhancing access to targeted therapies through policy changes are recommended to address disparities in availability and cost, and lastly, integrating genetic testing, when feasible, would allow more personalized treatment planning for patients with a strong family history of breast cancer

.6.2 Limitation of study

Despite its valuable findings, this study presents several limitations that must be acknowledged. The relatively small sample size and the fact that data were collected exclusively from Hiwa

Hospital in Sulaymaniyah limit the generalizability of the results to other populations or settings. Moreover, the retrospective design inherently depends on the completeness and accuracy of medical records, which in some cases were lacking in detail, especially regarding laboratory test results. The reliance on phone interviews for additional data introduces potential recall bias, as patients may have had difficulty remembering or articulating specific symptoms. Additionally, the study did not account for genetic or pharmacogenomic variations, such as BRCA mutations, that could influence treatment response and side effect profiles. It also excluded early-stage breast cancer patients and did not explore the effects of Palbociclib when combined with different hormonal therapies, limiting its scope. Furthermore, symptom grading was not based on standardized clinical criteria, which may affect the consistency of side effect reporting. Language and literacy barriers encountered during interviews also posed challenges to obtaining clear and accurate patient responses. These limitations should be addressed in future studies to improve the reliability and applicability of findings in similar clinical settings.

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Annex

Biography

- **Age**
- **Sex**
- **Smoking**(Yes/No,Former)
- **Family History Of Cancer:**(Yes/No,specify type)
- **Comorbidities** (e.g hypertension , diabetes , autoimmune disease)
- **Clinical Presentation Before Starting Palbociclib**

Identification of Side Effects:

- **Neutropenia occurrence:** (Yes/No)
- **Symptoms experienced:** (Fatigue, fever, infections, etc.)
- **Time to onset of neutropenia:** (After how many cycles?)
- **Did neutropenia require:**
 - Dose reduction? (Yes/No)
 - Treatment delay? (Yes/No)
 - Treatment discontinuation? (Yes/No)
 - G-CSF (granulocyte colony-stimulating factor) support? (Yes/No)

Complications of Neutropenia:

- **Infections due to neutropenia?** (Yes/No)
- **Type of infection:** (Bacterial, viral, fungal)
- **Hospitalization required?** (Yes/No)
- **Duration of hospitalization (if applicable):**
- **Antibiotic or antifungal treatment needed?** (Yes/No)

Impact on Quality of Life:

- **Did neutropenia affect daily activities?** (Yes/No)
- **Psychological impact on patient:** (Anxiety, fear of infections, treatment stress)
- **Patient's perception of treatment and side effects:**
- **Would the patient continue treatment despite side effects?** (Yes/No)