

DRUG UTILIZATION EVALUATION OF ANTICANCER DRUGS IN KARACHI

A dissertation submitted for the Degree of Masters of Philosophy



By

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CERTIFICATE

This is to certify that **Ms. Asma Khatoon D/o Syed Tameez Uddin** research work entitled **“Drug Utilization Evaluation of Anticancer Drugs in Karachi, Pakistan”** under my supervision and guidance in the Department of Pharmaceutics, Faculty of Pharmacy, Federal Urdu University of Arts and Science and Technology. Her research work is original and her thesis is worthy of presentation to the GRMC, Federal Urdu University of Arts, Science and Technology for the award of degree of Masters of Philosophy in Pharmaceutics.

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Dedication

This work is dedicated to my Mother Nasim Nilofer, my Husband Syed Zaryab Danish and My daughters (Simrah & Aghniya) who have made me stronger, better and more fulfilled than I could have ever imagined.

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List of Acronyms

5-FU	5-Fluorouracil
5-HT3	5-hydroxytryptamine 3 receptor antagonist
6-MP	6 - Mercaptopurine
ACDs	Oral Anticancer Drugs
ADRs	Adverse drug reactions
ALL	Acute lymphocytic leukemia
AML	Acute myeloid leukemia
APL	Acute Promyelocytic Leukemia
ASR	Age-standardized-rates
BSA	Body surface area
CA	Carcinoma
CCRT	Concurrent chemoradiation therapy
CINV	Chemotherapy-induced nausea and vomiting
CLL	Chronic lymphocytic Leukemia
CML	Chronic myeloid leukemia
DDIs	Drug-Drug Interaction
DLBCL	Diffuse large B-cell lymphoma
DNA	Deoxyribose nucleic acid
DUE	Drug Use Evaluation
DUR	Drug Utilization Review
EPV	Epstein–Barr virus
ER	Extended Release
FDA	Food and Drug Administration
FEC	Fluorouracil + Epirubicin + Cyclophosphamide
GC	Gastric Cancer
GIT	Gastrointestinal Tract
HER2	Human epidermal growth factor receptor 2
HNC	Head and Neck Cancer

HOME	Home Oncology Medical Extension.
HPV	Human papillomavirus
HPV	Human Papilloma Virus
ICDs	International Classification of Disease
INRUD	International Network for Rational Use of Drugs,
IR	Immediate Release
KCR	Karachi Cancer Registry
LPG	lowest price generics
mCRC	Metastatic Colorectal carcinoma
MRM	Modified Radicle Mastectomy
mTOR	Mammalian Target of Rapamycin
MUE	Medication use evaluation
NCCN	National Comprehensive Cancer Network
NEDL	National Essential Drug List
NSAIDs	Nonsteroidal anti-inflammatory drug,
NSAIDs	Non-Steroidal Inflammatory Drugs
OAMs	Oral Anticancer Medications
OBs	Originator Brands
OPSCCs	Oropharyngeal squamous cell carcinomas
OPSs	Oncology pharmacy specialist
QALY	Quality-Adjusted life-years
ReDO	Repurposing Drugs in Oncology
Rx	Prescription
SOB	Shortness of breath
TDM	Therapeutic drug monitoring
Tx	Treatment
WHO EML	World Health Organization-Essential Medicine List

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ABSTRACT

Irrational drug use is a major problem all over the world. The constant elevation in the number of medicines and options of use in the treatment protocol increases the irrational medicine treatment or irrational prescription, which results in poor-patient-outcomes and much waste of money, time and resources. The effect of improper medicinal use on the healthcare system is a decline in the quality of medicine therapy which enhances morbidity and mortality, the elevated cost of therapy, and a higher risk of untoward medicinal effects such as adverse drug reactions (ADRs). Especially, in specified a developing country like Pakistan, an irrational drug prescription is a frequent obstacle where the study of drug evaluation and its use can be useful.

On realization of the significance of research on drug utilization evaluation for creating an effective, reliable, and beneficial healthcare system. Various developed countries have initiated competent drug utilization review boards to deliver information regarding drug utilization data at the national level. The study is designed to focus on the main area of a pharmacist, to facilitate cancer patients in quality care enhancement, also aid as an education contributor, and help in cost reduction with emphasis on rational therapy.

This study's objective is to evaluate rational drug use for the identification and promotion of advancement in practice, in the cancer ward of private and public sectors in Karachi.

A retrospective research-based study was conducted on patients diagnosed with Cancer in the Department of Medicine in a tertiary care hospital. The patient's files were obtained from the Medical Records Department after getting a proper ethical endorsement from the hospital Institutional Ethics Committee. A minimum no. of 164 patient records was randomly collected for the period of 6 months from the public sector and 22 patient records for 2 months from the private sector in Karachi. A modified data collection record form was used to collect the information on patients' demographics and prescribed drugs. Results were analyzed on excel 2016 and SPSS 21 and prescriptions were analyzed by WHO (World Health Organization) core drug indicators.

In both sectors, females were observed to be more susceptible to cancer than males. More than 50 diverse types of cancer were observed in the public sector, and 14 types of cancers were noted in the private sector. The most prevalent and frequently diagnosed carcinoma was cancer of the head and neck, the incidence rate in both genders was 42 (25.06%), followed by breast cancer in females 36 (21.34%).

A total of 325 cytotoxic medicines were prescribed with an average of 1.98 drugs per prescription in the public sector and 69 total medicines were prescribed in the private sector with an average of 3.13 medicines per prescription. The group alkylating agent of cytotoxic drugs was the most frequently prescribed (36.0%) in the public sector and (29.40%) in the private sector. The average number of medicines prescribed from the World Health Organization (WHO) model list of essential drugs per prescription for the public sector is 1.98 and in the private sector is 3.13 due to the combination of other drugs antibiotics per prescription was 7.30 for the public and no antibiotic had used by the private sector. Injectables prescribed were 91.46% and 92.70% respectively. According to the policy of hospital, the brand names used to prescribe chemotherapeutics drugs. The cytotoxic agents prescribed from the Essential Drug List of Pakistan were 79.07% for the public sector and 92.70% for the private sector

Keywords: Cancer, Cytotoxic drugs, Pakistan.

خلاصہ

ادویات کا غیر معقول استعمال پوری دنیا میں ایک بڑا مسئلہ ہے۔ ادویات کی تعداد اور علاج کے پروٹوکول میں استعمال کے اختیارات میں مسلسل اضافہ غیر معقول ادویات کے علاج یا غیر معقول نسخے کو بڑھاتا ہے، جس کے نتیجے میں مریض کے نتائج خراب ہوتے ہیں اور پیسے، وقت اور وسائل کا بہت زیادہ ضیاع ہوتا ہے۔ صحت کی دیکھ بھال کے نظام پر دواؤں کے نامناسب استعمال کا اثر دوائیوں کے علاج کے معیار میں گراوٹ ہے جس سے بیماری اور اموات میں اضافہ ہوتا ہے، علاج کی بلند قیمت، اور منفی دواؤں کے رد عمل (ADRs) جیسے ناخوشگوار دواؤں کے اثرات کا زیادہ خطرہ ہوتا ہے۔ خاص طور پر، پاکستان جیسے ترقی پذیر ملک میں، دواؤں کا غیر معقول نسخہ ایک بڑی رکاوٹ ہے جہاں ادویات کا صحیح استعمال کا مطالعہ مفید ہو سکتا ہے۔

ایک مؤثر، قابل اعتماد، اور فائدہ مند صحت کی دیکھ بھال کے نظام کی تشکیل کے لیے منشیات کے استعمال پر تحقیق کی اہمیت کے احساس پر مختلف ترقی یافتہ ممالک نے قومی سطح پر ادویات کے استعمال کے اعداد و شمار کے حوالے سے معلومات فراہم کرنے کے لیے ادویات کے استعمال کے جائزہ بورڈز کا آغاز کیا ہے۔ مطالعہ کو فارماسٹ کے اہم شعبے پر توجہ مرکوز کرنے، معیار کی دیکھ بھال میں کینسر کے مریضوں کو سہولت فراہم کرنے، ایک تعلیمی شراکت دار کے طور پر مدد کرنے، اور تھراپی پر زور دینے کے ساتھ لاگت میں کمی میں مدد کے لیے ڈیزائن کیا گیا ہے۔

اس مطالعے کا مقصد کراچی میں نجی اور سرکاری شعبوں کے کینسر وارڈ میں عملی طور پر پیشرفت کی شناخت اور فروغ کے لیے ادویات کے استعمال کا جائزہ لینا ہے۔ ہسپتال میں شعبہ طب میں کینسر کی تشخیص کرنے والے مریضوں پر ایک تحقیق پر مبنی مطالعہ کیا گیا۔ ہسپتال کی انسٹیٹیوٹیشنل اینڈکس کمیٹی سے مناسب اخلاقی توثیق حاصل کرنے کے بعد مریض کی فائلیں میڈیکل ریکارڈ ڈیپارٹمنٹ سے حاصل کی گئیں۔ ایک کم از کم نمبر کراچی میں 164 مریضوں کے ریکارڈ 6 ماہ کے عرصے کے لیے پبلک سیکٹر سے اور 22 مریضوں کے ریکارڈ 2 ماہ کے لیے نجی شعبے سے جمع کیے گئے۔ ایک ترمیم شدہ ڈیٹا اکٹھا کرنے کا ریکارڈ فارم مریضوں کی آبادی اور تجویز کردہ دوائیوں کے بارے میں معلومات اکٹھا کرنے کے لیے استعمال کیا گیا تھا۔ نتائج کا تجزیہ ایکسل 2016 اور SPSS 21 پر کیا گیا اور نسخوں کا تجزیہ ڈیپلو ایج او (ورلڈ ہیلتھ آرگنائزیشن) کے بنیادی منشیات کے اشارے کے ذریعے کیا گیا۔

دونوں شعبوں میں، خواتین کو مردوں کے مقابلے کینسر کا زیادہ شکار دیکھا گیا۔ کینسر کی 50 سے زیادہ اقسام سرکاری شعبے میں دیکھی گئیں، اور پرائیویٹ سیکٹر میں کینسر کی 14 اقسام نوٹ کی گئیں۔ سب سے زیادہ عام اور اکثر تشخیص شدہ سر اور گردن کا کینسر تھا، دونوں جنسوں میں واقعات کی شرح 42 (25.06%) تھی، اس کے بعد خواتین میں چھاتی کا کینسر 36 (21.34%) تھا۔

پبلک سیکٹر میں اوسطاً 1.98 ادویات فی نسخہ کے ساتھ کل 325 (سانٹوٹوکسک) کینسر کی ادویات تجویز کی گئیں اور پرائیویٹ سیکٹر میں فی نسخہ اوسطاً 3.13 ادویات کے ساتھ 69 کل ادویات تجویز کی گئیں۔ سانٹوٹوکسک ادویات کا گروپ اکانٹیننگ ایجنٹ سب سے زیادہ تجویز کردہ (36.0%) پبلک سیکٹر میں اور (29.40%) نجی شعبے میں۔ ورلڈ ہیلتھ آرگنائزیشن (ڈیپلو ایج او) کی ماڈل لسٹ سے تجویز کردہ ادویات کی اوسط تعداد پبلک سیکٹر کے لیے فی نسخہ 1.98 ہے اور پرائیویٹ سیکٹر میں 3.13 ہے جس کی وجہ دیگر ادویات اینٹی بائیوٹک کے امتزاج کی وجہ سے عوام کے لیے فی نسخہ 7.30 تھی اور نجی شعبے نے کوئی اینٹی بائیوٹک استعمال نہیں کی۔ تجویز کردہ انجیکشن بالترتیب 91.46% اور 92.70% تھے۔ ہسپتال کی پالیسی کے مطابق، کیموتھراپیٹک ادویات تجویز کرنے کے لیے استعمال ہونے والے برانڈ نام۔ پاکستان کی ضروری ادویات کی فہرست سے تجویز کردہ سانٹوٹوکسک اینجینس سرکاری شعبے کے لیے 79.07% اور نجی شعبے کے لیے 92.70% تھے۔

مطلوبہ الفاظ: کینسر، سانٹوٹوکسک ادویات، پاکستان۔

CHAPTER 1

INTRODUCTION

1 Introduction

Drug utilization pattern emphasizes the issues that occur from the usage of the drug in the delivery system of health care and focused on the existing current approaches to the use of rational drugs. (1) Prescribing pattern or system where medicines are used from EDL (essential drug list), will indicate the result of rational drug use is obtained. Recognizing a set amount of EDL will promote better supply, cost-effectiveness, and more rational use. (2) Medications in the EDL are expected should satisfy the true needs of diagnostic, therapeutic, prophylactic, and rehabilitative administrations accomplishing criteria such as risk-benefit ratios, quality cost-effectiveness, tolerance, compliance, as well as most important acceptance.

The World Health Organization (WHO) has described the drug utilization evaluation/ review research work as the marketing of drugs, their distribution, consumption, and prescription in society, with special emphasis on the consequences of medical, social, and economical results.

Drug utilization is divided into descriptive (quantitative) and analytical (qualitative) studies (3). The accentuation of past *descriptive* studies describes patterns of drug utilization and recognizes the problems in more detail and in a specific way, on the other hand, it is useful in describing the existing situation related to the trends in drug prescribing and drug use at the different stages of the health care system.

While *analytical* findings will link the data of drug utilization facts of the diseased state, quality care, and treatment outcomes, with the goal of either therapy is rational or irrational or the appropriateness of utilization of the drug. The Pharmacoepidemiology of drug utilization concerns patient condition (with age, gender, and lab tests), prescriber's (quality prescription), and the dose (effect per concentration).

Towards analyzing drug utilization data from diverse localities, it may be frequently expected to identify substantial differences that oblige further evaluation, which may be prompted the identification and promotion of further practice (4)

The sources of data on drug utilization differ from country to country depending on the complexity level of record keeping, statistics collection, reporting, analysis, and the operational concerns of the health care system.

DUE also referred to as DUR (Drug utilization review) is a structured, authorized, in-progress evaluation of prescribing, dispensing, and utilizing of medication. DUR deals with:

Review of drugs against predetermined criteria of the use, if the criteria are not followed, then changes will be applied to the drug therapy. It is a quality assurance measure, which will provide corrective actions, prescriber opinion, and further evaluations. (5)

1.1 DUR is classified into three classes

- Prospective-drug therapy reviews a patient's planned therapy prior to a medication is dispensed.
- Concurrent - ongoing monitoring of therapy during the treatment course in the institutional setting.
- Retrospective - drug therapy reviewed after the patient has completely received the medication, used to compare the high-cost drugs with the low-cost classes and monitor the pharmacotherapy recommendations for disease treatment of the same condition.(6)

1.2 Steps involved in the drug utilization study

Step 1- Selection of drugs or therapeutic areas of practice for consideration in the system.

Step 2- Design an outline of the study.

Step 3- Describe criteria and norms.

Step 4- Design the information collection form.

Step 5-Data collection.

Step 6- Estimate results.

Step 7- Impart views of the results.

Step 8- Development and execution of interventions.

Step 9- Reassess to conclude whether drug usage has improved.

Step 10-Reconsider and revise the DUE program.

Step 11- Feedback results. (5, 7, 8)

1.3 Cancer

Cancer is described as a neoplasm or tumor, which is composed of new actively growing tissues in which cell multiplication is defined as uncontrolled, progressive, or faster than normal tissues(9). It is classified in many ways, but the simplest is its origin and whether it is benign or malignant. Benign has a slow growth rate, is non-invading or nonmetastatic, and is treated by medicine, surgery, or by radiation. While malignant tumors are poorly differentiated, grow rapidly in disorganized manners, and have a massive need for nourishment. So necrosis, metastases, and invasion of neighboring tissues rapidly convert their state from a malignant tumor to cancer. According to the National Cancer Institute (NCI), cancer is a collection of related diseases in which an uncontrolled growth of abnormal cells arises anywhere in the body(10).

1.4 Global Burden of Disease

1.4.1 Mortality rate

According to the research Global Burden of Disease, 9.6 million people in the year 2017 were estimated to have *died* from numerous forms of cancer. In the realm every sixth death cause is cancer, making it the second most prominent cause of death globally – after

cardiovascular (CVS) diseases. While In 2019, the rise of the mortality rate was 0.48 million increased over two years. Pulmonary cancer persisted as the prominent cause of cancer death, estimated at 1.8m mortalities (18%), then colorectal (9.4%), hepatocarcinoma (8.3%), abdominal (7.7%), and other cancers (6.9%) (11).

1.4.2. Incidence rate

The estimated *incidence* of new cancer cases was 23.6 million globally. Breast carcinoma has outstripped lung carcinoma as the most prevalent cancer, with an estimated 2.3m new cases (11.7%), followed by pulmonary cancer (11.4%), colorectal carcinoma (10.0 %), prostate carcinoma (7.3%), and abdominal carcinoma (5.6%) (11).

1.5 Cancer in Pakistan

As cancer is a worldwide disease, there are remarkable differences in both the overall *incidence rate* of cancer and the incidence of various *types* of cancer in different countries. This ranking of most prevalent cancers was considered separately when figured for a *developed and developing country* (12). As Pakistan, is included in developing countries, so the leading causes were poverty, illiteracy, ignorance, socio-economic burden, inappropriate health system, poor diagnosis, religious beliefs, and many other factors (13).

In Pakistan, from the period of 1990-2019, the third deadly disease which causes death was cancer. The *mortalities* were 179,733, which was a pressing challenge to make progress against this disease (15,16)

In genders-wise *incidence* breast cancer (17) was the most identified cancer in Pakistan with 14.5% (32,118) patients, and same the *death rate* was 11.7% ranked first as a fatal type of cancer, while the cancer of head and neck was frequently diagnosed (9.5%) (16,959) in males in 1 lac patients over 10 years, with (9.1%) death rate due to betel nut, pan, gutka, mawa, and other prohibited materials, (18). Then lungs and gastrointestinal carcinomas were (5.9%) (10,538) and (5.7%) (10,117), due to the exaggerated use of tobacco, smoking, air pollution, family history, environmental exposure, and other toxic materials while the

increased rate of junk foods, fizzy drinks, spices, late night intake of meals, lack of physical activity, obesity, sunlight exposure were the causative reasons of other types of cancer.

It has been evident that changes in lifestyle, dietary habits, cessation of smoking, and environmental considerations of good air quality, food, and hygiene could reduce the incidence of different types of cancers by as much as 50% (11).

1.6 Cancer Categories

More than 100 types of cancer were diagnosed. Types of cancer are usually named for the organs or tissues where they appear or form. Broadly it is distinguished into major five groups

- *Carcinomas* are identified by the cells that cover internal and external body parts such as lung, breast, and colon cancer(19).
- *Sarcomas* are described as cells that are found in the bone, cartilage, fat, muscle, connective tissue, and other supportive tissues (20).
- *Lymphomas* are those cancers that are initiated in the lymph nodes and immune system tissues.
- *Leukemias* are a type of cancer that begins in the marrow of the bone and has often accumulated in the bloodstream(21).
- *Adenomas* are characterized that develop in the thyroid, parathyroid, pituitary gland, adrenal gland, and other glandular tissues. (22,23)

1.7 Cancer staging

Staging of cancer is the most important tool in defining the type, rate, and extent of spread and in determining treatment protocol. On the other hand, the prognosis of cancer can range from excellent to poor, as it is between 0-4. Higher the number of 3-4 the more aggressive the cancer case or the more extensive is the cancer in the organic structure (24)

1.8 Signs and symptoms

Signs and symptoms depend on the specific type and grade. The physical signs of cancer are local lumps or general swellings, ulcers, tender, and loss of blood from the bowel, urine, and uterus but in general, symptoms are fatigue, weight loss, pain at the site, fever, change in bowel habit, cough, etc (22,23,25).

1.9 Treatments of cancer

The cancer treatment protocols depend on the type, site, size, and stage of cancer (how much and to what extent it has spread), along with age, health status, and other personal characteristics. For cancer, there is not any single treatment protocol, patients most often receive a combination or multiple therapies and palliative care. Treatments are usually classified into the following classes (26):

- Surgery: An instrumental method to control symptoms if the cancer is not metastasized, removing tissues or sometimes organs such as the breast, prostate, testicles, etc.
- Radiation: Focus of high radiation rays on the cancerous site to destruct the cell.
- Chemotherapy: Use of cytotoxic chemical agents that interfere with the division of cell process-damaging proteins or DNA so that cells deplete. This technique is used to cure, eradicate of start stage of metastasis, palliation of symptoms, and in combination sensitize radiotherapy(27)

1.10 Chemotherapy is mainly of three types:

- Neo-adjuvant type: given before surgery to shrink the cell, so removal of tissues will be less.
- Adjuvant type: given after procedure/surgery to reduce the recurrence risk.
- Palliative type: Used only to control cancer cells in periodic manners which have a chance of spreading in localized lymph nodes and breast. (28)

- Immunotherapy: Used local immunotherapy Injections to boost the body's immune system to fight against the target, e.g. *Small-molecule drugs, and Monoclonal antibodies*
- Hormone therapy: alteration in the hormone production site to stop the growth or killing of a cancerous cell. E.g. testosterone, estrogen, etc.
- Gene therapy: The damaged gene is replaced by the one that is working, with no successful outcomes, but researchers still working on this treatment to achieve the goal.(29)

1.10.1 Role of Combination therapy in treatment of Carcinoma:

The priority use of chemotherapeutics with hormonal therapy and immunotherapy in the treatment protocol of cancer has proven results indicating that combination therapy is superior to single-agent use. These combinations were selected, based on an active single agent which produces complete remission. With the different mechanisms of action, drugs should be combined in optimal dosage and range. This will minimize the resistance possibilities. In addition, for limiting the toxicities of drugs, different doses were added which allowed drugs to give at or near full therapeutic effects.

The aim is to achieve complete remission in the advanced disease state, with high dose intensities for several cycles. Combinational therapy is also designed to combat the chance of drug resistance to chemotherapy.

1.11 Drugs used in cancer treatment

1. *Alkylating agents* are classified as antineoplastic drugs which are highly reactive and play a role by inhibiting the transcription of DNA into RNA and destroying or stopping the protein synthesis in cancerous cells (carcinogenicity) (30,31).

They are *used* in the treatment of brain cancer, lymphoma, testicular cancer, breast cancer leukaemia, and melanoma (32).

2. ***Antitumor Antibiotics*** or anticancer antibiotics are natural products obtained from the fermentation of *Streptomyces* species. It has a structurally diverse range of products, and complex mechanisms of action (33). It blocks cell growth by interfering with DNA.

These anti-tumour antibiotics are *active* against leukaemia, sarcomas lymphoma, and most solid tumors (34).

3. ***Antimetabolites*** are a substance that is structurally like a metabolite (such as a coenzyme) and that interfere to inhibit a specific cellular function (such as the synthesis of DNA) by intervening with or blocking the metabolite's action (35).

They are most *effective* against hematologic malignancies, and solid tumors, like head and neck cancer, breast cancer, and osteosarcoma (36).

4. ***Plant alkaloids*** are made from several types of plants. Plant alkaloids compel microtubule proteins during their metaphase, triggering mitotic arrest. The cell cannot split and dies. They are effective against blood cancers, breast and testicular cancer, and others (37,38).

5. ***Topoisomerase inhibitors*** prevent the enzymes (topoisomerases) break down, which reconnect DNA strands that are required for cell division and growth (39,40). These are used in lung cancer, leukemia, lymphoma, testicular cancer, etc (41).

6. ***Targeted therapy*** is a type of treatment that uses particular medications designed to "target" neoplastic cells directly without affecting nearby normal cells. It works by stopping cancer cells from copying themselves. They are applied against blood carcinoma, brain cancer, GIT cancer, Head and Neck, etc (42).

7. ***Hormonal Therapy*** or anti-estrogen therapy is based on drugs that add, block, or cut off hormones, to reduce or stop the progress of cancer cells that demand hormones to grow(43).

Table 1.1: Description and Classification of Alkylating Agents:

S.No.	Types of Alkylating Agent	Generic Name	Dosage	Therapeutic Indications	Toxicities \ Side Effects
1	Platinum Complex	Cisplatin	15-20mg/m ² /day (5 days) repeated every 3-4 weeks 50-120 mg/m ² IV as single dose repeated every 3-4 week	Testicular Cancer, Ovarian Cancer, Bladder Cancer, Head & Neck Cancer	Nausea & Vomiting, Nephrotoxicity Ototoxicity Neurotoxicity
		Carboplatin	Upto 100 mg/m ² /day IV (repeated every 5-6 weeks) 400-500 mg/m ² IV single dose repeated every 4 weeks	Ovarian cancer	Myelosuppression, Nausea & Vomiting
		Oxaliplatin	130 mg/m ² IV Every 3 weeks	Cervical carcinoma Ovarian cancer,	Bone marrow depression
2	Nitrogen Mustard	Cyclophosphamide	1500 mg/m ² IV single dose repeated every 3 weeks 50-200 mg/m ² /d IV as continuous	Malignant lymphoma, Multiple myeloma leukemia, breast cancer, ovarian cancer	Myelosuppression Cardiac arrhythmias Thrombocytopenia, Hemorrhagic cystitis
		Ifosfamide	8 to 12 g/m ² IV 3 to 5 days repeated every 2 to 4 weeks	Breast cancer, Cervical carcinoma,	Myelosuppression,
				Chronic lymphocytic leukaemia Lung cancer Soft tissue sarcoma, Testicular cancer, Ovarian cancer,	Impaired renal function
3	Triazines	Decarbazine	2 to 4.5 mg/kg /24 hourly For 10 Days, repeated per month	Hodgkin's disease melanoma, Soft tissue sarcoma.	Photosensitivity. Moderate Myelosuppression Hepatotoxicity

Table 1.2: Description and Classification of antitumor antibiotics

S. No	Types of Antitumor Antibiotics	Generic Name	Dosage	Therapeutic Indications	Toxicities \ Side effects
1	Anthracycline	Doxorubicin	60 to 75 mg/m² IV Every 3rd Week	Leukemia, Sarcoma	Bone marrow suppression,
				Lymphoma, ovarian cancer	Mucositis, Cardiotoxicity
				Solid Tumors - Broad Spectrum	Nausea, Vomiting, Alopecia, etc
		Donorubicin	30 to 45 mg/m² IV For 3 Days, (repeated after 3 to 6 weeks)	leukemia	Congestive heart failure
				Kaposi sarcoma	Bone marrow suppression
					Neutropenia
					Nausea, Vomiting, Mucositis
2	Miscellaneous	Bleomycin	10-20 IU/m² weekly or twice weekly	Hodgkin's disease,	Pulmonary Fibrosis
				Squamous cell carcinoma,	Anaphylaxis
				Testicular carcinoma	Mucositis, Cardiotoxicity
				Lymphoma, ovarian cancer	Alopacia
				Head & Neck Cancer	

Table 1.3: Description and Classification of antimetabolites

S.No	Types of Antimetabolites	Generic Name	Dosage	Therapeutic Indications	Toxicities \ Side Effects
1	Folic Acid Antagonist	Methotrexate	2.5 mg/kg hourly 24 IV In leukemia every 14 days	Bone marrow transplantation,	Hepatotoxicity, Coma, Seizures,
			3-10 mg/day upto 30 mg/m² twice weekly	Breast cancer,	Neurotoxicity, Hepatotoxicity,
				Head and neck cancer,	Myelosuppression
				Leukaemia, Lymphoma	Nausea, Vomiting
				Osteosarcoma, etc	
2	Pyrimidine Antagonist	5-FU	upto 500mg/m² (5 days) every 4 week	Carcinoma of Breast, Colon,	Myelosuppression
				Stomach & Pancrease	Nausea, Vomiting
					Mucositis, Pneumonitis
		Cytarabine	100 mg/m² IV For 5 days. Repeated every 2 weeks total 12 doses	Acute leukemia,	myelosuppression
				Lung cancer and pancreatic cancer	Nausea, Vomiting
				Non-hodgkin's lymphoma,	CNS toxicity, Pulmonary toxicity,
		Gemcitabine	1 g/m² 0.8 hourly, Once a week for 3 weeks.	Pancreatic cancer	Thrombocytopenia,
				Lung cancer	Pneumonitis,

S.No	Types of Antimetabolites	Generic Name	Dosage	Therapeutic Indications	Toxicities \ Side Effects
				Breast cancer,	Leukopenia
				Head and neck cancer,	
3	Purine Antagonist	Mercaptopurine	upto 50 to 175 mg/m ² PO 24 hourly	Acute leukemia, ,	Liver dysfunction,
				Crohn's disease,	Interstitial pneumonitis,
				Non-hodgkin's lymphoma	Pancreatitis, Anorexia,
		Thioguanine	100 mg/m ² Over 3-5 days in conjunction with other	Acute(AML), Chronic leukaemia (CML),	Myelosuppression
			cytotoxic drugs. 12 HOURLY	Myeloblastic leukemia.	Nausea, Vomiting

Table 1.4: Description and Classification of plant alkaloids

S. No	Types Of Plant Alkaloids	Generic Name	Dosage	Therapeutic Indications	Toxicities \ Side Effects
1	Vinca Alkaloids	Vincristine	1.4 to 1.5 mg/m ² IV Once in a Week.upto 2mg	Breast cancer, Neuroblastoma,	GI symptoms, Neurotoxicity.
				Hodgkin's disease, Leukaemia,	Nausea ,Vomiting,
				Non-hodgkin's lymphoma,Lymphomas,	
				Rhabdomyosarcoma, Solid tumor,	
		Vinblastine	3.7-7.4 ug/m ² IV Once in a Week.upto 18.5mg/m ²	Solid tumor, Testicular cancer	GI symptoms.
				Hodgkin's disease, Kaposi's sarcoma,	Myelosuppression
2	Taxanes	Paclitaxel	175 mg/m ² IV If, Over 3 hrs., repeated every 3 weeks	Breast cancer, Ovarian cancer,	Cardiac arrhythmias, Anemia
					Neutropenia,
					Bone marrow depression.
		Docetaxel	60-100 mg/m ² every 3 weeks for 6 cycles	Gastric cancer,	Neurotoxicity, Sensory neuropathy
				Ovarian cancer, Pancreatic cancer	Nausea, Vomiting
				Metastatic carcinoma of breast	Mucositis
3	Podophyllotoxins	Etoposide	50 to 120 mg/m ² on days 1, 3, and 5 every 3 to 4 weeks	lung cancer, Gastric cancer	Nausea, Vomiting, Hypotension
				Testicular cancer	Alopecia,
4	Camptothecin Analogogs	Topotecan	1.5 mg/m ² by IV Inf over 30 min daily on days 1 to 5 of each 21-day cycle	Lung cancer, ovarian cancer.	Hyperbilirubinemia,
					Thrombocytopenia

1.12 Objective of the Study

A Retrospective observational study was conducted to evaluate the cost-effective rational use of the drug for the identification and promotion of advancement in practice, in the cancer ward of private as well public sectors in Karachi.

1.13 Specific Objectives

- To promote adherence with rational drug use.
- To increase the risk-benefit ratio.
- To increase the goal of therapy or compliance with therapy.
- To reduce adverse drug reactions and drug interactions.
- To increase the role of education providers.
- To provide response/feedback.

CHAPTER 2

LITERATURE REVIEW

Al-Shahri et al. in 2020 described the change in prescription patterns of opioids in palliative care teams (PCT) previously not examined in the Middle East. He explained the changes in the pattern of opioid prescription and the scores of pains before and after stating inpatients to a PCT. Patients records file was taken, newly referred all inpatients ≥ 15 years to the PCT for 21 months at Specialist Hospital King Faisal and Research Center of Riyadh. Of a total of six hundred and thirty-one patients observed, where females were 52.3%, 54 years was the median age, and 96.7% had positive cancer. The ratio before referral of patients on drug opioids (83.4%) was enhanced to 93.3% in the period of post-referral, $P < .0001$. Regularly patients receiving drug opioids before referral from 31.9% increased, to 49.9% after the recommendation to the PCT, $P < .0001$. The opioid Morphine was prescribed regularly as pre-and post-referral. The route of drug administration of opioids upon referral, was subcutaneous, elevated from 3.7% to 10.9%, $P < .0001$. Pain scores on the median were decreased by 1 point on a scale of 0 to 10 by the PCT within 48 hours (about 2 days) of screening a patient, $P < .0001$. APCT-referred individuals are liable to get optimized prescriptions of opioids and shortly improved pain grades after the PCT involvement. Cancer-related pain individuals with opioids requiring were referred to a PCT as soon as possible. (44)

Bepari et al. in April 2019 defined the key burden of Cancer and the threat to overall society. A wide range of multiple chemotherapeutic agents was used to alleviate cancer at various stages. The drug used inappropriately leads to raised concerns about medical care, adverse drug events, and patient mortality rates. Hence, drug utilization studies have become a potential tool used in different healthcare systems for the evaluation of cancer. The study objectives were to recognize the cancer of different types, the frequently prescribed drugs, the use of rational anticancer drugs, and analyze the prescribing patterns in a tertiary care hospital, in India. Diagnosed patients, new cancer and/or known carcinoma cases of both sexes which required medication protocol with chemotherapy aged

> 18 yrs. In Radiotherapy Department shifted for a 5month period and was analyzed for prescribing indicators. The cancers most prevalent types were head & neck cancers observed with more dominance among males. Mostly o patients were prescribed a single anticancer drug. The most used cytotoxic drug was Cisplatin pursued by carboplatin and antimetabolites. The adjuvant drugs most commonly used were anti-peptic ulcer and anti-emetics drugs. More Than 82% of anticancer agents were used from the essential drug list and were recommended in generic names, suggesting rational drug use (45).

Elahi, et, al. on December 30, 2019, from the city Lahore, Pakistan stated that the shortages of drugs in tertiary care hospitals constantly limited the capability of the health system to deliver quality support to suffering patients. In Pakistan, subsequently, the shortage exists of 5 different oncology drugs many patients were in a desperate state of not any cure for their depriving illness. For this regrettable situation, Cardinal factors were responsibly comprised of interruptions in supplies from the vendor and the regulatory bodies' issues associated with approvals and costings. The regulatory authorities, effectively review policies for the availability of oncology drugs that will avert the future miserable condition and assure high-quality care to affected patients by healthcare systems (46).

Sarwar, M. R., et, al., 2018 studied anticancer medicines to evaluate their availability in public and private sectors hospital in Punjab, Pakistan. The affordability with various income levels among patients. In 22 cancer care hospitals, both descriptive and cross-sectional surveys were conducted. 18 public hospitals, 04 private hospitals, and 44 private pharmacies were observed. All ($n=4400$) affiliates were of an age of ≥ 18 years. At multiple interval data were obtained and analyzed by (SPSS Statistics Version 21.0). In their result, they contacted a total of 4913 patients, and of them, 4400 takes part in the survey (rate of response = 89.6%). Lymphoma Non-Hodgkin (12.3%), cancer breast (8.6%), and blood leukemia (7.6%) were the most prevalent types of cancer. Medicines like cyclophosphamide, cisplatin, and etoposide were the most recommended medicines. To suggest newer anticancer medicines oncologists were very reluctant due to their unaffordable prices. More readily available were (52.5%) Originator brands (OBs), but less affordable were (53.4%); whereas, less available were (28.1%) lowest price generics (LPG) but most affordable (67.9%). For patients of the high-income class, anticancer medicines

were more reasonable than those of the low-income class. They explained at the end **the** availability of both OBs and LPG was greater at private hospitals and pharmacies as compared to public hospitals. Of both, OBs, and LPGs the high-income class had affordability more, while for all income classes LPGs were better affordable (47)

Balkhi, et. al. in June 2020 at (KSUMC) King Saud University Medical City studied a retrospective study, for 1 year. A total of 101 patients of breast cancer, female patients diagnosed were observed. Most patients were administered three cytotoxic drugs. Fluorouracil was the most recommended medication, followed by Epirubicin, and then the cyclophosphamide (FEC) regimen, used in almost 81% of patients. Combination therapy of FEC anticancer + docetaxel and another regimen FEC+ trastuzumab + docetaxel was received by 43% of patients and 23%, respectively. In the neoadjuvant setting, docetaxel was the highly used drug, whereas in hormonal and targeted therapies letrozole and trastuzumab were more prescribed, respectively. The anticancer therapy, total drug expenditure was around 3.8m Saudi Riyals (S.R), constituting adjuvant therapy more than half of the overall spending. In neoadjuvant settings, hormonal therapy was the highest paying cost. The condition was improved in most breast cancer patients in that period, whereas only 29% progressed. FEC was the commonest set of regimens, consistent with the guideline of the National Comprehensive Cancer Network (NCCN) recommendation. In their results, recommended medication regimens and adherence to guidelines enhance patient's outcomes. Findings analyzing the pattern of drug utilization, assist institutions in handling their inventory and by using resources of the health care system. (48)

Carlotta P, in 2019 demonstrated cancer as the major cause of millions of mortalities globally, and, even though need much advancement in medicine, still many highlighted issues persist to improve cancer therapy. Oncological researchers are making efforts toward new advanced efficient therapies which relieve side effects, that occurred by treatment protocols. Many technologies are in clinical trials. Hence, nanomedicine are contributing to the biocompatible materials development both for diagnostic and therapeutic uses, bioengineering of cells derived and extracellular vesicles from individuals has permitted univocal targeting strategies and the designing of ad hoc systems. They

provide the most innovative advancement in an in-depth analysis of applied and basic cancer research (49).

Yen Ang, C, et al. in 2019 stated Cancer disease is one of the main diseases that need a lot of scientific attention. Cancer therapeutics are conventional and deal with surgical tumor removal followed by treatment of chemotherapeutics. During anticancer drug chemotherapy, patients suffer from various undesirable side effects that damage organs. Thus, to overcome the side effects, there was an ultimate requirement for the development of novel strategies. Among others, the utilization of anticancer nanocarriers drug delivery is shown improved therapeutic drug efficiency with minimal unwanted side effects. They introduced targeting ligands that were functionalized on nanocarrier specificity for targeted delivery of the drug. They highlighted a few therapeutic cargoes used in cancer treatment. Interesting stimulus strategies at tumor sites, for controlled release of drug therapeutic cargoes. They reviewed efficient cancer therapy with the approach of nanomedicine. (50)

Pellino, A, et, al. in 2019 represented Gastric cancer (GC) as a principal cause of cancer-related mortality and morbidity globally, accounting for newly diagnosed cases of more than 1 million and thousands of decreases every year. In the last era, the optimization of available chemotherapeutic drugs and the advancement of targeted therapies has extended the treatment options for advanced-stage GC and provided better survival prospects to the patients. However, the epigenomic and genomic assortment of this disease resulted in the identification of new sensitive and specific predictive and prognostic biomarkers and classifications based on innovative molecular gene expression profiling. It is essential to improve the GC subgroups of molecular characterization to provide medical oncologists and researchers with new tools for patient stratification and selection in future clinical programs and trials. This delivered a global overview of classifications, in present developments in the targeted therapies and immunotherapy in metastatic GC(20)

Cool. L, et, al, stated in 2018 that in society increasing burden of cancer and Home-hospitalization become a patient-centred approach, described that oncological home hospitalization depends how organized and its quality and cost evaluation. They have included twenty-four papers explaining the administration of parenteral cancer drugs to

adult/elderly patients at their homes. They concluded that home hospitalization of oncological patients had no considerable effect on (7/8 = 88%) quality of life, but most patients (12/13, 92%) were satisfied and the home treatment preferred (7/8, 88%). With home hospitalization (10/10, 100%) no safety risks were related. In five clinical trials the home-hospitalization cost was beneficial (5/9, 56%); others reported no fiscal effect (2/9, 22%). For an oncological home-hospitalization maximum of stated models demonstrated an equivalent, safe and acceptable substitute to hospital ambulatory care. To evaluate, economic impact needs more well-designed trials. (51)

The study conducted by Babasahib, et. al. in October'2018 defined, patterns of prescribing anti-cancer drugs. Furthermore, was conducted to evaluate anticancer drug use in rational form, identify various kinds of cancers, and examine the expense and cost-effectiveness of anti-cancer medicines. The study was performed on 200 prescriptions in the department of oncology. From case findings reports, the records were collected. The drug prescriptions and medication charts were in particularly designed forms. Overall, from 200 enrolled patients, the majority were females (59.5%), and the respective ages limit of 40-60 years (52%). GIT carcinoma (25%) was frequently diagnosed, pursued by breast carcinoma (18.5%) and genitourinary carcinoma (16.5%). Cisplatin (35%) was the most prescribed anticancer drug, trailed by paclitaxel (18.5%), then carboplatin (14%), the 5-fluorouracil (12.5%), and oxaliplatin. Cancer is ranked highest amongst non-communicable ailments and lots of individual in India received treatments for cancer per year (52)

Manichavasagam n.d, et al., 2017 determined the role of drugs in society and their prescribing trend which is an important common tool that must be performed at any hospital from time to time. They intended the pattern to prescribe antitumor drugs in the department of medicine-oncology in a reputed tertiary care hospital in Tamilnadu (India). Every drug prescription was comprehensively studied for the patient's demographic details, drugs name, dosage form, dose, incidence reported, duration of disease, etc. Usually, anticancer medications and several types of neoplasm were noted and the ratio of prescribed drugs from the national essential drug list (NEDL) was estimated. Their research showed that the maximum number of carcinoma cases was evident in the age limits of 55 to 65 years. Of 328 individuals, females were 179, and 149 were males. The most

widespread was found Breast cancer to be females pursued by ovary and stomach carcinoma. In the male population, lung cancer was more identified, which is followed by stomach cancer. Maximum prescribed drugs were alkylating agents trailed by antimetabolites, cytotoxic antibiotics, plant derivatives, and glucocorticoids. The utilization of prescribed anticancer drugs in this setup was noticed to be rational and in addition, 70% of drugs were prescribed as on the National essential drug list. Pattern evaluation of prescribing drugs must be performed from time-to-time frame to minimize the undesired consequences at least to some extent. (53)

Kulkarni et al., determined in 2017 that the drug utilization of anti-neoplastic agents in the department of oncology outpatient (OPD) of Aurangabad Government Medical College. Prescription patterns of 512 patients were selected and examined as per the study outline. Anticancer drugs frequently used were recorded; moreover, diverse types of neoplasm were observed. The age limit of patients was shown that among 30 and 70, out of 267 were females and 245 were males. The most common kind of cancer was carcinoma of the breast (17.9%) and the most prescribed anti-cancer drug was Carboplatin (26.56%). Almost three anticancer drugs were given to each cancer patient. Recommended WHO drug utilization studies were desirable in each health-care sector. For an emerging country National Drug list/Policy, Drugs, and Therapeutics Committees are the prior requirement (54)

Pantziarka et al., in 2018, the project Repurposing Drugs in Oncology (ReDO) developed a literature-based technique to classify non-cancer licensed drugs of antitumor activity along with published evidence. Total 268 drug data entailed in a database (ReDO_DB) that was created by the ReDO project. The majority (73%) of drugs had some indications of anticancer activity from case reports, clinical trials, or observational studies. Moreover, 32% are involved in the WHO EML and most of them (84%) are off patent. Most drugs had human data, were off-patent, and involved in the WHO EML 67, indicating 25% of the total database. This study implies a hopeful trend of potential additional treatments in the oncology field (55)

Kumar, n.d et, al, in June 2018 determined the prescribing trends of cytotoxic drugs and patterns to differentiate various kinds of cancers and assess the cost distribution of

antineoplastic drugs. The Prospective and observational study was performed in the department of oncology on 300 patients. They gathered data from case reports, medication charts, and prescriptions. Of a total of 300 patients enrolled, females were in majority (59.5 %) in the age set of 40-65 years (52 %). Most observed was GI carcinoma (25 %), followed by breast carcinoma (18.5 %) and genitourinary carcinoma (16.5%). The frequently prescribed anticancer drug was Cisplatin (35%), pursued by paclitaxel (18.5%), then carboplatin (14%), subsequently 5-fluorouracil (12.5%), and then oxaliplatin (7.5%). Palliative therapy was used as Ranitidine, dexamethasone, and ondansetron to avert or manage the anticancer drug's adverse reactions. The major expense was (Rs. 4 50 000) of Trastuzumab contributes to drug protocol. The drug's typical cost per prescription was Rs. 11 135. The general prescribing indicators indicated that the average sum of total drugs, antibiotics, and anticancer drugs were 12.22, 0.43, and 1.73. The utilization of drugs was remarked to be rational and almost 99.38 % of the medicines prescribed were from the hospital formulary. The prescribing trends seemed suitable and respective to World Health Organization (WHO) guidelines. Their study outcomes support the most excellent prescribing procedures to improve healthcare delivery and promote cost-efficient treatment (56).

Sun, J, et al. in October'2017 described anticancer drugs FDA-approved for systematic analysis. They gathered 150 anticancer drugs and analyzed which were endorsed by the Food and Drug Administration US (FDA). Depends on the mechanism of action of the drug, these were separated into the two main groups: 89 target-based drugs and 61 cytotoxic-based drugs. In current years, the targeted agents were increased and delivered as a signal drug. They collected 102 effect-mediating drugs from 89 target-based drugs, that are found in the individual genome, and nearly all targets were placed on the plasma membrane and enzyme, especially tyrosine kinase. Built a drug-to-cancer network from 150 drugs, which confined 183 nodes (33 cancer types and 150 drugs) and associations of 248 drug-cancer. This indicated that the cancer types are more used to treat cytotoxic drugs than targeted drugs. Of the targeted 89 drugs, created a network of cancer-drug-target, which confined 214 nodes (23 cancer types, 102 targets, and 89 drugs,) and edges 313 (associations of 118 drug-cancer and 195 drug-target). The network of 133 novel drug-

cancer discovered associations between 16 cancer types and 52 drugs by the approach of general target-based. Drug-cancer novel associations (116, 87%) were encouraged by one study of a clinical trial (57)

In 2016 Mugada, et al Drug Utilization Evaluation (DUE) endorsed the use of rational drug. The study aimed to perform the DUE of anticancer. Recently diagnosed and/or recognized cases of neoplasm, required treatment with chemotherapeutics, both genders, and aged >18 years were involved in the study. Patients who were diagnosed with carcinoma, needed surgical intervention, radiotherapy, or another form of management were excluded. Core prescribing indicators of WHO were used to understand polypharmacy, the proportion of drugs, and extra use of antibiotics, prescribed by the Essential Drugs List (EDL). Females were more impacted than males. The age limit 41-50 years of patients (mean 52.43, SD ± 7.77) comprised the highest number, 34% and 14% in urban and rural areas of populations. Cisplatin and 5-Fluorouracil were the most used chemotherapeutics followed by Cyclophosphamide. The most adjuvant drugs were Diclofenac, Ranitidine, Granisetron, B-Complex, Mannitol, Ondansetron, and Dexamethasone. The cytoprotectant drugs identified in the study were Leucovorin, Peg-Filgrastim, and Mesna. The number of anti-cancer drug was 1.97. per prescription, the number of overall drugs prescribed was 8.16 per prescription. A percentage of 88.4% was prescribed from the Essential Drugs List (EDL). The proportion of antibiotics was 54.8%. They do not observe Injection prescribing, Polypharmacy, and unnecessary antibiotic (58)

Daniel M. et al. explained in 2016 that Oral anticancer medications (OAMs) were usually prescribed for many cancers. They performed retrospective study to evaluate viable interruptions in treatment (Tx). They involved patients of kidney and prostate cancer on-label OAMs at an academic institution. The result was taken from nursing notes and the patient charts, in which demographic details, initial dose date, date of OAM prescription, number and the justification for which phone calls to staff need to take on OAM, economic support, and company amount were demanded. The test they used was Kruskal-Wallis and Fisher's exact to relate the differences between OAM. As the result there were 116 patients (55% nephrocarcinoma, 45% prostate carcinoma) with 149 rare prescriptions, the median age was 65 (27-88), 85% male, 89% white, and 78% had drug coverage. In the patients

with data accessible (56 distinctive prescriptions), cited average/median that copay/month was declined to \$42/\$3 per month after the co-payment, support program utilization. At the start of on-label OAMs, there was a labor-intensive procedure that took 15 days to obtain the drug. The important OAM were differences associated with the specific drug plans, unmeasured variables, support programs, or requirements to be more validated in the bigger samples. The Out-of-budget expenses were remarked variable and need organization efforts to reduce through financial aid. The practice of beginning Oral Anti-cancer Medicines can be an obstacle to consideration and must be important to the quality improvement initiatives (59)

DZ, Louis, et al. in aug'2016 reported that most of the patients who wanted to die at home, with advanced stage cancer, need management and undergo to critical procedures, admitted to the intensive care unit (ICU) and go dead in the hospital. The study aim was to examine the difference in hospital utilization and, death places for patients dying with cancer of poor prognosis in Italy. They conducted a study of retrospective, population-level utilizing administrative data. Patients who died were included with at minimum one hospital admission for poor prognosis or metastatic carcinoma within three months or 180 days (about 6 months) of death. Intensive care, differences in the admission of the hospital, and techniques performed there were evaluated. A total of 11,470 patients died with poor prognosis or metastatic carcinoma. Of 50.7% cancerous patients died in the hospital while 78% were hospitalized in a hospice in the end of their life. The results differed from 38.3% to 69.3% in local health authorities. Of those patients who stayed in ICU, 55.1% of them stayed in community hospitals, and in teaching hospitals, 59.8% individuals were admitted on the day of their death in the ICU or the day prior to death. In the last 30 days (about 4 and a half weeks) of life, 7.5% of patients experienced a most important procedure. At the end-of-life substantial variation, overall elevated expenses, and in-hospital care offered an opportunity to estimate the accessibility of palliative care. Patient education, along with the care-taker, could reduce utilization of high-cost care in hospital and enhance the satisfaction of patient and family (60)

A. Shumaila, et.al in June 2016 reported Rational Drug use in Pakistan in a systematic way. They summarize reviews based on rational drug use in Pakistan and their consequences on

health. A published research work was undertaken from 1990 to 2015 which concentrated on various aspects of the use of rational drugs. Computerized databases and Annals of (INRUD) International Network for Rational Use of Drugs, PubMed, Science Direct, and WHO were assessed for same research reports, journal articles, and newsletters. They utilized Google's general search engine to enlarge and fortify the search process. Initially, from electronic databases, 60 articles were regained by the authors. These articles were compared with the objectives of the study. After this, 20 articles were selected, and 15 relevant findings were added to the review. They found that a hefty sum of drugs was used in the wrong way. In community pharmacies of Pakistan, the current paper emphasized the quality of services offered was not satisfactory. They focused on intervention to improve the situation and urgent needs (61)

Nishita, A. A., et al. 2016 performed a study on the utilization & evaluation of drug and cost analysis of the antiemetic group of drugs given in the oncology ward of a quaternary care hospital. They emphasized the drug utilization and cost comprised for antiemetic drugs on patients in the oncology ward undergoing chemotherapeutics. Their method was a prospective, observational, and non-interventional study. A total of 141 patients, out of which female was 77 (54.6%) patients while males were 64 (45.4%) patients. In the age group of 40-49 (29%) the majority number of patients were from 60-69 years (20%). They compared according to the standard protocols for use of antiemetics in the patients. They found a deviation from standard protocol 137 (97%) inpatient profiles, and only 4 patient profiles (3%) pursued the standard protocol because of prochlorperazine which was not stated in the standard protocol. They suggested a future approach, physician's education with the use of rational drugs and to assess the medication chart which will be effective in cost-effective treatment (62)

Patel, et al., in 2016 evaluated the drug utilization prescribing pattern and appropriateness of anti-cancer drugs as an adjuvant therapy and neoadjuvant therapy in breast carcinoma patients. In their study orders of medications in a chemotherapy regimen for breast carcinoma patients were considered and interrogated to assess the treatment plans and their appropriateness in an oncology ward of the hospital sector. The clinical disease stage of the illness, tumor characteristics, drug choice, route, dose prescribed, administration

method, and anti-emetics given were studied per standard international references to estimate the appropriateness of the designed chemotherapy. Up to 06 months 100 patients were observed. Anthracycline-based regimens used were found to be higher (92%) as compared to methotrexate, cyclophosphamide, and 5-fluorouracil regimen (6%). Prescribed targeted drug therapy was only 33% of positive tumor patients with HER2. In addition, endocrine therapy, as either aromatase inhibitor or anti-estrogens was given to 18 patients (100%) along with hormone-responsive tumors and 7 out of 13 cancer patients with an unidentified hormone response status. Chemotherapy treatment choices were suitable for 84% of patients. Therapy Costs were the limiting factor to choose a suitable treatment for the other patients. Anti-cancer agent doses were not estimated as per body surface area (BSA) during the consequent cycle for 22% of cases. Improper drug administration was found owing to extra dilutions of drugs (25%) and inappropriate time of infusion (29%). Choices of anti-cancer agents were detected to be well-yielding with standard international references. Although, a lack of adherence was reported to the prescribed chemotherapy due to inaccurate administration. Targeted therapy use was limited due to financial considerations. To improve chemotherapy delivery appropriate training can be offered to nurses (63)

Pentareddy, et al. studied in 2015 the most common factor of mortality and morbidity is Cancer all over the world. They discussed Chemotherapy as a vital element of treatment with additional tactics in the management. They evaluate anticancer drug prescribing patterns in their study. A retrospective observational study was done in the department of oncology for one year of ESI hospital. Patients with records of more than 19 years of age, diagnosed with carcinoma were involved. The majority were females (134, 68%), Out of 197 enrolled cancer patients, and in the age set of 41-60 years (147, 74.61% patients). Breast Carcinoma (58, 29.44%) was frequently pursued by head and neck carcinoma (46, 23.35%), and cervix carcinoma (34, 17.25%). As a combination regimen of drugs (160, 81.21%) chemotherapy was frequently used. Platinum-based and 5-Fluoro Uracil (5-FU) combinations were very commonly provided (60, 30.45%) exclusively in carcinoma of the head and neck (46, 23.35%). In lung carcinoma management Platinum-based combinations

were used. Ranitidine, Dexamethasone, and Ondansetron were applied as palliative therapy of anticancer drugs to manage or prevent adverse reactions (64)

Ades, et al., in 2014 explained the major elevation in the new cases of carcinoma because of the Demographic alterations in the global population. Societies are required to modify how they move towards cancer preventive measures and treatment goals, with alterations to the advancement and application of innovative chemotherapeutic drugs that play a key role. Although, there are difficulties in utilizing innovative cancer drugs in clinical practices. Before being used in regular practice, the medicines need reimbursement, and regulatory approvals to achieve fluctuation in the prescribing habits of physicians and eventually earn the compliance of cancer patients. It is essential to have a summary of the full procedure to enhance treatment goals and surge the likelihood of executing health innovation. This analysis aims to define the method and demonstrate the hurdles arising at each step. (65).

Mori, Tanimoto et, al, in 2015 in Japan stated all-case post-marketing surveillance of anticancer drugs performed on all patients. They studied all-case post-marketing surveillance or earlier market access and identified lethal adverse drug reactions (ADRs). They reviewed the post-marketing surveillance findings and identified the timeline where adverse drug reactions were primarily reported. From January 1999 and December 2009 set of total 25 all-case post-marketing surveillance was done. The result of 08 all-case post-marketing surveillances was comprised of information on each fatal case. Hence, only four warning letters were released by the regulatory authority, and two were prompted by all-case post-marketing surveillance. Current permitted anticancer in Japan of all-case post-marketing surveillance were useful evidence for the severe compilation of non-certain type of adverse drug reactions, but it is hard to detect clinically important fatal adverse drug reactions (66)

Miyamoto, Y, et, al, in 2016 stated that during gestation cancer diagnoses were rare; with the increase in maternal age, it is increasing and was a subject of international concern. In certain instances, the administration of chemotherapeutics was unavoidable, nevertheless there was a relative scarcity of indications concerning the administration of

chemotherapeutics during pregnancy. They interpreted the appropriate timings for the chemotherapy drugs administration, the medicinal regimens that were administered additionally with relative efficacy, safety, drug choices, and the effects on both the mother and the fetus, more cases have gathered gradually, and additional research had done. Although, new challenges had arisen, like the findings of novel antitumor medications and therefore the wish for children throughout drug therapy. During analysis, defines the outcomes of administering molecularly targeted medications and cytotoxic anti-tumor medication to pregnant women and fetuses, moreover the problems involving patients (67)

Siddique et al., reported in May 2014, Drug Utilization Evaluation of Anticancer drugs reduces polypharmacy, interactions of different drugs and also reduced hospitalization. The study was to identify the pattern of incidence of different cancerous disorders and to control the irrational use of medicine. It was an observational prospective study, which was performed at Yashoda Cancer Institute, in Hyderabad for 6 months. They have included 100 prescriptions in their research. The criteria were the inpatients up to 90 years of age of both genders. They obtained the relevant Patient data for the study from patient case files. Corresponding to their collected data, males (54%) predominated over the females (46%) and individuals from the 41-60 age group were more prominent in their study. The anticancer drugs used were rational and more than 50% of the drugs were prescribed from the essential drugs on the National drug list. They concluded that the Pharmacist was the main person for the management of therapy in a better way considering the stages and conditions and can manage the raised expenses of therapy and risk of potential reactions. They encouraged pharmacists for a sincere work to reduce untoward events (at least to certain extent) (28)

Builders, M., et al. (2015) performed Drug Utilization Study at Bingham University Teaching Hospital and evaluated the pattern of utilization of therapeutic agents in the health care delivery system. Worked on 417 record files where they assessed; age, gender, clinical findings, the drug regimen, and therapy duration which was used to collect primary data. Their assessment showed that 77.7% were females and that 22.3% were males. (44.1%) were in the age limit of 20-29yrs. Very cases were of gynecological diseases (58.1%). There were 2127 drugs in 417 prescriptions, the highest prescriptions were in March, other

drugs (58.0%) were the most prescribed drugs, and the highest prescribing drug being anti-anemic (15.2%). 56.7% of the drugs prescribed were with generic names as well 45.8% were orally administered (68)

Aggarwal, and et.al., evaluated the pattern of prescribing chemotherapeutics to inpatients receiving chemotherapy. The Method was an observational study, performed in the radiotherapy department. Of admitted cancer patients and 101 newly identified cases were taken, drug utilization was considered using core indicators of WHO. As a result, the average number of other drugs and anticancer drugs, given per patient were 9.2 and 2.97 respectively. Prescribed 94% of the drugs were advised from the essential medicines list, by their generic names (70%). The most prescribed anticancer group was Platinum compounds (27.6%) followed by antimetabolites (24.3%), then taxanes (15%), antitumor antibiotics (13%), observed by alkylating agents (10%), next to epipodophyllotoxins (3.7%), then vinca alkaloids (2.7%), steroids (1.7%), immunomodulators (1%), camptothecins (0.7%) and monoclonal antibody (0.3%). Cytotoxic agent Cisplatin (20%) was the most prescribed. Of cytotoxic drugs, 96% were given intravenously and 4% were given orally. Amongst the adjuvant group of drugs, antiemetics (20 %) were given utmost frequently, after that drug reducing gastric acid secretion (16%), electrolytes (14%), subsequently steroids (12%), later diuretics (10%), then colony-stimulating factors (8%), next mesna (4%), then antiallergics (4%), after that nutritional supplement (3%), minerals and vitamins (3%), antimicrobials (2%), then analgesics (1%) and antianxiety (1%). In Conclusion, the Average number of adjuvant drugs prescribed was high as many were prescribed either to decrease the adverse drug reactions or to enhance the quality of life. Antimetabolites and Platinum compounds were the most frequently applied classes of anticancer drugs as they were an element of the regimens used to handle the most common cancers (69)

Hin, C, et. al. in 2019 explained an Oncology pharmacist, also recognized as an oncology pharmacy specialist (OPSs) has expertise in chemotherapeutics and their accountability in treating cancer. The OPSs extended his role as a specialist in drug therapy and categorizes it into several key components of medication supervision that include selection, storage, procurement, preparation, dispensing, dosing, transcribing, prescribing, administration,

and evaluation/monitoring/ education. As forward-facing line in ambulatory care, hospital, long-term care facilities, and/or community specialty pharmacies, the OPS helps individuals in areas of supportive care or symptomatic care like vomiting and nausea, hematological management, nutrition taken, and infection control. Their role helps in the recovery level of treatment cycles and adherence phase of the chemotherapy treatment schedules (70)

Goel A, et al 2014 demonstrated Carcinoma as the leading cause of death all over the world included India. Chemotherapy continues to be the key part of treatment with all other modalities in the management regimen. This study evaluated the drug utilization pattern in anticancer drugs. In the oncology department of a tertiary care hospital research was conducted for two and half years. Data from inpatients elder then 18 years identified with carcinoma was comprised in the study. Epidemiological data of the given drugs were compiled in a pre-designed case record form. Of 316 patients, male was (234, 74.05%) and the age set of 41-70 years males were (246, 77.85% patients). Lung Carcinoma (91, 28.8%) was most stated in the pharynx (52, 16.45%), oral cavity (32, 10.13%), and then breast region (27, 8.5%). Chemotherapy was used as a combination regimen (299, 94.62%). The most frequently prescribed Combination was 5-FU and platinum-based drugs were (124, 39.24%) in the head and neck carcinoma (89, 28.16%). Platinum-based drug combinations were given in the management of lung carcinoma. As palliative therapy ranitidine, chlorpheniramine maleate, granisetron, ondansetron, dexamethasone & furosemide with mannitol were used to manage or prevent drug-related adverse drug reactions (ADRs) of anticancer. The most used regimens were Platinum-based and 5-FU combination therapy. Antiemetic, antiallergic, antiulcer, and corticosteroids were recommended as palliative therapy (71)

Takizawa, et al in 2014 explained Japan Cancer care was changing from intravenous (IV) chemotherapy to oral anticancer medicines (OAMs), from branded OAMs to generic OAMs, from in-hospital patient care to outpatient care, from the in-hospital prescription of drugs to external prescription at outpatient pharmacies. The study described the utilization style of OAMs and the exercise of pharmacists at pharmacies. The method used was a cross-sectional drug utilization study using the database of dispensations at nationwide

included 489 pharmacies in Japan between 1 year. Surveyed the routine in the pharmacy practice using questionnaires that involved 29 elements including background, training, medication counseling, opinions about generic OAMs, and communication with prescribers. The results were 31628 patients and approximately 156904 dispensations were recognized in the database. The individuals who received therapy for molecularly targeted drugs (n = 1716, 5.4%), hormone therapy (n = 19899, 62.9%), anti-metabolic drugs (n = 9002, 28.5%), 394 (80.6%) alkylating compound drugs (n = 839, 2.7%), microtubular inhibitors (n = 148, 0.5%) were added and pharmacist responded to the questionnaires. The main advisors were the hospital setups (66.7%) or clinics (33.3 %). 60.2% of the pharmacists voluntarily received training on OAMs while an average pharmacy dispensed 1848.8 prescriptions per day. The counseling included usage and dosage, the adverse drug reactions, but 45.9% did not use any related material for patients. The main justification for these queries to medical service providers was usage and dosage varying with the drug inserts. With generic prescribing of OAMs, 48.7% of the pharmacies stated advantages in the price, but 50 % were concerned about safety measurement, efficiency, and steady supply. They stated in the Conclusions about 90 % of OAMs (oral anticancer medicines) dispensed at pharmacies in Japan were anti-metabolic drugs and hormone therapy. The study proposes the significance of pharmacy cooperation with the clinic and sharing medical records, medication counseling, and training of pharmacists (72)

Jiang Y, et. al. performed the novel molecularly targeted development of cancer therapeutics in 2022 that was expensive, slow, with many late-stage failures. They need to speed up the process by increasing early clinical evaluation of anticancer drugs over modern and rational trials which incorporate predictive, pharmacodynamic, pharmacogenomic pharmacokinetic, and end-point biomarkers. They discuss strategies that will enhance the benefit to patients and accelerate the regulatory endorsements of new anticancer drugs. The development of novel molecularly targeted cancer therapeutics remains slow and costly with many late-stage disappointments. Complications of neurological chemotherapy started with rise in the number of cancer patients. The reason was aggressive antineoplastic therapy, neurotoxic agents, and prolonged survival of patients. The complications were arisen from the lethal properties of the drug on the

nervous system or indirectly in metabolic derangements or cerebrovascular disorders made by the drugs. Early detection in evaluation may assist to avoid neurological problems (73)

Niki Carver, et.al., 2021 stated that drug utilization review (DUR), drug-use evaluation (DUE), and medication use evaluation (MUE) all are the systematic evaluation of medication, described as an authorized, structured, dispensing, ongoing review of prescribing and use of medication. DUR was a drug review against predetermined measures which lead to modifications to drug therapy. It includes a review of patients' prescribing patterns and medication data before, though, and after dispensing to guarantee suitable medication, decision-making, and positive patient results. They said as quality assurance measures, DUR programs deliver corrective action, prescriber feedback, and evaluations. Further, DUR is organized into three categories: · Prospective -evaluation of patient's drug therapy earlier medication is dispensed · Concurrent -ongoing checking of therapy during treatment protocols · Retrospective -review of therapy conducted when the patient has received medications. They evaluated why DUR is essential and plays a significant role in managed health care system understanding, evaluating interpreting, and improving the prescribing, administering, and use of medication. The findings are used to substitute for more efficient use of unusual health care resources. Additionally, Pharmacists play an essential role because of their medicinal proficiency in therapy and management. DUR offers managed care pharmacists the prospect to detect the trends in prescribing patterns within groups of patients with diabetes, asthma, hypertension, or drug-specific criteria. Then Pharmacists collaborated with prescribers, physicians, and other representatives of the allied health care team, to instruct action for the patients to improve drug therapies (74)

Chowdhury T, in 2018 defined that recent years' studies on drug utilization become a prospective means to be applied in the assessment of health systems. Further studies on drug utilization emphasis on factors linked to prescribing, administering dispensing, and medication intake, and its associated events. In addition, drug utilization data were taken from database of computer, from all these multiple types of information, quantitative or qualitative, or referring to the population data were obtainable. Patient record files and computer registries are extensively used as tools for collecting information on drug

utilization. Upon the records collection timings Retrospective, Prospective, or Concurrent Drug Utilization of studies depend. Drug utilization studies in pharmaco-epidemiology have been Importantly increasing because of their close association with other zones like public health, pharmaco-economics, pharmacovigilance, and pharmacogenetics. the review of this article highlights various aspects, types, scope, and future perspectives of DUR studies (75)

In 2021, Zhang Y, et, al., demonstrated new targeted therapy that changed the treatment protocol. Hence high prices, effects the policy limiting the reimbursement of certain medications on drug use, health outcomes, and health care utilization. They explored the 14 foremost websites and bibliographic containing databases. In their study they included policies of pharmaceuticals that limit reimbursement and coverage of various drugs or classes, they often used specific information of patients linked to physical condition, status, or need. They included non-randomized controlled trials, randomized controlled trials, interrupted time series (ITS) analyses, controlled before-after analyses set, and repeated measures studies in the large care system or jurisdictions. In this article two authors obtained data and evaluated the limitations of the study. Quantitative re-analysis of time sequence data was done for studies and efficient data. In their results, participants were mostly senior citizens or lower-income populations, or both, in publicly supported or administered pharmaceutical assistance plans. Impact of these policies diverse by the class of drug and restrictions applied or not. When policies reviewed of these non-steroidal anti-inflammatory drug classes, targeted gastric-acid suppressants, reduced drug use and savings on drugs happened immediately and afterwards for up to two years, without any raise in the use of other health services (7 studies). In addition, targeting antipsychotic second-generation drugs enhanced dealing discontinue, in addition usage of other health care facilities without dropping overall drug expenditures (2 studies), restrictions for antihypertensives reimbursement, and statins elevated use, outcomes in lesser overall drug expenditures. They concluded implementing limitations to coverage and reimbursement of medications can decline third-party drug misuse without raising the use of other health services (7 studies). Rules of calming reimbursement for drugs applied for secondary prevention can also eradicate barriers to access. Health impact assessment should be

performed where the medicines are not interchangeable. Health equity effects, relating to the reasonable use and distribution of health benefits in the social order also require clear measurement (76)

Faley B, et, al. described in 2017, Medication utilization rapidly developed over the last ten years to not only a new means of investigation and suggestive information for epidemiology for clinical pharmacology. The paper reviews the general relations of reference, with special importance on the WHO-recommended methodology founded on defined daily doses (D.D.D.), then focuses on antihypertensive therapy, antidiabetic treatment, and on the usage of drugs in psychiatry, pregnancy, cancer patients, and elderly people (77)

Bossaer, J, et, al. 2021 defined that electronic drug interaction databases were mostly practiced in clinical setting to detect the potential drug-drug interactions of the drug pairs. It is unsure that in clinical findings, interactions were important. To prove these matters, an electronic database used for comprehensive drug-drug interaction (DDI) to interpret the frequency of DDIs at a cancer care center in between oral anticancer drugs (ACDs) and antidepressants. The method was retrieved by Drug utilization reports to ascertain the patients who were recommended antidepressants and oral ACDs between 2016 till 2019 at a cancer care center. Retrospectively the treatment records of these patients were assessed using OncoRx, which is an internet-based oncology-specific database that allocates the identification of DDIs. In their findings, out of 910 patients with antidepressants medicine were one-third (281 patients, 30.9%) used an oral ACD concomitantly. One-fifth (21.0%) of these patients had lethal DDIs. These were consumers of 17 potentially interacting drug pairs. Where 10 out of the 17 drug pairs were potentially causing pharmacokinetic interactions, and the others were pharmacodynamic interactions, while only 3 out of those 17 drug pairs were clinically recognized to cause interacting incidents. They concluded, the lack of screening circumstances led to an over-detection of these drug-drug interactions (DDI) through databases of electronic, DDI. Numerous of these exposed interactions might not be believed of high-level significance in clinical practices. They highlighted the weakness of current electronic, DDI databases for noticing antidepressant DDIs and oral ACDs (78)

Negri, et al., n.d demonstrated in their studies that consequences of anticancer drugs may vary between clinical practice and clinical trials. The administrative databases provided long-term information on the effectiveness and safety of drug protocol in larger un-selected populations and designated subdivisions of patients. Furthermore, the data provided complementary and essential information on the topics, when data of randomized clinical trials tend to be unavailable. In their method, they investigated 17 new targeted high-cost drugs in oncology practice in Lombardy for 4 years. In their technique, they used records from electronic healthcare databases. Their purposes were 1) to assess the incidence of significant adverse events (ADRs) in clinical practice and their prognosticators; 2) to assess survival and the progression of free survivals and their predictors; 3) to evaluate major clinical results according to various regimens of therapy. They considered building a database by record - linkage of numerous regional health service platforms: the File F registry system (where the administration of the 17 targeted drugs was recorded), the drug prescription database, the regional hospitals discharge forms database, the outpatient's services database, and the registry office database. Individuals who were Lombardy residents received at least one chemotherapeutic drug in four years were judged. Complications warranting hospitalization were obtained from the patients' sdos when the first drug was administered. From the registry office database, Vital status was obtained. In their outcomes, they provided the incidence of severe adverse reactions of anticancer therapies, and overall disease-free persistence in clinical practice, in total and subgroups. The conclusion contributed to an improved effective evaluation, especially under-represented patients in clinical trials (79)

Kadam, et al., 2017 studied prescription patterns of chemo-drugs and their adverse events (ADRs) in breast cancer patients. This cross-sectional, observational study was conducted in the Radiotherapy department of a tertiary care teaching hospital for 02 months. Individuals diagnosed with breast cancer and arrived in the Radiotherapy section for chemotherapy treatment were included. Their prescriptions were studied, and particulars of prescribed drugs were documented. They questioned individuals about the incidence of any ADRs and given details were noted. Preventability and severity of ADRs were assessed by the modified Schumock and Thornton scale and Hartwig and Siegel scale, respectively.

Almost 70 patients were involved in this study. Cyclophosphamide was the highly mentioned chemotherapeutic agent (77.14%), pursued by Doxorubicin (68.57%) and 5-FU (flurouracil) (44.29%). The most prescribed regimen was Cyclophosphamide + 5FU + Doxorubicin trailed by Cyclophosphamide + Doxorubicin. The most reported ADRs were nausea with alopecia, blackening of nails, and vomiting. From reported ADRs, 60.11% belonged to the set of “definitely preventable” whilst 74.15% of ADRs were of a lesser amount of severity considered as “mild level 1”. Cyclophosphamide was the frequently recommended drug for breast cancer. The highest incidence of ADRs was noticed with Cyclophosphamide + Doxorubicin + 5 FU combination. Irrespective of antiemetic management of the patients who had vomiting and nausea specifies that further strong measures to prevent emesis need to be carried out, other than these ADRs of antineoplastic drugs are normally preventable (80)

Gao, Bo, et al. stated that Therapeutic drug monitoring (TDM) provides remarkable guidelines for the dose adjustment of certain antibiotics, antiepileptics, immunosuppressives, and other drugs, but its use in anticancer therapies had been limited. They identified obstacle, as the requirement of various blood samples to effectively define systemic exposure of drugs that have a short elimination half-life obtained by intermittent intravenous Injectable. On the other hand, the newer targeted anticancer therapies had distinct pharmacokinetic (PK) effect and dosing characteristics in contrast with traditional cytotoxic drugs, which made it possible with a single trough-level measurement to estimate the drug steady-state exposure. Current evidence showed that such PK parameters, including trough levels, were correlated with clinical consequences for various agents, including imatinib, rituximab, sunitinib, and cetuximab. Hence, the current result was not sufficient to mandate TDM in routine practice, an intensive investigation needed to determine the steady state through targeted agent's measurements which have a practical place in the clinical care setting of effected individuals with cancer. (81)

Khaliq et.al. performed Cancer types of Retrospective study in both genders & ethnic groups. They described the cancer pattern in genders & ethnic groups in the last eight years registered in hospitals of Karachi, Oncology wards. Cytologically and histologically established cancer of every male & female. Retrospective Data were composed by patient's

files & charts, demonstrating the population of cancer patients of Karachi, Interior Sindh region & Balochistan. A total of 5134 patients (Male = 2432 / Female = 2702) were scrutinized for cancer diagnosed with type, gender, age & ethnicity. Malignancy classification was accomplished as per coding system of W.H.O (ICD-10) International Classification of Disease performed statistical analysis for mean, proportions & standard error for genders & ethnic groups. In males ratio was 47.37%. Ethnic groups were 17% Sindhi, followed by 17% Immigrant 4% Baloch 3% Pukhtoon, \approx 4% Punjabi, 2% Minorities, 1% Siraiki, and females 52.62%, which prominent were 16% Sindhi, pursued by 21% Immigrant than Baloch 4%, Pukhtoon 3%, Punjabi 5%, Siraiki 1%, then 3% Minorities. The Mean age of male patients = 45.75 years, (standard error) $SE \pm 0.227$, and for female patients = 44.07, where $SE \pm 0.183$. In all cancers of males, the three most striking tumors were found Adenoma (Carcinoma of Glands), Head & Neck, GIT, & Body cavity membranes, and in females Breast, Adenoma (Carcinoma of Glands), Head & Neck, GIT & Body cavity membranes. The data indicated among males Head & Neck was the most occurring cancer, while the most prominent malignancy among females was Breast cancer (82)

Dranitsaris, George, et al. explained improving access of patients to cancer drugs therapy in India. The economic modeling to calculate more reasonably priced drug based on societal value. They determined the cost-efficacy of anticancer drugs and established a model for overall survival and progression-free in mCRC metastatic colorectal carcinoma patients who received chemotherapy with/without the new drug. The extent of chemotherapy and its side-effects management was attained from both private and public hospitals in India. They assessed quality-adjusted life-years (QALY) which was concluded by oncology twenty-four nurses interviewing, who managed the Time Trade-Off technique. The estimated monthly expenditure of new drugs by the target threshold of US\$9, which was 300 per QALY gained, three times than the Indian per capita GDP. The expense of per dose US\$98.00 would be measured, as prospective cost-effective for Indian public healthcare. To improve the patient's quality of life more than the norm of survival from 3-6 months, the per-dose price increased to US\$253 and US\$170 to offer the same value. They also mentioned the WHO criteria for the cost estimation of a new drug

established on economic value for the developing countries, which was feasible and be used to assess a more acceptable cost on societal value thresholds. (83)

Khan, Gulam Muhammad, et al. 2016 worked in the Central Region of Nepal, on Cancer Evaluation of Cytotoxic Medication, Prevalence, and Prescribing. They evaluated the inpatient cancer prevalence and prescribing patterns of medicines that are cytotoxic for cancer treatment in tertiary care hospitals. They modified the data collection form to collect the patient evidence on demographics and prescribed drugs. Females were observed to be more exposed to carcinoma than males. Cancer of 58 distinct kinds were noted reproductive, pulmonary, and digestive cancers being prevalent. Cytotoxic drugs 427 were prescribed. The alkylating cytotoxic group was repeatedly prescribed drug (45.67%). The average number per prescription of overall drugs was 10.77, cytotoxic group of drugs was 1.78, antibiotics 0.37 and other per prescription drugs were 8.99. The cytotoxic drugs prescribed were by brand names. The essential drugs given from the model list of (WHO) the World Health Organization were approximately 67.40% and from Nepal's essential drug list was 73.72%. Antibiotics were 31.25% and Injections given were 100 %.(84)

Sahoo, A, et, al. discussed in the 2020 drug utilization study in a Tertiary Care Center: For Improving Drug Dispensing Policies of Hospitals, discussed drug therapy plays a key part in health expenditure. The cost-efficient useful strategy for health care was research on drug utilization that formed amendments in drug policies and was helpful in the rational use. To gather the data, study was conducted on drug utilization in inpatients of the tertiary care hospital to warn potential targets for prescribing drug patterns improvement. Randomly selected 231 medical records of Retrospectively Data were collected from inpatients of various hospital wards. WHO Defined Daily Dose/Anatomical Therapeutic Chemical methodology was utilized there to assess utilization data of drugs while prescriptions of the drug were evaluated by core drug indicators of WHO. More frequently prescribed Antibiotics were accounted for drug prices. Many of the antibiotics that were prescribed as a daily dose corresponded to the defined (DD) daily dose, and adherence to international recommendations. They are prescribing polypharmacy, the Brand name was quite common. Of the total drugs, prescribed 78% were from the 2003 National List of Essential Medicines. The restricted use of expensive and branded drugs, newer antibiotics,

and polypharmacy of drugs per prescription was targeted to low down the drug cost therapy (85).

Ramesh, Ambili. In 2017, worked on anticancer drug toxicities and their management. The characteristic observed was major side effects of anticancer agents that have severity and rigorousness at the level of therapeutic doses. Most anticancer drugs are cytotoxic agents targeted at rapidly multiplying cancer cells and the alleged targets are the nucleic acids and their precursors, which are synthesized rapidly during cell division. A lower growth fraction in solid tumors than the tumor of the gastrointestinal lining, normal bone marrow, gonads, and reticuloendothelial system. In a dose-dependent manner, drugs affect these tissues and there was also an individual susceptibility. More frequently associated toxicities were with these types of tissues. They stated that side effects may be self-limited, acute or chronic, mild or potential, permanent, or life-threatening. Utmost importance is the management of the side effects because they influence the tolerability, treatment, and overall quality of life (86)

Fernandez, M, et, al. in 2019 discussed a survey that was done in a university hospital for 10 years, patients were treated for solid tumors for 4 consecutive weeks. Off-label, 33% of anticancer drugs were used. The heterogeneity-approved labeling of the different anticancer drugs and the lack of drugs in many cancers described those results. In a randomized clinical comparative trial, the level of evidence is considered the finest to obtain a label. It is not feasible always in oncology, particularly in rare tumors. Another side is to ask for a label used for the pharmaceutical firm are even not obliged to an anticancer drug even if a prominent level of proof. A label used for anticancer drugs with its references prescribing, therapeutic innovation can be accomplished in the label before use and dissemination (87).

Frey, Simon et.al. 2016 studied a literature review in Economic evaluations of Leukemia, stating lymphoma and multiple myeloma, were hematological malignancies of the blood-forming organs. They explained four kinds of leukemia: acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), chronic lymphocytic leukemia (CLL), and chronic myeloid leukemia (CML). Hence, on the health economic evidence, no comprehensive

review was accomplished for the disease. They analyzed and reviewed the economic evaluations of the literature on different types of leukemia. They recognized published cost analyses of leukemia treatments and economic evaluations through electronic databases, a systematic literature search was used. Sixty studies were selected for the review purpose. The evaluations for economic data, specifically for ALL and AML, analyzation for cost-minimization, they compared the expenses of various strategies of treatment. While in CML, imatinib, a new treatment, was introduced, and with previous first-line treatments, several cost-effectiveness analyses was done compared with imatinib. This indicates a shortage of information related to cost-effectiveness in leukemia. The initiation of new therapies needed for additional economic evaluations of this disease. Moreover, the total costs, indirect costs, and quality of life (QOL) would be beneficial evaluations in leukemia. (21)

Seow, H, et.al. 2017 defined the analysis of prospective comparative data of home and hospital treatment for developed non-ambulatory care cancer patients. They assigned patients in hospitals (group A) and at-home (group B) treatment based on geographic location. Program Don Monti was provided for treatment by the (HOME) Home Oncology Medical Extension. A medically equipped van was transported to the home with a multidisciplinary health care team, comprising an oncologist, medical technologist, oncology nurse, dietitian, and social worker. Services included physical examinations, chemotherapy, pain control, psychosocial interventions, blood transfusions, bereavement counseling, and nutrition consultation. At home, one hundred seventy-four (174) patients were treated and 44 were in the hospital. For both groups, Pre-treatment characteristics were the same except age under 50 years was more regular in the hospital (group A), and home patients (group B) were more gastrointestinal (GI) cancer. For home treatment, medical benefits included reduced narcotic analgesic requirements, decreased length of stay and hospitalization, and for female patients improved amounts of fat stores. There was no variation in survival for lower performance sicker patients whether home or hospital treatment they received. Family and Patient acceptance were excellent for home treatment. A multispecialty oncology team provided Comprehensive home treatment that was effective for terminal stage cancer patients as an alternative to hospitalization.(88)

Sokol, et.al, in 2015 conducted a study on Healthcare Costs and Hospitalization Risk of Medication Adherence. A cohort retrospective analysis of patients was done, who were enrolled in prescription and medical benefit plans. For disease-specific evaluation, patients were identified claimed for inpatient, outpatient, or emergency room services in 12 months of the study. Using an integrated analysis data on drug utilization, and medical were determined. Medication adherence is characterized by the maintenance of medications by days' supply for each condition. The analysis consisted of 137,277 patients, a population-based sample of those under age of 65 years. All-cause and disease-related medical expenses, drug costs, and hospitalization risks were noted. Using regression analysis, at varying levels, these demonstrated medication adherence. For hypercholesterolemia and diabetes, with minor disease-related medical budgets, an important level of medication adherence was linked. For these conditions, elevated medication costs produce a net decrease in overall healthcare costs. Cost offsets were detected for hypertension, diabetes, and hypercholesterolemia, all-cause by medication adherence, costs at prominent levels. For all, hospitalization expenses were lower for individuals with superior medication adherence.(27)

Scarborough BM; in 2018 explained that assessment of pain and its management is critical to enhanced the health consequences in all adult cancer patients. Their study of 160 patients described, approximately 80 (50%) reported mild or severe pain. Of those with pain 40% of them were not given any pain-relieving medication. Sixty percent (60%) of the patients had pain management appropriately. Inappropriate pain documentation emphasized the need for improvement in 57% of cases, of the patients. Some NSAIDs were prescribed to only 8 (5%) patients on pain medication. The most frequently used opioid was Transdermal fentanyl (21%) for pain moderate to severe. Therefore, in pain management despite published guidelines, many cancer patients receive inadequate analgesia. (89)

M M; Martin P et, al. described in 2017 the Anticancer Drugs Prescribing Pattern, Errors, its Clinical Outcomes in a Medicinal Oncology department. Each prescription was analyzed for demographic data, age, medicine given, dose, duration of medicine, etc. Different cancer types, most prescribed anti-cancer drug and their percentages of use were compared with essential Drug list and noted. The outcomes of ages were in between 55-65

years. Females were more prone to the disease, breast cancer, ovarian cancer and stomach cancer was highly identified. In contrast, lungs and stomach carcinoma were more noted in males. Alkylating agent was the most prescribed drug. The utilization of drugs was found 70% rational with national essential list. Periodic assessment was required for prescribing pattern for reducing unwanted drugs effects. (90)

Zaal R, et.al 2020 worked on the Acceptance of pharmacists' suggestions on the telephone on routine bases by prescribers in hospital practice. In clinical pharmacy setting, component of the evaluation was often overlooked. Research was performed for evidence on the topic, acceptance-based suggestion was a measure of pharmacist's recommendation for a prescriber's compliance with drug therapy. For drug costs or quality of patient care, the pharmacist's suggestions, need for the prescriber to admit them. Approximately 23 studies were related to the topic. The average acceptance rate was 85.5%. Acceptance factors involved communication, time, type of prescriber, solicited versus unsolicited endorsements, and type of pharmacist. Non-acceptance leading factors are lack of physician knowledge to pharmacokinetic parameters, negative attitudes regarding clinical pharmacy, quality of suggestions, and prescribers' exercise of caution regarding patient's safety and well-being. To evaluate the importance, more research needs to be done on these factors. (91)

CHAPTER 3

EXPERIMENTAL

3.1 Materials

3.1.1 Study type

A retrospective observational study was conducted, which assessed the prescription pattern and prevalence information of cancer in Karachi, Pakistan.

3.1.2 Study Period

6 months for the public sector, 2 months for private sector hospitals.

3.1.3 Departments Concerned

Department of Pharmacy Practice FUUAST Karachi, Department of oncology JPMC, Department of Oncology ZHC.

3.1.4 Ethical Clearance

The study was endorsed by the ethical committee and Departments Heads of Institutions.

3.1.5 Study Demographics

To attain the objective of a retrospective view, the research study was conducted in the public and private sectors of Karachi, Pakistan. Karachi is a metropolitan city that covers patients from all over Pakistan. It has many reputable hospitals, which provide all essential health facilities in an organized way. The need of this research is to find out the lacking and to suggest amendments for better outcomes in cancer. This study covered both sectors for improvements in all aspects of DUE.

- *Jinnah Postgraduate Medical Hospital*, Karachi, is the oldest, biggest, 1600-bedded, best-equipped public sector tertiary care hospital in Pakistan. It has 31 departments with an influx of over one million patients annually, Provide quality healthcare with 30,000/year surgeries, all free of charge. Its Oncology department covers OPD, IPD, Emergency, Chemotherapy unit, Radiation unit, and Pharmacy.
- *Zia-Uddin Group of Hospital*, Karachi is one of the largest private tertiary care hospitals in the country. Providing all oncology services of the highest quality at affordable prices. Its oncology is equipped with state-of-the-art equipment.

3.1.6 Study Parameters

In the beginning, the medical director of the hospital and procedure properly approved by duly signing the letter to conduct the study. A detailed data collection form was designed on an excel sheet to note down the requirements which include:

▪ Age	▪ Gender	▪ Status
▪ Cast	▪ Residents	▪ Phone #
▪ Date of Diagnosis	▪ Registration No.	▪ Family History
▪ Weight	▪ Height	▪ BSA
▪ Alive / Deceased	▪ Comorbid	▪ Cancer Type
▪ Diagnosis	▪ Stage	▪ Plan of Treatment
▪ Surgery	▪ Place of surgery	▪ Radiation Cycles
▪ Chemotherapy Cycle	▪ Immunotherapy	▪ Hormone therapy
▪ Targeted Therapy	▪ Name of Chemo Drug	▪ Classification of Drug
▪ Strength	▪ Route	▪ Direction/Purpose
▪ Name of Other Drugs	▪ Strength	▪ Route/Direction/Purpose
▪ Nausea/Vomiting	▪ Anti-Emetics	▪ Pain Management
▪ Addiction Type	▪ Intake Period	▪ Amount
▪ Side Effects		

3.1.6.1 Study assistance

This was collected with the help of patients, attendants, physicians, and nursing staff for missing information, in addition, their case sheets, lab results, and progress were also observed.

3.1.7 Source of Data

In the existence of the concerned oncologist and a duty doctor, documentation was composed. The patient registration numbers will also be allotted for concurrent measures of studies.

3.1.8 Sample Size

Overall, 164 cases were reviewed from the said public sector and 22 from the private sector were analyzed for further evaluation.

3.1.9 Operational Modality

This included the records of in-patients file, medical practitioner records, computerized records, and related health surveys of the concerned department.

3.1.10 Software Used

Microsoft Office Excel, Word (2016), SPSS 21.0

3.2 Methodology

A review of literature for the same context was studied to create and design the study demonstrating methodology and outcomes. The Procedure for the study map was prepared and submitted to the ethics committee of institutions for approval. Collection of data was done from the medical records department, from in-patient files of the Medicine unit. All data were sorted, categorized, and entered into an excel file and SPSS for analysis.

3.2.1 Statistical Methods

Different statistical analyses, various comparative tables, and graphs were designed to comprehend the prescription pattern, demographic details, and distribution among the patient sample population of both sectors.

3.2.2 Study Workflow Chart



CHAPTER 4

RESULTS & DISCUSSION

4.1 Results

A retrospective study was performed to compare and evaluate drug utilization of anti-cancer drugs in public and private sector hospitals in Karachi. Approximately, 186 cases were observed over six months, including 164 patients from the public sector and 22 from the private sector hospitals in Karachi. The study included male and female patients receiving treatment for cancer at different hospitals in Karachi.

4.2 Public Sector

4.2.1 Caste and Gender

Almost, 164 (88.17%) patients included in this study received their treatment from public sector hospitals, 84 (51.2%) being females among which 22 (13.4%) were Urdu Speaking, 20 (12.20%) were Sindhi, 19 (11.59%) were Punjabi, 13 (7.93%) were Pathan and 8 (4.88%) were Balochi. Male patients were 80 (48.8%), among which 23 (14.02%) were Urdu speaking/Muhajir, 23 (14.02%) were Sindhi, 13 (7.93%) were Punjabi, 10 (6.10%) were Pathan and 8 (4.88%) were Balochi.

Table 4.1: Distribution According to Caste and Gender in the Public Sector

Distribution According to Caste and Gender in the Public Sector				
Caste	Female	Male	Total	% Of Total
Muhajir	22	23	45	27.4%
Sindhi	20	23	43	26.2%
Punjabi	19	13	32	19.5%
Pathan	13	10	23	14.0%
Balochi	8	8	16	9.8%
Hindko	1	3	4	2.45
Saraiki	1	0	1	0.6%
Total	84	80	164	100.0

A) Highly exposed ethnic group

Cancer was the most prevalent in the ethnic group Muhajir which was 27.4% followed by Sindhi 26.2%, Punjabi 19.5%, Pathan 14.0%, Balochi 9.8%, Hindko 2.45%, and Saraiki 0.6%.

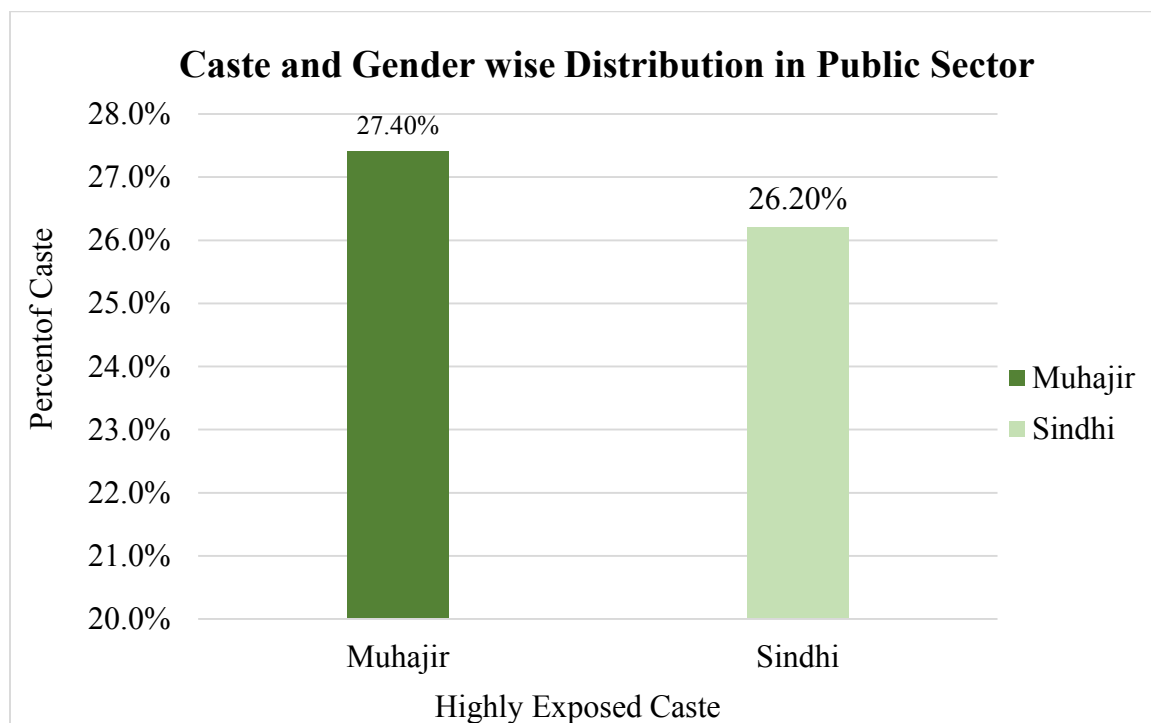


Figure 4.1: Caste and Gender-Wise Distribution in Public Sector

4.2.2 Age-wise Distribution

The study revealed that the most prominent age group was 41-50 (29.9%) years of age with 27 (16.4%) females and 20 (12.19%) males falling in this category. The next susceptible age groups for patients diagnosed with cancer were 31-40 (18.9%) and 51-60 (18.3%) years of age, with 14 (8.53%) females and 17 (10.3%) males in the former and 15 (9.14%) females and 13 (7.92%) males in the later age group.

Table 4.2: Age-Wise Distribution in the Public sector

Age-wise Distribution in the Public sector					
Age (Years)		Frequency	Percent (%)	Valid Percent	Cumulative Percent
Valid	10-20	13	7.9	7.9	7.9
	21-30	22	13.4	13.4	21.3
	31-40	31	18.9	18.9	40.2
	41-50	49	29.9	29.9	70.1
	51-60	30	18.3	18.3	88.4
	61-70	9	5.5	5.5	93.9
	71-80	6	3.7	3.7	97.6
	81-90	3	1.8	1.8	99.4
	Above 90	1	0.6	0.6	100.0
	Total	164	100.0	100.0	

4.2.3 Marital Status

Based on marital status, 128 (78.0%) married people were more carcinogenic, of which incidence rate was 63 (38.41%) females while 65 (3%) males, followed by single (unmarried) individuals were diagnosed with cancers of ratio 26 (15.9%) where females were 11 (6.7%) and males were 15 (9.14%) after that female widows were 10 (6.1%) average rates.

Table 4.3: Distribution According to the Marital Status in the Public sector

Distribution According to the Marital Status in the Public sector						
Status		Female	Male	Frequency	Percent	Cumulative Percent
Valid	Single	11	15	26	15.9	15.9
	Married	63	65	128	78.0	93.9
	Widows	10	0	10	6.1	100.0
	Total	84	80	164	100.0	

4.2.4 Resident of Cities

More than 50 city residents diagnosed with diverse types of cancers, belonging to all four provinces of Pakistan, came for diagnosis and treatment. But the maximum number of patients were from 5 major cities, Karachi, Quetta, Sukhar, Hyderabad, and Thatta, of region Sindh. From Karachi 74 (45.1%) residents shows the highest incident rate of which 41 (25%) were females and 33 (20.1%) were males. Subsequently in the order, the residents from Quetta 11 (6.7%) were entertained, of which 2 (1.2%) were females while 9 (5.4%) were males. Then Hyderabad 5 (3.0%) and Sukhar (3.0%) with 1 (0.6%) female and 4 (2.43%) males, and 3 (1.8%) females and 2 (1.2%) males. Later Thatta 4 (2.4%) of which 1 (0.6%) was female and 3 (1.8%) were male residents.

Table 4.4: Distribution According to the Resident of Cities in the Public sector

Distribution According to the Resident of Cities in the Public sector			
Residents	Female	Male	Grand Total
Karachi	41	33	74
Quetta	2	9	11
Hyderabad	1	4	5
Sukhar	3	2	5
Thatta	1	3	4
Grand Total	84	80	164

4.2.5 Family History of Cancers

Of the 17.1% of patients having a positive family history of cancer, 8 (4.87%) females and 2 (1.21%) males reported having a family history of breast cancer, while 6 (3.65%) females and 3 (1.82%) males had a family history of gastrointestinal cancer including liver cancer and esophageal cancer and 3 (1.82%) females and 2 (1.21%) males had a family history of head and neck cancer which includes carcinoma of tongue, cheeks, throat, and oral mucosa.

Table 4.5: Family History of Cancers in the Public Sector

Family History of Cancers in the Public Sector				
S. No	Family History	Females	Males	Grand Total
1	YES (CA Intestine)	2	1	3
2	YES (CA Liver)	0	2	2
3	YES (CA Brain)	0	1	1
4	YES (CA Breast)	8	2	10
5	YES (CA Esophagus)	4	0	4
6	YES (CA Head & Neck)	3	2	5
7	YES (CA Lungs)	1	0	1
8	YES (CA Bones)	1	0	1
9	YES (CA Blood)	0	1	1
	Grand Total	19	9	28

4.2.6 Diagnostic site of Cancer

Of 50 distinct types of cancers involving all body systems were observed in which carcinoma, sarcoma, adenoma, leukemia, and lymphoma were significantly identified consisting of the head and neck cancers, gastrointestinal tract, endocrine system, central nervous system, reproductive systems, pulmonary, blood cancers, lymphatic system, etc.

The most prevalent and frequently diagnosed carcinomas were head and neck cancer, the incidence rate in both genders was 42 (25.06%), followed by breast cancer at 36 (21.34%), afterward, leukemia was found to be dangerous that was 20 (12.10%), then gastrointestinal carcinoma 18 (10.09%), reproductive system 14 (9.14%), later on, CA brain, adenoma, sarcoma 6 (3.65%) was diagnosed, other striking carcinomas were lymphoma, pulmonary cancer 5 (3.04%), renal cancer 3 (1.08%) and chondrosarcoma, melanoma, myeloma was 1 (0.60%).

Table 4.6: Distribution According to the Site of Cancer in the Public sector

Distribution According to the Site of Cancer in the Public sector			
S. No	Cancer Site	Count of Cancer Type	% of Cancer Type
1.	CA Head and Neck	42	25.60%
2.	CA Breast	35	21.34%
3.	Leukemia (Blood Cancer)	20	12.10%
4.	CA Git	18	10.09%
5.	CA Reproductive Organ	15	9.14%
6.	Adenoma	6	3.65%
7.	CA Brain	6	3.65%
8.	Sarcoma	6	3.65%
9.	CA Pulmonary	5	3.04%
10.	Lymphoma	5	3.04%
11.	CA Renal	3	1.80%
12.	Chondrosarcoma	1	0.60%
13.	Melanoma	1	0.60%
14.	Myeloma	1	0.60%
	Grand Total	164	100.0%

4.2.6.1 CA Head & Neck

Cancer with the highest occurrence rate was Head and Neck Cancers 42 (25.6%) with 11 (6.7%) *females*, in which carcinoma of the tongue was significantly noted 5 (3.0%), followed by carcinoma of the cheeks 3 (1.8%), hard palate 2 (1.2%) and buccal mucosa 1 (0.6%).

While in *males* 31 (18.9%) were markedly identified with head and neck carcinoma with the most occurrence site being buccal mucosa 11 (6.6%), which was followed by carcinoma of cheeks 7 (4.2%), tongue, larynx, and nose 3 (1.8%), hard palate, mouth, lip, and nasopharynx were 1 (0.6%).

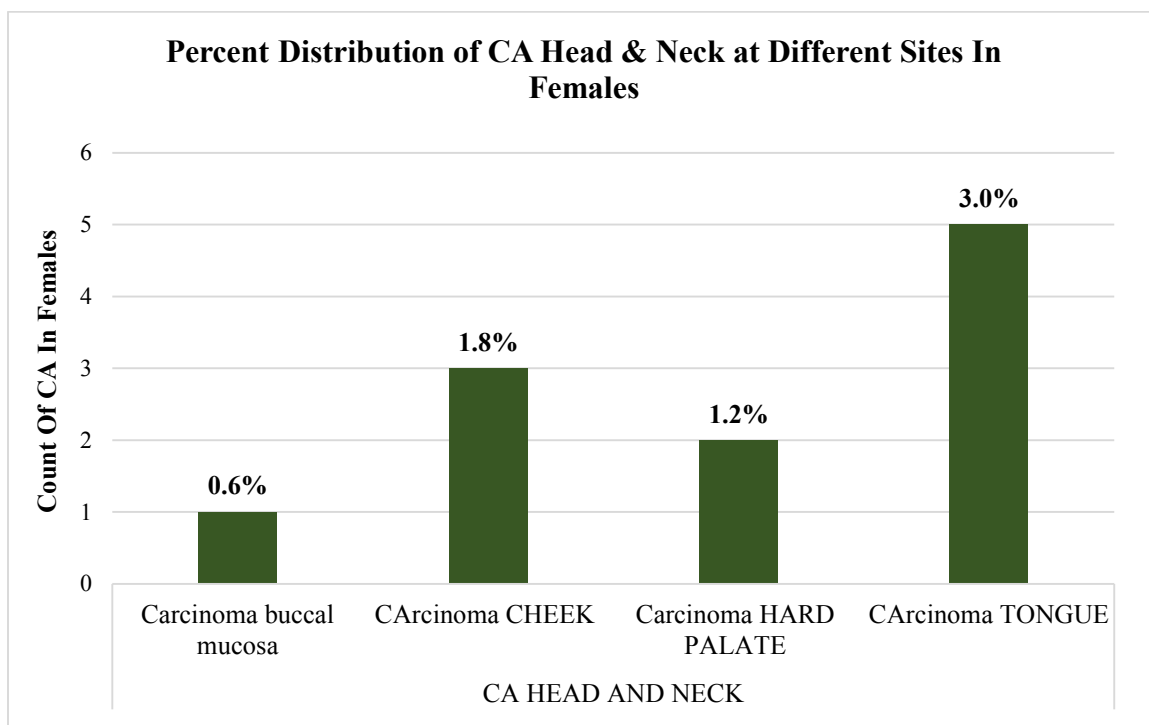


Figure 4.2: Percent Distribution of CA Head & Neck at Different Sites in Females in the Public Sector

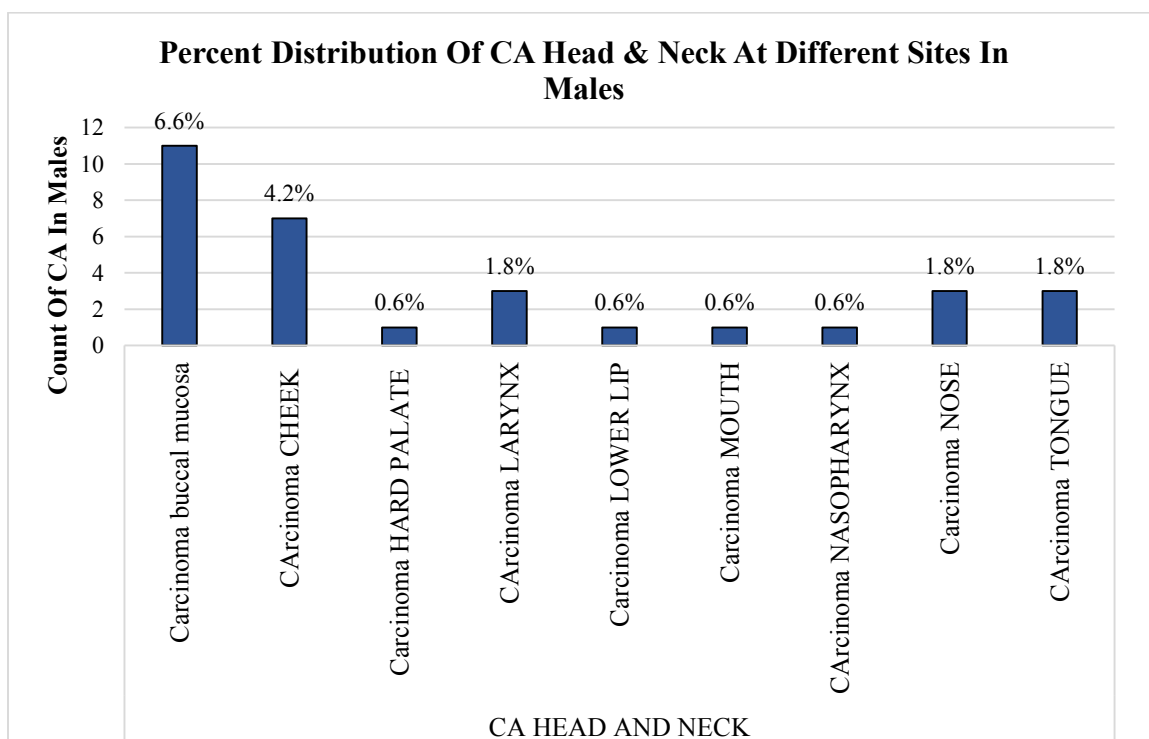


Figure 4.3: Percent Distribution of CA Head & Neck at Different Sites in Males in the Public Sector

4.2.6.2 CA Breast

Another high-incidence and commonly diagnosed cancer was breast Cancer, which was the most occurring type of cancer, especially in women, 35 (21.3%) were diagnosed with (20.12%) females and 2 (1.21%) males.

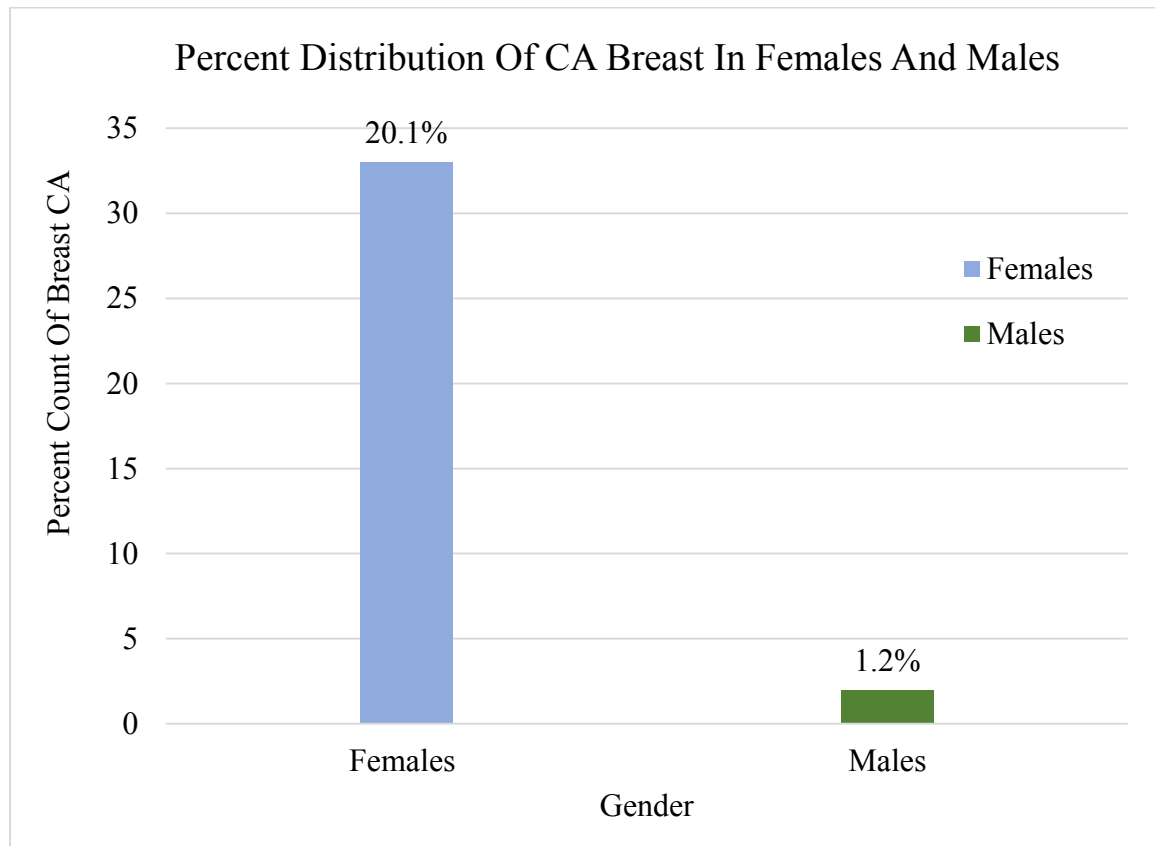


Figure 4.4: Percent Distribution of CA Breast in Females and Males

4.2.6.3 CA Blood

Diverse types of Blood cancer were also found to be quite common, analyzed in 20 patients, out of them 9 (5.45%) were females and 11 (6.6%) were males in which acute promyliotic leukemia (APL), chronic myeloid leukemia (CML), acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML) was identified.

Table 4.7: Distribution According to the Types of Blood Cancer in the Public sector

Distribution According to the Types of Blood Cancer in the Public sector			
Blood Cancer Types	Female	Male	Grand Total
(APL) Acute Promyliotic Leukemia	0	1	1
(CML Suspected) Myeloproliferative Disorder	0	1	1
(CML) Chronic Myeloid Leukemia	6	0	6
(ALL) Acute Lymphoblastic Leukemia	1	5	6
(AML) Acute Myeloid Leukemia	2	4	6
Grand Total	9	11	20

4.2.6.3.1 Gender-Wise Difference of Blood Cancer

The frequency of chronic myeloid leukemia *CML* was high in females which was 6 (3.63%), then AML and ALL 2 (1.21%) and 1 (0.6%).

While in males, *ALL* was often diagnosed with the frequency of 5 (3.03%), AML 4 (2.42%), and CML and APL 1 (0.6%),1 (06%).

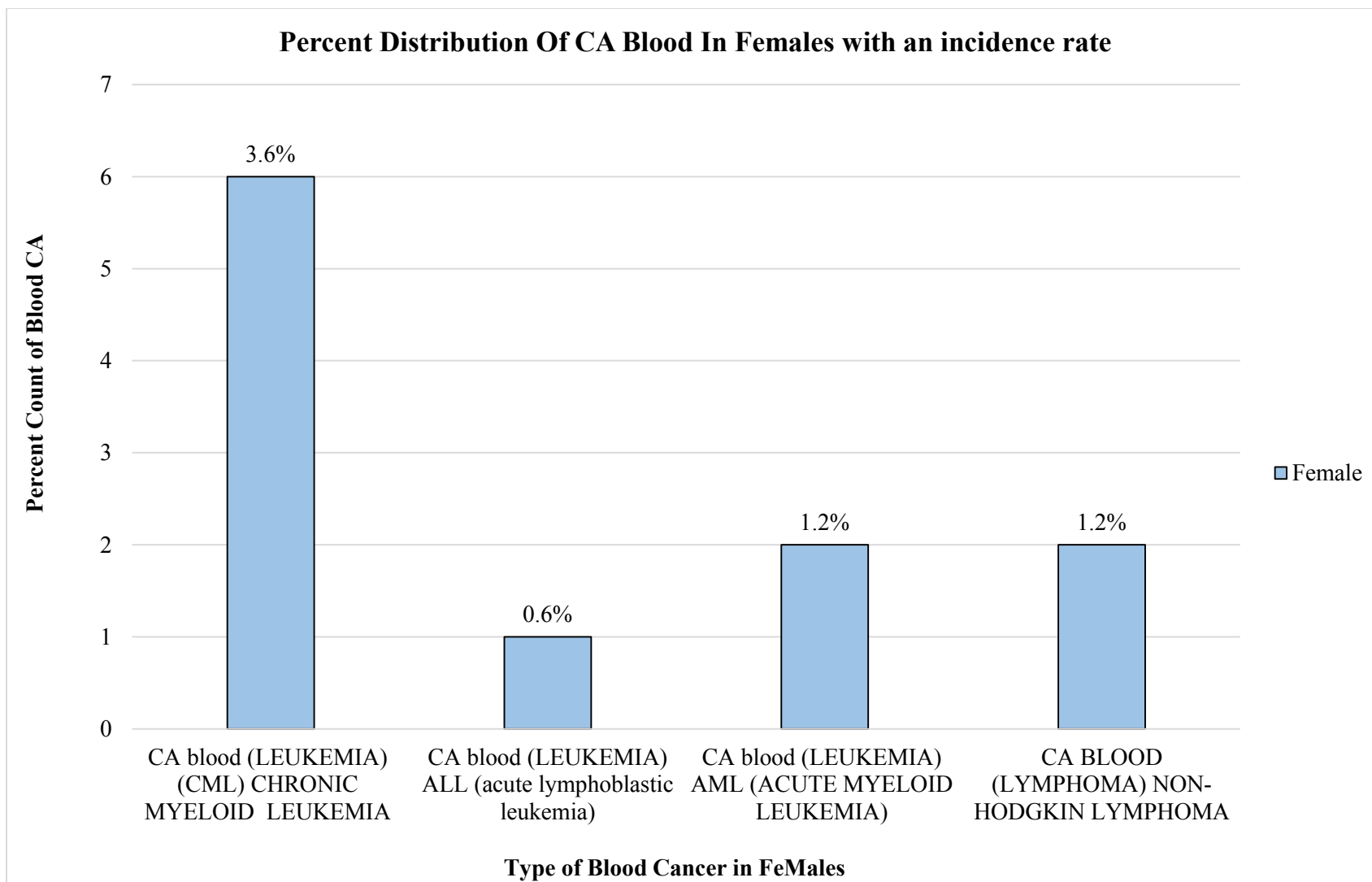


Figure 4.5: Percent Distribution of CA Blood in Females with an Incidence Rate in the Public Sector

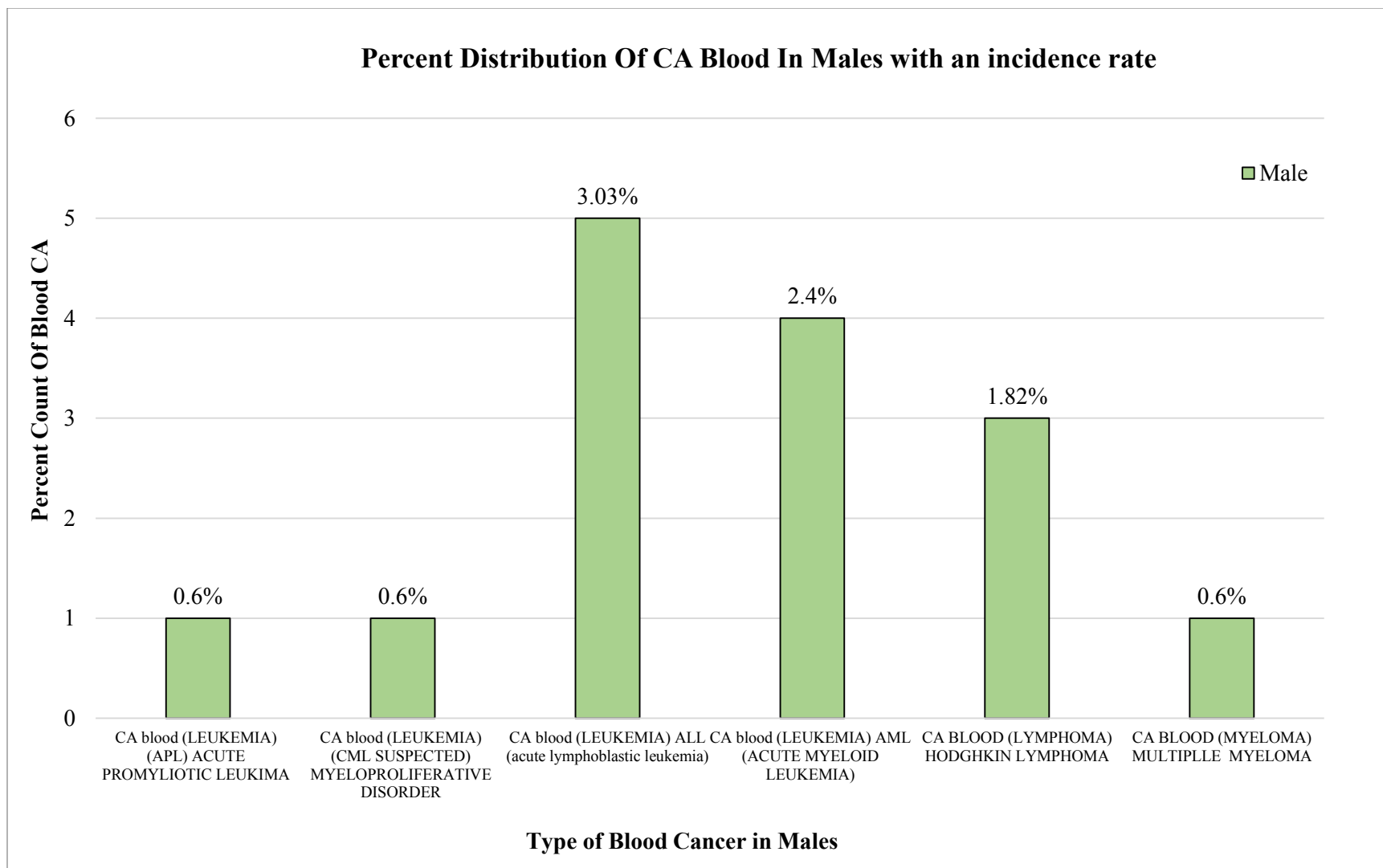


Figure 4.6: Percent Distribution of CA Blood in Males with an Incidence Rate in the Public Sector

4.2.6.4 CA Gastrointestinal Tract:

Another most predominant cancer type was the gastrointestinal tract 19 (11.5%), with 6 (3.6%) females and 13 (7.87%) males.

Most affected sites in females were esophagus 3 (1.8%) followed by rectum, liver, and biliary tract 1 (0.6%). While in male carcinoma of the rectum occurs, most was 5 (3.03%), and afterward esophagus and liver

2 (1.2%), then a colon, cecum, abdominal wall and adenocarcinoma of the stomach 1 (0.6%).

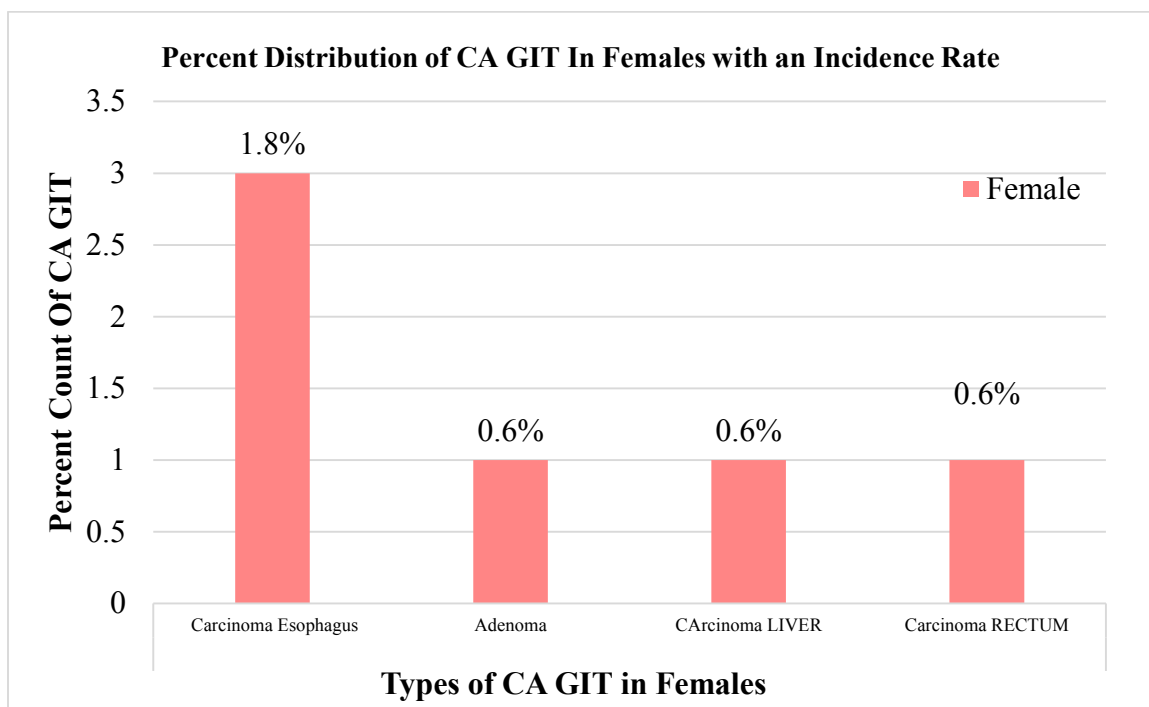


Figure 4.7: Percent Distribution of CA GIT in Females with an Incidence Rate in the Public Sector

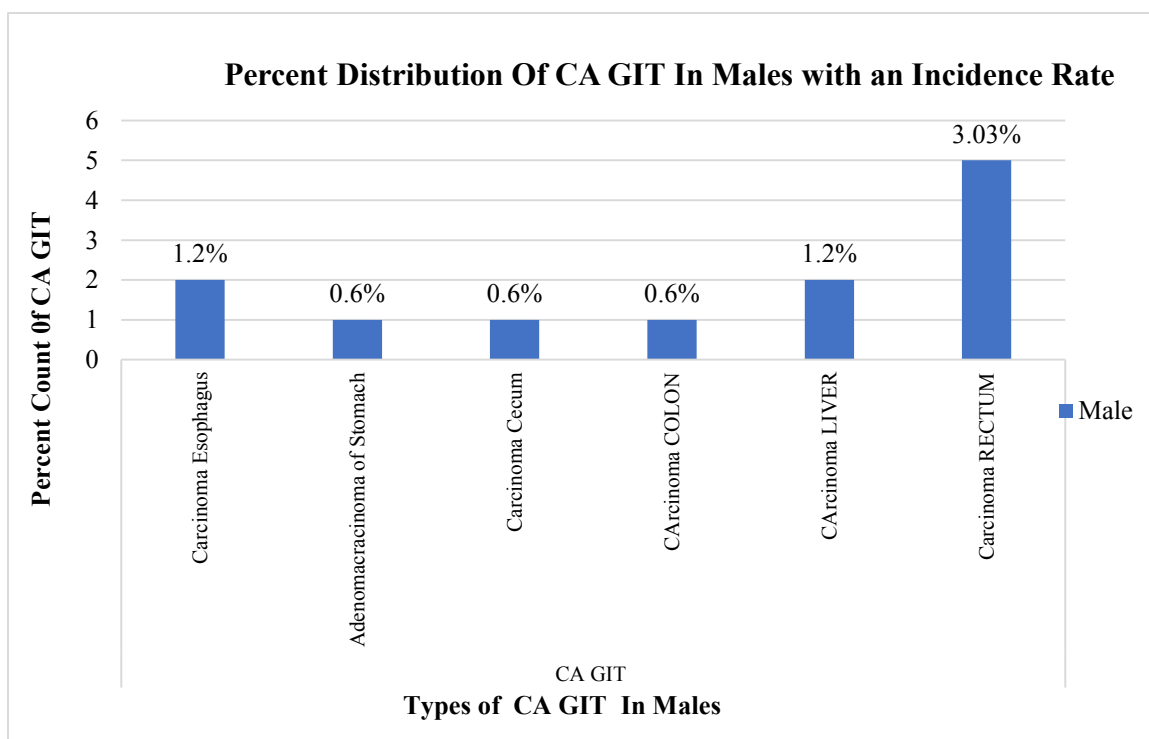


Figure 4.8: Percent Distribution of CA GIT in Males with an Incidence Rate in the Public Sector

4.2.6.5 CA Reproductive Tract

Reproductive tract carcinoma was also found in a considerable number, observed 12 (7.3%) where 10 (6.1%) females and 2 (1.21%) males. In females, carcinoma of ovary 6 (3.6%) was high in diagnosis, later are cervix and clitoris were classified with 3 (1.8%) and 1 (0.6%) ratio. On the other hand, most diagnosed in males were prostate and testis cancer which was 1,1 (0.6%).

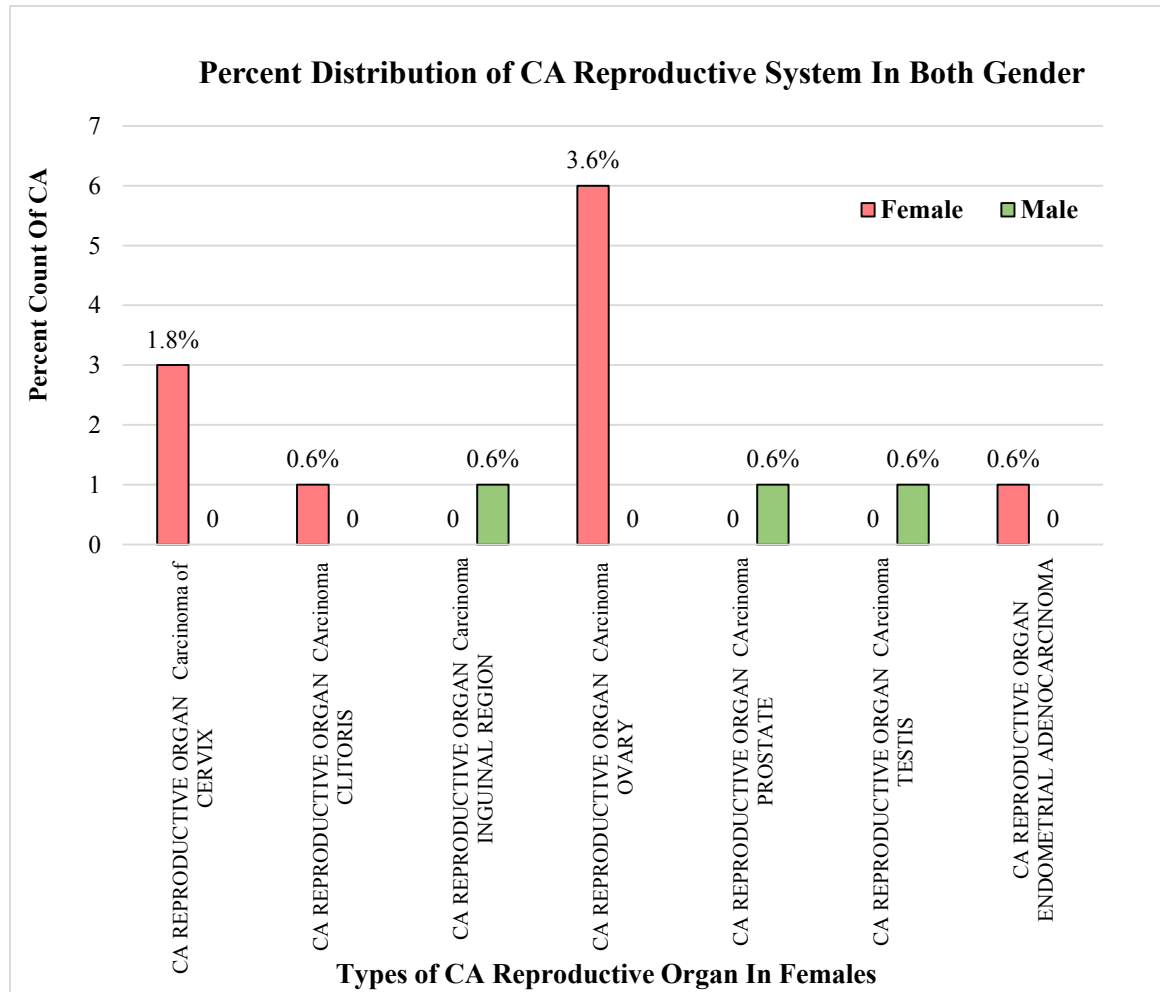


Figure 4.9: Percent Distribution of CA Reproductive System in Both Genders

4.2.6.6 Other Types of Cancer

In both genders, other cancers with significant occurrence were *CA brain, Adenoma, and Sarcoma* 6 (3.65%) The rate of affected gender in CA brain and adenoma was high in females 4 (2.4%) while males 2 (1.2%), in Sarcoma males, were more affected 5 (3.04%) than females 1 (0.6%).

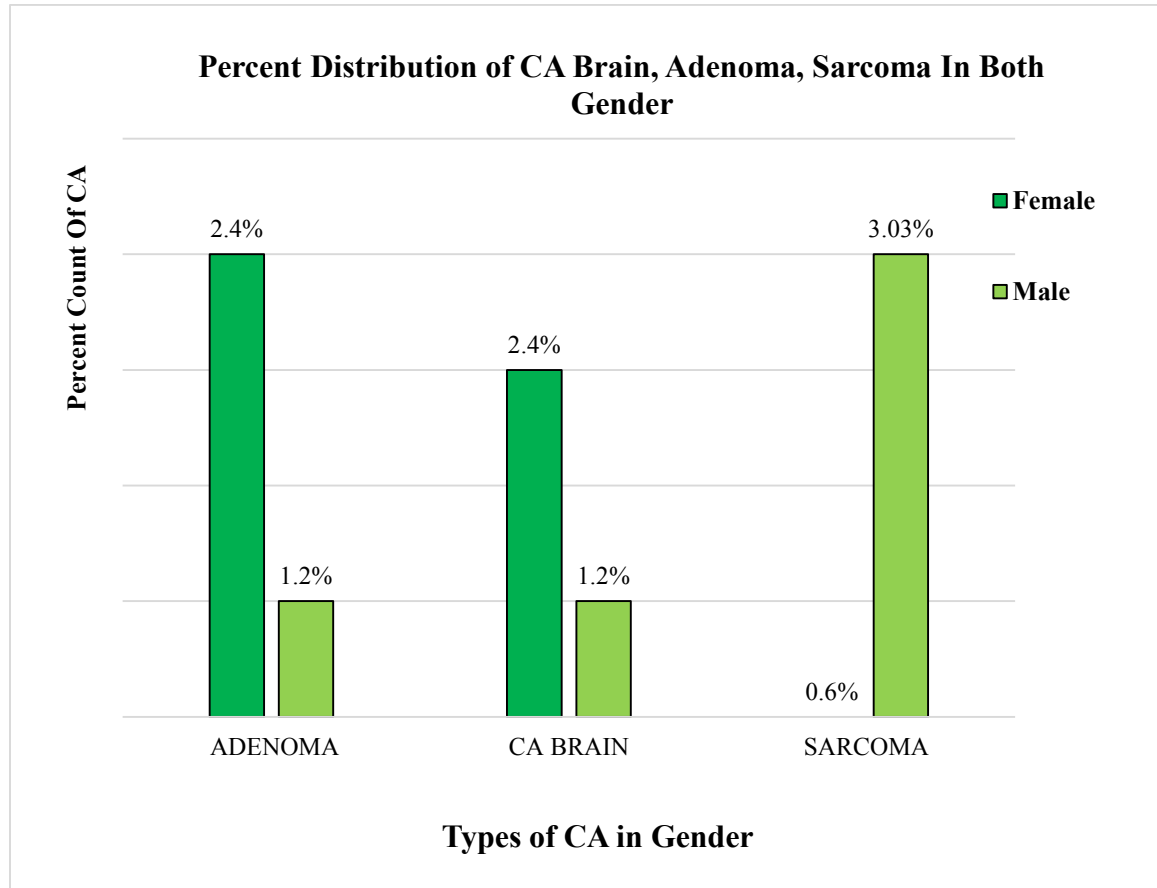


Figure 4.10: Percent Distribution of CA Brain, Adenoma, and Sarcoma in Both Gender

4.2.7 Stages of Cancer

Most patients had stage IV disease 66 (40.2%) with 33 (20.12%) females and 33 (20.12%) males, respectively. In contrast, 53 (32.3%) patients had stage III disease with 32 (19.51%) females and 21 (12.8%) respectively males at the time of diagnosis. Moreover, 30 (18.3%) patients had stage II disease with 16 (9.7%) females and 14 (8.7%) males. Patients had stage I disease with 13 (8.0%) which 2 (1.2%) were females and 11 (6.7%) males. while n pre-blastic stage 2 (1.2%) were identified where 1,1 (0.6%) were female and male.

Table 4.8: Distribution According to the Stages of Cancer in the Public sector

Distribution According to the Stages of Cancer in the Public Sector				
STAGE	Female	Male	Grand Total	% Of Total
0	1	1	2	1.2%
1	2	11	13	7.9%
2	16	14	30	18.3%
3	32	21	53	32.3%
4	33	33	66	40.2%
Grand Total	84	80	164	100.0%

4.2.8 Gender-Wise Difference of Stages:

Based on details, females were more provoked with cancer which was 84 (51.12%), more occurrences than males, despite them, 65 (40%) were analyzed on stage III and IV. While, on the other hand, 80 (48.8%) males were diagnosed, of which 54 (33%) were in stages III and IV.

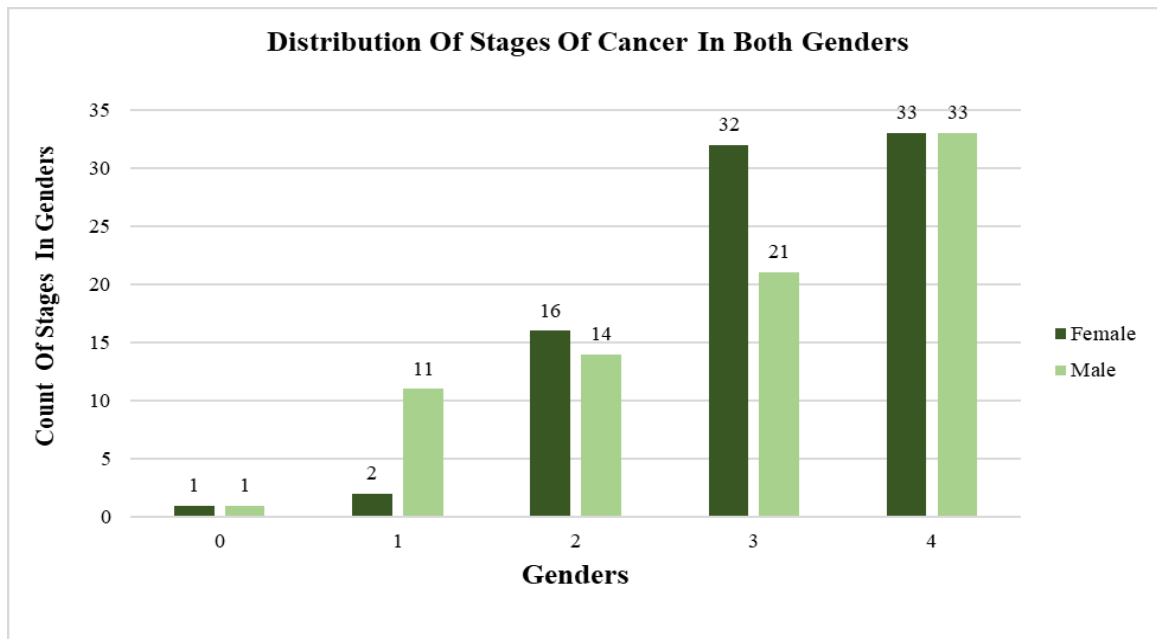


Figure 4.11: Distribution of Stages of Cancer in Both Genders in the Public Sector

4.2.9 Plans of Treatment

Consistent with the site, type, size, stage, and aggression of the disease, most of the patients received treatment plans which include chemotherapeutics alone or a combination of therapy. They were symptomatic, radicle, adjuvant, palliative, CCRT (Concurrent chemoradiation therapy), neo-adjuvant, Maintenance, induction, consolidation, and others.

The most significant treatment regimen was Palliative treatment 59 (36.0%) with 30 (18.2%) females and 29 (17.6%) males while 53 (32.3%) received Radicle/CCRT with 24 (14.6%) of those being females and 29 (17.6%) being males. Other treatment options were Radicle 25 (15.2%), in which 13 were females and 12 were males, followed by radicle/adjuvant 9 (5.4%), where 6 (3.6%) females and 3 (1.8%) males, then neo-adjuvant 6 (3.6%), induction 3 (1.8%), maintenance and symptomatic were 2 (1.2%).

Table 4.9: Distribution According to the Plans of Treatment in the Public sector

Distribution According to the Plan of Treatment in the Public sector					
S. No	Plan of Treatment	Female	Male	Grand Total	% Of Total
1	Symptomatic	2	0	2	1.2%
2	Radicle/Adjuvant	6	3	9	5.4%
3	Radicle / CCRT	24	29	53	32.3%
4	Radicle	13	12	25	15.2%
5	Palliative/ CCRT	1	2	3	1.8%
6	Palliative	30	29	59	36.0%
7	Neo-Adjuvant	6	0	6	3.6%
8	Maintenance	0	2	2	1.2%
9	Induction / Consolidation	1	1	2	1.2%
10	Induction	1	2	3	1.8%
	Grand Total	84	80	164	100.0

4.2.9.1 Gender-Wise Difference of Treatment Plan:

Treatment plan determined high in females were palliative 30 (18.2%) followed by radicle/CCRT 24 (14.6%), radicle 13 (8.0%), neo-adjuvant and radicle/adjuvant 6 (3.6%).

While in the male's treatment regimen

Observed more were radicle/CCRT 29 (17.6%) and palliative 29 (17.6%), afterward radicle 12 (7.3%) then radicle/adjuvant 3 (1.8%)

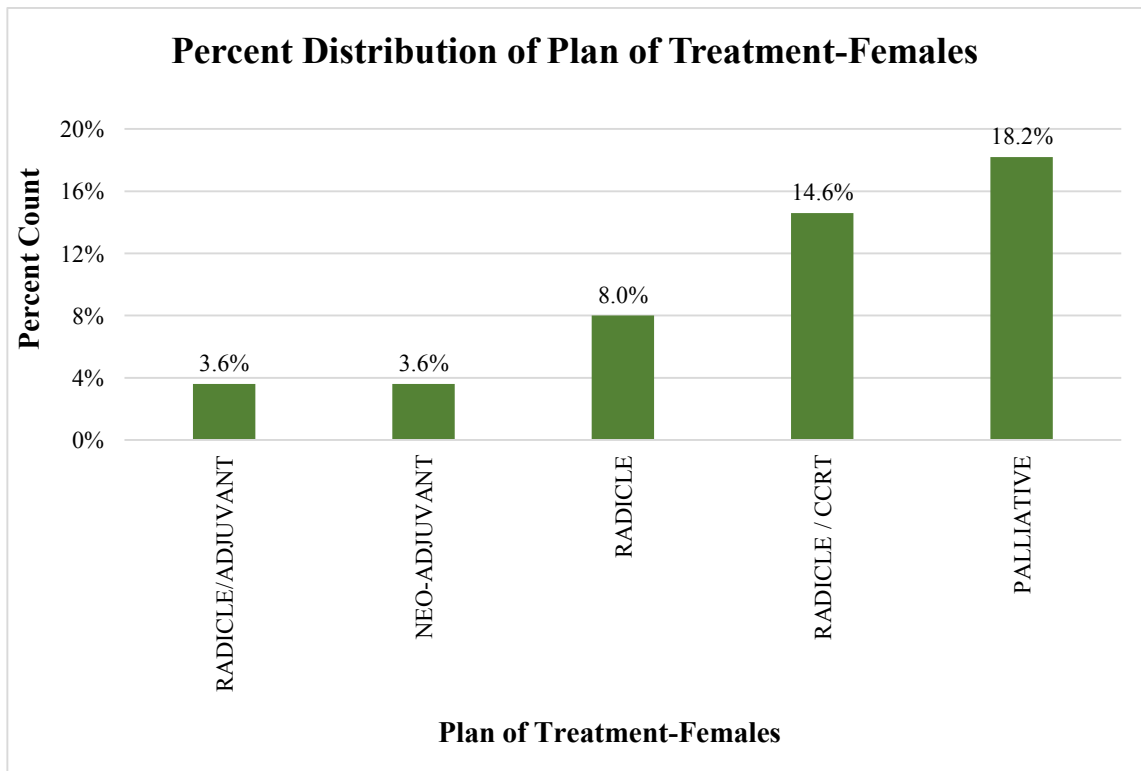


Figure 4.12: Percent Distribution of Plan of Treatment-Females

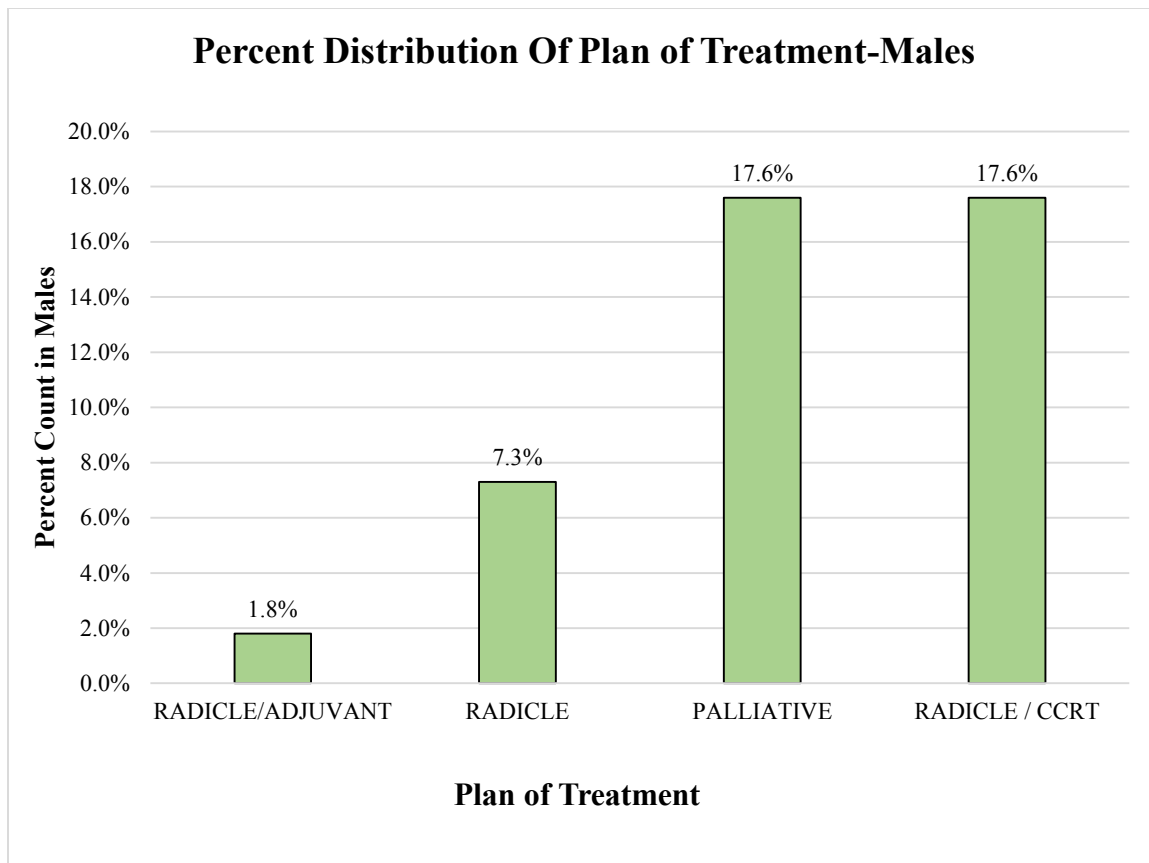


Figure 4.13: Percent Distribution Sof Plan of Treatment-Males

4.2.10 Surgical Procedures in Treatment Protocol

(A) Hospitals where surgeries performed

Under the treatment possibilities, 36.5% of patients went under surgical procedures, where decided 60 patients operated in different public and private sectors like Jinnah, civil, Liaquat national, AKU, baqai, Burhani, etc. The most burdened hospitals were in the public sector where surgeries were performed 33 (55%) in Jinnah hospital than in civil hospitals 6 (10%) followed by the private sector of LNH 6 (10%), then others.

Table 4.10: Distribution According to the Hospitals where Surgeries Performed by Patients from the Public sector

Distribution According to the Hospitals Where Surgeries Performed by Patients from the Public Sector		
S. No	Hospitals	Count Of Surgery
1	Agha Khan Hospital	1
2	Baqai Hospital Karachi	1
3	Burhani Hospital	1
4	Civil Hospital Karachi	6
5	Dar-Ul-Sehat Hospital	1
6	Federal Hospital	1
7	Jamshoro Sindh Hospital	1
8	JPMC	33
9	Lahore Medical Hospital	1
10	Liaquat National Hospital	6
11	Neurospinal & Cancer Care Institute	1
12	Niaz Hospital	1
13	Dow (OJHA)	1
14	PNS Shifa	1
15	South City Hospital	1
16	SIUT	1
17	T. Adam	1
18	Anklesaria	1
19	Grand Total	60

B) Surgical Procedures of Different Organ Sites

Out of 33 (55%), the surgical procedures of different sites performed in Jinnah hospital, noted were surgery of the brain, cheek, cholecystectomy, colectomy, esophagectomy, mastectomy, MRM, thyroidectomy, tongue, total hysterectomy.

The highest number of performing surgery was MRM (Modified Radicle Mastectomy) was 11 (18.3%), later, surgery of the head and neck 4 (6.6%), 3 (5.0%) (Cheeks, and tongue) then gastrointestinal sites, brain, thyroids 2 (3.33%).

Table 4.11: Distribution Burden of Different Types of Surgeries Performed under treatment protocol in JPMC

Distribution Burden of Different Types of Surgeries Performed under treatment protocol in JPMC		
S. No	Hospital	Count of Surgery / DATE
	Jinnah Hospital Karachi	
1	Brain	2
2	Cheek	4
3	Cholecystectomy	2
4	Colectomy	3
5	Esophagectomy	2
6	Mastectomy	2
7	MRM	11
8	Thyroidectomy	2
9	Tongue	3
10	Total Hysterectomy	2
	Grand Total	33

Other setups where surgeries were performed were Civil Hospital (public sector) and Liaquat National (private sector) 6,6 (10%), the procedures were MRM (Modified Radicle Mastectomy), laparotomy, head, and neck (buccal, cheek, hard palate).

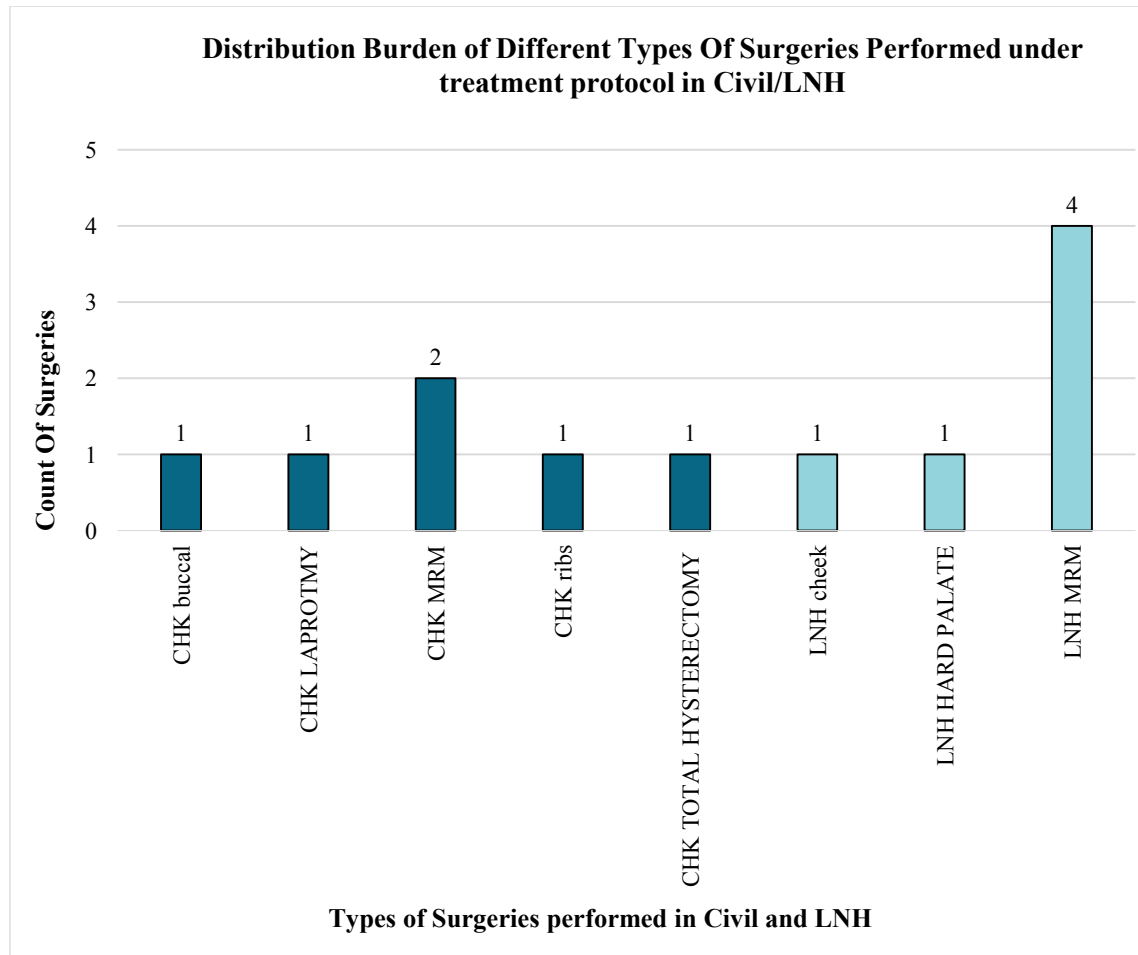


Figure 4.14 Distribution Burden of Different Types of Surgeries Performed Under Treatment Protocol in Civil/LNH

4.2.11 Classification of Anti-Cancer Drugs

More than 49 different agents were prescribed as a part of the chemotherapy regimen. In females, 149 (51.2%) drugs were given, which is slightly more than in males 142 (48.8%).

Inj. Cisplatin was the most prescribed, given to 44 (15.1%) patients with 12 (4.1%) females and 32 (11.0%) males. The other agents were, Inj. Doxorubicin was given to 34 (11.7%) patients including 25 (8.6%) females and 9 (3.1%) males, followed by cyclophosphamide 29 (10.0%) given to 23 (8.0%) females and 7 (2.4%) males.

Table 4.12: Distribution According to the Chemotherapeutic Agents Prescribed in Public Sector Hospitals.

Distribution According to the Chemotherapeutic Agents Prescribed in the Public Sector Hospitals.			
CLASSIFICATION OF DRUGS	FEMALE	MALE	GRAND TOTAL
ALKYLATING AGENT	50	55	105
Inj. Carboplatin	9	6	15
Inj. Cisplatin	12	32	44
Inj. Cyclophosphamide	23	6	29
Inj. Dacarbazine	0	3	3
Inj. Ifosfamide	2	1	3
Inj. Mesna (Cytoprotectant)	1	1	2
Inj. Oxaliplatin	0	4	4
Tab. Cyclophosphamide	0	1	1
Tab. Temozolomide	3	1	4
ANTI-TUMOR ANTIBIOTICS	25	19	44
Inj. Bleomycin	0	4	4
Inj. Daunorubicin	0	5	5
Inj. Doxorubicin	25	9	34
ANTIMETABOLITES	18	32	50
Inj. 5 FU (Fluorouracil)	5	7	12
Inj. Arsenic Trioxide	0	1	1
Inj. Cytarabine (Cytosar)	2	7	9
Inj. Gemcitabine (Gemzar)	6	4	10
Inj. L Asparaginase	0	1	1

Inj. Methotrexate	1	5	6
Tab. 6 MP (Mercaptopurine)	0	1	1
Tab Hydroxyurea	1	0	1
Tab. 6 Thioguanine	0	1	1
Tab. Capecitabine (Xeloda)	1	4	5
Tab. Methotrexate	2	1	3
HORMONAL THERAPY	12	2	14
Cap. Parlodel	1	0	1
Inj. Fulvestrant	1	0	1
Tab. Bicalutamide (Casodex)	0	1	1
Tab. (Letrozole) Femora	3	0	3
Tab. Exemestane	1	0	1
Tab. Tamoxifen A	6	1	7
IMMUNOTHERAPY	2	1	3
Inj. Zoledronic Acid	2	1	3
PLANT ALKALOIDS	19	18	37
Inj. Docetaxel	3	4	7
Inj. Paclitaxel	15	8	23
Inj. Vinblastine	0	3	3
Inj. Vincristine	1	3	4
TARGETED THERAPY	19	15	34
Cap. Nilotinib (Tasigna)	5	1	6
Inj. Bevacizumab	1	0	1
Inj. Cetuximab	5	1	6
Inj. Neupogen (Filgrastim)	4	3	7
Inj. Trastuzumab	0	1	1
Tab. Pazopanib (Votrient)	0	1	1
Tab. Everolimus (Afinitor)	2	2	4
Tab. Gefitinib	1	3	4
Tab. Lenvatinib (Lenvima)	1	2	3
Tab. Sorafenib (Nexavar)	0	1	1
TOPOISOMERASE INHIBITORS	3	1	4
Inj. Etoposide	1	1	2
Tab. Etoposide	2	0	2
GRAND TOTAL	149	142	291

4.2.12 Most Prescribed Class

Concerning the classification of chemotherapeutics, immunotherapy, hormonal therapy, and targeted therapy, 291 drugs were identified, of which the most prescribed was alkylating agent 105 (36.0%), followed by antimetabolites 51 (17.5%), antitumor antibiotics 44 (15.12%), plants alkaloids 37 (12.7%), targeted therapy 34 (11.7%), hormonal therapy 13 (4.5%), topoisomerase inhibitors 4 (1.4%), immunotherapy 3 (1.03%).

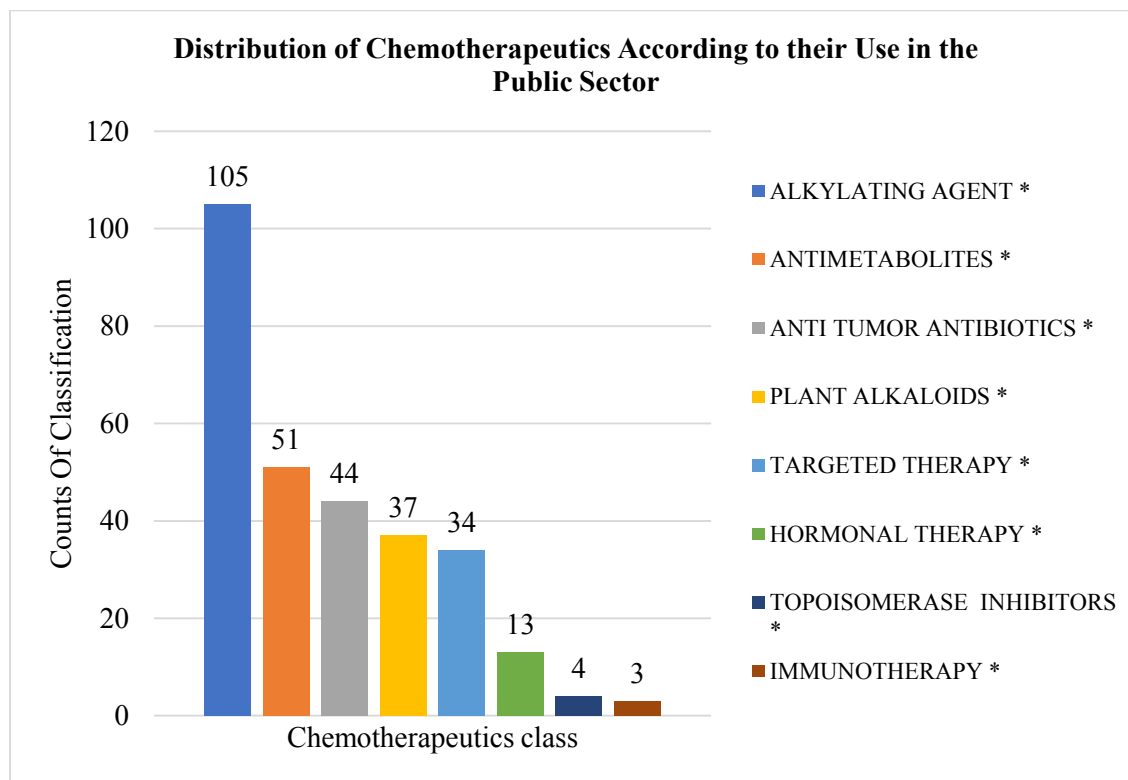


Figure 4.15: Distribution of Chemotherapeutics According to their Use in the Public Sector

4.2.13 Drug Administration Route:

Compared to the drug administration route, Intravenous 233 (80.0%) chemotherapeutics were used commonly as the safest route rather than the oral 51 (17.52%) and subcutaneous7 (2.40%) routes.

Table 4.13: Distribution of Anti-Cancer Drugs According to the Route of Administration in the Public Sector

Distribution of Anti-Cancer Drugs According to the Route of Administration in the Public Sector		
S. No	Row Labels	Count of routes (Total)
1	Intra Venous (IV)	233
	Alkylating Agent	99
	Anti-Tumor Antibiotics	44
	Antimetabolites	36
	Hormonal Therapy	1
	Immunotherapy	3
	Plant Alkaloids	37
	Targeted Therapy	11
	Topoisomerase Inhibitors	2
2	Oral	51
	Alkylating Agent	6
	Antimetabolites	12
	Hormonal Therapy	12
	Targeted Therapy	19
	Topoisomerase Inhibitors	2
3	Subcutaneous (Sc)	7
	Antimetabolites	3
	Targeted Therapy	4
	Grand Total	291

4.2.14 Chemotherapeutics Concerning Cancer Type:

According to the types, stage, age, and other factors, a combination of 291 chemotherapeutics was prescribed to 164 patients in the public sector. In CA Breast the highest number of combinations of chemotherapeutics were recommended 79 (27.1%), followed by CA Head & neck 63 (21.6%), CA blood (leukemia and lymphoma) 63 (21.6%), CA GIT 30 (10.3%), CA reproductive organs 23 (7.9%). Other common types of cancer were adenoma, sarcoma, CA brain, CA pulmonary, and CA renal chemotherapeutics were advised were 11 (3.0%), 11 (3.7%), 8 (2.7%), 7 (2.4%), 3 (1.0%).

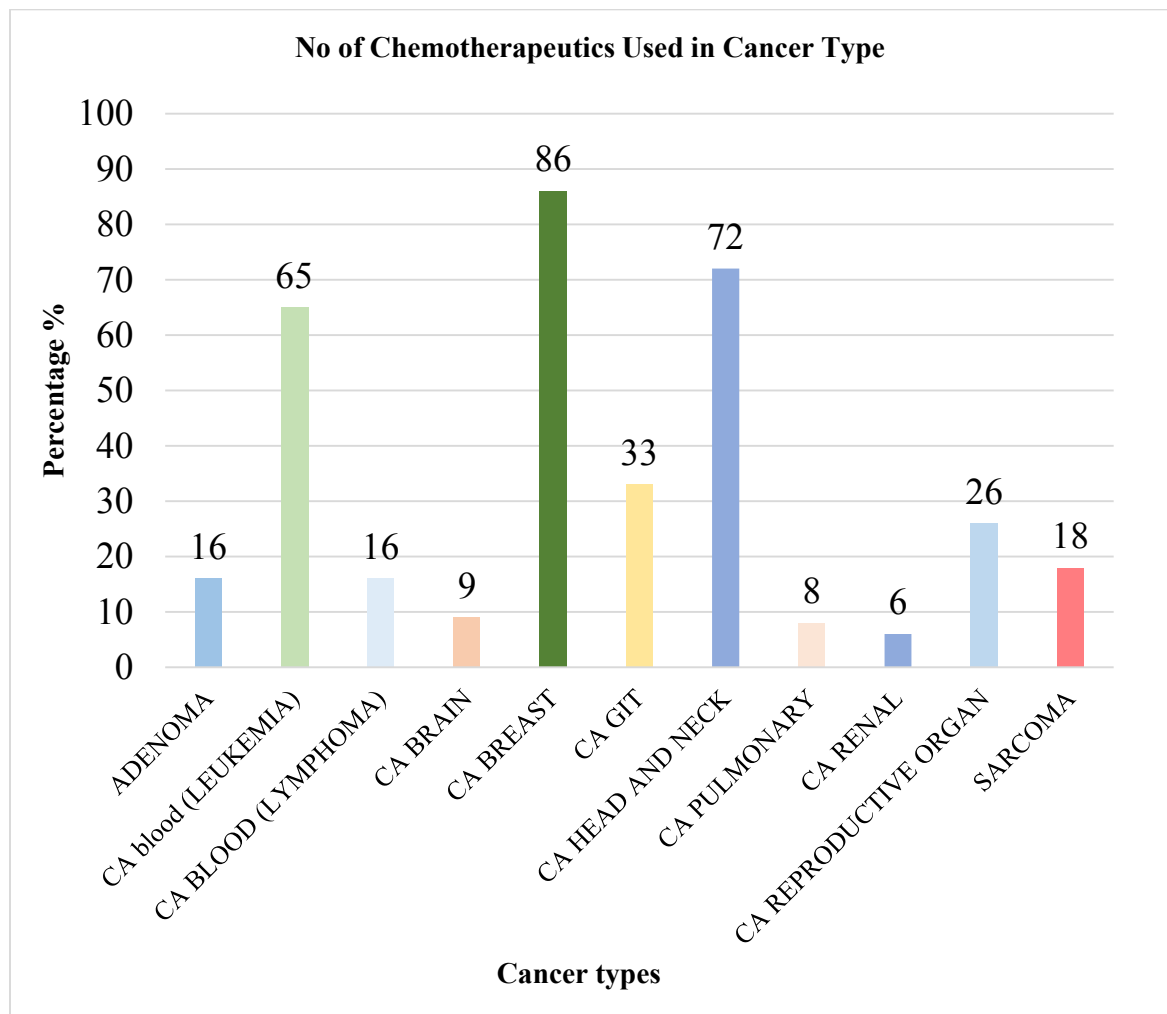


Figure 4.16: Number of Chemotherapeutics Used in Cancer's Type in the Public sector

4.2.14.1 CA Breast

In CA Breast, the major class of chemotherapeutics was prescribed like plant alkaloids, anti-tumor antibiotics, an alkylating agent, and hormonal therapy with other combinations of classes. Injection doxorubicin 22 (7.6%), cyclophosphamide 20 (6.9%), paclitaxel 11 (3.7%), tamoxifen 7 (2.4%), filgrastim 3 (1.0%), letrozole 3 (1.0%) and remaining others were given in single or in combination as a treatment regimen.

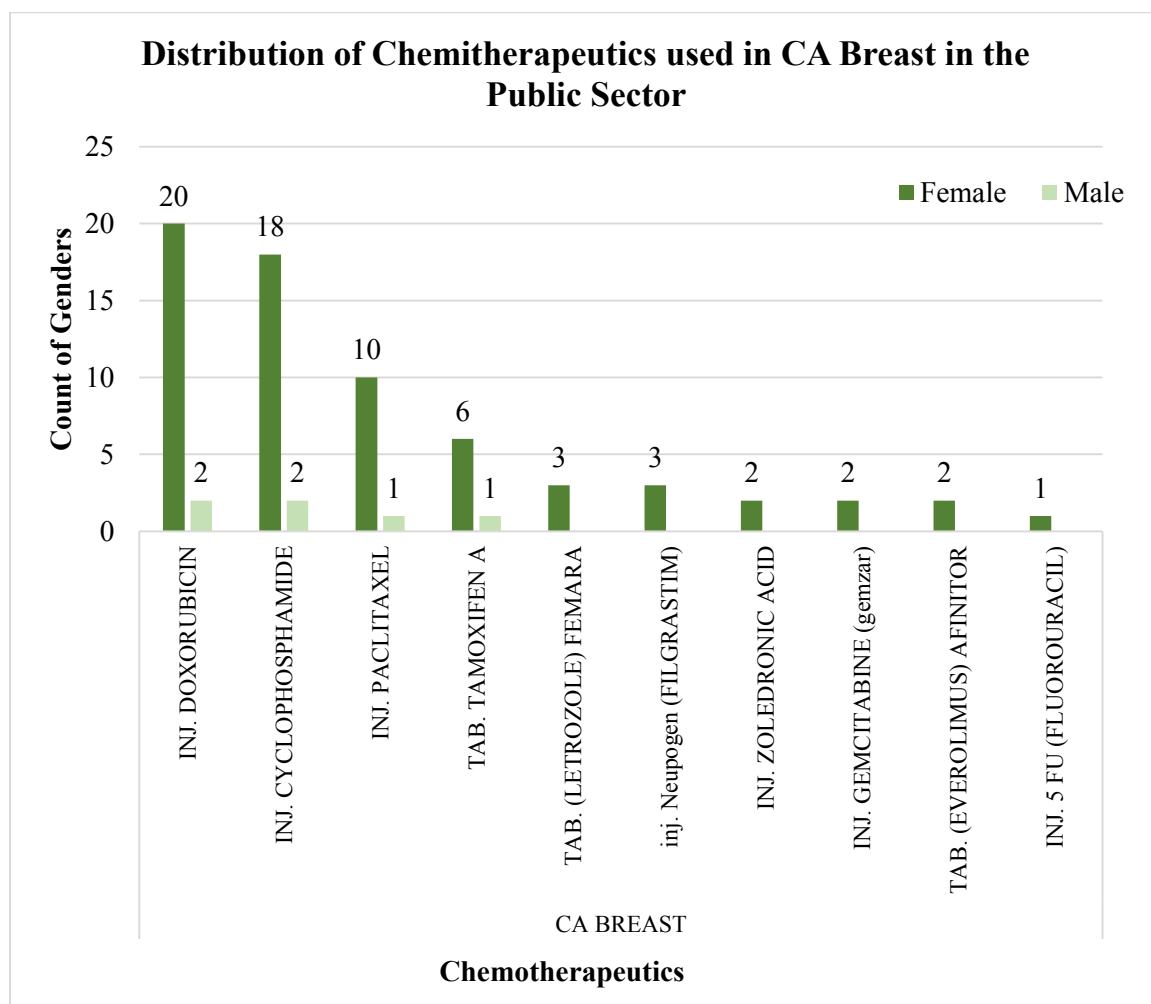


Figure 4.17: Distribution of Chemotherapeutics Used in CA Breast in the Public Sector

4.2.14.2 CA Head and Neck

In Head and Neck Cancer, the most recommended class was Inj. Cisplatin 30 (10.3%) is an alkylating agent only used in cervical cancer with other combinations of the drug like Inj.5-FU 6 (2.0%), Inj. cefutaximab 5 (1.7%), Inj. carboplatin 4 (1.4%), Inj. Taxotere, methotrexate 3 (1.0%), etc.

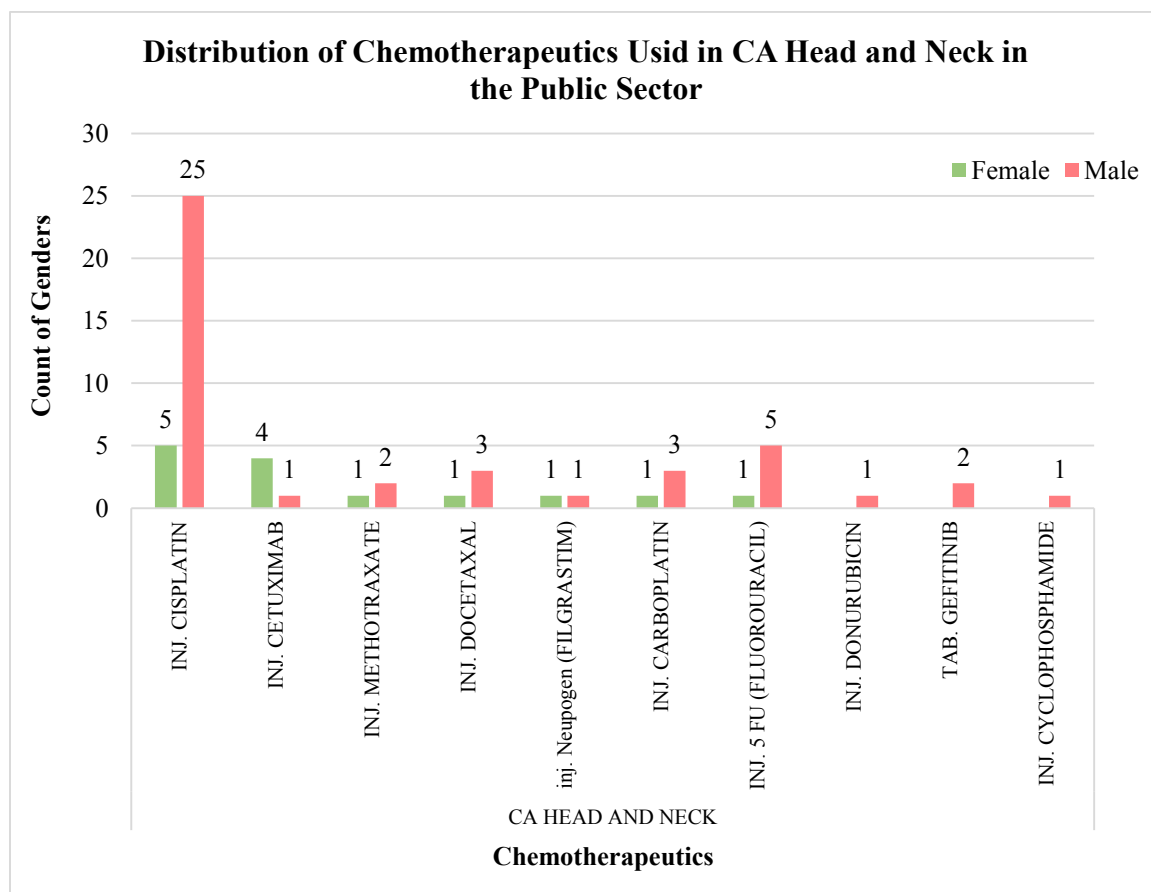


Figure 4.18: Distribution of Chemotherapeutics Used in CA Head and Neck in the Public Sector

4.2.14.3 CA Blood

In Blood carcinoma, chemotherapy is used in three phases, induction, consolidation, and maintenance. For this, a combination of powerful chemotherapeutics was recommended. Antimetabolites (cytarabine) were given 9 (3.0%), targeted drug, tyrosine kinase inhibitor (nilotinib) 6 (2.2%), anthracycline (daunorubicin) 4 (1.3%), an alkylating agent (cyclophosphamide), antimetabolites & plant alkaloids (methotrexate, vincristine) were given 3 (1.0%).

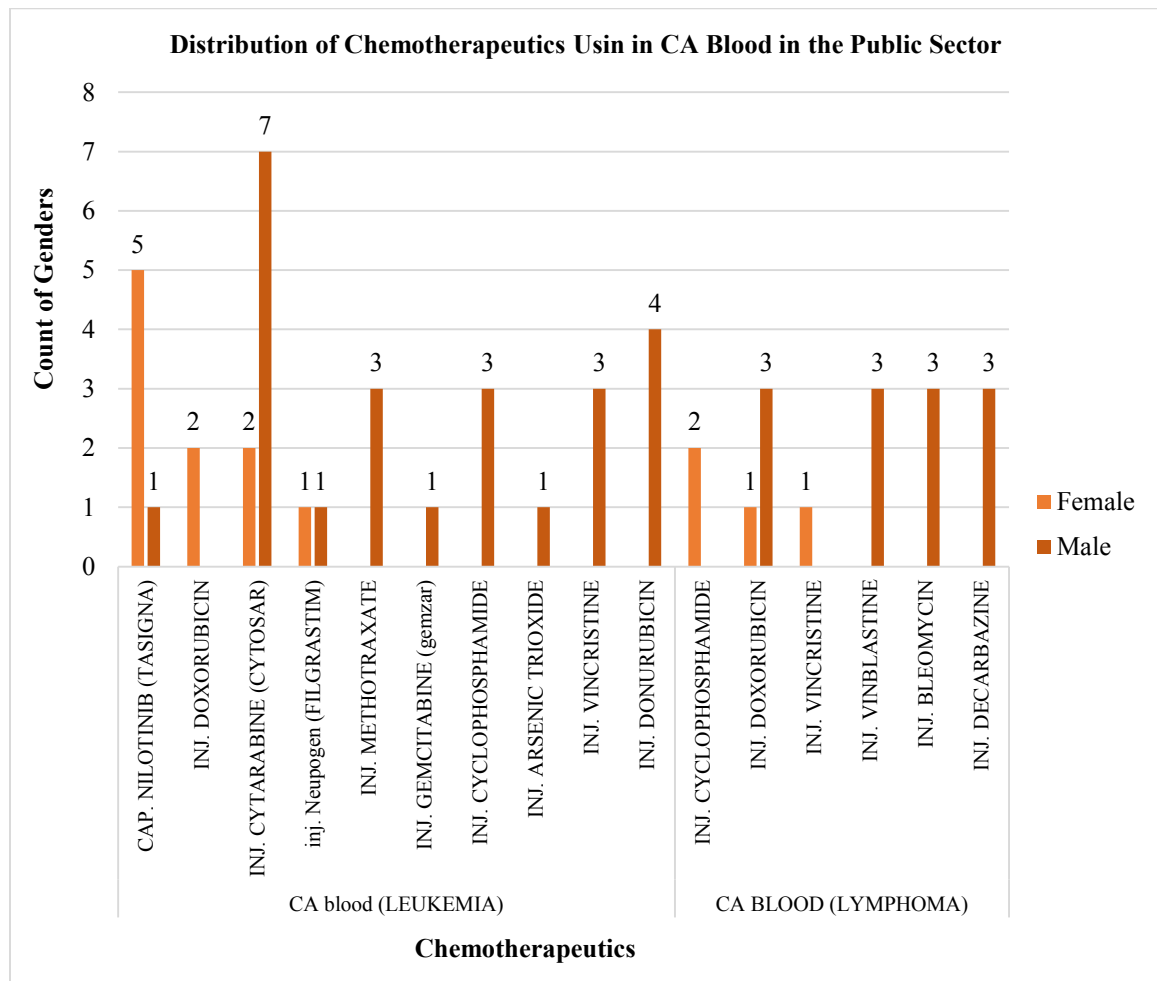


Figure 4.19: Distribution of Chemotherapeutics Used in CA Blood in the Public Sector

4.2.14.4 CA Gastrointestinal tract

In Gastrointestinal tract carcinoma combination of three classes was prescribed, Inj. Cisplatin 6 (2.0%) was used which was an antineoplastic in the class of *alkylating agents*, another class used commonly in metastatic cancer was *Antimetabolites*, tab. Xeloda (Capecitabine) 5 (1.6%), Inj. oxaliplatin 4 (1.3%), Inj.5-FU 3 (1.0%), followed by *Tyrosine kinase Inhibitor* Inj. Lenvatinib 3 (1.0%)

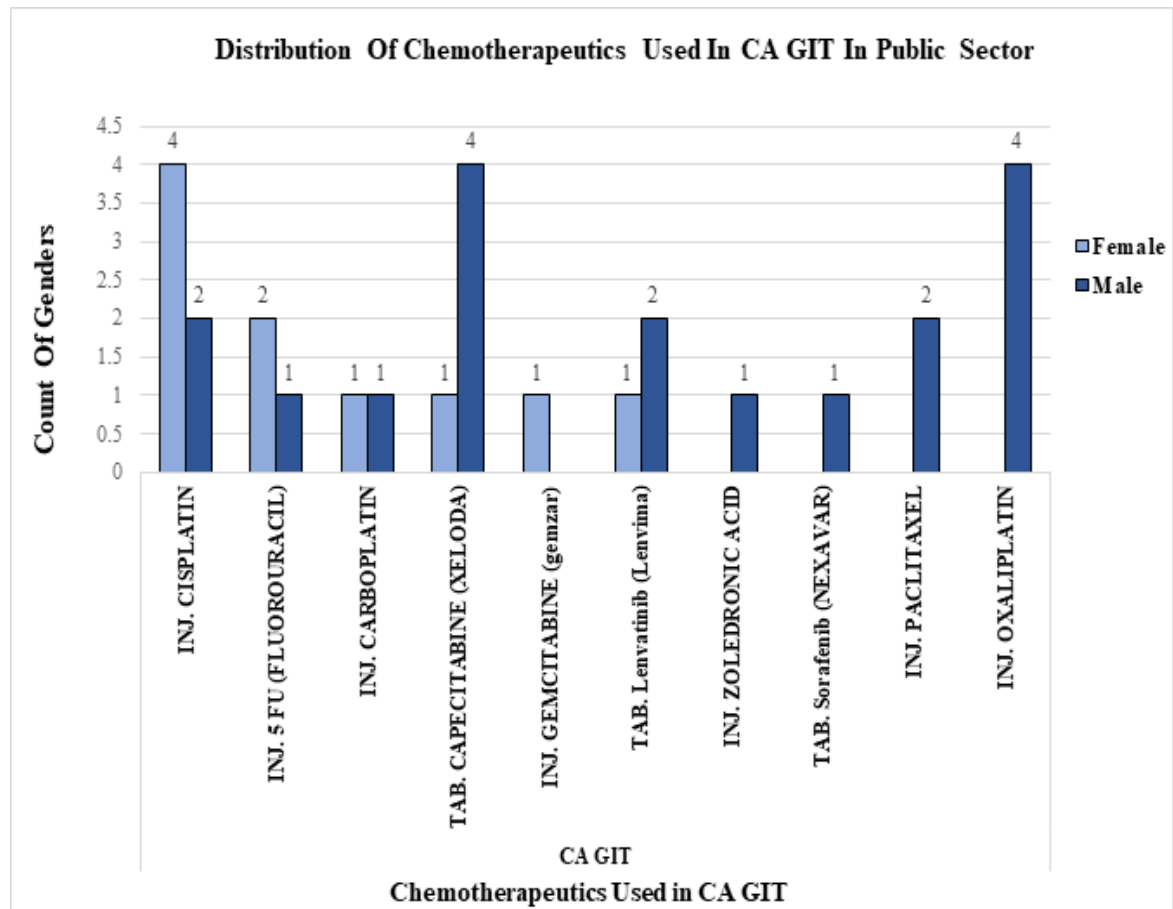


Figure 4.20: Distribution of Chemotherapeutics Used in CA GIT in Public Sector

4.2.14.5 CA Reproductive Organs

A combination of plant alkaloids with alkylating agents was used in the cancers of reproductive organs, in the alkylating group Inj. carboplatin 6 (2.1%), and cisplatin 3 (1.0%) were prescribed, while in plants alkaloids Inj. Paclitaxel 4 (1.4%) was used. In antineoplastic agent, Injectable and tablet Etoposide 3 (1.0%) was given. Others were gemcitabine 2 (0.6%) and Inj. 5-FU.

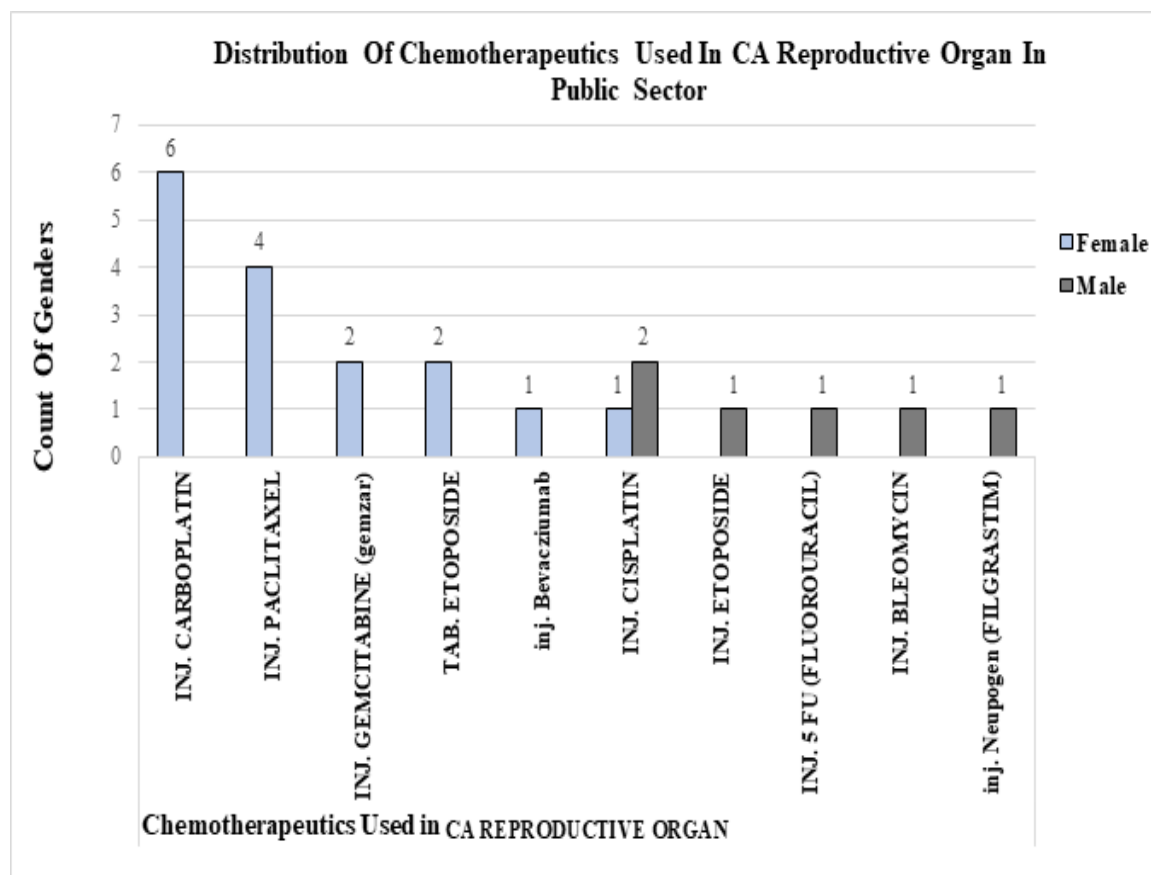


Figure 4.21: Distribution of Chemotherapeutics Used in CA Reproductive Organ in Public Sector

4.2.14.6 Adenoma and Sarcoma

In Adenoma, 11 chemotherapeutics were used, where alkylating agent Inj. Cisplatin and Inj. Carboplatin were 2 (0.6%), plant alkaloids, paclitaxel 2 (0.6%), and other classes of monoclonal antibodies Inj. Cefutaximab, anti-tumor antibodies 1 (0.3%) were given.

In Sarcoma, a combination of 2 or 3 drugs was given. Antitumor Antibiotics (anthracycline) doxorubicin 2 (0.6%), others were an alkylating agent, ifosfamide 1 (0.3%), Plant Alkaloids, Inj. Paclitaxel, docetaxel 1 (0.3%), antimetabolites, Inj. Gemcitabine 1 (0.3%), etc.

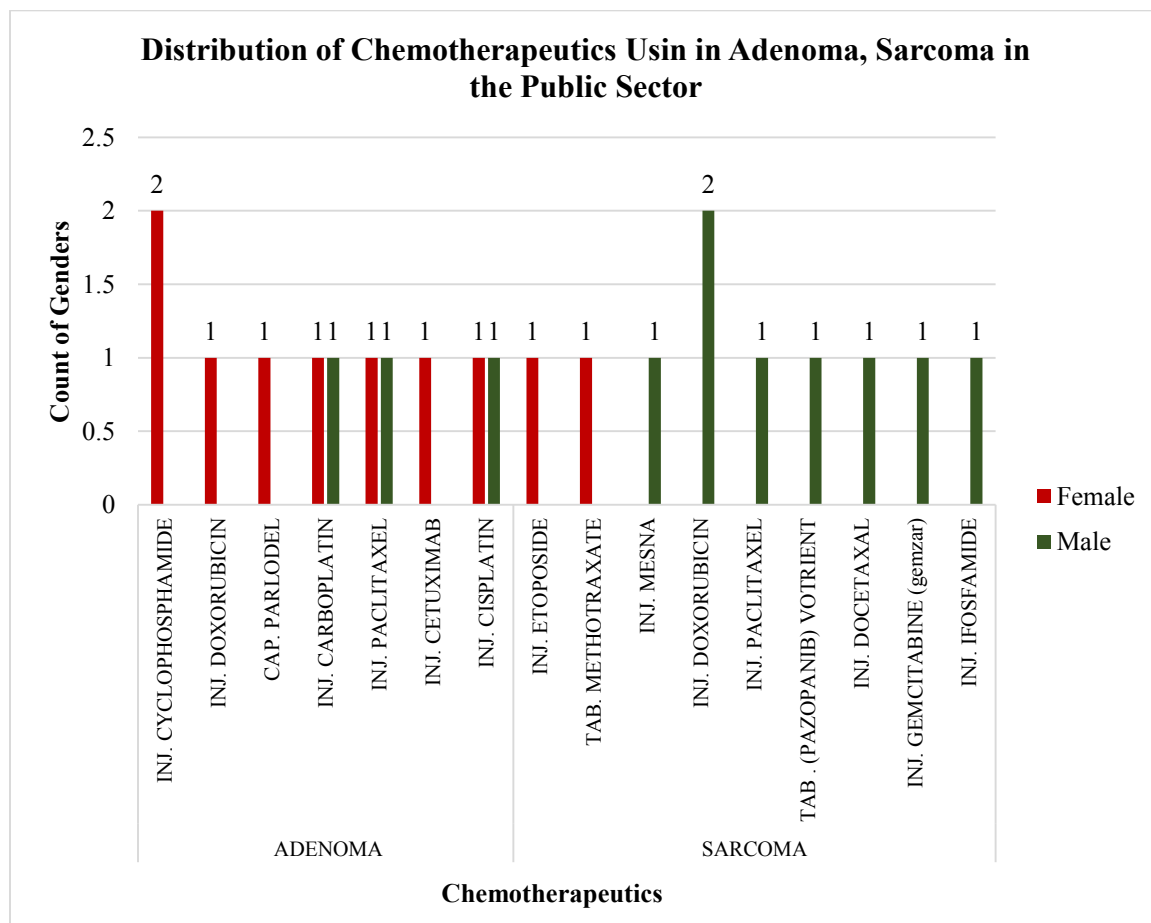


Figure 4.22: Distribution of Chemotherapeutics Used in Adenoma, Sarcoma in the Public Sector

4.2.14.7 CA Brain, Lungs, Kidneys

In carcinoma of the *brain* 8 drugs were used in both genders, in which alkylating agent, Inj. temozolomide 4 (1.3%), Inj. cyclophosphamide 1 (0.3%), antitumor antibiotics Inj. doxorubicin 2 (0.6%), plant alkaloid, Inj. docetaxel 1 (0.3%) was given.

In carcinoma of the *lungs*, 7 chemotherapeutics were used, an alkylating agent, Inj. cisplatin 2 (0.6%), Inj. Carboplatin1 (0.3%), in antimetabolites, Inj. gemcitabine 2 (0.6%), Inj. Paclitaxel 1 (0.3%) was given.

In *Renal* carcinoma antimetabolites, gemcitabine 1 (0.3%) was used, and the mammalian target of Rapamycin (mTOR) inhibitor, Afinitor 2 (0.6%) was given.

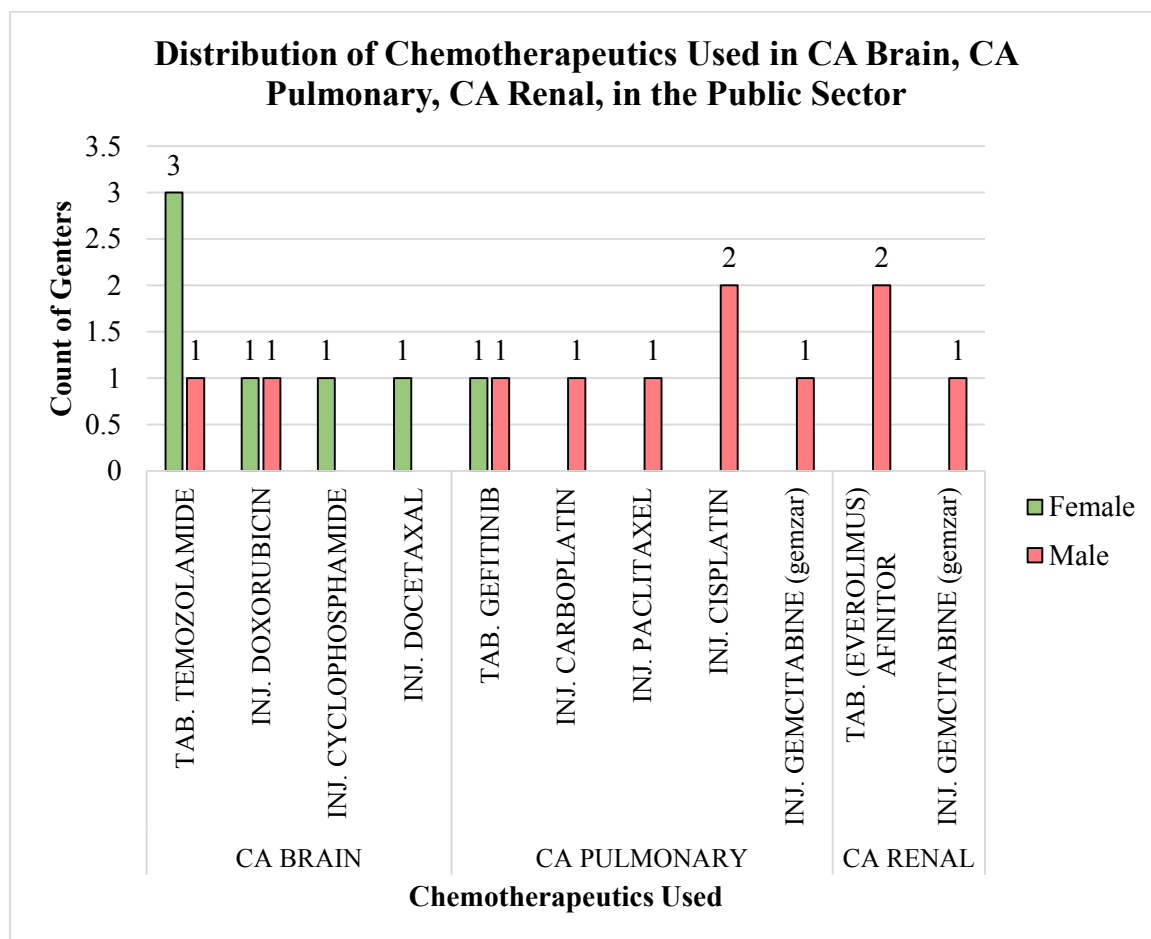


Figure 4.23: Distribution of Chemotherapeutics Used in CA Brain, CA Pulmonary, and CA Renal, In the Public Sector

4.2.15 Anti-Emetics

For receiving chemotherapy 76 (46.3%), patients reported having nausea/vomiting with 34 (20.7%) females and 42 (25.6%) males.

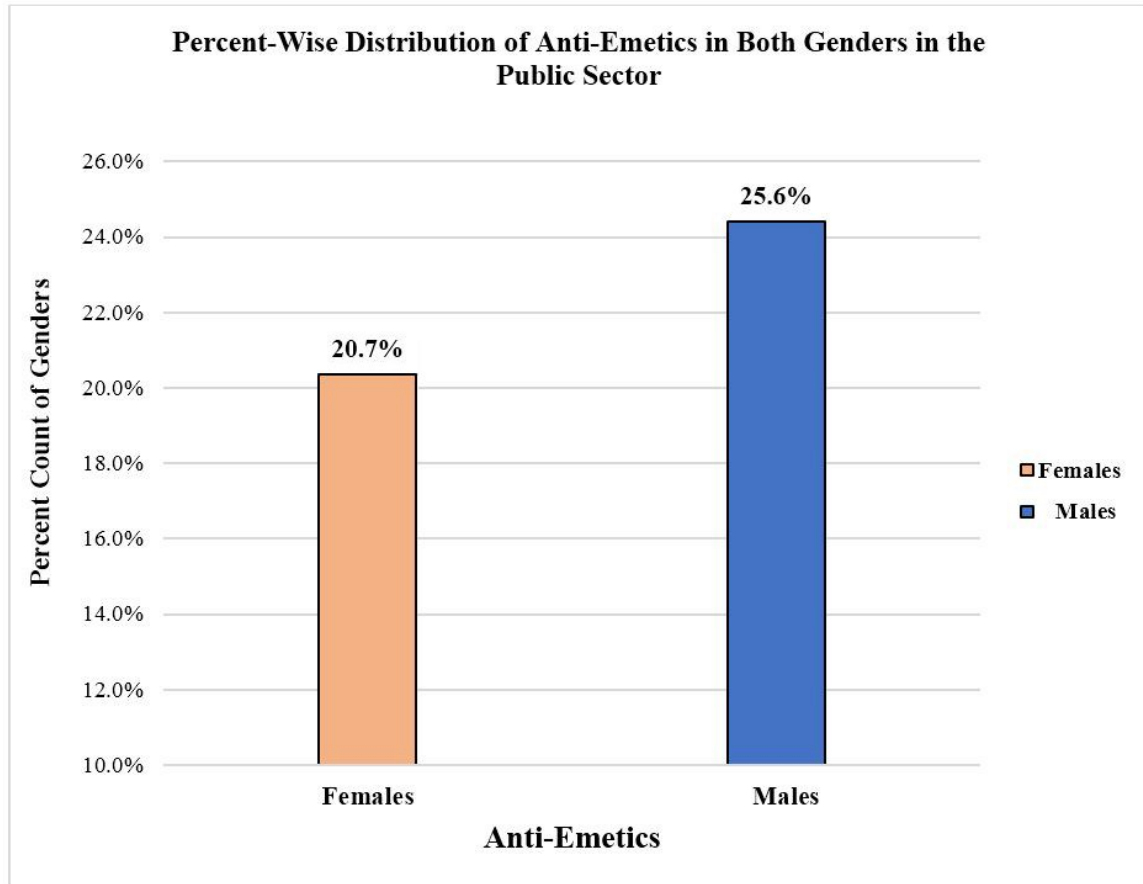


Figure 4.24: Percent Distribution of Anti-Emetics in Both Genders in the Public Sector

Different classes of anti-emetics were prescribed, the most used of which was Inj. Onset/Zofran (ondansetron) 8mg, given to 46 (28.0%) patients including 24 (14.6%) females and 22 (13.4%) males. Other agents prescribed were Inj. Ketryl (Granisetron) 30mg, 23 (14.0%); given to 10 (6.1%) female and 13 (7.9%) males, and Inj. Metoclopramide was given to 4 (2.42%) males.

Other than IV, oral antiemetics were also prescribed to 3 (1.82%), given to 2 (1.2%) females and 1 (0.6%) male.

According to this, in IV route Inj. Ondansetron was the most common antiemetics drug, used with chemotherapeutics in 46 (29.2%) of patients. While in the oral route tab. dimenhydrinate was given to only 3 (1.8%) patients.

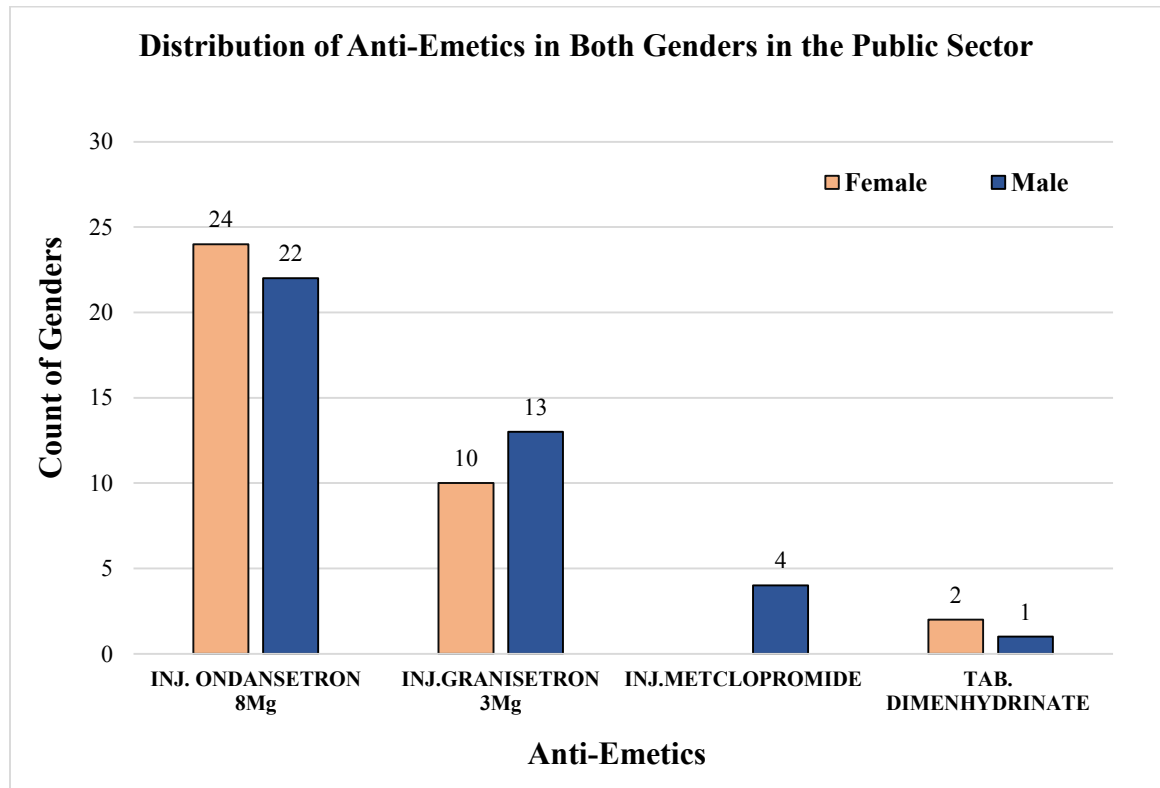


Figure 4.25: Distribution of Anti-Emetics in Both Genders in the Public sector

4.2.16 Pain Management

Only 20.7% of patients received analgesics, through parenteral and oral routes, of which 19 (11.5%) were females and 16 (%) were males. The most prescribed analgesic was NSAIDs, Inj. Tramal (tramadol) 12 (7.3%); given to 4 (2.4%) females and 8 (4.9%) males. Other analgesics prescribed were steroids like Inj. Dexta (dexamethasone) 12mg to 5 (3.0%); given to 4 (2.4%) females and 1 (0.61%) male, Inj. Toradol (ketorolac acid) 30mg 5 (3.0%); given to 4 (2.4%) females and 1 (0.61%) male, while orally; Tablet Tramal 4 (2.4%); given to 2 (1.23%) females and 1 (0.61%) male, other than this Syrup morphine elixir SOS was also given to 2 (1.23%) patients.

Table 4.14: Distribution According to Pain Management in the Public sector

Distribution According to Pain Management in the Public sector				
S. No	Pain Management	Female	Male	Grand Total
1.	Inj. Dexta 12mg IV STAT	4	1	5
2.	Inj. Toradol 30mg IV/ SOS	4	1	5
3.	Inj. Tramal IV SOS	4	8	12
4.	Inj. Voren 75MG SOS	1	1	2
5.	Syrup Morphine Elixirs SOS	1	1	2
6.	T. Rotec 100 Mg BID	1	0	1
7.	T. Tramal Plus (TDS)	2	2	4
8.	T. Nuberol Forte (TDS)	0	2	2
9.	T. Ponstan Forte BID	1	0	1
10.	T. Voren BD	1	0	1
	Grand Total	19	16	35

4.2.17 Side Effects of Anti-Cancer Drugs

The average prevalence of side effects was **18.3%**. Patients of Head and neck cancer 10 (6.1%) were more predisposed to the side effects of treatment protocols, followed by CA GIT 5 (3.04%), breast cancer 4 (2.4%), sarcoma 2 (1.2%), lymphoma, adenoma 1, 1 (0.6%) The most common side effects were nausea, vomiting, lethargic condition, and cough, 5 (3.0%). Others were fever, shortness of breath, swelling 4 (2.4%), constipation, bleeding, and diarrhea 3 (1.8%). Despite these swellings, allergies, pus, and oral thrust were also noted.

Table 4.15: Distribution According to the Side Effects of Different Cancer Types in the Public sector

Distribution According to the Side Effects of Different Cancer Types in the Public Sector		
S. No	Cancer Type and side effects	Count of side effects
1	ADENOMA	1
	Fever / Sob	1
2	CA BREAST	4
	Swelling	2
	Bleeding + Constipation	2
3	CA GIT	5
	Bleeding + Constipation	3
	Pus P/Rectal	2
4	CA HEAD AND NECK	10
	Swelling	3
	Diarrhea / Vomiting	2
	Generalized Weakness	1
	Oral Thrust	2
	Phlebitis In Arm	1
	Respiratory Distress	1
5	CA REPRODUCTIVE ORGAN	1
	Fever / SOB	1
6	LYMPHOMA	1
	Fever / SOB	1
7	SARCOMA	2
	Diarrhea / Vomiting	2
	Grand Total	30

4.3 Private Sector

4.3.1 Caste and Gender

This study includes 22 patients diagnosed with cancer who received their treatment from private sector hospitals in Karachi, 12 (54.55%) being females among which 4 (18.18%) were Punjabi, 3 (13.6%) were muhajir, 2 (9.09%) were Pathan and Balochi each and 1 was Sindhi. Male patients were 10 (45.45%) among which 6 (27.7%) were Urdu speaking, 2 (9.09%) were Pathan, and 1 (4.5%) were Punjabi and Sindhi.

Table 4.16: Distribution According to Caste and Gender in the Private sector

Distribution According to the Caste and Gender in the Private Sector				
Caste	Female	Male	Total	% Of Total
Muhajir	3	6	9	40.9%
Punjabi	4	1	5	22.7%
Pathan	2	2	4	18.2%
Balochi	2	0	2	9.1%
Sindhi	1	1	2	9.1%
Total	12	10	22	100%

4.3.2 Age-wise distribution

The high-risk age groups were 41-50yrs with 7 (31.8%) patients including 4 (18.2%) females and 3 (13.6%) males, then 51-60yrs with 6 (27.2%) patients including 5 (22.7%) females and 1 (4.55%) male, followed by 31-40yrs & 61-70yrs with 4 (18.2%) patients.

Table 4.17: Age-wise distribution of Patients in the Private Sector

Age-wise distribution of Patients in the Private Sector				
Age group	Female	Male	Total	%Of Total
21-30	0	1	1	4.5%
31-40	2	2	4	18.2%
41-50	4	3	7	31.9%
51-60	5	1	6	27.2%
61-70	1	3	4	18.2%
Total	12	10	22	100%

As compared to males, females were more prone to the disease, highly diagnosed age group was in between 51-60, while males are between 41-50 and 61-70 years of age.

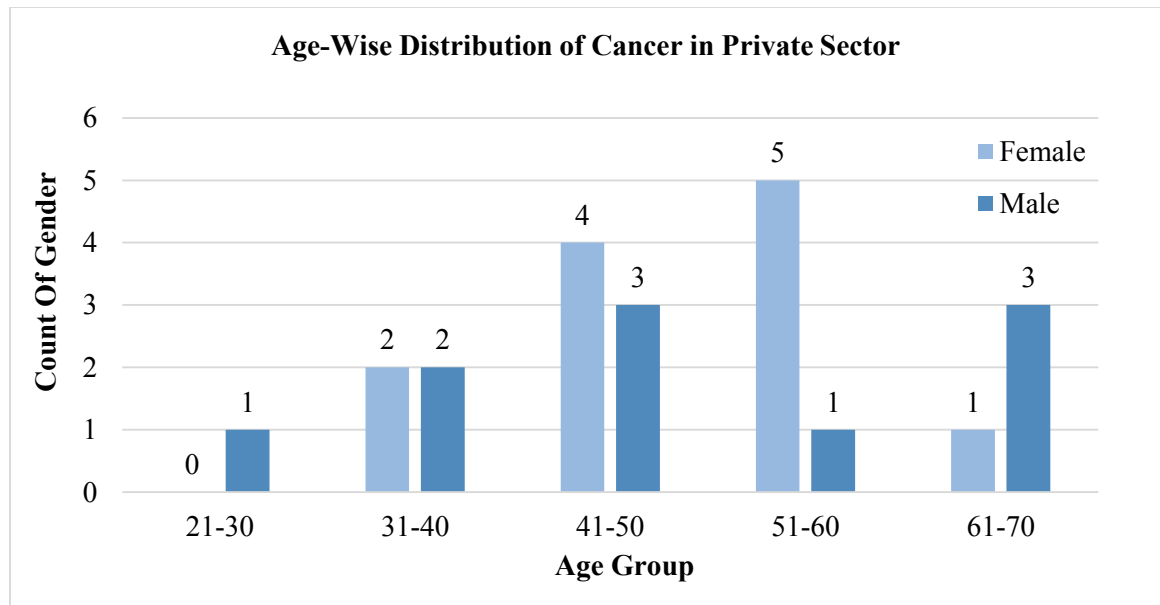


Figure 4.26: Age-Wise Distribution of Cancer in the Private Sector

4.3.3 Marital Status

Out of 22 patients, 12 (54.5%) were married females while married males were 8 (36.3%). Other than 2 (9.09%) were single males.

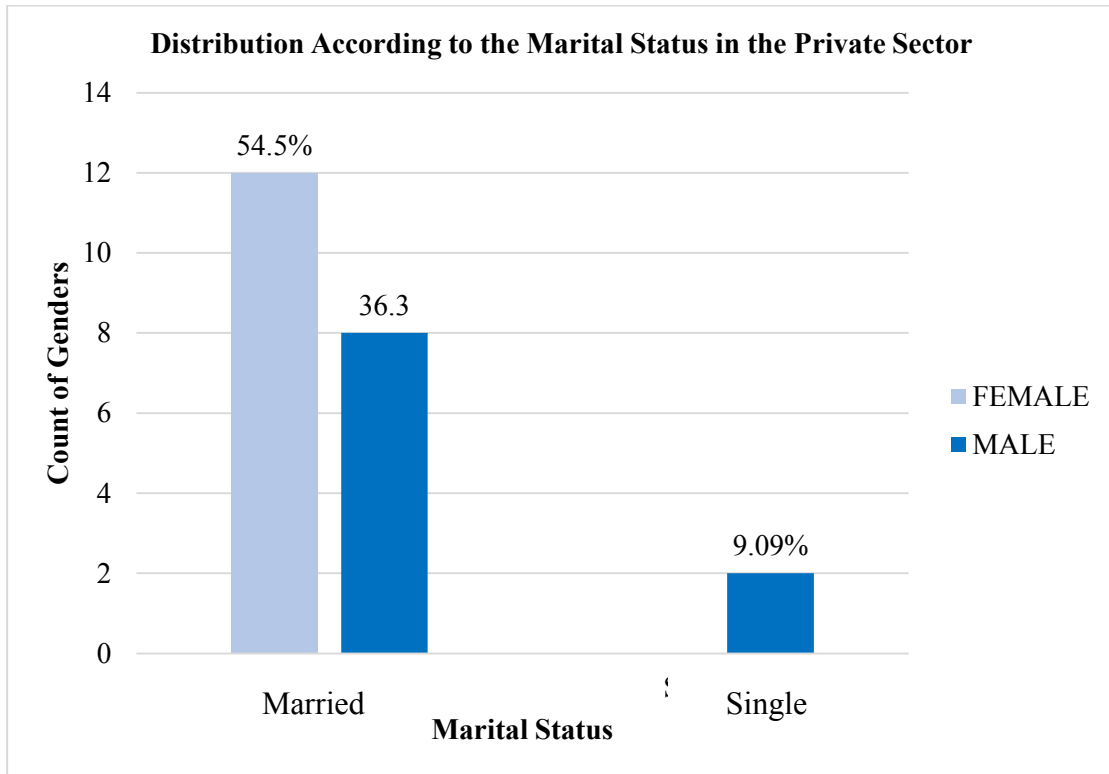


Figure 4.27: Distribution According to the Marital Status in the Private sector

4.3.4 Resident of Cities

Most of the residents 15 (68.1%) were from Karachi, out of them 8 (36.3%) were females while 7 (31.8%) were males. Despite them, other residents were from Hyderabad, Jamshoro, Khuzdar, Peshawar, Quetta, and Swat, 1 (4.5%) each.

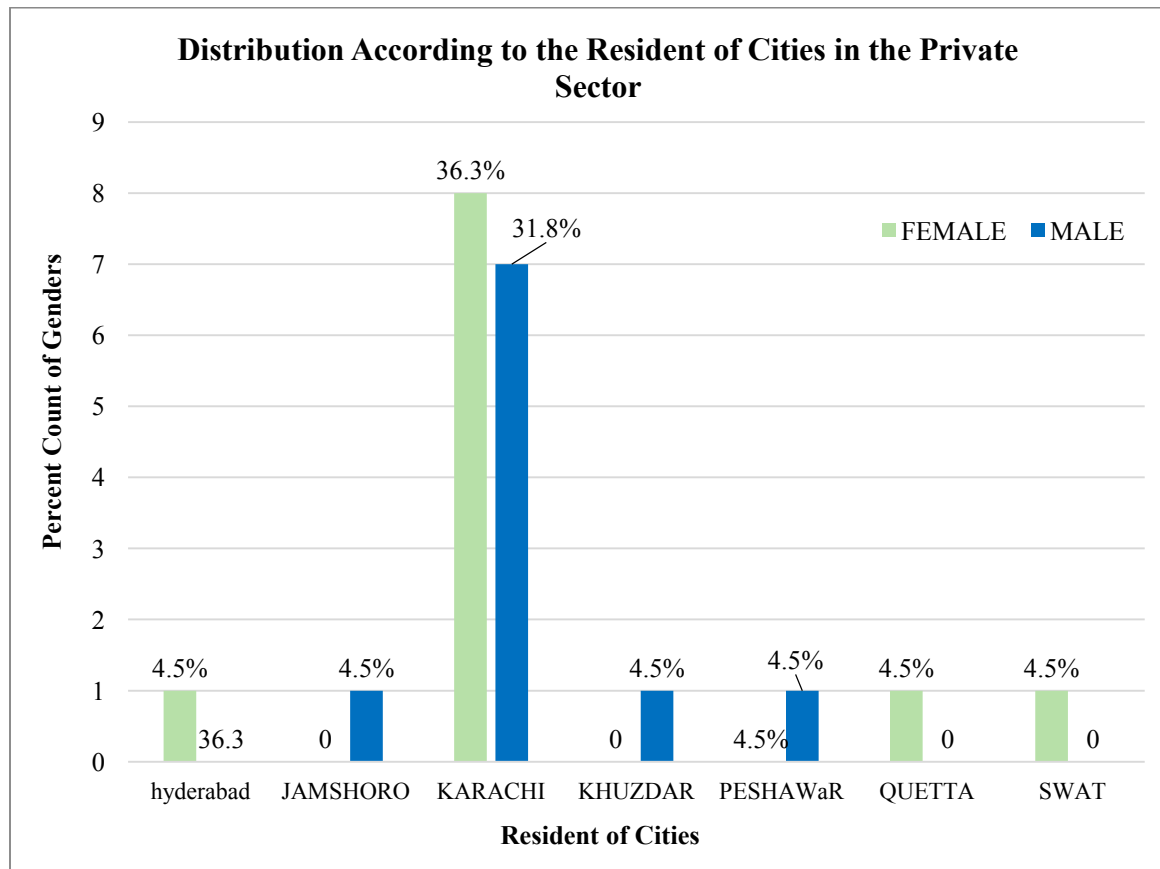


Figure 4.28: Distribution According to the Resident of Cities in the Private Sector

4.3.5 Family History of Cancer

27.2% of patients had a positive family of cancer with 2 (9.09%) females having a family history of breast cancer, 2 (9.09%) females having a family history of head and neck cancer, and 1 (4.5%) having a family history of lung cancer and 1 (4.5%) male with a family history of cancer of gastrointestinal tract.

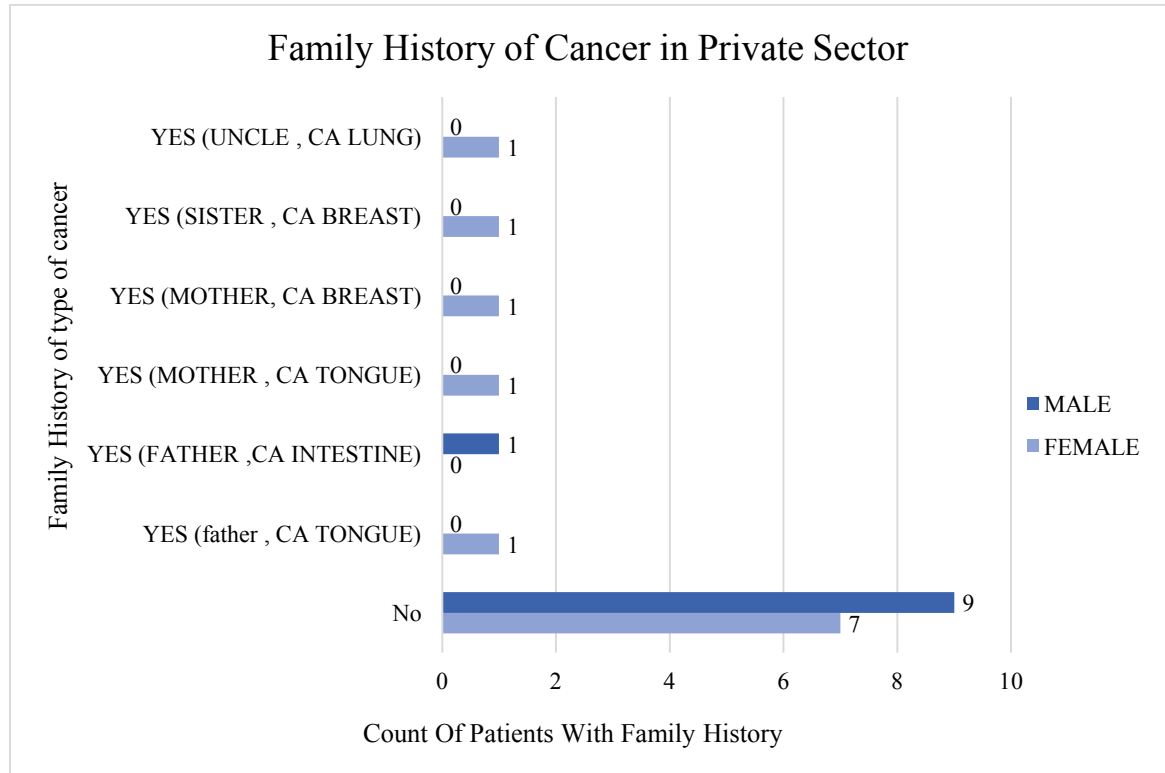


Figure 4.29: Family History of Cancer in Private Sector Hospitals

4.3.6 Types of Cancer

Distinct 14 types of cancers were observed involving the head and neck region, gastrointestinal tract, reproductive tract, blood, and breast tissue. Cancer with the highest occurrence was carcinoma of the gastrointestinal tract (22.7%) present in 3 (13.6%) females and 2 (9.09%) males, closely followed by Breast cancer (18.18%) present in 4 (18.18%) females, and Cancers of the reproductive tract (18.18%) with 3 (13.6%) females having ovarian cancer and 1 (4.5%) male having prostate cancer. Cancers of the head and neck region were only present in 3 (13.6%) of the included patients with 1 (4.5%) female and 2 (9.09%) males.

Concerning incidence types, females were more susceptible to carcinoma breast and ovary, on the other side males were more predisposed to carcinoma of the GIT (esophagus)

Table 4.18: Distribution According to the Types of Cancer in the Private sector

Distribution According to the Types of Cancer in the Private sector				
S. No	DIAGNOSIS	FEMALES	MALES	Total
1.	Carcinoma esophagus	0	2	2
2.	Carcinoma urinary bladder	0	1	1
3.	Carcinoma breast	4	0	4
4.	Carcinoma DLBCL (diffuse large b cell lymphoma)	0	1	1
5.	Carcinoma gall bladder	1	0	1
6.	Carcinoma larynx	0	1	1
7.	Carcinoma lungs	1	1	2
8.	Carcinoma ovary	3	0	3
9.	Carcinoma prostate	0	1	1
10.	Carcinoma rectum	1	0	1
11.	Carcinoma stomach	1	0	1
12.	Carcinoma t-cell / b-cell	0	1	1
13.	Carcinoma tongue	1	1	2
14.	Hodgkin lymphoma	0	1	1
	Total	12	10	22

4.3.7 Stages of Cancer

Most of the patients were diagnosed with Stage III disease (50%) with 6 (27,2%) being females and 5 (22.7%) being males. 22.7% of patients had a late diagnosis of stage IV disease with 3 (13.6%) females and 2 (9.09%) males while 27.2% of patients were diagnosed with stage II disease including 3 (13.6%) females and 3 (13.6%) males.

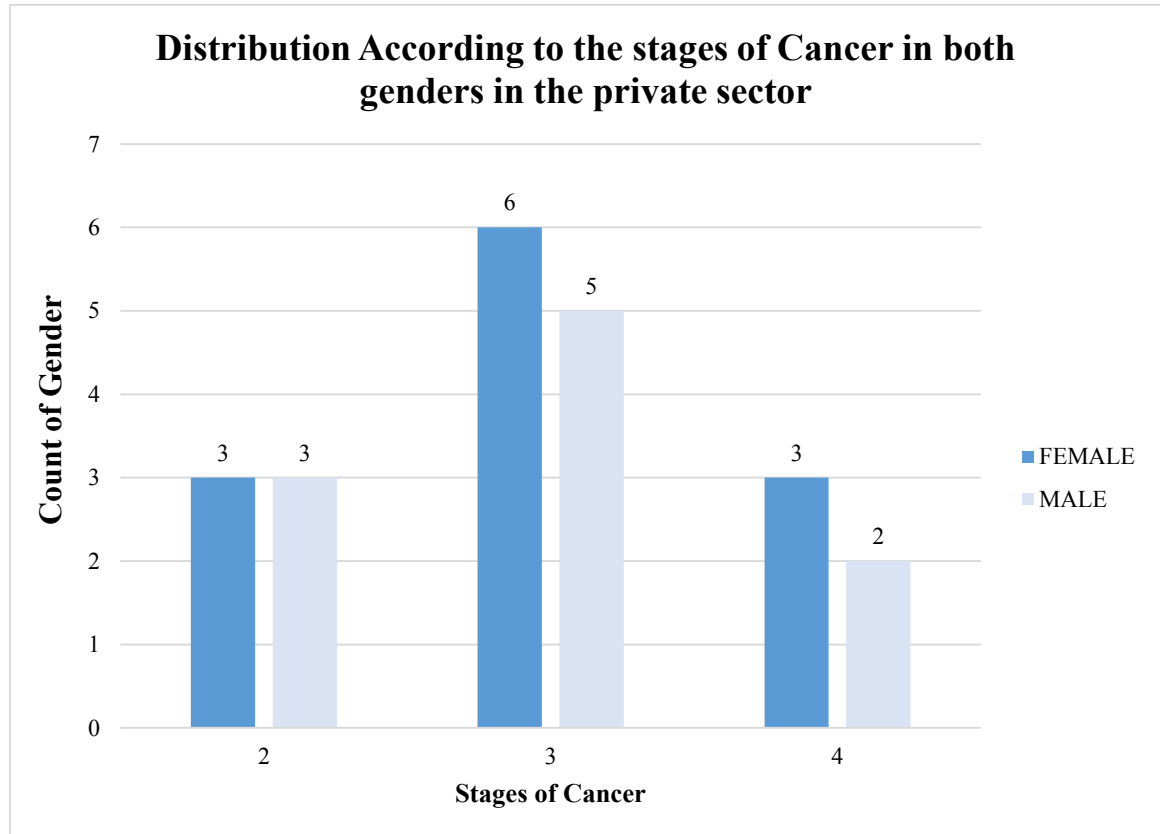


Figure 4.30: Distribution According to the Stages of Cancer in the Private sector

4.3.8 Plan of Treatment

Corresponding with the stage of disease at diagnosis, the treatment modality offered to most of the patients was Radicle/CCRT (59.09%) including 8 (36.6%) females and 5 (22.7%) males, while 7 (31.82%) patients were given Palliative treatment including 2 (9.09%) females and 5 (22.7%) males. Only 2 (9.09%) patients received Radicle treatment, were both female 16 (9.7%).

Table 4.19: Distribution According to the Plan of Treatment in the Private sector

Distribution According to the Plan of Treatment in the Private sector				
S. No	Plan of Treatment	FEMALE	MALE	Total
1.	Palliative	2	5	7
2.	Radicle	2	0	2
3.	Radicle / CCRT	8	5	13
	Total	12	10	22

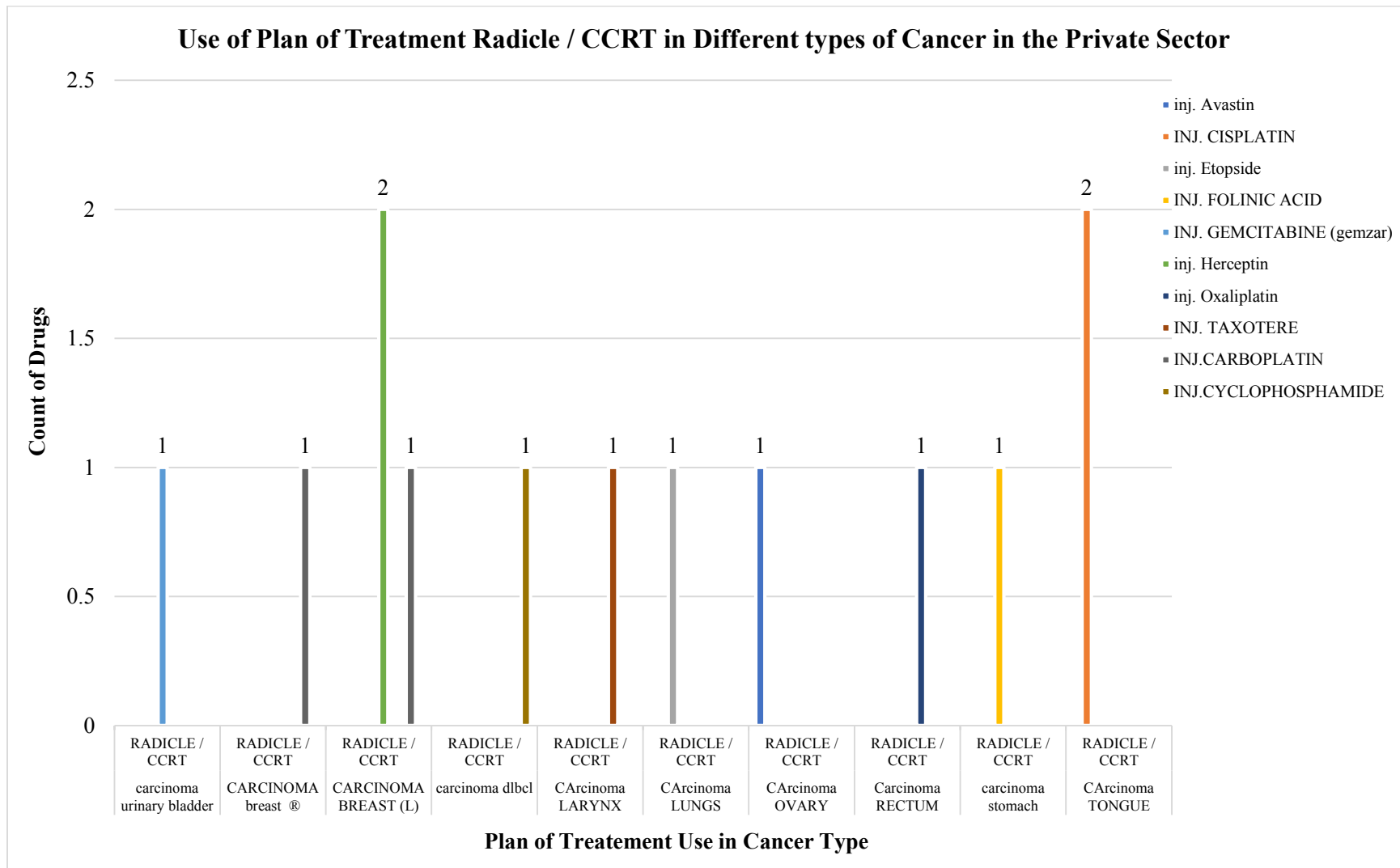


Figure 4.31: Use of Plan of Treatment Radicle/CCRT in Different Types of Cancer in the Private Sector

4.3.9 Classification of Anti-Cancer Drugs

Different 19 agents were used in the chemotherapeutic regimen including chemotherapy 46 (90.2%), targeted therapy 4 (7.84%), and immunotherapy (monoclonal antibodies) 4 (7.8%). Where alkylating agents were (32.6%), antimetabolites were (17.4%), plant alkaloids were (26.1%), antitumor antibiotics were (6.5%), and topoisomerase inhibitors were (4.3%).

Table 4.20: Chemotherapeutics, Targeted, and Immunotherapy Agents prescribed in the private sector

Chemotherapeutics, Targeted and Immuno Agents prescribed in Private Sector				
S. No	CLASSIFICATION OF DRUGS	FEMALE	MALE	Grand Total
1	ALKYLATING AGENT	7	8	15
	Inj. Cisplatin	2	4	6
	Inj. Ifosfamide	0	1	1
	Inj. Oxaliplatin	1	1	2
	Inj. Carboplatin	4	0	4
	Inj. Cyclophosphamide	0	2	2
2	ANTI-TUMOR ANTIBIOTICS	0	3	3
	Inj. Doxorubicin	0	2	2
	Inj. Epirubicin	0	1	1
3	ANTIMETABOLITES	5	3	8
	INJ. 5 FU	1	1	2
	Inj. Gemcitabine (Gemzar)	2	1	3
	Inj. Methotrexate	0	1	1
	Tab. Capecitabine (Xeloda)	2	0	2
4	PLANT ALKALOIDS	6	6	12
	Inj. Paclitaxel	5	0	5
	Inj. Cabazitaxel	0	1	1

Chemotherapeutics, Targeted and Immuno Agents prescribed in Private Sector				
S. No	CLASSIFICATION OF DRUGS	FEMALE	MALE	Grand Total
	Inj. Docetaxel	1	3	4
	Inj. Vincristine	0	2	2
5	TOPOISOMERASE INHIBITORS	0	2	2
	Inj. Etoposide	0	2	2
6	IMMUNOTHERAPY	3	1	4
	Inj. Neupogen (Filgrastim)	3	1	4
7	TARGETED THERAPY	3	1	4
	Inj. Bevacizumab	1	0	1
	Inj. Herceptin	2	1	3
	Grand Total	27	24	51

6.2.10 Most Used Class of Anti-Cancer

According to the classification of the drug, alkylating agent 15 (29.4%) was the highly prescribed class, followed by plant alkaloids 12 (23.5%), anti-metabolites 8 (15.6%), immune therapy 4 (7.8%), targeted therapy 4 (7.8%), anti-tumor antibiotics 3 (5.9%), topoisomerase therapy 2 (4.0%).

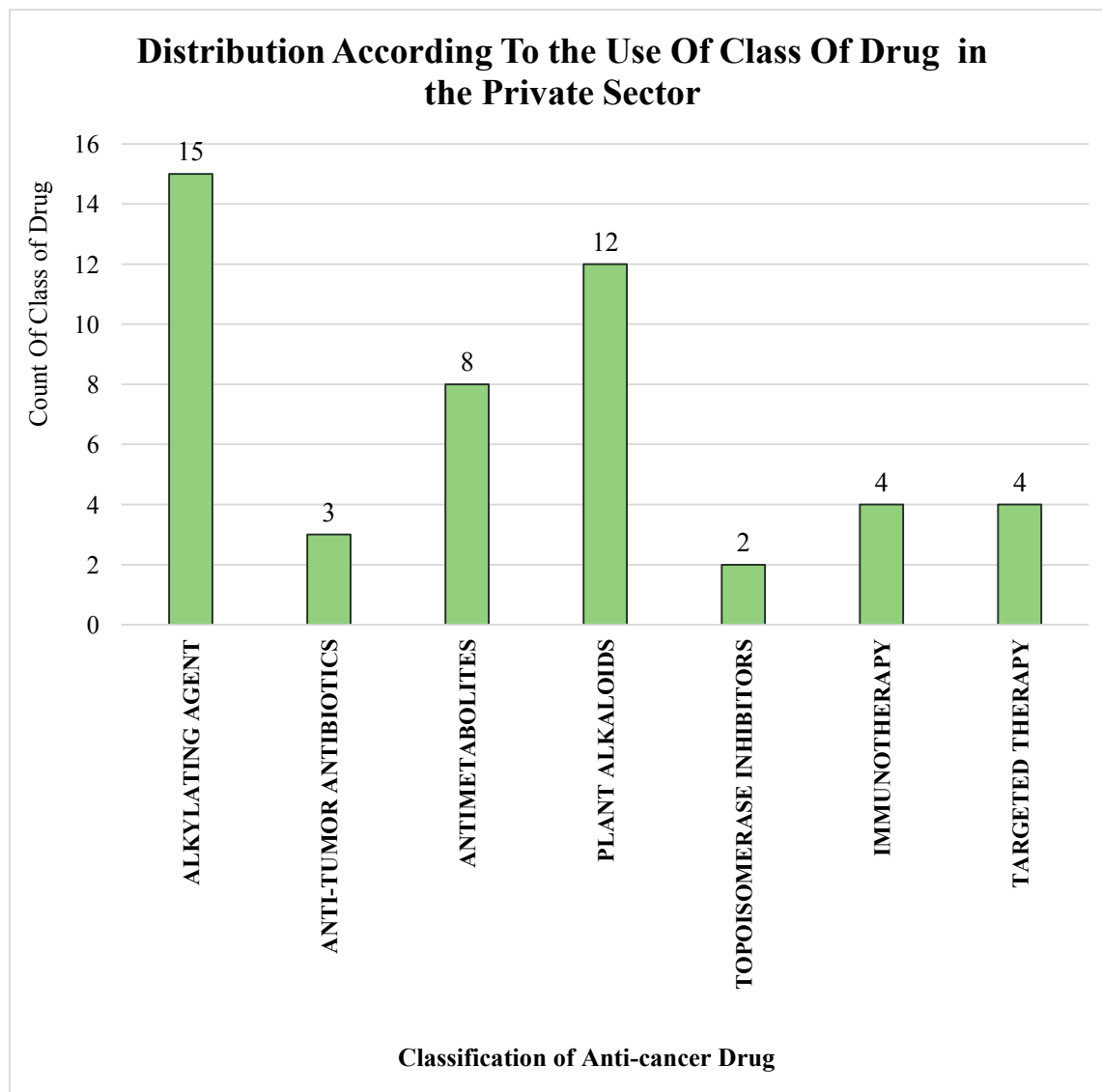


Figure 4.32: Distribution According to the Use of Class of Drug in the Private Sector

4.2.11 A) Frequently Used Chemotherapeutics in Both Genders

The most prescribed agents were Inj. Cisplatin (8.7%) and Docetaxel (6.5%) were given in males. While Inj. Paclitaxel (10.9%) and Cisplatin (8.7%), were given to females.

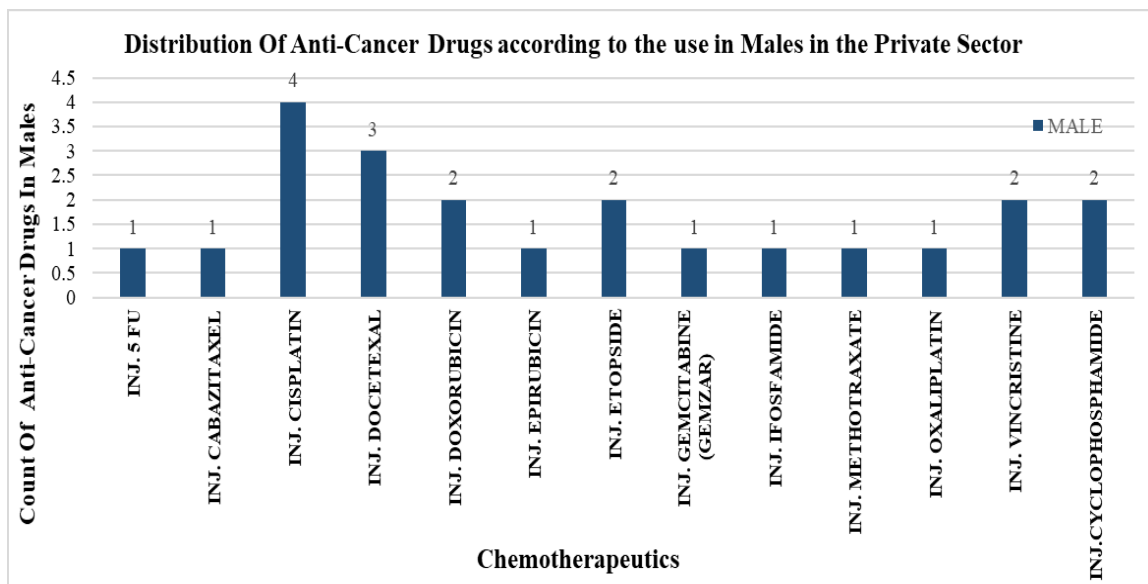


Figure 4.33: Distribution of Anti-Cancer Drugs according to their use in Males in the Private Sector

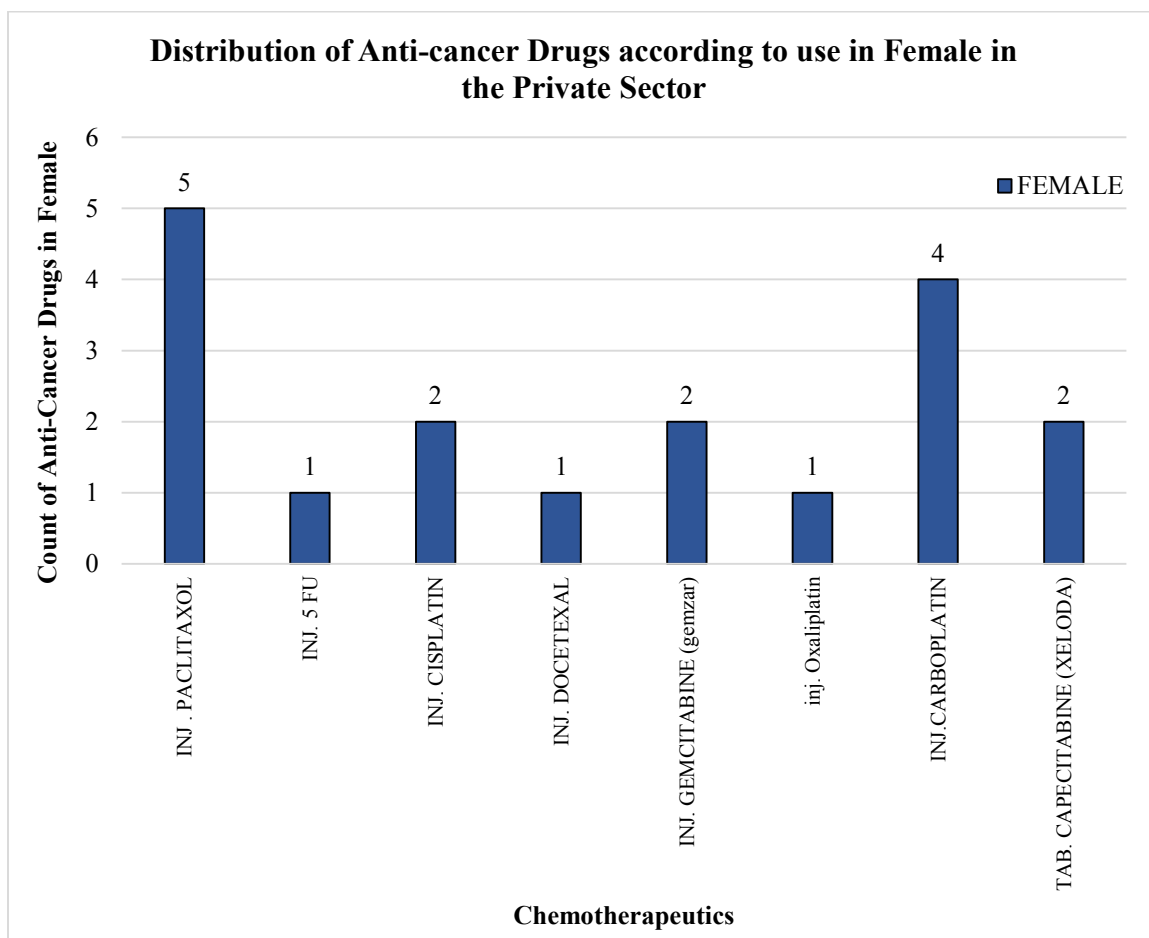


Figure 4.34: Distribution of Anti-Cancer Drugs according to their use in Females in the Private Sector

4.3.13 Types of Cancer

In the private sector, 22 patients with 7 diverse types of cancers were observed, and 48 different chemotherapeutic drugs were prescribed in respect of stage, prognosis, type, gender, age, and other factors. The highest number of drugs were prescribed in CA gastrointestinal tract 12 (23.5%), followed by CA Reproductive 11 (21.5%), CA Blood 10 (19.0%), CA Breast 9 (17.6%), CA Head and Neck Cancer 5 (9.8%), CA Renal 1 (2.0%), CA Pulmonary 3 (1.8%).

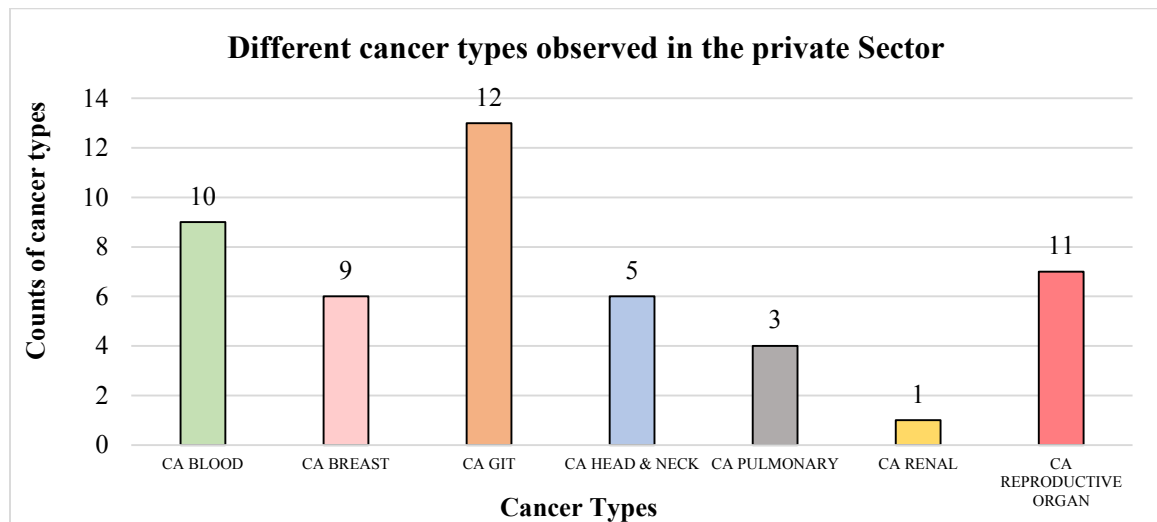


Figure 4.35: Different Types of Cancer Observed in Private Sector

4.3.14 Different Types of Cancer with Anti-Cancer regimen

In *CA Blood*, an alkylating agent, cyclophosphamide 2 (3.9%), plant alkaloids vincristine 2 (3.9%), and anthracycline which was Adriamycin 2 (3.9%) were used with another chemotherapeutic.

In *CA Breast* combinational therapy was used, monoclonal antibody Herceptin 3 (5.8%), alkylating agent carboplatin 2 (3.9%), and plant alkaloid Taxol 2 (3.9%%) were given as the main regimen.

In *CA GIT*, alkylating agent oxaliplatin 2 (3.9%), plant alkaloid docetaxel / Taxotere 2 (3.9%%), antimetabolites 5 fluorouracil 2 (3.9%) were prescribed with other chemo drugs.

Cisplatin (5.9%), the alkylating agent has been used as the main chemo drug in *Head & Neck cancer* while in *reproductive carcinoma*, colony-stimulating factor filgrastim 3 (5.8%) was used as supportive chemotherapy with plant alkaloid Taxol 2 (3.9%) and other chemo drugs.

**Table 4.21: Distribution of Different Types of Cancer with Anti-Cancer Regimens
Used in the Private Sector**

Distribution of Different Types of Cancer with Anti-Cancer Regimens Used in The Private Sector		
S.No.	Types of Cancer	Count of the drugs
1	CA BLOOD *	10
	Inj. Adriamycin	2
	Inj. Epirubicin	1
	Inj. Etoposide	1
	Inj. Ifosfamide	1
	Inj. Mesna	1
	Inj. Vincristine	2
	Inj. Cyclophosphamide	2
2	CA BREAST *	9
	Inj. Taxol	2
	Inj. Herceptin	3
	Inj. Neupogen (FILGRASTIM)	1
	Inj. Taxotere	1
	Inj. Carboplatin	2
3	CA GIT *	12
	Inj. Folinic Acid	1
	Inj. 5 Fu	2
	Inj. Cisplatin	1
	Inj. Folinic Acid	1
	Inj. Gemcitabine (Gemzar)	1
	Inj. Oxaliplatin	2
	Inj. Taxotere	2

Distribution of Different Types of Cancer with Anti-Cancer Regimens Used in The Private Sector		
S.No.	Types of Cancer	Count of the drugs
	Tab. Xeloda	2
4	CA HEAD & NECK *	5
	Inj. Cisplatin	3
	Inj. Methotrexate	1
	Inj. Taxotere	1
5	CA PULMONARY *	3
	Inj. Cisplatin	1
	Inj. Etoposide	1
	Inj. Gemcitabine (Gemzar)	1
6	CA RENAL *	1
	Inj. Gemcitabine (Gemzar)	1
7	CA REPRODUCTIVE ORGAN *	11
	Inj. Paclitaxel	1
	Inj. Taxol	2
	Inj. Avastin	1
	Inj. Carboplatin	1
	Inj. Cisplatin	1
	Inj. Jevtana	1
	Inj. Neupogen (Filgrastim)	3
	Tab. Emend	1
	Grand Total	51

4.3.15 Anti-Emetics

Of the 12 (54.5%) patients reported nausea/vomiting and were given anti-emetics. Out of 10 (45.4%) patients who received Inj. Zofran (ondansetron) 8mg, included 4 (18.1%) females and 6 (27.2%) males, while 2 (9.09%) patients who received Inj. Kytril (granisetron) included 1 (4.5%) female and 1 (4.5%) male.

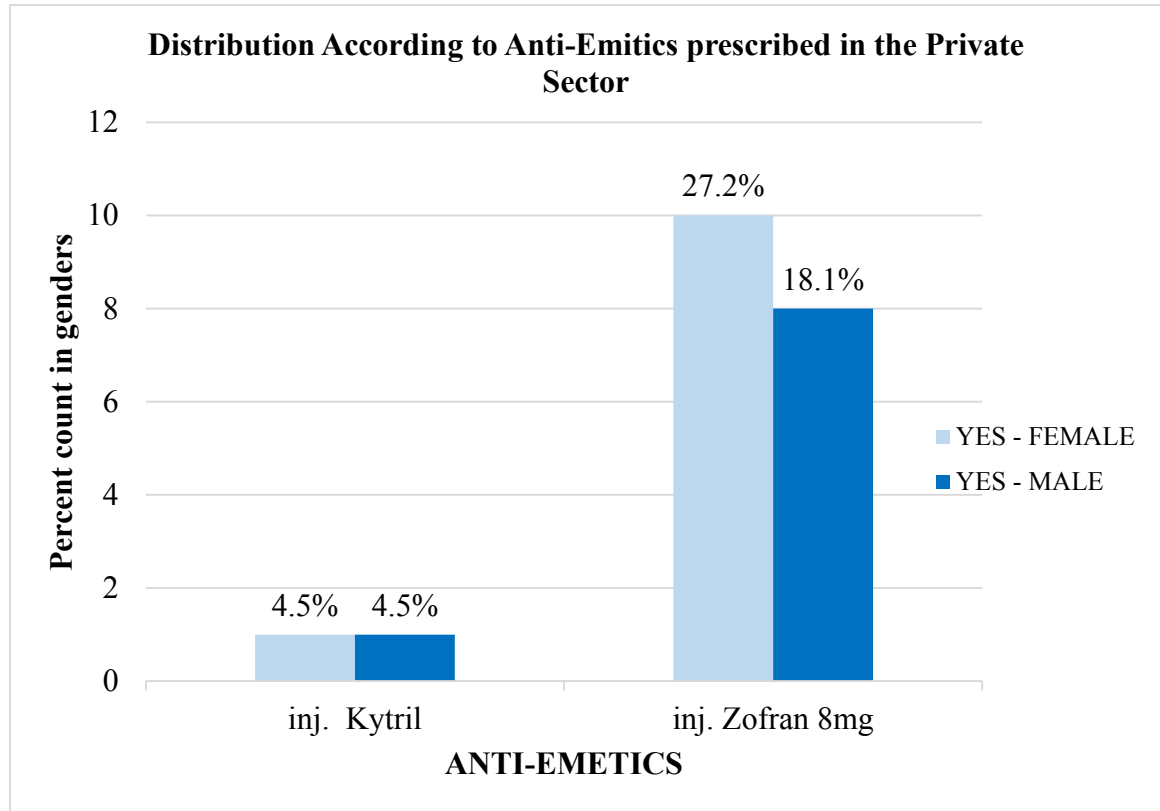


Figure 4.36: Distribution According to Anti-Emetics prescribed in the Private sector

4.3.16 Pain Management

Of cancer patients, 14 (64%) were given analgesics for pain management with Inj. Dexamethasone (Dexamethasone) 12mg was the most prescribed given to 9 (40.9%) females and 2 (9.09%) males. Inj. Toradol (ketorolac) 30mg was given to 3 (13.6%) patients including 1 (4.5%) female and 2 (9.09%) males.

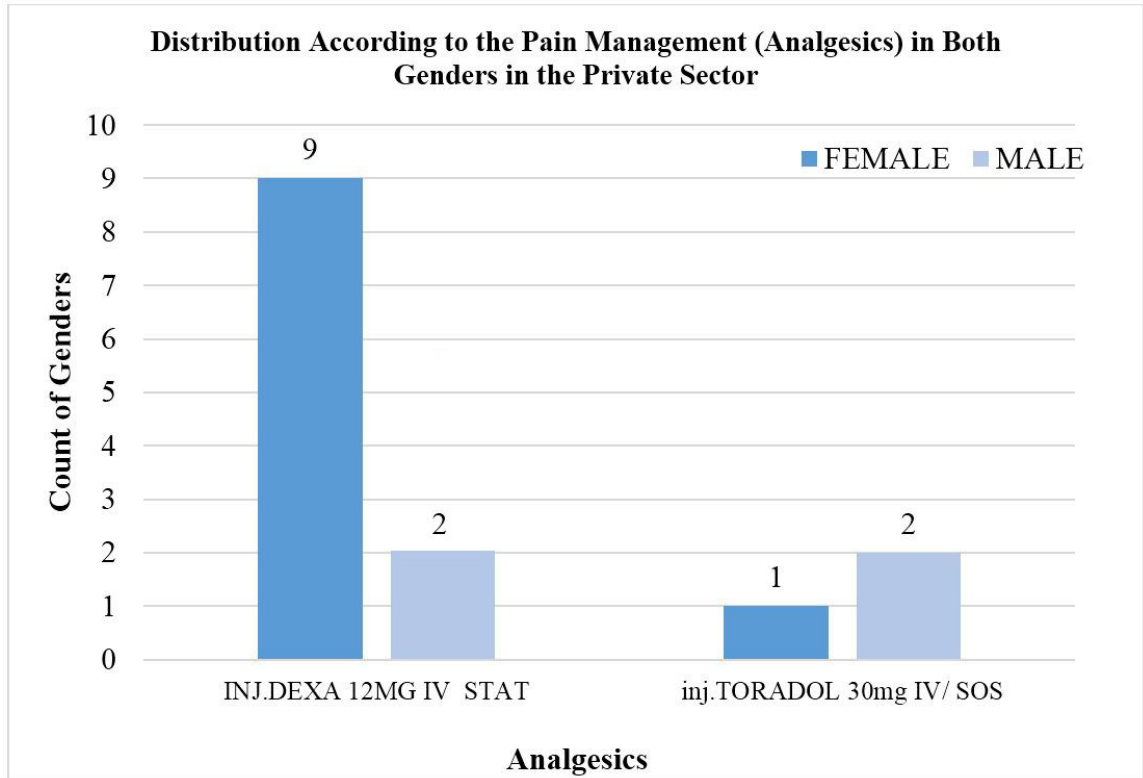


Figure 4.37: Distribution According to Analgesics Used in Private Sector

CHAPTER 5

DISCUSSION

5.1 DISCUSSION

The *gender-wise distribution* of patients is given in **Table 4.1** and for public sector and for **Table 4.16** private sector hospitals. On analyzing the distribution pattern of cancers, it became evident that cancer is more prevalent in females (51.6%) as compared to males (48.4%) in both public sector and private sector hospitals in Karachi, putting females in the higher risk group. A similar Karachi base study revealed that study from Jan 2017 to Dec 2019 malignant cases was recorded in the Karachi Cancer Registry (KCR) database comprising (52.5%) females and (47.5%) males (16). Similar research showed that the difference in gender in cancer susceptibility was one of the prominent findings in cancer epidemiology. (92) Another descriptive observational Study stated comparable results. (93). In susceptibility, to disease discernments, gender differences are a valuable piece of evidence that can be used to create the intended hypothesis for the ailment or to demonstrate subgroups at the highest possibility of risk for precautionary action. (93) In diagnosis, the gender variance in susceptibility can give significant clues to the etiology of cancers. (4) Breast cancers and cancers of reproductive organs are mostly seen in females while oral cancers are more common in males. (92) Another study stated that thyroid cancer is more prevalent in females compared to males. Concerning to Colo-rectal carcinoma, more recognized in male population. Increased awareness, lifestyle education, and screening tools should be made available and accessible to the female population to curb this increasing incidence.

The *Caste-Wise distribution* of patients is given in **Table 4.1** for public sector and **Table 4.16** for private sector hospitals. Where the caste Muhajir/Urdu speaking (29.0%), Sindhi (24.1%), and Punjabi (19.9%) were more affected groups in both sectors. Concerning this, similar studies reported similar data i.e.; 47.37% males and among which foremost ethnic groups were 17% Sindhi, 17% Immigrant, \approx 4% Punjabi, and 52.62% females, with which 16% Sindhi, 21% Immigrant, 5% Punjabi(82,94). This demonstrates marked variation in

cancer type, incidence, and mortality. A comparable study in the United States of America demonstrated that African-Americans have the greater incidence and mortality rate of Colo-rectal Cancer. This provides useful information about the development of therapeutic strategies against types of cancer with differences in the place of origin, and dominant ethnic group in that region and these differences are extremely statistically significant (94, 95).

The *age-wise distribution* of patients is given in **Table 4.2** for public and **Table 4.17 and Figure 4.26** private hospitals. The highest risk age group was 41-50 years of age for the public sector (29.90%) and private sector (31.80%). The next susceptible age groups were 31-40 years of age with equivocal percentages for both public and private hospitals were 18.90% and 18.18% respectively and 51-60 years of age at 18.30% and 27.27%. A connection was noted between increasing age and susceptibility to carcinoma (19). For most cancer classes, incidence rate and mortality rate raised with the age throughout all of adulthood and old age, with a tendency of turning-off at the highest years of ages (96). The Cancer Research UK website states that 'Older age is the primary risk factor for carcinoma' due to accumulating destruction to cell DNA with time (97). Hormonal, physiological, and biochemical changes due to aging coupled with decreased immunity may lead to the activation of pro-oncogenes. Based on similar research, the age limit 41-50 years should be pursued for screening carcinoma but widening this range to 30-60 years would be more effective (98).

Family history of cancer explained in **Table 4.5** for the public sector and **Figure 4.29** for the private sector was found positive in 17.1% of the public sector and 27.2% of patients in the private sector. In both sectors, females were more prone to cancer having a positive family history. In males, Head and neck cancer, and females Breast cancer was identified as the main risk of genetic changes or modifiable factors in family history.

The deviation in risk supported by commonly inherited variation is likely to rise soon (99). According to the National Health Services website of the UK, 'It is estimated that in between 3 and 10 in each 100 cancer types, analyzed are related with an inherited faulty gene. Almost 5% to 10% of cancers are relatable to the predisposition syndrome of

hereditary cancer (100). Identifying these has significant advantages both for the patient and for at-risk relatives. Furthermore, performing predictive genetic testing on affected family members effects in a more specific risk assessment and the beginning of appropriate screening and tests, and prevention measures (101).

Of 50 diverse types *of cancers* were observed in patients presenting to public sector hospitals **Table 4.6**, while 14 distinct types of cancers were observed in patients presenting to private sector hospitals **Table 4.18**. Cancer is classified highest among non-communicable ailments and millions of individuals get treatment for cancer diagnosis every year (52). Various systems of the body are affected exposing the non-specific kind of the disease (84). The most common cancer was found to be Breast cancer among females and Head and Neck cancers among males in both public sector and private sector hospitals, other cancers are of the gastrointestinal tract and the reproductive tract (CA ovary, cervix, endometrium for females, and prostate for males) closely following the lead. Similar results were obtained in a study (64) that reported cancer of the breast (29.44%) was the most detected cancer, followed by cancer of the head and neck (23.35%). Another study demonstrated that the highest occurrences of head and neck cancer (especially squamous cell carcinoma) were noted among males, while breast cancer was among females' gender (102). Head and neck cancers, especially oral cancers, have a strong association with tobacco, betel nut, pan, gutka, and mawa chewing. Human papillomavirus type 16 and Epstein Barr virus have also been correlated with the growth of oral squamous cell carcinoma (OPSCCs) (103,104).

Our study showed that 29.2% of the patients chewed pan/betelnuts/gutka or tobacco, 16 (9.7%) of those being females and 32 (19.5%) being males and 14.02% of patients reported smoking cigarettes or Huka with 3.04% females and 10.97% males. Oral cavity cancer of the lip are highest in Karachi males compared to any other male in the Asian population (105). A similar study indicated that 67.8% of males and 32.1% of females in Karachi chew either pan alone or pan with tobacco and approximately half of the cancers in males and a quarter of neoplasm in females are because of tobacco (16) develop malignancies in their body like reproductive organs, ovaries, prostate stomach, lungs, kidneys, and abdomen (106). Another Study from Karachi has shown that 21% of men and 12% of women use

betel, for both men and women 7.3% use pan, 6.7% chalia, 7.5% gutka, 14.6% naswar and use betel and chewed tobacco is 20% and 17%, respectively (107). As same incidence of cancers of the gastrointestinal tract is from 40% to almost 80% of patients, from early-stage colon cancer to advanced-stage cancer (106) is attributed to family history and lifestyle.

Pakistan should take necessary actions to counter this cancer (82), in the form of screening programs for high-risk groups and increased awareness with special emphasis on public awareness campaigns. Stricter regulations for tobacco use and stronger strategies for screening and its cessation should be put in place. Early Screening and vaccination programs are instrumental in dealing with these cancers. Additionally, Government policies and legislation, with cancer treatment challenges, and firm prevention and control must be revised seriously (106).

The ***stage of Cancer*** is a critical part of the prognosis, prevalence, and surveillance of cancer patients. Diagnosis at the earliest increases the chance of prolonged life and the quality of life, while delays increase morbidity and mortality. It is also a need in research work and cancer control activities (108). A Pakistan base study stated late diagnosis happened here are because of numerous factors like low health literacy, poverty, physical suffering, cultural ideas about health, in addition healthcare challenges, and environmental factors, are interconnected with each other. (109) In our study, **Table 4.8** and **Figure 4.11 and Figure 4.30** of diagnosed patients with stage IV 38.7% while stage III diagnosed patients are 31.7% in the public and private sectors. These stages are classified as advanced stages and alarming situations for the region. A study evaluated for head and neck carcinoma, examining the diagnostic delay impact on survival, estimates that the relative chance of mortality in head and neck carcinoma, related to any diagnostic delay was 1.34 folds, Referral delay increased three-fold, which indicates a fierce change in the stage of cancer. In head and cancers, pharynx cancer showed the highest association. Worldwide, it is the eighth leading reason of death and has a very narrow index in 5 years survival rate (110). Physicians emphasize the diagnosis and categorization of staging for successful cancer treatment. There are many kinds of cancer, and each class requires a different treatment approach, especially when a stage is considered because advancement in stages of any cancer could not be eradicated (111). In this context staging is a powerful tool in all

steps of survival and treatment protocols. Physicians emphasize the diagnosis and categorization of staging for successful cancer treatment. There are many kinds of cancer, and each class requires a different treatment approach, especially when a stage is considered because advancement in stages of any cancer could not be eradicated (111). In this context staging is a powerful tool in all steps of survival and treatment protocols. Proper screening, routine checkups and awareness of health issues will decrease the possibilities of carcinoma and fierce spreading at the diagnostic site.

An extensive variety of **anticancer agents** are significantly used to deal cancer of numerous types and stages. Inappropriate use of drugs may elevate cost of medical care, potent adverse drug effects, and patients rate of mortality (45). In our study, Alkylating agents in public (36.0%) **Table 4.12, Table 4.15 and Figure 4.18, 4.19** and Private (29.4%) sector hospitals **Table 4.20** were used equivocally where the major drug being Cisplatin and cyclophosphamide. Similar results were obtained in another study (58).

Another group of drugs given equivocally was antimetabolites, the prescribing percentage was 17.5% for the public sector while 15.6% for private sector hospitals followed by antitumor antibiotics where the prescribing percentage was 15.12% for the public while 5.9% for the private sector.

Affected **cancerous site**, like *breast carcinoma* in **Figure 4.17** the most prescribed agents were Inj. Doxorubicin (7.6%), cyclophosphamide (6.9%), and Inj. Paclitaxel (3.7%) for public sector while in **Table 4.21** Inj. Herceptin (trastuzumab) (5.8%) and Inj. Carboplatin (3.9%) was prescribed in the private sector. Doxorubicin is an anthracycline that is an important agent in the treatment protocol of both metastatic phase of every cancer and early breast cancer. (112) (113).

For cancers of the *gastrointestinal tract*, **Figure 4.20** the most prescribed agents were Inj. Cisplatin (2.0%), Inj. Capecitabine (1.6%) Inj. Oxaliplatin (1.3%) and, in the public sector while **Table 4.21** Inj. Docetaxel (3.9%) and, Inj. Oxaliplatin (3.9%) was prescribed in the private sector. In a study, it is stated that GI cancers are liable for the incidence of 26% of global cancer and 35% of all cancer-related mortalities (114). The treatment consists of surgical treatment plan of resectable gastric carcinoma, and the effect of pre-and post-operative chemotherapy or chemoradiation. Cisplatin class and fluoropyrimidine-based agents' chemotherapy with trastuzumab is the widely used treatment specifically in advanced stages (115).

For cancers of the *head and neck region*, **Figure 4.18** the most prescribed agents were Inj. Cisplatin (10.3%), Inj. 5-FU 6 (2.0%) and, Inj. Cetuximab (1.7%) in the public sector while Inj. Cisplatin (5.9%) and Inj. Docetaxel (2.0%) was prescribed in the private sector(112)

The innovative treatment of (Head and Neck) HNC consists of three procedures: surgery, radiotherapy, and systemic chemotherapy combine with immunotherapy, pembrolizumab with platinum and fluorouracil (antimetabolites) have been approved (116)

Cisplatin (alkylating agent) is an organometallic compound that is administered intravenously, and, used as first-line chemotherapy treatment for patients diagnosed with various types of malignancies, such as breast, blood cancers, gastrointestinal, reproductive tract cancers (testicular, ovarian, and, cervical), head, and neck cancers, and sarcomas (117). For effective prescription of drugs, several factors come into play like cost, availability, tolerance, and stage and progression of the disease.

In *Blood carcinoma*, chemotherapy is used in three phases, induction, consolidation, and maintenance. As **Figure 4.19** outlined, a combination of chemotherapeutics in the public sector. Antimetabolites (cytarabine) were given 9 (3.0%), targeted drug (nilotinib) given 5 (1.6%), daunorubicin 4 (1.3%), an alkylating agent (cyclophosphamide), antimetabolites & plant alkaloids (methotrexate, vincristine) given 3 (1.0%). In the private sector, **Table 4.21** equivocally used the treatment protocol. A similar study revealed that blood cancer has a high incidence rate of relapse, to an extremely low survival rate in patients. This

demonstrates an urgent demand for a targeted drug delivery system to intensify the safety measures and efficacy of drug therapeutics for blood cancers (73).

The most concerning untoward effects of chemotherapy are nausea/vomiting experienced by cancer patients which negatively impacts patients' quality of life and their adherence to therapy. Similarly, nausea and vomiting condition can result in anorexia, decreased performance status, metabolic imbalance, oesophageal tears, wound dehiscence, and the nutritional deficiency (118,119). Approximately 70-80% of individuals are at possibility for nausea and vomiting. During the initial cycles of chemotherapy individuals experienced the acute and delayed form of the symptom, and the frequency of nausea and vomiting enhanced during chemotherapy (120). The recommended anti-emetics are 5-HT₃ antagonists (granisetron and ondansetron) for acute and delayed form of nausea and vomiting and for moderately and highly emetogenic chemotherapy. (121) In *our* current study, (39.8%) of patients experienced chemo-related induced nausea/vomiting, for this **Figure 4.24, 4.25 & 4.36** the most prescribed anti-emetics were ondansetron (Inj. Zofran and Onset) 31.1% and granisetron (Inj. Ketril) 4.3% in both sectors. (122) Other studies stated that ondansetron and granisetron have equivalent antiemetic effects in reducing or eradicating chemotherapy-induced nausea and vomiting (CINV), Although the unwanted effects of ondansetron and granisetron have been reported, they normally are minor and of short-term duration, not severe or lasting enough to discontinuation warrant. (120) In a similar study, ondansetron 12 mg or granisetron 3 mg was intravenously given to cancer patients having cisplatin induce nausea and vomiting during 5 days of antiemetic treatment, complete prevention in 80% of the patients was observed. As well cost with a granisetron-based antiemetic treatment regimen was at a ratio of 10:1 higher compared with the one with ondansetron (123).

Other adjuvant drugs prescribed were cytoprotective agents such as MESNA (prevention of urothelial toxicity) and Filgrastim (treat chemo-related neutropenia) **Table 4.12 & Table 4.20**, these agents were used to stimulate mucus production by coating the lining of the gastrointestinal tract and reducing inflammatory response to enhance blood flow. (124) In a study of peptic ulcers, the cytoprotective agent Rebamipide was used for 12 months in

71.1% of patients against a placebo. Results in safety and may thwart peptic ulcers ≥ 5 mm in diameter. Additionally, no bleeding ulcers with two antiplatelets (124).

Filgrastim is used in myelosuppression to manage and treat neutropenia in patients who are on chemotherapy or radiation. In another study of solid tumors, blood count was analyzed on days 7 and 15 in each course of chemotherapy. All the hematologic components were noted. A reduction in the hematologic component and its increase after administration of GCF Injection was the prominent pattern of data (125).

Further categories of other drugs prescribed in our study were Anti-ulcer drugs (16%), Anti-allergies (10%), Analgesics (18%), antifungal (2%), antiviral (2%) Laxatives (6%), Antitussives (2%), Antidepressants (2%), Antidiarrheals (2%), Antihypertensives (2%), Anti-convulsants (1%), Mucolytic (1%), Diuretics (1%) and Multivitamins (9%) in overall patients. Only 7.30% of patients receive Antibiotics for chemotherapy-related infections. Similar studies define the same outcomes of the use of other drugs with anticancer drugs (28, 45, 126, 127).

Only 26.3% of patients received analgesics for *pain management* in both sectors. As described in **Table 4.14** analgesics were prescribed as opioids, non-opioids, and steroids for the public sector where tramadol (7.3%) and dexamethasone 12mg (3.0%) were used for relief in cancers patients while in the private sector dexamethasone 12mg (40.9%) and ketorolac acid 30 mg (9.09%) were given in **Figure 4.37**. There is no adjuvant analgesic therapy in patients with cancer-related pain stated in an article and are used on clinical judgment. Decisions are based on whether the patient has active cancer or is a cancer survivor. In active cancer patients, adjuvant analgesics added are opioids (morphine oral / IV, and transdermal patches as fentanyl) for moderate-to-chronic pain (128). In some cases, the use of a nonopioid analgesic and NSAIDS was sufficient and appropriate in low-to-moderate pain with the advanced technique of IR ‘immediate release’ to ER ‘extended release’ form of oral tablets (129).

5.1 Conclusion

Drug utilization review plays a vital role in the health care system and highlights the provision of optimal cost-effective drug therapy. Prescribing indicators provide an idea for general medicine prescribing patterns, innate flaws, and limitations. A total of 325 medicines were prescribed with an average of 1.98 drugs per prescription in the public sector and 69 total medicines prescribed in the private sector with an average of 3.13 medicines per prescription. The indicator is used to assess the extent and use of polypharmacy. For the private sector, the outcomes were above the mentioned range, but it cannot be termed polypharmacy considering combinational therapy and adjuvant drug therapies such as anti-emetics and analgesics. In our study, the prescribed antibiotics percentage was within range. Moreover, 79.07% were from the public sector and 92.7% of prescribed drugs were from the national essential medicine drug list. In this research work, the indicators were within the proposed range,

The conclusion of this study indicates that females were more susceptible to cancer with the highest incidence rate in breast and ovarian cancer while head and neck cancer in males. The main alarming situation was diagnostic stage 4, which was an advanced uncontrolled stage. Similarly, the elevated mortality rate is also considerable. There is a need for adherence to therapy with judicious intervention to halt the chronic progression of the disease, and continuous medical education to the health care providers and caretakers. Considering Pakistan is a developing country there must be a deemed requirement for successful cancer monitoring and prevention to decrease this persistent disease burden. There is also a demand for financial stress management to deal with the psycho-social fact of the patient's life, start-up of health policies from insurance companies and health cards from the government bodies will be a beneficial tool to minimize the rapid growth rate of the disease.

The union for international cancer control (UICC) should also monitor Pakistan closely to ensure a decrease in cancer burden which parallelly lowers the disease global rate.

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