

A Drug Utilization Study in Patients Suffering From Gastro-Intestinal (G.I.) Cancer at a Tertiary Care Teaching Hospital**Hardik Prajapati¹, Kamalesh Bhatt², Jatin Pathak³, Vidhi Thacker⁴, Minaxi Shah⁵
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Conflict of interest: Nil

Abstract:**Objective:** The objective of the study is to evaluate utilization patterns of drugs in patients suffering from Gastro-intestinal (G.I.) cancer at a tertiary care teaching hospital.**Materials and Methods:** This prospective, observational study was carried out at the Department of Pharmacology and Oncology, GCS Medical College, Hospital and Research Centre, Ahmedabad, to assess the drug utilization pattern in patients of cancer. The study was carried out over a period of 19 months from August 2019 to March 2021. A total of 43 patients were enrolled for the study. Patient's demographic, clinical, and therapeutic data were collected from the files and in person ward visit and analyzed in Microsoft Excel version 2015.**Results:** Diagnosis of G.I carcinoma was highest in age group of >60 years (44.19 %). Colon (23.26%) was commonest organ affected followed by esophagus (16.28%) and stomach (11.63%) subsequently. Family history of cancer was seen in 25.6% patients, while 51.2% gave history of Tobacco consumption. Oxaliplatin and CAP: Capecitabine (OXA + CAP) was the most commonly used initial combination followed by CAR: Carboplatin and PAC: Paclitaxel (PAC + CAR).**Keywords:** G.I. Cancer, Drug Utilization Study, Chemotherapy Regimen.

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Introduction

Investigator's view on Drug Utilization Research (DRC) importance had been significantly changed in the mid-1960, by the essential work of Arthur Engel in Sweden and Pieter Siderius in Holland. Comparing drug use between different countries and states or even different localised area in the same state can derive important data pertaining to that area.

Drug utilization research was defined by WHO in 1977 as "the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences." Drug utilization research is thus an essential part of pharmacoepidemiology and may provide insights into

- Pattern and Quality of drug use
- User, prescriber and drug characteristic
- Outcomes of use

This information might be beneficial to set priorities for the rational allocation of health care budgets. For the individual patient, the rational use of a drug implies the prescription of a well-documented drug at an optimal dose, together with the correct information, at an affordable price. (Introduction to drug utilization research, 2013)

Cancer also known as Neoplasm, is the appearance or development of a tumor. A tumor is an abnormal mass or piece of a tissue whose growth is found to be extreme and unstoppable or uncoordinated and continues or persists even after the cessation of the stimulus which gives rise to the change. Globally Non-Communicable Diseases (NCDs) accounted for 71% of total deaths and carcinoma is one of the most common causes of morbidity & mortality (Pentareddy MR et al, 2015). In India, NCDs were estimated to account for 63% of all deaths and cancer was one of the leading causes (9%) in previous years. Currently number of patients with

cancer in India is 13,92,179 for the year 2020 and the common 5 leading sites are breast, lung, oral cavity, cervix uteri and tongue (Mathur P et al, 2020). Most of the cancers can be categorized as follows according to the National Cancer Institute. There are generally 4 categories of cancer;

1. Carcinomas: Cancer that arising from epithelial cells of any tissue e.g., Lung cancer.
2. Sarcomas: Cancers that originates from “solid” mesenchymal tissues or its derivatives (i.e., cartilage, bone, muscle, fat& other connective tissues). e.g., Ewings sarcoma.
3. Leukemia: Cancers that originate in tissues of blood-forming such as bone marrow & causes large number of abnormal blood cells to be produced & enter the blood. e.g. Acute lymphoblastic leukemia.
4. Lymphomas & Myelomas: Cancers that originate in the immune system's cells. e.g. Non-Hodgkins lymphoma.

The main modalities used for cancer treatment include surgery, radiation, chemotherapy, immunotherapy and hormones. Cancer cells usually grow and divide faster than normal cells and chemotherapy works by preventing the cancer cells from growing, dividing and multiplying so chemotherapy is main stay of treatment which acts systemically to reduce the progress of disease and induces remission (Asmatanzeem Bepari et al, 2019). Chemotherapy can also have an unintentional harm on the other types of rapidly dividing cells possibly resulting in side effects.

If chemotherapy is given before surgery or radiation therapy with aim of to shrunk tumor it is called neoadjuvant chemotherapy while if given after surgery or radiation therapy to destroy any remaining cancer cells this is called adjuvant chemotherapy. Palliative chemotherapy is used to put a control (but not cure) to the cancer in periodic sittings in which the cancer might be spreading beyond the localized lymph nodes. In many cases, chemotherapeutic drugs are given in combination of more than one drugs, and these combinations are known as chemotherapy regimen and these can help in the regression of disease in about 30-60% of patients. The drugs, dose and treatment schedule depend on many factors. These includes

- Age & body weight of the patient
- Type of cancer
- Tumor size, location and spread (stage of cancer)

Thus, based on the growing incidence of cancer and implementation of newer cancer chemotherapeutic agents in clinical practice, we decided to do drug utilization research study in tertiary care teaching hospital in western area of

India to measures latest various parameters pertaining to drug utilization research.

Aim:

To evaluate utilization patterns of drugs in patients suffering from G.I. cancer at a tertiary care teaching hospital.

Primary Objective:

To evaluate drugs usage patterns in G.I. cancer patients of different age group admitted to oncology department in term of different anticancer drugs combinations (also known as regimen)

Secondary Objectives:

- To observe brief epidemiology of different cancers.
- To find out usage patterns of pre-chemotherapy agents, post-chemotherapy agents and supportive drugs.

Material & Method:

Study was carried out at chemotherapy ward (patients were admitted to receive their chemotherapy cycles) with collaboration of department of oncology and department of pharmacology, GCSMCHRC, Ahmedabad from August 2019 to March 2021. It was prospective observational study.

Following patients were included in the study:

- Patients of either gender who were willing to give consent for their participation in study
- Diagnosed patients of cancer of any G.I. system and confirmed by various investigations (e.g. histopathology reports, biomarkers etc.)
- Patients of G.I. cancer with any stage of cancer
- Patients requiring to receive anticancer drugs as their treatment plan

Following patients were excluded from the study

- Pregnant females and infants.
- Patients having insufficient records.
- Patients refused to give consent for their participation
- Anticancer drugs were not part as treatment plan (e.g. curative surgery in some cancer
- patients available)

Patients were explained about the study in their vernacular language and informed consent was obtained from them in form of signature or thumb impression by themselves or their relative in pre-defined informed consent form. Approval for study was obtained from Institutional Ethics Committee before starting the study.

All the necessary details include but not limited to only demographic details, chief complaints, provisional diagnosis/diagnosis, generic name,

brand name, dosage form, route of administration, duration etc. recorded in predefined case record form (CRF).

Analysis done for total 43 patient’s data e.g., their demographic pattern, diagnosis, comorbidity & drug usage pattern in the form of total drug, average drug, anticancer regimen, pharmacological classes, dosage form etc.

Data management and analysis: Data were recorded & analyzed through using Microsoft excel version 2015

Results: Total 43 patients were included in the study and categorized in different age group out of which highest number (19) of the patients were seen in age group D (>= 61 years) which indicate higher prevalence of G.I. cancers in older age group.

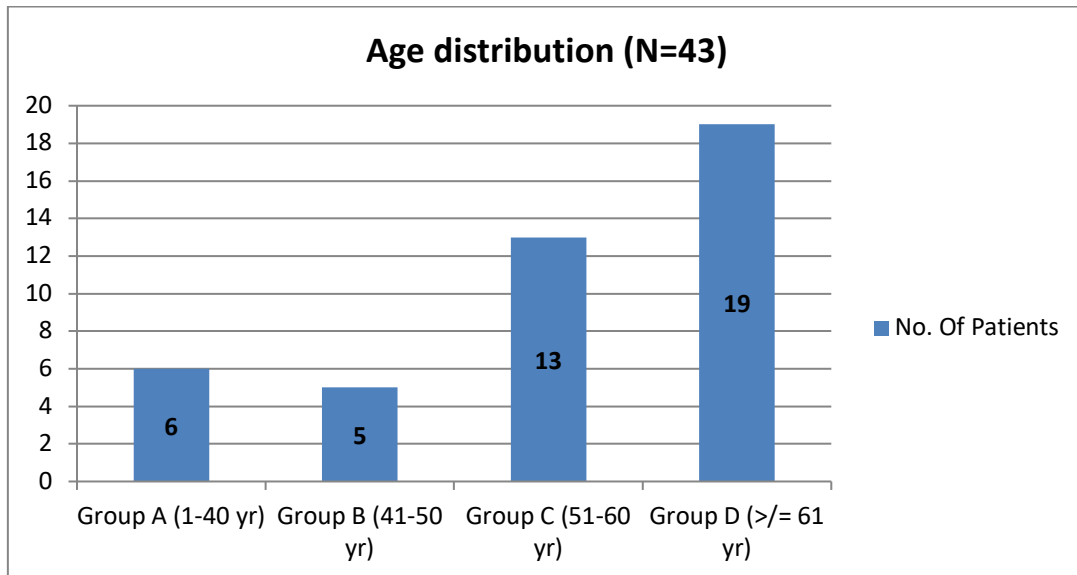


Figure 1: Age distribution (N=43)

Out of total 43 patients, 22 (51.2%) had history of tobacco consumption while 11 (25.6%) gave positive family history of cancer. So, total 33 (76.7%) patients had presence of any above-mentioned parameter. Thus, it is apparent that tobacco consumption in any form is strongly associated with occurrence of cancer and presence of any above-mentioned risk factor is associated with development of G.I. cancer. [Figure 2]

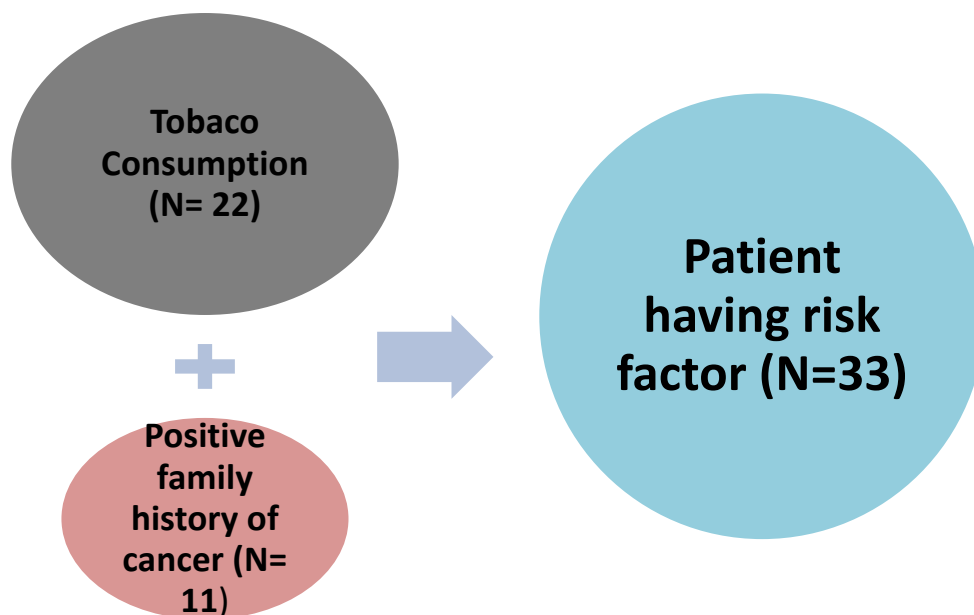


Figure 2:

Colon was commonest organ affected followed by esophagus, stomach, pancreas, appendix, rectum etc as shown in figure 3. Thus, organs falling in colorectal category were [10 (colon) +4 (pancreas) +4 (appendix) +3 (anal canal) +2 (caecum) =23] which was highest in our study.

Organ Distribution (N=43)

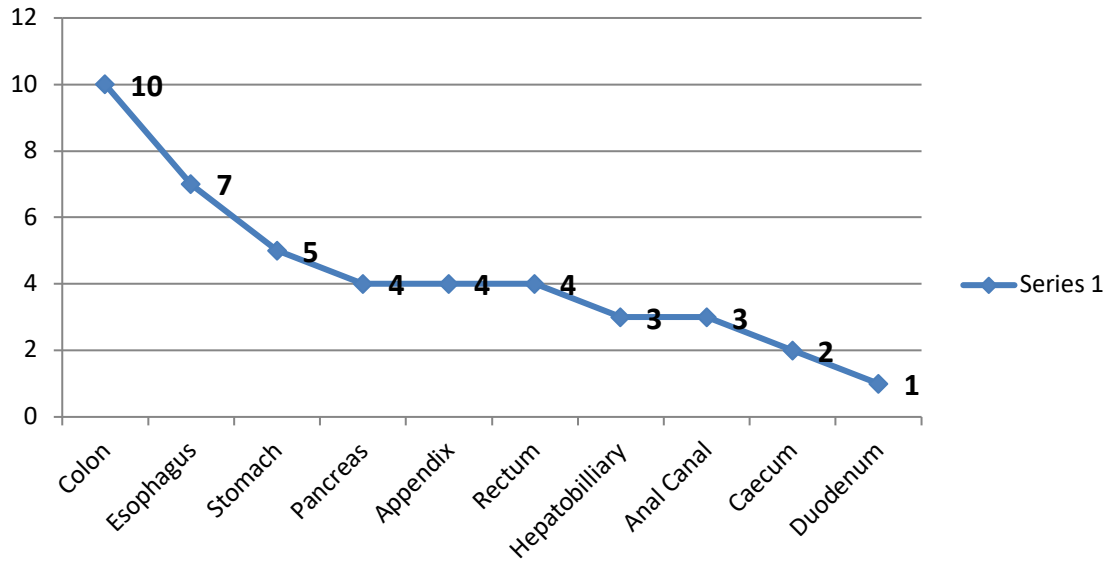


Figure 3:

Regimen means combination of different anticancer drugs prescribed to treat the cancer in individual patients. Where, regimen-1 is a initial combination of anticancer drugs and any subsequent changes made in regimen-1 afterward during the course of cancer chemotherapy in particular patient known as a regimen-2.

A. Regimen-1 (initial combination of anticancer drugs):

Total 100 anticancer drugs were used in regimen-1 in all patients (N=43).

So average anticancer drugs used per patients were 2.32. Using 11 different anticancer drugs, total 13

different combination of drugs were used in patients in initial cycle i.e. regimen-1. Out of which commonest prescribed regimen-1 shown in table 1.

B. Regimen-2 (first change in combination of anticancer drugs):

Total 30 anticancer drugs were used in regimen-2 in 13 patients. So average anticancer drugs used per patients were 2.30.

Using 7 different anticancer drugs, total 6 different combinations of drugs were used in patients in subsequent chemotherapy cycle i.e. regimen-2. . Out of which commonest prescribed regimen-1 shown in table 1.

Table 1:

Commonest regimen 1	Total patients	Commonest regimen 2	Total patients
OXA, CAP	18	Not Recorded	30
PAC, CAR	8	CIS, 5 FU	3
LEU, 5 FU	4	CAP	2

(Full forms: CAR: Carboplatin, OXA: Oxaliplatin, PAC: Paclitaxel, 5 FU: 5 fluorouracil, CIS: Cisplatin, CAP: Capecitabine, LEU: Leucovorin)

Out of both regimens, prescribed individual drug frequency also calculated which is shown in below figure. Oxaliplatin (30) was prescribed the highest followed by 5- Fluorouracil (26) while doxorubicin (02) was prescribed least.

Individual drug frequency

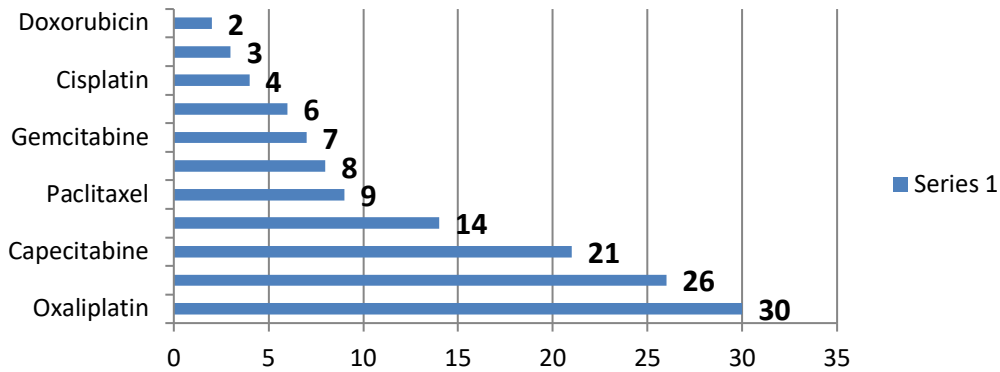


Figure 4: Individual drug frequency

All patients were prescribed pre-chemo and post-chemo treatment to counteract the nausea, vomiting, hypersensitivity reaction and other anticancer drug related side effects. Ondansetron, Dexamethasone & metoprolol were commonest prescribed drugs as shown in table 2.

Table 2:

Pre chemo drug	Total patients	Post chemo rug	Total patients
Ondansetron	43	Metoprolol	43
Dexamethasone	43	Magnesium sulphate	4
Prochlorperazine	01		
Pheniramine malate	35		

In all patients supportive drugs like prochlorperazine, domperidone, ondansetron, folic acid and rabeprazole had been prescribed after completion of indoor chemotherapy to combat toxicity. (Table 3).

Table 3:

Supportive drugs	Total patients	Supportive drugs	Total patients
Prochlorperazine	43	Niacinamide	16
Domperidone	43	Activated charcoal	8
Folic acid	43	Papain	8
Rabeprazole	43	Fungal Diastase	8
Dexamethasone	42	Pyridoxine	7
Riboflavin	16		

Discussion

The gastrointestinal (GI) cancers include cancer of the esophagus, stomach, small intestine, colon, rectum, anus & anal canal, liver & intrahepatic bile ducts, gall bladder, and pancreas.

21, 44 and 38% of oesophageal, gastric and colorectal cancer patients, respectively, were aged >75 years (Schlesinger et al, 2017) while in our study it 19 patients (44.2%) have age more than 60 years.

Esophageal, gastric, and liver cancers were more common in Asia than in other parts of the world, whereas of the burden from colorectal and pancreatic cancers was highest in Europe and North America. (Arnold et al, 2020) However, in our study colorectal (23 patients), esophagus (07 patients), gastric (05 patients) and liver cell

carcinoma (04 patients) were the commonest site involved.

One hundred sixty-two physicians (86%) treated patients with CRC. Of the 162 physicians, 92.6% (n = 150) recommended oxaliplatin-based regimens as first-line treatment for CRC due to perceived superior efficacy (66.9%; n = 107) or toxicity profile (17%; n = 27). Fluorouracil (FU), leucovorin (LV), and oxaliplatin (FOLFOX6) was the most popular regimen (59.3%; n = 98) (Field KM et al, 2008). In our study most common prescribed regimen was Oxaliplatin and Capecitabine. Nausea and vomiting are serious and directly related side effects of cancer chemotherapy. These adverse effects can cause significant negative impacts on patients' quality of life and on their ability to comply with therapy. Also, nausea and vomiting can result in anorexia, decreased performance status, metabolic

imbalance, wound dehiscence, esophageal tears, and nutritional deficiency (Williams & Wilkins; 1983, Fernández-Ortega P et al, 2012). To combat these side effects various anti-emetic drugs commonly used in clinical practice before starting of chemotherapy and after completing it. In our study, in all patient's dexamethasone and ondansetron were used as pre-chemotherapeutic agents while metoprolol used as post-chemotherapeutic agent in all patients.

As, chemotherapeutic agents are highly effective on rapidly multiplying cells, they also exert unwanted side effects towards the cells which have relatively short cell cycle (e.g., Cells of G.I. tract, Hair, Cells of bone marrow etc.) Thus, various supportive drugs are commonly prescribed after the chemo cycles. In our study, all patients received prochlorperazine, rabeprazole, domperidone and folic acid to neutralize the chemotherapeutics' agents effect on rapidly multiplying normal cells.

Advantage of the study: This study analysed the various chemotherapeutic drugs were used upto 8 chemotherapeutic cycles.

Limitation of the study: Relatively small sample size does not predict prevalence of various cancers accurately.

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