



## A Retrospective Study on Pharmacotherapeutic Outcomes in Colorectal Cancer Patients at Tertiary Care Hospital

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### ABSTRACT

**Introduction:** Colorectal cancer is the third most common cancer worldwide, accounting for approximately 10% of all cancer cases and is the second leading cause of cancer-related deaths worldwide. In our literature review we have noted some studies which are done to analyse the different clinical outcomes & disease prognosis of patients with CRC treated with FOLFOX chemotherapy based on different mutation patterns. Surgery and chemotherapy have long been the first choices for cancer patients.

### Aim:

1. To study the various patterns of drug therapy in colorectal cancer Patients.
2. To Understand the disease severity, Prognosis and the treatment outcomes in CRC patients

**Method:** A Retrospective, observational and single centered study was conducted in hospital to study the various patterns of drug therapy in colorectal cancer patients.

**Results:** In our study Where N=200, 146 underwent surgery, 77 were treated with chemotherapy and 33 received radiation therapy. The Patients diagnosed with CRC 18 were cured with the surgeries; 15 Patients received neoadjuvant chemotherapy and 62 patients received adjuvant chemotherapy. In this study 35 patients developed the recurrence at different sites.

**Conclusion:** The statistics of our study revealed that there is no significant effect of mutations on the survival rate of colorectal cancer. Patients diagnosed at stage 0, stage I are cured with surgery. Patients at stage III and IV are treated with the appropriate regimens of chemo and radiation therapy. Chance of recurrence occurred after 2-3 years of initial treatment.

**Keywords:** Colorectal cancer, FOLFOX, Mutations, Recurrence.

### INTRODUCTION

Uncontrolled cell division is a hallmark of the condition known as cancer. Colorectal cancer is the term for this kind of tumor that develops in the colon or rectum.<sup>1,2</sup> Worldwide, colorectal cancer is the third most diagnosed cancer. CRC is more common in males than in females.<sup>2,3</sup> An estimated 1,880,725 people were diagnosed with colorectal cancer in the year 2020. These numbers include 1,148,515 colon cancer cases and 732,210 rectal cancer cases.<sup>3</sup> Worldwide, colorectal cancer is the second leading cause of cancer death. About 915,880 deaths were reported with CRC in 2020.<sup>3</sup> Two-thirds of patients with newly diagnosed cancer report with localized disease, while 20% of patients have metastatic disease.<sup>4</sup>

In 1957 the American Joint Committee on Cancer (AJCC) adopted the tumour-node-metastasis (TNM) cancer staging system, and this has proven to be the most significant staging system we have to date.<sup>5</sup> The management of colorectal cancer (CRC) highly relies on the TNM staging system.<sup>6</sup> There are 5 stages: stage 0 (zero) and stages I through IV (1 through 4). The stage provides a common way

of describing the cancer.<sup>7</sup> Worldwide, the probability of suffering from colorectal cancer is about 4%–5%. The main risk factor for colorectal cancer is age: the risk of developing CRC is markedly increased above the age of 50 years and having certain inherited conditions like Lynch syndrome and familial adenomatous polyposis, but several other factors are also have been associated with increased risk, i.e., family history of the disease, excessive alcohol use, obesity, being physically inactive, cigarette smoking, and, diet. In addition, people with a history of inflammatory bowel disease such as ulcerative colitis or Crohn's disease have a higher risk of colorectal cancer.<sup>8,9</sup>

Many symptoms have been described, rectal bleeding, diarrhoea/ constipation — collectively sometimes named 'change in bowel habit' — loss of weight, abdominal pain<sup>10</sup>, published evidences are abdominal or rectal masses and iron deficiency anaemia as presenting features for colorectal cancer.<sup>11</sup>

The evidence is clearly stated the - screening for colorectal cancer may save life. Nowadays, an increasing proportion of people decide to undergo for colorectal cancer



screening. Consequently, the number of elderly individuals developing colorectal cancer and deaths from it are gradually decreasing. Two types of screening procedures commonly recommended for colorectal cancer Stool sample tests (FIT, Gfobt, mt-Sdna) and Visual screening procedures (Colonoscopy, Sigmoidoscopy, CT Colonography, MR colonography and PET CT).<sup>12</sup>

If cancer is detected, the biopsy samples may additionally undergo additional laboratory testing with a goal to improve the malignancy's classification and maybe identify certain treatment choices.

Biomarker tests are performed on tumor biopsies to identify gene mutations.<sup>13</sup> Whole-exome sequencing is an investigation that examines every gene in your cancer. Others, referred to as whole-genome sequencing, analyze all of the DNA (both within and outside of genes) in your malignancy. Some biomarker tests also measure the tumor-mutational load, or the genetic alterations present in your malignancy. Types of biomarkers used in CRC are KRAS, NRAS, BRAF, PIK3CA, MSI-High, CEA, HER2, TRK fusions.<sup>14</sup>

The main treatment modality for localized non-metastatic stage CRC is surgical resection at any age with acceptable performance status and optimized comorbidities. Adjuvant therapy is recommended for all CRC stage III (node-positive) and individualized by stage II with high-risk features.<sup>15</sup> There is no accepted neoadjuvant treatment for colon cancer. However, for rectal cancer, neoadjuvant radiotherapy or chemo radiotherapy are recommended for intermediate-stage and advanced-stage cancer to reduce the rate of local recurrence.<sup>15,16</sup> Surgery in conjunction with peri-chemotherapy may provide a curative option on oligo-metastatic lung and liver disease. Palliative systemic chemotherapy is recommended for non-surgical patients with substantial metastatic load or unresectable locally advanced cancer in order to increase their lifespan and enhance their standard of living. Individualized local-recurrent disease patients may achieve cure with further multimodality therapy.<sup>15</sup> Commonly used regimens for CRC are CAPEOX, FOLFOX, FOLFIRI, FOLFOXIRI, XELOX,...<sup>16,17</sup> Alongside these combined chemotherapy regimens, targeted agents are used for metastatic colorectal cancer treatment. Specifically, these comprise three main categories of medications: fusion proteins which focus on several proangiogenic growth factors (like aflibercept) and minor molecule-based multikinase inhibitors (like regorafenib), as well as monoclonal antibodies against EGFR (cetuximab and panitumumab) and VEGF-A (bevacizumab).<sup>16</sup>

## STUDY AIM & OBJECTIVES

### Study Aim –

To assess the pharmacotherapeutic outcomes in colorectal cancer patients.

### Objectives:-

1. To study the various patterns of drug therapy in colorectal cancer.

2. To study the treatment outcomes in colorectal cancer patients.

## STUDY METHODOLOGY

**Study design:** Retrospective, Observational study

**Study duration:** 6 months

**Sample size:** 200

**Study criteria:**

**Inclusion criteria:**

- The patients diagnosed and have been treated for CRC.
- The patients aged 18 years and above 18 years

**Exclusion criteria:**

- Pediatric patients
- Pregnant and lactating women

**Study site:** Apollo hospitals, jubilee hills, Hyderabad

**Sources of data:**

1. Patient files from medical records department.
2. Patient records from Information Technology department.
3. Patient available data on mutations from Molecular Biology department.

**Study procedure:**

After the protocol approval from the Institutional Ethics Committee, the medical records of the patients who meet the inclusion criteria were reviewed and analyzed.

Patient demographic details, Laboratory findings, and treatment given were collected from medical records of the patients.

The data collected from the medical records department and Molecular Biology department were reviewed and analyzed for the treatment outcomes in CRC patients.

**Statistical analysis:**

The data obtained was analyzed using MS-EXCEL as a statistical tool. Excel data sheet and SPSS version 28 (IBM Corp., Armonk, NY, USA) was used for data cleaning and data analysis respectively.

## RESULTS

A total of 200 patients who were admitted to the hospital between the years of 2010 and 2021 were the subject of our study, "A Retrospective Study on Pharmacotherapeutic Outcomes in Colorectal Cancer Patients at Tertiary Care Hospital."

Male patients are made up to 70% of the total and female patients 30%. Out of 200 patients, 94% were Asian, 4.5% were African, and 1.5% were Arab.



The age range of 59 to 68 years in our study had the highest risk of colorectal cancer, accounting for 30% of the patients, followed by the age range of 49 to 58 years with 24% of the patients, the age range of 69 to 78 years with 15.5% of the patients, and the age range of 89 to 98 years with the lowest risk.1% of the patients.

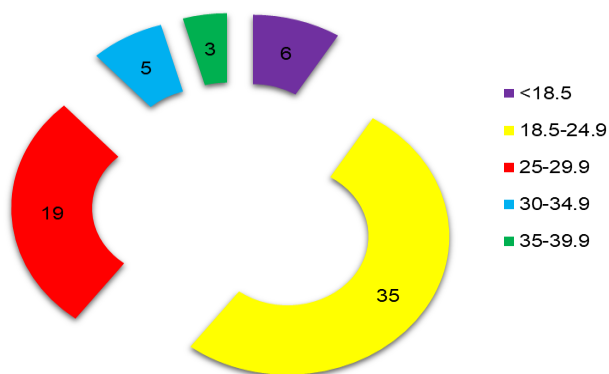
Out of 200 patients in our study, 29.5% were determined to have colorectal cancer as a prior condition, 9.5% had GI issues, and 5.5% had other malignancies. Patients were divided according to prior malignancies and GI issues.

In our study, out of 200 patients, approximately 72% of patients have never had surgery previously. 18.5% had colorectal surgery, 7.5% had Gastriintestinal surgery, and 2% had surgery due to other cancer.

200 individuals were diagnosed, with 63% receiving a diagnosis based on resection and 37% receiving a diagnosis based on a biopsy.

**Table 1:** Distribution of patients based on BMI

Criteria	Reference Values	No of Patients (%)
Under Weight	<18.5	6(8.8%)
Healthy Weight	18.5-24.9	35(51.4%)
Overweight	25-29.9	19(27.9%)
Obese Type I	30-34.9	5(7.35%)
Obese Type II	35-39.9	3(4.4%)



**Figure 1:** Distribution of patients based on BMI

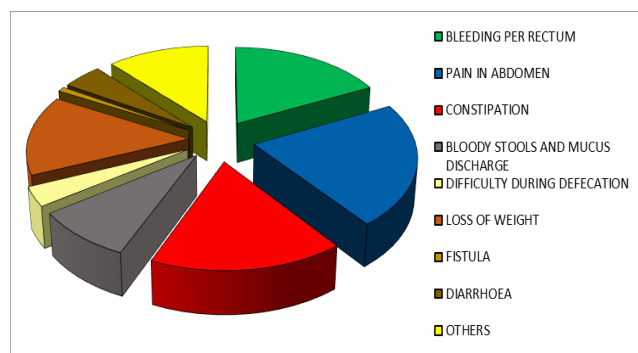
The above figure illustrates the distribution of patients based on BMI. From the total of 200 participants, about 8.8% were found to be underweight, about 51.4% were found to be with healthy weight, about 27.9% were found to be overweight, were as about 7.35% were found to be obese(type I) and about 4.4 % Patients were found to be type II obese.

The distribution of patients according to primary complaints is depicted in the pie chart above. Roughly 62 (31%) patients complained of rectal bleeding, 77 (38.5%) patients complained of abdominal pain, and 31 (15%) patients complained of bloody stools with mucus discharge. Approximately 12 (6% of people) reported having trouble urinating, 50 (25%) reported losing weight, about 3 (1.5%)

reported having a fistula, and about 16 (8%) reported having diarrhoea.

**Table 2:** Distribution of patients based on Chief Complaints

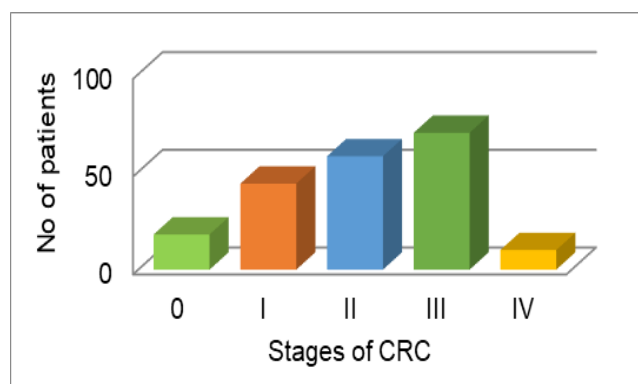
Patient Complaints	No of Patients (%)
Bleeding Per Rectum	62(31%)
Pain in Abdomen	77(38.5%)
Constipation	59(29.5%)
Bloody stools& Mucus Discharge	31(15.5%)
Difficulty during Defecation	12(6%)
Loss of Weight	50(25%)
Fistula	3(1.5%)
Diarrhoea	16(8%)
Others	41(20.5%)



**Figure 2:** Distribution of patients based on Chief Complaints

**Table 3:** Distribution of patients based on TNM Staging

TNM Stage	No of Patients Affected (%)
0	18(9%)
I	44(22%)
II	58(29%)
III	70(35%)
IV	10(5%)

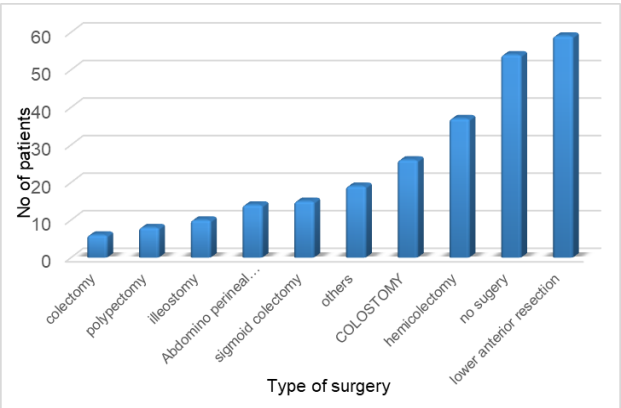


**Figure 3:** Distribution of patients based on TNM Staging

The distribution depending on TNM staging is depicted in the graph above. About 18(9%) of the patients were determined to be in stage 0, about 44(22%) were in stage I, about 58(29%) were in stage II, the highest percentage was about 70(35%) in stage III, and about 10(5%) were in stage IV.

**Table 4:** Distribution of patients based on Type of surgery

Type of Surgery	No of Patients (%)
Colectomy	6(3%)
Polypectomy	8(4%)
Ileostomy	10(5%)
Abdominoperineal Resection	14(7%)
Sigmoid Colectomy	15(7.5%)
Others	19(9.5%)
Colostomy	26(13%)
Hemicolectomy	37(18.5%)
No Surgery	54(27%)
Lower Anterior Resection	59(29.5%)

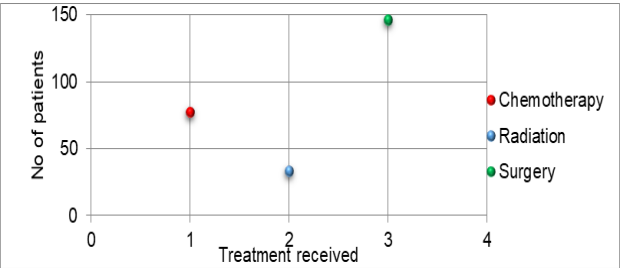


**Figure 4:** Distribution of patients based on type of surgery

According to the graph shown above, approximately 6 (3%) patients had colectomies, approximately 8 (4%) patients had polypectomy, approximately 10 (5%) patients had ileostomies, approximately 14 (7%) patients had abdominoperineal resection, 15 (7.5%) patients had sigmoid colectomies, approximately 19 (9.5%) patients had other surgeries, approximately 26 (13%) patients had colostomies, approximately 37 (18.5%) patients had hemicolectomy, and approximately 59 (29%) had lower anterior resection.

**Table 5:** Distribution of patients based on Treatment Received

Treatment Received	No of Patients (%)
Chemotherapy	77(38.5%)
Radiation Therapy	33(16.5%)
Surgery	146(73%)

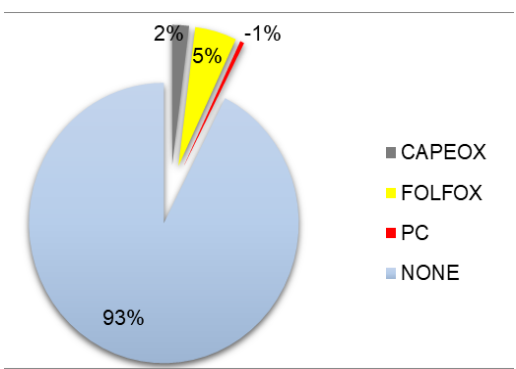


**Figure 5:** Distribution of patients based on Treatment Received

The above figure illustrates about the distribution of patients based on treatment received. About 77(38.5%) patients received treatment with only chemotherapy, about 33(16%) patients received treatment with Radiation therapy and about 146(73%) patients received treatment with surgery.

**Table 6:** Distribution of patients based on Neoadjuvant Chemotherapy

Regimen	No of Patients (%)
CAPEOX	4(2%)
FOLFOX	10(5%)
PC	1(1%)
None	185(92.5%)

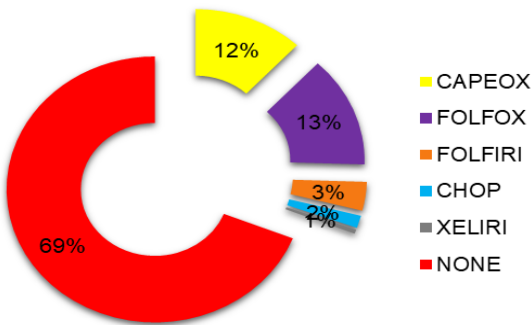


**Figure 6:** Distribution of patients based on Neoadjuvant Chemotherapy

In the picture above, it was determined that there were around 4 (2% of the total number of patients), 10 (5%), and 1 (1% of the total number of patients) receiving the CAPEOX, FOLFOX, and Paclitaxel regimens, respectively.

**Table 7:** Distribution of patients based on Adjuvant Chemotherapy

Regimen	No of patients (%)
CAPEOX	24(12%)
FOLFOX	27(13.5%)
FOLFIRI	7(3.5%)
CHOP	3(1.5%)
XELIRI	1(1%)
None	138(69%)

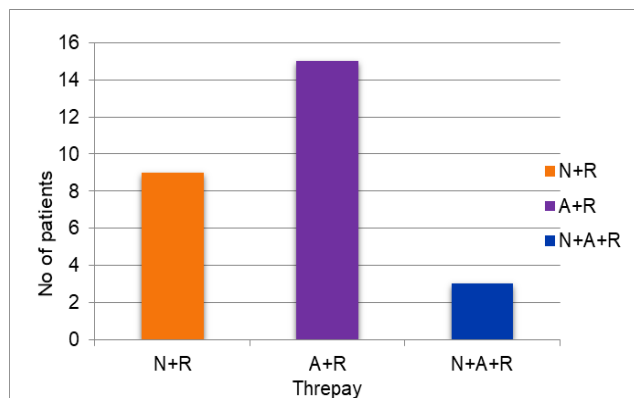


**Figure 7:** Distribution of patients based on Adjuvant Chemotherapy

The graph reveals that 24 patients, or 12% of them, had treatment with the regimen CAPEOX, 27 patients, or 13.5% with the regimen FOLFOX, 7 patients, or 3.5% with the regimen FOLFIRI, and 3 patients, or 2% with the regimen CHOP.

**Table 8:** Distribution of patients based on Chemo and Radiation Therapy

Therapy	No of Patients (%)
Neo+Radiation	9(4.5%)
Adjuvant +Radiation	15(7.5%)
Neo+Adjuvant+Radiation	3(1.5%)



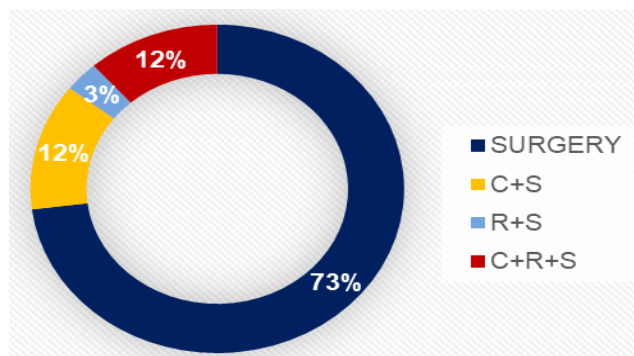
**Figure 8:** Distribution of patients based on Chemo and Radiation Therapy

N- Neoadjuvant Chemotherapy, A-Adjuvant Chemotherapy, R- Radiation Therapy

The data available represents that about 9(4.5%) patients received treatment with neoadjuvant + radiation therapy, about 15(7.5%) patients received treatment with adjuvant+ radiation therapy, about 3(1.5%) patients received treatment with neoadjuvant+adjuvant+radiation therapy

**Table 9:** Distribution of patients based on Various Treatment Approaches

Treatment	No of Patients (%)
Surgery	146(73%)
Chemo + Surgery	25(12.5%)
Radiation + Surgery	6(3%)
Chemo + Radiation+Surgey	23(11.5%)

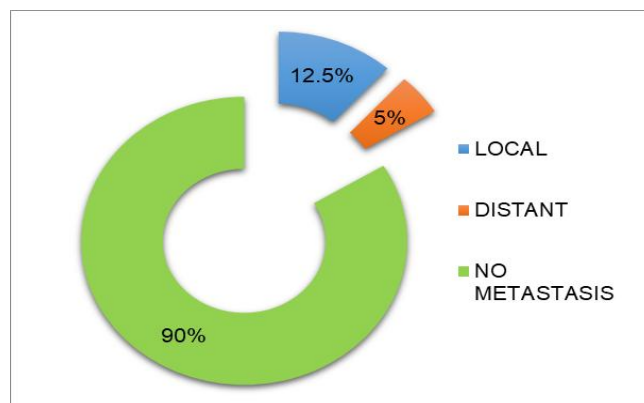


**Figure 9:** Distribution of patients based on Various Treatment Approaches

The graph illustrates that 146 (73%) of the patients had surgery as their primary form of treatment, 25 (12.5%) had chemotherapy and surgery, 6 (3%) had radiation and surgery, and 23 (11.5%) had chemotherapy and radiation therapy together with surgery.

**Table 10:** Distribution of patients based on Metastasis

Type of Metastasis	No of Patients (%)
Local	25(12.5%)
Distant	10(5%)
No Metastasis	180(90%)

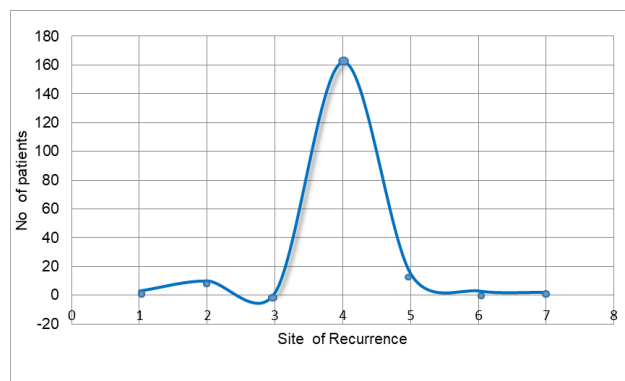


**Figure 10:** Distribution of patients based on Metastasis

From the above figure, the number of patients identified to have metastasis locally was found to be 25(12.5%), the number of patients identified to have metastasis distant was found to be 10(5%), the number patients with no metastasis was found to be 180(90%).

**Table 11:** Distribution of patients based on site of recurrence

Site of Recurrence	No of Patients (%)
Liver	3(1.5%)
Colon	10(5%)
Lung	2(1%)
None	162(81%)
Rectum	15(7.5%)
Others	3(1.5%)
Ovary	2((1%)

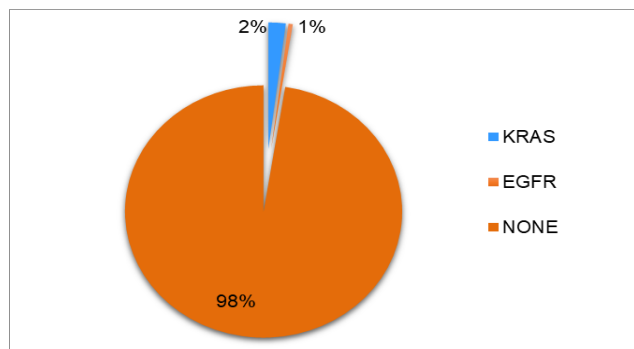


**Figure 11:** Distribution of patients based on site of recurrence

The figure shows that approximately 3 patients had recurrence in the liver, approximately 10 patients had recurrence in the colon, about 15 patients had recurrence in the part rectum, 2 patients had recurrence in the ovary and 3 patients had recurrence in some other parts, while about 162 patients did not have any recurrence.

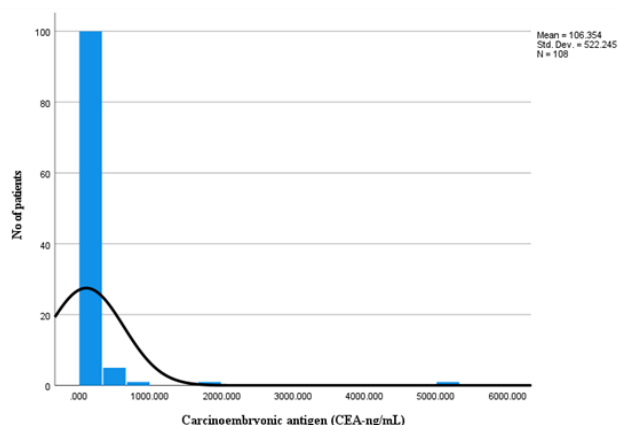
**Table 12:** Distribution of patients based on Mutations

Mutations	No of Patients (%)
KRAS	4(2%)
EGFR	1(1%)
None	195(97.5%)



**Figure 12:** Distribution of patients based on Mutation

According to the aforementioned statistic, around 4 (2% of patients) have KRAS mutations, approximately 1 (1% of patients) have EGFR mutations, and approximately 195 (97.5%) of patients do not have any mutations.



**Figure 13:** Distribution based of patients based on CEA

The above available data describes about the distribution of patients based on CEA. It shows that about 95(47.5%) patients had tested to have CEA value <100, about 8(4%) patients had tested to have CEA value between 101-500, about 2(1%) ateints had tested to have CEA value between 501-1000 and about 2(1%) patients had CEA value >1000.

## DISCUSSION

Our study entitled “A RETROSPECTIVE STUDY ON PHARMACOTHERAPEUTIC OUTCOMES IN COLORECTAL CANCER PATIENTS AT TERITIARY CARE HOSPITAL” is a retrospective observational study, conducted on 200

patients to understand the treatment approach, treatment outcomes and also mutation load in key genes associated with oncogenesis.

Among 200 patients 140(70%) were males and 60(30%) were female. This shows a higher prevalence of colorectal cancer among males than females. Our findings are in accordance with the statistics from CDC (Centre for Disease Control and Prevention).

The age group 59-68 has a higher number of patients accounting for 60. This is followed by 48 between 49-58, 31 between 69-78, 27 between 39-48, 13 between 29-38 and 79-88, 7 between 18-28 and 1 between 89-98.

Analysis of BMI showed that the majority of the patients i.e., 35(17.5%) are of normal weight. This followed by 19(9.5%) are of overweight followed by 5(2.5%) are of obese type 1 and 3(1.5%) obese type II. Patients with overweight and obese showed higher recurrence rate than other individuals. These findings are consistent with the observations of various works notable Dignam et al., reported a significant increased risk for recurrence and death from colorectal cancer in overweight and obese patients who receive adjuvant chemotherapy.

In our study, 77(38.5%) of patients presented with pain in abdomen, 62(31%) with bleeding per rectum, 59(29.5%) with constipation, 31(15.5%) with bloody stools and mucus discharge, 50(25%) with loss of weight, 12(6%) with difficulty during defecation, 16(8%) with diarrhoea, 3(1.5%) with fistula and 41(20.5%) with others. D Smith et al reported that early colorectal cancers do have significant symptoms which can early be captured by a PCQ and objective scoring tool in the Secondary Care Setting.

In our study 146 were underwent surgery, 77 were treated with chemotherapy and 33 received radiation therapy. The patients diagnosed with stage 0 18(19%) were cured with surgeries polypectomy and mesoresection, 15 patients received neoadjuvant chemotherapy and 62 patients received adjuvant chemotherapy. Among these individuals the commonly followed regimens are CAPEOX, FOLFOX, and FOLFIRI. CAPEOX stands for Capecitabine, Oxaliplatin. FOLFOX stands for Folinic acid, 5-fluorouracil, Oxaliplatin. FOLFIRI stands for Folinic acid, 5-fluorouracil, Irinotecan.

Different treatment approaches are followed which include N+R in 9(4.5%) patients, A+R in 15(7.5%), N+A+R in 3(1.5%), R+S in 6(3%), A+R+S in 15(7.5%), N+R+S in 6(3%), A+S in 24(12%), N+S in 1, N+A+R+S in 2(1%) patients.

In this study 33 patients developed the recurrence at different sites. Among these patients recurrence at local sites i.e., colon and rectum are 15, followed by 10 patients at lungs, 3 at liver, 2 at ovary and 3 at others. These findings are in consistent with the observations of the treatment with curative intent, 20% to 30% of the patients develop recurrence disease.

## CONCLUSION

We draw the conclusion from this study that mutations have no appreciable impact on the survival rate of colorectal cancer. Surgery is used to treat patients who have stage 0 or stage I diagnoses. Patients at stages III and IV received the proper chemo and radiation therapy treatments. After the first 2-3 years of treatment, there is a possibility of recurrence. Our study underscores the significant impact of body mass index (BMI) on the outcomes of colorectal cancer patients. Importantly, we observed that patients who were overweight and obese, including both obese type 1 and type II, had a higher recurrence rate compared to individuals with normal BMI.

Chemotherapy played a crucial role in the management of this patient population, with both neoadjuvant and adjuvant chemotherapy regimens such as CAPEOX, FOLFOX, and FOLFIRI being commonly employed. This underscores the importance of personalized treatment plans tailored to individual patient needs.

This study provides valuable insights into the prevalence and management of colorectal cancer and related conditions. It underscores the importance of a multi-modal treatment approach and the need for vigilant post-treatment surveillance to detect and manage recurrences effectively.

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