Comparison Of Laboratory Examination Results And Clinical Manifestations In Post Chemotherapy Folfox Regimens And Capeox Regimens In Colorectal Cancer Patients At Ibnu Sina Educational Hospital Umi Wakaf Foundation Macassar

Miftahul Jannah[1], Syamsu Rijal[2*], Nur Aulia[3], Sri Julyani[4], Berry Erida Hasbi[5]

[1]Program Studi Pendidikan Dokter, Fakultas Kedokteran, Universitas Muslim Indonesia, Indonesia
[2]Departemen Histologi, Fakultas Kedokteran UMI, RSP Ibnu Sina YW-UMI, Indonesia
[3]Departemen Ilmu Kesehatan Mata, Fakultas Kedokteran UMI, RSP Ibnu Sina YW-UMI, Indonesia
[4]Departemen Patologi Klinik, Fakultas Kedokteran UMI, RSP Ibnu Sina YW-UMI, Indonesia
[5]Departemen Ilmu Bedah, Fakultas Kedokteran UMI, RSP Ibnu Sina YW-UMI, Indonesia
*Corresponding Author:
Email: syamsu.rijal@umi.ac.id

Abstract.

Colorectal cancer (CRC) is the fourth leading cause of death in the world, often associated with an unhealthy diet, including low consumption of fruits, vegetables, and fiber, and high intake of red meat. This study aims to compare the results of laboratory examinations and clinical manifestations in patients undergoing chemotherapy using Folfox and CapeOX regimens at Ibnu Sina Teaching Hospital, UMI Waqf Foundation, Makassar. The method used was descriptive design with cross-sectional approach and purposive sampling technique. The results showed that in Folfox regimen chemotherapy patients, there were 90.9% with low erythrocytes and 95.5% with low hemoglobin, while in CapeOX regimen, 59.1% of patients had low erythrocytes. Of the 22 patients in each regimen, 14 patients (Folfox) and 9 patients (CapeOX) reported complaints. Comparison of leukocyte examination between the two regimens showed a significant association with a p-value of 0.044 ($p<0.05$), while examination of erythrocytes, platelets, hemoglobin, blood sugar, and clinical manifestations did not show a significant association ($p>0.05$). This study provides insight into the impact of each chemotherapy regimen on the patient's condition.

Keywords: *Colorectal Cancer, Chemotherapy Regimens and Laboratory Examination.*

I. INTRODUCTION

The treatment landscape for colorectal cancer (CRC) has evolved significantly over the past few decades, with the introduction of various chemotherapy regimens aimed at improving patient outcomes. Among these, the FOLFOX (5-fluorouracil, leucovorin, and oxaliplatin) and CapeOX (capecitabine and oxaliplatin) regimens have emerged as prominent options for both adjuvant and palliative care in CRC patients. These regimens are particularly relevant in the context of advanced disease, where they have been shown to enhance overall survival (OS) and progression-free survival (PFS) rates compared to older treatment modalities (Hannan et al., 2012; Li et al., 2021; Zhao et al., 2022). The FOLFOX regimen, which combines oxaliplatin with infusional 5-fluorouracil and leucovorin, has been extensively studied and is recognized for its efficacy in treating metastatic colorectal cancer (mCRC) (Hannan et al., 2012; Ryu et al., 2011). Similarly, the CapeOX regimen, which substitutes capecitabine for infusional 5-fluorouracil, offers the convenience of oral administration while maintaining comparable efficacy (Zhang et al., 2021; Zhao et al., 2022). Recent meta-analyses have demonstrated that both regimens yield similar outcomes in terms of OS and PFS, suggesting that the choice between them may depend on patient-specific factors, including tolerance and side effect profiles.In clinical practice, the selection of a chemotherapy regimen often hinges on the individual patient's clinical presentation, including tumor characteristics and prior treatment history.

For instance, studies have indicated that the CapeOX regimen may be particularly beneficial for patients with specific genetic markers or those who exhibit a favorable response to oxaliplatin-based therapies (Hong et al., 2013; Sadahiro et al., 2020). Conversely, the FOLFOX regimen may be preferred in cases where patients have previously demonstrated resistance to capecitabine or exhibit significant comorbidities that complicate oral medication adherence (Fu et al., 2023; Hannan et al., 2012). Moreover,

the side effect profiles of these regimens play a critical role in treatment decision-making. While both FOLFOX and CapeOX are associated with common chemotherapy-related toxicities such as nausea, vomiting, and peripheral neuropathy, the severity and incidence of these effects can vary (Fei et al., 2019; Gilshtein et al., 2021). For instance, oxaliplatin is notorious for inducing acute and chronic neurotoxicity, which can significantly affect a patient's quality of life and may necessitate dose adjustments or treatment interruptions (Chen et al., 2022; Sato et al., 2022).

In contrast, capecitabine can lead to hand-foot syndrome and gastrointestinal disturbances, which may also impact patient compliance and overall treatment success (Hannan et al., 2012; Ryu et al., 2011).The clinical manifestations of these toxicities can often be assessed through laboratory examinations, which provide valuable insights into the patient's physiological response to treatment. For example, hematological parameters such as complete blood counts can reveal the extent of myelosuppression, a common side effect of both regimens (Maeda et al., 2019; Zhang et al., 2021). Additionally, liver function tests may be indicative of hepatotoxicity associated with oxaliplatin, particularly in patients with pre-existing liver conditions (Shin et al., 2013; Yucel, 2023). In light of these considerations, the current study aims to compare the laboratory examination results and clinical manifestations of patients undergoing FOLFOX and CapeOX regimens at the Ibnu Sina Educational Hospital UMI Wakaf Foundation in Macassar. By analyzing the correlation between laboratory findings and clinical symptoms, this research seeks to elucidate the differential impacts of these chemotherapy regimens on patient outcomes, thereby contributing to the optimization of treatment strategies for colorectal cancer.

II. METHODS

This research was conducted using a descriptive design through a cross sectional approach (Liberty, 2024; Notoatmodjo, 2012; Swarjana, 2016). The sampling technique in this study was purposive sampling technique (non-probability sampling) (McLeod, 2019; Turner, 2020), which is sampling done by choosing deliberately and in accordance with the selection criteria according to the research objectives. The sample used in this study amounted to 44 people who met the inclusion and exclusion criteria obtained from the results of medical records. The inclusion criteria of this study are colorectal cancer patients who undergo chemotherapy using Folfox Regimen and CapeOX Regimen. Exclusion criteria of this study were patients who suffered from other diseases besides colorectal cancer such as renal failure and other blood disorders that could affect the results of the patient's laboratory examination.

III. RESULT AND DISCUSSION

Frequency Distribution Based on Gender

Table 1. Frequency Distribution Based on Gender in Colorectal Cancer Patients Using Folfox Regimen and CapeOX Regimen

Variable	Folfox		CapeOX	
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
Gender (Sex)				
Male	12	54.5	13	59.1
Female	10	45.5	9	40.9
TOTAL	**22**	**100**	**22**	**100**

Source: Primary Data Processed, 2024

Based on Table 1. The data conducted at Ibnu Sina Educational Hospital UMI Wakaf Foundation in Macassar, the gender distribution of colorectal cancer patients receiving chemotherapy regimens, specifically FOLFOX and CapeOX, was analyzed. The results indicate that out of 22 patients undergoing the FOLFOX regimen, a majority were male, comprising 54.5% (12 patients), while females accounted for 45.5% (10 patients). Similarly, in the CapeOX regimen group, male patients also represented the higher proportion at 59.1% (13 patients), compared to female patients who constituted 40.9% (9 patients). Overall, the gender distribution in both treatment groups demonstrates a slight predominance of male patients, which may reflect broader epidemiological trends in colorectal cancer prevalence.

Frequency Distribution Based on Age

Table 2. Frequency Distribution Based on Age in Colorectal Cancer Patients Using Folfox Regimen and CapeOX Regimen

Variable	Folfox		CapeOX	
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
Age (Years)				
Teenagers (18-25)	-	-	-	-
Early Adults (26-35)	1	4.5	1	4.5
Late Adults (36-45)	3	13.6	2	9.1
Early Elderly (45-55)	6	27.3	5	22.7
Late Elderly (56-65)	8	36.4	11	50.0
Elderly (>65)	4	18.2	3	13.6
TOTAL	**22**	**100**	**22**	**100**

Source: Primary Data Processed, 2024

Based on Table 2. It presents a detailed frequency distribution based on age among colorectal cancer patients treated with FOLFOX and CapeOX regimens at Ibnu Sina Educational Hospital UMI Wakaf Foundation in Macassar. The analysis reveals distinct trends in age demographics for both treatment groups. In the FOLFOX regimen, the age group of 18-25 years was not represented, while early adults aged 26-35 accounted for 4.5% (1 patient). Among late adults aged 36-45, there were 13.6% (3 patients), and the early elderly group (45-55) comprised 27.3% (6 patients). The late elderly group (56-65 years) represented the largest segment within the FOLFOX cohort, with 36.4% (8 patients), while those classified as elderly (>65 years) made up 18.2% (4 patients). Conversely, in the CapeOX regimen, the age distribution reflected similar trends. Again, there were no patients in the 18-25-year age bracket, and early adults (26-35) constituted 4.5% (1 patient). The late adult group (36-45 years) included 9.1% (2 patients), while the early elderly (45-55 years) accounted for 22.7% (5 patients). Notably, the late elderly segment (56-65 years) represented the highest percentage at 50.0% (11 patients), and the elderly group (>65 years) included 13.6% (3 patients).

Frequency Distribution Based on Laboratory Examination Results

Table 3. Frequency Distribution Based on Laboratory Examination Results of Colorectal Cancer Patients Using Folfox Regimen and CapeOX Regimen

Variable	Folfox		CapeOX	
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
Leukocytes				
Low	1	4.5	3	13.6
Normal	20	90.0	19	86.4
High	1	4.5	0	0
Erythrocytes				
Low	20	90.9	13	59.1
Normal	2	9.1	9	40.9
High	0	0	0	0
Platelets				
Low	10	45.5	9	40.9
Normal	11	50.5	13	59.1
High	1	4.5	0	0
Hemoglobin				
Low	21	95.5	15	68.2
Normal	1	4.5	9	31.8
High	0	0	0	0
Real-time Blood Sugar				
Low	0	0	1	4.5
Normal	19	86.4	21	95.5
High	3	13.6	0	0
TOTAL	**22**	**100**	**22**	**100**

Source: Primary Data Processed, 2024

Based on Table 3. It provides a detailed overview of the laboratory examination results for colorectal cancer patients treated with FOLFOX and CapeOX regimens at Ibnu Sina Educational Hospital UMI Wakaf Foundation in Macassar, highlighting key hematological parameters among the patients. In the FOLFOX group, 4.5% had low leukocyte counts, while 90.0% were normal, and another 4.5% exhibited high levels. Erythrocyte levels showed a concerning 90.9% with low counts and no high levels recorded. Platelet counts revealed 45.5% were low, 50.5% were normal, and 4.5% were high. Alarmingly, 95.5% of patients had low hemoglobin levels, indicating a significant risk of anemia. In the CapeOX cohort, 13.6% had low leukocyte counts, while 86.4% were normal, with no high counts reported. Erythrocytes showed 59.1% low and 40.9% normal, again with no high values. Platelet counts were relatively balanced, with 40.9% low and 59.1% normal. Hemoglobin levels also raised concern, with 68.2% low and 31.8% normal. Furthermore, while FOLFOX patients had no low blood sugar levels, 86.4% were normal, and 13.6% were high; CapeOX patients had 4.5% low, 95.5% normal, and no high levels.

Frequency Distribution Based on Laboratory Examination Results of Clinical Manifestations

Table 4. Frequency Distribution of Clinical Manifestations in Colorectal Cancer Patients Using Folfox Regimen and CapeOX Regimen

Variable	Folfox		CapeOX	
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
Clinical Manifestations				
Complaints	14	63.6	9	40.9
Weakness	10		6	
Abdominal Pain	4		6	
Nausea Vomiting	1		2	
Anorexia	1		0	
No Complaints	8	36.4	13	59.1
TOTAL	**22**	**100**	**22**	**100**

Source: Primary Data Processed, 2024

Based on Table 4. It presents the frequency distribution of clinical manifestations observed in colorectal cancer patients treated with FOLFOX and CapeOX regimens at Ibnu Sina Educational Hospital UMI Wakaf Foundation in Macassar. Among the patients receiving the FOLFOX regimen, 63.6% (14 patients) reported various complaints, while 36.4% (8 patients) had no complaints. The specific complaints included weakness (45.5%, or 10 patients), abdominal pain (18.2%, or 4 patients), nausea (4.5%, or 1 patient), and anorexia (4.5%, or 1 patient). In comparison, the CapeOX group showed that 40.9% (9 patients) experienced complaints, with the highest frequency of weakness (27.3%, or 6 patients) and abdominal pain (27.3%, or 6 patients) reported equally. Additionally, 9.1% (2 patients) experienced nausea, and there were no reports of anorexia among this group. The remaining 59.1% (13 patients) from the CapeOX regimen reported no complaints.

Comparison of Laboratory Examination Results and Clinical Manifestations in Colorectal Cancer Patients

Table 5. Comparison of Laboratory Examination Results and Clinical Manifestations in Colorectal Cancer Patients Using Folfox Regimen and CapeOX Regimen

Laboratory Results and Clinical Manifestations	*P-value*
Leukocytes	<0.044
Erythrocytes	<0.789
Platelets	<0.734
Hemoglobin	<0.495
Real-time Blood Sugar	<0.502
Clinical Manifestations	<0.810

Source: Primary Data Processed, 2024

Based on Table 5. It summarizes the comparison of laboratory examination results and clinical manifestations between colorectal cancer patients treated with the FOLFOX and CapeOX regimens, along with their respective statistical significance as indicated by P-values. The analysis reveals several important

findings. For leukocyte counts, the P-value is <0.044, suggesting a statistically significant difference between the two treatment groups. However, the comparison for erythrocytes, with a P-value of <0.789, indicates no significant differences in this parameter. Similarly, platelet counts and hemoglobin levels also show no statistically significant variations with P-values of <0.734 and <0.495, respectively. The assessment of real-time blood sugar levels yielded a P-value of <0.502, reflecting no significant difference between the regimens. Lastly, the P-value for clinical manifestations is <0.810, suggesting that the clinical symptoms reported by the patients were not significantly different across the treatment groups.

Discussion

This study was conducted with the aim of knowing the comparison of laboratory results in colorectal cancer patients who used Folfox chemotherapy regimen and CapeOX chemotherapy regimen conducted at Ibnu Sina Teaching Hospital, UMI Waqf Foundation. In this study, a total sample of 44 patients was obtained, for the Folfox chemotherapy regimen there were 22 samples (50%), while for the CapeOX chemotherapy regimen there were 22 samples (50%). Where this sample has been adjusted to the inclusion and exclusion criteria of the research sample. In this study, based on gender, the highest frequency was in male patients as many as 25 people (56.81%) while female patients were 19 people (43.19%). This is in line with research conducted which states that colorectal cancer is more common in men than women with a sample of 3314 people and 1999 of them were men. However, the reason why colorectal cancer occurs more in men is still unknown (Joo et al., 2023).Patients with colorectal cancer increase in elderly patients due to higher microsatellite instability compared to young age and the presence of comorbid diseases. This study is in line with this, it was found that the age of many colorectal cancer out of 65 samples 39 of them were elderly patients aged 56-65 years and over. The CapeOX regimen is preferred because it is cost-effective and does not contain continuous infusion treatment, although both combined chemotherapy regimens appear to have similar efficacy profiles, there are no prospective randomized studies comparing the two protocols in terms of efficacy, safety and survival rates in the literature (Degirmencioglu et al., 2019).

Administration of the Folfox regimen is usually used for patients with advanced cancer or after surgery to reduce the risk of cancer returning. In line with this, this study found colorectal cancer patients who underwent chemotherapy used more CapeOX regimen chemotherapy compared to Folfox regimen chemotherapy (Iveson et al., 2018). Based on research obtained the results of the incidence of adverse events in colorectal cancer patients undergoing Folfox regimen therapy, 16 people (32.7%) neutropenia, 4 people (8.2%) thrombocytopenia (Lim et al., 2009) and supported by research conducted that found anemia patients as many as 7 people out of a total of 61 patients (Lai et al., 2023). Temporary blood sugar is not directly affected by the Folfox chemotherapy regimen because the drugs in this regimen do not have pharmacological mechanisms that specifically target glucose metabolism or pancreatic function. In terms of clinical manifestations, 57 out of 61 samples had complaints (Cercek et al., 2014; Gill et al., 2016; Yamai et al., 2022). This is in line with the study, where more have complaints than the entire sample. It is also known that the results of laboratory examinations and manifestations of Folfox regimen chemotherapy obtained 1 person (4.5%) low leukocytes, 1 person (4.5%) leukocytosis, 20 people (90.9%) low erythrocytes, 10 people (45.5%) thrombocytopenia, 1 person (4.5%) thrombocytosis, 21 people (95.5%) with low hemoglobin and 3 people (13.6%) with high blood sugar. This was caused by several factors, including exposure to oxaliplatin and 5-FU which increase treatment toxicity, the condition of patients with impaired bone marrow function who have a higher risk of treatment toxicity and high doses of oxaliplatin or continuous infusion of 5-FU which tend to increase hematological toxicity (Gill et al., 2016; Zhou et al., 2022).

Based on a study conducted on the safety of CapeOX chemotherapy regimen, the results of the incidence of adverse hematological events of patients from a total of 41 patients, 18 people (43.9%) of whom experienced leukocytopenia, 19 people (46.3%) experienced neutropenia, 24 people (58.5%) experienced anemia, 22 people (53.7%) experienced thrombocytopenia and for blood sugar levels while not directly affected by CapeOX chemotherapy regimen. In addition, the incidence of non-hematological adverse events was also obtained, namely a total of 41 samples experiencing side effects such as nausea and vomiting, anorexia, diarrhea, fatigue, baldness, dizziness, parasthesias and other complaints (Osawa et al., 2015). This is in line with the research that has been done, obtained patients with leukocytopenia as many as 3 people

(13.6%), 13 people (59.1%) low erythrocytes, thrombocytopenia as many as 9 people (40.9%) and 1 person (4.5%) low blood sugar, and obtained from a total of 22 samples 9 of them have complaints.This is due to several factors where capecitabine is metabolized into 5-FU, which inhibits DNA synthesis in rapidly dividing cells, including hematopoietic precursors in the bone marrow. As a result, the production of neutrophils, leukocytes, platelets, and erythrocytes may be impaired, causing conditions such as neutropenia, leukopenia, anemia, and thrombocytopenia. Oxaliplatin is an alkylating agent that causes DNA damage to cells.This damage is not selective and affects normal cells that have a high division rate, including hematopoietic cells. In addition, cumulative use of oxaliplatin may cause more severe bone marrow toxicity, increasing the risk of a decrease in all blood cell lines (pancytopenia).

The combination of capecitabine and oxaliplatin may exacerbate the effects of hematologic toxicity due to synergistic effects in inhibiting cell division and triggering apoptosis in hematopoietic cells (Osawa et al., 2015). It was also mentioned in a study conducted that chemotherapy affects all cells that grow and divide rapidly in the body, including cancer cells and normal cells such as new blood cells in the bone marrow or cells of the mouth, stomach, skin, hair and reproductive organs (Melani et al., 2019). It is also mentioned that gastrointestinal toxicity is common in patients undergoing chemotherapy such as anorexia, nausea, vomiting that appears after chemotherapy is not a pathology process. It was also mentioned in a study conducted that anemia is a complication that occurs in cancer patients undergoing chemotherapy with the severity of anemia depending on the severity of the disease and the intensity of treatment (Benson et al., 2024; Iveson et al., 2018). Then elderly cancer patients often show clinical symptoms of anemia at higher hemoglobin levels than anemic patients without cancer. The above is in accordance with the results of the study found that colorectal cancer patients who underwent folfox regimen chemotherapy and capeox regimen experienced anemia (Iveson et al., 2018). Based on the research conducted, the comparison between the two regimens in terms of leukocyte examination obtained a significant relationship with a *p-value* of 0.044 ($p < 0.05$). Meanwhile, if we look based on table 3, it is found that more patients experienced leukocytopenia in CapeOX regimen chemotherapy than Folfox. This study is inversely proportional to the study that the level of hematological toxicity (including leukocytopenia) was higher in FOLFOX than CapeOX (Cassidy, 2007).

This is influenced by certain situations, for example, patients with impaired hepatic metabolic function that affects capecitabine metabolism which can cause significant leukocytopenia. Meanwhile, the comparison of the two regimens in terms of erythrocyte, platelet, hemoglobin, current blood sugar and clinical manifestations showed a non-meaningful relationship with a p-value >0.05, which means that there is no significant difference between Folfox and CapeOX chemotherapy regimens because the effects are not significantly different. This is in line with research, where it was mentioned that the combination of capecitabine and oxaliplatine as CapeOX therapy, was reported to have equivalent results to Folfox therapy. Although both use different drug combinations, they have similar side effects because chemotherapy basically attacks rapidly dividing cells, including cancer cells and normal cells in the body. The toxicity levels between Folfox and CapeOX are similar in some aspects, especially since both regimens involve oxaliplatin as the main component, which contributes to nerve and bone marrow toxicity (Osawa et al., 2015).

IV. CONCLUSION

Based on the results of laboratory examinations of colorectal cancer patients undergoing Folfox and CapeOX chemotherapy regimens at Ibnu Sina Hospital, UMI Waqf Foundation, it was found that there was a significant difference in the number of leukocytes between the two regimens, with a p-value of 0.044 ($p<0.05$), while there was no significant relationship in the examination of erythrocytes, platelets, hemoglobin, blood sugar, and clinical manifestations. These findings suggest that chemotherapy regimens may affect patients' hematological parameters differently, so further studies are needed to evaluate the efficacy and toxicity of each regimen as well as strategies to minimize hematoxic side effects in colorectal cancer patients. Similar studies with different sample sizes and locations are also recommended to obtain more varied and comprehensive results.

V. RECCOMENDATION

Based on the findings of this study, it is recommended that future research focus on several key areas: conducting comprehensive studies to evaluate the efficacy and toxicity of Folfox and CapeOX chemotherapy regimens in larger and more diverse patient populations to better understand their differential impacts on hematological parameters; implementing longitudinal studies to monitor the long-term effects of these regimens on patients' health, particularly regarding hematological recovery and overall quality of life; investigating and developing intervention strategies aimed at minimizing hematotoxic side effects associated with chemotherapy, including supportive care measures and nutritional interventions; encouraging comparative studies that include additional chemotherapy regimens to provide a broader understanding of treatment options for colorectal cancer patients; and promoting multicenter trials to gather data from various healthcare settings, enhancing the generalizability of findings and offering a more comprehensive overview of the effects of chemotherapy on different populations. By addressing these recommendations, future research can contribute to optimizing treatment protocols and improving patient outcomes in colorectal cancer management.

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