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Colorectal Cancer: Determinants of Delayed Diagnosis and Its Association with Survival in the Pakistani Population

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ABSTRACT

Background: New research indicates that Pakistan is seeing an increase in Colorectal cancer (CRC) cases among people older than 50. The main goal of this study is to find out the determinants of delayed diagnosis and their association with the survival of colorectal cancer patients in the Pakistani community.

Methods: A prospective, cohort study was conducted on biopsy-proven colorectal cancer patients, aged between 18-70 years old presenting at the surgery department of Al Tibri medical college and Hospital, Karachi from January 1st, 2023 till March 30th, 2024, with a sample size of 98 patients, follow up duration was 1 year. A purposive sampling technique was used. Statistical Package of Social Sciences (SPSS) version 22 was used to enter, sort, and analyze the data. Kaplain–Meier was generated for survival analysis for both colon and rectal carcinoma. A P-value of ≤ 0.05 was considered significant.

Results: Reasons for Delay in diagnosis were reported as misdiagnosis by a physician (OR 1.32, 0.24 – 2.16), poor knowledge of disease and symptoms (OR 2.48, 1.04 – 4.88), and herbal medication use to treat symptoms (OR 0.89, 0.047 – 1.89). Overall survival was reported as 74 (74.7%) for 1-year follow-up; however, Rectal cancer survival was 23 (23.7%), and colon cancer survival was 51 (51.3%) with a p-value of 0.365.

Conclusion: In conclusion, patients with colorectal cancer in Pakistan are often diagnosed at an advanced stage, with a dismal prognosis, due to a delay in presentation.

Keywords: Colorectal Cancer, Prevalence, Mortality, Survival Rate.

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INTRODUCTION

Colorectal cancer is the most frequently reported malignancy, with global prevalence as the third most common type of cancer among men and second in women[1]. Histologically CRC can be divided into 7 categories, Adenocarcinoma is the most common type of CRC ranging in approximately 95% of total reported cases, signet ring cell carcinoma is a rare and aggressive type of CRC, with prevalence rates of 10-15%, the lymph node involvements are higher with poor prognosis. Medullary carcinoma is another rare type of CRC, known for a relatively favorable prognosis and better outcomes as compared to other rare types. Squamous cell carcinoma, a rare type of CRC, may develop from pre-existing squamous metaplasia [2]. Regarding sites of CRC, the reported evidence reveals cecum and right colon cancer often at an advance stage due to minimal and/or neglectable symptoms, however, the left colon tumors are presented with altering bowel habits, bleeding from the rectum, and obstruction. Rectal tumor is diagnosed at a later stage[3]. The age-standardized incidence rate (ASIR) of colorectal cancer in Karachi is 7.70/100,000 for females and 12.35/100,000 for men, based on data from the Karachi Cancer Registry (KCR) for the years 2017–2019[4]. Patients' prognosis for colorectal cancer is influenced by several factors, such as the tumor anatomic location, stage, involvement of lymph nodes, and preoperative carcinoembryonic antigen (CEA) level[5]. Poor survival was linked to male gender, advancing age, and the severity of colorectal cancer, according to a study conducted among Malaysians[6]. Different variables contribute to the pathogenesis and prognosis of colorectal cancer (CRC) in third-world nations like Pakistan, particularly when the cancer manifests in younger age groups[7]. Although there is no national cancer registry in Pakistan, there are hospital-based and regional cancer registries that track cancer incidence, survival, and behavior in that area[8].

Similar professional and national health recommendations, however, are woefully absent from Pakistan's rural and urban regions, leading to a lack of knowledge about colorectal cancer (CRC) and unfamiliarity with the available CRC screening options. It has been shown that CRC screening adherence is a useful tactic for identifying precancerous polyps in people who are asymptomatic [9,10].

The incident rates of CRC are reported to range from 4-6.8% in the Pakistani population, the increasing incident rates are an alarming concern for healthcare providers especially due to the risk for the younger population. Identification of CRC at an early stage, proper diagnosis, and treatments necessary for preventive measures and managing incidents. The main goals of this study were to find out the factors associated with the overall survival of CRC patients; our secondary goals were to assess the factors contributing to the delayed diagnosis of CRC in the Pakistani community.

METHODS

A prospective, cohort study was conducted on biopsy-proven colorectal cancer patients, aged between 18-70 years old presenting at the surgery department of Al Tibri Medical College and hospital, Karachi from January 1st, 2023 till March 30th, 2024. The sample size was calculated using the WHO sample size calculator, keeping patients diagnosed with CRC in the last 6 months as population (n=130), confidence interval as 95%, and margin of error as 5%, the required minimum sample size is n= 98. Patients were identified through confidential medical files of the hospital, incomplete data or lost to follow-up patients were excluded from the study. A questionnaire was used to collect data after getting prior approval from the head of the department of Surgery. The questionnaire had three sections including demographic details, presenting symptoms, medical history of patients and family, histopathological features of biopsy, surgery outcomes, and intra-operative details, surgical records for tumor location, grade and lymph nodes involvement along with post-procedure outcomes were recorded. Radiological and laboratory investigations were performed pre and post-procedure, including complete blood count (CBC), liver function test (LFTs), ultrasound and CT abdomen. The American joint committee on Cancer Staging System (AJCC 7th edition) was used to stage the disease[11]. Follow-up was recorded for 1 year via regular telephone calls and clinic consultations, any additional information regarding symptoms, associated problems, side effects and/or evidence of relapse was documented as well.

SPSS version 22 was used to enter, sort, and analyze the data. Continuous variables were reported as mean and standard deviation, while proportions and percentages were used to present categorical variables. Kaplan –Meier were generated for survival analysis for both colon and rectal carcinoma.

Univariate analysis was used with the Cox proportional hazard model, to assess the prevalence ratio 95% confidence interval and 5% margin of error. p-value of ≤ 0.05 were considered significant.

RESULTS

Table 1: Demographic Details of Study Participants.

Variables		Frequency (%)
Gender	Male	58 (59.2%)
	Female	40 (40.8%)
Age	20-30 years	13 (13.2%)
	31-40 years	20 (20.3%)
	41-50 years	19 (19.3%)
	51-60 years	13 (13.2%)
	61-70 years	33 (33.8%)
Positive Family History		32 (32.7%)
Type of Cancer	Colon Cancer	66 (67.3%)
	Rectal cancer	32 (32.7%)
Stage of cancer	Stage I	24 (24.4%)
	Stage II	32 (32.6%)
	Stage III	32 (32.6%)
	Stage IV	10 (10.2%)
Presenting complaints	Bleeding per rectum	39 (39.4%)
	Abdominal lump	33 (33.7%)
	Intestinal obstruction	12 (12.1%)
Site of Tumor (Rectal)	Upper third	3(3%)
	middle third	6(6.1%)
	lower third	23(23.4%)
Site of Tumor (Colon)	ascending colon tumor	17(17.3%),
	Transverse colon	9(9.1%)
	descending colon	20(20.4%)
	Rectosigmoid	20 (20.4%)

Total of 98 patients were enrolled in the study with mean age of 47.7 ± 14.2 years and gender distribution of 58 (59.2%) male patients and 40 (40.8%) female patients. 32 (32.7%) had reported positive family history of cancer, age was categorized as 20-30 years including 13 (13.2%) patients, 31-40 years with 20 (20.3%) patients, 41 – 50 years with 19 (19.3) patients, 51-60 with 13 (13.2%) patients and 61-70 with 33 ((33.8%) patients respectively. Type of cancer was documented, reporting a higher prevalence of colon cancer with 66(67.3%) and 32(32.7%) rectal cancer cases only. Colorectal cancer stages were identified according to the American Joint Committee on Cancer Staging Sys (AJCC 7th edition) the reported frequency was 24(24.4%) as stage 1, 32(32.6%) as stage 2, and 32(32.6%) as stage 3 and 10 (10.2%) as stage 4.

Presenting complaints were reported as bleeding per reaction in 39(39.4%) patients, abdominal lump in 33(33.7%), and intestinal obstruction reported in 12(12.1%) patients respectively.BPR was reported in rectal cancer patients more frequently (25/14) as compared to colon cancer while intestinal obstruction was majorly reported in colon cancer (5/3) with altered bowel habits. Location of the tumor was reported as upper third 3(3%), middle third 6(6.1%), and lower third 23(23.4%) in rectal cancer, while colon cancer location was reported as ascending colon tumor 17(17.3%), Transverse colon 9(9.1%) descending colon 20(20.4%) & Rectosigmoid 20 (20.4%) respectively. Histopathology was reported as Adenocarcinoma 60 (61.2%), signet cell carcinoma 13 (13.2%), and mixed medullary Aden squamous 25(25.5%) **Table 1.**

Table 2: Factors of Delayed Diagnosis and Risk of Poor Survival in The Study Population.

Variables	Stage II (n=24)	Stage III (n=32)	Stage IV (n=42)	Mean Survival (weeks)	HR	CI 95% (Upper bound - lower bound)	P-Value
Misdiagnosed By Physician	14 (14.2%)	11 (11.2%)	13 (13.2%)	24.8 ± 18.2	1.32	0.24-2.16	0.23
Poor Knowledge	2 (2.0%)	8 (8.1%)	11 (11.2%)	34.5 ± 11.9	2.48	1.04 – 4.88	0.81
Herbal Medicine Use	1 (1.0%)	9 (9.1%)	13 (13.2%)	19.2 ± 8.52	0.89	0.047 – 1.89	0.047
Access To Healthcare Facility	5 (5.1%)	3 (3.0%)	2 (2.0%)	8.14 ± 9.24	1.85	0.46 – 2.88	0.299
Fear Of Hospital	2 (2.0%)	1 (1.0%)	3 (3.0%)	28.4 ± 12.9	1.99	0.67 – 3.61	0.082

Reasons for Delay in diagnosis were reported as misdiagnosis by a physician (OR 1.32, 0.24 – 2.16), poor knowledge of disease and symptoms (OR 2.48, 1.04 – 4.88), and herbal medication use to treat symptoms (OR 0.89, 0.047 – 1.89). Availability of healthcare institutes (OR1.85, 0.46 – 2.88) and fear of hospital (OR 1.99, 0.67 – 3.61) were reported as some other associated factors for delayed diagnosis in the study population (**Table 2**).

Socioeconomic status also played an important role and identified that poor SES (<50,000 / month or <200 USD / month) is a vulnerable group to get medical consultation and avoid regular check, the study population indicated higher frequency of poor SES patients with delayed diagnosis presenting with stage III (HR 2.41, 1.77 – 6.21) and stage IV (HR 3.41, 1.98 – 7.22) respectively.

Survival analysis was performed with the help of Kaplan-Meier test; associating type of cancer and stage of cancer, the results of the survival plot identified higher chances of mortality in stage IV patients, followed by stage III as compared to stage II and stage I. Similarly, higher mortality was reported in rectal cancer as compared to colon cancer (**Fig 1 and 2**).

Fig I: Survival analysis of study participants, the x-axis reported time in weeks (52 weeks = 1 year), while the y-axis reported many patients.

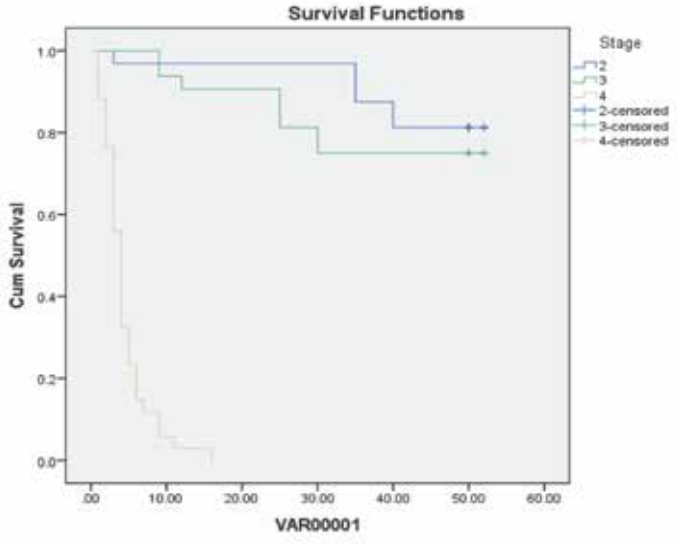

Fig 1: Survival Analysis of Study Participants, X-Axis Reported Time in Weeks (52 Weeks = 1 Year), While Y-Axis Reported Number of Patients.

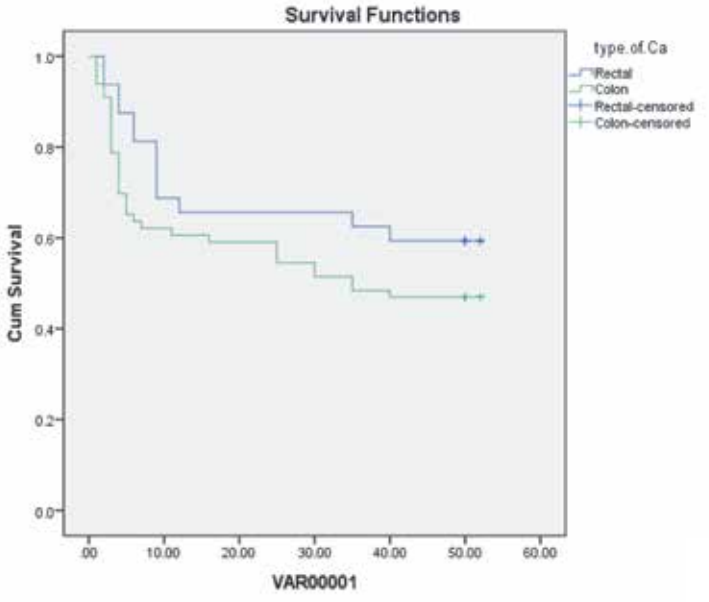

Fig 2: Overall Survival Analysis of Study Participants Categorized in Type Of CA, X-Axis Reported Time in Weeks (52 Weeks = 1 Year), While Y-Axis Reported Number of Patients.

Overall survival was reported as 74 (74.7%) for 1-year follow-up, however, Rectal cancer survival was 23 (23.7%) and colon cancer survival was 51 (51.3%) with a p-value of 0.365. The stage of CA was associated with overall survival, results reported 2/11 reported dead from stage I, 1/22 from stage II, 8/35 from stage III, and 13/30 from stage IV respectively (p-value 0.13).

DISCUSSION

This study assessed Karachi, Pakistan's colorectal cancer (CRC) patients' survival rates and determined the variables influencing this population's prognosis with a one-year survival rate of 74.4% in the study population[12]. The survival rate is comparable to other nations like Sweden (83%), Denmark (77.7%), England (74.7%), Australia (84.9%), and Norway (82.4%). The 3-year survival rate of colorectal cancer (CRC) patients in China was reported to be 74% and 42.20% in India for one and three years, respectively[13].

Study results discovered that there is a widespread lack of knowledge among the public about the signs and risk factors associated with colorectal cancer (CRC)[11]. This finding is consistent with certain studies carried out[14].

The main barriers to the successful uptake of screening were ignorance about the risk factors linked to colorectal cancer (CRC), the nature of screening techniques, and the related costs[15]. Our results did not significantly support the notion that social support from friends and family has a significant role in maintaining adherence to CRC screening, in contrast to two studies that discussed this topic.

According to this study, a major issue for CRC patients in our area is the delay in receiving a diagnosis. This is consistent with research, which found that 34% and 25% of patients, respectively, had a delay in diagnosis[16]. Following a review of the demographic characteristics of the patients in our research, low income was shown to be the primary cause of delayed diagnosis; in our region, around two-thirds of the population has low SES[17,18]. On the other hand, according to US statistics, only 17% of CRC patients experienced financial difficulties when seeking medical attention. Improving the availability of health care in isolated locations is necessary to close the gap between the populations of rural and urban regions[19,20,21].

According to the findings of another study patients' lack of desire to see doctors, a misdiagnosis made by doctors, and a lack of information were the main causes of the presentation's delay. According to our research, one of the worst effects of a delayed diagnosis is a presentation at the aggressive stage of CRC[22]. The observed findings align with other research indicating a connection between delayed diagnosis and delayed presentation.

In addition to poor poverty, our study revealed that misdiagnosis by medical professionals and patients' reluctance to attend doctors primarily because of symptoms they neglected to mention were other factors contributing to the diagnostic delay.

Considering misdiagnosis, the doctors misdiagnosed

a majority of patients with rectal cancer as hemorrhoids[23]. Hemorrhoids, affecting 4-5% of the general population, are the most prevalent cause of individuals presenting with bleeding PR[24]. The most frequent error for right-sided CRC was IBD, however, a significant portion of CRC patients had incorrect diagnoses of hemorrhoids (47%), Crohn's disease (15.1%), and ulcerative colitis (15.8%), according to studies[25].

In our study, the most often reported symptom among CRC patients was bleeding per rectum, which was followed by constipation and stomach discomfort. Other studies produced similar results as there is a delay between the emergence of a precancerous polyp and its development into invasive cancer, colorectal cancer (CRC) is seen as a disease that may be prevented and treated[26].

The study's limitations are the small sample size, and the inclusion of single-center, therefore its findings might not be universally applicable.

CONCLUSION

In conclusion, patients with colorectal cancer in Pakistan are often diagnosed at an advanced stage, with a dismal prognosis, due to a delay in presentation. Based on these results, national initiatives for CRC control and prevention must be launched, and universal access to healthcare should be made possible. The initiative should begin at the community level with print and electronic media to raise awareness of the substantial disease burden that colorectal cancer (CRC) causes among the general public.

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CONFLICT OF INTERESTS

The authors declared no conflict of interest.

FUNDING

There is nothing to declare.

PATIENT CONSENT

Informed consent in the language of understanding was obtained from patients.

ETHICAL APPROVAL

Approval for data collection was obtained from the Head of the department, Surgery, Al-Tibri Hospital, Karachi.

AUTHORS' CONTRIBUTIONS

RK initiated the study by creating objectives and collecting data, **HWA** documented surgical consultation and took care of ethical consideration.**SK** also had consultation and data collection with manuscript write-up while **ST** had entered, and analyzed the data and manuscript write-up.

REFERENCES

1. Hussain I, Majeed A, Rasool MF, Hussain M, Imran I, Ullah M, Ullah H. Knowledge, attitude, preventive practices and perceived barriers to screening about colorectal cancer among university students of newly merged district, Kpk, Pakistan–A cross-sectional study. Journal of Oncology Pharmacy Practice. 2021 Mar;27(2):359-67. https://doi.org/10.1177/1078155220922598
2. Miyakawa T, Kawamura H, Honda M, Takano Y, Kinuta S, Kamiga T, Yamazaki S, Muto A, Shiraso S, Yamashita N, Iwao T. Impact of histological subtype on prognosis in stage IV colorectal cancer: A population-based cohort study. PLoS One. 2022 Mar 3;17(3):e0264652. DOI: 10.1371/journal.pone.0264652.
3. Mezzapesa M, Losurdo G, Celiberto F, Rizzi S, d'Amati A, Piscitelli D, Ierardi E, Di Leo A. Serrated colorectal lesions: an up-to-date review from histological pattern to molecular pathogenesis. International Journal of Molecular Sciences. 2022 Apr 18;23(8):4461. DOI: 10.3390/ijms23084461.
4. Iqbal N, Berstad P, Solbjør M, Diaz E, Czapka E, Hofvind S, Bhargava S. Access to colorectal cancer screening for Pakistani immigrants in Norway–a qualitative study. BMC Health Services Research. 2024 Dec;24(1):1-2. https://doi.org/10.1186/s12913-024-11275-7
5. Shamsi U, Qureshi S, Moosaji M, Azam I, Idrees R. Colorectal Cancer Survival and Its Prognostic Factors in Karachi, Pakistan. Age (years). 2024 Jun 1;50(537):54-3. doi: 10.29271/jcpsp.2024.06.688
6. Tufail M, Wu C. Exploring the burden of cancer in Pakistan: an analysis of 2019 data. Journal of Epidemiology and Global Health. 2023 Jun;13(2):333-43. doi.org/10.1007/s44197-023-00104-5
7. Shaukat A, Levin TR. Current and future colorectal cancer screening strategies. Nature reviews Gastroenterology & hepatology. 2022 Aug;19(8):521-31. doi.org/10.1038/s41575-022-00612-y
8. Knudsen AB, Rutter CM, Peterse EF, Lietz AP, Seguin CL, Meester RG, Perdue LA, Lin JS, Siegel RL, Doria-Rose VP, Feuer EJ. Colorectal cancer screening: an updated modeling study for the US Preventive Services Task Force. Jama. 2021 May 18;325(19):1998-2011. doi:10.1001/jama.2021.5746
9. Cardoso R, Guo F, Heisser T, Hackl M, Ihle P, De Schutter H, Van Damme N, Valerianova Z, Atanasov T, Majek O, Mužík J. Colorectal cancer incidence, mortality, and stage distribution in European countries in the colorectal cancer screening era: an international population-based study. The Lancet Oncology. 2021 Jul 1;22(7):1002-13. DOI: 10.1016/S1470-2045(21)00199-6

10. Kanth P, Inadomi JM. Screening and prevention of colorectal cancer. Bmj. 2021 Sep 15;374. doi: https://doi.org/10.1136/bmj.n1855
11. Mascitti M, Rubini C, De Michele F, Balercia P, Girotto R, Troiano G, Muzio LL, Santarelli A. American Joint Committee on Cancer staging system 7th edition versus 8th edition: any improvement for patients with squamous cell carcinoma of the tongue?. Oral surgery, oral medicine, oral pathology and oral radiology. 2018 Nov 1;126(5):415-23. DOI: 10.1016/j.oooo.2018.07.052.
12. Harber I, Zeidan D, Aslam MN. Colorectal cancer screening: impact of COVID-19 pandemic and possible consequences. Life. 2021 Nov 26;11(12):1297. https://doi.org/10.3390/life11121297
13. Coleman MP, Forman D, Bryant H, Butler J, Rachet B, Maringe C, Nur U, Tracey E, Coory M, Hatcher J, McGahan CE. Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995–2007 (the International Cancer Benchmarking Partnership): an analysis of population-based cancer registry data. The Lancet. 2011 Jan 8;377(9760):127-38. DOI: 10.1016/S0140-6736(10)62231-3
14. Yuan Y, Li MD, Hu HG, Dong CX, Chen JQ, Li XF, Li JJ, Shen H. Prognostic and survival analysis of 837 Chinese colorectal cancer patients. World Journal of Gastroenterology: WJG. 2013 May 5;19(17):2650. doi: 10.3748/wjg.v19.i17.2650
15. Haggar FA, Boushey RP. Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. Clinics in colon and rectal surgery. 2009 Nov;22(04):191-7. DOI: 10.1055/s-0029-1242458
16. Muhamad NA, Ma'amor NH, Rosli IA, Leman FN, Abdul Mutalip MH, Chan HK, Yusof SN, Tamin NS, Aris T, Lai NM, Abu Hassan MR. Colorectal cancer survival among Malaysia population: data from the Malaysian National Cancer Registry. Frontiers in Oncology. 2023 Nov 29;13:1132417. https://doi.org/10.3389/fonc.2023.1132417
17. Kelty E, Ward SV, Cadby G, McCarthy NS, O'Leary P, Moses EK, Ee HC, Preen DB. Familial and non-familial risk factors associated with colorectal cancer survival in young and middle-aged patients. International Journal of Colorectal Disease. 2019 Oct;34:1673-80. https://doi.org/10.1007/s00384-019-03380-5
18. Holowatyj AN, Ruterbusch JJ, Rozek LS, Cote ML, Stoffel EM. Racial/ethnic disparities in survival among patients with young-onset colorectal cancer. Journal of Clinical Oncology. 2016 Jun 20;34(18):2148-56. https://doi.org/10.1200/JCO.2015.65.0994
19. Le H, Ziogas A, Lipkin SM, Zell JA. Effects of socioeconomic status and treatment disparities in colorectal cancer survival. Cancer Epidemiology Biomarkers & Prevention. 2008 Aug 1;17(8):1950-62. https://doi.org/10.1158/1055-9965.EPI-07-2774
20. Hall C, Clarke L, Pal A, Buchwald P, Eglinton T, Wakeman C, Frizelle F. A review of the role of carcinoembryonic antigen in clinical practice. Annals of coloproctology. 2019 Dec;35(6):294. doi: 10.3393/ac.2019.11.13
21. Kim HR, Joo JI, Lim SW, Oh BY. Prognostic value of carcinoembryonic antigen levels before and after curative surgery in colon cancer patients. Annals of Surgical Treatment and Research. 2021 Jan;100(1):33. doi: 10.4174/astr.2021.100.1.33
22. Basbug M, Arikanoglu Z, Bulbuller N, Cetinkaya Z, Aygen E, Akbulut S, Satici O. Prognostic value of preoperative CEA and CA 19-9 levels in patients with colorectal cancer. Hepato Gastroenterology-Current Medical and Surgical Trends. 2011 Apr;58(106):400. PMID: 21661403
23. Javanparast S, Ward PR, Carter SM, Wilson CJ. Barriers to and facilitators of colorectal cancer screening in different population subgroups in Adelaide, South Australia. Medical Journal of Australia. 2012 May;196(8):521-3. https://doi.org/10.5694/mja11.10701
24. Segura A, Siddique SM. Reducing disparities and achieving health equity in colorectal cancer screening. Techniques and innovations in gastrointestinal endoscopy. 2023 Jan 1;25(3):284-96. DOI: 10.1016/j.tige.2023.02.007
25. Khan AA, Macaron C, Burke CA, Singh A. Quality in Colorectal Cancer Screening. InQuality in Gastroenterology: A Concise Guide to Establishing High Value Clinical Care 2024 Aug 6 (pp. 133-153). Cham: Springer International Publishing.
26. Marinucci N, Moy N, Koloski N, Shah A, Austin G, Russell-Bennett R, McGraw J, Dulleck U, Holtmann G. Social determinants and participation in fecal occult blood test based colorectal cancer screening: A qualitative systematic review and meta-synthesis. Health Promotion Journal of Australia. 2024 Jan;35(1):9-36. doi: 10.1002/hpja.732.