Research Article

FACTORS AFFECTING DELAY IN DIAGNOSIS OF COLORECTAL CANCER; A CROSS SECTIONAL STUDY; FROM TERTIARY CARE HOSPITAL OF KARACHI PAKISTAN

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Short Title: *FACTORS AFFECTING DELAY IN DIAGNOSIS OF COLORECTAL CANCER*

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ABSTRACT

Background: CRC incidence is increasing in our region. There is no specific CRC control program or national cancer registry in Pakistan. Previously no data has been published on presentation and diagnosis delay of CRC in our region. This study is conducted to determine the factor affecting delay in presentation and diagnosis and to provide baseline information to launch a CRC control program. Primary objective is to determine factor causing delay in diagnosis of CRC. Secondary objective is to evaluate relationship between tumor site and stage of CRC with presenting symptoms and symptom duration.

Methods: This project is a prospective cross-sectional study on 113 biopsy-proven CRC patients admitted to the surgical ward of civil hospital Karachi.

Results: A total number of participants was 113. Presentation delay was observed in 83.2% of patients. The main reasons for a reported delay in the presentation were lack of patients' knowledge that these symptoms may be cancer (60.4%), the wrong diagnosis by the primary physician (34.6%), or the patient didn't want to visit the doctor (0.04%). Most tumors (95%) originated from the sigmoid and rectum. 38.9% and 44.2% of the patients diagnosed at Stage 4 and 3 respectively.

Conclusions: This study revealed that CRC patients in Pakistan are facing delays in presentation and diagnosis. This is the reason behind diagnosis at the advanced stage with a poor prognosis. Based on this study findings CRC control program should be introduced to detect CRC at an early stage.

What's already known about this topic?

- CRC patients diagnosed at the advanced stage with a poor prognosis.

What does this article add?

- CRC patients in Pakistan are facing delays in presentation and diagnosis.
- Reasons behind in delay in diagnosis are patient visits primary physician late, doctor makes wrong diagnosis and patient did not want to visit doctor.

1 | INTRODUCTION

Colorectal cancer is the second most common cancer worldwide [1]. In Pakistan, due to the lack of a national cancer registry, CRC data are scarce [2]. The single centered data of the last quarter of the century from the largest cancer institute "The Shaukat Khanum memorial hospital" of Pakistan reported CRC as the fourth most common cause of cancer in Pakistan [3].

Screening the general population for CRC lead to early detection at Duke's stage A or B consequently leading to a better prognosis. Few factors that are taken into consideration for early detection are as follows: [4]

(a)Patient interval/ delay: The time duration from the onset of symptom to first consult is referred to as patient interval, [5] and delay more than 3 months is called patient delay [6, 7].

(b)Diagnosis delay: The time interval of more than one month from the first consult until the histopathological diagnosis is stated as diagnosis delay [8].

(c)Treatment delay: the time duration longer than one month between diagnosis and initiation of treatment [9].

The most common presenting symptoms of CRC include Bleeding PR, altered bowel habits, weight loss, tenesmus, and change in the frequency & consistency of stools [10]. The resemblance of symptoms of CRC with diseases such as GI TB and IBD leads to misdiagnosis in many patients, and lack of radiological and endoscopic facilities in underdeveloped regions may aid in difficulty in reaching the correct diagnosis. [11] On the part of the health care provider, diagnosis can be delayed by attributing the symptoms to less serious diseases such as hemorrhoids, anal fissures, or fistula, etc [12].

In underdeveloped regions, the main factors in the delayed seeking of medical care for CRC include female sex, younger age, low socioeconomic status (SES), lack of resources and awareness among the general population, [13] and the taboo associated with the symptoms of CRC among the rural population which forms the majority of the population in Pakistan [14, 15].

There is no screening program for CRC patients in Pakistan. No study has been conducted focusing on reasons for diagnosis delay of CRC patients in our region.

The primary outcome is to determine causative factors involved in the diagnostic delay of CRC in an underdeveloped region. The secondary outcome was to evaluate the relationship between the tumor site and stage of CRC at presentation with the duration of symptoms and the presenting symptoms.

2 | MATERIALS AND METHODS

 A prospective cross-sectional study on 113 biopsy-proven CRC patients admitted in the surgical ward of civil hospital Karachi was conducted from June 2019 to May 2020. After IRB approval from the ethics review committee of the hospital. The sample size was calculated by using OpenEpi software with a confidence interval of 95%.

All biopsy-proven CRC patients admitted in the surgical ward of civil hospital Karachi were enrolled in the study. Participation was voluntary and written informed consent was taken from the patient in their

native language. The patient's identity was concealed, and the principal investigator filled the questionnaire after interviewing the participant and the remaining variable were filled from the patients' medical records.

An 18-point questionnaire comprising of three sections was formulated using a pre-formed questionnaire from a previously conducted study on a similar topic [15]. The first section comprised of demographic factors, duration of symptoms, the extent of disease, and clinical staging of CRC. The second section was based on the presenting symptoms of CRC which included (bleeding per rectum, abdominal pain, constipation or diarrhea, constitutional symptoms, perineal pain, and fecal incontinence). The third section encompassed various factors leading to delay in diagnosis of CRC among the general population. The variables evaluated involved lack of knowledge about the symptoms of CRC, a misdiagnosis by a physician, and the embarrassment associated with the symptoms of CRC deterring their visit to the physician.

2.1 | STATISTICAL ANALYSIS

Data analysis was done using SPSS (version 24, SPSS, Inc., Chicago IL). Continuous parametric data were analyzed as mean with standard deviation and categorical data as proportions. Chi-Square was used to assess the difference between categorical variables while the variance in continuous parametric variables was evaluated by the student's T-test. P-value <0.05 was considered statistically significant.

3 | RESULTS

A total of 113 biopsies proven CRC patients who matched the inclusion criteria were selected for the analysis. The mean age was 42.21±15.6 years. Of the 113 patients, 74 (65.5%) were male and 39 (35.5%) were female. 76.9% of patients belong to low socioeconomic status. Only 17.7 % of the patients presented within the first 3 months of development of symptoms while 82.3% of the patients presented after 3 months. 44.2% and 38.9% of the patients presented in Stage 3 and 4 respectively. The most common prevalent tumor site was the rectum while the least common was the transverse colon. See Table 1 for further results.

Table 2 demonstrates the relationship between the reasons for the delay in presentation of CRC with various clinical factors. Regarding the duration of symptoms, the lack of knowledge in the general population and misdiagnosis by the physician was found to be significantly associated with delayed presentation. The patients who did not want to visit the doctor were found to have a more severe stage of CRC (p=0.05). No statistically significant relationship was found between the reasons for the delay in diagnosis and population type, however, the patients having low income were found to have a lack of knowledge regarding CRC (p=0.03). See Table 2 for further results.

Table 3 describes the relationship of tumor sites with different variables. Regarding the duration of symptoms, no statistically significant association was found between the site of tumor involved and the delayed presentation. Similarly, no association between the site of tumor and severity of CRC was found. (P=<0.56) However concerning symptoms, bleeding PR was substantially associated with tumors involving the rectum, and abdominal pain was most prevalent in transverse colon cancer. The constitutional symptoms had a significant relationship with descending colon tumors. See table 3 for further results.

Table 4 reveals the association between the stage of CRC and various factors. There was no statistically significant difference found between the stage of CRC and duration of symptoms. There was no substantial relationship found between socioeconomic status with the stage of tumor and presenting symptoms. See table 4 for further results.

4 | DISCUSSION

This study revealed that one of the major concerns regarding CRC patients in our region is diagnostic delay. This is similar to studies conducted in Jordon and Denmark showing 34% and 25% of patients having a delay in diagnosis, respectively [15, 16]. After reviewing patients' demographic factors in our study, low income was the foremost factor responsible for delayed diagnosis, and our region has approximately two-thirds of the population belonging to low SES. In contrast to this, Siminoff et al in their results from the US reported that only 17% of patients having CRC had financial constraints while seeking medical care [12]. Access to health services in remote areas should be improved to overcome this difference between rural and urban populations.

However, the results are shown by Abu Helalah et; al described that the major reasons for the delay in the presentation were lack of knowledge, a misdiagnosis by physicians, and patients' lack of will to visit physicians [15]. One of the fearsome consequences of diagnostic delay is the presentation at the aggressive stage of CRC as stated in our results. These results are in concordance with the previously conducted studies stating that diagnostic delay is associated with the presentation at a late stage [17]. Apart from low income, the other reasons identified in our study for the diagnostic delay were misdiagnosis by physicians and lack of patients' will to visit doctors partly due to embarrassment and mainly due to negligence of their symptoms. These results are parallel to the studies conducted in Jordan and the USA by Abu Helallah et; al and Siminoff et; al [12,15].

Taking misdiagnosis into consideration, the physicians misdiagnosed a mainstream population of rectal cancer patients as hemorrhoids. This may be because hemorrhoids are the most common cause of patients presenting with bleeding PR affecting 4-5% of the general population. (18) While the most common misdiagnosis for right-sided CRC was IBD. E JF et; al and Wang et; al also reported that a major chunk of CRC patients was misdiagnosed as Hemorrhoids 47%, Crohn's 15.1%, and UC 15.8%. [19, 20]

Regarding the prevalence of symptoms among CRC patients in our study, the most common reported symptom was bleeding per rectum followed by constipation and abdominal pain. Similar findings were seen in a study conducted by Abu Helalah et; al in Jordon [15], Korsgaard et; al in Denmark [21], and Tomlinson et; al in Canada [22]. CRC is considered a preventable and treatable disease providing a lag time from the development of precancerous polyp to its progression into invasive cancer. A significant advancement in technology and vigilant screening test has increased the detection of these lesions at the pre-cancerous stage, if not at the early stage.

Now shedding light on the stage of CRC, two-third of our study population was detected at stage III and IV. This is consistent with the results conducted by Brandenburg et; al in the Dutch population [23] but in contrast to the study conducted by Tomlinson et; al in Canada which showed more than half of cancers were detected at Stage I and II [22]. The reason for this aggressive presentation may be the lack of a cancer screening program, and lack of adequate referral system, and a lack of access to oncology services [24].

More than two-thirds of the patient in our study population were below 50 years, the reasons may be hereditary and environmental factors such as physical inactivity, high fat diet, red meat, and smoking [25-27]. These results are consistent with a study from Saudi Arabia which has reported 63% CRC in younger population below 40 years [26].

A similar trend of increasing incidence of CRC in younger populations seen in the USA but expected rise to be seen in the younger population of 20-49 years till 2030.

The main strength of this study is that it is the first study conducted in Pakistan regarding presentation delay and diagnosis delay of CRC patients and its impact on morbidity. Factors predicting the delay were assessed. The limitation of this study, it is from a single-center study with a relatively small size and this may not be representative of the entire population. Another limitation of this study is recall bias. The patient may not recall the duration of the symptoms properly which may result in inaccurate answers. Another important concern is that this study is a cross-sectional one, and the patients have not been followed over a period. This makes its design relatively weaker than a cohort study design.

The few recommendations which the authors want to propose are: Our health care system must launch CRC screening program and its prevention on the national level to improve health care-related with CRC with key factor early diagnosis and management. Among children, curriculum-based health education should be introduced regarding the prevention of cancer and incorporate a healthy lifestyle into routine life. Social and mainstream media and awareness programs at a societal level can be used to enhance the cognizes of CRC among the general population. The general physicians should be aware of the burden of disease produced by CRC and seminars should be conducted to teach the General physician for keeping a very low threshold when a patient comes to the doctor with suspicious symptoms. The authors recommend that a prospective study should be conducted in this regard to increase the power of the results.

CONCLUSION

In Conclusion, CRC patients in Pakistan are experiencing a delay in presentation leading to diagnoses at the advanced stage with a poor prognosis. The low-income population living in rural areas face some difficulty in access to health care services. Based on these findings, future projects on CRC control and prevention at the national level must be started and, access to health services should be made feasible for the entire population. At community levels, the program should be started involving electronic and print media to create awareness of the significant burden of disease caused by CRC in the general population. This can also help to remove the taboo associated with symptoms of CRC that keeps the underprivileged population retreating to visit the hospitals for treatment.

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DISCLOSURE

The authors have no conflicts of interest to declare.

ETHICAL APPROVAL

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