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Do Younger Patients with Colorectal Cancer Presents with More Advanced Disease at Initial Presentation?

M. Shadab Khan[1*], Asma Sarfaraz[2], Ramna Nadeem[2], Bushra Shirazi[3] and Abdaal Waseem Khan[3]

[1]*Department of GI and HBP Surgery, University of Sindh, Institute of Medical Sciences, Karachi, Pakistan*

[2]*Department of General Surgery (GI&HBP), Sindh Institute of Medical Sciences (SIMS), Karachi, Pakistan*

[3]*Department of Surgery (GI&HBP), Sindh Institute of Medical Sciences (SIMS), Karachi, Pakistan*

Abstract

Introduction: Colorectal cancer the second most lethal malignancy widely considered a disease that affects people after the 4th decade of life but an interesting change in trend is observed and it was found that colorectal cancer rate has been increasing in young patients living under their 4th decade. These patients even present with more advanced diseases and generally have a poor overall prognosis compared to the older patients.

Materials and methods: Colorectal cancer patients presented in Sindh Institute of urology and transplantation's Oncology center from January 2011 till December 2020 were reviewed retrospectively. For data analysis, all patients were divided into two groups, Group A young age population (age between 18-50 years) Group B old age population (age 51 years and onward).

Subgroup analysis of the study period (from January 2011 – December 2015 first period while from January 2016 – December 2020 second period) was performed to check the progressive change in the trend of stage and clinical characteristics of colorectal cancer in young and old patients. Details were reviewed from the patient's files and all data was collected as per the Proforma requirement. Collected data was analyzed for results using SPSS version 23.0.

Results: Total of 612 patients with colorectal cancer presented between 2011 till 2020. Among these patients 243 (39.7%) presented between January 2011 till December 2015. Patients age 50 years and younger were 410 (66.8%).

Results showed a statistically significant association between patient age and tumor characteristics (histopathology and tumor differentiation). When data was analyzed over different study periods results showed that there is a statistically significant association between tumor differentiation and patient age. A change in the trend of clinical stage of the tumor with respect to patient age over this period of time was also noted.

Conclusion: The development and implementation of screening protocols and awareness programs will definitely have an impact to control disease incidence, patient prognosis, and survival outcome.

Keywords: Colorectal cancer • Young age • Old age • Advance disease

Introduction

Colorectal cancer (CRC) is the third most common and second most lethal malignancy, according to the 2018 global cancer incidence mortality and prevalence database. It is widely considered a disease that affects people after the 4th decade of life and screening is not indicated before 50 years of age [1]. But an interesting trend is being observed regarding CRC with a newly emerging high-risk group, Early-onset Colorectal Cancers (EOCRCs), regarded as patients with diagnosed CRC before the recommended screening age of 50 years. For example, in a study conducted in the USA, it was found that CRC rates have been increasing annually in individuals aged 20–39 and 40–54 since the mid-1980s and mid-1990s, respectively. Additionally, these individuals present with more advanced disease and generally have a poorer overall prognosis compared to the older patients [2]. This has recently led to a recommendation by the US Preventive Screening Task Force (USPSTF) for decreasing the age of colorectal screening to 45 years [3].

CRC is prevalent in 5% of the Pakistani population[4]. A study conducted among patients of early-onset colorectal cancer in Pakistan reported 74% of these patients had advanced disease of stage III/IV at presentation [5]. So theoretically earlier screening may help to detect earlier-stage disease, thus improving prognosis.

In recent years, alterations in diet, sedentary lifestyles, and the rising prevalence of obesity have been hypothesized to impact molecular and physiological characteristics influencing the risk of colorectal cancer and other cancer types in the young population. Taking into account the controversy on this subject and the dearth of literature in Pakistan, this study is being carried out in order to make a comparative analysis of these trends in CRC incidence between older and younger patient population groups.

Rationale of study

We intend to look at the stage at presentation, and tumor histology with differentiation at initial presentation among individuals diagnosed with colorectal cancer aged younger than 50 years at initial presentation and compare similar characteristics among those presenting at an older age. Hence the rationale is to provide objective data to inform screening and treatment recommendations with colorectal cancers in the younger age group.

Objectives: To compare the stage, Histological type, and differentiation of CRC at initial presentation between younger patients between 18 -- 50 years of age to those 51 years of age or older at the time of initial diagnosis.

***Address for Correspondence:** M. Shadab Khan, Department of GI and HBP Surgery, University of Sindh, Institute of Medical Sciences, Karachi, Pakistan; Email: drshadabkhan@hotmail.com*

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Materials and Methods

UA retrospective case-control study was conducted in the Sindh Institute of urology and transplantation GI surgery department on patients diagnosed case of colorectal cancer. All patients received in Hanifa Suleiman Oncology center fulfilling inclusion criteria from January 2011 till December 2020 enrolled in the study. The clinical record of all patients was retrieved from the Hanifa Suleiman Oncology clinic registry, GI clinic patient's registry, histopathology department, and hospital Record room. Variables mentioned in the questionnaire were all collected and stored with a given MR number maintaining data security and confidentiality. Approval for the study and exemption letter was obtained from Institutional Review Board (IRB) and from the ethical review committee (ERC). All variables mentioned in the questionnaire will be collected from the patient's files including age, Gender, endoscopy (colonoscopy/Sigmoidoscopy) findings, Histological Type, Grade, Site of Tumor.

For data analysis, all patients were divided into two groups, Group A young age population (age between 18-50 years) Group B old age population (age 51 years and onward).

Young age population further subdivided into three groups, A1 (age 18-30 years), A2 (age 31-40 years), A3 (age 41-50 years) while old age population also subdivided into three groups B1 (age 51-60 years), B2 (age 61-70 years) and B3 (age 71 years onward).

Subgroup analysis of study period (To check the progressive change in the trend of CRC in young patients) from January 2011 – December 2015 first period while from January 2016 – December 2020 second period. Subgroup analysis of study period (To check the progressive change in the trend of CRC in elder patients) from January 2011 – December 2015 first period while from January 2016 – December 2020 second period.

Table 1. Association of age and tumor characteristics.

Age	Tumour differentiation				P-Value
	Well diff	Mod diff	Poor diff	Undifferentiation	
≤ 50 years	70 (53.0%)	173 (66.2%)	153 (79.2%)	14 (53.8%)	0.000
≥ 51 years	62 (46.9%)	88 (33.7%)	40 (20.7%)	12 (46.1%)	
All ages	132 (100%)	261 (100%)	193 (100%)	26 (100%)	-
Age	**Tumour differentiation**				**P-Value**
	Adenocarcinoma	**Mucinous**	**Signet ring cell**		
≤ 50 years	301 (64.0%)	34 (80.9%)	75 (75.0%)		0.000
≥ 51 years	169 (35.9%)	8 (19.0%)	25 (25%)		
All ages	470 (100%)	42 (100%)	100 (100%)		-
Age	**Tumour differentiation**				**P-Value**
	Early stage			**Advance stage**	
≤ 50 years	66 (73.3%)			344 (65.9%)	0.154
≥ 51 years	24 (26.6%)			178 (34.0%)	
All ages	90 (100%)			522 (100%)	-

Table 2. Association of age and tumor characteristics over specified period of time.

Age	Year Of diagnosis	Tumour differentiation				P-Value
		Well diff	Mod diff	Poor diff	Undiff	
≤ 50 years	2011--2015	32 (53.3%)	61 (69.3%)	63 (82.8%)	11 (57.8%)	0.012
	2016--2020	38 (52.7%)	112 (64.7%)	90 (76.9%)	3 (42.8%)	
≥ 51 years	2011--2015	28 (46.6%)	27 (30.6%)	13 (17.1%)	8 (42.1%)	0.069
	2016--2020	34 (47.2%)	61 (35.2%)	27 (23.0%)	4 (57.1%)	
All ages	2011--2015	60 (100%)	88 (100%)	76 (100%)	19 (100%)	0.001
	2016--2020	72 (100%)	173 (100%)	117 (100%)	7 (100%)	
Age	**Year Of diagnosis**	**Tumour differentiation**				**P-Value**
		Adenocarcinoma	**Mucinous**	**Signet ring cell**		
≤ 50 years	2011--2015	122 (66.3%)	15 (83.3%)	32 (78.0%)		0.518
	2016--2020	179 (62.5%)	19 (79.1%)	43 (72.8%)		
≥ 51 years	2011--2015	62 (33.6%)	3 (16.6%)	9 (21.9%)		0.415
	2016--2020	107 (37.4%)	5 (20.8%)	16 (27.1%)		
All ages	2011--2015	184 (100%)	18 (100%)	41 (100%)		0.680
	2016--2020	286 (100%)	24 (100%)	59 (100%)		
Age	**Year Of diagnosis**	**Tumour differentiation**				**P-Value**
		Early stage	**Advance stage**			
≤ 50 years	2011--2015	34 (77.2%)	133 (66.8%)			0.037
	2016--2020	32 (69.5%)	211 (65.1%)			
≥ 51 years	2011--2015	10 (22.9%)	65 (32.6%)			0.403
	2016--2020	14 (30.4%)	113 (34.9%)			
All ages	2011--2015	44 (100%)	199 (100%)			0.036
	2016--2020	46 (100%)	323 (100%)			

Statistical Analysis

All data collected were analyzed using SPSS version 23.0. Frequencies and percentages were computed for categorical variables while mean ± standard deviation for quantitative variables. Chi-square or Fisher's Exact Test was used to determining the association between groups. An unadjusted odds ratio with a 95% confidence interval was employed to assess the direction and magnitude of association between variables. Significance based on p-value <0.05.

Results

During this study period between January 2011 till December 2020, 612 patients presented with the diagnosis of colorectal cancer in our institute. Among these patients 243 (39.7%) presented between January 2011 till December 2015 while 369 (60.3%) presented between January 2016 till December 2020. Patients age 50 years and younger were 410 (66.8%) while 202 patients (32.2%) were 51 years and above. The mean age of patients at the time of presentation was 44.46+/- 15.36 years. Out of total 386 (63.1%) were male. At the time of initial presentation, 80 patients (13.1%) were diagnosed to have right colonic cancer, 96 patients (15.7%) had left-sided colonic cancer and 436 patients (71.2%) had rectal cancer.

Results showed a statistically significant association between patient age and tumor characteristics (histopathology and tumor differentiation). Young patients have a greater proportion of moderately and poorly differentiated tumors (66.2 %and 79.2% respectively) compare to old age patients (33.7% and 20.7% respectively) similarly mucinous and signet ring cell histopathology is more pronounced in young patients (80.9% and 75% respectively)compare to older age patients (19% and 25%respectively). While there is no statistically significant association noticed between age groups and clinical stage of the tumor at initial presentation.

When data was analyzed over different study periods results showed that there is a statistically significant association between tumor differentiation and patient age. It is also concluded that there is a change in the trend of clinical stage of the tumor with respect to patient age over this period of time such that young patients are presenting with more advanced disease compared to older counterparts. When this change of time further compared with age subgroups results showed a statistically significant association between clinical stages of tumor inpatient age 31 – 40 years while there is no statistically significant association between other age subgroups.

Discussion

This study retrospectively reviewed colorectal cancer patients over a period of ten years from 2011 to 2020 and provided important information regarding the change of trend related to colorectal cancer incidence in our population. Our results showed that young patients with colorectal cancer had more advanced disease on initial presentation when trend assessed in ten years period and compared to their older counterparts. A similar change in trend has been reported in other international studies conducted in the United States [6] and Canada [7]. Decreased incidence of colorectal cancer in the elderly population is most likely related to the fact that this group has established screening programs while the opposite trend noticed in the younger population is because of the absence of any established screening programs for this population [8]. However colorectal screening protocols and even awareness programs in third-world countries like Pakistan are not routinely practiced or even exist. Even in the absence of such screening programs, our study results are in accordance with internationally published data in this regard [9]. Colorectal cancer screening for average-risk adults 2018 guidelines provides the guidelines specifically for an average-risk adult population which will help clinicians to refer patients for screening and hence leads to early detection and prevention of colorectal cancer in this population. Limited resources and a low health budget in our country restrict our intentions to develop a screening program for our general population. Keeping in view the advanced stage and aggressive nature of cancer in the young population we recommend awareness programs and our health care professionals should be more vigilant for early diagnosis of the problem which will lead to better treatment options for the problem.

Regarding tumor biology, a study comparing 59 patients younger than 40 years versus 416 older than 40 years during a 20-years period, found a higher frequency of tumors with poor differentiation. Mucinous adenocarcinoma and signet ring cell carcinoma were the most common variant noted in this young population In this study, we observe similar results that on initial presentation younger patients have a locally advanced tumor and unfavorable histopathological subtypes like a poorly differentiated tumor with mucinous or signet ring cell variety when compared to older patients. Ghodssi also reported similar results in his retrospectively conducted comparative study [10]. Our study has certain limitations, it is a retrospective study and hence the data has potential bias. Because of the retrospective nature of the study, we are unable to properly assess personal and family history and evaluate familial adenomatous polyposis syndrome. As this is a single-centered study with a limited number of cases, this study is not representing the true population as well as there is a lack of a national cancer registry. In this study, we only observe the trend of the disease over a specified period of time and are not able to address other associations.

However, this study is among the first to give an overview of colorectal cancer incidence in the younger population of Pakistan. The major strength of the study is that it will develop colorectal cancer awareness and screening information in the general population. Hence we favor the development of awareness programs, screening protocols for our population.

Conclusion

Considering this evidence of the rising incidence of colorectal cancer in the young population with even more advanced and aggressive disease steps need to be taken to control this change in disease pattern. It is of utmost importance to educate our population and especially our health professionals regarding this emerging issue. Development and implementation of screening protocols and awareness programs especially in third world country like Pakistan where no screening guidelines exist will have a major impact to control the incidence of colorectal cancer which ultimately influences disease prognosis and outcome.

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Conflict of Interest

Nothing to disclose.

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