

# Assessing demographic and socioeconomic factors in patients with advanced colorectal cancer

Evaluación de factores demográficos y socioeconómicos en pacientes con cáncer colorrectal avanzado

Mario Trejo-Avila\*, Danilo Solórzano-Vicuña, and Omar Vergara-Fernández Department of Colorectal Surgery, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

## Abstract

**Background:** The aim of the study was to determine the socioeconomic and demographic factors associated with advanced colorectal cancer (CRC) presentation at our institution. **Methods:** From January 2009 to January 2018, patients that underwent CRC surgery at our institution were included and retrospectively analyzed. Univariate and multivariate logistic regression were used to determine independent risk factors for presenting with advanced CRC. **Results:** A total of 277 patients were included, 53.5% presented with advanced CRC. The multivariate analysis identified that living in a rural area (odds ratio [OR] = 5.25; 95% confidence interval [95% CI]: 2.27-12-10; p < 0.001), weight loss (OR = 2.33; 95% CI: 1.35-4.09; p = 0.002), needing emergency surgery (OR = 4.68; 95% CI: 1.25-17.49; p = 0.022), location in the rectum in comparison with colon (OR = 2.66; 95% CI: 1.44-4.91; p = 0.002), and location in the mid rectum (OR = 6.10; 95% CI: 2.31-16.12; p < 0.001) were associated with higher odds of advanced CRC stage at presentation. **Conclusions:** Patients with lower socioeconomic status, with symptoms, and needing emergency surgery were associated with advanced CRC stage at presentation. Special interventions to improve access to care in this population should be planned to enhance CRC outcomes.

Keywords: Colorectal cancer. Socioeconomic factors. Advanced colorectal cancer. Health disparities.

## Resumen

**Introducción**: El objetivo del presente estudio es determinar los factores socioeconómicos y demográficos asociados con la presentación de cáncer colorrectal (CCR) en etapas avanzadas en nuestra institución. **Métodos**: De Enero 2009 a Enero 2018, aquellos pacientes operados por CCR fueron incluidos y analizados de forma retrospectiva. Se realizó análisis de regresión logística para determinar los factores de riesgo independientes para presentar CCR avanzado. **Resultados**: Se incluyeron un total de 277 pacientes, de los cuales 53.5% se diagnosticaron con CCR avanzado. En el análisis multivariable: vivienda en zona rural (OR = 5.25; 95% CI: 2.27-12-10; p < 0.001), pérdida de peso (OR = 2.33; 95% CI: 1.35-4.09; p = 0.002), necesidad de cirugía de urgencia (OR = 4.68; 95% CI: 1.25-17.49; p = 0.022), tumores en recto (OR = 2.66; 95% CI: 1.44-4.91; p = 0.002), fueron factores asociados a mayor probabilidad de presentación avanzada del CCR. **Conclusiones:** Pacientes con nivel socioeconómico bajo, aquellos que acuden sintomáticos, y los que requieren de inicio cirugía de urgencia, fueron factores asociados a cCR. Se requieren intervenciones especiales para mejorar el acceso a un diagnóstico temprano y oportuno en estos grupos poblacionales.

Palabras clave: Cáncer colorrectal. Factores socioeconómicos. Cáncer colorrectal avanzado. Disparidades en acceso a la salud.

 \*Correspondence:
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 Mario Trejo-Avila
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## Introduction

Colorectal cancer (CRC) is one of the most commonly diagnosed cancer in the world, representing the third most common cancer worldwide, and ranks second in terms of mortality<sup>1,2</sup>. Thus, there is a need to constantly improve screening programs and treatment outcomes of patients with CRC.

Regardless of the advances in screening strategies, chemotherapy, radiation therapies, and advanced surgical techniques, socioeconomic inequalities persist in cancer incidence, morbidity, mortality, and survival<sup>3-6</sup>. Socioeconomic status is considered a surrogate for the capacity of patients to seek and obtain appropriate medical treatment<sup>7</sup>. Social disparities in cancer incidence may be related to socioeconomic and demographic differences in cancer-related risk factors and behaviors<sup>3,8-11</sup>. Disparities in health care access and use, particularly in preventive services, may contribute to differentials in cancer stage distributions and prognosis<sup>3,6,12</sup>. Some previous studies have explored the relationships between race or ethnicity and socioeconomic status on the outcomes in CRC, mainly related to the decreased access to care<sup>2,6,7,13,14</sup>. In a previous study, rectal cancer patients with high socioeconomic factors had better survival, with almost a 4-year difference in median overall survival between the highest and lowest socioeconomic groups7.

Despite the fact that socioeconomic, demographic or ethnicity status have been previously explored in several articles, all the data come from developed countries<sup>2,3,7</sup>. Furthermore, the literature is more robust on outcome differences between African American and Caucasian patients<sup>2,13</sup>. The impact of those factors in underdeveloped or developing countries has not been widely studied.

In Mexico, it is estimated that nearly 70% of cancer cases are diagnosed in advanced stages<sup>15,16</sup>. Mexico does not have a single coordinating body for cancer prevention, there is no federal program for screening colonoscopy, no national policy nor a national cancer registry exists, and there are no complete and accurate data on the extent and social impact of CRC<sup>15</sup>.

The aim of the study was to assess the socioeconomic and demographic factors associated with advanced CRC presentation at a single center in a developing country.

### Methods

From January 2008 to January 2018, patients that underwent CRC surgery at Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán" in Mexico City, Mexico, were included in the study. Data for these patients were retrospectively retrieved and analyzed from the hospital medical records. Patients with incomplete data were excluded from the study.

Socioeconomic and demographic factors included in the study were as follows: Sex, age, presence of other comorbidities and previous diagnosis of another cancer, family history of cancer (first- and seconddegree relatives with any type of cancer), socioeconomic status divided in low, mid, and high (as determined by our social workers), marital status (single, married, divorced and widowed), place of residence (urban or rural), educational level (illiterate, literate, college, and above), and religion (catholic, muslim, jew, or others). The socioeconomic status was determined by the social workers of our institution and was calculated according with: mean familiar income, number of individuals depending on that income, mean monthly expense, employment status, and housing characteristics. Patients in our hospital do not have health insurance. Urban residency was considered when living in a place with more than 2500 inhabitants<sup>17</sup>. Rural residency was considered when living in a place with < 2500 inhabitants, and places located outside capital cities. Education level was divided in illiterate (patients unable to read or write), literate (we include in this definition to patients who read and write, and patients who had pre-college studies), and college (patients with university studies or more).

CRC diagnosis was confirmed with histology of the primary site (either with colonoscopy or after surgical resection). Staging evaluation included thoracic computed tomography (CT) scan, contrast-enhanced abdominal-pelvic CT scan, colonoscopic evaluation as required, carcinoembryonic antigen, and pelvic magnetic resonance for rectal cancer. CRC was categorized as localized (Stages I and II), and advanced (Stages III and IV). The stage at presentation was considered either during first clinical appointment or during emergency department consultation.

Factors associated with CRC diagnosis analyzed in the study were as follows: diagnosis of CRC by screening colonoscopy, initial symptoms related to CRC (patients debuting with: bleeding, weight loss, obstruction, perforation, anemia, abdominal pain, and change in bowel habits), colon cancer location (right, transverse, or left colon), and rectal cancer location (high, mid, or low rectum). Obstructing symptoms included those presenting with partial and total malignant obstruction. Symptoms of perforation included those of acute abdomen and peritonitis. Diagnosis by screening colonoscopy was considered when the recommendations of international guidelines were followed<sup>18</sup>.

Patients that underwent emergent surgical resection and that resulted in CRC diagnosis were also included in the study. Clinical stage was determined according with the American Joint Committee on Cancer (AJCC) Cancer Staging Manual eight edition and expressed as tumor, nodes, and metastasis<sup>19</sup>.

## Statistical analysis

All data were collected retrospectively in a digital database. Patients were divided in two groups depending on their clinical stage at presentation: Stages I and II (early CRC: E-CRC) and Stage III-IV (advanced-CRC: A-CRC). Categorical data were presented as totals (n) and proportions as percentages. Categorical data were compared using the Chi-square test or Fisher exact test (analyzing patients in two groups: E-CRC vs. L-CRC groups). All tests were two-sided and used an alpha of 0.05. Univariate binomial logistic regression analysis was performed. All variables with p-value inferior to 0.05 in the univariate analysis were considered as potential risk factors (predictors of advanced CRC presentation) and were entered manually into the multivariate forward logistic regression analysis. The variables representing the lowest risk for advanced CRC presentation were considered to be the reference group (odds ratio [OR] = 1.0). OR and 95% confidence intervals (95% CI) were calculated. Models were checked for goodness of fit using the Hosmer-Lemeshow test. Subgroup analysis examining the interaction between socioeconomic factors and stage at presentation, as well as symptoms at presentation and CRC stage, were performed. All p-values were two-tailed, and p < 0.05 was considered to be statistically significant. All data were analyzed using the Statistical Package for the Social Sciences Version 22.0 (IBM Corporation, Armonk, New York, NY).

## **Results**

A total of 277 patients who fulfill the inclusion criteria were analyzed in our study. Based on their clinical stage at presentation, 129 (46.5%) patients were included in the early CRC group (E-CRC), and 148 (53.5%) were included in the advanced CRC group (A-CRC). No differences were found on regard of sex and age at presentation between both groups. Table 1 describes the different socioeconomic factors

Table 1	. Patient	demographics	and	clinical	features
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Factors	Stage I-II (n = 129)	Stage III-IV (n = 148)	p < 0.05
Sex, n (%)	. ,	. ,	0.985
Female	60 (46.5)	69 (46.6)	
Male	69 (53.5)	79 (53.4)	
Age groups, n (%)	00 (15 5)	07 (10.0)	0.108
< 50 50-70	20 (15.5) 55 (42.6)	27 (18.2)	
> 70	53 (42.0) 54 (41.9)	77 (52) 44 (29.7)	
Other comorbidities, n (%)	01(11.0)	11(20.1)	0.362
Yes	92 (71.3)	98 (66.2)	
No	37 (28.7)	50 (33.8)	
Other malignancy, n (%)	04 (40 0)	00 (110)	0.746
Yes No	21 (16.3) 108 (83.7)	22 (14.9) 126 (85.1)	
Family history of cancer, n (%)	100 (03.7)	120 (00.1)	0.009
Yes	55 (42.6)	41 (27.7)	0.000
No	74 (57.4)	107 (72.3)	
Socioeconomic status, n (%)			0.028
Low	44 (34.1)	70 (47.3)	
Mid	68 (52.7)	69 (46.6)	
High Marital status, n (%)	17 (13.2)	9 (6.1)	0.446
Single	23 (17.8)	35 (23.6)	0.440
Married	70 (54.3)	76 (51.4)	
Divorced	12 (9.3)	17 (11.5)	
Widowed	24 (18.6)	20 (13.5)	
Place of residence, n (%)	4.04 (00.0)	100 (70)	0.004
Urban Rural	121 (93.8) 8 (6.2)	108 (73) 40 (27)	<0.001
Education level, n (%)	0 (0.2)	40 (27)	0.040
Illiterate	4 (3.1)	14 (9.5)	0.040
Literate	113 (87.6)	127 (85.8)	
College	12 (9.3)	7 (4.7)	
Religion, n (%)	/==		0.325
Yes	114 (88.4)	136 (91.9)	
No	15 (11.6)	12 (8.1)	
Diagnosed by screening			0.268
colonoscopy, n (%)	a (a a)	5 (0, 1)	
Yes No	8 (6.2)	5 (3.4) 143 (96.6)	
Initial symptoms, n (%)	121 (93.8)	143 (90.0)	
Bleeding	68 (52.7)	98 (66.2)	0.022
Weight loss	70 (54.3)	102 (68.9)	0.012
Obstruction	19 (14.7)	37 (25)	0.034
Perforation	2 (1.6)	12 (8.1)	0.013
Anemia Okasasi kasasi kasi	63 (48.8)	76 (51.4)	0.676
Change in bowel habit Pain	89 (69) 72 (55.8)	108 (73) 92 (62.2)	0.466 0.284
Colorectal tumor site, n (%)	12 (00.0)	52 (02.2)	0.029
Right colon	54 (41.9)	52 (35.1)	0.020
Transverse	8 (6.2)	5 (3.4)	
Left colon	43 (33.3)	38 (25.7)	
Rectum	23 (17.8)	50 (33.8)	
Synchronic Rectal cancer location in (%)	1 (0.8)	3 (2)	0.010
Rectal cancer location, n (%) High rectum	6 (4.7)	4 (2.7)	0.019
Mid rectum	6 (4.7)	29 (19.6)	
Low rectum	11 (8.5)	17 (11.5)	
Emergency surgery, n (%)	. ,		0.005
Yes	3 (2.3)	16 (10.8)	2.000
No	126 (97.7)	132 (89.2)	

Factors	Univariate ana	alysis	Multivariate logistic regression		
	Unadjusted OR (95% CI)	p value	Adjusted OR (95% CI)	p value	
SE status					
High	1 (Reference)				
Mid	1.91 (0.79-4.59)	0.145			
Low	3.00 (1.23-7.33)	0.016			
amily history of cancer		0.010			
Yes	1 (Reference)				
No	1.94 (1.17-3.20)				
Place of residence				< 0.001	
Urban	1 (Reference)		1.00		
Rural	5.60 (2.51-12.49)	< 0.001	5.25 (2.27-12.10)		
Education level					
College	1 (Reference)				
Literate	1.92 (0.73-5.06)	0.183			
Illiterate	6.00 (1.40-25.58)	0.015			
Bleeding	1.75 (1.08-2.85)	0.023			
Weight loss	1.86 (1.14-3.05)	0.013	2.33 (1.35-4.09)	0.002	
Dbstruction	1.93 (1.05-3.56)	0.035			
Perforation	5.60 (1.23-25.52)	0.026			
Emergency Surgery				0.022	
No	1 (Reference)		1.00		
Yes	5.09 (1.44-17.89)	0.011	4.68 (1.25-17.49)		
CRC Tumor site				0.002	
Colon	1 (Reference)	0.003	1.00		
Rectum	2.35 (1.33-4.13)		2.66 (1.44-4.91)		
Rectal cancer location					
High rectum	1 (Reference)		1.00		
Mid rectum	5.22 (2.08-13.13)	< 0.001	6.10 (2.31-16.12)	< 0.001	
Low rectum	1.67 (0.74-3.74)	0.212	0.89 (0.23-3.44)	0.877	

SE: socioeconomic. For multivariable logistic regression analysis odds ratio (OR) and 95% confidence interval (CI) are presented. Odds ratios are calculated for CRC late stage presentation. Only significant results are shown. The reference category has an odds ratio of 1.00. Backward conditional. CRC: colorectal cancer.

evaluated in the study and their association to the stage at diagnosis.

In the unadjusted analyses (Table 2), low socioeconomic status, no history of cancer in the family members, living in a rural area, being illiterate, presenting with bleeding, weight loss, obstruction, and perforation, the surgery performed as an emergency, and tumor located in the mid rectum were associated with advanced CRC presentation. The multivariate logistic regression analysis identified five independent risk factors for advanced CRC presentation: living in a rural area (OR = 5.25; 95% CI: 2.27-12-10; p < 0.001), presenting with weight loss (OR = 2.33; 95% CI: 1.35-4.09; p = 0.002), the CRC surgery performed as an emergency (OR = 4.68; 95% CI: 1.25-17.49; p = 0.022), location in the rectum in comparison with colon (OR = 2.66; 95% CI: 1.44-4.91; p = 0.002), and location in the mid rectum (OR = 6.10; 95% CI: 2.31-16.12; p < 0.001).

In the subgroup analysis combining the effect of only the socioeconomic factors (Table 3), multivariate analysis identified two independent risk factors for advanced CRC presentation: living in a rural area (OR = 5.28; 95% Cl 2.35-11.84; p < 0.001) and no history of cancer in the family members (OR = 1.77; 95% Cl: 1.05-2.97; p = 0.031).

When only the symptoms at presentation were combined (Table 4), the multivariate analysis revealed that presenting with bleeding (OR = 1.93; 95% CI: 1.16-3.21; p = 0.010), weight loss (OR = 1.97; 95% CI: 1.19-3.28; p = 0.008), and signs of perforation (OR = 8.05; 95% CI: 1.68-38.39; p = 0.009) were independent risk factors for advanced CRC.

Socioeconomic factors	Multivariate logistic regression			
	Adjusted OR	95% CI	p value	
Income status				
High	1 (Reference)			
Mid	1.78	0.65-4.83	0.258	
Low	4.11	0.89-18.86	0.069	
Place of residence			< 0.001	
Urban	1 (Reference)			
Rural	5.28	2.35-11.84		
Education level				
College	1 (Reference)			
Literate	1.78	0.65-4.83	0.258	
Illiterate	4.11	0.89-18.86	0.069	
Family history of cancer			0.031	
Yes	1 (Reference)			
No	1.77	1.05-2.97		

Table 3. Subgroup analysis: Combined effect of socioeconomic factors on late stage CRC at presentation

For multivariable logistic regression analysis odds ratio (OR) and 95% confidence interval (CI) are presented. Odds ratios are calculated for CRC late stage presentation. Only significant results are shown. The reference category has an odds ratio of 1.00. CRC: colorectal cancer.

Table 4. Subgroup analysis: Combined effect of debuting symptoms on late stage CRC at presentation

Multivariate logistic regression				
Symptoms at presentation	Adjusted OR	95% CI	p value	
Bleeding	1.93	1.16-3.21	0.010	
Weight loss	1.97	1.19-3.28	0.008	
Obstruction	1.88	0.99-3.56	0.053	
Perforation	8.05	1.68-38.39	0.009	

For multivariable logistic regression analysis odds ratio (OR) and 95% confidence interval (CI) are presented. Odds ratios are calculated for CRC late stage presentation. Only significant results are shown. The reference category has an odds ratio of 1.00. CRC: colorectal cancer.

## Discussion

In our study, 53.5% of CRC cases were diagnosed at an advanced stage. We found that patients with the lower socioeconomic status, living in a rural area, illiteracy, not having family members with history of cancer, as well as patients consulting with symptoms (bleeding, weight loss, obstruction, and perforation), needing emergency surgery, and tumors located in the mid rectum, were associated with advanced CRC stage at presentation. The findings of this study are concordant with the patterns identified in previously published studies<sup>2,3,5,7</sup>. Socioeconomic, racial, and demographic disparities in the survival of patients with CRC have been documented in the previous publications<sup>2,9-11,20</sup>. These disparities may be attributed to many factors including differences in socioeconomic status, disease stage at diagnosis, tumor biology, screening programs, access to care, quality of care, and post-treatment surveillance<sup>9-11,20</sup>. In a 2014 systematic review<sup>2</sup>, the impact of socioeconomic status on incidence, mortality, and survival of CRC patients was analyzed. They included 62 studies, being the majority from the USA and Europe, and only 1 study from South America (Puerto Rico)<sup>2,21</sup>. This reflects the lack of data from developing countries.

Authors from developed countries have suggested that a substantial proportion of the socioeconomic disparity of new onset CRC may be attributable to the higher prevalence of adverse health behaviors on low socioeconomic status populations<sup>2,22</sup>. We believe that the conclusions from other studies are not applicable to underdeveloped countries, because there is more social inequity, more poverty, less appropriate healthcare services, less educational level, as well as different patterns of risk behaviors. This highlights the importance of our results.

The previous studies have shown that the diagnostic interval (time from presentation with symptoms to diagnosis) is inversely related to survival<sup>23,24</sup>, the socalled "waiting time paradox." This paradox refers to a scenario, in which patients with shorter diagnostic interval have more advanced disease and poorer outcomes<sup>23</sup>. Although we did not have data to estimate the diagnostic interval, we found that patients presenting with symptomatic disease (bleeding, weight loss, obstruction and perforation) were associated with advanced CRC stages. This seems related to the fact that most patients with CRC are diagnosed after presentation with symptoms<sup>23,25</sup>.

Asymptomatic patients are usually diagnosed with CRC screening programs and generally had earlier and more treatable disease<sup>5,25</sup>. In the USA, approximately 34-59% of Americans for whom screening is recommended undergo recommended CRC screening<sup>25,26</sup>. Unfortunately, we found in our study an alarmingly low rate of cancer detected by screening colonoscopy (overall 4.7%). Under this scenario, we should remark that there is no mass population screening strategy for CRC in Mexico. As previously stated, the Mexican health system has serious deficiencies in its physical infrastructure and medical personnel that will be difficult to amend in the short term<sup>15</sup>.

An estimated 15% of CRCs present as a surgical emergency in the USA<sup>25,27</sup>. We found in our cohort an overall 6.8% (E-CRC 2.3% vs. A-CRC 10.8%) of patients presenting as a surgical emergency. Despite the number of patients that required emergency surgery in our cohort is lower than that reported in the USA, this could be the result of a selection or information bias in our study.

Although this study provides some evidence that lower socioeconomic status and some demographic factors are associated with advanced CRC stages, due to the nature of the study, it could not be possible to generalize the results to a national population. The fact that this study is based on retrospective data from a single center predispose to several bias (selection bias, information bias) inherent to the design. It is important to consider that there is a lack of a uniform set of indices for measuring socioeconomic status<sup>2</sup>, so the comparability between this and other studies may be compromised. This is also true for comparisons between larger studies in developed countries.

A large population-based study could provide more data about the social, demographic, and economical factors related to late CRC presentation in developing countries. Unfortunately, nation-wide databases or CRC registries are not available in our country<sup>15,28</sup>. The implementation of a national cancer registry program is of utmost importance to understand the detailed burden of cancer in our country<sup>28,29</sup>.

Despite these limitations, our results add to the published literature that in a developing country patients living in rural areas, with low socioeconomic and educational status, those needing an emergency surgery, and those presenting with symptomatic disease were associated with higher risk of advanced CRC stage presentation. Although we found some associations with advanced CRC presentation, more research is needed to determine the causal factors underlying socioeconomic and demographic risk gradients in our institution and in our country. Special focus to these vulnerable groups should conduce to health care improving policies and reduction in disparities in cancer care access and outcomes. There are several strategies that could be recommended to reduce the risk of CRC in vulnerable populations. One strategy is to perform massive screening programs in rural areas either by FIT test (fecal immunochemical test) or rectosigmoidoscopy. Other strategy is creating educational programs with massive diffusion to inform about the risks of CRC and the importance of scrutiny in rural and urban areas. A complementary strategy is to improve the primary prevention with lifestyle habits modifications, avoiding alcohol and smoking, take control of the weight (reducing obesity), and improve eating habits. Focusing in screening programs and primary prevention instead of building costly third level hospitals or paying expensive surgeries and chemoradiation should be considered as a cost-effective alternative to this problem.

#### Conclusions

In our study, patients with features related to lower socioeconomic status (low status, rural residence, and illiteracy), as well as patients consulting with symptoms and needing emergency surgery (history of bleeding, weight loss, obstruction, and perforation), were associated with higher odds of advanced CRC stage at presentation. Special interventions to improve access to care in this population should be planned and executed to enhance CRC outcomes.

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## Conflicts of interest

The authors declare that they have no conflicts of interest.

#### Ethical disclosures

**Protection of human and animal subjects.** The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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