

Early Onset Colorectal Cancer: A Major Health Problem



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Introduction

Colorectal cancer (CRC) was long considered a disease of aging population. Incidence is now declining in individuals above 50, while it is actually sharply rising below 50. The cut-off age for early-onset colorectal cancer (EOCRC) is not well defined, ranging between < 40 and < 50 , but generally most data available rose from research using the value of 40, except data from USA. Reports earlier in this century reported that 2-10% of all colorectal cancers are young patients [1,2] Colorectal cancer incidence trends were analyzed from data provided by the Surveillance, Epidemiology, and End Results (SEER) program registries of 490,305 people aged 20 and older diagnosed with colon or rectal cancer from 1974 to 2013 [3].

Among adults between the ages of 20 and 39, colon cancer rates increased by 1% to 2.4% annually since the mid-1980's. Rectal cancer incidence rates among adults in their 20s have risen even more sharply, increasing by 3.2% per year from 1974 to 2013. Based on SEER data, a predictive model was set suggesting that if the observed trends persist between 2010 and 2030, the incidences of colon cancer and of rectal/rectosigmoid cancer will rise by 90% and 124%, respectively among 20- to 34-year-olds, and by 28% and 46%, respectively, among 35- to 49-year-olds. An analysis of the "Cancer Incidence in Five Continents" database shows an increase in CRC incidence in resource-constrained countries, with a significantly higher proportion of early-onset cancers [4].

Data from other highly populated resource-constrained countries in Asia and Africa, such as Nepal [5], Pakistan [6], Taiwan [7], Jordan [8], Singapor [9], Bangladesh [10], and Nigeria [11] reveal also high patterns of incidence. Also reports from Middle-Eastern area show higher CRC rates in younger patients than in the West. CRC was diagnosed in patients aged 40 years or younger in 17-36% in Saudi Arabia, Sudan and Iran [12-16]. In Egypt reports showed that CRC was diagnosed in 25-38% of patients aged 40 years or younger [17-23].

It was found that the increase in incidence among young was predominantly driven by distal colon especially rectal, and it is predominantly mucinous type, poorly differentiated, many with signet ring features, and advanced stage at diagnosis. Prognosis of early onset CRC in literature has contradictory results, but in general, better 5 years survival rates in Duke's A and B, and worse prognosis for advanced/ metastatic disease. Etiology of EOCRC is not yet well known. It could be genetic, behavioral, environmental, or all of them. Little data about the genetic and epigenetic alterations in CRC from resource-constrained countries, but -in general- based on the literature available, it was found that MSI and BRAF mutations were uncommon and seen in 5.0% and 2.5% , respectively, high frequencies of overall KRAS mutations (67.5%), higher codon 15 and 18 KRAS mutations versus codon 12 and 13 in West, while only 54.6% of cases exhibited substantial b-catenin nuclear localization in contrast to 80%-100% reported in the Western literature.

Regarding hereditary syndromes, like Lynch, FAP, attenuated FAP, more than 75% of EOCRC don't have family history, and are not a member of hereditary syndrome. In addition, Lynch syndrome is predominantly on the right side. The results of Abou-Zeid et al. [23] who conducted a 7 years review to CRC patients at Ain Shams surgical department, Cairo, Egypt, showed that 38% of the tumors occurred in patients aged less than 40 years (highest incidence of EOCRC in Egypt). The authors observed that the high prevalence in young population couldn't be explained on a hereditary basis or be attributed to bilharziasis, and that the disease was usually presented at an advanced stage, and that predisposing adenomas were rare [23].

Two meta-analyses with data from 16 and 37 studies showed a 10-fold [24] and 6-fold [25] higher risk of CRC with human papilloma virus (HPV) positivity, respectively. More specifically, HPV prevalence varied by geographical region, with the highest prevalence in South America, followed by Asia and the Middle

East, suggesting a possible correlation linking high-risk sexual behavior, lifestyle, and HPV infection with CRC rates in resource-constrained countries [26]. Laskar et al. [26] detected HPV DNA in 31.2% of patients with RC in their study, of which 76% had HPV subtype 18, 8% had subtype 16, 8% had both subtypes 16 and 18, and 8% had subtypes other than 18 and 16. Many other environmental factors could be involved in the etiology of EOCRC, among of which are: chlorinated water, dumping sites for industrial wastes with subsequent soil and water pollution, and occupational exposures.

A recent review suggests that occupational exposures increase the risk of CRC by 11%-15% among laborers working in leather, basic metals, plastic, and rubber-manufacturing industries, including workers in the sector of repair and installation of machinery who are exposed to asbestos [27]. Regarding pesticide pollution of food, an epidemiologic correlation study was conducted, investigators from Egypt reported a high incidence of young-onset CRC, with over a third of patients younger than age 40 with a rectal preponderance, and noted a substantially elevated risk in people with pesticide exposures (odds ratio [OR] = 2.6) and in agricultural workers who ate food items from the field for half the time or more (OR = 4.6) [28].

Other known risk factors for CRC like obesity, diabetes, inflammatory bowel disease, decrease in milk consumption, lack of exercise, consumption of high fat, more red meat, processed meat, alcohol, smoking were not well studied in this subpopulation. Current research is also exploring association between CRC and variations in gut microbiome, and changing patterns in the use of statins and antibiotics during the past decades. Immediate attention is needed. Without increased research and education, EOCRC will become a major health problem in the very near future.

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