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Demographic, histopathological and staging analysis of colorectal carcinomas in a Tertiary Care Hospital, Mumbai

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Abstract

Background: Carcinoma of the colon and rectum is a relatively uncommon malignancy in India when compared with the western world. Colorectal cancer is generally a disease affecting individuals 50 years of age and older and is much less common in persons under 40 years of age.

Aims: To study relative frequency of colonic carcinoma with regard to demographic data, histological types and pathologic stages.

Materials and methods: We studied total of 409 colorectal carcinomas (CRC), diagnosed during the past 15 years i.e., from January 2001 to December 2015. The records were analysed in detail for age, gender, site of primary tumour, histopathological type, and pathological stage.

Results: Four hundred and nine patients were diagnosed to have CRC. Majority were males (54.77%), rectum was commonest site (57.7%). Most of them were adenocarcinoma (54.52%) followed by mucin-secreting adenocarcinomas (22.49%) and squamous cell carcinoma in 9.29%. Most of them presented at IIB stage (40.09%). Patients less than 40 years (30.81%) showed less favourable histology and higher grade of tumor.

Conclusions: In CRC, rectal cancers are the most common cancers. Incidence of CRC in young is increasing. Screening for colorectal cancers and early evaluation of symptomatic cases need to be defined in developing countries.

Keywords: Adenocarcinoma, Colorectal carcinoma, Demography, Young age

Introduction

Worldwide, colorectal cancers are the third most common cancers and the third leading cause of cancer related death, contributing 8.9% of all cancers in both males and females.(1) Incidence of varies widely with higher incidence rates in North America, Australia and Europe(2). Developing countries have lower rates; particularly Africa and Asia.(3)

In India, the annual incidence rates (AARS) for colon cancer and rectal cancer in men are 4.4 and 4.1 per 100000, respectively. In the 2013 ICMR report, the highest AAR in men for CRCs was recorded in Thiruvananthapuram (4.1) followed by Bangalore (3.9) and Mumbai (3.7)(4) per 100000. Generally, cancer incidence and mortality rates have been higher in economically advantaged countries(5). This may be related to consumption of a high-fat and high red meat diet, lack of physical activity with resulting obesity, and variations in mortality causes over a longitudinal period of time.(6)

Material and Methods

This study was conducted in the department of pathology of one of major tertiary care hospital, Mumbai, India. Histopathological records of all cases of malignant colorectal tumour which were received and diagnosed during last 15 years i.e., from January 2001 to December 2015 were studied. The demographic information, such as age and gender and site of primary tumour were noted. The anatomical location of the malignancy noted was as cecum, ascending colon, hepatic flexure, transverse colon, splenic flexure to sigmoid colon and rectum. Then, four major anatomic sites of the tumours were recognized, namely: (1) the right colon including the cecum, ascending colon and hepatic flexure, (2) the transverse colon, (3) the left colon including the descending colon, splenic flexure and the sigmoid colon and finally (4) the rectum. All the slides had been routinely stained with H & E. The slides of all patients with CRC were reviewed for typing of malignancy and pathologic staging. The carcinoma was staged according to the AJCC staging system. Only carcinomas were included in the study. Clinical details were obtained from case records.

Results

There were 409 patients with colorectal cancer in total 15 year period. The age group varied from 14 to 78 years with a mean age of 51 years for males and 49 years for females. The commonest age group affected is 51-60 years, followed by 61-70 years in our study. Less than 40 years age group constituted 30.81% of the cases (126 patients). Five of which were diagnosed in the paediatric (defined as <18 years) age group.

Below 40 years, female predominance was seen (56.35%), while male predominance was seen in patients above 40 years (59.72%). Of the 409 cases, 224

(54.77%) were males and 185 (45.23%) were females, with a male to female ratio of 1.21:1. [Fig. 1]

On comparison of community wise distribution of cases, it was seen that majority of patients belong to Hindu community (79.46%) followed by Muslims (17.68%) and Christians (0.93%). Comparing diet wise distribution of colorectal carcinomas, it was found that the majority of population affected were non vegetarians, accounting for 68.95% of all cases. While vegetarians were 31.05% of total patients. [Table 1]

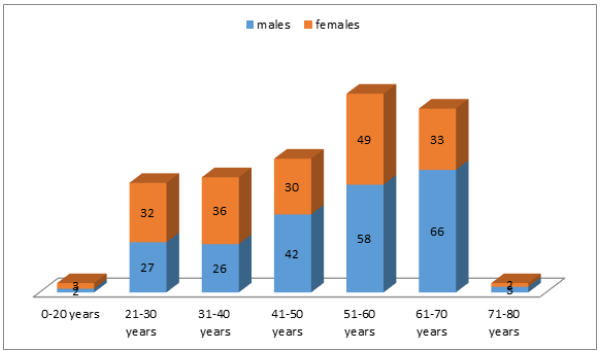

Fig. 1: Age wise & Sex wise Comparison of CRC

Table 1: Incidence of CRC with respect to community & diet

	Community			Diet	
	Hindu	Muslim	Christian	Veg	Non veg
No	325	72	12	127	282
%	79.46	17.6	2.94	31.05	68.95

We studied the location of tumour. The majority of tumours, 236 (57.70%) occurred within the rectum and anal canal, and 173 involving colon. Rectal carcinomas mainly involved lower and middle rectum. In colon cancers, most commonly involved is sigmoid colon in 48 cases (11.74%) followed by cecum with 43 cases (10.51%). Thus in colonic cancers overall, right colon (caecum, ascending colon, hepatic flexure) was more commonly involved in 86 cases than left colon (splenic flexure, descending colon and sigmoid colon) 65 cases. Transverse colon was involved in 22 cases. [Table 2]

Table 2: Distribution of Different morphological types of colorectal carcinomas

	Adeno Ca	**Mucinous Ca**	**Signet Ring**	**Adenosq**	**Sq**	**Melanoma**	**Basaloid**	**Carcinoid**	**NHL**	**Mets**	**No**	**%**	
Caecum	11	7	0	0	2	0	0	0	1	1	43	10.52	Right sided = 86 (21.03%)
Asc colon	7	11	0	0	0	0	0	1	1	2	39	9.58	
Hep flx	2	1	1	0	0	0	0	0	0	0	4	0.93	
Trans col	5	5	0	0	0	0	0	0	0	2	22	5.26	22 (5.26%)
Spln flx	3	2	0	0	0	0	0	0	0	0	5	1.5	Left sided= 65 (15.89%)
Desc col	4	5	0	0	0	0	0	0	0	0	12	2.81	
Sigm col	20	6	0	0	0	0	0	0	0	0	48	11.66	
Rectum & Anal canal	66	33	16	1	2	3	2	0	1	0	236	57.74	236 (57.74%)
Total	223	92	10	2	48	6	4	5	14	5	409 (100 %)		
%	54.52	22.49	7.34	0.49	9.29	1.47	0.98	1.22	3.42	1.71			

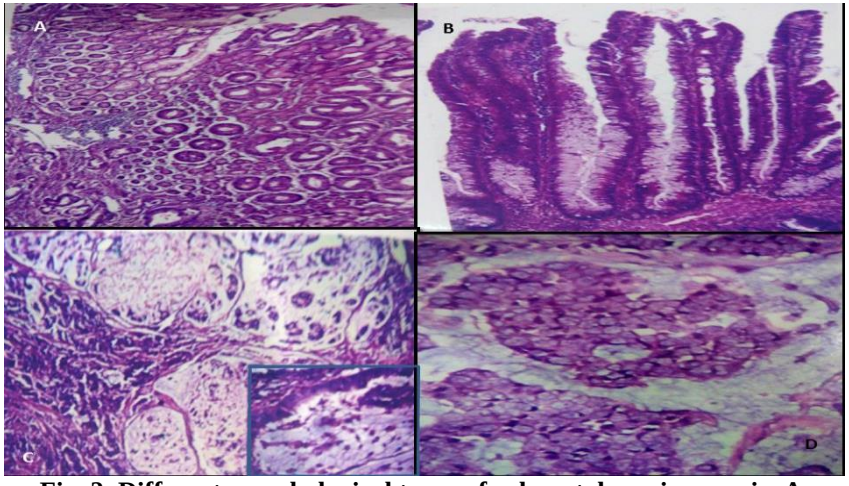

Fig. 2: **Different morphological types of colorectal carcinoma viz. A. Adenocarcinoma B. Papillary adenocarcinoma, C. Mucinous carcinoma & D. Signet ring carcinoma**

The duration of symptoms at presentation ranged from 2 weeks to 1 year with mean duration of 6 months. The most common symptom of CRC was abdominal pain (33.5%) followed by bleeding per rectum in 15.5% of the patients. Other symptoms were altered bowel habits, weight loss, palpable mass in 12, 10 & 10.4% of cases respectively. In right sided, the most common presenting signs and symptoms were abdominal pain and palpable mass followed by altered bowel habits and bleeding per rectum (PR). While in left colon, common signs symptoms were bleeding PR and altered bowel habits.

Most common gross morphological type was ulceroproliferative (56.77%) followed by exophytic type (24.32%) and annular type (18.91%). There was no much difference of gross morphology of tumour when compared location, as cecum, rectum, anal canal, hepatic & splenic flexure, all showed ulceroproliferative type most commonly followed by exophytic one. But in descending colon, annular type of growth (66.68%) superseded the ulceroproliferative and exophytic type (16.66% each).

Histopathological examination showed majority of tumours to be adenocarcinomas (54.52%), followed by mucinous carcinoma (22.49%). Adenocarcinomas were further divided into three grades. In our study, 40.46% were moderately differentiated (grade II), 36.74% well differentiated while 22.80% were of poorly differentiated (grade III) histology. Among those above 40 years also majority were having well to moderately differentiated adenocarcinomas. However, among those below 40 years of age, majority had poorly differentiated adenocarcinomas. There were 4 cases of papillary type and 1 case of tubo-papillary type of adenocarcinoma. Two cases were of villous adenoma with invasion of basement membrane and microscopically was well differentiated adenocarcinoma.

The third common histological type encountered was squamous cell carcinoma (11.74%) of all microscopic cases. All cases were found in anal canal, with age range of 42-69 years and equal male female incidence. Bleeding PR, pain and mass lesion was commonest presenting symptoms.

There were 6 cases (1.47%) of malignant melanoma, all found in rectum and anal canal of elderly patients of more than 60 years of age. Other uncommon tumours seen were signet ring carcinoma (7.34%), carcinoid & adenosquamous carcinoma (5 & 4 cases each) and 2 cases of Basaloid carcinoma of anorectal region.

In our study, there were 14 cases of Non-Hodgkin's Lymphoma (NHL), accounting for 3.42% of all tumours. It usually seems to be affecting younger age group of less than 60 years, with 10 males and 4 females. 10 cases presented with polypoidal mass while 4 had exophytic growth. Histologically 10 had diffuse large b cell lymphoma, 1 case of Burkitt's lymphoma, 3 was labelled as NHL only on histology.

There were 5 cases of metastasis, comprising 1.22%. One case was of metastasis from mucin secreting carcinoma, 2 cases each of adenocarcinoma of unknown primary and 2 cases of squamous cell carcinoma from operated cases of carcinoma oesophagus. The age group was 70,60,65,16 & 55 years.

Majority of cases in our study belongs to AJCC stage II A (40.09%), followed by stage IIIB (18.05%). The majority of tumours in stage III B, were located on the right side of the colon. When we compared patients who were above 40 years of age to those who were under 40 years of age, higher pathological t stage with more advanced n stage was seen in the younger age group when compared with patients above 40 years. [Table 3]

Table 3: Comparison of colorectal carcinoma patients below and above 40 years of age

Particulars	Age below 40 yrs.	Age above 40yrs	Total
Adenocarcinomas	(N =100)	(N =123)	223 (54.52)
Well	23 (45.1)	28 (54.9)	51 (22.87)
Moderately	32 (35.6)	58 (64.4)	90 (40.36)
Poorly	45 (54.9)	37 (45.1)	82 (36.77)
Staging AJCC	(N=126)	(N=283)	409
I	09 (7.14)	43 (15.19)	52 (12.72)
IIA	28 (22.22)	136 (48.05)	164 (40.09)
II B	14 (11.11)	20 (7.06)	34 (8.32)
IIIA	2 (1.58)	2 (0.71)	4 (0.98)
IIIB	40 (31.74)	34 (12.01)	74 (18.09)
IIIC	23 (18.25)	40 (14.13)	63 (15.4)
IV	10(7.94)	8(2.83)	18(4.4)

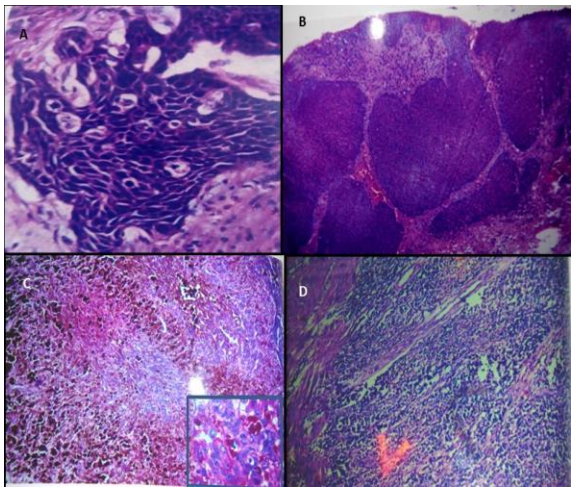

Fig. 3: Other histological types like A. Squamous cell carcinoma, B. Basaloid carcinoma, C. Malignant Melanoma (inset showing nuclear pleomorphism with intra & extra cellular melanin pigment) and D. Non-Hodgkin's Lymphoma

Discussion

Incidence of colorectal cancer varies throughout the world. The incidence of cancers of colon in males and females is 32.9 and 24.4 per 100,000 in us and lowest in Africa and South- Central Asia[8]. The trend is increasing in developed Asian countries like Japan, South Korea and Singapore[9]. Among the Asian population, Singaporeans have higher incidence of colorectal carcinoma than the Malays and Indians[10]. In our study, the incidence of CRC was 5% of overall

malignancies. It was comparable with Goldsbury[11], Goh[12], Leishram[13], Suryadevara[14], Sudarshan[15].

Although changes in dietary habits and lifestyle are believed to be the reasons underlying the increase, the interaction between these factors and genetic characteristics of the Asian populations might also have a pivotal role.[13] Predominance of Hindu population and non-vegetarian diet is also comparable with other studies by Rasool et al[6], Goldsburry et al[11] and Jing Jiang et al.[16] Ganesh et al[17] stated that cabbage; sprout and fresh fish eaters had 40–70% reduction in risk of CRC while 1.6-2.4 fold enhanced risk among those who ate dry fish and meat. Dark-green-leafy-vegetables and 'other vegetables' did not show any protective effect for colorectal cancer in their study. Overall it is a well-known fact that the excess of red meat intake, increased calorie intake and lack of physical activity are potential risk factors for colonic malignancy.[18,19] For decades it has been believed that the predominantly vegetarian diet with high fibre and low meat intake is responsible for the low CRC incidence in India. Finding the factors responsible for the low incidence of CRC in India will help in primary prevention of CRC.[1]

Bleeding per rectum is the commonest presentation, which is in agreement with other studies reported in developing countries.[20,21]

The commonly affected age group in our study was 51-60 years of age. The mean age of presentation was 69 years in the western population, whereas in our study the mean age is around 51 & 49 years, for males and females respectively. The male predominance is in accordance with the many studies.[10] Less than 40 years age group constituted 30.81% of the cases. This was comparable with those reported by Pal et al.,[22] Nath et al.[23] Gupta et al.,[24] and Laskar et al[25] But was higher than those in the Population based cancer registry (PBCR)[15] from in 2004-2005[26] as well as in 2006-2008[27] [Table 4].[15,22,23,24,25,26,27]

Table 4: Demography of colorectal carcinomas compared with population-based studies

Study	No of cases	CRC Incidence	M:F ratio	% of patients <40 years
Ahmedabad[15,26]	21	1.47	2:1	28.57
Banglore[15,26]	379	4.97	1.32:1	14.2
Barshi[15,26]	14	2.76	1:1	21.42
Bhopal[15,26]	79	3.66	1.46:1	15.18
Chennai[15,26]	409	4.34	1.45:1	12.95
Delhi[15,26]	857	3.66	1.43:1	18.90
Delhi[27]	91	--	--	25.9
Mumbai[15,26]	1019	5.15	1.38:1	12.26
Mumbai[27]	793	--	--	14.3
Kolkatta[15,26]	159	4.33	1.18:1	25.15
Kolkatta[27]	102	--	--	30.3
Chattisgharh[15]	233	6.09	1.35:1	39.05
Kashmir[6]	446	--	1.3:1	15.69
Manipur[3]	54	5.6	1.16:1	33.33
Manipur[27]	95	--	--	21.1
Gupta et al, Kolkata[24]	305	--	--	36.00
Nath et al[23]	287	--	--	35.5
Southern East Aasam[27]	144	--	--	48.6
Kamrup[27]	80	--	--	26.2
Dibrugarh[27]	55	--	--	21.7
Mizoram[27]	81	--	--	26
Present study (2016)	409	5	1.13:1	30.81

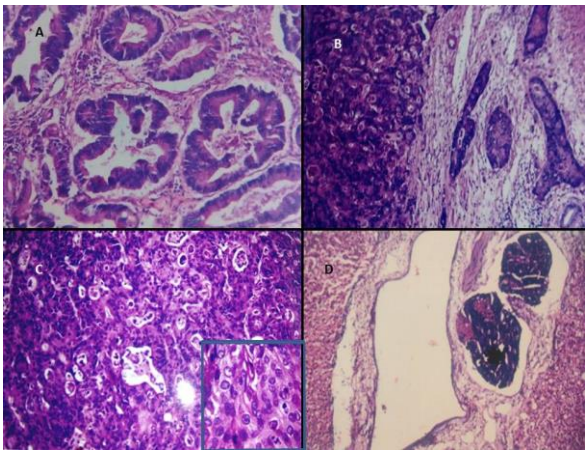

Fig. 4: Histological Grading of adenocarcinoma as A. Well differentiated showing glandular pattern, B. Moderately differentiated infiltrating submucosa, C. Poorly differentiated with no glandular formation, loss of polarity & inset showing nuclear pleomorphism with high mitotic activity and D. Vascular Tumor emboli

Regarding anatomical location of the tumour, rectal cancers predominate than colonic cancers in our study group. In colonic cancers, right sided were commoner than left sided one, which was concordant with west, where right sided colonic tumours predominate. In Indian studies, predominance of rectal cancers can be seen in Suryadevara et al (80%)[14], Leishram (53.71%)[13], while Rasool et al[6], Goh et al (68.5%)[12] and Tarek et al[1] showed predominance of colonic cancers to rectal one. Amongst them, Rasool et al[6], Suryadevara et al[14] and Leishram et al[13] had right sided growth common than left one, while Tarek[1] and Goh et al[12] had left sided colonic cancers as commoner location. [Table 5]

Table 5: Comparative studies about site distribution of colorectal carcinomas

Location	Rasool[6] (n=446)		Suryadevara[14] (n=171)	Tarek[1] (n=215)	Leishram[13] (n=54)	Goh[12] (n=228)	Present study (n=409)	
Caecum	6.28	Right 34.78	Right 10.52	Right 14.9	-	6.9	10.52	Right 21.03
Ascending colon	24.01				Right -22.22	7.3	9.58	
Hepatic flexure	4.49				-	-	0.93	
Transverse colon	2.02			7.9	12.96	6.0	5.26	
Splenic flexure	2.47	Left 23.1	Left- 9.48	Left- 30.2	-	-	1.5	Left 15.97
Descending colon	8.74				Left 11.11	11.3	2.81	
Sigmoid colon	11.89			20	-	32.3	11.66	
Rectum	40.14		80	27	53.71	36.3	57.74	

In Asian countries, for example Japan and Korea, a right-sided shift in the distribution of tumours has been demonstrated.[28,29] the anatomic location of the is tumour is important. The proximal and distal colon has different embryological origins and morphology, and different implications with respect to etiopathogenesis of cancer.[12] The predominantly distal location is of practical significance in the choice of CRC screening methods, where a flexible sigmoidoscopy and faecal occult blood testing may be more cost-effective compared with screening colonoscopy.[30,31]. The higher incidence in our region may also be due to increased adoption of western life style such as increased consumption of foods with little nutritional value and high on calories. Another possible explanation for the increase in incidence of the rectal cancers that we observed could be because of increased availability of colonoscopy for diagnosis.

In accordance with other studies[12,13,14,15,31,32], in our study 54.52% of the colorectal malignancies are adenocarcinomas. Other colorectal malignant pathologies observed in our study group are mucinous carcinomas, squamous cell carcinoma, signet ring carcinomas, lymphoma, and malignant melanoma of the ano-rectal junction. Total of 40.09% of the patients presented at stage IIB and 18.09% stage IIIA.

Advanced stage of presentation with poorly differentiated morphology of tumour was seen in patients less than 40 years of age, which could be attributed to a higher growth rate of colorectal cancer in young patients. Pal et al[22], Nath et al[23], Gupta et al[24] and Laskar et al[25] also reported a proportionate increase in incidence of colorectal cancer at an age below 40 years. Al-Jaberi et al[33] Minardi et al[34] also reported that 68% & 37% of the patients, who presented with colorectal cancers younger than 40 years, already had an advanced stage (C Or D) of CRC compared to those who were above 40 years of age. The concern for colorectal cancer affecting young population below 40 years old was due to the poor prognosis attached to it. [Table 6]

Table 6: Comparison Histological grading & staging of colorectal carcinoma in patients below 40 years of age in various studies

Particulars	Age below 40 yrs. (%)					
	Sudarshan et al[15]	Leishram et al[13]	Gupta et al[24]	Nath et al[23]	Laskar et al[25]	Present study
Total	233	54	305	287	144	409
<40 years	39.05	33.34	39.02	35.5	48	30.81
Histological grading						
Well	8.79	17.64	50	48	22.9	45.1
Moderately	10.98	40			21.4	35.6
Poorly	80.21	41.17	50	52	55.7	54.9
Staging	TNM	Duke's	TNM	TNM	TNM	AJCC
I	28.57	14.28	40	18.9	4.8	7.14
II		21.05			17.7	33.33
III	54.94	57.14	60	62.3	41.9	51.57
IV	16.48	57.14		19.7	35.5	7.94

Patients with familial adenomatous polyposis (FAP) are known to have a greater proportion of right-sided colon lesions, with fewer cancers diagnosed in rectum and microsatellite instability has been identified in most of the patients with early onset of CRC at least some young rectal cancers in India, Suggesting genetic etiology[35]. The Bethesda criterion recommends that all patients who develop CRC before age 45 undergo testing for tumour microsatellite instability to identify individuals at risk for HNPCC (hereditary non-polyposis colorectal cancer)[36].

Conclusion

Incidence of colorectal cancer in Indian older age group is lower than western population. There is increase in incidence younger age CRC and having

distinct clinic-pathological differences with the older patients. As there are no routine screening programmes available for CRC in India, clinicians should give more emphasis on rectal examination by sigmodoscopy or colonoscopy in all patients including younger patients with rectal symptoms. Detailed epidemiological and molecular studies need to be done to identify the aetiology of young age rectal cancer in India.

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