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Original Research Paper

Pathology

A HISTOPATHOLOGICAL STUDY ON COLORECTAL CANCER AT A TERITIARY CARE CENTRE

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ABSTRACT **Background:**Colorectal cancer (CRC) is one of the leading causes of cancer-related mortality worldwide. There are different histopathological variants of CRC that differ in their behaviour and means of management. Therefore, the aim is to study different histopathological types of CRC in relation to age and gender in our hospital. **Methodology:**It is a retrospective and prospective study carried over a period three years from 2019 to 2021. Numberof case files were retrieved and clinical details along with histopathological findings were collected. **Results:** Most patients presented with colonic site tumours constituting 34/50(68%), followed by Rectum and Rectosigmoid representing 15/50(30%) and 1/50(2%) respectively. Adenocarcinoma (AD) was diagnosed in 35/50(70%).The great majority of patients were categorized with moderately differentiated carcinoma representing 14/50(28%), followed by well differentiated and poorly differentiated carcinomas constituting 12/50(24%) and 12/50(24%), respectively. **Conclusion:** Asram medical college patients majority with CRC were of younger and middle age groups and presented with advanced stages of the disease in contrast to Western populations, which presented more frequently in an extra advanced stage in older patients. . Such findings suggest that comprehensive awareness program accompanied by screening program are required to control this disease.

KEYWORDS : Colorectal Cancer; Adenocarcinoma; Colon

INTRODUCTION

Colorectal cancer (CRC) is one of the most common cancers worldwide [1]. CRC ranks third most common cancer in men and the second most common cancer in women [2]. CRC has multifactorial etiology linked to lifestyle, genetic and environmental factors. Although, there are hereditary and non-hereditary CRC types, but the majority is non-hereditary and commonly caused by somatic mutations in response to environmental factors. In the past few years, scientists have concentrated their thoughtfulness on the mechanisms behind these factors and the methods of enhancing disease prevention and treatment [3]. CRC is not a homogenous disease, but can be classified into different subtypes, which are characterized by specific molecular and morphological alterations [4]. Although outcomes of CRC have improved, it is clear that from a genomic standpoint CRC is not one disease, but a heterogeneous group of malignancies that arise within one organ. This means that different subtypes have different outcomes; the ability to subtype tumours in the clinic would be highly favourable, enabling optimal treatment for individual patients [5].

The most common (about ~84 % of sporadic CRC) is characterized by chromosomal instability (CIN), with gross changes in chromosome number and structure. These are often detectable as a high frequency of DNA somatic copy number alterations (SCNA), which are a hallmark of most tumours that arise by the adenoma-carcinoma sequence [4,6]. Previous molecular genetic studies have associated CIN with inactivating mutations or losses in the Adenomatous Polyposis Coli (APC) tumour suppressor gene, which occurs as an early event in the development of neoplasia of the CRC in this sequence. The second group (around 13-16 % of sporadic CRC) are hyper-mutated and show microsatellite instability (MSI) due to defective DNA mismatch repair (MMR), often associated with wild-type TP53 and a near-diploid pattern of chromosomal instability [6,7].

With regard to epidemiology of CRC, countries with the highest incidence rates include Australia, New Zealand, Canada, the United States, and parts of Europe. The countries with the lowest risk include China, India, and parts of Africa and South America [8,9]. This has a major implication for decisions about the threshold age for screening [10]. Therefore, the aim of this study was to determine the different types CRC in relation to age and gender in Asram medical college.

Materials and Methods

This was a descriptive retrospective study conducted in Asram medical college. Sample size represents a full coverage of the available cases with completed required data (including full histopathology report, age, sex etc.). Any patient underwent colonoscopy or/ and biopsy due to the presence of colon lesion for the purpose of diagnosis was included. A total of fifty cases (50) were found to be referring to colonoscopy or/and biopsy. All information of the patients was retrieved from hospital. All fifty (50) patients were confirmed by conventional histopathology. Conventional histopathology was re-assessed. The histological examination of biopsy specimens were done to achieve the assessment process role, by giving a pathology category classification (types of malignant lesions).

RESULTS

This study investigated fifty (50) CRC patients their ages ranging from 20 to 90 years with a mean age of 63 years old.

Out of the 50 patients, 37/50(74%) were males and 13/50 (26%) were females with males to females ratio of 2.84: 1. Most of the study population were found in age range 41-50 years representing 16/50 (32%) followed by age ranges 51-60, less than 40, 61-70 years, 71-80 years & 80+ constituting 12/50(24%), 11/50(22%), 7/50 (14%)&3/50 (6%) and 1/50(2%), respectively as indicated in Table 1,2 & Figure 1. Most of patients presented at age group 41-50 years (32%). The distribution of males and females in each age group was relatively varied. High variations were encountered in age group 41-50 years and <40 years. In age range 41-50 years, the proportions of males and females were 35% and 23% in this order. In age group <40 years, the proportions of males and females were 46% and 13% in this order. The remaining age groups, however, showed relatively similar proportions, as shown in Figure 1.

With regard to the site of the tumour, most of them were upraised in the colon constituting 34/50(68%), followed by Rectum and Rectosigmoid representing 15/50(30%) and 1/50(2%) respectively, as indicated in Table 4. Out of the 34/50(68%) presented with colonic lesions, 25/34 (73.5%) were males and 9/34(26.4%) were females. Of the 15/50(30%) identified in rectum, 11/15 (73.5%) were males and 4/15(26.6%) were females, as indicated in Table 4 Figure 2. Rectosigmoid were 1/50 males (2%), as shown in Table 4 & Figure 2.

On the other hand, Adenocarcinoma (AD) was diagnosed in 35/50(87.5%) of the patients, of whom 27/35(77%) were males and 8/35(23%) were females. AD was the commonest CRC histological type Asram hospital patients. Signet ring cell AD was also diagnosed in 1/50 as indicated in Table 5 & Figure 3.

Table 6, summarizes the distribution of the study subjects by age and pathology. The majority of the patients with colonic site tumors were identified among age group 41-50 years constituting 10/34(29.4%), followed by age ranges 51-60, <40 ,71-80 years and 61-70 years representing 10/34(29.4%), 9/34(26.4%) , 3/34(10.4%) and 2/34 (5.8%) respectively. Most of the cases of rectum site were also found in age group 41-50 years, representing 6/15(40%) followed by 61-70 , <40 years , 51-60 years and 81+,representing 4/15(26.6%)&2/15(13.3%) ,2/15(13.3%) and 1/15(6.6%) respectively. One case of rectosigmoid site was found in age group 61-70 years as indicated in Table 7& Figure 5.

Out of the 35 patients diagnosed with adenocarcinoma, 10/35(28.5%) were identified among age group 51-60, 9/35(25.7%) were found among age group <40 years, 8/35 (22.8%) among 41-50, 5/35 (14.2%) among 61-70 years, in 71-80 years, 2/35 (5.7%) as indicated in Table 7 & Figure 6. Of 12 well differentiated carcinomas , 4/12(33.3%) were found among age groups 51- 60 years, <40 years followed by ages 41-50years and 71-80 years constituting 2/12(16.6%) each, in this order, as shown in Table 7 & Figure 7.

Table 1: Distribution of the study subjects by sex and age

Age Group	Males	Females	Total
<40	5	6	11
41-50	13	3	16
51-60	9	3	12
61-70	6	1	7
71-80	3	0	3
81+	1	0	1
Total	37	13	50

Table 2: Percentage of distribution of the study subjects by sex and age

Age Group	Males		Females		Total
	Number	Percentage	Number	Percentage	
<40	5	13.5	6	46.2	11
41-50	13	35.1	3	23.1	16
51-60	9	24.3	3	23.1	12
61-70	6	16.2	1	7.7	7
71-80	3	8.1	0	0.0	3
81+	1	2.7	0	0.0	1
Total	37	100.0	13	100.0	50

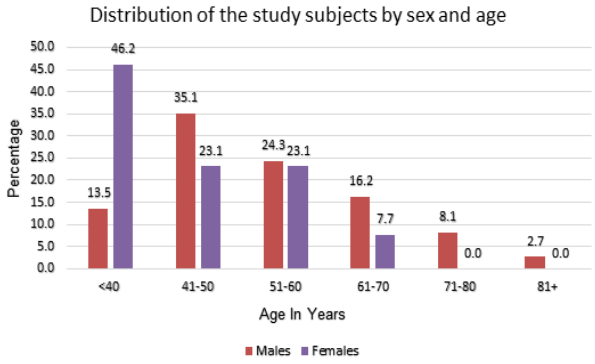

Fig 1: Percentage of distribution of the study subjects by sex and age

Table3: Male to Female ratio

Male	Female	Male: Female
37	13	2.85:1

Table 4: Distribution of the study subjects by sex and pathology

Category	Variable	Males	Females	Total
Tumor Presentation				
	Colon	25	9	34
	Rectum	11	4	15
	Rectosigmoid	1	0	1
	Total	37	13	50
Diagnosis				
	Adenocarcinoma	27	8	35
	AD Signet ring type	1	0	1
	Basaloid Squamous Cell Carcinoma	0	1	1
	Carcinoid tumor	1	0	1
	Adenomas	9	3	12
	Total	38	12	50
Tumor Differentiation				
	Well Differentiated	9	3	12
	Moderately Differentiated	10	4	14
	Poorly Differentiated	9	3	12
	Total	28	10	38

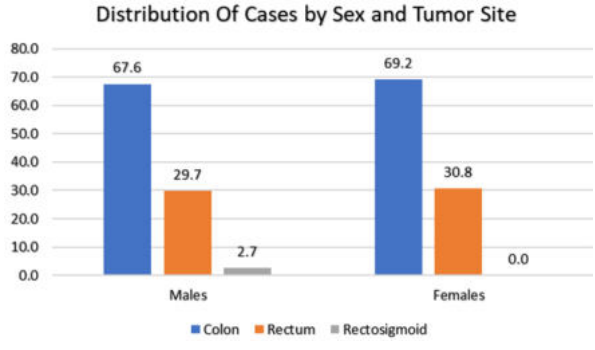

Fig 2: Percentage distribution of the study subjects by sex and pathology

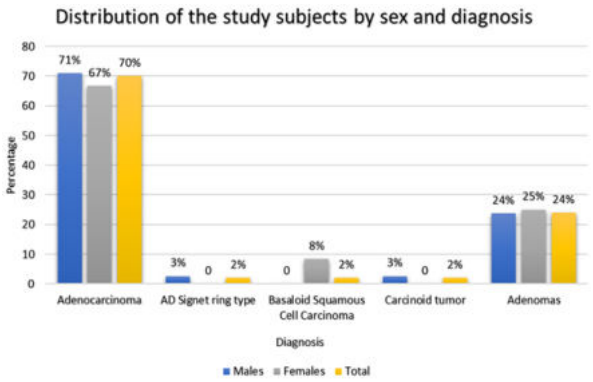

Fig 3: Distribution of the study subjects by sex and diagnosis.

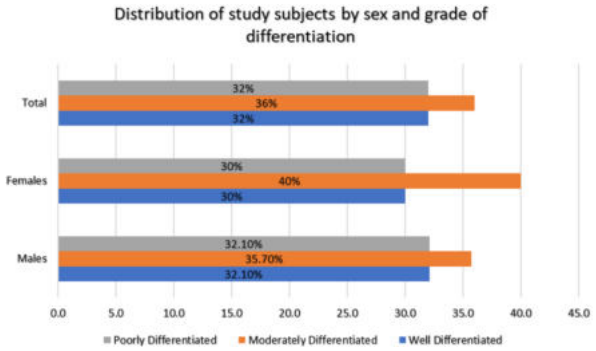

Fig 4: Distribution of study subjects by sex and grade of differentiation

Table 5: Percentage Distribution of the study subjects by sex and pathology

Category	Variable	Males		Females		Total
Tumor Presentation		Number	Percentage	Number	Percentage	
	Colon	25	67.6	9	69.2	34
	Rectum	11	29.7	4	30.8	15
	Rectosigmoid	1	2.7	0	0.0	1
	Total	37	100	13	100	50
Diagnosis						
	Adenocarcinoma	27	71.1	8	66.7	35
	AD Signet ring type	1	2.6	0	0.0	1
	Basaloid Squamous Cell Carcinoma	0	0.0	1	8.3	1
	Carcinoid tumor	1	2.6	0	0.0	1
	Adenomas	9	23.7	3	25.0	12
	Total	38	100	12	100	50
Tumor Differentiation						
	Well Differentiated	9	32.1	3	30	12
	Moderately Differentiated	10	35.7	4	40	14
	Poorly Differentiated	9	32.1	3	30	12
	Total	28	100	10	100	38

Table 6: Distribution of the study subjects by Age and pathology

Category	Variable	<40	41-50	51-60	61-70	71-80	81+	Total
Tumour Presentation								
	Colon	9	10	10	2	3	0	34
	Rectum	2	6	2	4	0	1	15
	Rectosigmoid	0	0	0	1	0	0	1
	Total	11	16	12	7	3	1	50
Diagnosis								
	Adenocarcinoma	9	8	10	5	2	1	35
	AD Signet ring type	0	0	0	1	0	0	1
	Basaloid Squamous Cell Carcinoma	0	1	0	0	0	0	1
	Carcinoid tumor	0	1	0	0	0	0	1
	Adenomas	2	6	2	1	1	0	12
	Total	11	16	12	7	3	1	50
Tumour Differentiation								
	Well Differentiated	4	2	4	0	2	0	12
	Moderately Differentiated	2	3	4	5	0	0	14
	Poorly Differentiated	3	5	2	1	0	1	12
	Total	9	10	10	6	2	1	38

Table 7: Percentage distribution of the study subjects by Age with percentages and pathology

Category	Variable	<40		41-50		51-60		61-70		71-80		81+		Total
Tumor Presentation		Number	%	Number	%	Number	%	Number	%	Number	%	Number	%	
	Colon	9	81.8	10	62.5	10	83.3	2	28.6	3	100	0	0	34
	Rectum	2	18.2	6	37.5	2	16.7	4	57.1	0	0	1	100	15
	Rectosigmoid	0	0.0	0	0	0	0.0	1	14.3	0	0	0	0	1
	Total	11		16		12		7		3		1		50
Diagnosis														
	Adenocarcinoma	9	81.8	8	50.0	10	83.3	5	71.4	2	66.7	1	100	35
	AD Signet ring type	0	0.0	0	0.0	0	0.0	1	14.3	0	0.0	0	0	1
	Basaloid Squamous Cell Carcinoma	0	0.0	1	6.3	0	0.0	0	0.0	0	0.0	0	0	1

	Carcinoid tumor	0	0.0	1	6.3	0	0.0	0	0.0	0	0.0	0	0	1
	Adenomas	2	18.2	6	37.5	2	16.7	1	14.3	1	33.3	0	0	12
	Total	11		16		12		7		3		1		50
Tumor Differentiation														
	Well Differentiated	4	44.4	2	20	4	40	0	0.0	2	100	0	0	12
	Moderately Differentiated	2	22.2	3	30	4	40	5	83.3	0	0	0	0	14
	Poorly Differentiated	3	33.3	5	50	2	20	1	16.7	0	0	1	100	12
	Total	9		10		10		6		2		1		38

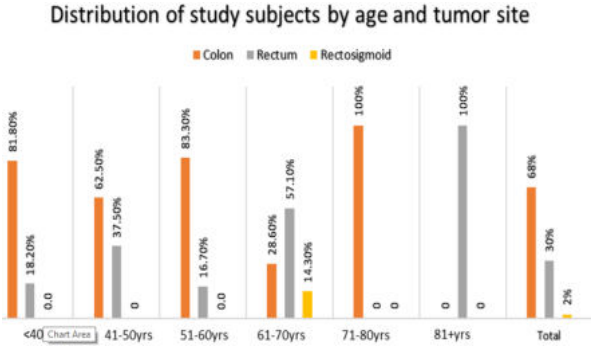

Fig 5: Distribution of study subjects by age and tumour site

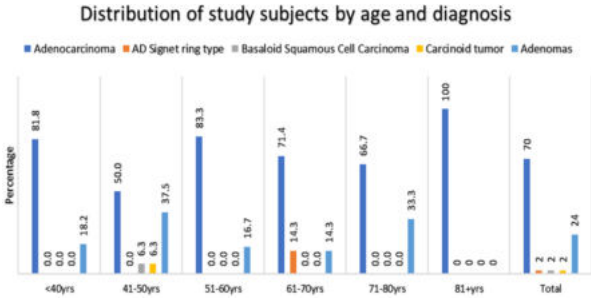

Fig 6: Distribution of study subjects by age and diagnosis

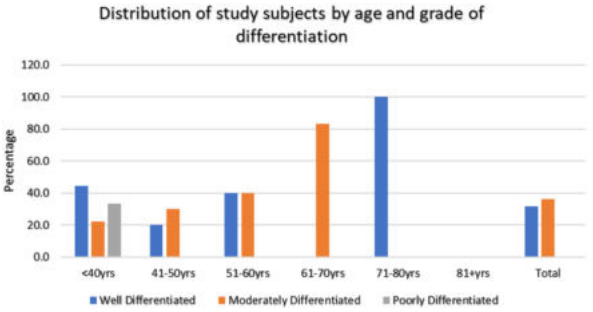

Fig 7: Distribution of study subjects by age and grade of differentiation

DISCUSSION

In the present study we have assessed the different patterns of CRC in Asram hospital, as well as, the relation between these CRC types and demographical characteristics, particularly gender and sex. In this study, patients present with different colorectal sites. The great majority presented with colonic site lesions followed by rectum and recto-sigmoid sites. Right colon tumours spread to local and distant sites in 90% of autopsies, and to distant sites alone in 10%. Rectal tumours spread locally only in 25% of cases, to distant site alone in 25%, and to both in 50%. Regardless of the origin of the primary tumour, the liver is the most common site of metastasis, followed by the regional lymph nodes and the lungs. Two-thirds of the patients with right colon lesions died of liver metastases, and three-quarters of those with rectal tumours succumbed to disseminated disease [11]. Generally, colorectal carcinoma is thought to be a malignancy that primarily occurs in patients older than 50 years of age [7]; likelihood of the disease is unusual in patients under 40 years of age. It has been estimated that between 2 and 3% of colorectal cancers occur in patients younger than the age of 40 years [8]. However, current studies suggested that an increased incidence of colorectal cancers in younger age groups in India as well as all over the world [9, 10]. In our study there is highest incidence in fourth decade followed by fifth decade. One possible explanation could be increased use of endoscopy in diagnosis of colorectal lesion and timely biopsy of suspected growth. Therefore the colorectal malignancy are getting diagnosed at an earlier age and at early stage than what was done in past.

Generally, incidences of colorectal cancer ascended sharply after the age of 45 years, and 90% of cases occur in persons over the age of 50 years [16, 17] but its reported incidences among patients of 20–40 years of age increased by 17–20% now-a- days [18]. Several studies in India also reported that incidences of colorectal cancer in younger individuals escalated in recent years [19, 20].

Most of patients in this series were diagnosed with adenocarcinoma. Colon adenocarcinoma is the most common histopathological type of colorectal cancer. Colon was most common site of involvement in our study and moderately differentiated adenocarcinoma most common histological type.

The study of Falterman et al, also shows that the commonest histological type of colorectal carcinoma was adenocarcinoma followed by mucinous carcinoma which is correlating with the present study [22].

Most patients having mucinous adenocarcinoma, present late, and have rapid disease progression and poor outcome [12, 13]. AD may be well-differentiated, frequently rising within a villous adenoma, or poorly-differentiated. The poorly-differentiated lumps (such as, AD-signet ring type) have a poor prognosis and tend to affect younger patients. Most are well-differentiated AD and are classified according to mucin content. Mucin-secreting ADs have less than 50% mucin production, mucinous carcinomas have more than 50% extracellular mucin, and AD-signet ring types have intracellular mucin that shifts the nucleus to one side [14]. Diagnosis of AD-signet ring types is made when at least 50% of the cells are of the signet ring type [15]. We had a single case of adenocarcinoma signet ring cell type.

Although the age of patients is relatively similar in all age groups, but it was observed that there was an increase in the younger age group. Moreover, though the males were more than females, but many females present at younger age. There has been a slight predominance among men with an average ratio of 116:100 over the years (range: 99:100-132:100). In our study also males were more commonly affected than females. The male to female ratio is 2.84:1 .The overall age-standardized rate (ASR) approached a plateau of 9.6/100000 in 2010. The ASR has increased, but is still much lower than in developed countries [10, 16]. In the present study the mean age was 63years and the great majority of the males were found in age range 41-50 years, followed by 51-60 years & 61-70 years, hence the great majority of females were

observed at age range 51-60 followed by 61-70 & <40 years. With regard to the lesion site, colon was frequently involved followed by rectum and recto sigmoid junction.

The diagnosis of different carcinomas (adenocarcinoma, basaloid squamous cell carcinoma) was relatively similar among both sex except for carcinoid tumour and adenocarcinoma signet ring cell type which was only seen in males in our study.

Tumour differentiations were relatively similar for both sex, but what is excitingly, that most cases present in advanced stage of the disease, which might be due to the lack of screening programs as well as, the low levels of awareness. Similar findings were reported from our institute [17]. Nationwide awareness campaigns and screening programs for CRC are critical for prevention, early detection and adequate management of CRC [18, 19].

On the other hand, the age distribution by site of the lesion has showed great variation. Most of those with colonic sites were diagnosed at age range 41-50 and 51-60 years, hence, most of the those with rectum lesion site were diagnosed at the age range 41-50 years followed by <40 years, 51-60 years. Nevertheless, most of the cases of AD diagnosed at age over 50 years. Though all cases of adenocarcinoma were diagnosed at age over 50 years, we noticed that the cases of carcinoid and SCC were diagnosed at age less than 50 years [20, 21].

For tumour differentiation most cases of the poorly differentiated presented at younger stages of the disease which might be attributed to non-expectation of the disease.

CONCLUSION

Asram hospital patients with CRC were presented with more advanced stages of the disease at younger and middle age group compared to Western populations, which presents more frequently in an extra advanced stage and poorly differentiated type than in older patients The above observation implies for a greater emphasis on early recognition of signs and symptoms, to facilitate for early diagnosis so that curative resection can be attempted for the patient to enjoy a better prognosis and better quality of life.

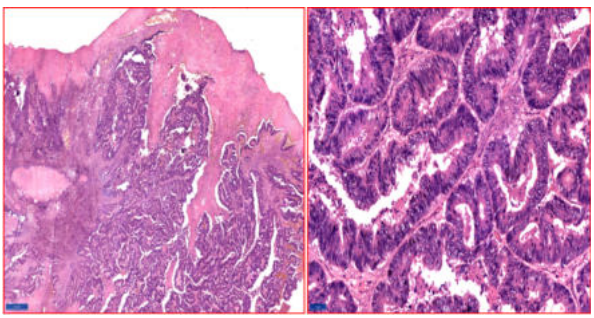

Fig 8 & 9: Haematoxylin & Eosin histopathology pictures of adenocarcinoma colorectum power X 10, X40, showing glandular and papillary patterns.

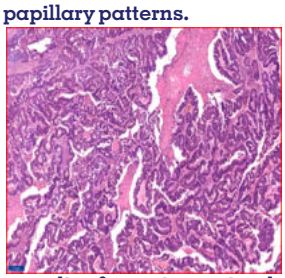

Fig10: Haematoxylin & eosin stained histopathology pictures of well differentiated adenocarcinoma , power X 10, showing glandular and papillary patterns

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