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Demographic Association of Laterality and Histopathology in Metastatic Colorectal Carcinoma Patients

Boskey Pancholi[1], Harish Gautam[2], R K Tanwar[3], Manish Gautam[4]

[1]Department of Zoology, Lzebra College, Kota
Corresponding Author Email: *boskey.pancholi[at]gmail.com*

[2]Department of Zoology, Government College, Kota

[3]Department of Radiation Oncology, Maharao Bhim Singh (MBS) Hospital, Kota

[4]Department of Medical Oncology, Shree Kalyan Cancer Hospital, Kota

Abstract: ***Colorectal cancer becomes third most fatal cancer type and leads to high mortality rates in India as well as worldwide. For proper prognosis and management detection of tumour staging is necessary. In this research paper concluded histopathological aspect of metastatic colorectal carcinoma (mCRC). In this four-year histological study included 51 forth stage colorectal cancer patents were selected. Tissue sample was received from biopsy procedure followed by immediate preservation in formalin solution. After tissue section preparation using microtomy apparatus diagnosis was given according to TNM staging. Fifty-one patients of IV stage colorectal cancer were examined during the period of January 2022 to December 2025. Patients with more than 18 years of age groups were selected. Tissue sample were selected using biopsy sampling and types of malignancy were diagnosed. Most of the patients showed left side laterality (72.55%) and 42 (76.47%) of patients had Adenocarcinoma (NOS) histology followed by mucinous and signet ring adenocarcinoma (15.69% and 7.84% respectively). The most common symptoms are abdominal pain (41.17%) and bleeding per rectum (33.33%). The study of colorectal carcinoma in Hadoti region conclude that the mean age of the patients is 58 ± 0.24 (in male) 54 ± 0.45 (in female) and proportion of male is slightly higher than the female. Adenocarcinoma lesion and left laterality was more common in TNM staging criteria.***

Keywords: Biopsy, TNM staging, Adenocarcinoma, colorectal cancer, malignancy, rectal bleeding

1. Introduction

Colorectal cancer is the second most frequent cause of cancer death in the western countries as well as sharp rising in India too. The incidence of Colorectal cancer is third to lung and prostate (in male) and the prevalence of breast cancer in females. The global incidence rates are 10,45,413 in male and 8,26,706 in female in year 2022. Annual age adjusted rates per 1,00,000 (AAR) is 17.8 with mortality of 7.8. as it counts 9% of the world cancer mortality in year 2022[1,2]. Several factors such as tumour invasion depth, involvement of lymph nodes, as well as host factors such as age, gender, food habits, smoking, co- morbidities (such as diabetes, CVD, ulcerative colitis, hypertension) plays an important role in determining the survival rates [3]. The overall survival in this operable disease also depends upon stage of the cancer along with systemic and inflammatory responses. In this study the histological analysis of stage IV colorectal cancer patients tissue samples has been conducted to specify:

1) To conduct a prognosis analysis of venous invasion in colorectal cancer.
2) Detailed analysis of age, gender and laterality analysis of the stage IV colorectal cancer patients.
3) Types and frequency and types of cancer cells present in stage IV cancer patients at the time of presentation.
4) The symptoms of the patients at the time of presentation and their corelation with laterality.

2. Materials and methods

In the current study WHO Classification have been used [4]. According to this plan Tissue samples have been taken from Maharo Bhim Singh Hospital, Kota (MBS, Kota) between the period of January 2022 to December 2025. As this is the oldest and largest Government Hospital in Hadoti region. Due to proper facilities and implementation of Government Health schemes large number of Urban and Rural population referred here for their treatment. As the histological analysis of colorectal carcinoma is already available across the globe, the main purpose of the study is to estimate the histological pattern, frequency of various types of colorectal carcinoma in the region and nearby cities (Kota, Baran, Jhalawar and Bundi).

The tissue sample was taken from Colonoscopic/ Sigmoidoscopic biopsy procedure using specific needle that is inserted into Tumour Lesion. The biopsy tissue sample is preserved using formalin (10% v/w) solution. The tissue is placed on a glass slide and dyed with the appropriate stain to show the essential component of the tissue such as nuclei and cytoplasm. The paraffin blocks were cut into sections of 3-5 µm Thickness using microtome apparatus. For staining protocols Haematoxylin and Eosin (H&E) is used to highlight nuclei and cytoplasm. Haematoxylin stain the nuclei with a purple colour and eosin stain cytoplasm with pink colour. Most common stains are Hematoxylin and Eosin. These stains highlight nuclei (blue color) whereas eosin stain cytoplasm pinkish color.

After preparing the glass slide, tissue sample was viewed under the microscope scanned by digital scanner. Scanners read the whole tissue section slide by converting it into high resolution image more than 5 X, 10 X, 45 X and 100 X. The basis of the study was conducted on bases: (a) Data were withdraw as retrospective as well as observational studies (b) the tissue collection procedure does not interfere patients' treatment (c) administration of any foreign substances is restricted during tissue collection procedure (4) data collection method was confidential so that patient's identity should not be disclosed.

The criteria for data collection were (1) age and gender of the patients (2) Location of tumour, pathological features of the resected tumour, presence of distant metastases and (3) presence of associated comorbidities in the subjects. The tumour differentiation grades were classified as well-differentiated, moderately differentiated, and poorly differentiated. Staging criteria was determined using eighth edition of "TNM Classification of Malignant Tumours" described in Union for International Cancer Control [5].

Inclusion criteria:

- Biopsy confirmed metastatic colorectal carcinoma,
- Age of the patient should be more than 18 years at the time of presentation.
- The location of the tumour in the right colon (caecum, ascending colon, hepatic flexure) or left colon (splenic flexure, descending colon, sigmoid colon).

Exclusion criteria:

- Presence of other malignancies.
- Inappropriate/incomplete history at the time of diagnosis.
- Patient taking alternative treatment.

3. Results

3.1 Histological analysis

3.1.1 Tumour appearance: Right side colon cancer appeared as huge tissue masses that grows outwards or in the form of polypoid tissue in the cavity of the colon with ulceration. Right side colon cancer often developed in the form of serrated adenomas or polyp. The cancer tissue is soft and easily bleed so iron deficient anaemia is the major symptoms (Figure 1a, 1b).



Figure 1a, b: Tissue damage in **Right side colon cancer** where ulcer cells emerge from colon (1a) Adenomas or polyp tissue constrict the passage of stool causing bleeding.

Left side colon cancer these tumours give an appearance of polypoid tissue grow with the wall of intestine and make a shape of "napkin ring". They have a localized appearance of polyps or outgrowth of the cells in the lumen of the colon. The circumferential growth of the cells in the colon forming a constriction that narrows the passage of lumen (Figure 2a, 2b).



Figure 2a, b Local protruding lesion with exophytic growth in **left side colon cancer** of the tissue (2a) A characteristic appearance of "Napkin-ring" like structure that narrows the passage of lumen (2b).

3.1.2 Histological differentiation

a) Well differentiated adenocarcinoma: These tumor cells are slow growing and resembling the basic glandular cells. Narcotic bodies or branching glands were also observed that showed slow growth as compared to moderate or poorly differentiated cells (Figure 3).

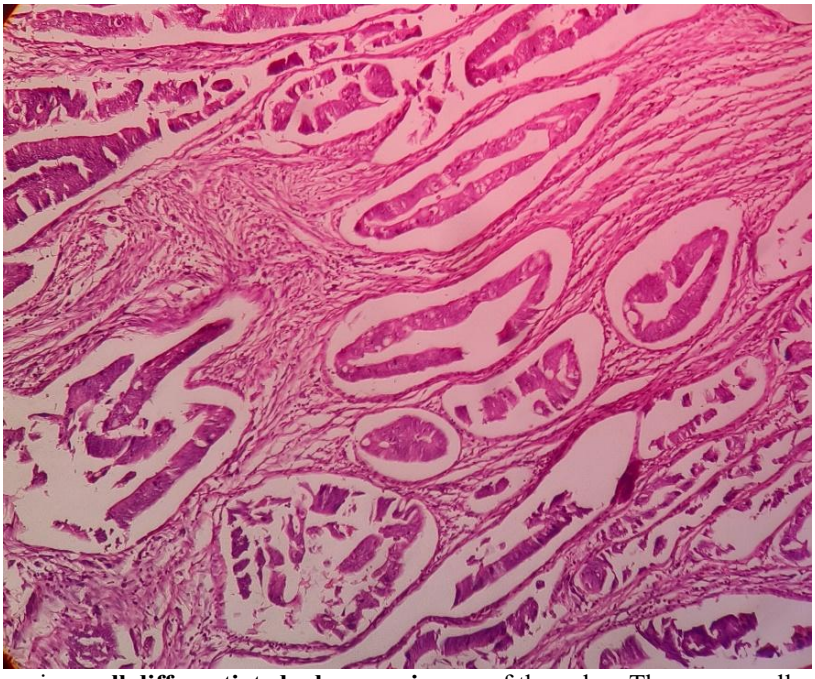


Figure 3: Micrograph showing **well differentiated adenocarcinoma** of the colon. The cancer cells shown in the micrograph are tubular, branched glands lined by malignant cells. The oncogenic cells infiltrate into surrounding stromal cells.

2) Moderately Differentiated adenocarcinoma: Fast growing cells but poor prognosis because they are moderately different form the glandular cells. They show characteristic "Cribriform" (gland within gland pattern) or presence of cellular debris. The tumor cells showed nest or island of epithelial cells infiltrate the surrounding connecting tissue. The shape of the cells was polygonal and round in shape commonly called as "Keratin pearls". The neoplastic cells demonstrated variation in nucleus size and shape (nuclear pleomorphism) with hyperchromatic nuclei (Figure 4).

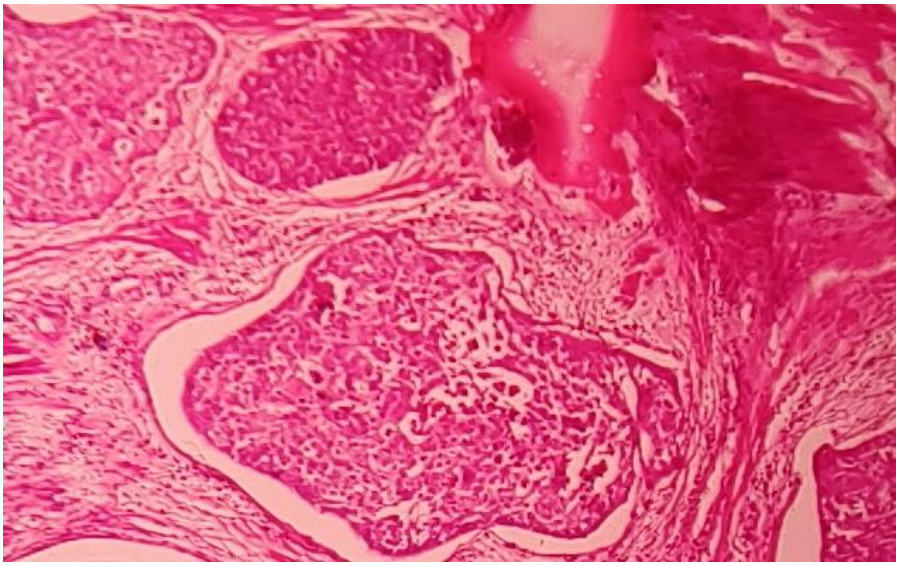


Figure 4: Micrograph showing **moderately differentiated** cluster of abnormal, keratin producing cells, surrounding to the fibrous stroma cells. The cancer cells are characterized as irregular, tubular and sieve-like structures. Elongated nucleus, diverse cell size and shape along with some of the cells still maintain gland forming patterns.

3) Poorly differentiated adenocarcinoma aggressive type of histological subtype displaying dense poorly differentiates tissue that is characterized by co-existence of malignant glandular and squamous cells.

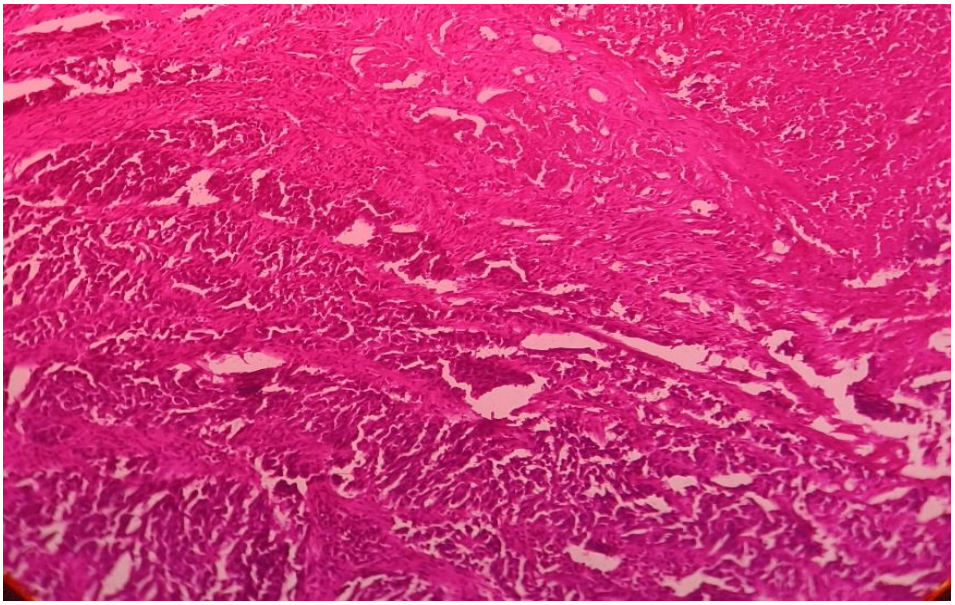


Figure 5: Poorly differentiated cell with characteristic of high nucleus to cytoplasm ratio, cellular pleomorphism (disturbed cell size and shape). Poorly differentiated adenocarcinoma loss the ability of gland formation as possess high grade tumor formation

3.1.3 Histologic types demonstrated by the CRC patients

1) Adenocarcinoma (Not Otherwise Specified - NOS): Most frequently found adenocarcinoma and well known for its aggressiveness. Most common symptoms are pain, continuous weight loss and digestive changes. In the micrograph prepared in histology laboratory pinkish, lobulated cells with rounded appearance covered in fibrous tissue were observed (Figure 8). The presence of Keratin pearls i.e. bright pink central areas surrounded by tumor cells is the identifying feature demonstrated in the colon cancer patients.

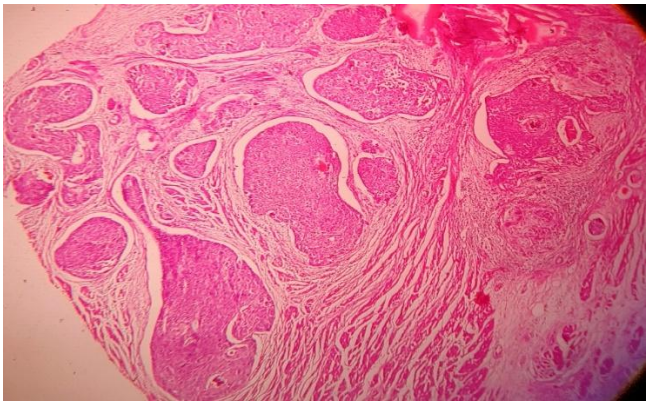


Figure 8: The tissue demonstrated characters of Adenocarcinoma (NOS).

2) Mucinous adenocarcinoma showing abundant extracellular mucin (40 × magnification). The extracellular mucin is present in > 50% of the tumor volume. Small nest, cords and malignant epithelial cells appeared in floating condition in large "lakes" or pools of light stained mucin (Figure 9).

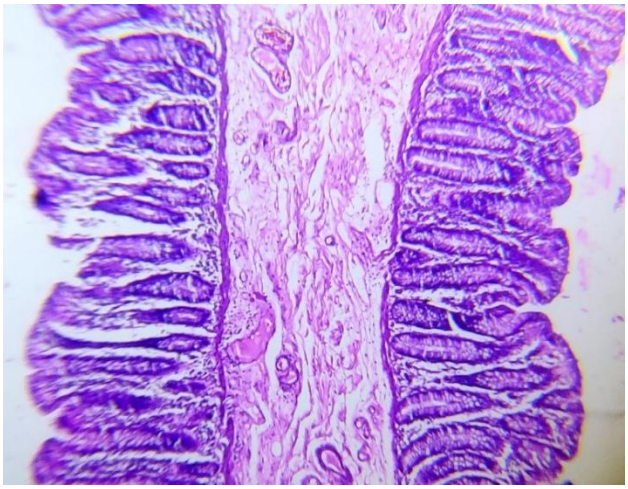


Figure 9: Mucinous adenocarcinoma cells in the pool of mucin tissue

3) Signet ring cell adenocarcinoma more than 50% of the cells are of signet ring cell structure. In this type of cell structure mucin vacuole pushes the nucleus to periphery. It is diagnosed mostly in advanced stages. Lymphatic invasion, venous invasion and perineural invasion is seen in the microscopic studies (Figure 10).

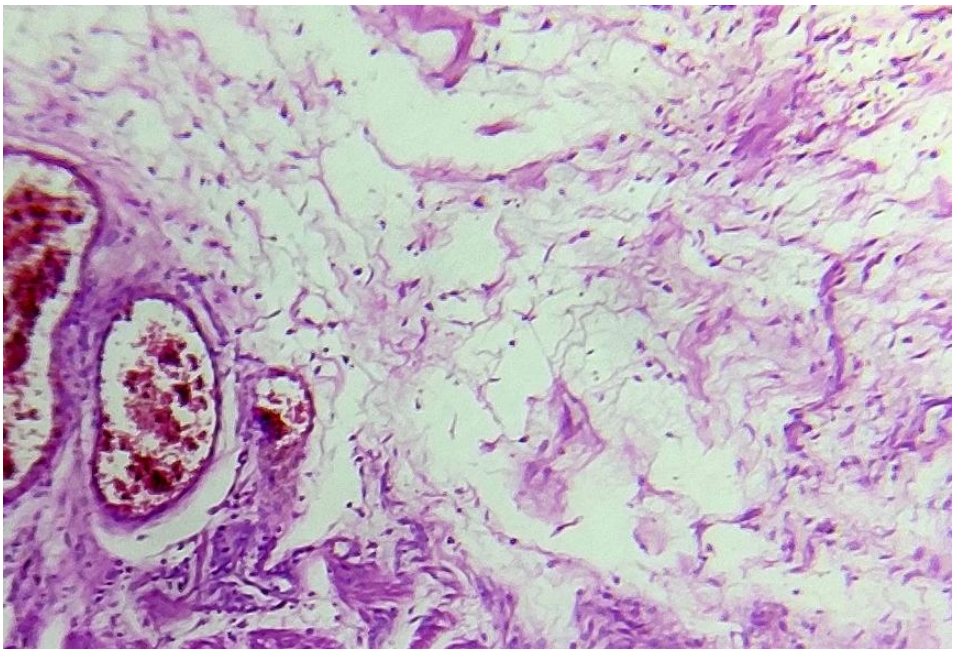


Figure 10: Signet ring cell adenocarcinoma (40 X magnification)

3.2 Clinical characteristics

Along with the histological analysis clinicopathological studies were also conducted so as to give an insight the correlation of laterality with colon cancer symptoms and presentation (Table 1).

On comparison with **age** right side colon cancer patients were more aged then compared to left side colon cancer patients. There is slight variation in age group where female was more affected with right side colon cancer as compared to males.

3.3 Clinical presentation

Table 1: Demographic characteristics

Characteristic	Right side colon cancer	Left side colon cancer
Age (Mean ±SD)	58 ± 0.24	54 ± 0.45
Gender		
Female	9 (17.64%)	15 (29.41%)
Male	5 (9.80 %)	22 (43.13%)

Table 2: Distribution of patients according to laterality

Laterality	Number	Percentage (%)
Right	14	27.45
Left	37	72.55
Total	51	100

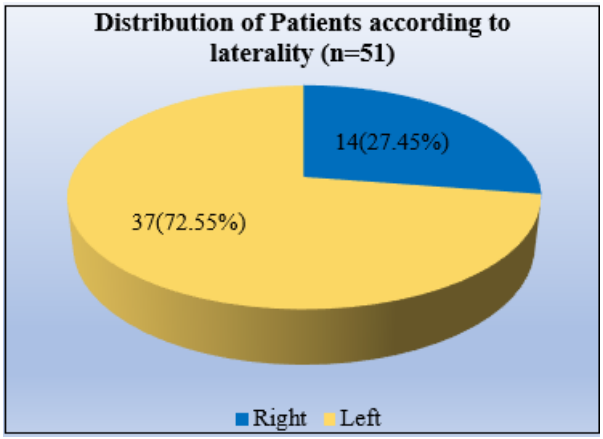


Figure 11: Laterality: In present study 37 (72.55%) patients were involved left side of the colon while 51 (27.45%) patients have right side of colon involvement.

Table 3: Distribution of mCRC patients according to Histopathology

Histopathology	Number	Percentage (%)
Adenocarcinoma (NOS)	39	76.47
Mucinous Adenocarcinoma	8	15.69
Signet ring cell carcinoma	4	7.84
Total	51	100

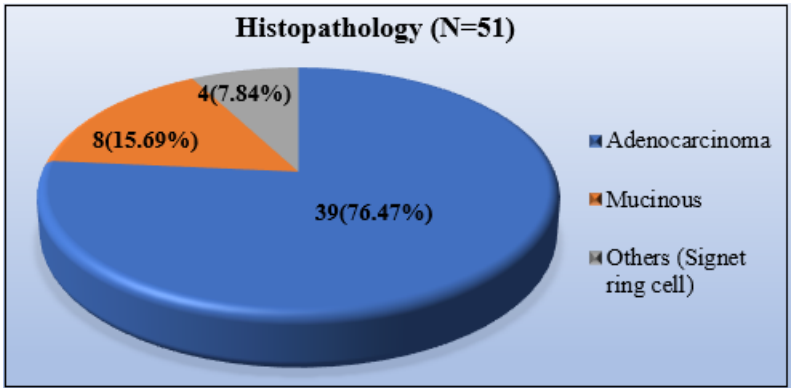


Figure 12: Histopathology: 42 (76.47%) of patients had Adenocarcinoma (NOS) histology followed by 8 patients (15.69 %) with Mucinous cell carcinoma and 4 (7.84%) patients with signet ring cell carcinoma histopathology.

Table 5: Distribution according to presenting complaints

Clinical presentation	Number of patients	Right side colon cancer	Left side colon cancer
Abdominal pain	21 (41.17%)	13 (25.49%)	8 (15.68%)
Change in bowel habits	16 (31.37%)	5 (9.8%)	11 (21.56%)
Bleeding per rectal	17 (33.33%)	7 (13.72%)	10 (19.6%)
Anaemia	5 (9.80%)	4 (7.84 %)	1(1.96%)
Loss of weight/Loss of appetite	12 (23.52%)	6 (11.76%)	6 (11.76%)
Obstruction	1 (1.96%)	1(1.96%)	0

4. Discussion

Mortality rates and disease progression can be reduced only by using proper screening procedures [6]. In developed countries appropriate screening measures reduced the mortality rates on the other hand developing countries like Eastern European region reports marked rise in CRC cases [7]. Histology is the backbone of cancer diagnosis process. It is helpful in the identification of abnormal cells in the tissue under microscope. In addition to diagnosis, pathologic staging, surgical margins, prognostic parameters, lymphovascular and perineural invasion lastly assessing therapeutic effect of neoadjavant therapy [8]. The most common symptoms are obstruction large bowel, anemia, blood in stool, Malena (blackening of stool), perforation and hemorrhage [9,10]. In addition to adenocarcinoma NOS, which accounts for the overwhelming majority of cases, nine other specific subtypes are recognized, all with distinct morphologies and differences in natural histories. These comprise mucinous adenocarcinoma, signet ring cell adenocarcinoma, medullary carcinoma, serrated adenocarcinoma, micropapillary adenocarcinoma, adenoma-like adenocarcinoma, adenosquamous carcinoma, carcinomas with sarcomatoid components, and undifferentiated carcinomas [11]. Among them adenocarcinoma (NOS) was the most commonly presented (76.47%) in our results which is co related to the standard findings [12,13] In the previous findings older age patients reports right side pathology more as compared to left side pathology (58 ± 0.24 with compared to 58 ± 0.24). The patients in young age had a prominence of tumor formation in sigmoid colon whereas caecum is the main region of tumor occurrence in older patients [14].

According to study conducted by gonzalez et al.,[15] the proportion of male and female colon cancer occurrence is similar but in worldwide crc occurrence analysis male proportion is higher than female. the occurrence of right-side tumor occurrence is higher in female as compared to male patients (male patients' hand more left side tumor predominance) [15]. the major symptoms for colorectal cancer presentation are rectal bleeding, anemia, abdominal constriction and change in bowel habits [18]. in both the groups

anemia is the major clinical symptom which is due to ulceration in colon and rectum. right side colon cancer patients showed anemia and weight loss as a major clinical manifestation whereas right side colon cancer patients demonstrated change in bowel habits and rectal bleeding [16]. similar observation was found in our findings where 72.55 % patients showed left side laterality and 27.45% patients showed right side laterality. complication of abdominal pain was reported in 21 out of 51 patients 13 patients of right-side laterality and 8 patients of left side laterality. another major complication was rectal bleeding. out of 17 patients 10 patients demonstrated left side and 7 right side laterality. the current finding makes more accordance with the previous findings.

5. Conclusion

The anatomical location has a significant impact on behavior, molecular and immunological feature of the tumor. In the current study we can conclude that colorectal carcinoma has a prominent occurrence between the age group of 50-60 years. Left side laterality is more phenomenon than the right-side laterality. Abdominal pain and rectal bleeding are the common complication at the time of presentation. Not otherwise specified (NOS) adenocarcinoma is the most common circumstance in our case. Recognizing these important factors help in optimizing treatment strategy plan, designing personalized medicine and improving diagnostic blueprint that enhance patient lifespan.

Conflict of Interest
None.

Source of Funding
None

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