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Clinicopathological profile of colorectal cancer managed at a university teaching hospital, Nepal

Sanjaya Paudyal[1], Shiva Raj KC[2], Shantabir Maharjan[3], Surendra Shah[3], Niraj Giri[4], Samyukta KC[4], Bidhan Sigdel[5]

[1]Assoc. Prof., [3]Asst. Prof, [4]Lecturer, [5]MS Surgery Resident, Dept. of Surgery
[2]Assoc. Prof., Dept. of Pathology and Lab. Medicine, Patan Hospital, Patan Academy of Health Sciences, Lalitpur, Nepal

Correspondence
Dr. Sanjaya Paudyal
Dept. of surgery
Patan Hospital
Patan Academy of Health Sciences, Lalitpur, Nepal
Email: sanpau3003@gmail.com

Peer Reviewers
Prof. Dr Jay N Shah
Patan Academy of Health Sciences

Asst. Prof. Dr Ashis Shrestha
Patan Academy of Health Sciences

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Abstract

Introductions: Colorectal carcinoma is the third most common cancer worldwide. The incidence is increasing in developing countries including Nepal. The aim of this study is to find out the clinicopathological pattern of colorectal carcinoma locally.

Methods: Data were recorded retrospectively by reviewing the charts of the patients who were diagnosed and treated for in patients having colorectal cancer managed during three years period of 2016-9 at Patan Hospital, the university teaching hospital of Patan Academy of health sciences, Nepal. Clinicopathological profile, age, gender, surgery, histopathological findings were descriptively analised.

Results: There were 36 colorectal cancer patients, male 20 (56%) and females 16 (44%), mean age 56.9 years (range 24 to 89). Curative surgery was possible in 17 (47.2%) and adenocarcinoma of moderate differentiation was found in 25 (70%) of the resected specimen.

Conclusions: Colorectal carcinoma was found in old age, slightly more in male than female, adenocarcinoma being most common histology type.

Keywords: adenocarcinoma, colorectal carcinoma (CRC), curative resection

Introductions

Colorectal carcinoma (CRC) is more common in elderly with a median age of 68 years (range, 25-93 years).[1] Around 15 to 30% of CRCs present as a surgical emergency, as obstruction (78%), perforation (10%), or bleeding (4%).[2,3]

In WHO South east Asia region the reported proportion of colorectal cancer in men is 56.7%and in women 43.2% among 120225 case of colorectal cancer. Similarly, in India which is similar to our geographical region the proportion is 57.4% in male and 42.6% in female among 64332 detected colorectal cases.[4] The overall incidence is increasing in developing countries including Nepal.[5] Epidemiological change of colorectal cancer has been observed in the past with increased incidence in young age.[6]

This is a followup study of similar study done at our institute.[7] The aim of this study was to analyse the clinicopathological pattern of CRC in local scenario, to find out changing trends in the CRC especially pathological aspects and surgery so as we can plan for better management accordingly.

Methods

An institution based retrospective study was performed on all the patients managed at the department of surgery, Patan hospital, Patan academy of health sciences Nepal during three years period from Aug 2016 to Sept 2019. Patients preoperative diagnosis of CRC by Colonoscopy/Contrast enhanced computed tomography (CECT)/ Magnetic resonance imaging (MRI) or pre-operative Histopathological examination (HPE) and Fine needle aspiration cytology (FNAC) (in advanced disease) were included, as well as who were diagnosed intraoperatively. Incomplete records or patients charts which were not available for analysis were excluded.

Medical records were retrieved by searching a hospital computer database using International Classification of Diseases, 10th revision (ICD 10 code) “C20” for rectal and “C18” for colon carcinoma. Institutional review committee approval was obtained. Patients files were reviewed for demographics (age and sex), duration of symptoms (days), presenting symptoms (pain abdomen, PR bleeding, abdominal mass, rectal mass and pallor, associated symptoms (weight loss, pre-treatment diagnostic findings (Ultrasongram (USG), CT/MRI, colonoscopy biopsy, level of carcinoembryonic antigen(CEA), involved part of colon, type of surgery, surgical clearance in curative, histological tumor type, post-operative adjuvant treatment, palliative treatment, recurrence and followup were recorded. Last date of followup was recorded and duration was calculated from the date of initial diagnosis and start of treatment or surgery. Recurrence of the operated patient was noted if there was an obvious diagnosis of recurrence at the time of last followup. Data were descriptively (mean and percentage) analyzed using SPSS 20.

Results

Record of 42 patients were found by ICD 10 search “C20 and “C18” but only 36 patients’ charts could be retrieved for final analysis. Out of 36 CRC, male was 20 (56%) and female 16 (44%), mean age 56.9±16.9 years (range 24-89). Six (16.7%) patient were below 40 years of age, thirteen (36.1%) were between 40-60 years and 17 (47.2%) were above 61 years of age. Altogether, majority (83.3%) were above 40 years.

Abdominal pain was present in 31 (86%), followed by per rectal (PR) bleeding in 20 (55%), Table 1.

Table 1. Presenting signs and symptoms of CRC (N=36)

Presenting signs symptoms	N	%
Pain abdomen	31	86%
PR bleeding	20	55%
Palpable abdominal mass / rectal mass	7	19%
Pallor	8	22%

Table 2. Location of CRC (N=36)

Involved segment	N	%
Rectum including rectosigmoid	23	63.8%
Ascending colon	7	19%
Descending colon	4	4%
Ca caecum	1	2%
Transverse colon	1	2%

Table 3. Types of surgery performed for CRC (N=36)

Type of surgery		N	%
Right hemicolectomy		4	20%
Left hemicolectomy		4	20%
Anterior resection (AR)		4	20%
Low anterior resection (LAR)		3	15%
Ultra LAR		1	5%
Sigmoidectomy		1	5%
Palliative surgery	Diverting colostomy	1	5%
	Transvers colon mass excision with en block partial gastrectomy	1	5%
	Non curative right hemicolectomy	1	5%

Table 4. Histology type of CRC after surgery (N=20)

Histology type	N	%
Moderately differentiated	14	70%
Mucinous adenocarcinoma	4	20%
Poorly differentiated	1	5%
Complete response after neoadjuvant treatment (no tumour cells)	1	5%

Table 5. Tumor (T stage) and lymph node (N) status in curative surgery of CRC (N=17)

Tumor Stage		N	%
T stage	T0	1*	5.8%
	T1	2	11.7%
	T2	4	23.5%
	T3	6	35.3%
	T4	4	23.5%
N stage	N0	8	47%
	N1 (1-3 nodes)	5	29%
	N2 (4-6 nodes)	4	23.5%

*No residual tumor, Post CTRT

Rectum and rectosigmoid involvement was found in 23 (63.8%). Overall, left colon was affected in 27 (75%) and right in 9 (25%). (Table 2)

All patients had preoperative colonoscopy or sigmoidoscopy and biopsy, showing malignancy in 31 (86.1%) and 5 (13.9%) had acute on chronic colitis.

All the patients (36) had undergone a CECT examination with diagnosis of CRC. Among 36 CECT, 20 were done prior to surgery, and 16 before neoadjuvant or palliation. In 28 (77.8%) patients CEA was done, of which 18 (64.2%) it was ≥4 ng/ml, in 10 (35.7%) <4 ng/ml.

Surgery was done in 20 (55.5%), of which 17 (85% of 20) were curative resection, Table 3.

Out of 36 patients, 20 patients underwent surgery in our hospital, 17 had curative resections and 3 had palliative care.

The HPE in 20 surgery showed moderately differentiated adenocarcinoma in 14 (70%). One patient who had neoadjuvant treatment, HPE showed no residual microscopic tumor cells, Table 4. Lymphovascular invasion (LVI) was seen in 5 (25%), perineural invasion (PNI) in 4 (20%) and 2 (10 %) had both LVI and PNI. Surgical margin was free in 19 patients (R0) and one patient with en bloc partial gastrectomy showed positive resection margin. In curative resection, the lymph node yield ranged from 1 to 37, mean 12.5±9.1. Among them mean lymph node positivity was 1.87±2 ranging from 0-5. Two patients had T1 and eight N0, Table 5. Out of twenty operated patients, six had adjuvant chemotherapy.

Followup was available in 30 (83.3%) patients, average 36.2 weeks (range 1-156). Short followup was noted in the patients with the advanced disease 16 (44.4%) and 9 (25%) had palliative care and 7 (19.4%) referred to other center for chemotherapy and radiotherapy. Among 20 operated patients one death occurred within one year of surgery.

Discussions

In our study we found that 6 (16.7%) patients were below 40 years of age. However, earlier study[7] at our center showed 29% of patients were below 40 years of age. This may be due to smaller sample size of 36 and lesser duration of 3 years in present study, than earlier study at our center with sample size of 73 during 8 years. And so, this is not necessarily the real decline of CRC in younger age of <40 years locally. Literatures show CRC is rare before the age of 40 years, and the incidence begin to increase significantly between the age of 40 and 50 years and age-specific incidence rates increasing in succeeding decades thereafter.[8] It has been seen that 90% of new cases are diagnosed in patients over 50 years of age, but now incidence in the younger population is increasing and they present in a more advanced stage.[9] Worldwide, CRC is the third most common cancer and the third leading cause of cancer-related death in both males and females.[10,11] Globally, the highest incidence of CRC rates are in North America, Australia, and Europe, and the lowest rates in Africa and Asia.[10,11] So far there is lack true incidence of CRC in Nepal. Data from our center, 73 during 2004-12 earlier study,[7] plus 36 during 2016-2019 in present study, total 99 in 11 years, suggest that it is not uncommon and number of CRC is in the rise.

Study with larger sample size of 22432 cases of CRC between 2000 and 2011 from China found that the age-specific rates were relatively low in populations younger than 40 years for both males and females and a dramatic increasing incidence after 40 years of age, which peaked at 80 years, and declined after 85 years of age.[12] A multicenter study involving 1525 CRC cases between 2005 and 2014 as part of genetic and epidemiological studies from Colombia reports average age at diagnosis was 57.4 years, with 26.5% of cases having early-onset diagnosed by the age of 50 years).[13]

We found male (20) and female (16) ratio is near equal (1:1.2). A study done in US in 373,956 patients over 40 years of age diagnosed with malignant CRC between 1975

and 2006 who resided in one of the nine Surveillance, Epidemiology and End Results (SEER) regions of also had equal numbers of men (187973) and women (185983), however, men had significantly higher age-adjusted CRC incidence rates across all categories of age, race, tumor sub-site, stage, and SEER region. Gender differences in CRC incidence rates for the 40–49 and 50–59 age categories were small and increased only slightly over time.[14]

Our analysis showed that 31 (86%) patients came with abdominal pain and 20 (55%) with notable PR bleeding, Table 1. A retrospective study involving 236 patients reports that the most common symptom is abdominal pain 121 (51.3%) followed by weight loss 77 (32.6%) and change in bowel habit 34 (14.5%). The noticed bleeding, change in bowel habit and weight loss occurred more in left than right colon.[15]

However, in our analysis even though 55% of patients had PR bleeding, less than 19% had a mass per rectum in DRE. Our policy is to do at least sigmoidoscopy in all the patients with PR bleeding after exclusion of fissures even if DRE negative and proctoscopy revealing hemorrhoids. A review article (on the basis of other non- English article) states- the importance of DRE (digital rectal examination) along with the case history recognized 70% of rectal cancers and 30% of CRCs and the accuracy of the examination increases with the experience of the doctor.[16]

All our patient during study period had undergone CECT prior to treatment. Based on CECT findings, 20 (55.5%) underwent surgery of out 36. Out of 20 surgeries, 17 (85%) had curative resection and three palliations for obstructive symptoms. In difference to earlier study when there was lack of CT facility at our center.

All our 36 CRC had colonoscopy or sigmoidoscopic examination. This is important both for detection and confirmation of CRC. It is recommended internationally and nationally by gastroenterology and cancer societies as an initial screening modality.[17] Identification of CRC on screening colonoscopy has advantage of detection at lower-stage and better outcomes.[18] However, there has been an increasing concern about the effectiveness of endoscopy in detecting adenomas and CRC in the right colon.[19]

We found that out 30 CRC patient tested for CEA, 18 had more than 4 ng/ml. Our practice is to do CEA in all suspected CRCs, but six reports were missing in present study. High preoperative levels of CEA correlate with adverse prognosis. Serial measurements can detect recurrence with a sensitivity of 80%, a specificity of 70%. It also provides a lead time of approximately 5 months and currently, the most useful application of CEA is in the detection of liver metastasis from colorectal cancers.[20]

We use CEA value of >4 ng/L as cut off for CRC. Systematic Reviews of 52 studies reports overall sensitivity of 41% to 97% and specificity from 52% to 100% in detection of recurrence of CRC.[21] The review further mentions that based results of seven studies with a threshold of 2.5 ng/L, had sensitivity of 82% and specificity 80%. Other 23 studies with a threshold of 5 ng/L, sensitivity was71% and specificity 88%. Yet another seven studies with 10 ng/L, had sensitivity of 68% and specificity 97%. Thus, CEA is insufficiently sensitive to be used alone. Therefore, recommendation is to monitor recurrence with more than one diagnostic modality but applying the highest CEA cut-off value of 10 ng/L.[21]

Our study shows more left sided malignancy i.e. 27 (75%) including descending, sigmoid colon and rectum. In a review article, the rectal cancers, once accounting for more than 50% of CRCs in the West, have now decreased to less than colon cancers. This review emphasizing the three entity of CRC, namely 1) right sided proximal to the splenic flexure - Caecum, Ascending colon, Transverse colon; 2) left sided distally to this site descending colon and sigmoid colon; and 3) rectum.[22]

The CRC registry of SEER including 220000 cases reported proximal colon carcinoma rates were higher than distal colon or rectal

carcinoma, throughout the study period in the US.[23] However, according our study left sided 27 (75%), Table 2.

In present study, among 20 operated patients of CRC, 70% were moderately differentiated adenocarcinoma, Table 4. Literature shows, more than 90% of CRC are adenocarcinomas and most colorectal adenocarcinomas (70%) are moderately differentiated, whereas well and poorly differentiated carcinomas account for 10% and 20%, respectively.[24] Out of 20 patients, LVI was seen in 5 (25%), PNI in 4 (20%) and only two had both (PNI+LVI). The LVI and PNI represents advanced stage of CRC and risk of recurrence. In a study of 2649 patients regarding LVI and PNI in rectal cancers, concluded that Stage II rectal cancer patients with LVI and PNI had increased risk of recurrence.[25] Another study reported that LVI was positive in 26.3% out of 139026 patients, PNI was positive in 11.1% out of 142034 patients. The PNI is an independent poor prognostic marker for survival in CRC.[26] We did not analyze LVI and PNI positivity with outcome in our study because of retrospective nature and short followup.

In a phase-3 non inferiority trial of 6088 patients (receiving CAPEOX vs FOLFOX and 3 vs 6 months) concluded that 3 months of oxaliplatin-containing adjuvant chemotherapy was non-inferior to 6 months of the same therapy for patients with high-risk stage II and stage III colorectal cancer and was associated with reduced toxicity and improved quality of life.[27] In our study, 12 patients were referred for adjuvant treatment at other center and detail were not available.

Out of 36 patients, we could trace 30 till their last followup visit, with average of 36 weeks and maximum 156 weeks. Our institute lacked both medical and radiation oncology services earlier during the study period. Now we have started medical oncology service since last six months. Majority of patients who were sent for neoadjuvant treatment were lost to follow, 12 (of 17 curative resections i.e. 70.5%) who were referred out for adjuvant treatment did not come for regular followup. Also there was no mechanisms to trace them.

Comparing earlier study[7] from our center reported 52 (71.2%) CRC in >40 years and 21 (28.8%) in <40, similar to present study with majority 30 (83.3%) >40 years and 6 (16.7) and no difference in sex in both the studies. Moderately differentiated adenocarcinoma is the most common (70%) histologic type found in current study as compared to earlier study (22.2%). In current study out 20 surgeries, 17 (85%) had curative resection, possibly due to better CECT staging and segregation for adjuvant or palliative treatment avoiding non-curative resections, this data was lacking in earlier study.

Even though this is a low volume center with small sample size the findings are comparable, and a multicenter pooled data will provide better understanding of the CRC in Nepal. Limitations of present study is inherent of retrospective analysis of missing data and incomplete followup.

Conclusions

Our findings show CRC is still the disease of older age (>40 years) seen in 83.3% with a nearly equal incidence between male and female, though younger age (<40) is not spared and seen in 16.7%. Early detection confirms a high chance of curative surgery. Moderately differentiated adenocarcinoma is the most common variety.

Conflict of Interests

None

Fundings

None

References

1. Smith D, Ballal M, Hodder R, Soin G, Selvachandran SN, Cade D. Symptomatic

presentation of early colorectal cancer. Ann R Coll Surg Engl. 2006;88(2):185-90. DOI PubMed GoogleScholar
2. Scott NA, Jeacock J, Kingston RD. Risk factors in patients presenting as an emergency with colorectal cancer. Br J Surg. 1995;82(3):321-3. DOI PubMed GoogleScholar
3. Wong SK, Jalaludin BB, Morgan MJ, Berthelsen AS, Morgan A, Gatenby AH, Fulham SB. Tumor pathology and long-term survival in emergency colorectal cancer. Dis Colon Rectum. 2008;51(2):223-30. DOI PubMed GoogleScholar
4. International Agency for Research on Cancer (WHO). Cancer today: colorectal cancer [internet]. Cancers Fact Sheets. 2012;1-10. Weblink
5. Pradhananga KK, Baral M, Shrestha BM. Multi-institution hospital-based cancer incidence data for Nepal - an initial report. Asian Pac J Cancer Prev. 2009;10(2):259-62. DOI PubMed GoogleScholar Weblink
6. Larsen IK, Bray F. Trends in colorectal cancer incidence in Norway 1962-2006: an interpretation of the temporal patterns by anatomic subsite. Int J Cancer. 2010;126(3):721-32. DOI PubMed GoogleScholar
7. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin. 2011;61(2):69-90. DOI PubMed GoogleScholar
8. Kamangar F, Dores GM, Anderson WF. Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. J Clin Oncol. 2006;24(14):2137-50. DOI PubMed GoogleScholar
9. Boyle P, Langman JS. ABC of colorectal cancer: epidemiology. BMJ. 2000;321(7264):805-8. DOI PubMed GoogleScholar
10. O'Connell JB, Maggard MA, Livingston EH, Yo CK. Colorectal cancer in the young. Am J Surg. 2004;187(3):343-8. DOI PubMed GoogleScholar
11. Zhou Q, Li K, Lin GZ, Shen JC, Dong H, Gu YT, Liu HZ. Incidence trends and age distribution of colorectal cancer by subsite in Guangzhou, 2000-2011. Chin J Cancer. 2015;34(8):358-64. DOI PubMed GoogleScholar
12. Shah S, Shrestha S, Shah JN, Paudyal S. Clinico-pathological characteristics of colorectal carcinoma at university teaching hospital, Nepal. Journal of Patan Academy of Health Sciences. 2015;1(2):35-8. DOI GoogleScholar Weblink
13. Bohorquez M, Sahasrabudhe R, Criollo A, Sanabria-Salas MC, Vélez A, Castro JM, et al. Clinical manifestations of colorectal cancer patients from a large multicenter study in Colombia. Medicine (Baltimore). 2016;95(40):e4883. DOI PubMed GoogleScholar
14. Abotchie PN, Vernon SW, Du XL. Gender differences in colorectal cancer incidence in the United States, 1975-2006. J Womens Health (Larchmt). 2012;21(4):393-400. DOI PubMed GoogleScholar
15. Ben-Ishay O, Peled Z, Othman A, Brauner E, Kluger Y. Clinical presentation predicts the outcome of patients with colon cancer. World J Gastrointest Surg. 2013;5(4):104-9. DOI PubMed GoogleScholar
16. Świderska M, Choromańska B, Dąbrowska E, Konarzewska-Duchnowska E, Choromańska K, Szczurko G, et al. The diagnostics of colorectal cancer. Contemp Oncol (Pozn). 2014;18(1):1-6. DOI PubMed GoogleScholar
17. Triantafillidis JK, Vagianos C, Malgarinos G. Colonoscopy in colorectal cancer screening: current aspects. Indian J Surg Oncol. 2015;6(3):237-50. DOI PubMed GoogleScholar
18. Amri R, Bordeianou LG, Sylla P, Berger DL. Impact of screening colonoscopy on outcomes in colon cancer surgery. JAMA Surg. 2013;148(8):747-54. DOI PubMed GoogleScholar
19. Lakoff J, Paszat LF, Saskin R, Rabeneck L. Risk of developing proximal versus distal colorectal cancer after a negative colonoscopy: a population-based study. Clin Gastroenterol Hepatol. 2008;6(10):1117-21. DOI PubMed GoogleScholar
20. Duffy MJ. Carcinoembryonic antigen as a marker for colorectal cancer: is it clinically useful? Clin Chem. 2001;47(4):624-30. DOI PubMed GoogleScholar Weblink
21. Nicholson BD, Shinkins B, Pathiraja I, Roberts NW, James TJ, Mallett S, et al. Blood CEA levels for detecting recurrent colorectal cancer. Cochrane Database Syst Rev. 2015;12: CD011134. DOI PubMed GoogleScholar
22. Li FY, Lai MDe. Colorectal cancer, one entity or three. J Zhejiang Univ Sci B. 2009;10(3):219-29. DOI GoogleScholar
23. Troisi RJ, Freedman AN, Devesa SS. Incidence of colorectal carcinoma in the U.S.: an update of trends by gender, race, age, subsite, and stage, 1975-1994. Cancer. 1999;85(8):1670-6. DOI PubMed GoogleScholar
24. Fleming M, Ravula S, Tatishchev SF, Wang HL. Colorectal carcinoma: pathologic aspects. J

Gastrointest Oncol. 2012;3(3):153-73. DOI PubMed GoogleScholar
25. Nikberg M, Chabok A, Letocha H, Kindler C, Glimelius B, Smedh K. Lymphovascular and perineural invasion in stage II rectal cancer: a report from the Swedish colorectal cancer registry. Acta Oncol. 2016;55(12):1418-24. DOI PubMed GoogleScholar
26. Al-Sukhni E, Attwood K, Gabriel EM, LeVea CM, Kanehira K, Nurkin SJ. Lymphovascular and perineural invasion are associated with poor prognostic features and outcomes in colorectal cancer: a retrospective cohort study. Int J Surg. 2017;37:42-9. DOI PubMed GoogleScholar
27. Iveson TJ, Kerr RS, Saunders MP, Cassidy J, Hollander NH, Tabernero J, et al. 3 versus 6 months of adjuvant oxaliplatin-fluoropyrimidine combination therapy for colorectal cancer (SCOT): an international, randomised, phase 3, non-inferiority trial. Lancet Oncol. 2018;19(4):562-78. DOI PubMed GoogleScholar