

Large Intestine Malignancies in Dar es salaam, Tanzania.

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Background: Large intestine malignancies basically can be defined as cancer of the large bowel. It includes all malignant conditions originating from the ileocaecal valve down to the anus. In the year 2000, colorectal cancer was ranked the third most common form of cancer in adults world-wide in terms of incidence. This study aimed to document the profile of large intestine malignancies and early treatment outcomes among patients attended in major hospitals in Dar es Salaam, Tanzania.

Methods: This was a one year hospital based retrospective cross sectional study conducted by using a structured data collecting tool. The data were analyzed using SPSS software.

Results: A total of 102 patients with Large intestine malignancies were enrolled in our study. Both sexes were affected equally. The overall mean age was 51.23 (SD $\pm$ 15.5) years with a range of 22 to 80 years with those aged between 60 to 79 being the most affected group by 40.2%. Most tumours were located in the rectum and anal canal constituting 49.3% in males and 50.7% in females. DUKES C accounted for 79.4% of the cases with Adenocarcinoma being the commonest histopathological diagnosis accounting for 82.4% of the cases with Colo-Rectal tumours. Hemicolectomy was the most performed surgery by 57.1% with good outcomes at a follow up of thirty days. Only one death occurred in patient who underwent a low anterior resection.

Conclusion: From our study Large bowel malignancy is no longer a rare condition with no gender bias. Majority of our patients with large intestine malignancies still presents with advanced disease, we therefore call for high index of suspicion among clinicians for early diagnosis and prompt treatment to improve survival of patients.

Key words: Large intestine malignancies, treatment outcome

Introduction

The large intestine extends from the ileocaecal valve to the anus. It is divided anatomically and functionally into the colon, rectum and anal canal. Large intestine malignancies can be subdivided into colon cancer, which ranges from caecum to the sigmoid colon, rectal cancer that involves the rectum and anal cancer within the anal canal¹⁻⁴. In the year 2000, colorectal cancer was ranked the third most common form of cancer in adults world-wide in terms of incidence (after prostate and lung cancer in males and breast and lung cancer in females)⁵. Among both men and women, incidence rates were nearly fourfold higher in more-developed compared with less-developed countries of the World, whereas mortality rates were only two-and-a half-fold higher⁶. In United States about 72% of cases arise in the colon and about 28% in the rectum³. Anal canal cancer usually appears in the 6th and 7th decades of life with prevalence double in women compared to men, mainly attributed to Human Papilloma Virus (HPV) infections⁶. An increase has also been found in geographical areas where HIV prevalence is high, and among homosexuals⁶. Worldwide it is estimated that 30,400 new cases of anal canal cancer occur annually with 15,900 cases in developing countries and 14,500 in developed countries^{3,6}. The lowest rates of colorectal cancer are reported to occur in Sub-Saharan Africa, South America and Asia, but they are said to be on the increase in these countries probably due to change in life-style and dietary habits⁷.

The major clinical features of large intestines malignancies are rectal bleeding, change in bowel habits, abdominal pain, bowel obstruction, weight loss, anorexia, anaemia, tenesmus and rectal mass depending on the site of location of the tumor. Silently, patient may have occult blood in

stool, and persistent anaemia⁸⁻⁹. The diagnosis of large intestine malignancies, as with all malignancies, requires a high index of suspicion and diligent follow-up of all symptoms, especially in high-risk individuals¹⁰. A logical approach to early diagnosis is through routine screening tests. The most widely used screening tests for asymptomatic individuals are: Digital rectal examination (DRE) which is inexpensive and useful form of examination as well as Faecal Occult Blood Test (FOBT) used to detect tiny amounts of invisible blood in the stool. Blood vessels at the surface of colorectal polyps or cancers are often fragile and easily damaged by the passage of faeces¹¹. Proctosigmoidoscopy, Colonoscopy and Double contrast barium enema studies are useful for diagnosis¹².

Management of large intestine malignancies is based on the location and the stage of the tumor. Cancer of colon is a highly treatable and often curable disease when localized to the bowel.¹³ Standard treatment of colon cancer has been surgical resection of the primary and regional lymph nodes for localized disease and the procedure results in cure in approximately 50% of patients¹³. Laparoscopic resection has been employed and found to yield the same results as open resections for such lesions¹⁴. Regional lymph node dissection needs to be performed to determine staging, which guides decisions about adjuvant therapy. Up to 20% of isolated hepatic metastasis may be cured with resection or cryosurgical ablation of hepatic lesion¹⁵⁻¹⁶. Even patients with extensive metastatic disease may benefit from resection of colonic tumors to reduce the likelihood of intestinal obstruction or serious bleeding^{13, 15}.

For rectal carcinoma, the operative approach depends upon the level of the tumor proximal to the anal verge, the size of the tumor, the depth of penetration and the patient's general condition. For patients with less than 3 cm, well-differentiated, less than 7.5 cm from the anal verge shown by endosonography and CT imaging to be localized to the rectal wall, trans-anal excision may be the surgery of choice¹³. All other patients require either a low anterior resection with colorectal anastomosis or an Abdomino-perineal resection (APR) with a terminal colostomy, depending on how far above the anal verge the tumor is located¹³. Both respectability and operability of rectal tumors have been shown to be improved by Neo-adjuvant radiotherapy followed by Total Mesorectal Excision (TME). The use of staplers has also improved functional outcome and quality of life after rectal surgery by bowel anastomosis instead of a permanent colostomy.

Adjuvant chemotherapy and radiotherapy have been demonstrated to improve overall disease free survival in selected patients with large intestines malignancies. Patients with stage I colon cancer have excellent 5-year survival rates (80-100%) and no adjuvant therapy is recommended. Usually patients with advanced stage II and stage III benefit most with postoperative adjuvant chemotherapy. There is evidence that stage III patients have 33% reduction in mortality with adjuvant therapy. Stage IV patients can also benefit from adjuvant chemotherapy^{13, 17}.

Recurrence of large intestine malignancies following surgery is a major problem and often is the ultimate cause of death. So, patients who have undergone resections with curative intention should be followed-up closely indefinitely for evidence of tumor recurrence and spread¹³. The use of tumor markers before initiation of therapy is very important in the follow up period as well as endoscopic procedures that are now readily available in developing countries including Tanzania. The characteristics of colorectal and anal cancer patients in Tanzania have not been documented and local observation is lamenting on low resection rates of the patients that are attended, citing late presentation. The immediate outcome of our patients is also not known. So this study aimed to address these gaps and come up with suggestions to improve colorectal and anal cancer surgery in Tanzania.

Patients and Methods

A hospital based descriptive, retrospective study was carried out in five major hospitals in Dar es Salaam that perform large intestines cancer surgery, only one being a public facility, namely Muhimbili National Hospital, TMJ, Hindu Mandal, Tumaini, and Aga Khan hospitals for a period of eleven months. Those that were referred to the only cancer institute were also followed up to their discharge. There was no direct patient contact, treatment records was obtained by reviewing their case notes where information regarding age, location of tumor, histological confirmation, HIV status, treatment offered, dukes classification and immediate outcome. All patients with histological confirmation of malignancy of the large intestines were included in the study.

The study protocol was presented to IRB of Muhimbili University of Health and Allied Sciences, MUHAS, where approval was obtained. This study carried no risk to the patients as only their records were being reviewed, but had the benefits of showing deficiencies in our practice for the benefit of future patients with large intestines malignancy. No direct patients' identifiers were used in this study, and confidentiality was maintained even after the study period. Data was collected using a structured questionnaire, cleansed, coded and entered into EPI Info 2002 and exported into SPSS version 16 for analysis where cross-tabulations were generated. This study did not look at why surgery was not offered to patients, no views of surgeons was gathered, patients risk factors not assessed and reason for patients refusing proposed treatment and the nature of the proposed treatment.

Results

A total of 102 patients were treated for large intestines malignancy during the period of 12 months with equal sex distribution. The age ranged from 22 to 80 with a mean of 51.2 ± 15.5 , with the mean age in males lower than in females at 50.5 (SD ± 15.8) years and 51.9 (SD ± 15.2) years respectively. Over a quarter of the study subjects were below forty years of age while the majorities were sixty years and above at 43(42.1%) (Figure 1). Adenocarcinoma was the most prevalent histological diagnosis by 84(82.4%), with slight male predominance at 43(51.2%) for colorectal cancers, while squamous cell carcinoma was dominant in the anal canal in 13 (12.7%), with female predominance, 8 (61.5%). Four cases with tumor in the colon and rectum respectively had Gastro-Intestinal Stromal Tumors (GIST) one in the sigmoid colon and three being rectal region.

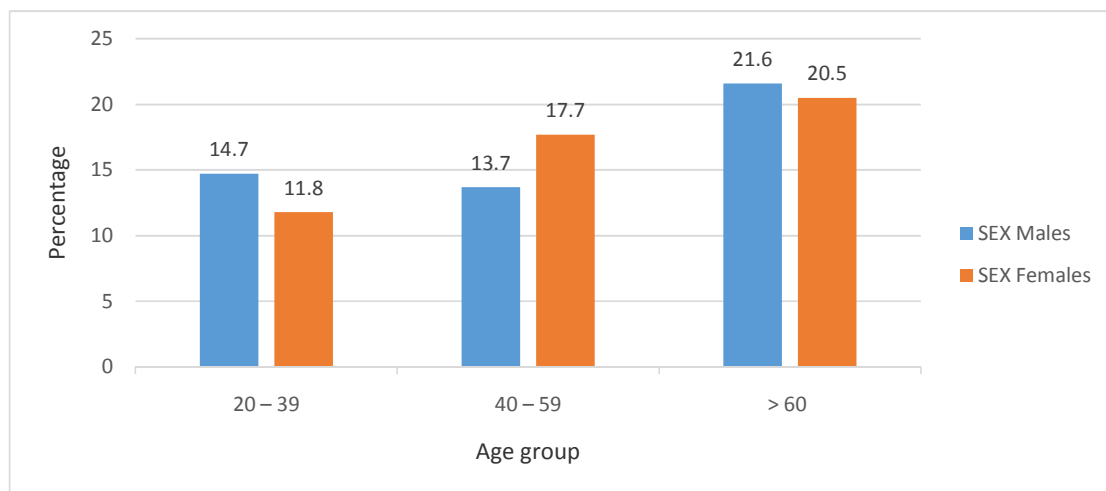


Figure 1: Age and sex distribution (n=102)

Table 1. Anatomical Location of the Tumour.

	Anatomical Location						
	Caecum N=09	Ascending N=02	TC N=01	DC N=01	Sigmoid N=09	RA N=79	Multiple N=01
Age							
20 – 39	02	01	0	0	1	23	0
40 – 59	02	01	01	0	02	25	01
>60	05	0	0	01	06	31	0
Sex							
Male	06	01	0	0	05	38	01
Female	03	01	01	01	04	41	0

Key: TC - Transverse colon; DC - Descending colon; RA- Rectum and Anus

Table 2. DUKES stage in Relation to Age and Sex of the study patients with colorectal tumors.

		DUKE'S STAGE		
		CN=81 (%)	D N=16 (%)	Unclassified N=5
Sex	Male	38 (46.9)	10 (62.5)	03
	Female	43 (53.1)	06 (37.5)	02
Age group				
	20 – 39	21 (25.9)	04 (25.0)	02
	40 – 59	25 (30.9)	07 (43.8)	0
	60 – 79	35 (43.2)	05 (31.2)	03

Table 3. Types of Curative Surgical Treatments Offered

Variable	APR (9)	LAR(3)	HC(16)	Total (28)
Age group				
20 – 39	02	01	04	07
40 – 59	03	0	07	10
>60	04	02	05	11
Sex				
Male	05	02	09	16
Female	04	01	07	12
Death	0	01	0	01

Key: APR – Abdomino-Perineal Resection, **LAR:** Low Anterior Resection, **HC:** Hemi-Colectomy

Only one case of Melanoma of the anal canal was also found. Majority of the study subjects had tumors in the Anorectal region, 79 (77.5%) most of whom were sixty years and above. Slightly more female patients had tumors in that region at 41 (51.9%) (Table 1). Nearly all patients with colorectal tumours, 95.1%, had Dukes staging performed with the majority being in stage C, 81(79.4%), followed stage D by 16 cases (15.7%) of which 12 were due to liver metastasis and four lung metastasis (Table 2).

Only 28 (27.5%) of the patients had tumor resection done with Hemicolectomy being the most performed procedure in 16 (57.1%), followed by Abdomino-perineal resection in 9 (32%) and the least was Low anterior resection in 3 (10.7%). All the surviving patients were referred for chemoradiotherapy. Forty seven patients received palliative treatments in the form of colostomy and chemoradiation (Table 3).

Discussion

While this study did not aim to document on the incidence of colorectal and anal malignancy, it has shown that the problem might be of significant health concern to health planners. The study has shown that these cancers affect people in their middle age of life when they are still productive and useful to their societies, contrasting with most studies which have reported the disease to be occurring in advances of age¹⁸⁻²⁴. A quarter of the study patients were well below forty years of age, but it was not uncommon among those over sixty years. This pattern is difficult to explain in this study but can be a focus of another study to explore on the risk factors for the development of the malignancy including molecular and genetic characteristics of these patients. While some studies suggest that large intestines cancer is largely a disease of the male⁷, our study has shown equal sex predilection. This finding is similar to those from India and Thailand²⁵⁻²⁶. While it is postulated that estrogen hormones are protective against the cancer, why our women were not protected remains unknown to us and is another area for future studies.

Clinically, most of our patients with large intestine cancers presented late making it difficult to differentiate between anal tumors extending upwards to the anus or vice versa. Due to this, more than two thirds of the tumors were classified as Anorectal which is the most preferred terminology here. The second most common site was the sigmoid colon, therefore making left sided tumors to be the most common just like in other studies²⁷. Differentiation between anal and rectal tumor was then only made after histological diagnosis, where by squamous cell carcinoma would be considered as anal in origin and Adenocarcinoma as rectal in origin. In this study, Adenocarcinoma constituted more to more than four fifth of the histological diagnosis to patients who had colorectal tumours, with slight male predominance. This is similar to other studies which have shown that more than three quarters were Adenocarcinoma¹⁹. There were 12.5% cases of squamous cell carcinoma of the anal canal in this study with majority occurring in the female population. This in other literature was explained by the occurrence of Human Papiloma Virus in the female population. A thorough examination would have been ideal to rule out co-existence of cervical cancer because undocumented observation in our centers has shown cases of the later infiltrating the anal canal and admitted in surgical wards. Our study has also reported the occurrence of GIST in sigmoid colon and for the first time in this country melanoma in the anal canal.

Almost all of our patients with colorectal tumours presented late with dukes stage C and D in spite of most of them having tumors on the left side which usually present early due to bleeding per rectum, mass sensation, and bowel obstruction; though the exact nature of presentation was not documented. However, our findings are similar to those reported from other low incidence areas where screening is not being practiced^{14, 25-27}. General patient interview to know of their presenting symptoms, health seeking behavior, medical attention before referral and physicians index of suspicion should be investigated to address this problem of late presentation. Similarly, a prevalence study should be carried out at multiple centers in the country to identify at risk patients and carry out surveillance and screening.

Just well over one fifth of the patients had surgical resection of the tumor whether with palliative or curative intent. The reason for this low resection rate was not explored, undocumented reports from the physicians report patients refusal to accept proposed

treatment modalities, especially if it involved permanent colostomy. This is usually the standard of care offered to lower rectal and anal tumors since bowel anastomosis after resection of lower rectal tumors is usually hand sewn. Uses of stapling devices is not very famous due to their high cost, and are not being stocked by hospitals hence patients have to buy one and bring it with them for surgery. In the country as a whole, there are no specialist colorectal and anal cancer surgeons, hence no dedicated team of providers who have developed interest and expertise in the management of these patients. This resulted into longer waiting lists for surgery and possibility of stage shift of the disease. The most commonly performed procedure was a palliative colostomy due to what was perceived to be inoperability. The practice of offering Neo-adjuvant radiation therapy is not very popular as it can be seen that only 19.5% of the study subjects underwent it, unlike in other places where it was offered to more than half of the patients^{17, 28}. Observation from local experience after both Neo-chemotherapy and/or radiotherapy is a no change in tumor status.

Adjuvant chemotherapy and radiotherapy have been demonstrated to improve overall disease free survival in selected patients with large intestine malignances. Patients with stage I colon cancer have excellent 5-year survival rates (80-100%) and no adjuvant therapy is recommended. Usually patients with advanced stage II and stage III benefit most with postoperative adjuvant chemotherapy. There is evidence that stage III patients have 33% reduction in mortality with adjuvant therapy. Stage IV patients can also benefit from adjuvant chemotherapy^{13, 17}. Recurrence of large intestine malignances following surgery is a major problem and often is the ultimate cause of death. So, patients who have undergone resections with curative intention should be followed-up closely indefinitely for evidence of tumor recurrence and spread¹³. The use of tumor markers before initiation of therapy is very important in the follow up period as well as endoscopic procedures that are now readily available in developing countries including Tanzania. In our study the role of adjuvant chemotherapy was not studied.

The questions remain whether we are using the right drugs and doses, and whether EBRT can deliver enough doses to shrink a tumor has not been studied here. But since two thirds of patients with colon cancers had received a Hemicolectomy leaves a lot of questions as to whether it was inoperability or lack of expertise which led to low resection rates as those factors may influence the outcome²⁹. Leaving the general surgeons to do advanced surgeries like recto-anal procedures should be looked at especially in tertiary level facilities to improve resection rates.

Conclusion

Large intestines malignancy is a common disease occurring in Tanzania with equal sex distribution, affecting the middle age. It occurs most commonly on the left side, with rectum being the commonest. Most of large intestine cancer patients present with advanced stages of the disease with adenocarcinoma being the most common histological diagnosis for those who had colorectal tumours. A need for high index of suspicion among clinicians so as to ensure early diagnosis of large intestines cancers and prompt treatment is required. Health education to the population should be offered to promote awareness of early signs and symptoms of large intestines cancers hence increase rate of early diagnosis.

More studies are needed to investigate on long term outcomes of these patients in terms of morbidity and mortality with respect to the available treatment options.

Recommendation

- Establishment of a surgical gastroenterology unit that will only be dealing with GIT surgery including large bowel surgery should be considered.
- There is a need to train surgeons on lower bowel surgery.
- Locally developed protocol for the management of large intestine cancer should be developed to improve and standardize type of care offered to the patients.

Acknowledgements

We would like to extend our sincere gratitude and appreciation to the Ministry of Health and Social Welfare for sponsoring this study without conflict of interest known to us. We also wish to thank members of the department of surgery MNH, Dr. Jafferji the Chairman TMJ Hospital, Dr Chahya pathologist at TMJ Hospital, members of staff at Ocean Road Cancer Institute, Aga Khan Hospital, and Tumaini Hospital. We express our thanks to all the patients and caregivers.

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