Addis Ababa University

College of Health Science and School of Medicine

Department of pathology

Histopathologic pattern of Neoplastic Colorectal Lesions in Resection Specimens at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, over a 5 year period, 2016-2020

A Thesis submitted to the Department of Pathology, College of Health Sciences, School of Medicine Addis Ababa University in Partial fulfillment of the requirements for the Specialty Diploma in Pathology.

Investigator: Zekarias Yitbarek (MD, Pathology resident)

Advisor: Dr Mullugeta Temesgen (MD, Assistant professor of pathology)

Acknowledgement

I would like to express my deepest gratitude to my instructor and advisor, Dr (MD), Assistant Professor of pathology for his expertise, guidance and constructive advice in the course of this Study. Next, I would like to extend my sincere gratitude to college of health sciences, Addis Ababa University.

Contents

List of Tables

List of Figures

Abbreviation

CRC-Colorectal cancer

CC-Colon cancer

RCC-Right colon cancer

LCC-Left colon cancer

HDI-Human development index

PNI-Perineural Invasion

LVI-Lymphovascular Invasion

WHO-World Health Organization

AJCC- American Joint Committee on Cancer

NHL-Non Hodgkin Lymphoma

DLBCL-Diffuse Large B cell Lymphoma

GIST-Gastro Intestinal Stromal Tumor

MALT-Mucosal Associated Lymphoid Tissue

ABSTRACT

Background: Adenocarcinoma of the colon is the most common malignancy of the gastrointestinal tract and is a major contributor to morbidity and mortality worldwide. By contrast, the small intestine, which accounts for 75% of the overall length of the gastrointestinal tract, is an uncommon site for benign and malignant tumors **[1]**

Over 1.8 million new colorectal cancer cases and 881000 deaths are estimated to occur in 2018 accounting for about 1 in 10 cancer cases and deaths. Overall colorectal cancer ranks third in terms of incidence but 2nd in terms of mortality. During 2018, according to Globocan report on Ethiopia 2878 and 1671 new cases of colon and rectal cancers were diagnosed making colon and rectal cancers 5th and 11th in overall cancer incidence .In the same year 2371 and 1067 cases of colon and rectal cancer patients died which makes them 5th and 12th commonest causes of cancer related death. [2]

Objectives: The aim of this study is to determine Histopathologic patterns of Neoplastic Colorectal Lesions in resection specimens in Tikur Anbessa Specialized Hospital.

Methods and materials: The study applies retrospective cross-sectional descriptive method to review Histopathologic reports of patients with Neoplastic Colorectal Lesions at resection specimens in the five years period (January 2016 to August 2020).The reports are collected from the pathology data archives and data analysis is done by Using IBM SPSS 23.0.

Result: A total of 208 colorectal resections fulfil the study criteria in the study period. From this 117 were males and 91 were females. Majority of the cases are in the 5th decade of life (41-50 years), 25%. The age of the study subjects ranges from the minimum of 19 to the maximum age of 87 forming the range of 68 and mean of 52.13. The Rectum is most common location (29.5%) of the lesions followed by the Sigmoid Colon (24.4%).

Adenocarcinoma (194, 93.3%) is the most common Histopathologic pattern followed by Neuroendocrine Tumors (7, 3.4%) and 2 cases (1%) of High risk GIST. From the 194 cases of Adenocarcinoma 111 (57.2%) are Males and 83(42.8%) are Females, male to female ratio 1.34:1. The mean age patients with Adenocarcinoma is 51.73 and age range is 19-87.The Rectum 56(30.9%) followed by Sigmoid Colon 47 (26 %) are most common locations. From the total cases of adenocarcinoma 41 of them (21.1%) are aged below 40 while 153(78.9%) are aged above 40.
Adenocarcinoma NOS is most common histologic subtype of Adenocarcinoma 165(85.1%) followed by mucinous Adenocarcinoma 26(13.4%) and Signet Ring Cell Carcinoma 3(1.5%).

Conclusion: This study reveals that majority of the colorectal cancers occur in the Recto Sigmoid area, in the 5th to 7th decades and more common in males. Adenocarcinoma is by far the most common Histopathologic pattern.

1. Introduction

1.1Background

The large bowel comprises the terminal 1–1.5 m of the gastrointestinal tract and is divided into the following regions: cecum, ascending (right) colon, transverse colon, descending (left) colon, sigmoid colon, and rectum. The hepatic flexure is at the junction of the ascending and transverse colon, and the splenic flexure is at the junction of ***the transverse*** and descending colon [29]. If we consider the distal transverse colon as the boundary between the right colon and left colon, the right colon includes the cecum, ascending colon, liver flexure, and transverse colon, and the left colon includes the splenic flexure, descending colon and sigmoid colon [3] .The rectum forms the distal 8–15 cm of extra peritoneal large bowel that lies within the pelvis and ends at the anal canal [29].

The large bowel wall is composed of four layers: mucosa, submucosa, muscularis externa (propria), and serosa (or, in the rectum, perimuscular tissues) [29].

The mucosa has three components: epithelium, lamina propria, and muscularis mucosae. The mucosal surface is covered by a single layer of low columnar to cuboidal epithelium into which the crypts of Lieberkuhn open, either on the surface itself (the majority) or onto the innominate grooves. This surface epithelium is composed of absorptive cells (with basally located nuclei, mucin-negative acidophilic cytoplasm, and luminally directed apical striated borders) and goblet cells (which synthesize, store, and secrete mucin granules). Lymphocytes and occasional eosinophils may be present between the surface epithelial cells, which rest on a continuous thin basement membrane. The crypts have a tubular, test tube-like shape, and are arranged parallel to each other. The lamina propria contains a few lymphocytes (both T and B cells), plasma cells, histiocytes, and mast cells scattered in a network of collagen fibers, smooth muscle bundles, vessels, and nerves [29]. Intramucosal ganglion cells can also be seen, isolated or in clusters, but they carry no pathologic significance [28].

The submucosa is composed of loose connective tissue having cell constituents similar to the lamina propria [30]. It also contains the sub mucosal neural plexus of Meissner. The muscularis externa (propria) includes a circular inner layer and a longitudinal outer layer, with the myenteric neural plexus of Auerbach lying between them. The serosa is composed of a single layer of flattened to cuboidal mesothelial cells and the subjacent fibro elastic tissue. Interstitial cells of Cajal are present scattered throughout the wall, as they are in other portions of the gastrointestinal tract [29].

The lymphatic drainage of the colon is mainly through the mesentery into the paracolic groups of lymph nodes located along the marginal vascular arcades. The lymphatic drainage of the rectum is toward the inferior mesenteric artery nodes, the superior hemorrhoidal chain, and the hypogastric and common iliac nodes [29].

Colorectal cancer is the most common type of gastrointestinal cancer [5]. Due to changes in life style incidence is rising worldwide [5]. It is the 2nd most common cancer in women and 3rd most common cancer in men with highest incidence rates seen in highest income countries [5].

Established risk factors include consumption of processed and red meat, alcohol and excess body fat, genetic predisposition (e.g. FAP), chronic bowel inflammation, pelvic irradiation [5].
Patients with colorectal cancer have varied clinical presentations, in part depending on primary site. Anemia and weight loss are common to cancers throughout the colon, whereas hematochezia
and constipation are most typical for Rectosigmoid cancers. Some patients present with obstruction or perforation [4].

Colorectal carcinomas show a range of gross appearances, including fungating, intraluminal masses; ulcerating tumors with heaped-up edges ; and circumferential, stricturing tumors. They are usually firm, with a uniform, white cut surface. Around 10% of colorectal cancers (mucinous adenocarcinomas) have a soft, mucoid cut surface [4].

The majority (90%) of colorectal carcinomas are adenocarcinomas, predominantly Adenocarcinoma NOS [5]. Histopathological subtypes include Mucinous Adenocarcinomas, Signet-ring cell carcinoma, Medullary carcinoma, serrated adenocarcinoma, Micropappilary adenocarcinoma, Adenoma-like adenocarcinoma, Adenosquamous carcinoma and carcinomas with sarcomatoid components [5].

Most colorectal cancers develop via the conventional pathway through the classic adenoma-carcinoma sequence of pathogenesis. The most frequent and characteristic Genetic changes in conventional adenoma-carcinoma pathway include Chromosomal instability pathway (84%), Microsatellite instability (MSI) pathway (13%) and Ultramutant pathway (3%) [5].

1.2 Statement of the problem

Over 1.8 million new colorectal cancer cases and 881000 deaths are estimated to occur in 2018 accounting for about 1 in 10 cancer cases and deaths. Overall colorectal cancer ranks third in terms of incidence but 2nd in terms of mortality. Colorectal cancer incidence rates are about 3 fold higher in transitioned versus transitioning countries; however with average case fatality higher in lower HDI settings, there is less variation in the mortality rate During 2018, according to globocan report on Ethiopia 2878 and 1671 new cases of colon and rectal cancers were diagnosed making colon and rectal cancers 5th and 11th in overall cancer incidence. In the same year 2371 and 1067 cases of colon and rectal cancer patients died which makes them 5th and 12th commonest causes of cancer related death [2].

1.3 Significance of the study

Colorectal cancer is a major cause of morbidity and mortality throughout the world [5]. Colorectal carcinoma, historically a cancer typical of the industrial countries, is now among the common newly diagnosed cancers and causes of cancer death globally. The evidence that the disease is significantly increasing in most developing countries heralds an even more remarkable disease burden in the near future [6]. Environmental factors such as changes in life style and diet, are proposed to play major roles in the current transition of CRC epidemiology [8].

The increase in CRC incidence in developing countries, that are often equipped with fewer resources, are paralleled by an increase in the mortality rates, as indicated by studies from South America and Eastern Europe[7]

Despite the increasing trend of colorectal carcinoma in developing countries there is no recent study at Pathology department of this institution.

2. Literature review-

The crude incidence of CRC in Sub-Saharan Africa is 3.69/100,000 for women and 4.38/100,000 for men (overall 4.04/100,000) with a wide variation in the geographical distribution of CRC reported on the African continent. A high incidence in South Africa of 11.9/100,000 whilst low incidences reported in East Africa (6.5/100,000) and West Africa (3.8/100,000 in women; 4.5/100,000 in men) has been reported[9,10,11].However, in a recent study by Siegel from Sub-Saharan Africa has shown that in urban areas the incidence of colorectal carcinoma is indeed increasing[12]. Generally, in many East African Countries there has been an increased incidence in the incidence rate of CRC [31]. The male to female ratio in East African studies currently report a ratio of 1.2:1 to 1.88:1[31]

In East Africa a significant proportion of patients are young with a median age at diagnosis of 41-59 years [13,14,15,16]. Between 19% to 38% of patients younger than 40 years of age present with CRC[14,15]. This is in contrast to only 1.9% of patients in the USA who are younger than 40 years and present with CRC [17]. Among African-American patients, early onset CRC has also been described [18].

In one study done Fatimah Biade Abdulkareem and colleagues in Lagos and Sagamu, Southwest Nigeria There were 420 cases (237 males and 183 females) of CRC. It peaked in the 60-69 year age group (mean: 50.7; SD: 16.2), M: F ratio 1.3:1 and 23% occurred below 40 years. Left-sided (distal colon) tumor 261 (62%) was more common than right-sided (proximal) ones 58 (14%). More than half of the cases were located in the Rectosigmoid region 246 cases (58.6%) followed by caecum 34 cases (9%), ascending colon 24 cases (6%), transverse 19 cases (4.5%) and descending colon 15 cases (3.6%) each. Macroscopically ,the right sided tumors were fungating nodular lesions with surface ulcerations while the left sided tumors were flat and infiltrating or constricting. Microscopically, the tumors were adenocarcinoma of varying grades. Majority were well differentiated adenocarcinoma in 233 (55.5%), 88 (21%) were moderately differentiated and 34 (8%) were poorly differentiated carcinoma. Mucinous and Signet ring carcinomas accounted for 45 cases (10.7%) and 5 cases (1.2%), respectively and more common in patients under 40 years compared to Well Differentiated tumors. Fifteen cases (3.6%) were anaplastic (undifferentiated) tumors. Mucinous carcinoma accounts for (19%) and signet ring carcinoma (3%) under 40 years; compared to 4% & 0.6% record in patients above 40 years. On the other hand, well differentiated adenocarcinoma was more common in patients above (59%) than those below 40 years (43%). The male to female ratio is also less for younger patients. The cases less than 40 years also tended to be located in the cecum (11%) compared to older patients (7%) [19].

In a study which compares 17,641 Patients With Right- and Left-Sided Colon Cancer: Differences in Epidemiology, Perioperative Course, Histology, and Survival done by Frank Benedix and colleagues Between January 1, 2000 and December 31, 2002 all consecutive patients with CC (N 17,641) were analyzed for this study. Of this 12,719 Patients undergo Elective Operations with Curative Intent. Overall, 8297 (47.0%) had RCC and 9344 (53.0%) had LCC. With respect to anatomical site, sigmoid colon cancer was found to be the most frequent tumor accounting for 42.5%. RCCs were more frequently diagnosed in women (55.3%), and LCCs were found predominantly in men (54.1%). Patients with RCC were significantly older

with total median age of 71 years as compared to LCC patients which has a median age of 68.5. This age difference
(RCC vs LCC) was more pronounced in women than in men, median age of 73 and 69.7 years for RCC and LCC in females. Histologically, the majority of all CC were adenocarcinomas with a higher proportion in the LCC group (RCC 86.8% vs LCC 91.7%). Mucinous (RCC 10.6% vs LCC 6.3%), undifferentiated (RCC 0.7% vs LCC 0.2%), and signet-ring cell carcinomas (RCC0.9% vs LCC 0.3%) were more frequently diagnosed in patients with RCC. Tumor grade for RCC was grade I,II,III and IV in 5.5%,65.9%,27.8% and 0.8% of the cases respectively and tumor grade for left LCC was grade I,II,III,IV in 6.2%,76.8%,16.8% and 0.3% of the cases respectively, revealing a higher proportion of poorly differentiated tumors in the RCC group.
According to TNM classification PT1, PT2, PT3 AND PT4 tumor was seen in 7.4%, 16.5%, 64.8%, 11.3% respectively for RCC, and the respective numbers for LCC were 13.9%, 19%, 58% and 9%. RCC showed locally advanced tumor growth (pT3/4 76.1% vs 67.0%) and lymph-node-positive disease more frequently (36.1% vs LCC 33.6%). The median number of lymph nodes examined in surgical specimens of RCC was 17, compared with 14 in LCC [20].

Population-Based Analyses of Lymph Node Metastases in Colorectal Cancer done by ROCCO RICCIARD and colleagues done at the Department of Surgery, University of Minnesota Medical School, Minneapolis, Minnesota; and the ‡Department of Surgery, St. Michael's Hospital, University of Toronto, Canada In a cohort of 124,180 CRC patients diagnosed from 1988 through 2002 treated with radical surgery without Neo adjuvant irradiation, assesses the proportion of patients who were lymph node positive and determined factors that influenced the risk of lymph node metastases including patient anatomic location, and Histopathologic factors. Of the 124,180 patients with CRC who met the selection criteria, 43% had proximal colon tumors, 43% had distal colon tumors, and 14% had rectal tumors. Overall, 34.5% of patients were node positive. Patients with T4 tumors were much more likely to be node positive (50%) than those with T1 tumors (8%). Patients with poorly differentiated tumors were much more likely to be node positive (52%) than those with well-differentiated tumors (20%). Patients with poorly differentiated tumors were at least twice more likely to be node positive at any T stage than those with moderately differentiated tumors [21].

In a study done by Iris D. Nagtegaal and colleagues and the Pathology Review Committee for the Cooperative Clinical Investigators of the Dutch Colorectal Cancer Group on Macroscopic Evaluation of Rectal Cancer Resection Specimen, the data of 180 non irradiated rectal cancer patients was analyzed .From the 180 patients for whom information was available about the quality of the Mesorectum in the reports, 102 specimens (56.6%) were classified as complete, 35 (19.4%) as nearly complete, and 43 (23.9%) as incomplete Mesorectum.The distance of the tumor from the anal verge is strongly associated with quality of the Mesorectum. Lower tumors (distal border 5 cm from the anal verge) showed only 39% complete excision, compared with 67% in the group of tumors located more than 10 cm from the anal verge. Forty-one patients had a positive resection margin, defined as tumor cells within 1 mm of the inked resection margin. In patients with a positive resection margin, 44% of the specimens were incomplete, compared with 11% in the patients with margins greater than 1 cm [22].

In a Histopathological study done by DN Dijxhoorn and colleagues on colorectal cancer in patients from Uganda Histopathological specimens of 81 Ugandan patients with CRC (2006-

2010) were retrospectively reviewed. The ages were not available in 9 out of 81 patients diagnosed with Adenocarcinoma. The median age at which colorectal cancer was diagnosed in the other 72 patients were 55 years (range 20-89). Patients aged under 50 years were 22 (30.6%) while 5 (6.9%) were < 30 years. Fifty (69.4%) of the patients were aged 50 years and above. The sex was not available in 8 out of 81 patients diagnosed with Adenocarcinoma. Of the other 73 patients, 34 were male (46.6%) and 39 women (53.4%). There was no significant difference in age of diagnosis between female and male .Mucinous adenocarcinoma was more common in younger compared to older patients (9.7% vs. 5.6%), though the presence of signet ring cells was similar. A total of 72 (88.9%) of cases were moderately differentiated and 9 (11.1%) were poorly differentiated. Younger patients were more likely to have a poorly differentiated adenocarcinoma than those diagnosed at an older age (8.3% vs. 4.2%) [23].

In a study by D. Zemenfes and colleague A Two- year review of Colorectal Cancer was done at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. A retrospective cross-sectional study design, by reviewing of patient records collected from 2010 to 2011 was used. There were 142 patients in two years' time but the records of only 120 (86%) patients could be retrieved for analysis. According to this study the age range of the patients is between 18 and 83 years. A third was below the age of 40 years, 69 (58%) were men with a male to female ratio of 1.3:1. Fifty six (49%) of the study subjects were between the age group of 40 and 60, while 44(36.6%) were under the age of 40 years. 48.3% of the tumors were located in the rectum. The caecum was the seat of the tumor in 12.5% of the cases. The sigmoid and the recto sigmoid junction were seats of tumor in12.5% and 10.8% respectively. Hence sigmoid, Rectosigmoid and rectum combined were the commonest (71.6%) sites involved in this study. According to this study Adenocarcinoma (94.8%) was the most frequently reported cancer. Other histological types include 2 cases of carcinoid, 1 case of lymphoma, 1 case of sarcoma and 1 case of Maltoma/MALT Lymphoma [24].

A research was done at Wuhan China by Zhiqiang Liu and colleagues on Colonic Gastrointestinal Stromal Tumor: A Population-Based Analysis of Incidence and Survival. In this study a total of 10046 GIST patients were collected in which 56 cases with an unknown tumor site were excluded. 249 colonic GIST and 9741 other GIST cases were included. Colonic GISTs were found to be more common in males with a slight male predominance (male 51.41%, female 48.59%) which was consistent with previous studies. The age of onset ranged from 21 to 93 with a median (mean) age of 67.5 (65.56) in colonic GISTs [25].

In a study done by M. T. C. Wong and K. W. Eu Department of Colorectal Surgery, Singapore General Hospital on Primary colorectal lymphomas, during the 10-year period from 1989 to 1999, 14 cases of primary colorectal lymphomas were identified. This comprised 0.44% of all colorectal malignancies (14 of 3199 cases) seen in the department during this period. Their mean age at presentation was 61 years. The two most common sites of involvement were the caecum (57.1%) and the rectum/sigmoid colon (21.4%). The lesions manifested in a variety of ways, ranging from solitary fungating masses to multiple colonic polyps. All but one patient underwent attempted curative surgical resection. All cases were non-Hodgkin's B-cell lymphomas, with a majority being diffuse large B-cell lymphomas (57.1%). The diagnoses were established through laparotomy in all cases. All cases presented with evidence of spread to regional lymph nodes or beyond [26].

In a study done by Osnat Bairey MD and colleagues At Institute of Hematology, Rabin Medical Center (Beilinson Campus) in Israel on Non-Hodgkin's Lymphomas of the Colon, Seventeen patients were identified over a 13 year period, comprising 1.4% of the total NHL registry. Fourteen patients had primary intestinal lymphoma, and in 3, colonic involvement occurred at relapse or progression. Diagnosis was established by colectomy in 11 patients and by colonoscopy with biopsy in the remaining 6.Ninety-four percent were of B cell origin; 88% had aggressive histology : DLBCL in 11, MCL in 3, and peripheral T cell lymphoma in 1.Two patients had indolent lymphomas: MALT in one and small lymphocytic lymphoma in the other. The most frequently involved site at diagnosis was the ileocecal region in 8 patients (47%), followed by the cecum in 5 (29%), the sigmoid in 3 (18%) and the colorectal area in 1 patient (6%)[27]

In a study done by Senait Ashenafi on Tumor characteristics of CRC in Ethiopia and Switzerland the overall M: F ratio of 1.1:1 and 1.3:1 was observed in Luzern and Addis Ababa respectively. The mean age for CRC in Luzern was 69 years while in Addis Ababa it was 46 years. However there was a female predominance in those under 4o years of age. The male to female ratio in Luzern was 1:3.5(2:7) and in Addis 1:2(10:19). In Addis 39.2% (29) cases of CRC were seen in patients under 40 years of age, where as in Luzren only 2.4% (9 cases) of CRC were in patients under 40 years. In Luzren 93.5% (347 cases) were Low Grade, 6% (22) High Grade, 0.5% (2) were Mucinous and there were no case of Signet Cell Carcinoma. In Addis 84% (62) were Low Grade, 7% (5) were high grade, 5% (4) were Mucinous, and 4% (3) were Signet Ring Cell Carcinoma. In those less than 40 years Higher Grade Tumors were seen in 28% (8) of cases from Addis while none were seen from Luzern. While in those over 40 years of age the Higher Grade Tumors accounted for 6.6% (24) of the cases from Luzern and 9% (4) of the cases from Addis [32].

In a study done by Michael Adloff and colleagues on colorectal cancer in patients under 40 years of age from the department of surgery Schiltigheim/Strasborg, France in a review of 1037 patients with colorectal cancers the age range was from 19 to 90. There were 32 patients (3%) below the age of 40 years. Mucinous carcinoma accounts for 34.5% and 8.6 % of adenocarcinoma cases before and after the age of 40 [33].

In a study done by Patricia and colleagues in Atlanta Georgia on Adenocarcinomas of the colon and rectum in persons under 40 years 87% of cancers were adenocarcinomas of the usual type 10% were mucinous adenocarcinomas, and 1.7% were signet ring carcinomas. Among those 40 years or older 94% were adenocarcinomas usual type, 5% were mucinous adenocarcinomas 0.2% were signet ring carcinomas [34]. In this study among the 106,760 colorectal adenocarcinomas in persons 40 years and older, the overall proportion of the 105,001 cancers with a known site in each location was similar to that for the younger patients: rectum, 20%; recto-sigmoid junction, 11%; sigmoid colon, 26%; descending colon, 6%; splenic flexure, 3%; transverse colon, 8%; hepatic flexure, 3%: ascending colon, 9%; cecum, 16%; and appendix, 0.3%[34].

In a study done by Aliyu and colleagues on the burden of Colorectal Carcinoma in Nigeria Abubakar Tafawa Balewa University Teaching Hospital, Bauchi, Nigeria, A total of 65 patients were studied. 44(67.7%) were males and 21(32.3%) were females, with a male-

female ratio of 2:1.The mean age was 50.5, with an age range of 16-79 years. The most common of CRC in Northeastern Nigeria is rectal cancer (33.8%). Adenocarcinoma is the most common histological variant (86.2%), followed by Gastro-intestinal Stromal Tumors (GIST) at 4.6%. From Adenocarcinomas 10.8% and 4.6% are Mucinous and Signet ring type [35].

In a study done by Renan Cascaes Lopes on the incidence of Angiolymphatic Invasion In Colorectal Cancer in Brazil Two hundred and fifty one patients were submitted to CRC resection from 2000 to 2010, and the mean age was 60 years old, (+/ – 15 years). ALI was present in 112 patients (44.6%) and perineural invasion was seen in 22 patients (8.8%). In this study 184(73.3%), 50(19.9%), 15(5.9%), 2(0.7%) are well, moderately and poorly differentiated and undifferentiated [36].

In a population based study done by K. DeCaria and colleagues on rectal cancer resection and circumferential margin rates in Canada the percentage of rectal cancer cases with a positive CRM ranged from a low of 7.7% in Manitoba to a high of 21.1% in Nova Scotia. The wide range persisted even when the comparison was limited to larger provinces with higher volumes of rectal surgery. For example, the positive margin rate in British Columbia was nearly twice the rate reported in Alberta (17.0% and 8.7% respectively) [37].

In a study done by Ramzi Amri and colleagues in USA, Harvard Medical School on association of radial margin positivity with colon cancer, radial margin was involved in 52 (5.3%) of the 984 patients included in the study [38].

In a study done by Paul M. Johnson and colleagues On adequacy of nodal harvest from 569 primary colorectal cancer resection specimens in Canada the mean number of lymph nodes harvested was 8.3 nodes per patient and the range was between 0-60 [39].

In the study done by B.S.Nedrebo and colleagues on risk factors associated with poor lymph node harvest after colon cancer surgery in a national cohort, Oslo, Norway on 2879 colon cancer patients the median number of harvested lymph nodes was 14 [40].

In a study done by Nancy N Baxter on lymph node evaluation in 116,995 colorectal cancer patients in the US the median number of lymph nodes examined was nine[45].

In a study done by Hui-Hong Jiang and colleagues on Prognostic significance of lymphovascular invasion in colorectal cancer and its association with genomic alterations in Shanghai, China Of the 1219 CRC patients included in the retrospective analysis, 714 (58.6%) were male and 505 (41.4%) were female, with a median age of 62 years (range, 21-92 years). In this study there were 569 (46.7%) colon cancers and 650 (53.3%) rectal cancers. Histologically, 894 (73.3%) cases were well or moderately differentiated, and 325 (26.7%) were poorly differentiated or mucinous. LVI was detected in 150 tumors, with a presence of 12.3% (10.5%-14.2%) [41].

In a study done by Catherine and colleagues in Houston, Texas on 269 consecutive patients with CRC the Rectosigmoid and the rectum accounts for 35.7% and 26.5% of the cases. Perineural invasion was identified in less than 0.5% of initial pathology reports and on re review 22 % of

the tumors are were found to be PNI positive. In this study 9.6%, 13.8%, 9.6%, 56.9% and 10% of the cases are pTis, pT1, pT2, pT3 and pT4 respectively. From a total of 269 cases 36.1% and 58.6% are node positive and node negative respectively and 5.2% are pNx [42].

A study done by Senait Ashenafi at Addis Ababa University Pathology Department reviewed the biopsy reports of 255 patients having CRC in the years between 1973 to 1978 and 1989 to 1993.

In that study CRC constituted 0.8% of the total number of biopsies and 34% of "colorectal biopsies and was diagnosed in 164 males and 90 females. The male to female ratio was about 2:1; and did not show a major difference between the two study periods. The mean age of CRC in this study was 47 years with no difference seen between the two study periods. Even 35% of the carcinomas were seen below the age of 40 and 16% below 30 years of age. This younger age at presentation was consistent for both rectal and colon carcinoma. Most CRC were found in the rectum (66.7%). Left sided, mainly Rectosigmoid carcinomas accounted for 76% while right sided carcinomas (caecum and ascending colon) accounted for 8% only [44].

3. Objective of the study

3.1. General objective

- To determine Histopathologic Patterns of neoplastic colorectal lesions in resection specimens diagnosed in Tikur Anbessa Hospital from January 2016 to August 2020.

3.2 Specific objectives

- To show distribution of various neoplastic colorectal lesions at resection specimens by age and gender, gross specific location in colorectum, by Histopathologic pattern.
- To show the frequency of T and N pathologic staging of malignant neoplasms at colorectal resections and relative frequency of lymph node involvement with increasing depth of invasion.
- To show the frequency of radial margin involvement, mean number of lymph nodes harvested, frequency of lymphovascular and perineural invasion of colorectal neoplasms in resection specimens and to assess the relative frequency of quality of Mesorectal excision in rectal cancer resections.
- To compare right colon cancers and left colon cancers with age, sex, histologic subtype, pathologic T and pathologic N staging.
- To compare and contrast results from other similar studies done from different parts of the world with that of the result from the present study.

4. Methodology

4.1 Study Area

This study is conducted at Black Lion (Tikur Anbessa) specialized teaching Hospital. Tikur Anbessa (Black Lion) Specialized Hospital is located in Addis Ababa at Lideta sub-city opposite to Immigration office Ethiopia. It is the teaching hospital of the Addis Ababa University and the largest referral hospital in the country with over 700 beds, and serves as a training centre for undergraduate and postgraduate medical students, dentists, nurses, midwives, pharmacists, medical laboratory technologists, radiology technologists, and others who shoulder the responsibilities to solve the health problem of the community and the country at.

4.2 Study Design and Period

The study is a cross-sectional retrospective descriptive study where data will be retrieved from the archive of the department of pathology that are registered from Sep 2016 up to August 2020.

4.3 Source Population

All patients whose biopsy specimens were submitted to the department of pathology

4.4 Study population

All patients who undergo colorectal resections for neoplastic lesions and their specimens submitted to the department in the study period from January 2016 to August 2020.

4.5. Inclusion and exclusion criteria

4.5.1 Inclusion Criteria

- Complete medical records of patients
- All cases with definitive Histopathologic diagnosis

4.5.2 Exclusion criteria

- Cases lacking documentation of age and sex
- Cases with no pathologic staging and descriptive diagnosis.

4.6 Sample size estimation

All patients fulfilling the criteria during the study period will be included.

4.7 Sampling procedure

All the hard copy of colorectal excisional neoplastic histopathology reports from January 2016 to August 2020 will be reviewed from the archive of pathology department.

4.8 Data collection tools and procedures

Demographic data, clinical presentation of the patients and histopathology diagnoses will be extracted from the hard copy using data extraction sheet.

4.9 Study variables

Age, gender, location of the tumor, histologic type, grade of the tumor, pathologic T, N, M group, radial margin status, quality of Mesorectal excision for rectal tumors

4.10 Data analysis

The data sheets is coded and data entry, cleaning and analysis is done using the Statistical Package for the Social Sciences (SPSS)

4.11 Ethical consideration

Ethical permission is sought from the Department of Pathology, College of Health Sciences, Addis Ababa University, and ethics committee at Tikur Anbessa hospital. Names of patients or their chart numbers are not mentioned in the study to keep the confidentiality of the patients.

5. RESULTS

A total of 214 cases of colorectal resections were done for neoplastic lesions in the study period. From this 4 were excluded because of incomplete Histopathological diagnosis; as absence of the grade and pTNM staging and the other 2 cases were excluded because of incomplete demographic data. From the 208 cases which fulfil the inclusion criteria 117 were males and 91 were females. Majority of the cases are seen in the 5^{th}, 6^{th}, and 7^{th} decades accounting for 25%, 19.2 and 22.1% of the cases.

Table 1-Frequency of neoplastic lesions by sex

	Sex	Frequency		Cumulative Percent
Valid	Male	117	56.3	56.3
	Female	91	43.8	100.0
	Total	208	100.0	

Table 2-Frequency of total cases by age group

		Frequency	Percent
Valid	11-20	5	2.4
	21-30	15	7.2
	31-40	31	14.9
	41-50	52	25.0
	51-60	40	19.2
	61-70	46	22.1
	71-80	16	7.7
	81-90	3	1.4
	Total	208	100.0

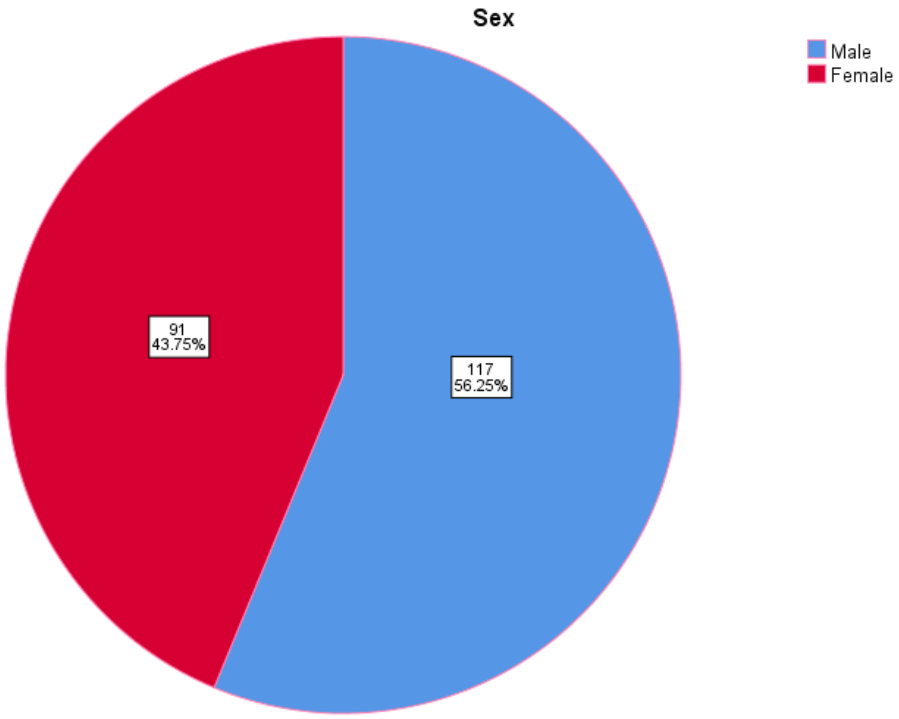

Figure 1: Neoplastic Lesion Distribution by Gender

Specific site of the tumor were not known in 15 of the cases with 6 of them labeled as colonic lesions, 5 of them right colonic lesions and 4 of them labeled as left colonic lesions. From the rest 193 cases the rectum is the most common site of the lesions (57cases, 29.5%) followed by Sigmoid Colon (47, 24.4%).

Table 3: Specific Site of the tumor

		Frequency	Valid Percent
Valid	Caecum	24	12.4
	Ascending COLON	10	5.2
	Hepatic Flexure	7	3.6
	Transverse Colon	8	4.1
	Splenic Flexure	10	5.2
	Descending Colon	10	5.2
	Sigmoid Colon	47	24.4
	Recto sigmoid	20	10.4
	Rectum	57	29.5
	Total	193	100.0

The age of the study subjects ranges from the minimum of 19 to the maximum age of 87 forming the range of 68 and mean of 52.13.

Adenocarcinoma (194, 93.3%) is the most common Histopathological pattern followed by Neuroendocrine Tumors (7, 3.4%) and 2 cases (1%) of High risk GIST. There are 1 cases (0.5%) for each of High Grade NHL, Mixed Neuroendocrine Non Neuroendocrine Carcinoma, Sub mucosal Lipoma, Villous Adenoma with High Grade Dysplasia and Desmoid Type Fibromatosis.

Table 4 : Histologic type frequency

		Frequency	Valid Percent
Valid	Adenocarcinoma	194	93.3
	High Grade NHL	1	0.5
	Neuroendocrine Tumors	7	3.4
	Mixed Neuroendocrine Non Neuroendocrine Carcinoma	1	0.5
	Submucosal Lipoma	1	0.5
	High risk GIST	2	1.0
	Villus Adenoma with High Grade Dysplasia	1	0.5
	Desmoid Type Fibromatosis	1	0.5
	Total	208	100.0

From the 194 cases of adenocarcinoma 111 (57.2%) are Males and 83(42.8%) are Females, male to female ratio 1.34:1.The mean age patients with Adenocarcinoma is 51.73 and age range is 19-87. The highly affected age group is the 5^{th} followed by, 6^{th} and 7^{th} decades of life.

Table 5: Mean Age Across Different Histopathological Types

Histopathological Type	Mean Age	N
Adenocarcinoma	51.73	194
Neuroendocrine Tumors	56.86	7
High Risk GIST	64.50	2

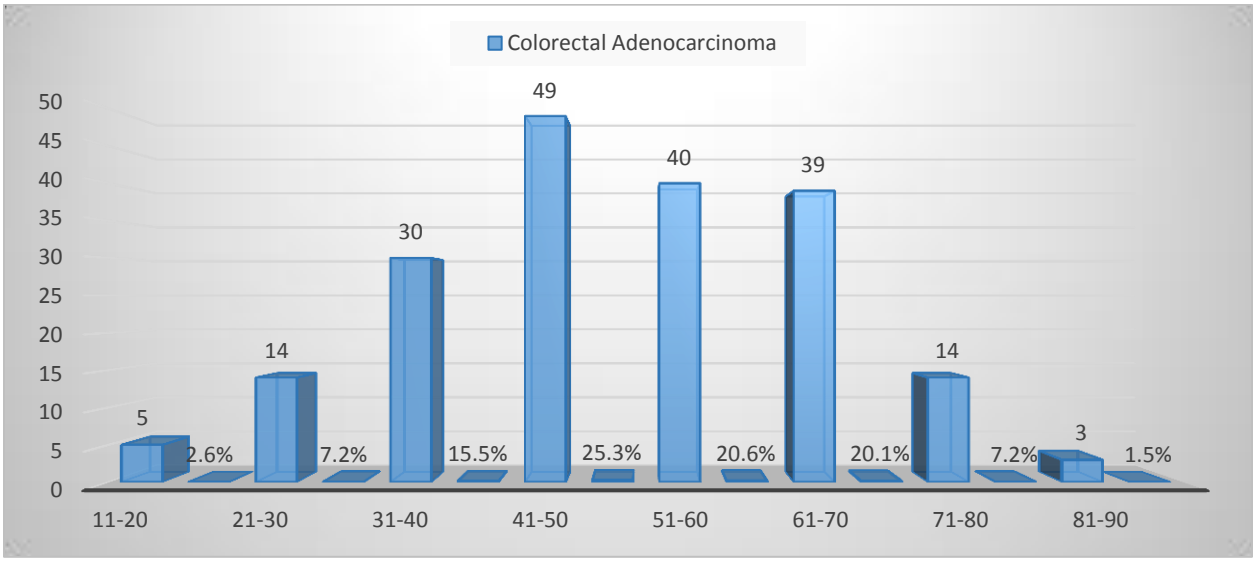

Figure 2: Colorectal Adenocarcinoma distribution across age groups

Specific location of the colorectal adenocarcinoma was known in 181 cases. From this the most common location of Adenocarcinoma is the Rectum 56(30.9%) followed by the Sigmoid Colon47 (26 %), Recto sigmoid area 20 (11%) and the Caecum 18(9.9%). The Rectum, Recto sigmoid and Sigmoid Colon are the sites of Adenocarcinoma in 67.9 % of Adenocarcinoma cases.

Adenocarcinoma NOS is the most common histologic subtype of Adenocarcinoma 165(85.1%) followed by Mucinous Adenocarcinoma 26(13.4%) and Signet Ring Cell Carcinoma 3(1.5%).

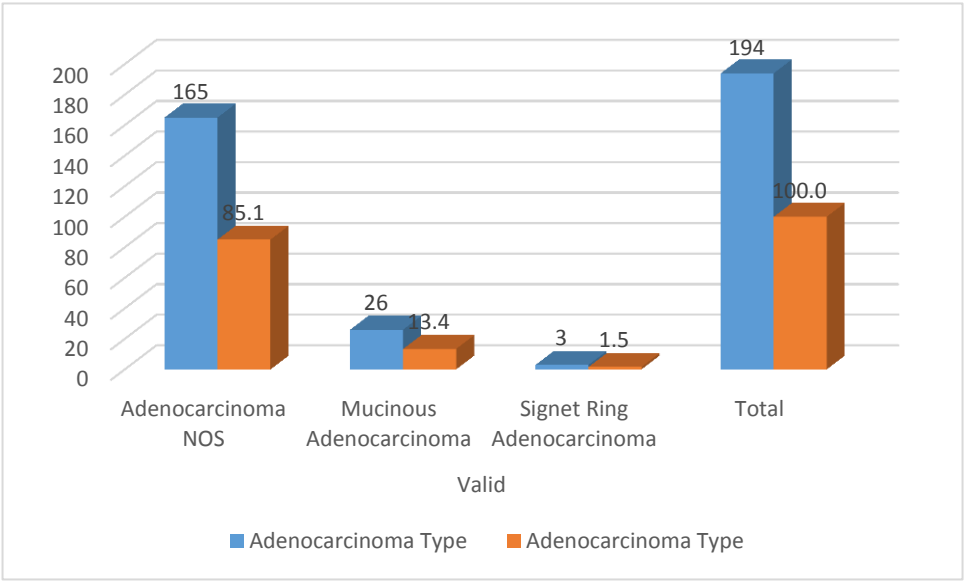

Figure 3: Histologic Subtypes of Adenocarcinoma

The mean age of subtypes of Adenocarcinoma is 52.22, 51.58, and 27.67 for Adenocarcinoma NOS, Mucinous Adenocarcinoma and Signet Ring Cell Carcinoma respectively.

From the total cases of adenocarcinoma 41 of them (21.1%) are aged below 40 while 153(78.9%) are aged above 40. From the 26 cases of mucinous adenocarcinoma 7 (26.9%) are below 40 while the rest 19(73.1%) are above the age of 40. All of the 3 signet ring carcinomas occur below the age of 40, while 31(18.8%) and 134 (81.2%) of Adenocarcinoma NOS cases are below and above 40 ages respectively.

From the 41 cases of adenocarcinoma under the age of 40 Mucinous Carcinomas account for 17.1% of Adenocarcinoma cases while after the age of 40 it accounts 12.4% of the cases.

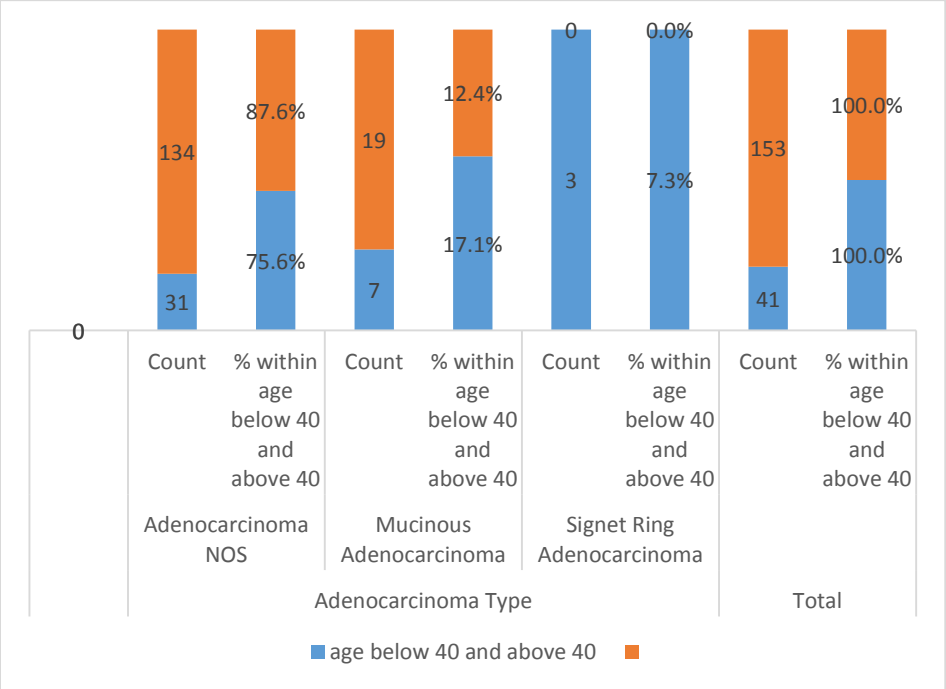

Figure 4: Adenocarcinoma Subtypes with age under 40 and above 40 years

From the 194 cases of adenocarcinoma 45(23.2%) located in the Right Colon, 67 (44.8%) in the Left Colon, 56(28.9) in the Rectum, 20 in the Recto Sigmoid and the Rest 6 (3%) were known to arise from the colon with no specification whether they are located in the right or left, which makes 118 colonic, 20 Recto Sigmoid and 56 Rectal Adenocarcinomas.

From the 118 colonic Adenocarcinomas 45(38.1%) are RCC, 67 (56.8%) are LCC, 6(5.1%) were labeled as Colonic with no specification of their location as either RCC or LCC.

From the 112 adenocarcinomas labeled as either right or left colon 45(40.2%) are right colonic cancers which includes the caecum, ascending colon, hepatic flexure and transverse colon (RCC), 67(59.8%) are Left colonic cancers which includes splenic flexure, descending colon and sigmoid colon (LCC).

The mean age patients with RCC is 54.18 and with LCC 51.73 years.

From the 45 Right Colon adenocarcinomas 34 (75.6%) are Adenocarcinoma NOS and the rest 11(24.4%) are Mucinous Adenocarcinomas. From the 67 cases of Left Colonic Adenocarcinomas 60(89.6%) are Adenocarcinoma NOS, 5(7.5%) are Mucinous Adenocarcinomas, 2(3%) are Signet Ring Cell Carcinomas. From the 56 rectal adenocarcinomas 47(83.9%), 8 (14.3%), 1(1.8%) are

Adenocarcinoma NOS, Mucinous Adenocarcinomas and Signet Ring Cell Carcinomas respectively.

From the 45 cases of RCC 22(48.9%) are Males while the rest 23(51.1%) are Females. From the 67 LCC cases 38(56.7%) are Males and the rest 29(43.3%) are Females. Therefore RCCs are more frequently diagnosed in women (51.1%), and LCCs were found predominantly in men (56.7%).

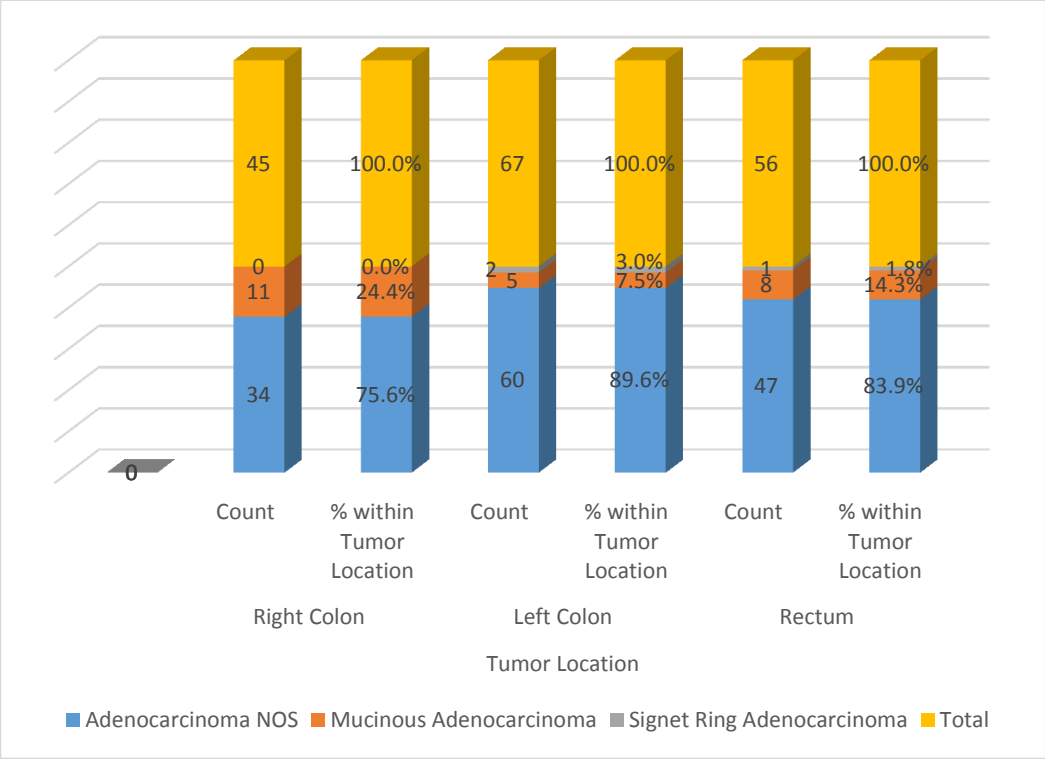

Figure 5: Distribution of Adenocarcinoma Subtypes at the Right Colon, Left Colon and Rectum

From the 34 cases of Adenocarcinoma NOS of the Right Colon 30(88.2%) are Low grade and 4(11.8 %) are High grade. From the 60 cases of Left Colonic Adenocarcinoma NOS 58 (96.7%) are Low Grade, 1(1.7%) High Grade, 1(1.7%) is not Graded.

RCCs show locally advanced tumor growth (pT3/4, 71.1%) while LCCs show advanced tumor growth (pT3/4, 73.1%). Lymph node positive disease is seen in 44.4% and 35.9% of RCCs and LCCs.

Table 6: Pathologic N staging for RCCs and LCCs

			Pathologic N Staging				Total
			NX	N0	N1	N2	
For Colonic Adenocarcinomas the distribution of RCC and LCC	RCC	Count	7	18	15	5	45
		% within For Colonic Adenocarcinomas the distribution of RCC and LCC	15.60%	40.00%	33.30%	11.10%	100.00%
	LCC	Count	12	31	19	5	67
		% within For Colonic Adenocarcinomas the distribution of RCC and LCC	17.90%	46.30%	28.40%	7.50%	100.00%
Total		Count	19	49	34	10	112
		% within For Colonic Adenocarcinomas the distribution of RCC and LCC	17.00%	43.80%	30.40%	8.90%	100.00%

Table 7: Pathologic T staging for RCCs and LCCs

For Colonic Adenocarcinomas the distribution of RCC and LCC * Pathologic T Staging Crosstabulation							
			Pathologic T Staging				Total
			T1	T2	T3	T4	
For Colonic Adenocarcinomas the distribution of RCC and LCC	RCC	Count	1	12	22	10	45
		% within For Colonic Adenocarcinomas the distribution of RCC and LCC	2.20%	26.70%	48.90%	22.20%	100.00%
	LCC	Count	4	14	37	12	67
		% within For Colonic Adenocarcinomas the distribution of RCC and LCC	6.00%	20.90%	55.20%	17.90%	100.00%
Total		Count	5	26	59	22	112
		% within For Colonic Adenocarcinomas the distribution of RCC and LCC	4.50%	23.20%	52.70%	19.60%	100.00%

In those less than 40 years the higher grade tumors were seen in 3 (7.3%) of cases. While in those over 40 years of age higher grade tumors were seen in 6(4%) of cases. In those less than 40 years of age Mucinous Carcinoma were seen in 7 cases (17%) while in those over 40 years of age Mucinous Carcinomas were seen in 19 cases (12.75%).

From 194 cases of adenocarcinoma 38(19.6%), 74 (38.1%), 52 (26.8%), 28 (14.4%) and 2 (1%) are pNX, pN0, pN1, pN2, ypNO respectively, making the total Lymph node involvement, (N1+N2) - 80(41.2%).

Table 8: Pathologic N Staging for Colorectal Adenocarcinoma

Pathologic N Staging	NX	Count	38
		% within colorectal adenocarcinoma	19.6%
	N0	Count	74
		% within colorectal adenocarcinoma	38.1%
	N1	Count	52
		% within colorectal adenocarcinoma	26.8%
	N2	Count	28
		% within colorectal adenocarcinoma	14.4%
	yPN0	Count	2
		% within colorectal adenocarcinoma	1.0%
Total		Count	194
		% within colorectal adenocarcinoma	100.0%

From the total 194 cases of Adenocarcinoma 152(78.4%) are Low Grade, 9 (4.6%), are High Grade the rest 4(2.1%) were not graded, 26 (13.4%) are mucinous and 3(1.5%) are signet ring adenocarcinomas.

From the 152 Low Grade tumors 32(21.1%), 67 (44.1%), 35(23%), 17(11.2%), 1(0.7%) are pNX, pN0, pN1, pN2 and ypN0 respectively, making total lymph node involvement (N1+N2) 34.1%.

From the 9 High Grade Adenocarcinomas 1(11.1%),0(0%),3(33.3%),4(44.4%),1(11.1%) are NX,N0,N1,N2 and YPN0 respectively making total lymph node involvement (N1+N2) 77.7%.

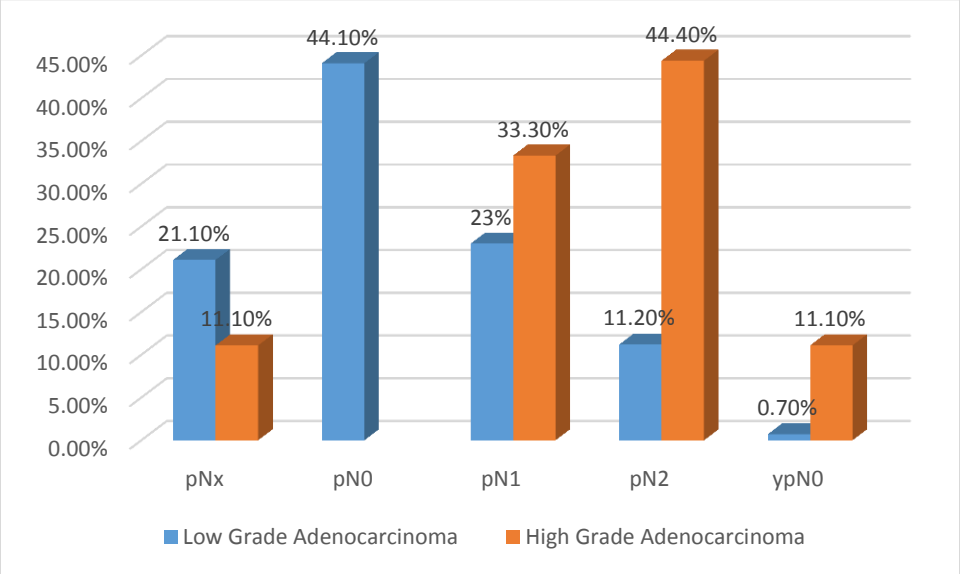

Figure 6: Grade of adenocarcinoma with pathologic N staging

From the low grade tumors 6(3.9%), 40(26.3%), 87(57.2%), 18(11.8%), 1(0.7%) are pT1, pT2, pT3, pT4 and ypt0 respectively. From the High Grade Adenocarcinomas 0(0%),1(11.1%),2(22.2%),5(55.6%),1(11.1%) are T1,T2,T3,T4 and Ypt3 respectively.
Lymph node involvement (N1+N2) is 33.3%, 34%, 45.9%, 48.4% within T1,T2,T3 and T4 tumors(including Adenocarcinomas and Neuroendocrine Tumors).

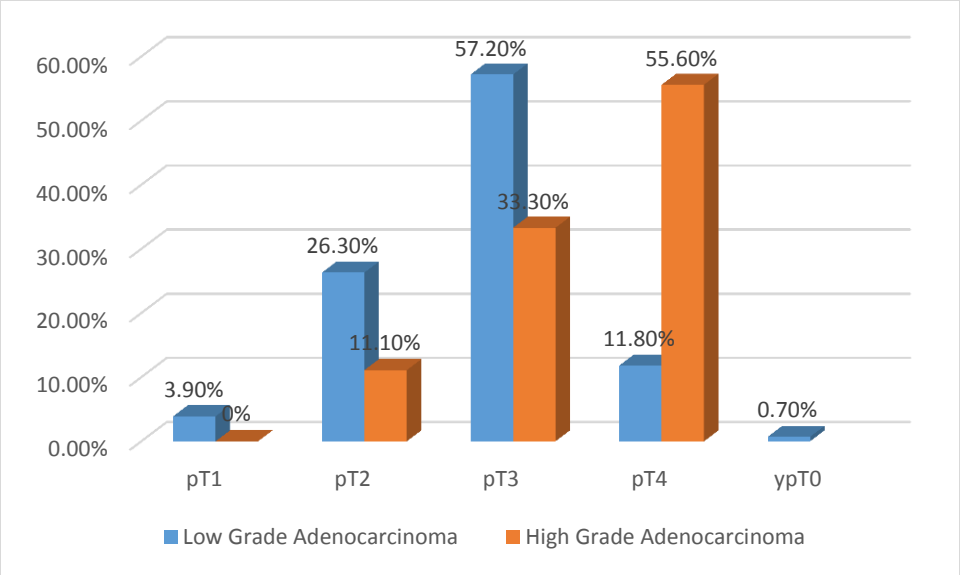

Figure 7: Grade of Adenocarcinoma with pathologic T staging

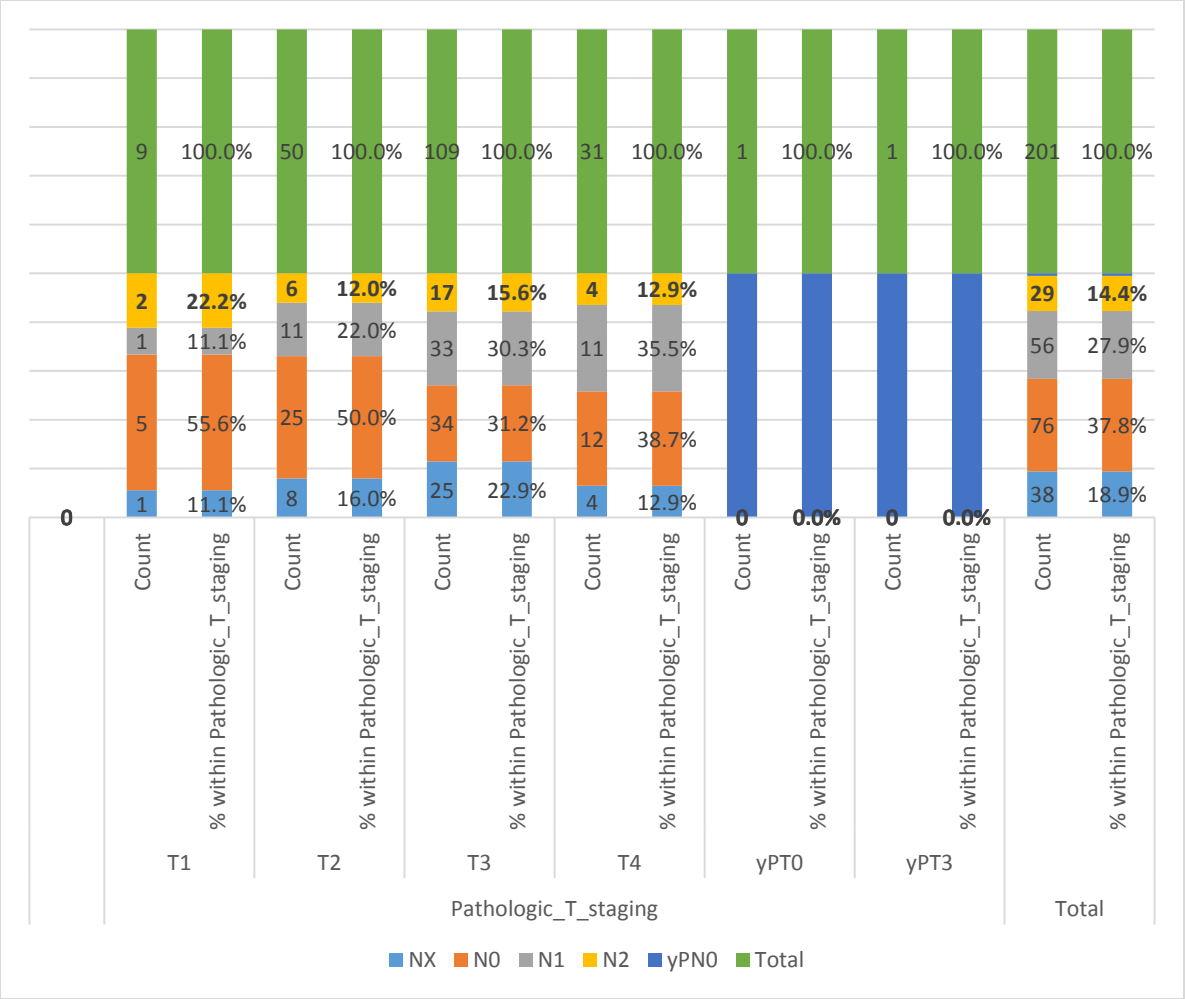

Figure 8: Frequency of pathologic N staging Across Different T staging

Table 9: Type of Neuroendocrine Neoplasm frequency

		Frequency	Valid Percent
Valid	Large Cell Neuroendocrine Carcinoma	1	14.3
	Typical Carcinoid	1	14.3
	Well Differentiated Neuroendocrine Tumor	1	14.3
	Well Differentiated Neuroendocrine Tumor Grade 2	1	14.3
	Well Differentiated NET grade 3	2	28.6
	Neuroendocrine Carcinoma	1	14.3
	Total	7	100.0

From the neuroendocrine tumors two cases were diagnosed as Well Differentiated Neuroendocrine tumor grade 3,1 case large cell Neuroendocrine Carcinoma,1 case Neuroendocrine Carcinoma,1 case Typical Carcinoid and another 1 as Well Differentiated Neuroendocrine Tumor.

From a total of 204 Neoplasms(excluding Submucosal Lipoma, Villous Adenoma with High Grade Dysplasia, Desmoid Type Fibromatosis, and High Grade NHL) status of Lymphovascular Invasion was present in 36(17.6%), Absent in 38(18.6%) and was not stated in 130(63.7%).

Table 10:Status Of Lymphovascular Invasion

		Frequency	Valid Percent
Valid	Present	36	17.6
	Absent	38	18.6
	Not stated	130	63.7
	Total	204	100.0

From a total of 194 cases of Adenocarcinoma Lymphovascular invasion was not stated in 121(62.4%) of them and was stated in 73(37.6%). From those with known Lymphovascular status 35(47.9%) have Lymphovascular Invasion and the rest 38(52.1%) do not show Lymphovascular invasion.

Perineural Status is not stated in 168 (86.6%) and was stated in 26(13.4%). From those with known status of Perineural Invasion 6(23.1%) of them has Perineural Invasion while the rest 20(76.9%) do not have Perineural Invasion.

From a total of 56 Rectal Adenocarcinomas gross quality of Mesorectal Excisions was not stated in 18(32.1%) and was stated in the remaining 38(67.9%). From those with a stated quality of Mesorectal excision 12(31.6%), 9 (23.7%), 17(44.7%) have incomplete, near complete and complete Mesorectal Excisions respectively.

From the 56 cases of Rectal Adenocarcinomas Microscopic Radial Margin/CRM was not stated in 5 (8.9%) of them and was stated in the remaining 51(91.1%) of them. From those 51cases 9 (17.6%) of them show Microscopic Radial/CRM involvement and the rest 42(82.4%) are not involved.

From 118 colonic adenocarcinomas microscopic radial margin status was not stated in 37(31.4%) stated in 81(68.6%) cases. From the 81 cases the Radial margin is involved in 12(14.8%) not involved in 69(85.2%).

From the total of 204 cases (194 adenocarcinomas, 2 High Risk GISTs and 7 Neuroendocrine neoplasms, 1 Mixed Neuroendocrine Non Neuroendocrine Neoplasm) the average number of lymph nodes harvested is 10.65 nodes per patient. It ranges from 0-32 and the median is 9. From the 204 cases 34(16.7%) has 0 lymph node harvested.

6. Discussion

In this study the total number of cases is 208 with minimum and maximum age of 19 and 87 and mean age of 52.13 which is comparable to the study done by Aliyu and colleagues in Nigeria (50.5)[35] but lower than a study in china (62)[41]. About 43(20.7%) are below the age of 40 which is comparable to the study done in Lagos Sagammu (23%) [19] but lower than that of A study done by Senait Ashenafi that reviewed the biopsy reports of 255 patients having CRC in the years between 1973 to 1978 and 1989 to 1993 in Addis Ababa University, Pathology Department (35%) [44]. While the rest 165(79.3%) are above the age of 40, 117(56.3%) are males with a male to female ratio of 1.3:1 comparable to the study done by D. Zemenfes and colleague two year review of Colorectal Cancer at Tikur Anbessa Specialized Hospital (1.3:1)[24] .

The Caecum and ascending colon are the site of the tumors in 17.6% of the cases which is higher than the study by Senait Ashenafi (8%) [44] and lower than a study by Patricia and colleagues in Atlanta Georgia (25%) [34] and a study in Houston, Texas (26.1%)[42]. The Sigmoid and Recto Sigmoid Junctions are seats of the tumor in 47(24.4%) and 20(10.4%). The rectum is the location of 57(29.5%). Hence Sigmoid, Recto Sigmoid and Rectum combined were the commonest (64.3%) sites involved in this study. This finding is comparable to the study done by Sagamu Nigeria (60.5%) [19].

In the present study Adenocarcinoma is the most frequent Histopathological pattern 194(93.3) which is comparable to study done by D. Zemenfes and colleague (94.8%) [24] and a study done by Aliyu and colleagues in Nigeria (86.2%)[35].

From the 194 cases of adenocarcinoma 111 (57.2%) are males and 83(42.8%) are females, with age range 19-87 which is comparable to the study done by DN Dijxhoorn and colleagues on Colorectal cancer in patients from Uganda (19-87) [23] and a study done by Michael Adloff and colleagues on colorectal cancer in patients under 40 years at Schiltgheim/Strasborg, France (19-90) [33] and a study from china, (21-92)[41]. Male to Female ratio and the mean age of patients with Adenocarcinoma is (1.34:1, 51.73) which is comparable to the study Lagos, Sagamu, southwest Nigeria (1.3:1, 50.7)[19] and also study by Senait Ashenafi (1.3:1, 46)[32].

The rectum is the site of colorectal Adenocarcinoma (from the 181 cases with known specific site of adenocarcinoma) in 30.9% of the cases which is comparable to the study in north eastern Nigeria (33.8%)[35] and a study in Houston, Texas(26.1%) [42]. The Rectum, Recto sigmoid and Sigmoid colon account for about 67.9% of the cases followed by caecum(9.9%) which is comparable to the study done by Fatimah Biade Abdulkareem and colleagues in Lagos and Sagamu, Southwest Nigeria (58.6% and 9%)[19].

In this study from the 194 cases of adenocarcinoma 4 were not graded from the rest 190 cases 152 (80%) are Low Grade and (4.7%) are High Grade, which is comparable to the study by Senait Ashenafi in Addis 84% and 7%[32] and also the study from china[41].

In this study Adenocarcinoma NOS and Mucinous Adenocarcinomas account for 85.1% and 13.4% from total adenocarcinoma cases which is comparable to the study done by Aliyu and colleagues (86.2%, 10.8%)[35].

Mucinous carcinoma and signet ring carcinoma accounts for 17% and 7.3% of cases of Adenocarcinomas below the age of 40, while in the Lagos and Sagamu its 19% and 4% [19] and in a study done by Patricia in Atlanta, Georgia its 10 and 1.7% [34] . After the age of 40, Mucinous Carcinoma accounts for 12.4% of Adenocarcinomas which in the Micheal Adloff and Collogues study was 8.6% [33] and in a Study by Patricia its 5% [34].

In this study the mean age of patients with RCC is higher than LCC patients (54.18, 51.73) comparable to the study by Frank Benedix and colleagues which compares right and left sided colon cancers, Germany (71, 68.5) [20]. Histologically, the majority of all CC were Adenocarcinoma NOS with a higher proportion in the LCC group (RCC 75.6% V LCC 89.6%) which in Frank Benedix and collogues study is (RCC 86.8% vs LCC 91.7%) [20]. In our study Mucinous adenocarcinomas are more common in the RCC group (24.4%) than LCC group (7.5%) while in the Frank Benedix and collogues study the respective figures are (RCC 10.6% vs LCC 6.3%) [20].
In this study RCCs are more frequently diagnosed in women (51.1%), and LCCs were found predominantly in men (56.7%) this is comparable to Frank Benedix and collogues study which shows RCCs frequently diagnosed in women (55.3%), and LCCs were found predominantly in men (54.1%) [20].RCCs show Locally advanced tumor growth less commonly (pT3/4, 71.1%) than LCC (pT3/4,73.1%) in contrast to Frank Benedix and collogues study which shows (RCC pT3/4 76.1% vs LCC 67.0%)[20] .RCCs show Lymph node positive disease more frequently than LCCs (44.4% and 35.9%) and this is comparable with similar study (RCC 36.1% vs LCC 33.6%)[20].

From a total of 194 cases of adenocarcinoma 80 (41.2%) are node positive which is comparable to study by Rocco Ricciardi and colleagues on analysis of lymph node metastasis in Canada Which shows node positive disease in 34.5%[21]. Node positive disease is seen in 48.4% of T4 disease which is comparable to Rocco study (50%)[21].In our study Node positive disease is seen in 3 (33.3%) of T1 which in the Rocco study is (8%)[21] this discrepancy may be due to small number of T1 tumors(9) in this study which is difficult to interpret.

In this study from the 73 Adenocarcinoma cases with known Lymphovascular status 35(47.9%) have Lymphovascular Invasion which is comparable to the study done by Renan Cascaes Lopes in Brazil (44.6%) [36] but higher than that reported in a study done by Hui-Hong Jiang and colleagues on Prognostic significance of lymphovascular invasion in colorectal cancer and its association with genomic alterations (12.3%)[41]. From 26 cases with known status of Perineural Invasion 6(23.1%) of them has Perineural Invasion which is higher than Renan Cascaes Lopes study (8.8%) [36] but comparable to the study by Cathrine and colleagues (22%)[42].

From a total of 56 Rectal Adenocarcinomas gross quality of Mesorectal Excisions was not stated in 18(32.1%) and was stated in the remaining 38(67.9%). From those with a stated quality of Mesorectal excision 31.6%, 23.7%, 44.7% have incomplete, near complete and complete Mesorectal Excisions respectively which is comparable to the study done by Iris D. Nagtegaal and colleagues and the Pathology Review Committee for the Cooperative Clinical Investigators of the Dutch Colorectal Cancer Group on Macroscopic Evaluation of Rectal Cancer Resection Specimen with respective figures being 23.9%, 19.4%, 56.6% [22].

From the 51 Rectal Adenocarcinomas with known Microscopic Radial/CRM status 9(17.6%) of them show positive margin which is comparable to the rate in British Colombia Province in Canada (17%) in a study done by K. DeCaria and colleagues [37].

From the 81 cases of colonic adenocarcinomas radial margin was involved in 12(14.8%) of the cases which is higher than the study done by Ramzi Amri and colleagues (5.3%) [38].

In our study the average number of lymph nodes harvested per patient from the 204 neoplasms (excluding Desmoid type Fibromatosis, Submucous Lipoma, Villous Adenoma with high grade dysplasia and High Grade NHL) is 10.6 nodes per patient and the range is from 0-32 which is comparable to the study by M. Johnson and colleagues On adequacy of nodal harvest in primary colorectal cancer resection specimens (8.3 nodes per patient, 0-16) [39]. The median number of harvested lymph nodes in our study is 9 which is similar to a study by Nancy N Baxter and colleagues in the US(9)[45] but lower than the study done by B.S.Nedrebo and colleagues in Oslo, Norway (14)[40]. The mean number of lymph nodes harvested per patient in our study is lower than the minimum number recommendation of 8th edition of AJCC (12LNs) [43].

7. Conclusion

In this study the minimum and maximum age of patients with colorectal cancer is 19 and 87. Male to female ratio for the total 208 cases is 1.3:1, and for 194 Adenocarcinoma cases is 1.34:1, Mean age of patients for the total cases and for Adenocarcinoma cases is 52.13 and 51.73 years respectively. The Rectum followed by Sigmoid and Recto sigmoid junctions are the commonest sites of colorectal cancer. Adenocarcinoma is by far the most common Histopathological pattern with Adenocarcinoma NOS being the commonest subtype followed by Mucinous Adenocarcinoma.

Mucinous adenocarcinomas and Signet Ring Cell Carcinomas are more common under the age of 40 than above the age of 40.

In this study RCCs are more frequently diagnosed in Women and LCCs were found predominantly in men, with the mean age higher in the RCC group. In our study Mucinous Adenocarcinomas and lymph node involvement more common while locally advanced tumor growth (T3/T4) is less common in the RCC group than the LCC group.

Lymphovascular and Perineural invasion by Adenocarcinomas is 44.6 and 23.1% respectively.

8. Recommendation

The majority of patient's medical records in our department were incomplete and misplaced. Therefore, the record archiving of the department needs to be improved. Implementing a sustainable digital data archiving system, and providing continuous training and audit is the recommendation of this study.

Most of the data sent to the Department of Pathology are incomplete especially the specific site of the tumor, the type of the procedure, demographic data and in few gender and age, clinical presentation and radiology reports are missing. The radial margin in the retroperitoneal segments of bowel may be difficult to detect in a formalin-fixed specimen so it will be good if the surgeons apply a mark on it. It is also necessary if the surgeons tell us if a tumor site perforation is iatrogenic during the surgical procedure or if it's genuine perforation because this may affect the pathological report. Hence, it would be helpful to have interdepartmental communications between the clinicians and Pathologists to solve such problems

Angiolymphatic invasion (ALI) and Perineural invasion in colorectal cancer (CRC) is considered as an important independent prognostic factor after controlling for gender, age, tumor site, differentiation, and may influence therapeutic decisions. Despite this for significant number of cases the status of lymphovascular invasion and perineural invasion is not known, so we should improve on that.

In the literature the number of retrieved LNs is related to oncological outcomes in patients with colorectal cancer without distant metastasis. Low numbers of retrieved lymph nodes (LNs) have been linked to poor outcomes in patients with colorectal cancer. In our study the mean number of harvested lymph nodes is a bit lower than the minimum number AJCC recommendation which is 12 and 16.7% of the cases has 0 harvested lymph nodes, so this should be improved.

The circumferential resection margin (CRM), also called the radial margin is very important in rectal cancer surgery, being a prognostic factor in patients who undergo such surgery. A CRM of less than 1 mm has been shown to be a strongly negative prognostic factor: specifically, it predicts for subsequent loco-regional recurrence distant metastasis and poorer overall survival. The CRM is not stated in few of the rectal cancer resections so we should improve that.

A strong relationship between poor total Mesorectal excision quality and a positive CRM, Recurrence and survival rates has been documented in the literature. One of the factors influencing quality of Mesorectal excision is lower limit of the tumor above the anal verge. So Quality of Mesorectal excision and distance of the lower part of rectal tumor from the anal verge should be mentioned.

Using Standard Grossing and Pathologic Reporting Dataset will help us to write a complete pathological report.

It will be advisable to work on community awareness creation and to have colorectal cancer screening as the disease burden is increasing.

9. References

1. Kumar V, Abbas AK, Aster JC, editors. Robbins and Cotran Pathologic Basis of Diseases.9thed. Faridabad: Elsevier; 2014. 961-9.
2. Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A., & Jemal, A. (2018). Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: A Cancer Journal for Clinicians. doi:10.3322/caac.21492
3. Bufill JA. Colorectal cancer: evidence for distinct genetic categories based on proximal or distal tumor location. Ann Intern Med. 1990; 113: 779–88.
4. Christopher D.M. Fletcher, Diagnostic Histopathology of Tumors, fourth edition volom1, Elsevier, 2013.
5. Cheung,ANY.WHO classification of tumours 5th edition, digestive system.Geneva,Switzerland:World Health Organization.2018
6. Center MM, Jemal A, Ward E. International trends in colorectal cancer incidence rates. Cancer Epidemiology Biomarkers Prev. 2009; 18 : 1688–1694.
7. Center MM, Jemal A, Smith RA, Ward E. Worldwide variations in colorectal cancer. CA Cancer J Clin. 2009;59:366–378
8. Bishehsari, F. (2014). Epidemiological transition of colorectal cancer in developing countries: Environmental factors, molecular pathways, and opportunities for prevention. World Journal of Gastroenterology, 20(20), 6055. doi:10.3748/wjg.v20.i20.6055
9. Ferlay J, Soerjomataram I, Dikshit R, et al.Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. In J. Cancer.2015;136:E359-86.
10. Center M, Jemal A, Smith R, Ward E.Wordwide variations in colorectal cancer.CA Cancer J Clin. 2009;59:366-78.
11. Weitz J, Koch M, Debus J, Hohler T, Galle PR, Buchler MW. Colorectal cancer. Lancet. 2005;365:153-165.
12. Siegel RL, Miller KD, Jemal A. Cancer statistics.CA: A Cancer Journal for Clinicians. 2015;65(1):5-29.
13. Walker A, Segal I. Colorectal cancer in an African city population in transition. Eur. J. Cancer Prev. 2002;11:187-91.
14. Chalya PL, Mchembe MD, Mabula JB, Rambau PF, Jaka H, Kay M, Mkongo E, Masalu N. Clincopathological patterns and challenges of management of colorectal cancer in a resource-limited setting: A Tanzanian experience. World Journal of Surgical Oncology. 2013;11:88. Available:http://www.wjso.com/content/11/1/88
15. Saidi HS, Karuri D, Nyaim EO. Correlation of clinical data, anatomical site and disease stage in colorectal cancer. East African Medical Journal. 2008;85(6).

16. Ashenafi S. The frequency of large bowel cancer as seen in Addis Ababa University, Pathology Department, Ethiop. Med. J. 2000;38:277-282
17. Siegel RL, Fedewa SA, Anderson WE, Miller KD, Ma J, Rosenberg FS, Jemal A. Colorectal cancer incidence patterns in the United States, 1974-2013. J Natl Cancer Inst. 2017;109(8). DOI: 10.1093/jnci/djw322
18. Siegel RL, Jemal A, Ward EM. Increase in incidence of colorectal cancer among young men and women in the United States. Cancer Epidemiol Biomarkers Prev. 2009;18(6):1695-8 DOI: 10.1158/1055-9965.EPI-09-0186
19. Abdulkareem FB, Abudu EK, Awolola NA, Elesha SO, Rotimi O, Akinde OR, Atoyebi AO, Adesanya AA, Daramola AO, Banjo AAF, Anunobi CC. Colorectal carcinoma in Lagos and Sagamu, Southwest Nigeria: A histopathological review. World J Gastroenterol 2008; 14(42): 6531-6535
20. Benedix, F., Kube, R., Meyer, F., Schmidt, U., Gastinger, I., & Lippert, H. (2010). Comparison of 17,641 Patients With Right- and Left-Sided Colon Cancer: Differences in Epidemiology, Perioperative Course, Histology, and Survival. Diseases of the Colon & Rectum, 53(1), 57–64. doi:10.1007/DCR.0b013e3181c703a4
21. Ricciardi, R., Madoff, R. D., Rothenberger, D. A., & Baxter, N. N. (2006). Population-Based Analyses of Lymph Node Metastases in Colorectal Cancer. Clinical Gastroenterology and Hepatology, 4(12), 1522–1527. doi:10.1016/j.cgh.2006.07.016
22. Iris D. Nagtegaal, Cornelis J.H. van de Velde, Erik van der Worp, Ellen Kapiteijn, Phil Quirke,and J. Han J.M. van Krieken and the Pathology Review Committee for the Cooperative Clinical Investigators of the Dutch Colorectal Cancer Group, Macroscopic Evaluation of Rectal Cancer Resection Specimen: Clinical Significance of the Pathologist in Quality Control ,J Clin Oncol 20:1729-1734. © 2002 by American Society of Clinical Oncology.
23. DN Dijxhoorn, A Boutall, CJ Mulder, R Ssebuufu, A Mall, S Kalungi, C Baigrie, PA Goldberg, Colorectal cancer in patients from Uganda: A histopathological study. Department of Pathology, Makerere University College of Health Sciences, Kampala, Uganda. COSECSA/ASEA Publication -East and Central Africa Journal of Surgery.March/April 2014 Volume 19
24. D. Zemenfes, B. Kotisso, A Two- year review of Colorectal Cancer at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, Addis Ababa University, CHS, SOM, Addis Ababa, Ethiopia ,COSECSA/ASEA Publication-East and Central African Journal of Surgery, July/August 2015 Volume 20 (2).
25. Liu, Z., Sun, Y., Li, Y., Zhao, J., Wu, S., Meng, Z., & Wu, H. (2019). Colonic Gastrointestinal Stromal Tumor: A Population-Based Analysis of Incidence and Survival. Gastroenterology Research and Practice, 2019, 1–10. doi:10.1155/2019/3849850
26. Wong, M. T. C., & Eu, K. W. (2006). Primary colorectal lymphomas. Colorectal Disease, 8(7), 586–591. doi:10.1111/j.1463-1318.2006.01021.x

27. Osnat Bairey MD1, Rosa Ruchlemer MD2 and Ofer Shpilberg MD MPH1, Non-Hodgkin's Lymphomas of the Colon, Institute of Hematology, Rabin Medical Center (Beilinson Campus), Petah Tiqva, Israel,IMAJ • Vol 8 • December 2006
28. Tunru-Dinh V, Wu ML. Intramucosal ganglion cells in normal adult colorectal mucosa. Int J Surg Pathol 2007, **15**: 31–37.
29. Juan Rosai: Rosai and Ackerman's Surgical Pathology, tenth edition, Philadelphia: Elsevier; 2011.
30. Lord MG, Valies P, Broughton AC. A morphologic study of the submucosa of the large intestine. Surg Gynecol Obstet 1977,**145**: 55–60.
31. Richard Wismayer, Colorectal Adenocarcinoma in East Africa: A Narrative Literature Review, School of Biomedical Sciences, College of Health Sciences, Makerere University, Kampala, Uganda. Department of Surgery, Masaka Regional Referral Hospital, Masaka, Uganda, Journal of Advances in Medicine and Medical Research 32(6): 1-11, 2020; Article no.JAMMR.56736, 30 April 2020.
32. Senait Ashenafi and colleague, tumor characteristic of colorectal carcinoma in Ethiopia and Switzerland, department of Pathology, Addis Ababa University, Faculty of Medicine, Ethiopia, Pathology Institute Kantosipital Luzren, Switzerland, Ethiopian Journal of Health Development,2001,15(3):223-225
33. Michael Adloff and colleague, colorectal cancer in patients under 40 years of age, From the Department o] Surgery, Centre M'edico-Chirurgical et Obsfe trical de la S'ecurigeSociale, Schiltigheim/ Strasbourg, France, November 1985.
34. Patricia M. Griffin and colleague , Adenocarcinoma of the Colon and Rectum in persons under 40 years old,Emory University, School of Public Health,Atlanta, Georgia,American Gastroenterological Association, 1991
35. Aliyu S1 and colleagues The Burden of Colorectal Cancers in Nigeria: Patterns and Presentations in North-Eastern Nigeria, Journal of Cancer Research and Oncobiology, march 2020
36. Renan Cascaes Lopes1 and colleagues, Incidence of angiolymphatic invasion in colorectal cancer, *Medical School of Universidade do Sul, in Santa Catarina (Unisul) – Tubarão (SC), Brazil,* **J Coloproctol**, 2012;32(3): 240-245.
37. *K. DeCaria phd and colleagues Rectal cancer resection and circumferential margin rates in Canada: a population-based study*, February 2015 *Curr Oncol*, Vol. 22, pp. 60-63; doi: http://dx.doi.org/10.3747/co.22.2391
38. Ramzi Amri, MD and colleagues, Association of Radial Margin Positivity With Colon Cancer, J*AMA Surg*. doi:10.1001/jamasurg.2015.1525
39. Johnson, P. (2002).Adequecy of Nodal Harvestin Colorectal Cancer A consecuative cohort study. Journal of Gastrointestinal Surgery, 6(6), 883-890.doi:10.1016/S1091-255X(02)00131-2
40. B.S.Nedrebo and colleagues, risk factors associated with poor lymph node harvest after colon cancer surgery in a national cohort. Colorectal Disease, 15(6),e301-e308.doi:10.1111/codi.12245, November 2012
41. Hui-Hong Jiang and colleagues, Prognostic significance of lymphovascular invasion in Colorectal cancer and its association with genomic alterations *World J Gastroenterol* 2019 May 28; 25(20): 2402-2538.doi:10.3748/wjg.v25.i20.2489

42. *Catherine Liebig***,** Perineural Invasion Is an Independent Predictor of Outcome in Colorectal Cancer, Michael E. DeBakey Veterans Affairs Medical Center**,***J Clin Oncol 27:5131-5137. © 2009.*DOI: 10.1200/JCO.2009.22.4949
43. *AJCC Cancer staging manual (8th edition).Springer Internartional Publishing: American Joint Commission on cancer;2017*
44. Senait Asheaafi, Frequency of Large Bowel Cancer as seen in Addis Ababa University,Pathology Department, Ethiop Med J, 38,2000
45. Nancy N Baxter and colleagues, Lymph node evaluation in colorectal cancer patients, 2005 Feb 2;97(3):219-25. doi: 10.1093/jnci/dji020.