

Epidemiological and Histopathological Features of Small Intestine Cancer in Cameroon: About 47 Cases

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Abstract: Background: The small intestine represents the longest part of the digestive tract. The small bowel cancer is rare, but is increasing worldwide. Methods: Data was analysed retrospectively from the medical records concerning cancer of the small intestine histologically proven, from different histopathology laboratories in Cameroon, for 13 years (2004-2016). The variables studied were the frequency, age, gender, risk factors, location and histopathologic type Results: 3.34% (47 cases /1407) of digestive cancers observed during the period of study. There were 23 female and 24 male patients, with a mean age of 49,77±15,84 (11 to 78 years), the sex ratio of men to women 1.04. The main risk factors were Intestinal polyp, adenomatous polyp and polyposis with 6 cases 25.00%, respectively. The ileum location was the most represented with 47.37%. Adenocarcinoma was the most frequent histological type with 33 cases (70.21%). Conclusion: Small intestine cancer is the sixth malignant tumor of the digestive tract in Cameroon. The mean age of onset is 49.77 years with a relative male predominance. The most common histological type is adenocarcinoma.

Keywords: Small Intestine, Small Bowel, Cancers, Epidemiology, Histopathology, Cameroon

1. Introduction

Malignant tumors of small bowel are less frequent. Small intestine malignancies represent only 3 percent of all gastrointestinal tract neoplasms [1, 2]. Despite that, small intestine cancers are increasing in developed world, with over 100% estimated incidence growth in the past four decades [3]. International data shows that the incidence is higher in North America, western Europe and Oceania than

in Asia [4, 5]. Males are more likely to be diagnosed and die from, small intestine cancer than females [6]. In USA, the median age was 66 [3]. In some others African countries, the average age was 46 years (15 – 70 years), 41,75 years (5 et 77 years) and 36 years old, in Morocco, Togo and Madagascar respectively [7-9]. Several authors have shown a link between some lesions and SBC like adenoma, familial polyposis, Crohn's disease, and coeliac disease [10-13]. Cancers of the small intestine are primarily of two etiologies:

small bowel adenocarcinoma (SBA) which account for 40% of cases, and neuroendocrine tumors, accounting for another 40% [14, 15]. In Cameroon, a study conducted by Ngowe Ngowe et al in 2001 on 10 cases of tumors small Bowel in general at the Yaounde General Hospital, found only two malignant tumors including a carcinoid and Kaposi Angiosarcoma [16]. The scarcity of data on this pathology in Cameroon has led us to conduct this multicenter study to provide information on the epidemiology and histopathology of this disease in this part of the world.

2. Methods

This is a retrospective descriptive and analytical study of histologically proven malignant tumors of small bowel, diagnosed between January 2004 and December 2016. Data was obtained from histopathology, urology and oncology records of different health centers in five regions of Cameroon. The samples generally come from previously unresolved surgery, cancerology or gastroenterology departments. Once in the pathology departments, they are fixed at 10% formalin, and then the macroscopic study in

which the pieces are cut. The pieces are dehydrated by passing through several tanks of alcohol at increasing concentrations, then included in paraffin, then cut with a microtome to a thickness of 5 micron. They are then deparaffinized by xylene lightening, and the staining is done with haematin-eosin followed by reading made using a microscope. The parameters studied were frequency, age, sex, histological type of the tumor. Data entry was done using computer based statistical Package for Social Sciences (SPSS) version 20. The elements of descriptive statistics were used to calculate the frequencies and proportions.

3. Results

3.1. Frequency of Cancers by Segment of the Digestive Tract

In total, 1407 cases of cancers of the gastrointestinal tract were collected, from 2004 to 2016. Small intestine (12 cases, 3.34%) was in the sixth position after the stomach, the colon, the rectum, the anal and the esophageal cancer.

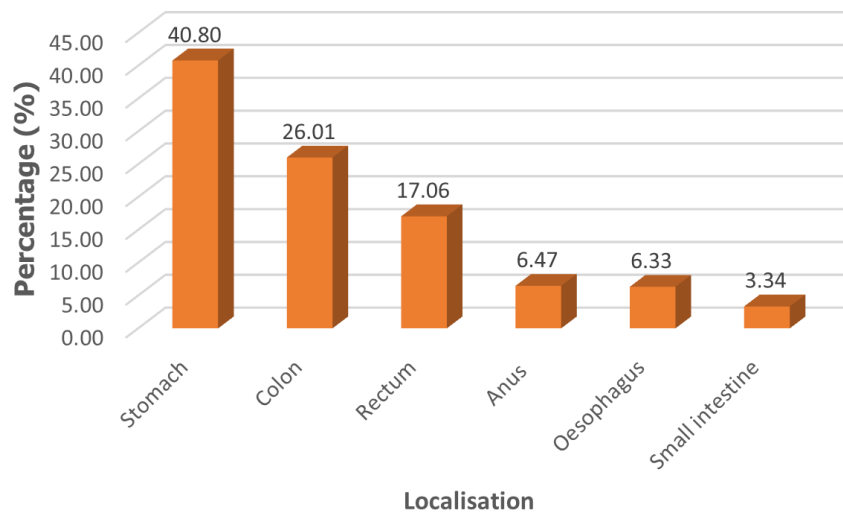


Figure 1. Distribution of cancers according to the segment of the digestive tube.

3.2. Distribution by Sex

As shown in table 1, the male sex was represented by 24 cases (51.06%) or 1.71% of all digestive cancers. The sex ratio was 1.04.

Table 1. Distribution of digestive tract cancers by sex.

Organ	Stomach		Colon		Rectum		Anus		Oesophagus		S intestine		Total
	H	F	H	F	H	F	H	F	H	F	H	F	
Effective	312	262	193	173	130	110	42	49	67	22	24	23	1407
% Effective	22,17	18,62	13,72	12,30	9,24	7,82	2,99	3,48	4,76	1,56	1,71	1,63	100
Total	574		366		240		91		89		47		1407
% Total	40,80		26,01		17,06		6,47		6,33		3,34		100

3.3. Distribution by Age

As shown in the Figure 2, the average age of diagnosis was 49,77±15,84 (11 to 78 years). The majority of patients were

between 50 and 59 years old (11 cases; 23.40%).

In men, the average age was 51,52±13,67 years with extremes ranging from 23 to 70 years old. In women the mean age of diagnosis was 48,17±19,33 years with extremes ranging from 11 to 78 years old.

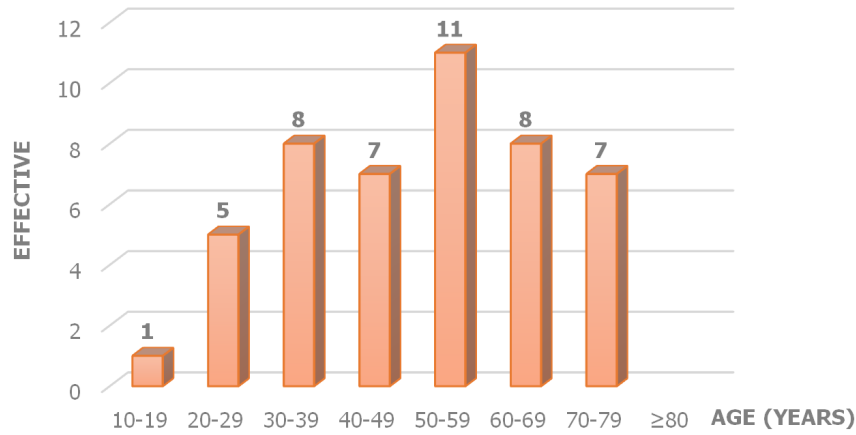


Figure 2. Distribution of patients by age group.

3.4. Distribution According to Risk Factors

Risk factors were highlighted in 24 patients. The most common were Intestinal polyp, adenomatous polyp and polyposis with 6 cases 25.00%, respectively (Table 2).

Table 2. Factors associated with the risk of small intestine cancer.

Risk Factors	Effective	Percentage %
intestinal Polyp	6	25.00
Polyposis	6	25.00
adenomatous polyp	3	12.50
Delicatessen	3	12.50
Alcohol	3	12.50
HIV	3	12.50
Total	24	100.00

3.5. Tumor Localization

Of the 19 lesions localized, as shown in Figure 3, the tumor was ileum localization in 47.37% of cases (9 cases), jejunum (7 cases, 36.84%).

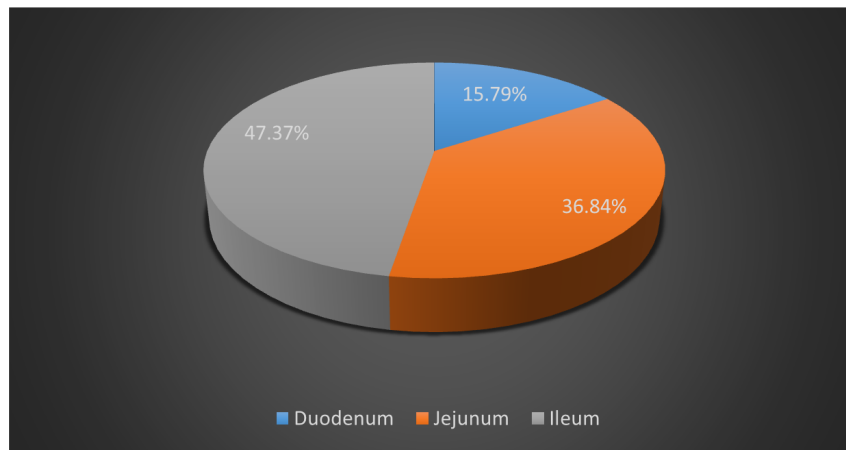


Figure 3. Distribution by localization.

3.6. Anatomopathology

3.6.1. Types of Sampling

The type of sample was specified on 30 cases, of which 18 (60.00%) were derived from operative specimens and 12 (40.00%) were biopsies.

3.6.2. Histological Type

The most common varieties were adenocarcinomas (33 cases, 70.21%), followed by Non-Hogdgin’s Malignant Lymphoma (NHML). Carcinoid was found principally before 40 and after 70 years old (Table 3).

Table 3. Distribution by histological type.

Histological Type	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	Total	%
Adenocarcinoma	-	-	1	6	5	11	7	3	33	70,21
NHML	-	1	3	1	2	-	1	1	9	19,15
Carcinoid	-	-	1	1	-	-	-	3	5	10,64
Total	-	1	5	8	7	11	8	7	47	100,00

NHML - Non-Hodgkin's Malignant Lymphoma

At the 3 principal subsites, all tumors showed a predilection for the ileum (Table 4).

Table 4. Distribution of histological types by location.

Location	ADK		LMNH		T Carcinoide		Total
	H	F	H	F	H	F	
Duodenum	1	2	-	-	-	-	3
Jejunum	3	2	1	1	-	-	7
Ileum	5	1	-	1	1	1	9
Total	9	5	1	2	1	1	19

4. Discussion

The small bowel represents approximately 75 percent of the length and over 90 percent of the surface of the alimentary tract (90% of the absorptive surface area of the gastrointestinal tract) [1, 2]. The small intestine is located between the stomach and the large intestine and is the primary site of end absorption of nutrients from food, including proteins, lipids, and carbohydrates. It is comprised of three distinct regions: the duodenum, jejunum, and ileum. The duodenum is where most of the body's digestive enzymes are released [17].

In our study, cancer of the small intestine (12 cases, 3.34%) was in the sixth position after the stomach, the colon, the rectum, the anal and the esophageal cancer. According to Neugut, malignant tumors of that organ account for less than 5% of all gastrointestinal cancers (GI) cancer cases [18]. Raghav and Siegel in their studies indicated that small bowel malignancies represent only 3 percent of all gastrointestinal tract neoplasms [1, 2]. In others series, Cancers of the small intestine or small bowel cancer (SBC) account for only 0.42% of total cancer cases and 2.3% of cancers of the digestive system in the United States; while in Canada, 0.37% and 1.78% respectively [19, 20]. Finally, we can say that, malignant tumors of the small intestine are very rare compared to other gastrointestinal organs.

Several hypotheses have been put forward to explain the relative infrequency of small bowel. A small food transit time in the small intestine, which shortens the exposure of the mucosal lining to carcinogens, in addition to fluid circulation of alkaline intestinal chyme [21, 22]. The small intestine has a much lower bacterial load, thus has decreased concentration of potential carcinogens from bile acid breakdown [23]. Authors evocated rapid turnover of the small bowel mucosa which inhibits the growth of cancer cells, high concentration of microsomal hydrolases likely to inactivate some carcinogens and high level of Ig A, that is evidence of an important anti-virus activity. Meaning these tumors are more frequent in patients with congenital or

acquired immuno-deficiency [23-25]. Studies also demonstrate that the small intestine generates less endogenous reactive oxidative species (ROS) than the colon does, which may handle oxidative stress more effectively than the colon resulting in less oxidative damage during exogenous oxidant stress [26].

Males are more likely to be diagnosed with, and die from, small intestine cancer than females [6]. In our study, the male sex was represented by 24 cases (51.06%) or 1.71% of all digestive cancers. The sex ratio was 1.04:1. In Japan, Terada found that the male to female ratio was 14: 8 [27] and in Morocco - 1.6:1 [28]. The gender discrepancy in incidence is about 1.3:1 and in mortality about 1.6:1, suggesting lower survival rates among men [16]. Interestingly, in the United Kingdom, while men are still more likely to be diagnosed, survival rates for men are actually higher than those for women [29]. But, in some African countries, researchers found a female predominance, such like in Togo (0.6:1), Madagascar (0.76:1) and Tunisia (0.81:1). However, it is important to note the low number of cases in those studies 8, 25 and 20 respectively [8, 9, 30]. Differences in diet, carcinogen exposure, and metabolic rate, among others, may underlie the sex difference in small intestine bowel incidence and mortality [6].

The median age for small intestine cancer diagnosis we found was 49,77±15,84 (11 to 78 years). In some others African countries, the average age was 46 years (15 – 70 years), 41,75 years (5 et 77 years) and 36 years old, in Morocco, Togo and Madagascar respectively [7-9]. In the USA, the median age was 66 [3]. The majority of our patients were between 50 and 59 years old (11 cases; 23.40%). The most common age for incidence in the United Kingdom was 80–84 [29].

Some factors are classified like Non-Modifiable Risk Factors. Around 1% of people with larger (20mm+) adenomas, or adenomas with high-grade dysplasia, develop bowel cancer within 4 years after removed adenomas [10]. As in the colon, adenoma in the small intestine appears to be a precursor of adenocarcinoma [31]. A large fraction of villous adenomas of the small intestine has been shown to progress to malignancy [32]. Villous histology, increasing size and a higher grade of dysplasia of the adenoma increase the risk of neoplastic transformation from adenoma to carcinoma [31, 33].

The risk of advanced bowel cancer is 80% higher in people with low-risk polyps detected at first colonoscopy, compared with people with no polyps detected at first colonoscopy [34]. Those with familial adenomatous polyposis (FAP) have a germline APC mutation that predisposes towards the

growth of adenoma polyps. Familial adenomatous polyposis (FAP) is an autosomal dominant genetic disorder caused by mutations of the APC gene on the long arm of chromosome 5. Patients with FAP have thousands of polyps growing in their intestinal lining by the age of 10–12. Over time, the risk of these adenomas transforming to adenocarcinoma grows exponentially, and by age 40, virtually all patients with FAP will have received a colorectal cancer diagnosis [35, 36]. In our study, many patients developed polyps; 25% had polyposis, 12.5% adenomatous polyps. The small intestine is the second most common site for adenocarcinoma among those with FAP. In a study of 1255 patients, about 5% had been diagnosed with small bowel adenocarcinoma (SBA). Half of those cancers were found in the duodenum [11]. The risk of small intestine adenocarcinoma among those with FAP is 330 times higher than for the general population [37, 38]. The prevalence of duodenal adenomatosis in FAP patients are 50%-90% and 3%-5% of these patients develop duodenal cancer; however, periampullary adenomas seem to have a high risk of malignant transformation [39].

In our series, we found that 12.5% of patient consumed delicatessen. Dietary factors have been suggested to be related to the risk of small bowel cancer. Diets that have a high content of animal fat and protein have been associated with a higher risk of that pathology with correlation coefficients of 0.61 and 0.75, respectively [40]. Chow *et al* observed two-to three-fold increases in SBC risk with frequent intake of red meat and salt-cured/smoked foods [41]. Others authors reported a significant increase in risk associated with frequent intake of foods rich in heterocyclic aromatic amines (based on the combined intake of fried bacon and ham, barbecued and/or smoked meat and smoked fish) in males only and with total sugar intake [42]. Processed meat was designated as a carcinogen, and red meat as a probable carcinogen, due to their likely effect on the development of cancers of the small and large intestine [43].

A few studies have observed a positive association between alcohol consumption and SBC, either adenocarcinoma or carcinoid tumors [42, 44]. In our study, 12.5% of patients recognized their alcohol consumption. Several studies do not find a relationship between alcohol intake and SBC risk [41, 45, 46]. Heavy alcohol consumption had been found to increase the risk of CRC by 20–40%, leading many to assume it has a similar effect on SBA, even if small sample sizes due to the rarity of the disease preclude definitive results [6, 47].

Many factors have been suggested to be a risk factor or promoter of SBC, such as Inflammatory bowel diseases, Celiac disease, Peutz-Jeghers syndrome, other cancers, [31, 48-50].

SBC can be found in different locations. According to Hatzaras *et al* findings, the most prevalent anatomical tumor site in this study was the ileum (374 cases; 29.7%), followed by the duodenum (320 cases; 25.4%), and then the jejunum, affected in 193 cases (15.3%) [51]. Raharisolo Vololonantenaina *et al* found 50% in duodenum, 10% in jejunum, 25% in ileum and 15% diffuse repartition. In

Tunis, in their series Haoues *et al* discovered Malignant tumors of the small bowel most commonly arise in the ileum (60%) followed by the jejunum (35%) [30]. In our study the tumor was ileum localization in 47.37% of cases, jejunum - 36.84% and 15.79% - duodenum. This site dispersion is particularly interesting and may be explained by the fact that the segments of the small bowel in proximity to the stomach and large bowel are exposed to higher concentrations of carcinogens [51]. Other possible mechanisms for explanation of this phenomenon are that the jejunum may be protected by the continuous and rapid turnover of its epithelial cells (life span range, 2-5 days), which confers a unique resiliency of this part of the bowel and that the jejunal mucosa has an enhanced ability to digest, metabolize, and/or detoxify potential carcinogenic byproducts of dietary ingestion [41].

Adenocarcinoma (33 cases, 70.21%) was the most common histological type in our study, followed by Non-Hodgkin's Malignant Lymphoma (NHML). Carcinoid was found principally before 40 and after 70 years old. Instead of that, all tumors showed a predilection for the ileum. Hatzaras *et al* histologically, discovered that carcinoid tumors were the predominant form of small-bowel neoplasms (417 cases; 33%), followed by adenocarcinomas (379 cases; 30.1%) and, all tumors showed a predilection for the ileum, with the exception of adenocarcinoma, for which the highest incidence was in the duodenum and then progressively decreased throughout the rest of the more distal small intestine [51]. For Haoues *et al*, carcinoid tumor was the main histological type (8 cases), followed by leiomyosarcoma (7 cases), giant B-cell lymphoma (2 cases), malignant stromal tumor (2 cases) and malignant myxoid schwannoma (1 case). However, according to many authors, approximately 30%-40% of the cancers observed in the small intestine are adenocarcinomas, a percentage much lower than the proportion in the colon where the overwhelming majority is adenocarcinomas. Most of the tumors located in the duodenum and the duodenal-jejunal junction are adenocarcinomas [5, 14, 33]. Carcinoid tumors accounts for some 35%-42% of neoplasms in the small intestine, most of which occur in the ileum and rarely in the duodenum [5, 14, 33]. About 15%-20% of cancers of the small intestine are lymphomas with most occurring in the ileum and jejunum [5, 14]. Some authors attributed the prevalence of adenocarcinoma in the duodenum to the early metabolism of ingested carcinogens and the interactions of carcinogens with pancreaticobiliary secretions [52]. Ribeiro *et al* [11] reported a significant exception in patients with long-standing Crohn disease. Seventy percent of the patients that develop a change in their clinical status, such as small-bowel obstruction refractory to usual treatment, were found to have developed an adenocarcinoma of the ileum at the site of the primary inflammatory process [12].

5. Conclusion

Cancers of the small intestine are is the sixth malignant

tumor of the digestive tract in Cameroon. The mean age of onset is 49.77 years old with a relative male predominance. They are comprised of 3 major histological types (adenocarcinomas, Non-Hodgkin's Malignant Lymphoma and Carcinoid), the most common is adenocarcinoma. The establishment of a real cancer registry will provide better coordination in the control of the epidemiology of this pathology, and in the development of means to fight it.

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