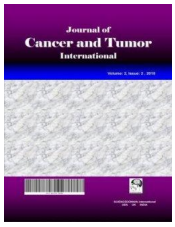

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# Colon Cancers: Epidemiological and Histopathological Aspects in Cameroon

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***Authors' contributions***

*This work was carried out in collaboration between all authors. Author JPNE designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors ODN, BDD, RGA, SG and AM participated in data collection supervision and analysis. Authors AF and AH contributed in literature search. Authors DA and JLOE reviewed the final manuscript. All authors read and approved the final manuscript.*

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## ABSTRACT

**Objective:** To determine the epidemiological and histological profile of colon cancer in Cameroon.
**Materials and Methods:** It was a retrospective descriptive and analytical study on cancers of the colon, histologically proven for 13 years (2004-2016), listed in the registers laboratories of

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pathology and Oncology of the national territory. The variables studied were the frequency, age, gender, risk factors, location and histopathologic type.
**Results:** We identified 1047 cases of digestive cancers. The colon with 366 cases (26. 01%) was the second most common location behind the stomach. The average age of the patients was 52. 82 ± 15. 92 years, with extremes ranging from 6 to 89 years old. The male was the most represented with 52. 73% (193 cases), with a male-to-female sex ratio of 1.12. A tumour was sigmoid localisation in 37. 59% of the cases (100 cases on 266 listed locations). Adenocarcinomas were the first histological type with 311 cases (84. 97%) followed by the Kaposi Sarcoma (21 cases; 5.74 percent) and lymphomas (17 cases; 4.65%).
**Conclusion:** Colon cancers remain a relatively common pathology in Cameroon where it ranks second among malignant tumours of the digestive tract. Women remain less affected than men by this pathology whose dominant histological type is adenocarcinoma. However, these data remain relative given the absence of a cancer register at the national level.

*Keywords: Cancer; colon; epidemiology; histopathology; Cameroon.*

## 1. INTRODUCTION

Colon cancers are the most common malignant tumour of the digestive tract, developing from cells lining the inner lining of the colon [1,2]. It accounts for 9.7% of all cancers globally [3-5] and ranks third after lung (13%) and breast (11.9%) cancers [6-8]. Malignant colon tumours represent the third most common disease in men and the second in women with an estimated incidence of 1.4 million cases in 2012, the sex ratio M / F is 3/2 with almost 95% of patients diagnosed after 50 years [1-3]. Incidence rates vary from continent to continent, and high incidence countries are Western Europe, North America, Australia, New Zealand and Japan [4-8]. In France, the sex ratio M/ F is 1.22 with a mean age of diagnosis of 71 years in men and 73 years in women [3,9,10]. In Canada it is the 2nd most diagnosed form of cancer (13% of all cancers combined) with more than 90% of patients older than 55 years; the male-to-female sex ratio is 1.25 [11,12]. In Africa the incidence is lower; this is the case of Togo, the sex ratio M / F is 3/2 with an average age of 46.7 years [13]. In Morocco the mean age of onset 54.48 ± 14.75 with slight female predominance [14]. In 2012, according to the International Agency for Research on Cancer (IARC), colon cancers were the 4th leading cause of death in the world with 694,000 deaths behind lung, liver and stomach cancers [1]. In West Africa, there is a low mortality rate for colon cancers of 3.5 per 100,000 men and 3 per 100,000 women [15]. Although colonic polyposis is considered to be the major risk factor for the development of colon cancer (HNPCC: hereditary non-polyposis colorectal cancer) [16,17], other risk factors are incriminated in the genesis of this pathology in particular, age> 50 years, obesity, a diet low in fruits and vegetables, sedentary lifestyle and smoking [18,19]. The diagnosis of certainty is colonoscopic associated with an anatomopathological examination. The most common histological types are adenocarcinoma in more than 90% of cases (Liberkhunien, colloid or mucinous, with kittens ring cell contingents) [20]. The most frequent locations are the ascending colon, the descending colon, and the sigmoid [21,22]. The primary means of treatment are surgery for locoregional forms, chemotherapy and radiotherapy for extended forms, including palliative care [23]. In Cameroon, the incidence of colon cancer is estimated in Yaoundé at 2.9% [24]. In the littoral region, it ranks 2nd in digestive cancers behind stomach cancer with an incidence of 22.79%; the mean age of onset is 51.83 ± 17.34 years with a sex ratio of 1.69 [25]. However, it should be noted that these two studies are regional and we do not have data at the national level. It is therefore essential for us to study through this work the epidemiological profile and histopathological aspects of this severe condition over a period of 13 years (2004-2016) in Cameroon to have recent data, which would allow a better control of this pathology in our context.

## 2. MATERIALS AND METHODS

This is a retrospective descriptive and analytical study of histologically proven malignant colon tumors, diagnosed between January 2004 and December 2016. The study took place in the main public and private pathological anatomy laboratories in Cameroon. We needed the reports of histopathological examinations of the various laboratories solicited, all the necessary documentation relating to our subject (books, journals, specific publications ...), and a well-

defined office equipment. 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 a reading made using a microscope. Only patients for whom the diagnosis was confirmed by histology were included in the study. The information obtained included 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

At the end of our study, we collected 1407 digestive cancers, 366 of these cancers were colon cancers with a frequency of 26.01% making it the second digestive cancer after stomach malignant tumours (Fig. 1).

The frequency of onset was 28.15 cases / year. We have seen an increase over the years from about 22 cases / year in the first seven years of our study to 35 cases / year for the last five years (See Fig. 2).

### 3.2 Distribution by Sex

Of the 366 cases of colon cancer found, the male sex was represented by 193 cases (52.73%) or 13.72% of all digestive cancers and the female sex represented by 173 cases (47.27% or 12.30% of all digestive cancers. The male-to-female sex ratio was 1.12. (Table 1).

### 3.3 Distribution by Age

As shown in the Fig. 3, the average age of diagnosis was 52.82 ± 15.92 years, with extremes ranging from 6 to 89 years. The majority of patients were between 50 and 59 years old (86 cases; 24.57%).

In men the average age was 53.62 ± 15.38 years with extremes ranging from 6 to 89 years; the majority of cases were between 50 and 59 years old, its means 52 patients (27.6%). In women, the mean age of diagnosis was 51.90 ± 16.49 years with extremes ranging from 7 to 88 years; the majority of cases were between 40 and 59 years old with 68 patients (41.46%).

### 3.4 Distribution According to Risk Factors

Risk factors were highlighted in 235 patients. The most common were cold cuts (21.28%), alcohol (17.02%), obesity (13.62%) and smoking (12.34%) (Fig. 4).

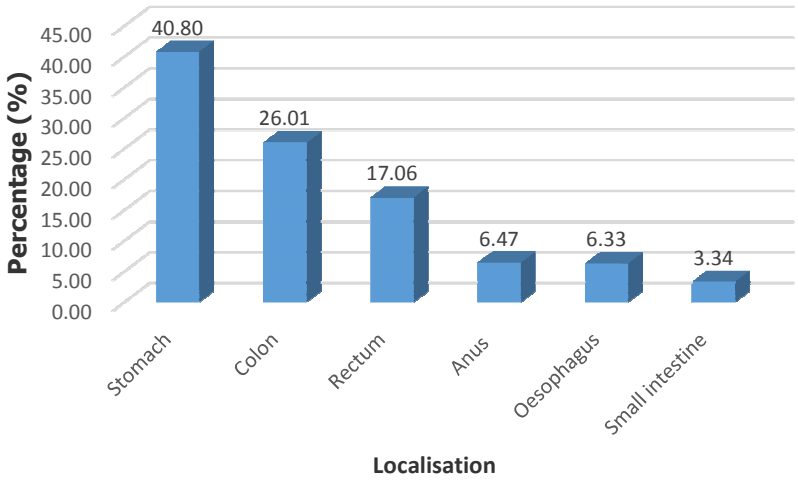


**Fig. 1. Distribution of cancers according to the segment of the digestive tube**

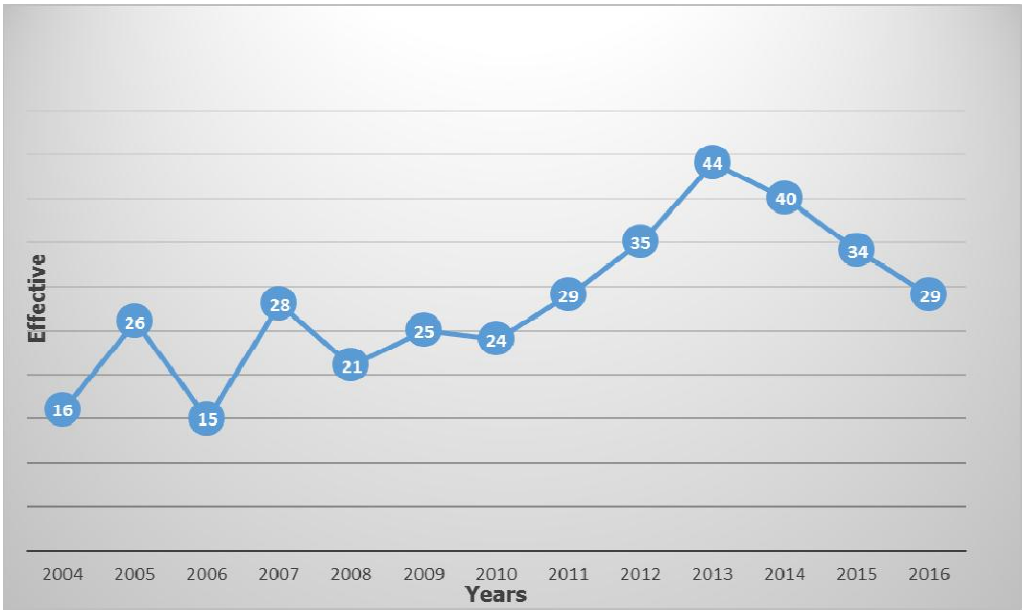


**Fig. 2. Evolution of colon cancer in the years from 2004 to 2016 (n = 366)**

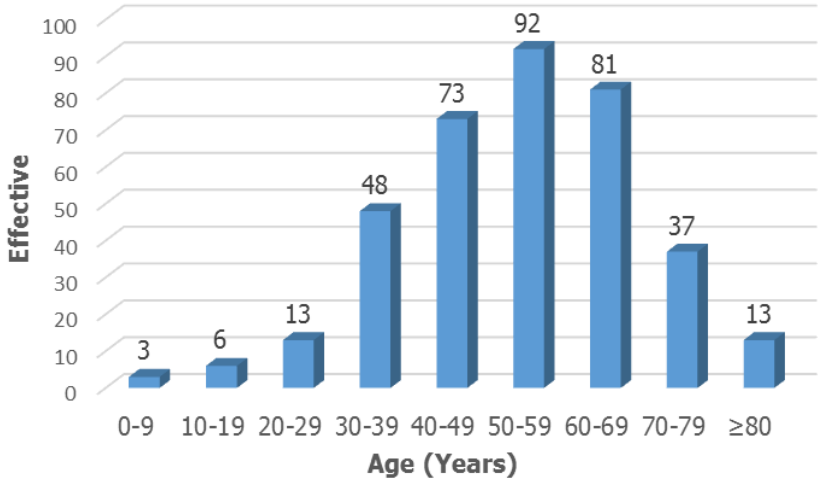


**Fig. 3. Distribution of patients by age group. n = 366**

**Table 1. Distribution of digestive tract cancers by sex**

| Organ | Stomach | | Colon | | Rectum | | Anus | | Œsophagus | | S intestine | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sex | 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 |

*S-Small*

### 3.5 Tumor localization

In the study, 266 localizations were highlighted in this study. As showed in Fig. 5, the tumor was sigmoid localization in 37.59% of cases (100cas / 266).

### 3.6 Anatomopathology

#### 3.6.1 Types o sampling

Of the 366 cases of colon cancers identified in our study, the type of sample was specified on 357 cases, of which 191 (52.19%) were derived from operative specimens and 166 (45.35%) were biopsies.

#### 3.6.2 Histological type

The most common varieties were adenocarcinomas, the most common subtype being Liberkhunien. In patients whose age range varies between 0 and 9 years. It should also be noted the census of a case of the type Leiomyosarcoma or 0.27% of all histological types encountered (Table 2).

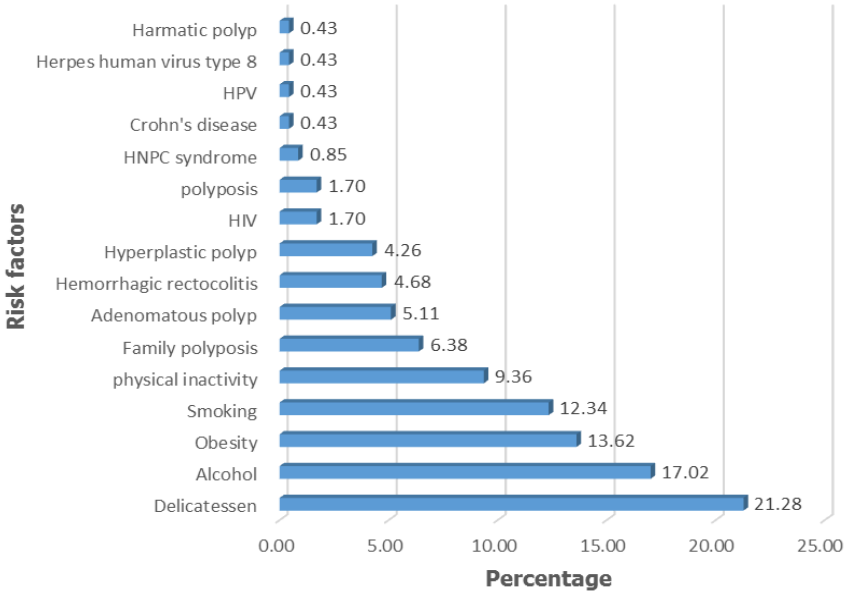


**Fig. 4. Distribution of Risk Factors n = 235**

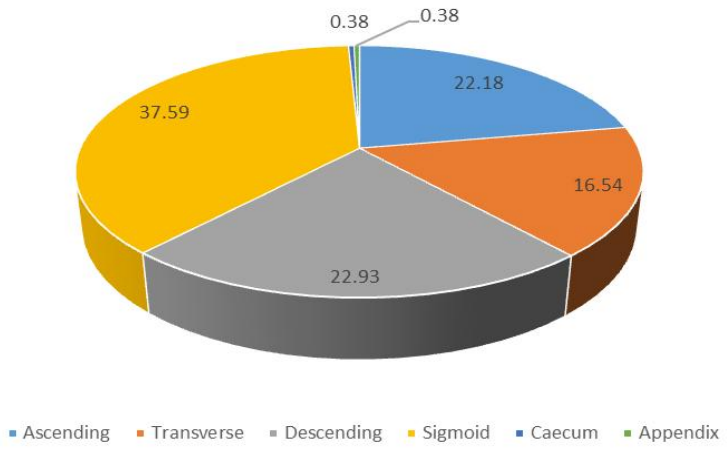


**Fig. 5. Distribution by localization n = 266**

## 4. DISCUSSION

In the study, colon cancers accounted for 26.01% of all malignant digestive tumors, ranking 2nd after the stomach. Several other studies in the African territory rank them second but with varying frequencies (Peghini et al., Ayite et al., Harouna et al., Sani et al. [26-29]). Similarly, in Niger they represent 28.8% of the digestive tract behind the stomach [30-31]. Globally and in the West, particularly in France, they occupy the first place in digestive cancers [2,4,32]. This epidemiological difference could be explained by the high incidence of colic polyposis, whether familial or not in the West, which would raise colon cancer to the highest level of digestive tumoral pathologies on a global scale [16-18].

We collected a total of 366 cases of colon cancer in Cameroon over a period of 13 years or 28.15 cases / year. Indeed, in 2000, Takongmo et al. found an incidence of 7 cases / year over 10 years (1987-1996) in Yaoundé [33]. More recently Engbang et al. found 7.5 cases / year over 12 years (2004-2015) in the Littoral region [25]. It should be noted, however, that these two studies are regional whereas ours is of a national character. This epidemiological observation can be explained on the one hand by an increase in the reference due to training and awareness activities on cancer and on the other hand a better knowledge of the diagnostic methods of the pathology, as well as the presence of cancer centers. pathology in the territory.

Moreover, their distribution per year shows a growing increase in the number of cases from 22 cases / year in the first seven years to (2004-2010) to 35 cases / year for the last five years (2011-2016), a rate of increase of 37.14%. African cohort studies are piecemeal; that of Bamako has shown an increasing trend in the number of cases from 0 cases in 2005 to 34 cases in 2011 [22]; in Uganda, Wabinga et al. also demonstrated in 2000 an increase in the incidence of this pathology [34].

We noted a male predominance with a sex ratio M / F of 1.12. Globally, the sex ratio is 1.5 [35]. In western Algeria there is a male predominance with 272 cases of colon cancer in men and 229 in women out of 501 cases recorded from 2000 to 2007, a sex ratio of 1.2 [21]. In Dakar in 2014, Ibo et al. had found a sex ratio M / F of 1.31 [36]. Given these figures, we conclude that our results are close to those of the literature review. This predominance could be explained by the presence of high-risk factors in men as in women.

The patients in the study were aged 6 to 89 years. The mean age was 52.82 ± 15.92 years. Engbang et al. in the Littoral-Cameroon region had a mean age of patients of 51.83 ± 17.10 years with extremes ranging from 7 to 86 years. Similar retrospective studies in Congo, South Africa, and Tunisia found similar comparable age averages of 55, 59, and 58 years, respectively [37-39]. In Togo there is a lower average age of 48.7 years whereas in Senegal there was a higher average age [13,36]. Thus, colon cancer appears at a relatively lower age among Africans than among Westerners whose peak frequency is between 60 and 70 years [40,41]. This difference could be explained by the low life expectancy in our regions, but should also look for local factors of carcinogenesis.

The most reached age group was between 50 and 59 years old with 86 cases listed. There is also a high representativeness of young subjects with an unexpected peak of incidence between 30 and 39 years. Subjects under 40 years of age represent 20.06% of cases. The figures found by Takongmo et al. found a significantly higher incidence in the under 40 years of 47.61% [33], as well as two Nigerian studies also reporting a significant subgroup of patients under 30 years old [42,43]. The fact that the cases of colon cancer observed in young people are often associated with genetic markers and particular clinical aspects, invites us to conduct prospective studies on the genetic factors associated with this pathology in Cameroon [16]. We also note in our results 51 cases among those over 70 years of age (14.41% of the population of age). Age is a very questionable prognostic factor; studies have concluded that the occurrence of colon cancer in an elderly person is a factor of poor prognosis [14,18]. On the other hand, several authors agree to highlight the seriousness of colon cancers in subjects under 40 years of age due to the frequency of histologically aggressive forms such as mucinous and undifferentiated forms [13,37].

The most common risk factors are excessive consumption of cold cuts, smoking and alcohol. These results are similar to the review of the literature [18,44]. However, there are also 2 cases (0.85%) of HNPCC syndrome, which differs somewhat from Western analytical studies according to which this syndrome is one of the important risk factors for colon cancer [16,45].

**Table 2. Distribution of histological types by age group**

| | 0-9 | 10-19 | 20-29 | 30-39 | 40-49 | 50-59 | 60-69 | 70-79 | ≥80 | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| Lieberkühn's ADK | 2 | 2 | 6 | 34 | 57 | 64 | 61 | 27 | 11 | 264 |
| Mucinous ADK | 1 | 2 | 3 | 9 | 9 | 13 | 6 | 4 | | 47 |
| UDT Carcinoma | | | | | 1 | 1 | | | | 2 |
| Squamous cell carcinoma | | | | | 1 | 1 | | | | 2 |
| AQM carcinoma | | | | 1 | | | | | | 1 |
| Carcinoid tumor | | | 1 | 1 | 2 | 1 | 3 | 1 | | 9 |
| NHML | | 2 | 2 | 2 | 1 | 3 | 4 | 2 | 1 | 17 |
| Kaposi's sarcoma | | | 1 | 1 | 2 | 8 | 7 | 2 | | 21 |
| Leiomyosarcoma | | | | | | 1 | | | | 1 |
| Liposarcoma | | | | | | | | | 1 | 1 |
| Stromal tumor | | | | | | | | 1 | | 1 |
| | 3 | 6 | 13 | 48 | 73 | 92 | 81 | 37 | 13 | 366 |

*NHML - Non-Hogdkin's Malignant Lymphoma; ADK – Adenocarcinoma; UDT - Undifferentiated; AQM - Adenosquamous*

Indeed the risk of occurrence of a malignant colon tumor is very high in case of a history of polyposis or lynch syndrome. Few studies have been done on the incidence of this polyposis in our country. In 2014 in the city of Douala, 86 cases of rectocolic polyps were identified and the most common types were inflammatory (48.83%) and adenomatous (30.23%) polyps [46].

Several mechanisms have been proposed to explain the association between red and processed meat with colon cancer. Potential factors such as heterocyclic amines (HCA) and polycyclic aromatic hydrocarbons (PAH) arising in meat cooked at high temperatures, heme iron or nitrates and nitrites used in meat processing have all been hypothesised to play a role [47-50]. Red meat is abundant in heme iron which has been suggested to mediate the formation of intestinal carcinogenic compounds [47]. Egeberg et al. has hypothesised that since different red meats contain differing amounts of heme iron, the risk for colon cancer may therefore vary according to the red meat subtype [51]. A more recent hypothesis proposed to explain the relation of red meat consumption and colon cancer suggests that a specific bovine infectious factor may be involved in colon cancer development. Based on the fact that chemical carcinogens (HCA and PAH) as the sole player in colon cancer risk have been questioned and the fact that the increased risk for colon cancer is restricted to populations with high beef consumption the author concludes that a specific beef factor may contaminate the meat which could then be potentially carcinogenic upon transmission to humans [47,52].

Concerning alcohol, that product can act as a pro-oxidant in tissues, including lung tissue [53,54], and on lipids, including lung membrane lipids [55,56]. Alcohol can induce the expression of enzymes that are related to carcinogen metabolism, and compounds other than ethanol that are contained in alcoholic beverages may have carcinogenic effects. some mechanisms may explain the alcohol-colon cancer relationship. First, acetaldehyde, an oxidation product of alcohol, may be responsible for colorectal carcinogenesis [55]. Homann et al. reported that high levels of acetaldehyde in rat colon degrade folate, a nutrient that is hypothesized to reduce the risk for colorectal cancer [57]. Second, alcohol is an antagonist of methyl-group metabolism and may contribute to abnormal DNA methylation, an early step in colonic carcinogenesis [58]. Finally, greater alcohol intake may increase the risk for colorectal cancer indirectly through immune suppression, delay of DNA repair, activation of liver procarcinogens by induction of cytochrome P-450 enzymes, or changes in bile acid composition [55].

Colon cancer risk is 18% higher in men who are overweight (body mass index [BMI] 25-29.9) and 48% higher in men who are obese (BMI 30+), compared with men of a normal weight (BMI 18.5-24.9) [59]. Colon cancer risk is 12% higher in women who are obese, compared with women of a normal weight [59]. The association in obese women may be stronger in premenopausal than postmenopausal women [60]. The study results showed that there was a strong risk for proximal colon cancer or distal colon cancer higher with high BMI or WC levels [61]. Obesity is considered one important risk factor for many types of solid cancers, especially for colon [61]. Previous reviews have indicated that obesity is associated with 7% to 60% greater risk of colon cancer compared with normal weight individuals [62]. Currently, several possibilities have been hypothesized. Two hormonal systems – the insulin/insulin-like growth factor (IGF) axis and adipokines (adiponectin and leptin) – are the most studied candidates. First, the involvement of insulin and IGF-1 in colorectal carcinogenesis has been supported by experimental and clinical studies [63]. Circulating total IGF-I, a major determinant of free IGF-I concentrations, is associated with increased risk of colorectal advanced adenomas and cancer [61]. The main reason is that increased free IGF-I with concomitant changes of environment mitogenesis and anti-apoptosis in the cellular favouring tumour formation . Moreover, there is an increased risk of colon cancer development associated with type 2 diabetes [61]. Previous studies have demonstrated that the fat itself can also influence colon cancer risk [64,65]. Adipocytes and preadipocytes could promote proliferation of colon cancer cells [66]. For Ogino et al., fatty acid synthase overexpression has been shown to be associated with colon cancer phenotype [67]. Adipokines such as adiponectin, leptin are also associated with the risk of colon cancer. Adiponectin as an insulin-sensitizing agent and a negative regulator of angiogenesis is secreted mainly from visceral adipose tissue, which could inhibit colon cancer growth in animal models, and its circulating concentrations was associated with colon cancer risk in clinical trials [68]. Leptin could also favour that pathology growth in vivo and in vitro experiment as a

pleiotrophic hormone being mitogenic, anti-apoptotic, pro-angiogenic, and pro-inflammatory in various cellular systems [69]. The relationship between circulating leptin concentrations and colon cancer risk has been demonstrated [70].

The association between cigarette smoking and colon cancer risk has been shown to be dose-dependant [71]. Cigarette smoking strongly associated with molecularly defined subtypes of colorectal cancer, such as MSI-high, CIMP-positive, and BRAF mutation-positive, that originate through epigenetically mediated carcinogenic pathways. These subtypes are more prevalent among women and are more often located in the proximal than the distal colon [72,73]. For Samadder et al. cigarette smoking may be a stronger risk factor for KRAS mutation-negative tumors located in the proximal colon than in the distal colon [74]. Evidence is emerging in support of a strong association between smoking and proximal colon cancer, especially among female smokers [71].

We found in our study 266 localizations out of 366 registered cases. The sigmoid location ranked first with 37.59% (100cas / 266) followed by descending and ascending settlers representing 22.93% and 22.18% of the total proportion. Ele et al., Barth et al. And Brunet et al. Find frequencies approximating ours [37,75, 76]. There is no clear explanation because there is little data available on the factors associated with the occurrence of colon cancer by sub-location [77].

Of the 366 cases reported, liberkhunien adenocarcinoma is the histological variety that dominates colon cancer in our series with 72.13% (264 cases). In parallel with the literature, this type of histology is the most important, but nevertheless Amegbor, Diallo Owono and Darré report higher percentages, especially 89.9%, 98% and 91.2% [13,78,79].

Lymphomas account for 46.5% (17 cases) of colonic malignancies, superior to data in the literature which states that they are rare with a rate of 2% [80]. They are observed at any age with great frequency between 40 and 60 years [66]; In our study non-Hodgkin's Malignant Lymphomas are observed at younger age groups (<20 years).

According to the literature, sarcomas are extremely rare histological varieties of primary colorectal cancers; Viguier et al. reported a frequency of 0.09% [81]. In contrast to these studies, we find 22 cases of sarcoma including 21 of Kaposi (5.74% of the total proportion). Studies on etiological factors of sarcoma would allow us to explain and understand a high incidence of this histological type.

## 5. CONCLUSION

This study conducted on colon cancer in Cameroon has noted that that pathology has a high incidence of digestive tumors (26.01%) with male predominance. This pathology occurs mainly in people in their fifties with a relatively high frequency in people under 40 years. Predominant sigmoid localisation, they are primarily dominated by adenocarcinoma. However, these data remain relative given the absence of exhaustive information on several clinical and epidemiological aspects, hence the need for confirmation of these results by the installation of a national cancer registry. Besides, the fact that colon cancer cases are observed in young subjects invites us to conduct prospective studies on the genetic, environmental and food factors associated with this pathology.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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