

# Histological Types of Gastric Cancer and *Helicobacter pylori* Infection in Yaoundé

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## Abstract

**Introduction:** The diffuse type of gastric adenocarcinoma has been found to be more prevalent in low risk countries like Cameroon. The objective of this study was to determine the most frequent histological type of gastric cancer found in Yaoundé and its association to the *Helicobacter pylori* infection. **Materials and Methods:** The registries of histopathology laboratories of 4 reference hospitals in Yaoundé, Cameroon have been reviewed for registered primitive gastric malignancies from July 2009 to May 2014. Paraffin blocks mounted on slides and stained with Hematoxylyn and Eosin of gastric cancer cases were re-stained Giemsa to search for *Helicobacter pylori* and they were classified using the criteria of Lauren in intestinal type or diffuse type. **Results:** Forty-two cases were reviewed: 25 (59.5%) of them were intestinal type of gastric adenocarcinoma, 11 (26.2%) were diffuse type, 4 (9.5%) were malignant gastric lymphoma, 1 (2.4%) was a stromal tumor, and 1 (2.4%) was a colloid carcinoma. The most common site of location was the proximal gastric portion (52.2%). The overall prevalence of *Helicobacter pylori* infection was 88.1%, most common with the intestinal type (100%) and malignant lymphoma (100%) than with the diffuse type (72.2%) ( $p = 0.007$ ). **Conclusion:** The most common type of gastric adenocarcinoma in Cameroon is the intestinal type and *Helicobacter pylori* infection is more common in the intestinal type and malignant gastric lymphoma than in the diffuse type. The *Helicobacter pylori* eradication campaigns are needed.

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## Keywords

***Helicobacter pylori*, Stomach Neoplasms, Adenocarcinoma, Lymphoma, Non-Hodgkin, Cameroon**

### 1. Introduction

Despite a steady decline in the annual incidence in the last 2 decades, gastric cancer remains a public health problem worldwide [1]-[4]. Nearly one million of new cases were recorded in 2012 (6.8% of all cancers), making gastric cancer as the fifth most common cancer in the world, behind lung cancer (13.0%), breast (11.9%), colon and rectum (9.7%) and prostate (7.9%) and the 3rd leading cause of cancer death [5]. In Africa, in 2012 the incidence of gastric cancer was estimated to be 3.78 cases per 100,000 adults per year, far behind Asia (15.78 cases/100,000) and Europe (9.38 cases/100,000) [5]. Compared to other continents the incidence regresses very slowly in Africa [1] [4]. In Cameroon, although tumor registration is not common practice, gastric cancer represents 2% of all cancers and is in the 11<sup>th</sup> position behind breast cancer, cervix, lymphoma, prostate and liver, and it is responsible of minimum 256 deaths per year [6].

The main risk factors of gastric cancer are environmental factors. The offending factors are salted and smoked nutrition (rich in nitrates) and low vegetables and fruits diet. Alcohol consumption, smoking and low socioeconomic level are also cited [2] [7] [8]. *Helicobacter pylori* (*H. pylori*) infection which is associated with the distal form of intestinal type gastric cancer is a specific factor [9]-[11]. The sequence that leads to cancer has been well defined. It goes through atrophic gastritis, intestinal metaplasia and dysplasia. There is an ongoing controversy on the low prevalence of gastric cancer in Sub-Saharan Africa a region with a high prevalence of *H. pylori* infection [12] [13].

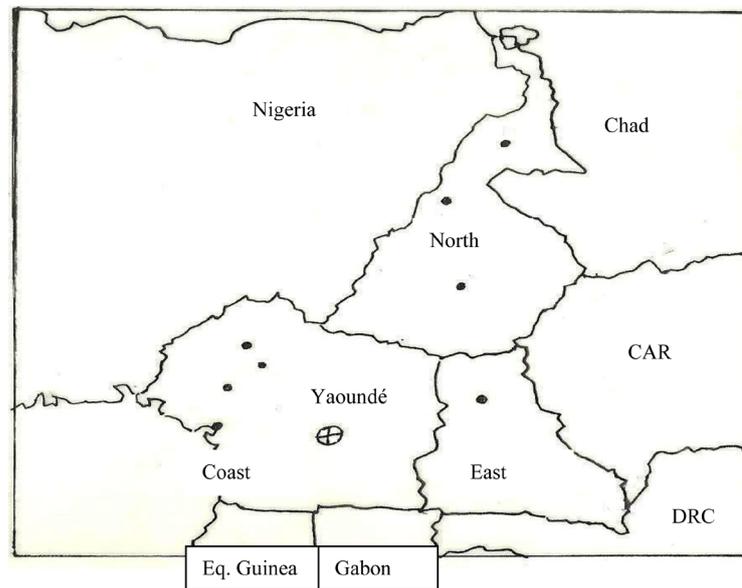
The histological classification of gastric cancer is based on the criteria proposed by Lauren in 1965 [14] and the World Health Organization (WHO) [15]. Lauren's classification distinguishes two main types of adenocarcinoma: the intestinal type and the diffuse type. The term gastric cancer or gastric carcinoma refers to adenocarcinoma of the stomach, which represents nearly 90% of malignant lesions of the stomach. Other malignant lesions of the stomach are malignant lymphomas (2% - 7%) which are in most cases of mucosa-associated lymphoid tissue lymphoma (MALT), gastric stromal tumors (GIST) and carcinoid [1]. In Cameroon adenocarcinoma is the most common type of gastric cancer but little is known about the epidemiology of the different histological types [16] [17].

The objective of this retrospective and descriptive study was to describe the epidemiological and histological aspects of gastric cancer and its association to the *Helicobacter pylori* infection in the histopathology services of four university hospitals in Yaoundé.

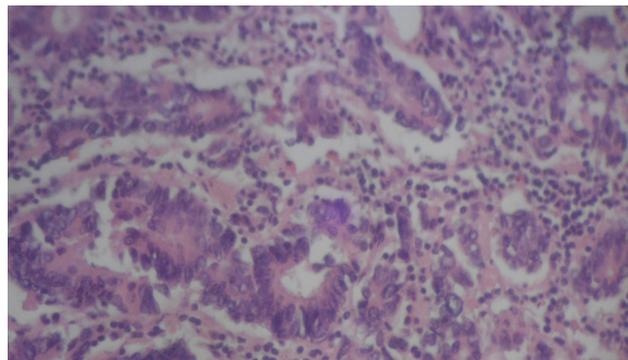
### 2. Materials and Methods

#### 2.1. Context of the Study

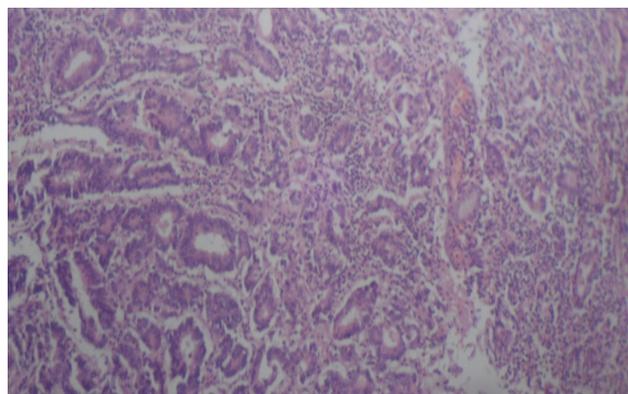
We have conducted a retrospective and descriptive study in four university hospitals in Yaoundé, Cameroon (Figure 1). Yaoundé, the political capital of Cameroon, is located in the Central Region. It covers 304 km<sup>2</sup> and hosts a cosmopolitan population, estimated in 2005, during the 3rd population and habitat census of March 2010, at 1,817,524 inhabitants. Records of pathology were reviewed for cases with primary malignant tumors of the stomach in the period from July 2009 to May 2014. Forty-two patients with precise socio-demographic and registered for histopathological proven malignant tumors of the stomach were included in this study. The fragments of biopsies and surgical specimens were fixed in 10% formalin. After gross examination, the tissue fragments were subjected to dehydration techniques then included in paraffin blocks. The obtained paraffin blocks were cut by a rotary microtome and mounted on slides before being stained with Hematoxylyn and Eosin. Reading was made using an optical microscope at low and at high magnification. Primary gastric malignant lesions found on biopsy material was classified according to the Lauren classification criteria (1965) in intestinal type, diffuse type and mixed type of adenocarcinoma. These two main histological types are illustrated in Figures 2-4. Slides of Hematoxylyn and Eosin stains of gastric cancer cases were re-stained Giemsa to detect *H. pylori* in the bottom of the crypts and in the upper pole of the cells.



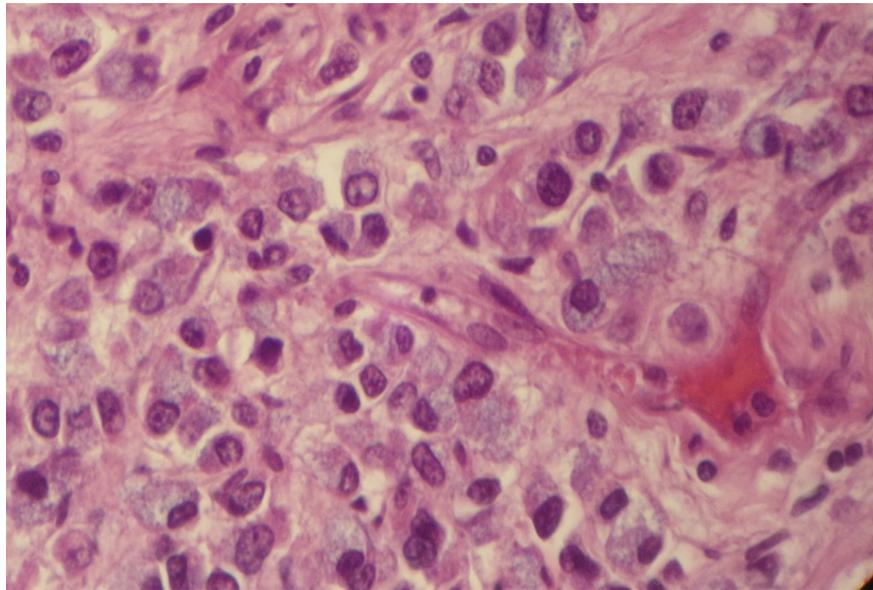
**Figure 1.** Physical map of Cameroon showing the central position of Yaoundé, the east region, the coastal region and the neighboring countries of Cameroon. CAR: Central African Republic; DRC: Democratic Republic of Congo; Eq.: Equatorial.



**Figure 2.** Adenocarcinoma of the stomach. Intestinal type with well-formed glandular structures. Hematoxylyn and Eosin stain,  $\times 25$ . Courtesy of the Histopathology Laboratory of the University Hospital Teaching of Yaoundé.



**Figure 3.** Adenoarcinoma of the stomach. Intestinal type with well-formed glandular structures. Hematoxylyn and Eosin stain,  $\times 10$ . Courtesy of the Histopathology Laboratory of the University Hospital Teaching of Yaoundé. .



**Figure 4.** Adenocarcinoma of the stomach. Diffuse type, absence of cohesion of cells. Hematoxylyn and Eosin stain,  $\times 40$ . Courtesy of the Histopathology Laboratory of the University Hospital Teaching of Yaoundé.

## 2.2. Statistical Analysis

Data were entered and analyzed using SPSS 20.0 (IBM Corporation, NY, USA) software and Microsoft Excel 2007. For quantitative variables the mean and standard deviations were calculated. The proportions have been established for categorical variables.

Comparisons of proportions and means were performed using  $\chi^2$  or Student test. Yates correction and Fisher exact test were used for small numbers. The significance level was set at 5%.

## 2.3. Ethical Considerations

The study was approved by the Ethics Committee of the Faculty of Medicine and Biomedical Sciences of the University of Yaounde 1, Cameroon. A research authorization was obtained from the managers of the various hospitals.

## 3. Results

Of the 42 primary malignant tumors of the stomach, 18 (42.9%) were found in the age group a 50 - 59 years and 30 (71.4%) of these specimens were found in men. The mean age (standard deviation) was 53.4 (9.3) years. Among the histological types, 25 (59.5%) were intestinal type of gastric adenocarcinoma, 11 (26.2%) were diffuse type, 4 (9.5%) were malignant gastric lymphoma (MALT), colloid carcinoma and stromal tumor represent 1 each (2.4%).

The distribution of gastric adenocarcinoma by sex and sites in the stomach is shown in **Table 1**. The sex ratio (M/F) of gastric adenocarcinoma was 3:1; the main location was the proximal gastric region that accounts for 52.2% (19/36) ( $p = 0.672$ ).

The mean age, peak frequency and the sex ratio M/F for the two histological main types of gastric adenocarcinoma are compared in **Table 2**. We found that 76% (19/25) of the cases of intestinal type were diagnosed in patients of more than 50 years, while 63.6% (7/11) of cases of diffuse type were diagnosed in those under 50 years.

**Table 3** shows the prevalence of *H. pylori* infection according to the histological types of primary malignant lesions of the stomach. The overall prevalence of *H. pylori* infection was 88.1% (37/42), *H. pylori* infection was more frequent in intestinal adenocarcinoma (100%) and malignant lymphoma (100%) than diffuse type adenocarcinoma (72.2%).

**Table 1.** Gastric adenocarcinoma by sex and by gastric sites location (n = 36).

Variables	Gastric carcinoma		
	Number of cases	Percentage (%)	p value
<b>Sex</b>			
Male	27	75	0.166
Female	9	25	
Sex-ratio M/F	3:1		
<b>Location</b>			
Cardia	6	30.4	0.672
Proximal	19	52.2	
Distal	11	17.4	

M: male; F: female.

**Table 2.** Mean age, peak frequency and sex-ratio of intestinal and diffuse types of gastric cancer.

	Intestinal type	Diffuse type
Mean age (yr)	54.1	45.2
Younger than 50 yr (%)	24	63.6
Older than 50 yr (%)	76	36.4
Age of peak frequency (yr)	50 - 59	40-49
Peak frequency (%)	44	45.5
Sex-ratio M/F	2.6:1	4.5:1

yr: year; %: percent; M: male; F: female.

**Table 3.** Histological types of primary gastric malignant tumors and *Helicobacter pylori* infection.

	Number examined	<i>H. pylori</i> (+ve)	<i>H. pylori</i> (-ve)	p value
Intestinal adenocarcinoma (%)	25	100	---	0.007
Diffuse adenocarcinoma (%)	11	72.2	23.7	
Malignant lymphoma (%)	4	100	---	
Others (%)	2	---	100	
<b>Total (%)</b>	42	88.1	11.9	

*H. pylori*: *Helicobacter pylori*; +ve: positive; -ve: negative; %: percent.

## 4. Discussion

Demographic characteristics and histological aspects of gastric cancer were examined in several epidemiological studies in Africa [18]-[20] and worldwide [1] [2]. Data from the International Center for Research on Cancer (IARC) in 2012 showed that gastric cancer is relatively rare in Africa compared to Asia and Europe. Thus, according to these data, gastric cancer accounts for 2.0% of all cancers in Cameroon, 1.9% in Nigeria, 2.0% in Chad, 5.0% in the Democratic Republic of Congo, 2.2% in Central African Republic, 0.5% in Mozambique, 1.6% and 4.5% in Egypt and Ivory Coast [5]. The reasons for this geographic disparity and these low impacts are unknown. Cohort studies conducted in several countries are pointing the finger primarily to environmental factors and specifically the *H. pylori* infection [9] [10] [20]. Because of the low socioeconomic levels, extension of refrigeration in the food preservation is not effective in sub-Saharan Africa and also chronic *H. pylori* infection is endemic in the population with approximately 80% of infected individuals since childhood [21]. In Cameroon both risk factors for gastric cancer exist, especially at the Coastal region and in the forest of the East region.

However, studies comparing the populations of the Coast and East eating salted food and smoked fish or meal to the rest of the population do not exist.

The results reported here are from hospitals in Yaoundé in the Central Region. Patients in this study are certainly not all natives of the Central region, but come from different regions of Cameroon; due to lack of technical platforms that can support oncology patients. Yaoundé regroups a cosmopolitan population of cancer patients.

The predominance of adenocarcinoma among primary malignant lesions of the stomach was reported in several clinical studies [1] [22]. Our results indicate a clear predominance of adenocarcinoma among our patients that accounts for around 86% of all stomach malignant tumors. The male is the most represented among these cases; three times more than women. This is similar to what we have previously reported [16].

In 1965, Lauren reported the prevalence of intestinal type adenocarcinoma in Finland [14]. The intestinal type usually predominates in high-risk areas of gastric cancer; the relative frequencies are approximately 54% for the intestinal type, 32% for the diffuse type and 15% for the mixed type [23] [24]. Our results show that the intestinal type is predominant in Cameroon, a low risk country, with 59.5% of cases, while the diffuse form represents 26.2% of cases. Similarly in previous study, Mabogunje *et al.* [25] reported in northern Nigeria, a neighboring country of Cameroon a frequencies of 61.5% for the intestinal type, 24.6% for the type diffuse and 3.1% for the mixed type.

Some evidences have shown that, the diffuse type of adenocarcinoma of poor prognosis, is most often encountered in women and in younger patients [14] [26], and the intestinal type is most often associated with *H. pylori* infection, intestinal metaplasia, male sex and elderly [14] [27] [28]. Our results indicate a male predominance, regardless of the type of adenocarcinoma, with a 3:1 and 5:1 respectively for intestinal type and diffuse type. Over 60% of all gastric cancer cases were diagnosed in patients older than 50 years including in 76% of intestinal type adenocarcinoma, while 63.6% of diffuse type adenocarcinoma were found in subjects under 50.

The decrease in the incidence of gastric cancer in the United States of America and Western Europe largely reflects the decline of distal gastric lesions; in contrast, however, the proximal location of adenocarcinoma of the stomach is increasing. Advanced explanation is an inverse relationship with *H. pylori* infection, the incidence is decreasing in industrialized countries, including Switzerland following the *H. pylori* eradication campaigns [1] [4] [29] [30]. In this study, the proximal location was predominant with about 52% of cases. In our environment where *H. pylori* infection is endemic we expected a predominance of distal location rather than the proximal one. We have no arguments to explain the predominance of proximal gastric location of adenocarcinoma in this study. Environmental factors in synergy with *H. pylori* infection may explain this fact than *H. pylori* infection alone. There is controversy on the high prevalence of *H. pylori* infection and the low frequency of gastric cancer in population in Africa; this contributes to the “Africa enigma” [12] [13] [21].

This is a retrospective study and as such it carries some limits. First it was conducted in the city of Yaoundé, far from other parts of the country; second, the number of cases was very small for a five years study. This is because tumors registration’s and reporting are very limited in Cameroon and almost not existing, making epidemiological studies a great need to map the distribution of gastric cancer in all regions of Cameroon.

## 5. Conclusion

In this study, we have found that the intestinal type of gastric adenocarcinoma is the predominant histological form in Cameroon. Also, the *H. pylori* infection is frequently associated with it and malignant gastric lymphoma than with the diffuse type. This finding suggests that the main risk factor of gastric cancer in our country may be the *H. pylori* infection. We believe that *H. pylori* eradication’s campaigns are needed and further studies conducted among populations with environmental risk factors as in the Coast and the forest area to the East may be necessary.

## Conflict of Interest

The authors declare no conflict of interest.

## Acknowledgements

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