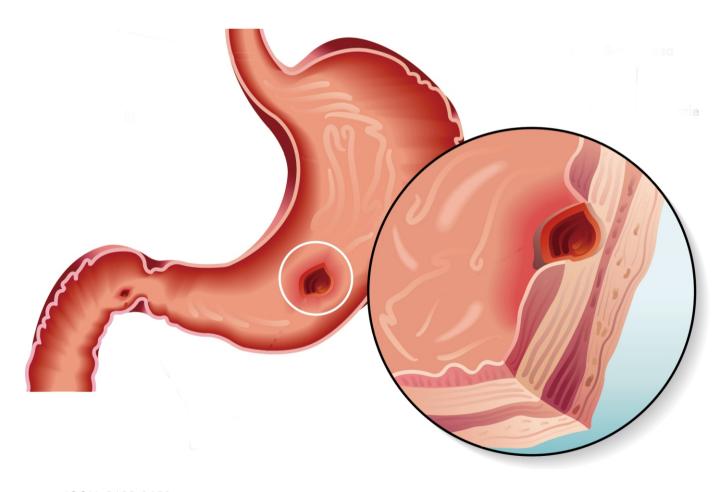


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Helicobacter Pylori Infection: Epidemiological, Clinical and Endoscopic Aspects in Brazzaville

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Abstract

Introduction: Helicobacter pylori infection is a real health problem worldwide. It is the most common chronic bacterial infection in the world, and is particularly prevalent in developing countries. Objective: To determine the frequency of Helicobacter pylori infection and to study the epidemiological, clinical and endoscopic characteristics associated with this infection in Brazzaville. Patients and Methods: This was a descriptive cross-sectional study conducted from January to November 2020, i.e. 11 months. This work focused on 100 symptomatic patients over 18 years old referred for upper GI endoscopy. Gastric biopsies for biological study by urease test and molecular study by real time PCR technique were taken. Results: With a mean age of 46.32 \pm 15.20 years, the frequency of Hp infection was 91%, with a female predominance of 53%. The sex ratio was 0.92. The average age was 46.32 \pm 15.20 years. Carriage of the infection was more important in households with more than 3 persons, in patients consuming public tap water and in those using both types of sanitary facilities. Endoscopy was indicated for epigastralgia in 93.1% of cases. About 56.14% of the infected patients had normal mucosa versus 12.28% with ulcerated lesions and 22.81% with gastritis. Conclusion: The prevalence of Helicobacter pylori infection is significant in Congo, justifying early detection in order to improve management.

Keywords

Helicobacter pylori, Carriage, Chronic Gastritis, Gastric Ulcer, Brazzaville

1. Introduction

Hp infection is a real human health concern worldwide. It is the most common chronic bacterial infection, particularly in developing countries [1]. However, this prevalence can vary considerably, both between different countries in the world and even within a country, depending on the age and socio-economic conditions of the population [2]. Indeed, more than 50% of the world's population is thought to be infected and 20% - 90% of people are infected depending on the country, with infection being more common in poor and low socio-economic environments [3] [4] [5] [6] [7].

In Africa, several studies conducted from 2005 to 2019, place the prevalence of *Hp* infection between 60% and 91% [8] [9] [10] [11]. In Congo, several studies have investigated the frequency of *Hp* infection. Ibara *et al.* in 2005 reported a frequency of 48.7% in children [12]; Ontsira Ngoyi *et al.* in 2015 estimated a frequency of 89% in adults [13]. Ngala Itoua-Ngaporo *et al.* in 2018 estimated that *Hp* occurs in up to 79.6% of the population [14] and the most recent by Ontsira Ngoyi *et al.* in 2019 estimated the prevalence at 75.5% [15].

The mode and routes of transmission of *Hp* infection are known. Infection occurs mainly in childhood, via the oral or faecal-oral route. Factors influencing the incidence and prevalence are age, gender, geographical location, promiscuity, poor hygiene and low socio-economic status [16].

Hp infection has been implicated in a wide range of gastric mucosal diseases, such as acute and chronic gastritis, gastric ulcer, gastric cancer [16] [17].

The aim of this work is to improve the management of patients infected with *Helicobacter pylori* by studying the epidemiological, clinical and endoscopic features associated with *Hp* infection.

2. Patients and Method

This was a descriptive and cross-sectional study from January to November 2020, a period of 11 months. The study was conducted in the cities of Brazzaville and Pointe-Noire. The upper digestive endoscopy and biopsy samples were taken in three endoscopy centres in the city of Brazzaville, namely the Schnell Foundation Medical and Social Centre, the OCH Gastroenterology Medical Centre, and the Gastroenterology and Internal Medicine Department of the Brazzaville University Hospital. The molecular study was carried out at the Hugues Dieudonné Loemba (HDL) laboratory of the Fondation Marie Madeleine Gombes (FMMG) in Pointe-Noire. The study population consisted of all patients received for oesogastroduodenal endoscopy (EOGD), regardless of the indication, in one of the exploration centres during the study period. We included any consenting patient over 18 years of age, symptomatic patients and those with histologically confirmed gastric cancer. Patients who had taken a PPI and/or antibiotic in the month prior to endoscopy, patients in whom oesogastroduodenal endoscopy was incomplete and biopsy could not be performed, and patients in whom biopsies were not usable were excluded from the study. Our sample size was estimated at 100 patients. Consecutive sampling of patients meeting the inclusion criteria was performed until the estimated number was reached. The study required the opinion of the Health Sciences Research Ethics Committee (N°303/MRSIT/IRSSA/CERSSA).

The data were collected by the same investigator using a pre-established survey form. The form was used to collect information on the risk factors of contamination, *i.e.* socio-economic and epidemiological aspects, but also certain habits and lifestyle of the patients that could influence the frequency of *Hp* infection.

The digestive symptoms were dyspeptic syndrome, nausea, vomiting, digestive haemorrhage, type and location of abdominal pain. Upper GI endoscopy was performed using FUGINON video endoscopes in the Brazzaville University Hospital and Olympus[®] GIF V2, GIFQ 145 in the other centres, as well as accessory equipment that was carefully disinfected and sterilised before the examination according to SFED recommendations. During the examination, samples were taken with a single-use biopsy forceps from two sites: the antral mucosa and the fundic mucosa. For each site, two biopsy fragments of approximately 0.5 mm in diameter were taken. For each of the two sites, one fragment was taken for urease testing and one fragment for molecular biology. Biopsies for molecular study were cryopreserved, frozen at -32° C.

The rapid urease test was performed in the endoscopy room immediately after the examination, using the Pronto Dry New, Cadrex test. This test allowed rapid detection of the bacteria based on its main property, urease production. The test was positive when the indicator (ring) with a yellow base gradually turns from pink to purplish red at room temperature.

The molecular study was carried out on fresh cryopreserved biopsies using the real-time PCR technique in two consecutive steps: DNA extraction using the "ReliaPrepTM gDNA tissue Miniprep system from Promega" and DNA amplification for *Hp* detection using the "TechneTM PrimePRO qPCR DNA detection Kit, H Pylori".

3. Results

Of the 100 patients in our study population, 84 patients were positive by urease test and 91 by PCR. Based on our variable of interest, PCR, the overall frequency of Hp infection was 91% (**Table 1**). Our study population was predominantly female, 53% of the women were carriers of the bacteria. The mean age of the patients was 46.32 ± 15.20 years with a peak of infection (32.97%) between 40 and 49 years (**Figure 1**). Hp infection was higher in patients with an average so-cio-economic status of 61.54%.

Regarding household size, the frequency of *Hp* infection was 86.9% for households with more than 3 persons. *Hp* infection was found in 59% of patients using tap water, 45% using modern toilets and 42% using latrines (**Table 2**).

Out of a total of 100 patients included in our study, 87 patients presented with abdominal pain. *Hp* was found in 92.5% of the patients with epigastric pain, 65%

Table 1. Frequency of infection according to the results of the two Hp tests in the study population.

VARIABLES –		PCR	
	Positive	Negative	Total
Urease positive	79	5	84
Urease negative	12	4	16
Total	91	9	100

p = 0.01.

Table 2. Distribution of infection by household size and living arrangements.

	PCR result			
VARIABLES	Positive $(N = 91)$	Negative (N = 9)	p-Value	
	n (%)	n (%)		
Household size				
<3	11 (13.1)	7 (43.8)	0.003	
3 - 7	60 (71.4)	8 (50)	0.09	
>7	13 (15.5)	1 (6.2)	0.3	
Types of sanitary facilities				
Latrines	42 (46.15)	6 (66.67)	0.2	
Modern	45 (49.45)	3 (33.33)	0.3	
Both	4 (4.40)	-	0.5	
Modern Water Source				
Public tap	59 (64.84)	7 (77.78)	0.4	
Mineral water	24 (26.37)	2 (22.22)	0.7	
Well	3 (3.30)	-	0.5	
*Other	5 (5.49)	-	0.4	

of which was burning (**Table 3**). The frequency of *Hp* infection was higher in patients with nausea/vomiting followed by dyspeptic disorders, however, 74% of GI bleeding was related to *Hp*, and 81% of melenas presented by patients were related to *Hp*. All patients included in the study had undergone upper GI endoscopy. Endoscopy was normal in 70% of the patients, and revealed pathological mucosa in 30% of the patients. Endoscopy was indicated for epigastralgia in 93.1% of cases. It revealed normal mucosa (56.14%), ulcerated lesions (12.28%) and gastritis (22.81%) in infected patients. The bacterium was exclusive in acanthosis (100%) and frosted lesions (100%). This result is shown in **Table 4** & **Table 5**.

4. Discussion

Considered the only carcinogenic bacterium to date, Hp infection is a major

public health concern in developing countries. The aim of this study was to investigate the epidemiological, clinical and endoscopic factors associated with Hp infection.

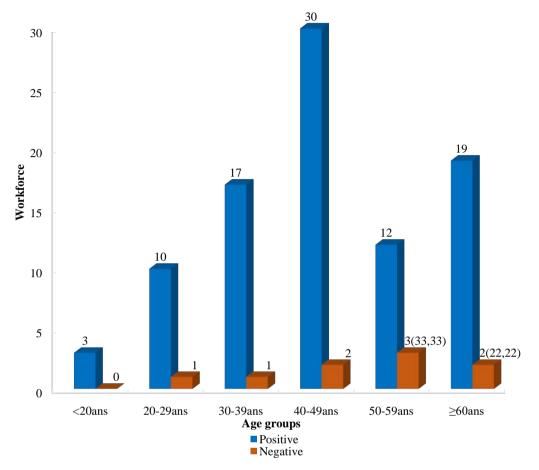


Figure 1. Age distribution of infection. p = 0.567.

	PCR result			
VARIABLES	Positive $(N = 91)$	Negative (N = 9)	p-Value	
	n (%)	n (%)		
Location of pain				
Epigastrium	74 (92.5)	8 (100)	0.4	
Right hypochondrium	2 (2.5)	-	0.6	
Available at	4 (5.0)	-	0.5	
Type of pain				
Burn	52 (65)	3 (42.86)	0.2	
Cramp	25 (31.25)	4 (57.14)	0.1	
Vice	1 (1.25)	-	0.7	
Not specified	2 (2.50)	-	0.6	

	PCR result			
VARIABLES	Positive $(N = 91)$	Negative $(N = 9)$	N = 9) <i>p-Value</i>	
	n (%)	n (%)		
Digestive symptoms				
Nausea	34 (25.19)	4 (17.39)	0.6	
Early feeling of fullness	29 (21.48)	5 (21.75)	0.1	
Feeling of fullness in the stomach	22 (16.30)	4 (17.39)	0.1	
Vomiting	30 (22.22)	3 (13.04)	0.9	
Hematemesis	7 (5.19)	4 (17.39)	0.0007	
Méléna	13 (9.62)	3 (13.04)	0.1	

Table 4. Distribution of infection according to symptoms.

Table 5. Distribution of infection according to endoscopy findings.

	PCR		
VARIABLES	Positive $(N = 91)$	Negative $(N = 9)$	p-Value
	n (%)	n (%)	
Endoscopic aspects of patients			
Normal mucosa	64 (56.14)	6 (37.5)	0.8
Ulcerated lesion	14 (12.28)	3 (18.75)	0.1
Budding lesion	3 (2.63)	2 (12.5)	0.01
Frosted lesion	1 (0.88)	-	0.7
Erosive aspect	12 (10.53)	1 (6.25)	0.8
Congestive aspect	14 (12.28)	1 (6.25)	0.7
Infiltrated appearance	1 (0.88)	2 (12.5)	0.0003
Acanthosis lesion	2 (1.75)	-	0.6
*Other	3 (2.63)	1 (6.25)	0.2

Two identification techniques (urease and PCR) were used to assess the carriage of *Helicobacter pylori* infection in the study population. Of the 100 patients in our study population, 84 were urease positive and 91 were PCR positive. Some patients (11) were urease negative and PCR positive. The high frequency of *Helicobacter pylori* by PCR demonstrates the improved sensitivity of PCR and the limitation of the urease technique which can only detect secreting strains. Furthermore, there was a statistically significant difference between these two tests (p = 0.01). The variable of interest being the PCR, the frequency of *Helicobacter pylori* infection was 91%. This frequency was higher in women (53%). Aguemon *et al.* in Benin and Bommelaer *et al.* in France also reported a female predominance of infection [8] [18], while ATTAF N *et al.* in Morocco and Ould Bouh *et al.* in Mauritania reported a male predominance [19] [20].

All age groups were affected, with a higher frequency in younger patients, par-

ticularly those under 50 years of age, with a peak between 40 and 49 years of age (32.97%). No significant difference was found between age and *Hp* infection (p = 0.567). This result is similar to those reported by some studies in Africa, which found no significant difference between the presence of *Hp* and age [8] [9] [21].

Hp infection was higher in patients with an average socioeconomic status of 61.54%. This result is similar to that obtained by Bagny *et al.* in Togo who obtained a higher frequency of *Hp* infection in the middle socio-economic class in 63.3% of cases [22]. On the other hand, Ankouane *et al.* in Cameroon and Ilboudo *et al.* in Burkina Faso obtained a frequency of 73.9% and 77.9% respectively in patients with a low socio-economic level [21].

Regarding patients' lifestyle, our results showed that regardless of household size or lifestyle, these factors were not directly related to Hp infection. However, a higher tendency of infection was observed in patients using tap water (59%) compared to those using other water sources. This result can be explained by the fact that more than half of the Congolese population uses this water source. This result can be explained by the fact that more than half of the fact that more than half of the Congolese population uses this water source. This result can be explained by the fact that more than half of the Congolese population uses this source of water, as reported by Aguemon *et al.* in Benin [8] who found an association between Hp infection and latrine use.

Of the 43.86% of Hp-positive patients with abnormal endoscopy, a statistically significant difference was observed with patients with infiltrated (p = 0.0003) and budding (p = 0.01) lesions. Carriage of Hp infection was exclusive in acanthosis (100%) and frosted lesions (100%). In addition, Hp was strongly implicated in the occurrence of gastric ulcers, accounting for more than 80% of ulcers.

5. Conclusion

Helicobacter pylori occur at a frequency of 91% in the Brazzaville population. This study also showed that certain epidemiological factors such as the patients' lifestyle, including promiscuity, tap water consumption, and the use of latrines and sanitary facilities were associated with the occurrence of *Hp* infection. Epi-gastric pain, dyspeptic disorders and digestive bleeding were the symptoms experienced by *Hp-infected* patients. Although the mucosa was normal in most cases, the lesions identified were ulcers, gastritis, and ulcerative and frosted lesions. The search for *Hp* should be routine in cases of suspected Hp infection, and improve the management of *Hp-infected* patients.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Neuroendocrine Tumor of Small Intestine, a Diagnostic Challenge

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Abstract

Incidence of neuroendocrine tumors (NET) has significantly increased in the past three decades. In the small intestine, NET are the most frequent tumors, even more frequent than adenocarcinomas. Due to atypical presentations and late symptoms, NET in the small intestine frequently represent a diagnostic challenge. It is important to take these tumors into consideration in differential diagnosis of gastrointestinal neoplasms. Surgeons, oncologists, endocrinologists, and gastroenterologists should understand the disease characteristics and management alternatives. This document aims to review the key points of NET and main diagnostic tools. We present the case of a 50-year-old male who presented lower gastrointestinal bleeding. Imaging and endoscopic studies showed no conclusive findings. A capsule endoscopy showed multiple ulcered lesions with neoplastic aspect in the distal jejune. Due to the multifocal nature of the lesions, clinicians suspected NET-associated digestive bleeding. The patient underwent exploratory laparoscopy with ileectomy and radical abdominal lymphadenectomy. Histopathologic examination confirmed the suspected diagnosis of NET. This case reflects the complexity of diagnostic approach and differential diagnoses for these tumors.

Keywords

Neuroendocrine Tumor, Carcinoid Tumor, Intestinal Cancer, Diagnostic Laparoscopy, Case Report

1. Introduction

Neuroendocrine tumors (NET) are malignant epithelial neoplasms that arise from enterochromaffin cells with neuroendocrine differentiation. These tumors may release vasoactive peptides, such as serotonin, tachykinins, and bradykinins. The NET may present in different body areas, and they were once considered infrequent in the small intestine. In the past 35 years, however, small intestine NET incidence has increased from 300% - 500%, and they now represent 37% of small intestine tumors [1]. Such an increase is probably due to improved detection of new cases thanks to better imaging techniques and a higher frequency of endoscopic procedures [2].

Intestinal neuroendocrine tumors (iNET) may involve the jejunum, ileum, appendix, and proximal colon. Of all iNET, 89% are present in the ileum, commonly 100 cm from the ileocecal valve. Peculiarly, iNET present as multiple tumors in 30% - 56% of cases, and 50% of iNET have metastasis at diagnosis. Despite the more aggressive presentation, patients with metastatic iNET who receive timely surgical treatment have good long-term survival, reaching more than 50% at 5 years [2] [3].

Usually, diagnosis of NET is delayed due to their small size and unspecific symptoms. Manifestations include abdominal pain, gastrointestinal bleeding, and intestinal obstruction, as well as symptoms secondary to metastasis, carcinoid syndrome, or anemia [2] [4]. Variable presentation leads clinicians to initially consider other diagnoses.

Diagnostic aids, such as endoscopy, computed tomography (CT), magnetic resonance image, and capsule endoscopy, are essential in determining the NET location. Locating the tumor may be challenging even with those methods and may require exploratory surgery. Surgery may be curative, and liver metastasis resection may improve survival [5].

2. Case Presentation

A 50-year-old male patient came to the emergency room for consultation due to hematochezia in the previous four days. The melena was accompanied by nonirradiated, 6/10-intensity pain in the right hypochondrium. Systems review did not reveal constitutional symptoms, functional class deterioration, or bowel habit changes. Past medical and social history included overweightness and alcohol consumption every week. Family history included pancreatic cancer in his maternal grand-mother.

General examination showed vital signs within normal ranges, generalized pallor, and dry mouth. Deep palpation of the abdomen revealed pain in the left flank and left hypochondrium, with no masses or signs of peritoneal irritation. Due to lower digestive bleeding, the patient received intravenous hydration and proton-pump inhibitor.

Laboratory tests showed normocytic anemia with hemoglobin at 7.7 mg/dl (normal range: 13.5 - 18 mg/dl), mean corpuscular volume at 87.5 femtoliter (normal range: 79 - 101 ft), and hematocrit at 22.3% (normal range: 42% - 52%). An upper endoscopy revealed a 2-cm hiatal hernia, antral and corporal erythematous gastropathy, as well as urease-positive erythematous duodenitis. A colonoscopy reported abundant digested blood that impeded view of the mucous

layer. An ileocolonoscopy showed no lesions or active bleeding. Given the lack of conclusive findings, a capsule endoscopy was performed. This exam revealed multiple 1 - 1.5-cm large, ulcered masses with neoplastic aspect at the jejunum/ proximal ileum (**Figure 1**). Secondary neoplastic involvement of the thorax was ruled-out. A CT enterography evidenced segmentary thickening of the small intestine walls with no enlarged lymph nodes. A retrograde enteroscopy attempted to obtain a sample for histopathological examination, but it was not possible to reach the lesions. Blood chromogranin level was 240.75 ng/l (reference value: <100 ng/l).

Differential diagnoses of the intestinal masses included NET, lymphoma, gastrointestinal sarcoma, and intestine adenocarcinoma. Due to the gastrointestinal bleeding at presentation, the patient underwent an exploratory laparoscopy. This procedure evidenced multiple nodules in an 80-cm segment of the proximal ileum. All the intestine was then explored with video-assisted manual palpation. It identified approximately 18 whitish lesions involving the serosa. These lesions were 3 - 20 mm in diameter and produced no apparent stenotic effect. The mesentery of the involved segment had multiple visible nodes as large as 2 cm (**Figures 2(a)-(c)**).

Histopathological examination of the surgically removed section revealed grade I, well-differentiated NET. The biggest lesion was 1.2 cm, extending from the muscularis propria to the subserosa, with vascular and perineural invasion. Surgical margins were free of tumoral involvement. The mitotic count showed <2 mitoses per 2 mm².

Of 22 removed nodes, 8 had tumoral involvement. Additional immunohistochemical studies found positive synaptophysin, chromogranin, the cytokeratin monoclonal antibodies AE1/AE3, and the CD56 antigen. There were tumoral cells in the blood vessels with positive D2-40, CD31, and CDX2. The PHH3 showed <2 mitoses per 2 mm² and the Ki67 proliferative index was <3%. With this information, the tumor was classified as a well-differentiated, stage III, jejunal NET, pT3N1M0.



Figure 1. Capsule endoscopy imaging shows masses in jejunum/proximal ileum.



(a)



(b)

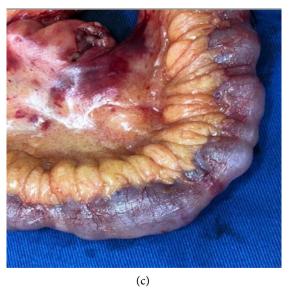


Figure 2. (a) Small intestine specimen; (b) Nodularity in small intestine; (c) Enlarged nodes in the mesentery root.

In the post-operative period, the patient had modulated pain with no emesis or respiratory distress. He progressively tolerated oral diet and, on the sixth post-operative day, was discharged from the hospital. At a 6-month follow-up, the patient had continued with adequate evolution.

3. Discussion

It appears that tumors in the small intestine present more frequently in association with 1) Genetic diseases, such as the familial adenomatous polyposis, and Peutz-Jeghers syndrome. 2) Intestinal inflammatory diseases, such as Crohn's disease and celiac disease. Primary tumors of the small intestine, such as adenocarcinomas, NET, leiomyosarcomas, and lymphomas may have an insidious presentation. Unspecific manifestations may include intestinal obstruction, jaundice, bleeding, or abdominal pain when they achieve local infiltration [6].

According to 2019 statistics of the United States National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) Program [7], less than 5% of gastrointestinal cancers are in the small intestine. Cancers of the small intestine are primarily small bowel adenocarcinoma accounting for 40% of cases and NET which account for another 40%. The remaining 20% is attributed to stromal tumors, sarcomas, and lymphomas [8]. Most of the NETs are in the gastrointestinal (GI) system (55%) or in the bronchopulmonary system (25%). In the GI tract the most common site is the small intestine (45%), rectum (20%), appendix (16%), colon (11%), and stomach (7%) [9]. These tumors can secrete a variety of hormones including serotonin, somatostatin, gastrin and substance P, also Carcinoid tumors exhibit immunoreactivity to chromogranin A [6] [10].

There are several nomenclatures and staging systems for NET, depending on the involved area. No system is standardized in the scientific community. The European Neuroendocrine Tumor Society (ENETS) recommends the World Health Organization (WHO) classification system. The North American Neuroendocrine Tumor Society (NANETS) proposes the American Joint Committee on Cancer (AJCC) staging system, adding basic pathological elements. These include proliferation rate, extension, and immunohistochemical markers [11]. **Table 1** and **Table 2** present NET nomenclature systems.

 Table 1. Gastroenteropancreatic NET nomenclature system.

Grade	ENETS, 2010	WHO, 2010
Low grade	Grade 1 NET (G1)	G1 Neuroendocrine neoplasm
Intermediate grade	Grade 2 NET (G2)	G2 Neuroendocrine neoplasm
High grade	Grade 3 neuroendocrine carcinoma (G3), small-cell carcinoma Grade 3 neuroendocrine carcinoma (G3), neuroendocrine large-cell carcinoma	Grade 3 neuroendocrine carcinoma, small-cell carcinoma Grade 3 neuroendocrine carcinoma, neuroendocrine large-cell carcinoma

Kulke, M. H., Anthony, L. B., Bushnell, D. L., et al. & North American Neuroendocrine Tumor Society (NANETS), 2010 [13].

Stage	Description		
Primary tumo	70		
TX	Not classifiable.		
Т0	No evidence of primary tumor.		
T1	Tumor invades lamina propria or submucosa and tumor size ≤ 1 cm.		
T2	Tumor invades muscularis propria or tumor size > 1 cm.		
T3	Tumor invades muscularis propria and subserosa, no invasion of serosa		
T4	Tumor invades visceral peritoneum (serosa) or invades other organs.		
Lymph node	S		
NX	Regional lymph node involvement cannot be assessed.		
N0	No regional lymph node involvement.		
N1	Regional lymph node involvement <12 nodes.		
N2	Large mesenteric tumor (>2 cm) and/or \ge 12 nodal deposits (especially		
	those encasing the superior mesenteric vessels).		
Metastasis			
M0	No distant metastasis.		
M1	Distant metastasis.		
M1a	Metastasis confined to liver.		
M1b	Metastasis in at least one extrahepatic site.		
M1c	Hepatic and extrahepatic metastases.		
Stage			
Ι	T1, N0, M0.		
II	T2/T3, N0, M0.		
III	T4, N0, M0.		
	Any T, N1/N2, M0.		
IV	Any T, any N, M1.		
Tm	Multiple tumors.		

Table 2. Small intestine NET staging AJCC 2018.

Amin MB, Edge SB, Greene F, et al. (2017) AJCC Cancer Staging Manual (ed 8). New York, NY: Springer.

The iNET frequently arise in the distal ileum, less than 80 cm from the ileocecal valve. The majority of these are carcinoids of serotonin-producing enterochromaffin cells [12].

By the former ENETS classification, the clinical case presented in this paper was a low-grade, well-differentiated iNET. This type of NET may release hormones, such as serotonin, gastrin, and P-substance, as well as serum markers [12].

Chromogranin A (CgA) is present in endocrine, neuroendocrine, and immune cells. The CgA may be segmented in biologically active peptides, such as vasostatin and pancreastatin. Because of its sensitivity, the CgA is the most-used marker for NETs and is suitable for NET diagnosis and follow-up. A study published in Frontiers in Oncology retrospectively reviewed CgA levels in patients with grade 1 and grade 2 NET. The study showed that CgA levels had a diagnostic sensitivity of 73% for secreting tumors and 45% for non-secreting tumors (p < 0.004). The cutoff value in that study was 130 ng/ml [13]. The patient in this clinical case presented elevated chromogranin.

As with this clinical case, 60% of NET do not present clinical manifestations. Conversely, as many as 21% of well-differentiated (G1) and 30% of moderately differentiated NET debut with metastasis and unknown primary location [14]. Like in this clinical case, where 18 lesions were macroscopically identified, multiple tumors present in 15.6% of cases of stage I-IIIA NET [15].

Imaging studies for iNET detection are anatomical and functional. Anatomical studies include CT scan which is useful for staging and operative planning. The sensitivity ranges from 7% to 38% but can be improved to 82% if there are mesenteric lymphadenopathy//fibrosis as evidence of small bowel primary tumor. CT enteroclysis has better sensitivity: 50% - 85% [16]. Abdominal CT may show mesenteric tumors with attachments to the bowel, lymphadenopathies, and liver metastases. The masses, however, may not be visible due to their extraluminal location. Occasionally, these anatomical imaging techniques provide little preoperative visualization. Such was the situation in the present clinical case.

Functional studies include ⁶⁸Ga-DOTATATE PET/CT scanning. The radiomarked somatostatin analogue is useful to identify the primary tumor. It is also valuable to detect metastases, mainly hepatic, that may be treated with somatostatin analogues, interventionist radiology, or surgery. Also, this scan has 92% sensitivity and 83% specificity for diagnosis of metastatic node disease [17]. This exam is very effective for identification of well-differentiated, less aggressive NET, due to higher cell-membrane expression of somatostatin receptors (SSTRs) by these tumors. Conversely, FDG PET/CT scan is best for poorly differentiated, more aggressive tumors, with worse prognosis and lower marker intake [18].

Surgery with curative or palliative intention is recommended as the first line of treatment for iNET. Results may be better with a laparotomy, since it allows exploration of all the small intestine by palpation, and it also guarantees appropriate node resection. This clinical case combined that approach with video-assistance, allowing proper exploration and tumor resection [4].

Surgery principles include 1) Complete resection of the primary tumor. Bidigital palpation is necessary to assess all the small intestine, given the high incidence of multifocal tumors. 2) Radical lymphadenectomy of mesenteric nodes. A minimum of 7 nodes includes those in group 1 (peri-intestinal nodes), group 2 (mesenteric nodes), and group 3 (mesenteric root nodes). 3) In case of metastatic liver disease, metastasis resection may be considered [4] [19].

Favorable oncological results in patients with NET depend on tumor location, extent of local/metastatic disease, tumor functional status, and viability of complete tumor resection [20]. Clinicians should recognize the particular manifestations of NET. Timely diagnosis and treatment prevent complications and improve the patient's quality of life.

The case in this paper posed a challenge for the treating medical team. The patient's symptoms were unspecific, and the tumor was hardly visible in routine imaging. Also, obtaining a sample for histopathological examination was not

possible on the first attempt. This case underscores the importance of surgical exploration for iNET diagnosis.

4. Conclusion

This clinical case highlights challenges in the diagnostic approach for iNET. This paper reminds healthcare professionals to more consciously consider this condition among differential diagnoses of small intestine tumors. In case of suspected NET of the small intestine, a diagnostic algorithm should include imaging and endoscopic studies aiming to define the lesions' locations and characteristics. Finally, surgical excision employing oncologic principles followed by a histopathological examination of the surgical specimen is paramount for accurate diagnosis and specific management.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Esophagogastric Reconstruction in Cobra-Head Shape with Toupet-Like Partial Anti-Reflux Technique for Resection of Proximal Gastric Tumors. Experience with Three Cases from a Non-Asian Population

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Abstract

Background: Proximal gastrectomy is a rarely performed procedure but a feasible option in benign tumors and malignant neoplasms in the proximal third of the stomach since novel options of reconstructions are available nowadays with fewer long-term sequels. Methods: Report of three cases of proximal gastric gastrointestinal stromal tumors (GIST), with a description of its presentation, histological characteristics, and follow-up after being treated with proximal gastrectomy with cobra head reconstruction. Results: Case 1: A 62-year-old woman with epigastric pain of four months with endoscopic evidence of a cardia GIST. The surgery was performed without complications. The histopathological report confirmed a fusiform GIST of $3.2 \times 3 \times 2.5$ cm, stage IA. No adjuvant treatment was considered. An esophagogram showed no evidence of reflux and no stenosis, and no disease recurrence after 40-months follow-up. Case 2: A 66-year-old woman with dyspepsia and a palpable tumor in the epigastrium. The surgery was performed without complications. The pathology report confirmed a proximal gastric GIST of $13 \times 8 \times 7$ cm, staged II. She received adjuvant treatment with imatinib for 36 months without recurrence and no reflux or stenosis. Case 3: A 55-year-old woman with intermittent hematemesis and right subscapular pain. The surgery was performed without complications. The histopathological report concluded that a

GIST tumor of the cardia, 1.4×1.2 cm, staged IA. She was left in observation. At a 6-month follow-up, she does not report dysphagia, reflux, or stenosis, and no locoregional recurrence. **Conclusions:** Open and laparoscopic proximal gastrectomy is a safe therapeutic option for GIST. Furthermore, the reconstruction of the esophagus-gastro anastomosis in the cobra head after proximal gastrectomy is feasible and secure in our population, with good functional results in a short follow-up.

Keywords

GIST, Gastric Cancer, Laparoscopy, Proximal Gastrectomy, Cobra Head Reconstruction

1. Introduction

The stomach has several regions where different tumors can grow, from adenocarcinoma, the most frequent (95%), to lymphomas or gastrointestinal stromal tumors (GIST) [1] [2]. Tumors in the esophagogastric junction, cardia, and fundus are considered proximal [3]. The increase in obesity rates worldwide predisposes to more significant reflux disease associated with an increased incidence of proximal gastric adenocarcinoma [4]. When tumors present at an early stage, conservative surgery is an option to preserve as much of the stomach as possible without neglecting the oncological principles (respecting surgical margins and a correct lymph node dissection) [5]. It also adds the benefit of improving the quality of life since these patients maintain the digestive and endocrine function of the stomach; however, this type of early-stage patient is rare in our environment, and gastric preservation is not indicated [6] [7]. Despite this, other less frequent tumors with more favorable tumor biology are ideal candidates to try to preserve the most significant amount of gastric tissue, for example, GIST or leiomyomas [8] [9].

Proximal gastrectomy is a frequent procedure in Japan and Korea due to the high incidence of early gastric cancer. There are several reconstruction techniques to reduce pathological acid or bile reflux since several physiological anti-reflux mechanisms are eliminated after a proximal gastrectomy [10] [11]. However, they are complex techniques, such as the "Kamikawa" reconstruction, that increase the surgical time and the risk of late stenosis [12] [13]. That is the reason a Japanese group, in 2016, described a minimally invasive technique to create a gastric tube 3 cm wide by 20 cm long with a cobra head termination to fix the esophagus to the gastric tube as a partial anti-reflux procedure. As a result, from their 13 patients with early proximal gastric cancer (T1N0M0) without esophageal invasion, there was no leak or stenosis of the anastomosis and no intra-abdominal collections. Furthermore, at 1-year follow-up, only three patients presented reflux esophagitis (Los Angeles Classification grade B and C) with adequate pharmacological control [14].

This novel technique has good preliminary results (in open and minimally invasive approaches) since creating a thin gastric tube reduces the area to produce acid. Also, adding a partial anti-reflux procedure such as a Toupet-Type, minimizes the risk of reflux, the main complication in patients undergoing proximal gastrectomy. In addition, linear anastomosis decreases the stenosis rate in short- and long-term follow-up [15] [16]. Another important matter nowa-days is evaluating the quality of life after oncological procedures since life expectancy has increased with the improvement of surgical and systemic treatments [17]. Some studies have reported less post-gastrectomy syndrome with proximal gastrectomy, resulting in enhancing wellbeing [18].

In this article, we used this type of reconstruction in 3 patients with proximal GIST tumors who underwent proximal gastrectomy by combined open and laparoscopic approach.

2. Surgical Technique

Proximal gastrectomy follows the oncological principles of the Japanese school to treat proximal gastric tumors. The stomach is released at the greater curvature by cutting the greater omentum 3 to 4 cm below the right gastroepiploic artery, which is preserved, but the left gastroepiploic artery is cut. In the lesser curvature, we preserve the right gastric artery, and the posterior gastric surface is dissected from the pylorus to the esophagus, including the section of the posterior gastric, left gastric, and short gastric vessels. The phreno-esophageal membrane is opened to release the esophagus at least 5 cm, and the vagus nerves must be sectioned for a better release. Measuring two to three centimeters of the distal esophagus proximal margin, it is cut with a 60 mm linear stapler.

The distal cut of the stomach is performed by designing a thin gastric tube 3 centimeters wide with a length of 20 centimeters on the greater curvature and 5 cm on the lesser curvature from the pylorus using a linear stapler to intermediate tissue thickness of 45 or 60 mm and the proximal part of the gastric tube should have a 6 centimeters wide base that will simulate the cobra head. In minimally invasive surgery, we perform the gastric tube by extracorporeal approach (Figure 1). Subsequently, for the esophagogastric anastomosis, an enterotomy will be performed in the middle third on the staple line of the esophagus, another on the anterior gastric face in the 6 cm area closer to the greater curvature to introduce 45 mm linear stapler, performing the anastomosis between the posterior surface of the esophagus with the anterior surface of the stomach. The closure of the enterotomy will be with a continuous surge using a barbed suture (3-0 monofilament) from the left staple line to the right staple line. Finally, individual stitches will be placed with a 3-0 monofilament suture to invaginate or fix the esophagus with the anterior surface of the stomach, simulating a Toupettype partial fundoplication (Figure 2). This reconstruction is possible by minimally invasive surgery where we performed the reconstruction tube using a 5 cm subxiphoid incision and finally intracorporeal lineal anastomosis plus Toupet-type partial fundoplication (Figure 3).

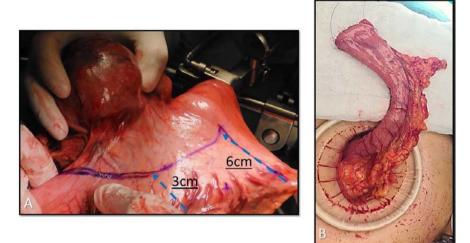
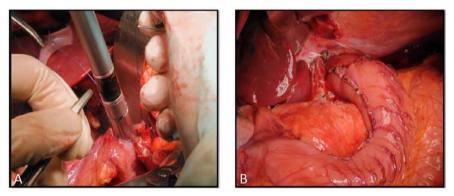
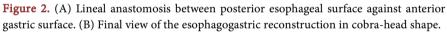


Figure 1. Performing gastric tube cobra-head. (A) Showing the 6 and 3 cm width of the gastric tube (B) Extracorporeal approach in minimally invasive surgery.





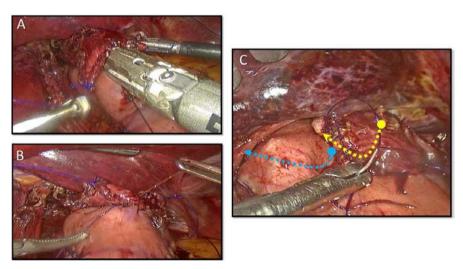


Figure 3. Minimally invasive reconstruction. (A) Intracorporeal lineal anastomosis. (B) The closure of the enterotomy with a continuous barbed suture. (C) Showing the Toupet-type partial fundoplication using individual stitches where invaginate the esophagus with the anterior surface of the stomach.

3. Case Presentation

3.1. Case 1

A 62-year-old woman with a history of laparoscopic cholecystectomy eight years ago began with abdominal distension and epigastric pain over four months of evolution. The endoscopy showed a submucous gastric lesion. The endoscopic ultrasound (EUS) showed a 3 cm calcified lesion in the upper third of the lesser gastric curvature dependent on the muscularis propria layer. A fine needle aspiration biopsy was performed, reporting a GIST (Figure 4). Contrast-enhanced tomography of the chest/abdomen ruled out regional and distant metastatic disease. A proximal gastrectomy was performed by laparoscopic approach with conversion to open surgery to achieve the esophageal-gastro anastomosis reconstruction in the cobra head with a partial anti-reflux procedure. There were no postoperative complications, and she was discharged on the tenth postoperative day. The histopathology report confirmed fusiform GIST of $3.2 \times 3 \times 2.5$ cm, with one mitosis/50 fields and 19 negative nodes, negative margins, and the staging was pT2 pN0 M0. The patient was placed in a low-risk group and was left under surveillance. An esophagogram showed no evidence of reflux and no stenosis. The disease-free period (PLE) was 40 months, and she only reported mild symptoms of reflux controlled with medical treatment (omeprazole) and nutritional changes for the first six months.

3.2. Case 2

A 66-year-old woman presented with dyspepsia after three years of evolution. She had a previous history of a low-grade papillary urothelial carcinoma of the bladder diagnosed a year earlier and treated by transurethral bladder resection (TURB) and intravesical BCG application. In the last three months, she increased

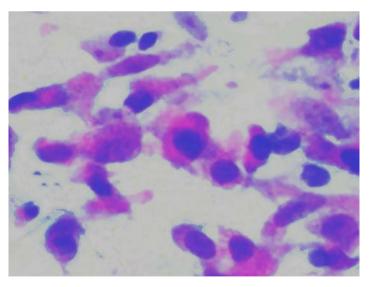


Figure 4. Fine needle aspiration biopsy of proximal gastric GIST. The image shows spindle cells without atypia in a fibrous matrix in the background: Hematoxylin and eosin, 200×.

postprandial fullness and progressive palpation of a solid tumor in the epigastrium, slightly mobile at 10 cm in size. A endoscopy and EUS confirmed a heterogeneous tumor, with a hypoechoic center in the gastric fundus with involvement of the lesser curvature, size 8×6 cm, which depended on the muscle layer. A CT scan confirmed a calcified tumor of $11 \times 8.8 \times 6$ cm, suspicious for gastric GIST in lesser curvature, between the proximal and middle thirds that contacted the left hepatic lobe (**Figure 5**). A proximal gastrectomy was performed by laparotomy and reconstruction of the esophagus-gastro anastomosis in the cobra's head. No postoperative complications were reported during the eight days of hospitalization. The pathology report confirmed spindle cell GIST, with three mitoses/50 fields, size $13 \times 8 \times 7$ cm, four lymph nodes negative, and negative margins with intermediate risk staging (pT4 pN0 M0) (**Figure 6**). She received adjuvant treatment with oral imatinib 400 mg to complete three years and no recurrence at 37 months of follow-up and not presenting reflux or stenosis.

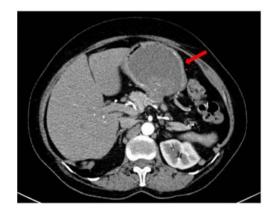


Figure 5. Abdominal CT scan demonstrating a proximal gastric calcified tumor of $110 \times 88 \times 60$ mm, suspicious for gastric GIST at the lesser curvature in contact with the left hepatic lobe.

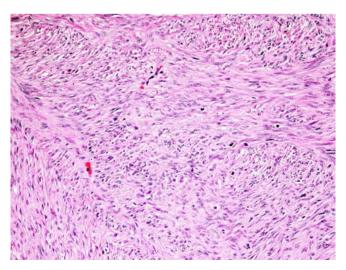


Figure 6. Photomicrography of gastric GIST showing a low-grade spindle-cell neoplasm composed of cells in short fascicles and whorls; the cells have pale eosinophilic fibrillary cytoplasm, ovoid nuclei, and ill-defined cell borders: Hematoxylin and eosin, 100×.

3.3. Case 3

A 55-year-old woman with a history of two cesarean sections and an open appendectomy began five months previously with intermittent hematemesis and two weekly episodes of right subscapular pain without improvement with pump inhibitor plus intermittent dysphagia to solid foods. The endoscopy observed a 2-cm subepithelial tumor in the cardia. It was complemented with EUS confirming a subepithelial tumor in the cardia of 1.5×1 cm, hypoechoic, lobulated, and defined borders, with 50% partial obstruction and positive biopsy for low-grade GIST. An abdominal CT scan reported a 1.4×1.1 cm nodular tumor in the cardia, with no tumor activity elsewhere. Laparoscopic proximal gastrectomy was performed with reconstruction by esophagogastric anastomosis in the cobra head with an anti-reflux procedure. The patient did not develop postoperative complications and was discharged on the seventh day. The histopathological report concluded a GIST tumor of the cardia of 1.4×1.2 cm, without mitosis/5 mm², or necrosis, unifocal, negative margins, and three negative pericardial nodes with a pathological stage IA (pT1 pN0 M0). Therefore, it was classified as low risk remaining under surveillance. In the first month after surgery, she reported mild dysphagia to solids that improved with changes in diet and prokinetic medication. At a three-month follow-up, she did not report dysphagia, reflux, or stenosis.

4. Discussion

The best surgical experience in proximal gastrectomy for the cardia or gastric fundus tumors is in Japan and Korea, where the incidence of early gastric adenocarcinoma is high and does not require a D2 lymph node dissection [19]. This type of resection can apply to tumors with better oncological prognosis due to less aggressive behavior and minimum capacity for lymph node invasion, such as GIST or well-differentiated neuroendocrine tumors [20] [21]. The optimal surgical management of gastric GIST includes a complete surgical resection with negative margins and it is not necessary a lymph node dissection for small tumors (less than 5 cm) because <2% are metastatic to regional lymph nodes [22] [23].

Among the benefits observed with these limited gastric resections is the possibility of preserving a functional gastric remnant with an adequate excretory and reserve function by preserving the pyloric innervation of the celiac hepatic and vagal branches after limiting the extent of the gastric resection and lymph nodes at the level of the pylorus [24]. Clinically, it translates into less long-term weight loss, with lower rates of protein-calorie malnutrition [25] [26].

Concerning the type of reconstruction of the gastroesophageal anastomosis, this novel technique involves only one anastomosis, which reduces the risk of anastomosis leakage compared to other reconstruction techniques, such as Roux-en-Y [27]. In addition, the reconstruction of the proximal portion of the gastric tube has an amplitude twice that of the distal portion (6 cm vs. 3 cm),

reducing the incidence of stenosis of the anastomosis.

The significant morbidity in proximal gastrectomy is related to the possibility of gastroesophageal reflux in the short and long term, which leads to esophagitis [28]. This problem occurs after removing the angle of His and the lower esophageal sphincter as anti-reflux mechanisms [29] [30]. This problem was addressed by the original Japanese surgical team by adding a partial anti-reflux fundoplication with the cephalic surface in gastric reconstruction. The initial report of this technique was published in 2016; however, in 2021, the same group reported an update and extension of the laparoscopic technique, including some selected locally advanced cases of gastric adenocarcinoma. In this study, it was compared with the reconstruction of the conventional esophagogastric anastomosis with a circular stapler; the results showed the same rate of postoperative complications (11% vs. 10%), with no anastomosis leak and stenosis in both groups. Furthermore, esophagitis occurs less than circular anastomosis (10% vs 33%) [14] [31]. We reproduced this technique in three patients with proximal GIST gastric tumors. Early results in the follow-up have shown specific morbidities with this new surgical reconstruction. One patient reported esophagogastric reflux in the first six months that remitted after dietary modifications and proton pump inhibitor plus prokinetic without evidence of esophagitis in the annual endoscopic control. Furthermore, a second patient presented self-limited dysphagia to solids but we did not have evidence of stenosis and only we did some changes in the type and frequency of the diet.

Regarding the oncological safety of the cobra head reconstruction technique, in Asian cases of gastric carcinoma, it has shown similar long-term rates in locoregional recurrence of up to 7%, without a statistically significant difference, even for patients with locally advanced stages [31]. In our three cases treated with this technique, after a median follow-up of 26 months (2 - 40 months), no patient has shown locoregional or distant recurrence, even in the patient with the high-risk GIST that was receiving adjuvant therapy with Imatinib. Therefore, we are confirming the safety of this procedure from the oncological point of view for proximal gastrointestinal stromal tumors localized in the stomach.

One limitation of this case report is that we only have performed this surgical technique in GIST histopathology because these tumors have less aggressive biological behavior, and in our center, most of the gastric adenocarcinomas are locally advanced, with diffuse histology and require a total gastrectomy with D2 lymph-node dissection.

5. Conclusion

Open and laparoscopic proximal gastrectomy is a safe therapeutic option from the oncological point of view for gastrointestinal stromal tumors and early gastric cancer. Furthermore, to our knowledge, we are the first oncology group replicating in Latin America the reconstruction of the esophagus-gastro anastomosis in cobra head after proximal gastrectomy in gastric GIST tumors, with shortand medium-term functional and quality-of-life results similar to those of the Japanese population, which has shown a lower incidence of gastroesophageal reflux and postoperative esophagitis in longer follow-up in a large population included.

Declaration of Authorship

All authors meet the criteria for authorship as per the guidelines of the International Committee of Medical Journal Editors (ICMJE); all have participated at 1) the Conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND 2) Drafting the work or revising it critically for important intellectual content; AND 3) Final approval of the version submitted; AND 4) Agreement to be accountable for all aspects of the work regarding the accuracy or integrity of the research.

Acknowledgment of Patient Consent

The authors confirm that the patients involved in this publication have given their consent for the information presented in the Case reports to be published.

Conflicts of Interest

The authors declare no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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Patient Experience at Endoscopy Centers in Three West African Countries during the COVID-19 Pandemic

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Abstract

Corona virus infection and the risk of contagiousness to medical personnel or patients during endoscopy necessitated further measures in the endoscopy rooms. The objective of this study was to assess the experience of patients in endoscopy rooms during the COVID-19 epidemic in West Africa. Patients and Methods: This was a multicenter cross-sectional study that took place over a period of 3 months (June to August 2020) in endoscopy centers in Burkina Faso, Benin and Niger. An online questionnaire was sent to patients who had performed upper digestive endoscopies, in 8 digestive endoscopy centers including private, public and religious structures. Depending on the choice of patients, questionnaires were either sent electronically or completed in the endoscopy room with the help of field investigators. The choice of centers was random from the list of centers and descriptive analyses were carried out. Results: A total of 294 patients responded to the online questionnaire. There were 37 lower and 257 upper gastrointestinal endoscopies. The female sex represented 52.1%. The wait times for obtaining an endoscopy appointment were considered satisfactory by 281 patients 95.6%. In the endoscopy departments, 112 patients, or 38.1%, were questioned about the risk factors for contamination of SARS-CoV-2. Among the risk factors found, 6 patients (2.0%) would have traveled abroad in the 2 weeks preceding the examination, 4 patients 1.4% had already been in contact with a subject at risk. The most frequent symptoms were chest pain (80 cases; 27.2%), flu-like syndrome (29 cases; 9.9%), cough (40 cases; 13.6%), fever (46 cases; 15.6%). In contrast, ageusia (7 cases; 2.4%) and anosmia (5 cases; 1.7%) were only found in very few patients. Twenty-two patients (7.5%) felt highly exposed to COVID-19 during the endoscopy examination and 144 patients (48.9%) rated the examination as satisfactory. **Conclusion:** Gastrointestinal symptoms initially described as rare are being reported with increasing frequency in studies and may motivate the request for endoscopy examinations. However, the risk associated with infection with SARS-CoV-2 does not seem to have been sufficiently taken into account in endoscopy centers in the 3 countries.

Keywords

Endoscopy, COVID-19, Patients, Exposure, Symptoms

1. Introduction

In December 2019, the outbreak of several cases of pneumonia of unknown origin in Hubei province in China led to the identification in January 2020 of a new coronavirus [1], named SARS-CoV-2 by the Coronavirus Working Group of the International Committee on Taxonomy of Viruses [2]. SARS-CoV-2 causes sometimes a severe respiratory disease, named "COVID-19" by the World Health Organisation (WHO). After Asia, Europe, the United States and Iran are the most affected regions of the world [3].

COVID-19 is rapidly creating great concern in African countries [4] where health systems are not sufficiently prepared to deal with health crises [5]. The exposure of health workers to infection in the context of the COVID-19 epidemic has been discussed in several studies. Indeed, the Center for Disease Control and Prevention in China (CDC-China) confirmed in a report that less than two months after the outbreak of COVID-19, a total of 1716 health care workers had been infected with the virus, and five of them had died [6].

Burkina Faso recorded its first case on 09 March 2020 [7] and as of 02 January 2021 the number of cases was still increasing with 7126 confirmed cases including 86 deaths [8]. The outbreak of COVID-19 and the risk of contagiousness of medical staff or patients during endoscopy required new measures in endoscopy rooms. As health workers are in the front line of the fight against the epidemic and are highly exposed, they themselves can become a source of COVID-19 contamination for the population if not properly protected. The highly contagious COVID-19 is transmitted from person to person, mainly by direct contact or by droplets spread by coughing or sneezing from an infected person [9]. Although this risk of contagiousness was considered low in Europe, it was important to better understand the realities in West Africa. The aim of this study was to assess the experience of patients in endoscopy rooms in three West African countries during the COVID-19 epidemic.

2. Patients and Methods

This was a multicenter cross-sectional study that took place over a 3-month period (June to August 2020) in endoscopy centers in Burkina, Benin and Niger. An online questionnaire was either sent electronically to the patients at the end of the endoscopic examination or filled in the endoscopy room with the help of field investigators. The study took place in 8 digestive endoscopy centers including private, public and faith-based facilities. During the study period all patients received in health centers during the period were surveyed after giving their informed consent. The data studied concerned sociodemographic and clinical variables, risk factors for COVID-19 infection, indications for endoscopy examination, difficulties in having an appointment at this time, the existence of a triage center in the structure, means of protection, barrier measures used in the health structure, the feeling of exposure to COVID-19 and the suggestions made by patients. The perception of risk (level of exposure) of the respondents was explored and each response was scored from 0 (low) to 10 (high) for the level of exposure during the examination. The maximum score that patients could obtain was 10, the minimum was 0. For the level of exposure: people with a score of 0 to 3 were classified as having low exposure, a score of 4 to 6 moderately exposed and a score of 7 to 10 highly exposed. Descriptive analyses were conducted using SPSS software.

3. Results

In total, 294 patients responded to the online questionnaire. The maximum number of patients was found in Burkina Faso with 106 respondents or 36% of cases (Figure 1).

There were 37 lower and 257 upper gastro-intestinal endoscopies. The average age of the patients was 41 years with extremes of 11 and 76 years. Females represented 52.1%.

In Niger and Burkina Faso we found a male predominance with 49 patients (51.6%) and 54 patients (50.9%) while in Benin, woman were more represented with 48 patients (51.6%). The patients came from religious structures 147 (50%), public 101 (34.4%) and private 46 (14.6%) (Figure 2).

For all three countries, the waiting time for an endoscopy appointment was considered satisfactory by 281 patients (95.6%). They were fairly short, *i.e.* within 48 hours for 111 patients (37.7%) and within 72 hours for 70 patients (23.8%). In Niger 89 patients (93.7%) were satisfied with the time taken to obtain an appointment, in Benin 88 or 94.6% and in Burkina Faso 104 or 98.1%.

One hundred and eight patients (108), or 36.7%, stated that there was no sorting center in the health facilities before they went to the endoscopy departments for their examination and 143 patients, or 48.6%, had not used the sorting

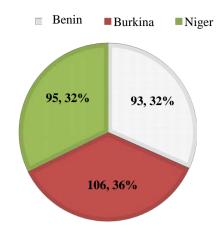


Figure 1. Breakdown of patients by country.

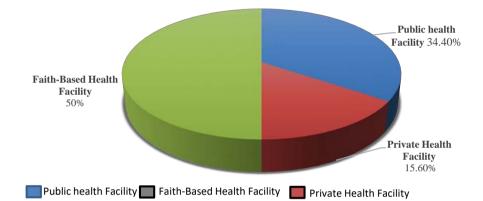


Figure 2. Distribution of patients by type of health facility.

center when it existed. Only 23 patients in Burkina Faso (21.7%) had used the screening center, while in Niger and Benin no patient had done so.

In the three countries, very few patients were questioned during endoscopy about risk factors for SARS-CoV-2 infection, with 27 patients (25.5%) in Burkina Faso, 75 patients (80.6%) in Benin and 10 patients (10.5%) in Niger.

Among the risk factors found in the three countries, 6 patients (2.0%) had travelled abroad in the 2 weeks preceding the examination, 4 patients (1.4%) had already been in contact with a subject at risk.

In all three countries, when asked about clinical signs that might be suspicious for COVID-19, 67 patients (22.8%) reported having none of the symptoms. The most frequent symptoms were chest pain (80 cases; 27.2%), flu-like syndrome (29 cases; 9.9%), cough (40 cases; 13.6%), fever (46 cases; 15.6%). On the other hand, ageusia (7 cases; 2.4%) and anosmia (5 cases; 1.7%) were found in very few patients.

The indications for examination were dominated by digestive signs with abdominal pain in all three countries (156 patients; 53.1%). Only in Benin were other signs such as chest pain found in 15 patients (16.1%).

Regarding the digestive signs encountered by patients in the three countries, abdominal pain (162 patients; 55.1%) and nausea (48 patients; 16.3%) were the

two most common signs.

In Niger and Burkina, respectively 31 patients (32.6%) and 70 patients (66%) were afraid of the endoscopy but the reasons given were all related to the endoscopic procedure and not to the risk of COVID-19 infection. In Benin 34 patients (36.5%) who were afraid of the examination, only 8 patients reported a link with the COVID-19 infection

A total of 56 patients (19.1%) in the three countries felt highly exposed to COVID-19 at the end of the endoscopy examination. In Niger 7 patients (7.4%), in Benin 13 patients (14%) and in Burkina Faso 36 patients (34%). Table 1 summarises the exposure levels of the patients.

For the suggestions that could improve management in the three countries, 133 patients gave their opinion, and the emphasis was mainly on compliance with barrier measures and awareness rising for 26.10% and 11.53% of patients respectively.

4. Discussion

A total of 294 patients responded to the questionnaire. We believe that the low number of patients could be explained on the one hand, by the fact that online surveys generally have a lower participation rate than face-to-face surveys [10] and on the other hand by the fact that the COVID-19 crisis led to a significant drop in the use of health services in several countries of the world due to the fear of infection [11]. Indeed, according to a global survey conducted by WHO, 90% of countries have suffered disruptions to their essential health services since the start of the COVID-19 pandemic [11].

Thirty-seven lower and two hundred and fifty seven upper gastro-intestinal endoscopies have been achieved. In general, in endoscopy centers, lower endoscopies are less frequent than upper endoscopies, partly due to the much greater difficulty in performing lower gastro-intestinal endoscopies (Much longer examination time and need for prior colonic preparation).

The average age of the patients was 41 years with extremes of 11 and 76 years. The young age of our population can also be explained by the fact that the elderly had been identified as being at high risk of death in the event of infection, and

COVID-19 exposure levels	Frequence	Pourcentage
1 - <3	109	37.1%
3 - <5	47	15.9%
5 - <7	82	27.9%
7 - <9	34	11.6%
9 - <10	10	3.4%
>10	12	4.1%
TOTAL	294	100.00%

Table 1. COVID-19 exposure levels during the examination.

it was only in emergencies that they went to the health centers at that time. In Niger we found a male predominance with 49 patients (51.04%) while in Benin and Burkina Faso women were the most represented with respectively 48 patients (51.61%) and 52 patients (55.91%). The predominance of females in our study population is also reported by other African authors [12] [13] [14] and may be related to the high level of attention women pay to their health status. On the other hand, in a hospitalized SARS-CoV-2 infected population, there was a clear male predominance (63.7%) in univariate analysis in the study by Wu *et al.* and 58.1% and 62% in the studies by Guan *et al.* and Zhou *et al.* respectively [15] [16] [17]. This difference is possibly explained by the higher frequency of risk factors for disease severity in the male population.

The patients came from religious facilities 147 (50%), public facilities 101 (34.3%) and private facilities 46 (14.6%). Our sample is fairly representative of the different types of facilities existing in our working context.

Regarding the delays in obtaining appointments for examination, the availability of hepato-gastroenterologists in our study allowed more than half of the patients to undergo digestive endoscopy within a short waiting period (less than 72 hours). We believe that this can be considered as a near-normal continuation of activity in the three countries given the good level of patient satisfaction. In Niger 89 patients (92.71%) were satisfied with the time taken to obtain an appointment, in Benin 88 patients (94.62%) and in Burkina Faso 104 patients (98.11%).

One hundred and eight patients (39.2%) stated that there was no sorting center in the health facilities before they went to the endoscopy departments for their examination and 143 patients (52%) had not used the sorting center when it existed. Only 23 patients in Burkina Faso (21.7%) had used the screening center, while in Niger and Benin no patient had used it.

The absence of triage centers in health facilities remains a major shortcoming given the existing risk of infection with COVID-19. Despite the fact that COVID-19 has rapidly created great concern in African countries [4], very little concrete action has been observed on the ground. The health systems in our countries were not prepared to deal with this health crisis [5]. This should challenge us to prepare ourselves in order to be able to better respond to other possible health crises.

However, exposure of health care workers to infection during the COVID-19 epidemic has been reported in the literature, according to CDC-China, less than two months after the outbreak of COVID-19, a lot of health care workers had been infected with the virus

Health care workers are on the front line in the management of the COVID-19 epidemic. Through case surveillance and patient care, they are exposed to the risk of contagion on a daily basis. In case of infection, they can become potential transmitters of the virus. They therefore play an essential role in the implementation of adequate infection prevention and control measures in health care facilities [5]. But in all the three countries of our study, very few patients were

asked during endoscopy about risk factors for SARS-CoV-2 infection. In African countries, 40% of healthcare workers are infected with the SARS-CoV-2 virus. In comparison, the infection rate of healthcare workers in Europe is 20% in the most affected countries [6]. Although this risk of contagiousness was judged to be low during endoscopy in Europe, we believe that precautions are still necessary as this infection has not yet revealed all its secrets.

Among the risk factors found, 6 patients (2.0%) had travelled abroad in the 2 weeks preceding the examination, 4 patients (1.4%) had already been in contact with a subject at risk. The awareness of the population at the beginning of the COVID-19 pandemic about the risk of contamination by travelling to certain destinations and the closure of borders have considerably reduced the mobility of the population in our regions. The majority of patients (98.7%) had any contact with a person at risk in the 15 days preceding the examination. This result could be explained by the lack of knowledge of people at risk (sometimes asymptomatic disease), or by the fear of being exposed to stigma and isolation. Indeed, these figures may be underestimated because some patients may hide this information for fear that it will be an obstacle to obtaining care. The psychosis associated with COVID-19 infection at this time could justify such attitudes.

In all three countries, the most common suspected symptoms of COVID-19 were chest pain (80 cases; 27.2%), flu-like illness (29 cases; 9.9%), cough (40 cases; 13.6%), and fever (46 cases; 15.6%). In the three studies by Wu *et al.*, Guan *et al.* and Zhou *et al.*, the cardinal signs of COVID-19 combined fever greater than 37.5°C (88.7% - 4%), cough (67.8% - 81.1%), sputum (23% - 41.3%) and dyspnoea (18.7% - 39.8%), occurring within the first few days of infection [13] [14] [15]. These relatively low rates in our study could be explained by the fact that our population was not diagnosed as COVID-19 positive but just at risk.

On the other hand, very few patients had ageusia (2.3%) and anosmia (1.6%). An increase in medical consultations for anosmia/ageusia without nasal obstruction has been reported in the context of the SARS-CoV-2 pandemic, reminiscent of the olfactory impairment that was reported for SARS-CoV-1. [18] [19]. These are symptoms that often go unnoticed and may be underestimated in our study.

The presence of asymptomatic patients 22.7% in our study, could not eliminate the possibility of SARS-CoV-2 infection in these patients. Indeed this has already been demonstrated in a study in Japan, where among 634 confirmed cases of SARS-CoV-2 infection, 17.9% were asymptomatic [20]. A confirmatory test for infection in these asymptomatic patients will have proved the existence of infection in some of them.

Abdominal pain was the most frequent reason for the examination. The same observation has also been reported in the literature by several authors in the pathologies of the upper digestive tract outside the health crisis [12] [21].

In Niger and Burkina Faso, respectively 31 patients (32.29%) and 70 patients (66.04%) were afraid of endoscopy but the reasons given were all related to the endoscopic procedure and not to the infectious risk linked to COVID-19. We

believe that the population did not clearly perceive the risk of COVID-19 infection in our context. For some it was just another infection and for others their daily difficulties went beyond "this disease of Europe". Indeed, the low rate (7.46%) of patients who felt that they were heavily exposed to COVID-19 during endoscopy attests to this.

Compliance with barrier procedures and awareness were the suggestions of some patients. This should alert us to the need to reinforce preventive measures in digestive endoscopy centers in our African context.

5. Conclusion

Gastrointestinal symptoms initially described as rare are increasingly reported in studies and could be the reason for requesting endoscopic examinations. However, the risk related to SARS-CoV-2 infection does not seem to have been sufficiently taken into account in the endoscopy centers of the 3 countries.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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