

Helicobacter Pylori Infections in Peptic Ulcer Perforations: A Retrospective Analysis in Two Referral Hospitals in Douala, Cameroon

Francois Adrien Morel Bokalli^{1,2}, Chi Fru McWright¹, Jerry Brown Njoh Aseneh¹, Takere Maseoli Mbachan¹, Ngomba Divine Mokake³, Jules Clément Assob Nguedia⁴, Marcelin Ngowe Ngowe⁵

¹Department of Medicine, Faculty of Health Sciences, University of Buea, Buea, Cameroon

²Laquintinie Hospital, Douala, Cameroon

³Department of Surgery, Faculty of Health Sciences, University of Buea, Buea, Cameroon

⁴Department of Biomedical Sciences, Faculty of Medicine and Pharmaceutical Sciences, University of Douala, Douala, Cameroon

⁵Department of Surgery, Faculty of Medicine and Pharmaceutical Sciences, University of Douala, Douala, Cameroon

Email: francois_boks@yahoo.fr, chimcwright@gmail.com, jbaseneh@gmail.com, mbachan_takere@yahoo.com, divymoks2001@yahoo.fr, juleclement@yahoo.fr, nkouki2002@yahoo.fr

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Abstract

Background: Perforations are major complications of peptic ulcer disease and surgical emergencies with important mortality and morbidity. *Helicobacter pylori* (*H. pylori*) has been identified as one of the commonest factors associated with peptic ulcer disease. However, little is known about its implication in cases of perforations in Cameroon. We aimed to determine the frequency of *Helicobacter pylori* infections in cases of perforated peptic ulcers, describe clinical features and outcomes of these cases in Cameroon. **Method:** A hospital-based retrospective cross-sectional study was conducted through the review of patients' records admitted for peptic ulcer perforations in Laquintinie and Douala General Hospitals over a period of 5 years (January 2014 - December 2018). We defined *H. pylori* infection as; positive result on tissue biopsy at time of surgery. We used SPSS version 23.0 to analyse data and set an alpha value at $P = 0.05$. **Results:** We reviewed 115 cases of peptic ulcer perforation, with a mean age of 40 years and sex ratio (M:F) of 5:1. All patients underwent emergency laparotomy, 48 (41%) cases had a biopsy report and the prevalence of *H. pylori* infection in these cases was 47.9 %. Smoking, alcohol consumption and Non-Steroidal Anti-inflammatory Drugs (NSAIDs) use, were not associated with peptic ulcer perforation. The morbidity was at 43.7% and mortality at 14%. Mortality was increasing with a higher Mannheim Peritonitis Index score (OR: 23.51, 95% CI: 4.197 -

143.003, P-value: 0.000). **Conclusion:** We observed a high prevalence of *H. pylori* infection in patients with peptic ulcer perforations. We recommend systematic *H. pylori* screening in cases of perforations and that larger studies should be carried out to evaluate the association of *H. pylori* infection with peptic ulcer perforation in Sub-Saharan Africa.

Keywords

Perforated Peptic Ulcers, *Helicobacter pylori* Infections, Clinical Features, Outcome

1. Introduction

Peptic ulcer disease (PUD) refers to a break in the mucosal lining of the stomach or duodenum and occasionally the lower part of the oesophagus [1]. There are five major complications of PUD; bleeding, perforation, penetration, obstruction and malignancy [2].

In 1983, the whole thinking regarding the pathophysiology and management of this disease was revolutionized when Warren and Marshall [3] reported *Helicobacter pylori* (*H. pylori*) infection plays a crucial role in the pathogenesis of PUD. The revolution in PUD treatment that occurred with the discovery of the role of *H. pylori* is yet to lead to any detectable changes in incidence or treatment of peptic ulcer perforations (PUP) [4] [5].

As such, notable factors associated with PUP are; drugs (use of Non-Steroidal Anti Inflammatory Drugs (NSAIDs), steroids), smoking, fasting, stress, alcohol and gastrinoma [6].

PUP occurs in 2% - 10% of patients with ulcer disease, it is the second most frequent complication after bleeding [7]. Gastroduodenal perforation, with leakage of alimentary contents into the peritoneal cavity, is a common surgical emergency associated with morbidity and mortality in 50% and 30% of cases respectively [8] [9]. PUP present as acute abdominal emergency conditions, with localized or generalized peritonitis and a high risk for further development of sepsis and death [10].

About 50% of the global population is colonized by *H. pylori* in the gastric mucosa, yet it causes diseases in only 10% - 20%. Nonetheless, it shows a variable prevalence (0 - 90%) in perforated ulcers [5] [11]. In addition, studies done in Africa have shown that the rate of *H. pylori* infections in patients with PUP ranges from 50% - 80% and *H. pylori* infections, as a risk factor for PUP, appear to be more relevant in younger patients [12] [13].

H. pylori is highly endemic in Cameroon [14] with a prevalence estimated at 72.5% with a slight male predominance and affecting the young adults of less than 40 years. It was also higher among people living in urban cities, with low level of education and of low socioeconomic status. The prevalence of *H. pylori* infections was 63% among patients with gastric ulcers and 50% among those

with duodenal ulcers [15].

Despite diagnostic and therapeutic advancements [16] [17], the role of *H. pylori* in the incidence of perforations and possible interactions with other known risks is yet to be ascertained. However, there is paucity of data regarding its burden in peptic ulcer perforations in Cameroon. Therefore, we sought to determine the influence of *H. pylori* infections in cases of peptic ulcer perforations in the city of Douala.

2. Materials and Method

2.1. Study Area

We carried out this study in two referral hospitals in Douala (the economic capital of Cameroon); the Douala General and Laquintine Hospitals. They host an extensive technical plateau and experimented specialists.

2.2. Study Design

This study was a hospital-based cross-sectional retrospective study carried out over a period from January 2014 - December 2018.

2.3. Study Population

We reviewed all records of patients hospitalized for peptic ulcer perforation in both hospitals from 1st January 2014 to 31st December 2018, excluded cases of perforations resulting from trauma and all cases managed conservatively (not surgically), as well as records with incomplete data. Where histopathology records were available, cases were classified as; infected with *H. pylori* if positive or not infected with *H. pylori* if negative.

2.4. Study Procedure

The study involved the use of patients' records who had been treated for PUP. Additional information was obtained from ward registers, histopathology reports and theatre records. Morbidity was considered as medical complications sustained postoperatively during the hospital stay. The Mannheim Peritonitis Index [18] was the scoring system used to predict outcome, we classified into 3 groups; those with a score <21, 21 to 28 and >28 corresponding to mild, moderate and severe respectively. These were collected with the help of a pre-established data collection form (**Appendix**).

2.5. Data Management and Analysis

The Data collection forms were checked on a daily basis to ensure correct entry of information and codes used to ensure confidentiality. Data were keyed into a computer, secured by a password known only to the primary investigator. Data collected were entered into Census and Survey Processing System (CSpro) version 7.0. and exported for analysis into Statistical Package for Social Sciences (SPSS) IBM version 23.0.

Data were summarized as frequencies and proportions for categorical variables. Continuous variables were summarized using means and standard deviation for parametric variables and median and interquartile range for nonparametric variables. Group comparison for categorical variables was done using Chi-square (χ^2) test and Fisher's exact test (where appropriate). The p-value < 0.05 was considered statistically significant.

The prevalence was determined by counting the number of patients in whom the bacteria were isolated divided by the overall number patients who were biopsied.

2.6. Ethical Statement

We obtained administrative clearance from the Faculty of Health Sciences of the University of Buea, followed by ethical clearance from the Institutional Review Board of the Faculty of Health Science. Then proceeded to obtain authorization from the administration of the Douala General and Laquintinie Hospitals.

3. Results

In, total, 176 cases of perforations were identified. 61 files were excluded (42 Traumatic perforations, 17 incomplete records and 2 conservatively managed). We retained 115 for analysis. 48 (41.2%) benefitted from a biopsy amongst which the prevalence of *H. pylori* infection was 47.9% (Table 2). Their mean age was 40.0 ± 16.5 years and Sex ratio (M:F) was 5:1 (Table 1).

Out of the 48 screened cases, 45 cases (93.8%) had gastric ulcer perforations,

Table 1. Age and gender distribution of study population.

Variables	<i>Helicobacter pylori</i>	
	Present (%)	Absent (%)
Age groups (years)		
15 - 30	7 (43.8)	9 (56.2)
31 - 45	11 (68.8)	5 (31.2)
46 - 60	2 (20)	8 (80)
60+	3 (50)	3 (50)
Gender		
Male	20 (50)	20 (50)
Female	3 (37.5)	5 (62.5)

Table 2. Relationship between type of perforation and *H. pylori* status.

Site of perforation	<i>Helicobacter pylori</i>		Total	P-value
	Present (%)	Absent (%)		
Gastric	22 (48.9)	23 (51.1)	45 (100)	1.000
Duodenal	1 (33.3)	2 (66.7)	3 (100)	
Total	23 (47.9)	25 (52.1)	48 (100)	

22 (48.9%) of which were positive for *H. pylori* infection while 3 cases (6.2%) had duodenal ulcer perforations, 1 (33.3%) of which was positive for *H. pylori* infection. 40/45 (88.9%) gastric ulcer perforation cases were pyloric perforations (Table 2).

Of the 11 with history of smoking, 5 were found to be *H. pylori* positive. Among 37 non-smokers, 18 were *H. pylori* positive. 24 persons had a known history of PUD or recurrent dyspepsia, among them 12 were *H. pylori* positive and among those with neither history, 11 were *H. pylori* positive. Among 11 patients with history of alcoholism, 8 were *H. pylori* positive and among 37 non alcoholics 15 had *H. pylori* infection. Among 15 patients with history of NSAIDs, 8 were positive for *H. pylori* and among 33 patients with no history of NSAIDs 15 tested positive for *H. pylori*. No significant association was found between the presence of *H. pylori* infection in peptic ulcer perforation with smoking, alcohol intake, history of PUD/dyspepsia or NSAIDS use (Table 3).

The median duration of hospital stay was 12.0 (9 - 18) days, which was shorter in the *H. pylori* negative population (median (IQR) = 10 (7 - 17) days). The morbidity was 43.7%, as 21 of the 48 cases developed some form of post-operative complication. Surgical site infection was the commonest complication among the *H. pylori* positive population and some developed two or more complications (Table 4).

The mortality in our study was 17% (7/48), with just one case registered as *H. pylori* positive. Mortality was found to be higher in patients with MPI greater than 29 compared to those with less (p = 0.000) (Table 5).

4. Discussion

Of the 115 patients treated for PUP, 48 (42%) were screened for the presence of *H. pylori* infection. This was relatively low and could be explained by financial

Table 3. Association of factors with *H. pylori* infection.

Factors	Helicobacter pylori		Total	P-value	
	Present (%)	Absent (%)			
PUD/Dyspepsia	Present	12 (50)	12 (50)	24 (100)	1.000
	Absent	11 (45.8)	13 (54.2)	24 (100)	
NSAIDs	Present	8 (53.3)	7 (46.7)	15 (100)	0.846
	Absent	15 (45.5)	18 (54.5)	33 (100)	
Smoking	Present	5 (45.5)	6 (54.5)	11 (100)	1.000
	Absent	18 (48.6)	19 (54.1)	37 (100)	
Alcohol	Present	8 (72.7)	3 (27.3)	11 (100)	0.125
	Absent	15 (40.5)	22 (59.5)	37 (100)	
Blood group O	Present	10 (50)	10 (50)	20 (100)	1.000
	Absent	13 (46.4)	15 (53.6)	28 (100)	

PUD: peptic ulcer disease, NSAIDs: non steroidal anti inflammatory drug.

Table 4. Follow-up and outcome in study population.

Variable	<i>Helicobacter pylori</i>	
	Present (%)	Absent (%)
Hospital stay (days)		
0 - 10	9 (41)	13 (59)
11 - 20	10 (59)	7 (41)
>20	4 (44)	5 (56)
Complication		
Surgical site infection	4 (44)	5 (56)
Respiratory infection	1 (20)	4 (80)
Septicemia	1 (14)	6 (86)
Renal failure	2 (100)	0 (0)
Cardiovascular	2 (50)	2 (50)
Enterocutaneous fistulae	0 (0)	3 (100)
MPI score		
<21	21 (64)	12 (36)
21 - 28	0 (0)	10 (100)
>29	2 (40)	3 (60)

MPI: Mannheim peritonitis index.

Table 5. Prognostic score (Mannheim Peritonitis Index) against Mortality.

MPI score	Death (%)	Discharged (%)	OR	CI	P-value
<21	1 (3)	33 (97)			
21 - 28	3 (30)	7 (70)			
>29	3 (75)	1 (25)	23.51	4.19 - 143.00	0.000*

MPI: Mannheim peritonitis index, OR: Odds ratio, CI: Confidence interval, *statistical significance.

constraints on the part of patients and a probable under-prescription on the part of the treating physician.

Among these 48 cases, 40 (83.3%) were males (M:F ratio of 5:1). This finding was similar to results obtained by Bekele *et al.* in Nigeria and Afuwape *et al.* in Ethiopia [7] [19]. This is likely owing to the fact that men are the breadwinners in the family, and are consequently prone to stress, drugs and alcohol abuse.

The mean age at presentation was 40 years with an age range of 17 to 80 years. Afuwape *et al.* [19] reported a mean age of 42.5 years and the highest incidence in the fifth decade. These results differed from those of Ghosh *et al.* in India [10] who showed most (45.1%) patients were in the 15 - 30 age group. In Europe however, majority (68%) of patients belonged to a much older age group (>60 years) [20]. These variations in the age may be attributed to the age at which the patients are exposed to various risk factors predisposing for peptic ulcer disease and subsequently perforation.

Prevalence of *H. pylori* infection in peptic ulcer perforation in our study was 47.9%. This was comparable to the study by John *et al.* probably due to a similar sample size [21] who had a prevalence rate of 46.9%. The prevalence according to the study by Dogra *et al.* had a prevalence of 92% [22]. This discrepancy could be accounted for by the fact that other diagnostic methods were used in that study.

Although the age groups 15 - 30 and 31 - 45 had equal number of participants, the percentage of 31 - 45 year positive for *H. pylori* infection was highest and agrees with the findings of Dogra *et al.* [22].

The association of *H. pylori* infection with gastric ulcer perforation was slightly more striking in that out of 43 cases of gastric ulcer perforation, *H. pylori* was detected in 22 cases (48.9%). But was less striking in cases of duodenal ulcer perforations where 1 out of 3 (33.3%) had *H. pylori* detected. These results were similar to the study of Rashim *et al.* [23] where *H. pylori* was isolated in 48.7% of gastric ulcer perforation.

Although treatment of patients with history of chronic dyspepsia should be individualized, a cost-effective initial approach is to test for *H. pylori* and treat the infection if the test is positive. If the *H. pylori* test is negative, empiric therapy with an acid suppressant is recommended. In our study, patients having history of dyspepsia had a high prevalence rate of 50% though Ullah *et al.* had a higher prevalence at 87% [24]. The differences in cultures could be an explanation to this.

Only 15 had positive history of NSAIDS use. Among these 15, 8 were positive for *H. pylori* infection (53.34%). 33 patients did not have any history of NSAIDS use, out of which 15 tested positive for *H. pylori* 45.5%. This observation is similar to what Rehmani and colleagues had in his study [3].

Bateson *et al.* reported strong association between *H. pylori* infection and smoking while in this study the association of *H. pylori* infection with smoking in perforated peptic ulcer disease patients was not found to be significant [25].

Among 11 patients with history of alcoholism, 8 tested positives for *H. pylori* infection and among 37 non-alcoholics, 15 were *H. pylori* positive. The difference was not statistically significant ($p = 0.125$). The study by Rashim and collaborators [23] showed inverse correlation between alcohol ingestion and presence of active *H. pylori* infection.

Duration of hospital stay was slightly higher in the *H. pylori* positive population who on average spent more time in the hospital compared to the *H. pylori* negative population. Prolonged hospital stay was seen to be associated with post-operative complications and some non-medical reasons (such as financial constraints).

The main complications observed were surgical site infection, respiratory infection and septicaemia. The reason for high rates of surgical site infection could be due to heavy contamination of the wound due to bacterial peritonitis.

The Mannheim peritonitis index is one of the simplest scoring systems in use

that allows the surgeon to easily determine the outcome risk during initial surgery. In theory the lower the score the lower the chances of morbidity or mortality from peritonitis and this was seen in practice in our study as the mortality rate was 1/48 (2%) for those with a score < 21 and 6/48 (12.5%) for those > 21. Those who were *H. pylori* positive had a better prognosis of survival from perforation peritonitis as shown by a Mannheim peritonitis index < 21 for a majority (60%) when compared to *H. pylori* negative and over 91% among those who tested positive. This could help conclude that *H. pylori* infection does not worsen the prognosis in cases of perforated peptic ulcer as this observation attained statistical significance. The mortality rate was higher compared to similar studies [21] [22].

All the cases in which the bacteria were isolated were systematically placed on *H. pylori* eradication therapy for 2 weeks, but follow up on this was not documented.

Study Limitations

1) The retrospective nature of this work made retrieval of some important data that would have been added value to the study difficult.

2) We assumed that all patients entered during the study had been subject to a fairly standard treatment commensurate with the individual diagnosis. Inadequate treatment could have negatively impacted on outcome, yet it was not a subject of evaluation in this study.

5. Conclusion

Peptic ulcer perforations are common findings in the male population of the fourth and fifth decades of life. Also, gastric perforations were more common than duodenal. The prevalence of *H. pylori* infection in cases of peptic ulcer perforations in which histopathologic biopsies were done was 47.9%. This is quite high given that *H. pylori* eradication therapy is systematically prescribed in PUD. However, smoking, NSAIDs use and alcohol ingestion were not associated with *H. pylori* infection.

Recommendations

Raise awareness on the importance of *H. pylori* screening in cases of peptic ulcer perforations.

To always send excised body tissues for histopathologic analysis.

Authors Contributions

BFAM participated in the conception, literature review, design of the study, data analysis and management. CFM participated in design of study, edition and revision of manuscript. JBNA participated in literature review and data analysis. MTM participated in drafting, editing and revising the manuscript for publication. MDN participated in drafting the topic, design of study and literature review. ANJC participated in conception of topic, study design, data management

and analysis. NNM participated in study design and conception, data analysis, editing and revising the manuscript for publication.

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Conflicts of Interest

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

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List of Abbreviations

H. pylori—*Helicobacter pylori*

MPI—Mannheim Peritonitis Index

NSAIDs—Non Steroidal Anti Inflammatory Drugs

PUD—Peptic Ulcer Disease

PUP—Peptic Ulcer Perforation

BFAM—Bokalli Francois Adrien Morel

CFM—Chi Fru McWright

JBNA—Jerry Brown Njoh Aseneh

MTM—Mbachan Takere Maseoli

MDN—Mokake Divine Ngomba

ANJC—Assob Nguedia Jules Clement

NNM—Ngowe Ngowe Marcelin

Urine output	Others (specify)	Rigidity
		Shifting dullness
2. Anthropometric Measurement		Absent bowel sounds
Weight		Anterior tenderness on DRE
Height		Others (specify)

**E. PARACLINICAL INVESTIGATION AND MANAGEMENT: PLEASE
FILL IN OR TICK (✓) THE APPROPRIATE ANSWER**

1. Radiological studies Tick Findings
 - Chest X-ray Pneumoperitoneum
 - Plain abdominal X-ray Intra-peritoneal fluid collection
 - Abdominal ultrasound Free gas in the abdomen
 - Others (specify) Others (specify)

2. Laboratory investigation(s) Findings
 - FBC (1), urea/creatinine (2)
 - serum electrolytes (3)
 - serum amylase (4) LFT (5)

3. Pre-Op diagnosis Tick 4. Pre-Op duration Tick
 - Localised peritonitis Less than 24 hours
 - Diffuse peritonitis 24 hours or more

5. Site of Perforation Tick Number(s)
 - Gastric perforation
 - Specific site
 - Duodenal perforation
 - Specific site

6. Histopathology Reports Tick
 - Biopsy performed
 - H. pylori* isolated

7. Color of Exudate Tick
 - Clear
 - Purulent
 - Fecal
 - Bloody

8. Intra operative procedure
 - Name

9. Post-op complications Tick
 - Wound infection/failure
 - Fecal fistula (enterocutaneous fistula)

Paralytic ileus
 Chest infection (lung abscess, pneumonia, ards)
 Anastomotic leak
 Post-op intra-abdominal collection
 Multi organ failure
 Burst abdomen
 Abdominal compartment syndrome
 Renal failure
 Neurologic deficit
 MI and cardiac failure
 DVT/pulmonary embolism
 Sub-phrenic/pelvic abscess
 Others (specify)

- | | | |
|--|------|-------|
| 10. Outcome | Tick | |
| Death | | |
| Discharge | | |
| 11. MPI score wise distribution | Tick | Score |
| <21 | | |
| 21 - 28 | | |
| >29 | | |
| 12. Duration of hospital stay | | |
| 13. <i>H. pylori</i> Eradication therapy | | |