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RAPID COMMUNICATION

Histopathological profile of gastritis in adult patients seen at a referral hospital in Kenya

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Abstract

AIM: To conduct a detailed histological study of gastritis in adult patients attending an endoscopy clinic at a Kenyan teaching and referral hospital.

METHODS: Biopsy specimens from consecutive patients were examined and graded according to the Updated Sydney System for *H pylori* infection, chronic inflammation, neutrophil activity, glandular atrophy and intestinal metaplasia. Also documented were gastric tissue eosinophil counts and presence of lymphoid follicles.

RESULTS: The rate of the graded variables, in the antrum and corpus respectively, were as follows: *H pylori* infection (91%, 86%), chronic inflammation (98%, 93%), neutrophil activity (91%, 86%), glandular atrophy (57%, 15%) and intestinal metaplasia (11%, 2%). Lymphoid follicles were noted in 11% of cases. Duodenal and gastric ulcers were documented in 32% and 2% respectively. The mean eosinophil count was 5.9 ± 0.74 eosinophils/HPF and 9.58 ± 0.93 eosinophils/HPF in the corpus and antrum respectively. Significant association was found between the degree of *H pylori* colonisation with chronic inflammation, neutrophil activity and antral glandular atrophy. Biopsies from the antrum and corpus showed significant histopathological discordance for all the graded variables. *H pylori* negative cases were associated with recent antibiotic use.

CONCLUSION: The study reaffirms that *H pylori* is the chief cause of gastritis in this environment. The majority of patients show a moderate to high degree of inflammation but a low degree of glandular atrophy and intestinal metaplasia. The study shows that inter-relationships between the histological variables in this African population are similar to those found in other populations worldwide including non-African populations.

Key words: *H pylori*; Gastritis; Stomach; Gastric atrophy; Intestinal metaplasia; Tissue eosinophils; Peptic ulcer; African enigma; Sydney system

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INTRODUCTION

H pylori has been implicated in the causation of various diseases since the Nobel-winning discovery by Warren and Marshall in 1981[1]. Ample evidence now exists linking the bacterium to the pathogenesis of chronic gastritis, peptic ulceration, gastric cancers and gastric MALT lymphoma[2-5]. Over half the world's population is infected with *H pylori* and the infection has been shown to follow a geographic and socio-demographic distribution[6]. Interestingly however, the infection rate in various populations does not parallel the incidence of morbidity caused by the infection. This has been termed by a number of authors and commentators as the 'African enigma' based on an apparently low incidence of gastric carcinoma and other *H pylori*-associated morbidities in the continent[7,8]. On the other hand, several commentators and investigators have questioned the realism of this enigma[9,10]. Both proponents and opponents of the 'Africa enigma', however, concede that there are insufficient data from the continent to allow a more critical analysis of the issue.There is thus a need for more data on gastritis from the African continent.

This study was to provide a detailed histological profile of patients with gastritis at Kenyatta National Hospital (KNH) using the histological criteria of the Sydney system and quantification of gastric tissue eosinophil counts in the endoscopic biopsies. In this study, we present a detailed histopathological assessment of gastritis in an African population within an African setup. There are very few histological studies on gastritis that have been published

from this part of the world. We believe that our findings will further contribute to the available body of world literature on gastritis particularly *H pylori* gastritis.

MATERIALS AND METHODS

Study design

This was a prospective descriptive cross-sectional study conducted on consecutive adult patients as per the inclusion/exclusion criteria. Patients who declined to give consent, those with gastric cancer and those with inadequate biopsies were excluded from the study.

The study was conducted in the Endoscopy Unit of KNH, which is the largest tertiary referral hospital in Kenya. The unit is the only public hospital endoscopy facility situated in the capital city of Nairobi.

Patients

A total of 71 consecutive patients were enrolled in this study between February and May 2004 through the Endoscopy Clinic at KNH. Of the 71 cases enrolled, five were excluded from the study on the grounds of inadequate tissue for proper examination. One patient was found to have normal gastric mucosa on histology and was also excluded from the study as this study was confined to patients with histological evidence of gastritis.

Of the 65 patients with histological gastritis analysed in this study, 32 were males and 33 females (male to female ratio: 1:1). The mean age was 43 years (± 16 years) with a median age of 42 years and an age range of 18 to 86 years. The majority of the patients reported symptoms consistent with dyspepsia (94%). Many of the patients used medication within three months preceding the endoscopy, including antacids in 70%, anti-secretory drugs in 63% (H_2-antagonists and proton pump inhibitors), antibiotics in 53% and *H pylori*-eradication treatment in 11%. The endoscopists reported gastritis in 77% of the patients, duodenitis in 32%, duodenal ulcer (DU) in 27% and gastric ulcer (GU) in one patient (2%).

Methods

Histological examination was done on formalin-fixed 4 μm-thick paraffin sections from the corpus and antrum mucosa, 52% of the patients had 3-site biopsies (one from the corpus and two from the antrum including the incisura angularis), while 48% had 2-site biopsies from the antrum and corpus respectively. Five patients did not have histologically-confirmed biopsies from the corpus. The assessment was done on HE-stained sections as per the Sydney System for graded variables of gastritis employing visual analogue scale charts[11]. Gastric tissue eosinophil count was recorded as the number of cells per × 400 high power field (HPF) using an Olympus Provis AX 70 with a field size of 0.344 mm^2. Modified-Giemsa stained sections were used for *H pylori* assessment[12]. The assessment was supervised and checked by an experienced consultant with over 15-year experience. At least 10 cases were randomly reviewed by an independent pathologist as part of quality assurance in the study.

Table 1 Frequency of graded histological variables in patients with gastritis *n* (%)

Variable	Score	0	1	2	3
Chronicity	Corpus (n = 59)	4 (7)	14 (24)	18 (30)	23 (39)
	Antrum (n = 65)	1 (2)	7 (11)	29 (44)	28 (43)
Activity	Corpus (n = 59)	11 (19)	13 (22)	13 (22)	22 (37)
	Antrum (n = 65)	9 (14)	5 (8)	25 (38)	26 (40)
Atrophy	Corpus (n = 59)	50 (85)	7 (12)	2 (3)	0
	Antrum (n = 65)	28 (43)	27 (42)	10 (15)	0 0
Metaplasia	Corpus (n = 59)	58 (98)	1 (2)	0 0	0 0
	Antrum (n = 65)	58 (89)	6 (9)	1 (2)	0 0
H pylori	Corpus (n = 59)	8 (14)	27 (46)	15 (25)	9 (15)
	Antrum (n = 65)	6 (9)	26 (40)	22 (34)	11 (17)

Statistical analysis

Chi-square test and Mann-Whitney *U* test were used to analyze differences and compare variables between various groups. Wilcoxon signed-rank test was used to compare histological findings between the related variables from the antrum and corpus. The eosinophilc counts were transformed to base 10 to make variation constant before subjected to statistical measures of associations. $P < 0.05$ was considered statistically significant (respective values shown). SPSS® version 10 was used for statistical analysis.

RESULTS

Gastric biopsies from 65 patients met the inclusion/exclusion criteria and were analyzed in the study. Most of the biopsies showed a moderate to severe degree of chronic inflammation and neutrophil activity (Table 1).

A total of 59 cases (91%) had histological evidence of *H pylori* infection, 59 (91%, n = 65) antrum infection and 56 (86%, n = 59) corpus infection. Most of the cases showed a mild degree of colonization by *H pylori* (40% and 46% for the antrum and corpus respectively). Severe colonization was seen in 17% and 15% of the cases respectively. Only 6 cases (9%) were *H pylori* negative, of them 4 recalled a history of antibiotic use within a month preceding the endoscopy but showed moderate to severe inflammation and neutrophil activity in the absence of *H pylori*, 2 having no history of antibiotic use had mild chronic inflammation but no neutrophil activity.

Glandular atrophy in the antrum was seen in 37 cases (57%), of them 27 (42%) were of mild degree and 10 (15%) moderate degree. Severe atrophy was not seen. Glandular atrophy in the corpus was seen in 7 cases (11%). A total of seven cases (11%) had antral intestinal metaplasia, one of them had concurrent mild intestinal metaplasia in the corpus. All but two of the cases showing intestinal metaplasia were of mild degree. No case of severe intestinal metaplasia was noted.

Significant association was found between the degree of *H pylori* colonisation and chronic inflammation in the corpus and antrum (corpus: $P = 0.012$, antrum: $P = 0.032$), as well as between *H pylori* colonisation, neutrophil activity and inflammation (corpus: $P = 0.000$, antrum: $P = 0.032$).

Table 2 Stratifying graded variables in relation to the presence of duodenal ulcer *n* (%)

Histology variable	Site	Category	0	1	2	3	*n*
	Corpus	DU - ve	3 (7)	12 (29)	12 (29)	14 (34)	41 (100)
Chronic	(*P* = 0.445)	DU + ve	1 (6)	2 (11)	6 (33)	9 (50)	18 (100)
inflammation	Antrum	Du - ve	1 (2)	6 (13)	21 (45)	19 (40)	47 (100)
	(*P* = 0.732)	DU + ve	0	1 (6)	8 (44)	9 (50)	18 (100)
	Corpus	Du - ve	10 (24)	12 (29)	5 (12)	14 (34)	41 (100)
Active	(*P* = 0.008)[a]	DU + ve	1 (6)	1 (6)	8 (44)	8 (44)	18 (100)
inflammation	Antrum	Du - ve	9 (19)	5 (11)	15 (32)	18 (38)	47 (100)
	(*P* = 0.061)	DU + ve	0	0	10 (56)	8 (44)	18 (100)

DU + ve: patients with duodenal ulcer; DU - ve: patients without duodenal ulcer. [a]*P* < 0.05 *vs* antrum.

Table 3 Distribution of eosinophils in the antrum and corpus

Eosinophils/HPF	Frequency	
	Antrum	Corpus
0	1	7
1-5	28	31
6-10	15	8
11-15	9	11
16-20	7	3
> 20	6	1
Mean	9.6	5.9
Standard error of mean	0.93	0.74
95% confidence interval	4.42-7.38	7.72-11.74

Glandular atrophy was significantly associated with *H pylori* colonisation in the antrum but not in the corpus (antrum: *P* = 0.031, corpus: *P* = 0.868). Intestinal metaplasia did not show any significant association with any of the other graded variables.

Biopsies from the antrum and corpus showed significant histopathological discordance as demonstrated using Wilcoxon signed-rank test comparing respective scores. The antrum consistently showed higher grades for all the graded parameters than the corpus: chronic inflammation (*P* = 0.010), activity (*P* = 0.013), intestinal metaplasia (*P* = 0.034) and *H pylori* (*P* = 0.002). Significant discordance was also observed between multiple antral biopsies from patients who had more than one antral biopsy. There was significant discordance for atrophy (*P* = 0.011) in 39 cases showing different scores. A difference in intestinal metaplasia was only recorded in one biopsy not being statistically significant (*P* = 0.317), demonstrating that multiple antral biopsies increase statistical probability for detecting glandular atrophy, but are not helpful for intestinal metaplasia owing to the low rate and degree of intestinal metaplasia.

Duodenal ulcer was significantly associated with higher grades of active inflammation in the corpus (*P* = 0.008) but not in the antrum (*P* = 0.061, Table 2). The association between duodenal ulcer and each of the other graded variables was not significant: chronic inflammation (antrum: *P* = 0.732; corpus: *P* = 0.445), glandular atrophy (antrum: *P* = 0.837; corpus: *P* = 0.527), intestinal metaplasia (antrum: *P* = 0.083; corpus: *P* = 0.504), and *H pylori* (antrum: *P* = 0.498; corpus: *P* = 0.369). No statistically significant association was found between any of the histological and endoscopic parameters with age or gender.

Significant association was demonstrated for chronic inflammation in the antrum with the use of proton pump inhibitors (*P* = 0.048), antibiotics (antrum *P* = 0.028) and eradication therapy (antrum: *P* = 0.023). Patients on these drugs exhibited lower grades of chronic inflammation in the antrum. The association was also significant between chronic inflammation and proton pump inhibitors in the corpus (*P* = 0.027) but not between antibiotics (*P* = 0.240) or eradication therapies (*P* = 0359). None of the above drugs showed any significant association with the other graded variables including active inflammation. Histamine receptor blockers and antacids did not show any significant association with the presence of duodenal ulcer.

The mean gastric tissue eosinophil count was 9.6 eosinophils/HPF and 5.9 eosinophils/HPF in the corpus and antrum respectively (Table 3). The highest density observed was 23 eosinophils/HPF in the corpus and 31 eosinophils/HPF in the antrum. Duodenal ulcer was associated with higher eosinophil counts in the corpus (*P* = 0.031). The eosinophil count was significantly associated with chronic inflammation and activity (*P* = 0.000 for both antrum and corpus), as well as *H pylori* colonization (antrum: *P* = 0.002; corpus: *P* = 0.012). Glandular atrophy was not associated with intestinal metaplasia.

Seven (11%) and three (5%) of the patients had lymphoid follicles within the lamina propria of antral and corpus biopsies respectively. Of the three patients with lymphoid follicles in the antrum, two had concurrent lymphoid follicles in the corpus biopsies. Mild dysplasia was found in 1 case and moderate dysplasia in 2 cases respectively, representing 5% of the patients. All these patients had *H pylori* infection.

DISCUSSION

The histopathology results from this study provide further evidence that *H pylori*-associated gastritis is the most common etiopathological type of gastritis among adults presenting to this main referral hospital in Kenya. The rate of 91% is consistent with high prevalence rates reported from previous endoscopic studies in the same hospital. A study around the same period as this study found *H pylori* positivity in 69% of patients with dyspepsia using the rapid urease test[13]. A previous study in the same setting found a rate of up to 73% and 85% among dyspeptic patients with and without HIV respectively[14]. Our high pickup rate of *H pylori* gives credence to histology as a sensitive method for diagnosing the bacterium, with the added advantage of enabling morphological assessment of the mucosa. It is, however, noted that antibiotic use prior to endoscopy may affect the sensitivity of histological diagnosis of *H pylori* in gastric biopsies.

The findings in this study reaffirm that *H pylori* is causally associated with chronic inflammation, neutrophil activity and glandular atrophy in the stomach. The findings are similar to those reported from elsewhere around the world. The study also highlights that gastritis in this environment is mainly antral-predominant with significant discordance in the severity of graded variables between

antral and corpus biopsies. The majority of patients undergoing endoscopy in this setting were seen to have moderate to severe gastritis, but much lower rates and severity of glandular atrophy and intestinal metaplasia. These findings are in agreement with the results from several other studies in similar environments[15]. Studies done in other parts of Africa have shown a mean rate of 28% for glandular atrophy (range 14%-70%) and 14% for intestinal metaplasia (2%-24%) respectively.

The low rate of severe glandular atrophy and intestinal metaplasia is important because progression of these variables has been linked to the development of gastric cancer[16]. The average age of our patients is much lower than that of patients from areas with a high incidence of *H pylori*-associated gastritis and gastric cancer. Nevertheless, in this study no association was found between the various histological parameters and age. An extensive collaborative study comparing various histological parameters with age and gender matched subjects from other regions would certainly be very informative[17,18].

Low incidence of gastric cancer is also associated with a low rate of GU as opposed to DU, a low rate and degree of glandular atrophy and intestinal metaplasia, and higher rates of corpus-predominant versus antral predominant gastritis[19]. In Africa, a wide range of DU: GU ratios have been reported varying from 3:1 to 15-20:1[9]. In this study, we found a strikingly low rate of GU compared to DU, a low degree of glandular atrophy, a markedly low rate of intestinal metaplasia, as well as antral-predominant gastritis in this population. The DU:GU ratio in this study is 13.5:1. The DU:GU ratio from previous studies in the same setting ranged from 11.5:1 in adults of all ages[20] to 3:1 in the young and 1:1 in patients over 50 years[21].

Unfortunately, the data are insufficient to establish the true incidence of gastric cancer in Kenya. However, the indirectly adjusted figures between 1991 and 1993 estimated an annual average crude incidence rate of 7.01 for per 100 000 males and 3.7 for females (compared to a world age-standardised rate, 14.3 for males and 7.1 for females)[22]. We are thus inclined to believe that the low rate of glandular atrophy, intestinal metaplasia and GU is similar to other parts of the world where the so called Africa enigma has been observed. As yet to be fully determined, host genetic, bacterial virulence and environmental factors underlie this enigma by affecting the progression of infection to neoplasms[23]. Further study needs to be conducted in order to elucidate the pathological basis of the disparity in the incidence of *H pylori*-associated glandular atrophy, intestinal metaplasia and gastric cancer among various populations of the world.

Lastly, this study demonstrated that gastric tissue eosinophils were significantly associated with the severity of chronic inflammation, neutrophil activity and bacterial colonisation[24]. Similar observations have also been reported by several other workers including recent experimental studies[25]. We are of the opinion that the body of knowledge on eosinopils in gastritis has grown sufficiently since the introduction of the Sydney System, and that more attention needs to be given to the utility of quantitative evaluation of eosinophils in gastritis. Because they are easily identifiable in the gastric mucosa, eosinophil counts may serve as a useful surrogate marker of the severity of inflammation in *H pylori*-associated gastritis.

H pylori is the chief cause of gastritis amongst patients presenting for endoscopy in Kenya. The majority of such patients have a high degree of chronic inflammation, neutrophil activity and *H pylori* infection. Quantitative evaluation of eosinophils may serve as an important surrogate marker of the severity of inflammation in *H pylori* gastritis. Gastritis in this population is significantly antral-predominant, while glandular atrophy, intestinal metaplasia and gastric ulcer are seen to occur at a relatively low rate. Our findings mirror those from other parts of the world with a low incidence of gastric cancer in high *H pylori*-prevalent populations. More studies specifically comparing various histological parameters with age and gender matched subjects from other regions are needed.

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