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ORIGINAL ARTICLES

# Prospective endoscopic study of duodenal ulcer in Zimbabwean Blacks

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### SUMMARY

One thousand seven hundred and fourteen Black Zimbabwean patients underwent upper gastrointestinal endoscopy. Demographic details of the patients were analysed. A randomly chosen cohort of 50 patients with duodenal ulceration was compared to age and sex matched controls regarding lifestyle and *H. pylori* infection. Five hundred and sixteen patients had active duodenal ulcers, giving a crude prevalence rate of ulceration of 456 per 100 000 new hospital cases.

There is a difference from the disease in Western countries in several respects. The incidence appears to be increasing in Zimbabwe. There was no significant difference between ulcer patients and controls in their association with alcohol consumption, cigarette smoking, urban residence and salicylate ingestion (p>(),1),

Ulceration was most strongly associated with *H. pylori* gastritis compared to control (p<0,001). Duodenal ulceration was most prevalent in the 21 to 30 year age group. The overall male to female ratio was 4,7:1. A significant proportion of patients had persistence of ulceration after a standard course of Cimetidine. Pain did not always correlate with presence or absence of ulcers.

# INTRODUCTION

Peptic ulceration is an important disease in the Southern African region, although the exact magnitude of the problem in the Black rural and urban population remains obscure. The aetiology of duodenal ulcer disease world-wide is uncertain although several hypotheses have been formulated particularly in the light of recent studies related to *Helicobacter pylori*. The epidemiology of peptic ulcer disease in populations not previously studied may be of help in identifying aetiological factors common to disparate populations.

The geographical distribution of duodenal ulceration may provide valuable clues with regard to its actiology. It may also be useful in identifying unique factors, thus contributing fresh perspectives and new hypotheses. Changes in prevalence of duodenal ulceration over the past century have been perceived by others.

Any historical changes in prevalence, associated with changes in the mode of living, may give useful additional information. The aetiology of duodenal ulceration is multifactorial, but the factors that are important in Southern Africa have not been established.

The clinical differentiation between duodenal ulceration and the various causes of non-ulcer dyspepsia is difficult and notoriously unreliable. The diagnosis of duodenal ulcer disease should be supported by good quality endoscopy or contrast radiology.

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No studies, which are supported by such investigations, on the basic demographic characteristics of patients suffering from duodenal ulceration, nor on the relative importance of various actiological factors have been performed in Southern Africa, including Zimbabwe.

It was the aim of the present study to: (a) determine the demographic characteristics of Black Zimbabwean patients suffering from endoscopically proven duodenal ulcer; (b) compare the relative frequency of possible actiological and other associated factors between patients with active duodenal ulceration and controls; and (c) assess the response of the ulceration to conventional treatment with Cimetidine.

# MATERIALS AND METHODS

(a) Patient Selection: One thousand seven hundred and fourteen Black Zimbabwean patients, aged 15 years and over, referred during a period of 12 consecutive months, from throughout the country to the central teaching hospitals in Harare, were admitted to the endoscopy units. The hospitals serve as the tertiary referral centres and derive most of their patients from two thirds of the country. The methods were in accordance with the ethical standards laid down by the hospitals' ethics committees, and in accordance with the Declaration of Helsinki. Written informed consent was obtained in each case.

At endoscopy, each patient's demographic details including age, sex and endoscopic findings were recorded. Of the patients found at endoscopy to have active duodenal ulceration, age and sex distribution were analysed and compared to the whole study population. A cohort of 50 patients who were ulcer-positive were randomly selected and studied in more detail to assess alcohol intake, smoking habits, urban or rural dwelling, and the presence of *H. pylori*.

Alcohol and smoking habits were established by means of a structured questionnaire to determine daily consumption and duration. This cohort was matched for age and sex with another group of 50 patients selected during the same study period and assessed in a similar manner.

The control group had negative endoscopic examinations and had been referred with symptoms identifiable clinically as non-ulcer in actiology. An ulcer was defined as denuded epithelium of more than 0,5 cm diameter, with or without scarring, or slough at the based. Patients with scars in the duodenal wall were not

used as controls. It was assumed that patients in the control group had symptoms unrelated to concurrent or previous duodenal ulceration.

The cohort of 50 patients with proven peptic ulcer were required to undergo repeat endoscopy after a six week course of Cimetidine to determine the proportion of patients who still had symptoms or persistent ulcers.

(b) Endoscopic Arrangements: During the period of study, an open referral policy operated, accepting patients from any medical practitioner (both hospital and community based) from any part of the country. It was a matter of policy in all public health institutions (catering for the vast majority of the Zimbabwean population) that before H<sub>2</sub>-receptor antagonists were prescribed for any patient, a positive result (endoscopy or barium study) should be available.

All patients underwent endoscopy within two weeks of referral to the unit. The procedure was performed by one of two experienced endoscopists (IG and CK) using one of three Olympus  $XQ_{10}$  or  $XQ_{20}$  forwardviewing gastroscopes. Prior to the examination, the patient's throat was treated with xylocaine anaesthetic spray and the examination was performed without sedation. The endoscope was sterilised between patients by soaking and cleaning it with 10 pc glutaraldehyde (Cidex, Johnson and Johnson, Harare) for a minimum of 20 minutes.

- (c) Investigations for Helicobacter Pylori: Endoscopic biopsies were obtained from the antrum at endoscopy. The presence of active chronic gastritis and H. pylori were sought in the biopsy specimens by histology, culture and rapid urease tests using standard methods. \*\*H. pylori\* was taken to be present whenever culture was positive, or when both histology and rapid urease test were positive.
- (d) Data Analysis: The mean ages of the male and female patients with active ulcers were calculated, and compared by the two-sample t test. The distribution of possible actiological factors in the cohort of 50 patients with proven ulcers was compared to those in the control group. Standard error of the difference was calculated and assessed for significance using the chi-square test, and the one-sided Fisher's exact test. An estimate of the point prevalence of duodenal ulcer in hospital patients was calculated using the total of in and out patients as the denominator.

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Figure 1: Study patients by age group

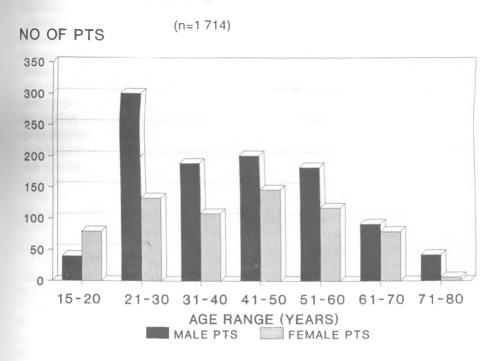
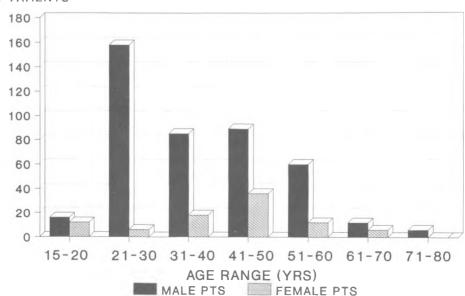


Figure II: Ulcer patients (by age group)

(n=516)

NUMBER

# OF PATIENTS



# RESULTS

One thousand seven hundred and fourteen patients were studied; 1 046 males and 668 females. The ages in the male group ranged from 15 to 78 years with a mean ( $\pm$ SE) of 41,0  $\pm$  1,4 years. The age range in the female group was 15 to 80 years with a mean ( $\pm$ SE) of 40,2  $\pm$  1,6 years. These findings are summarised in Figure I. Five hundred and sixteen patients were found to have active peptic ulceration on endoscopic examination.

During the study period, a total of 229 563 patients were seen in the hospitals. This gives a prevalence rate for duodenal ulcers of 456 per 100 000 new hospital cases. Of these patients with ulcers, 426 were male (41 pc of all male patients in the study), and 90 were female (13 pc of all female patients studied), giving a male to female ratio of 4,7:1. The mean age of the male patients with proven ulcers was  $36.9 \pm 1.9$ . The mean age of female patients who had ulcers was  $40.3 \pm 4.5$  years. This different was significant (p<0,0001), showing a male ulcer population about five years younger than the female population.

Duodenal ulceration was most prevalent in the 21 to 30 year age group in males. The distribution of the ages of women with active duodenal ulceration showed two peaks in the 41 to 50, and the 15 to 20 year age groups respectively (Figure II).

In comparison of the cohort of 50 patients who had proven duodenal ulcers and the matched control group, there was no significant difference in the mean ages nor sex distribution in the two groups (Figure III). Of the risk factors assessed (cigarette smoking, alcohol consumption, urban dwelling and presence of *H. pylori* associated chronic gastritis), only *H. pylori* positivity was significantly different in the two groups (p<0,01; see Figure III). Nine patients had a positive history of ingesting salicylates or non-steroidal anti-inflammatory drugs in the preceding year.

Figure III: Comparison of cohort of patients with ulcers and controls

	No. of Ulcer patients n=50	No. of Control Group n=50	Р
Mean age (Yrs)	39	38	
Males patients	24	24	
Smokers	13	11	>0,1
Drinkers	21	16	>0,1
H. pylori+	45	31	<0,01
Urban dwelling	41	39	>0,1

In the cohort of 50 patients with ulcers, 27 patients (54 pc of all patients, and 75 pc of patients who were reexamined) showed complete healing of the duodenal ulcer at six weeks following Cimetidine 800 mg nocte. Nine patients showed persistence of ulcers and 14 patients either failed to return or refused repeat examination.

Of the 27 patients with healed ulcers, two had persistent localised epigastric pain. Of the nine patients with persistent ulcers, two were completely free of symptoms (Figure IV). Only two patients in the ulcer group had a history of aspirin ingestion, compared to three patients in the control group.

Figure IV: Analysis of persistence of ulceration and symptoms in the cohort group: n=50

	No. with healed ulcers	No, with persistent ulcers
Symptomatic	2	7
Non-symptomatic	25	2
Totals	27	9
Non-return/refusals		14

### DISCUSSION

In reviewing the old medical literature, there are several assumptions and beliefs regarding duodenal ulceration in sub-Saharan Africa which appear at variance with the findings in this study. L2 Duodenal ulcer disease is commoner than was originally suspected from earlier reports. The prevalence of duodenal ulceration in Southern Africa may be increasing despite the reported falling prevalence in Western Europe. S.9

There is an obvious question of whether the relatively high prevalence rate in this study reflects a rate which is higher simply because of better accessibility to medical facilities of the study population as well as improved diagnostic investigations, or if this reflects a true increasing prevalence of the disease in recent years. It is highly probably that the prevalence of duodenal ulceration in Zimbabwe has long been far higher than previously reported.

It is often postulated that the changes in the lifestyles of people in sub-Saharan Africa has been markedly affected over the past three decades by Western influuences, and that this would help explain the apparent increase in the prevalence rates of duodenal ulceration.

Our study population includes people who come from widely different social environments. For example, the rural patient leads a lifestyle (particularly regarding diet, stress and drug use) that still closely resembles that in the last century. The urban patient sometimes has a way of life essentially indistinguishable from his Western counterpart. It would appear reasonable to suggest that if lifestyle had a strong influence on the prevalence of duodenal ulceration, then such a difference should be demonstrable between the urban and rural population in our study.

The present study failed to demonstrate such a difference. We conclude that Western influences on such factors as diet do not seem to have a detectable effect on the prevalence rate of duodenal ulcers.

There was a preponderance of male patients in the study population. This could not be explained by the selection policy on the part of the endoscopy units since we operated an open access policy. Neither is there any significant selection pressures on the patients who may be seen in the hospitals. During the period of study, free medical services were offered to patients who had no substantial regular income. During this time, endoscopy was offered free of charge to all patients. All district hospitals regularly sent patients to the two central hospitals, so that both men and women in remote areas had a comparable opportunity to seek medical advice. Hospital activity analysis shows that there was no significant difference in the number of male and female patients seen in the out patients department.

In calculating the ratio of male to female ulcer patients, an allowance was made for the different numbers of male and female patients presenting for endoscopy. We feel that the ratio of nearly 5:1 of male to female patients with ulcers reflects a genuine preponderance of duodenal ulceration in males.

The large standard error of the mean age of the female ulcer population raises the strong possibility that there is no true difference in the mean ages of the male and female patients with active ulcers. The male ulcer patients showed an age distribution which is significantly difference from that of the whole male study group, but this was not the case with the female patients. Thus the mean age of female ulcer patients may simply reflect the age distribution in the study population as a whole.

The association of duodenal ulceration with the widely accepted risk factors such as cigarette smoking, non-steroidal anti-inflammatory drug ingestion and *H. pylori* related chronic gastritis was assessed and revealed important differences in emphasis compared to the studies elsewhere.<sup>9</sup>

The strongest associated factor was the presence of *H. pylori* associated chronic gastritis in the pyloric antrum. Although this organism is ubiquitous in the general Zimbabwean population<sup>10</sup> (62 pc in our control group), the organism was shown to be present in all but five of the 50 patients with active duodenal ulcers. Of these five "negative" patients, three had a strongly positive rapid urease test but had negative histology and culture. One had positive histology but negative rapid urease test and culture, thereby making all four of them negative according to the working definition above. It is possible, however, that these four patients harboured *H. pylori* infection. None of these five patients had taken anti-inflammatory drugs.

A significant proportion of the Zimbabwean population smokes, but smoking is still very uncommon among women. Smoking can be confidently excluded from the list of possible risk factors in rural female patients with ulceration. There were more smokers, alcohol drinkers, and urban dwellers in the active ulcer group than in the control group; but significance testing consistently gave a p value of >0,100. Thus if there is an association between any of the risk factors and duodenal ulceration, then the power of the study was not sufficient to detect them. We strongly suspect, however, that these factors are in fact of marginal importance in the actiology of duodenal ulceration in the local population.

The need to search for factors with a stronger bearing on the development of duodenal ulceration remains undiminished. Although *H. pylori* would appear in this study to be one such factor, there clearly must be other important factors, as many control patients with no evidence of duodenal ulceration also harboured this organism. Furthermore, therapy was successful in the majority of cases even though Cimetidine has no effect on *H. pylori* activity. The role of a peptic acid environment appears crucial to the development of ulceration. Concurrent chronic gastritis due to *H. pylori* and hyperacidity seem to be important in the actiology of duodenal ulceration

Healing rates of duodenal ulcers following six weeks of Cimetidine was 75 pc in those patients who presented for repeat endoscopy. We found it interesting that some patients remained symptomatic from their epigastric pain despite endoscopic proof of ulcer healing. Similarly, a small proportion of patients were asymptomatic although an ulcer crater remained in evidence. This should serve to warn against making a straight inference on the persistence or resolution of ulcers on the basis of symptoms alone. Only follow-up endoscopy will resolve this question.

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