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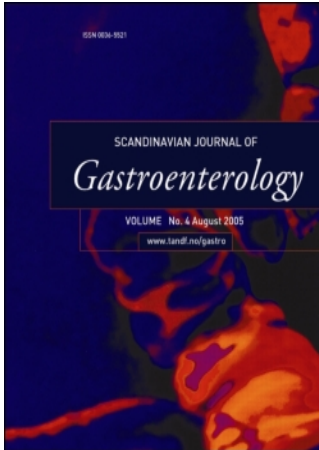
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Peptic Ulcer Disease Is Strongly Associated with Helicobacter pylori in East, West, Central and South Africa

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Peptic Ulcer Disease Is Strongly Associated with *Helicobacter pylori* in East, West, Central and South Africa

While 10–22% of *Helicobacter pylori*-infected persons are expected to develop upper intestinal ulcers, the impression has been that this rate is much lower in Africa (1–3). The large number of *H. pylori*-infected persons who are either symptomless carriers or 'only' suffering from non-ulcer dyspepsia has brought authors to question both the association between *H. pylori* infection and peptic ulcer disease and the significance of pathology related to *H. pylori* on this continent (4, 5). Because the assumed lack of pathological significance of this pathogen in Africa remained unexplained, the phenomenon was named the 'African enigma' (6).

Meanwhile, studies from different parts of Africa have appeared, and this paper is a review of 15 studies with a total of 5487 patients. Age is commonly not reported in African studies, but available demographic data from the studies included in the present paper are given in Table I. Mean age of the 3433 patients studied in the 9 papers presented in Table I was 38.4 years.

In one study (7), mean ages of the ulcer and control patient groups were found to be 39 and 38 years, respectively, and in another (8) 41 and 44 years, respectively. One study reported that the mean age of their ulcer patients was 36 years, while the mean age of the entire study population was 39 years (9). All other studies included in Table II failed to give the age of ulcer patients, which is unfortunate because the occurrence of peptic ulcer disease is dependent on age. In some of the studies, *H. pylori* infection rates for gastric and duodenal ulcers were not given separately. The odds ratio for duodenal and gastric ulcers therefore had to be given combined as peptic ulcer in a number of cases. In one study, patients with non-ulcer dyspepsia were regarded as controls because the *H.*

pylori infection rate for patients with a normal gastroscopy was not given (Table II).

The infection prevalence is high from early adolescence onwards in Africa, and no difference in the prevalence of infection has been noted in accordance with sex or age above 12–15 years (9, 10). The prevalence of peptic ulcer disease nevertheless depends upon age; one study clearly indicated a sex difference, as 41% of male patients and 13% of female patients had a duodenal ulcer (9). Important differences in the age distribution of ulcer patients and control groups cannot be excluded. An over-representation of men could increase the likelihood of identification of an association between infection and peptic ulcer disease, and the overall M:F ratio in the present papers was in fact 1.47:1. The studies are also hampered by a selection bias, as 20% of non-ulcer patients and 77% of ulcer patients are examined for the presence of *H. pylori* infection (Tables II and III).

The reason for the selection bias is that authors have aimed at testing ulcer patients for the presence of *H. pylori* infection whenever possible, while non-ulcer patients have been tested randomly. The importance of age and gender has largely been disregarded. The odds ratios are high, however, and the accordance between the different studies is reassuring (Table II). In spite of obvious structural shortcomings of the individual studies, it must therefore be concluded that these studies provide a good picture of the association between *H. pylori* infection and peptic ulcer disease in Africa. Based on figures given in Table II, the chi-squared value for an association between *H. pylori* infection and peptic ulcer disease in the four regions is 22.9–83.5 ($P < 0.0005$ – $P < 0.0001$). The amount of pathology that has been brought to our attention through these papers is also far from

Table I. Demographic profile of study populations

Reference	Country	n	Age (years)		M:F
			Mean	Range	
18	Malawi	160	37	18–70	1 : 0.72
26	Rwanda	184	35		1 : 1.19
7	Zimbabwe	1714	41	15–80	1 : 0.64
9	Zaire	324	39	10–88	1 : 0.80
14	Ivory Coast	277	37	13–80	1 : 0.74
29	Cameroon	93	41	16–79	1 : 1.02
5	Nigeria	213	31	13–75	1 : 0.92
27	Ghana	39	41	12–71	1 : 0.39
28	Ethiopia	440	35	14–75	1 : 0.44

Table II. Association between *Helicobacter pylori* infection and peptic ulcer disease in different African localities and regions. Prevalence of infection in patients with mild gastritis or normal endoscopic findings is compared with that in patients with duodenal ulcer or peptic ulcer

Reference	Location		Hp+	Hp-	OR	CI																																																																																																																																																																						
18	Lilongwe Malawi	DU	39	2	3.0	0.7–14.0																																																																																																																																																																						
		Normal	90	14			26	Kigali Rwanda	PU	45	0			Normal	12	13	7	Harare Zimbabwe	PU	45	5	5.5	1.9–16.3	Normal	31	19	9	Kivu Zaire	DU	38	0			Normal	58	9	7, 9, 18, 26	Central Africa	PU	167	7	6.9	3.0–15.5	Normal	191	55	14	Abijan Ivory Coast	PU	46	2	12.8	2.5–64.1	Normal	18	10	29	Banso Cameroon	PU	28	5	3.0	1.01–9.0	NUD	39	21	5	Maiduguri Nigeria	DU	16	0			Normal	82	24	27	Kumasi Ghana	DU	23	0			Normal	0	1	5, 14, 27, 29	West Africa	PU	113	7	6.5	2.9–14.8	Normal	139	56	13	Addis Ababa Ethiopia	DU	83	4	7.7	2.5–23.4	Normal	62	23	28	Arba Minch Ethiopia	PU	75	15	2.9	1.6–5.5	Normal	109	64	20	Yirga Alem Ethiopia	PU	161	13	7.3	3.7–14.4	Normal	73	43	8	Khartoum Sudan	DU	16	10	3.7	1.08–12.9	Normal	6	14	8, 13, 20, 28	East Africa	PU	335	42	4.6	3.1–6.7	Normal	250	144	19	Cape Town South Africa	DU	6	0			Normal	5	2	21	Durban South Africa	DU	65	2	10.4	2.3–47.1	Normal	53	17	19, 21	South Africa	DU	71	2	11.6
26	Kigali Rwanda	PU	45	0																																																																																																																																																																								
		Normal	12	13			7	Harare Zimbabwe	PU	45	5	5.5	1.9–16.3	Normal	31	19	9	Kivu Zaire	DU	38	0			Normal	58	9	7, 9, 18, 26	Central Africa	PU	167	7	6.9	3.0–15.5	Normal	191	55	14	Abijan Ivory Coast	PU	46	2	12.8	2.5–64.1	Normal	18	10	29	Banso Cameroon	PU	28	5	3.0	1.01–9.0	NUD	39	21	5	Maiduguri Nigeria	DU	16	0			Normal	82	24	27	Kumasi Ghana	DU	23	0			Normal	0	1	5, 14, 27, 29	West Africa	PU	113	7	6.5	2.9–14.8	Normal	139	56	13	Addis Ababa Ethiopia	DU	83	4	7.7	2.5–23.4	Normal	62	23	28	Arba Minch Ethiopia	PU	75	15	2.9	1.6–5.5	Normal	109	64	20	Yirga Alem Ethiopia	PU	161	13	7.3	3.7–14.4	Normal	73	43	8	Khartoum Sudan	DU	16	10	3.7	1.08–12.9	Normal	6	14	8, 13, 20, 28	East Africa	PU	335	42	4.6	3.1–6.7	Normal	250	144	19	Cape Town South Africa	DU	6	0			Normal	5	2	21	Durban South Africa	DU	65	2	10.4	2.3–47.1	Normal	53	17	19, 21	South Africa	DU	71	2	11.6	2.6–52.0	Normal	58	19						
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Hp = *Helicobacter pylori* infection. DU = Duodenal ulcer. PU = Peptic ulcer. NUD = Non-ulcer dyspepsia.

negligible, as 26% of the patients had a peptic ulcer (Table III). The African situation deserves our attention because *H. pylori*-related diseases need to be taken seriously on this continent, and also because there are epidemiological lessons to be learned.

The interplay between epidemiology and demography has many interesting aspects. The average life expectancy in many African countries is often less than 50 years (11). This is about the age by which Europeans on average develop a duodenal ulcer, while stomach ulcers and cancers usually appear a little later (12). This relative lack of patients old enough to develop ulcers or cancers in Africa is combined with extremely high transmission rates for *H. pylori*, commonly above 10% per year for certain age groups (10).

We would thus expect that the prevalence of peptic ulcer disease among those infected would be lower, and the afflicted patients younger in Africa than elsewhere. The mean age of patients with a duodenal ulcer was found to be 34 years in Addis Ababa, Ethiopia, and 35.9 years in Kivu, Zaire, where the mean age of patients with gastric cancer was 34.8 years (9, 13).

There are only a few reports about sex and age distribution of different patient groups. In one study, the mean age of patients with and without *H. pylori* infection did not differ significantly, being 36.3 and 39.9 years, respectively (14). In Harare, Zimbabwe, the mean age of duodenal ulcer patients was significantly higher for women than for men (40.3 versus 36.9 years, $P < 0.0001$) (7). The M:F ratio of this patient

Table III. Prevalence of peptic ulcer disease (%) among patients examined by gastroscopy in different African localities and regions

Reference	Location	n	DU	GU	PU
18	Lilongwe, Malawi	160	41 (25)	0	41 (25)
7	Harare, Zimbabwe	1714	516 (30)		
26	Kigali, Rwanda	166	43 (26)	2 (1)	45 (27)
9	Kivu, Zaire	324	38 (12)	5 (2)	43 (13)
7, 9, 18, 26	Central Africa	2364	638 (27)	7 (1)	129 (20)
1	Maiduguri, Nigeria	200			60 (30)
5	Maiduguri, Nigeria	213	22 (10)	2 (1)	24 (11)
27	Kumasi, Ghana	39	23 (59)	0	23 (59)
14	Abijan, Ivory Coast	277	26 (9)	22 (8)	48 (17)
29	Bonsa, Cameroon	93	26 (28)	7 (8)	33 (35)
1, 5, 14, 27, 29	West Africa	822	97 (16)	31 (5)	186 (23)
13	Addis Ababa, Ethiopia	200	87 (44)	0	87 (44)
28	Arba Minch, Ethiopia	440			90 (20)
20	Yirga Alem, Ethiopia	834	133 (16)	60 (7)	193 (23)
8	Khartoum, Sudan	100	32 (32)	3 (3)	35 (35)
8, 13, 20, 28	East Africa	1574	252 (22)	63 (6)	405 (26)
21	Durban, South Africa	224	67 (30)	21 (9)	88 (39)
19	Cape Town, South Africa	51	6 (12)	24 (48)	30 (60)
19,21	South Africa	275	73 (27)	45 (16)	118 (43)
All		5487	1105 (23)	148 (5)	965 (26)

DU = Duodenal ulcer. GU = Gastric ulcer. PU = Peptic ulcer.

group was found to be high in both Addis Ababa and Harare, being 3:1 and 4.7:1, respectively (7, 13). These ratios were astonishingly high, and could probably only to some extent be explained by African women being more reluctant than men in attending hospitals (Table I).

Patients with duodenal ulcers have high rates of *H. pylori* infection in Africa as elsewhere. *H. pylori* infection rates are commonly >90% in this group of African patients (Table II), while the sensitivity of diagnostic tests commonly used to detect *H. pylori* infection has been found to be 85–99% (15, 16). Because of the high transmission rates, there are also high, but variable, infection rates of control populations. This situation demands that studies are made with ample statistical power and careful interpretation of the data. When *H. pylori* infection rates for ulcer patients and controls are 94% and 77%, respectively, the required sample size is 150 ($\alpha = 0.05$, $\beta = 0.15$). When these infection rates are 94% and 87%, respectively, the sample size should be ≥ 600 (17). The reports from east, south, central and west Africa in Table II provide evidence of a strong association between *H. pylori* infection and peptic ulcer disease throughout Africa. The exceptions are a few reports that are all short in statistical power (5, 18, 19). In some of the smaller studies, the number of patients without *H. pylori* infection in the duodenal ulcer group was often found to be 0. In these cases, the odds ratio could not be calculated (Table II).

Rates of peptic ulcer disease >20% are usually reported when African dyspeptic patients have been examined by gastroscopy (Table III), while complications of peptic ulcer disease and cancers are commonly found in <10–15% (1, 20). Probably because of the young age of African populations, gastric ulcers

are not very common, but wherever life-span is increased, gastric ulcers are found (19–22). Cancer is usually found in <3% of patients, while higher figures are reported from hospitals situated in areas that have an increased prevalence of cardio-oesophageal cancers (23). Thus, in one recent report from south Ethiopia, 126 (15%) patients with cancer were found in a cohort of 834 patients examined by gastroscopy (20). The prevalence of patients with ulcers and severe diseases is therefore high in most of these studies (Table III).

The low mean age of African ulcer patients was explained by a reduced life expectancy and early acquisition of infection. One more condition might contribute, however. When low mean age of ulcer patients and/or high ulcer rates are found, an increased virulence of *H. pylori* infection could be the cause. The epidemiological diversity of *H. pylori*-related pathology world-wide has puzzled researchers for several years. Comparison of epidemiological patterns in Japan and The Netherlands has shown that increased infection rates (Japan) are associated with an increased risk for development of peptic ulcer disease (3). If virulence factors were randomly distributed, it could be assumed that repeated infections would be a risk factor for accumulation of virulent strains, because there is no evidence in the literature of existing infection of *H. pylori* being protective against re-infection by the same species. On the contrary, multiple strain infections are common (24). One recent study on chimpanzees has shown that natural colonization does not elicit protective immunity from subsequent *H. pylori* challenge (25). The only strong argument against an association between repeated infections and increased disease risk would be the assumption that Africans were harbouring less virulent

infections than patients elsewhere in the world in spite of high transmission rates, and this assumption has now been rejected. The time has therefore come to propose that repeated infections by different strains of *H. pylori* could increase the risk for accumulation of virulence factors and thus increased disease risk.

Because a large majority of children and adolescents are infected, the proportion of young patients who seek medical care for non-ulcer dyspepsia would be expected to be higher in Africa than in Europe. When young patients, who have a reduced risk for ulcer, are over-represented in a study population, the number of patients with peptic ulcers is reduced. The many infected patients with modest pathology have nourished the belief that *H. pylori* infection is a minor problem in Africa. However, because there is a strong association between infection and disease, and because a large majority of most African populations are infected, many patients are suffering from severe consequences of the infection. It is important that the management of these patients is not hampered by misinterpretation of African epidemiology: there is no African enigma.

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