

Clinical, microbiological and antibiotic susceptibility patterns of diarrhoea in Korem, Ethiopia

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Summary

Two hundred patients with diarrhoea in a rehabilitation camp in Ethiopia were studied in October 1985 to determine the presence of pathogens in the stool and their susceptibility to antibiotics. A total of 42 (21.1%) patients had a positive culture with enterobacteriaceae, the isolation rate was 15.6% for *Escherichia coli*, 3.5% for *Shigella* spp. and 2.01% for *Salmonella* spp. In-vitro antibiotic resistance was frequent among the 42 isolates: 53% of *E. coli* strains were found to be resistant to ampicillin, 47% to chloramphenicol, 30% to co-trimoxazole and 67% to tetracycline. Of the seven *Shigella*, three were resistant to chloramphenicol and four to tetracycline. Multidrug resistance (two or more antibiotics) was observed in 52.3% of the 42 isolates. The protocols used for the screening of dysenteric patients for *Shigella* spp. or *Salmonella* spp. were found to be specific but poorly sensitive. The opposite was observed for amoebiasis and giardiasis. The responsibility of widespread use of common oral antibiotics is discussed as one of the major factors of antibiotic resistance occurrence at Korem.

Introduction

In 1984/85 more than 50 000 people fleeing from the results of the 1984 drought gathered at Korem, Wollo Province, Ethiopia. Relief and assistance were provided to the Korem displaced community by the Relief and Rehabilitation Commission (RRC) which collaborated with

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international and non-governmental organizations. Poor nutritional status, overcrowding, lack of water and lack of adequate sanitation made this population highly vulnerable. Dysentery, defined as more than three mucous or bloody stools per day, was one of the major causes of death. The management of diarrhoeal cases was based on oral rehydration therapy (ORT). For dysentery, following Ministry of Health (1985) recommendations, antibiotics, either co-trimoxazole or tetracycline for *Shigella* spp. or *Salmonella* spp., were also given, and metronidazole for giardiasis or amoebiasis. The positive criteria for the indication of antibiotic treatment was dysentery with fever ($\geq 38^{\circ}\text{C}$) and for metronidazole treatment, dysentery without fever. In the field health workers evaluated dysentery through a patient (or relative, for children) interview. To assess the aetiology of dysentery, the validity of the clinical protocols for antibiotic and metronidazole treatment for dysenteric patients and the antibiotic resistance of diarrhoea associated bacteria, a survey was undertaken during 1985 with the collaboration of the National Research Institute of Health of Addis Ababa.

Materials and methods

A case of diarrhoea to be investigated was defined as any person living at Korem for more than 15 days who developed diarrhoea (three or more loose stools per day for at least 1 day) during October 1985. Cases were identified at the two camp dispensaries.

For each case a standardized questionnaire was completed by the dispensaries' doctors and nurses, under supervision. No controls were

Table 1. Resistance of enterobacteriaceae to antibiotics, among patients with diarrhoea, Korem, Ethiopia, October 1985 ($n = 199$ cases)

	<i>n</i>	Resistance to tested antibiotics									
		Ampicillin		Chloramphenicol		Co-trimoxazole		Tetracycline		Kanamycine	
Enterobacteriaceae	<i>n</i>	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)
<i>E. coli</i>	30	16	(53.3)	14	(46.6)	9	(30.0)	20	(66.7)	3	(10.0)
<i>Shigella</i> spp.	7	0	(0.0)	3	(42.9)	0	(0.0)	4	(57.1)	0	(0.0)
<i>Salmonella</i> spp.	4	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
<i>Salm. paratyphi</i>	1	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Total	42	16	(38.1)	17	(40.5)	9	(21.4)	24	(57.1)	3	(7.1)

selected. Demographic and clinical information was recorded. The hydration status was assessed using the WHO Control of Diarrhoeal Diseases program (WHO 1984) criteria and classifications.

Specimens of fresh stools were collected from each case. Direct macroscopic and microscopic stool examinations were done at Korem by a trained laboratory technician. All specimens were cultured and antibiotic sensitivity testing was performed at the National Research Institute of Health of Addis Ababa after transportation on Gary Blair media at 4°C. Each stool was cultured on a Shigella-Salmonella and a Mackonkey Agar at 37°C for 24 h. Api commercial tests were used for the differentiation of the colonies. Antibiotic sensitivity was determined with a commercial antibiotic stoke disk diffusion technique. Sensitivity to ampicillin, co-trimoxazole, chloramphenicol, tetracycline and kanamycine was tested. Statistical tests were performed using Fischer exact test and Mantel Haenzel chi square.

Results

Two hundred patients meeting the case definition were enrolled in the study during the first two weeks of October 1985. Complete information was available from 199 of them. The median age was 14 years (range 4 months to 70 years). Thirty-nine patients (19.6%) were less than 5 years old. The male to female sex ratio was 93:106 (0.88). The median number of stools per day was 4.7 (range: 4 to 10) while the median duration before consultation was 3 days

(range 1 to 15 days). Among the 199 cases, 31 (15.6%) had moderate or severe dehydration.

Forty-one patients were vomiting (20.6%), 31 had a temperature of 38°C or more (15.6%). On interview stools were reported as dysenteric (mucous or bloody) by 101 patients (51%) compared to 171 (86%) classified as dysenteric by the laboratory technician on macroscopic inspection. The agreement for these two ways of assessing the stools aspect is 59.1%.

Ninety-eight patients (49.2%) had at least one parasite in their stools. Among them 41 were trophozoite forms of *Gardia lamblia* and 16 were trophozoite forms of *Entamoeba histolytica*; both parasites were present among 53 patients (26.6%). Forty-two (21.1%) stool cultures grew Enterobacteriaceae (30 *Escherichia coli* spp., 7 *Shigella* spp. and 5 *Salmonella* spp. among which one was a *Salm. paratyphi*). The prevalence of resistance among these 42 isolates is shown in Table 1. Twenty-two of the 42 enterobacteria (53%) were resistant to two or more antibiotics.

The isolation rates of the micro-organisms according to age are shown in Figure 1. Enterobacteriaceae isolation rates were higher among under 5 years patients (59%) than among older patients (11.9%), ($P < 0.001$).

Table 2 shows the distribution of the patients hydration status according to the clinical and biological characteristics. Dehydration was more likely to be observed among patients less than 5 years of age, among patients who were vomiting, among patients with a more severe diarrhoea, among pyretic patients and among patients with a positive stools culture.

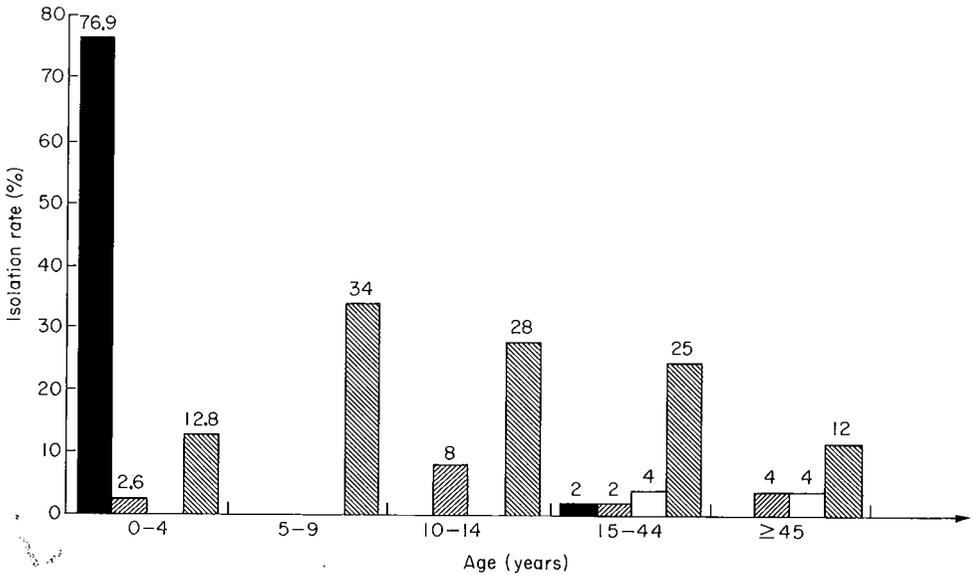


Figure 1. Distribution by age of patients of micro-organisms isolated, Korem, Ethiopia, October 1985. (■) *E. coli*; (▨) *Shigella* spp.; (□) *Salmonella* spp.; (▩) trophozoites of *E. histolytica* or *G. lamblia*.

Table 2. Hydration status according to clinical and microbiological characteristics, Korem, Ethiopia, October 1985

Characteristics	Dehydration (n=31)		No dehydration (n=168)		P value*
	n	(%)	n	(%)	
Age < 5 years	10	(32.3)	29	(17.3)	0.06
Vomiting	13	(41.9)	28	(16.6)	0.03
> 5 stools/day	10	(32.3)	21	(12.5)	0.009
Fever (≥ 38°C)	7	(22.6)	14	(8.3)	0.03
Enterobacteriaceae	11	(35.5)	31	(18.5)	0.04
<i>Escherichia coli</i>	8	(25.8)	22	(13.1)	0.07
Trophozoites of <i>E. histolytica</i> or <i>G. lamblia</i>	9	(29.0)	44	(26.2)	0.44

*Fischer exact test.

Table 3 shows the relationship of macroscopic dysentery and fever with the presence of *Shigella* spp. or *Salmonella* spp. in the stools. Patients with this clinical picture were more likely to have a positive culture for *Shigella* spp. or *Salmonella* spp. (21%) than patients without (4%) ($P < 0.05$). A good specificity (92%) and a low sensitivity (33%) was found for dysentery with fever for shigella or salmonella isolation.

Table 4 shows the relationship of dysentery with the presence of trophozoite forms of *E. histolytica* or *G. lamblia* in the stools of asexual

patients. Patients with dysentery were more likely to be infected with *E. histolytica* or *G. lamblia* (32%) than other patients (4%) ($P < 0.005$). For *E. histolytica* or *G. lamblia* the specificity of dysentery is low (19%), thus the sensitivity is higher (98%).

Discussion

The conditions of life in a place like Korem and the limited available facilities and resources reduced the technical feasibility of such studies.

Table 3. Distribution of shigella or salmonella isolation by clinical status among patients with diarrhoea, Korem, Ethiopia, 1985

Syndrome	Presence of shigella or of salmonella	No shigella and no salmonella	Total
Dysentery and fever	4	15	19
No dysentery, no fever	8	172	180
Total	12	187	199

Fisher exact test = 0.02.

Sensitivity = $4/12 = 33.3\%$.

Specificity = $172/187 = 92\%$.

Positive predictive value = $4/19 = 21\%$.

Negative predictive value = $172/180 = 96\%$.

Table 4. Distribution of trophozoite forms of *E. histolytica* or *G. lamblia* by clinical status among apyrexial patients with diarrhoea, Korem, Ethiopia, 1985

Syndrome	Presence of trophozoites of <i>E. histolytica</i> or <i>G. lamblia</i>	No trophozoites of <i>E. histolytica</i> and <i>G. lamblia</i>	Total
Dysentery	48	104	152
No dysentery	1	25	26
Total	49	129	178

$\chi^2 = 8.6$ ($P < 0.005$).

Sensitivity = $48/49 = 98\%$.

Specificity = $25/129 = 19\%$.

Positive predictive value = $48/152 = 32\%$.

Negative predictive value = $25/26 = 96\%$.

It did not allow an adequate follow-up of all the patients, therefore the outcome of the treatment is not reported. The limited bacteriological investigations and the lack of data on a control group do not permit any conclusion on the pathogenicity of the microorganisms isolated. The association of enterobacteria with dehydration could support their pathogenic role. Habte *et al.* (1981) and Thoren *et al.* (1982) showed on case control studies in Addis Ababa that diarrhoea among children was associated with enterobacteria in a respective proportion of 33.7 and 43%. These figures are quite comparable to the proportion of 54.8% found among the children of our study. Furthermore the age distribution of *E. coli* in our sample is similar to the findings of Stinzing *et al.* (1981) for enterotoxigenic *E. coli* in Addis Ababa on a larger population of diarrhoeal children. These

similar findings support the possible pathogenic role of some of the *E. coli* isolated among the children group of our study.

The prevalence of resistance to usual oral antibiotics used in Korem was high for *E. coli* and such a multidrug resistance is probably due to plasmid resistance factors that can be easily transferred from one strain to another. High levels of resistance to antibiotics have been reported for *E. coli* and shigella in other parts of the third world (Farrar 1985; Murray *et al.* 1985; Hassan 1985; Jerudason 1985). Drug sensitivity patterns of enteric organisms in Ethiopia have been studied for more than a decade (Gedebou *et al.* 1977; Gedebou & Tassew 1979; Gebre-Yohannes & Limenih 1980). In a recent study, in Addis Ababa, multidrug resistance for *Shigella dysenteriae* type 1 isolates was found among 84% of the isolates (Gebre-

Yohanes 1987, personal communication). In another study R-factor mediated multidrug resistance of *Salmonella typhimurium* isolates has been recognized in Ethiopia (Gebreyohanes *et al.* 1987). The potential threat of the emergence and spread of resistant strains of enteric organisms in Ethiopia, where antimicrobials are widely and indiscriminately used, is worrying. The population gathered in Korem had lived before in poor rural areas where antibiotics were not easily available. The relief programmes implemented to meet the tremendous health needs in Korem community, led to a large use of antimicrobials. This might have contributed to the acquired drug resistance found in our study. The shigella strains were not resistant to co-trimoxazole which is not the case in many other developing countries (Farrar 1985; Jerudason *et al.* 1985; Hassan 1985). Although the usefulness of antibiotics and antiparasitic drugs in diarrhoea management is limited compared to ORT they are recommended for dysentery when the disease is severe or the patient is vulnerable (WHO 1984). In field conditions, such as Korem, the use of these specific drugs was needed to reduce the high case fatality ratio. Their use should be based on valid, simple and adapted clinical protocols. Our study shows that macroscopic dysentery with fever is a specific but not sensitive criterion for the screening of *Shigella* spp. or *Salmonella* spp. among diarrhoeal patients. It indicates a low risk of treating false positive with antibiotics while many patients are false negative and will not be treated. We observe the opposite for the screening of amoebiasis or giardiasis. The low specificity may have induced many treatments with metronidazole that were not needed.

At Korem, stool aspects were assessed by interview. It has been found of poor value compared to the results of macroscopic examination and has probably impaired the adequacy of drug indication for dysenteric patients.

The high prevalence of resistance supports strongly the need for careful and discriminate use of antibiotics in emergency situations. Ideally the use of antibiotics or metronidazole in dysentery management in Korem, should have been based on the macroscopic aspect of the stools. This was feasible at the reference

level (hospital or medical centre) where the higher technical level of health workers might have improved on the criteria 'dysentery with fever' for the identification of the dysenteric patients related to shigella or salmonella. Other field studies are needed to further assess the validity of the relation of the diarrhoea clinical picture to the causative microorganisms. They should include a control group and a prospective follow-up of the cases.

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