Paper V

Scandinavian Journal of Infectious Diseases, 2005; 37: 262–268

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Antimicrobial resistance in urinary bacterial isolates from pregnant women in rural Tanzania: Implications for public health

BJØRN BLOMBERG[1,2], BJØRG EVJEN OLSEN[1,3], SVEN GUDMUND HINDERAKER[1,3], NINA LANGELAND[1,2], PETRO GASHEKA[3], ROLAND JUREEN[2], GUNNAR KVÅLE[1] & TORE MIDTVEDT[4]

From the [1]Centre for International Health and [2]Institute of Internal Medicine, University of Bergen, Norway, [3]Haydom Lutheran Hospital, Mbulu, Tanzania, and [4]Department of Medical Microbial Ecology, Karolinska Institute, Stockholm, Sweden

Abstract

Treatment of asymptomatic bacteriuria and urinary tract infections in pregnancy can prevent adverse outcome for mother and child. However, antimicrobial resistance can impede effective chemotherapy. From April 1995 to March 1996, urine specimens from 5153 pregnant women in a rural area in northern Tanzania were inoculated on dip slides. Bacterial isolates from 101 positive dip slides were identified and tested for susceptibility to antimicrobial agents by disc diffusion. In total, 107 bacterial isolates were recovered, 71 Gram-negative and 36 Gram-positive. The most frequent isolates were Escherichia coli ($n=27$) and enterococci ($n=15$). E. coli isolates showed low rates of resistance to ampicillin (17%), mecillinam (9%), cefalexin (0%), nitrofurantoin (4%), trimethoprim-sulfamethoxazole (0%), trimethoprim (13%) and sulfamethoxazole (0%). Other Gram-negative bacteria displayed higher rates of resistance to these drugs. All enterococcal isolates were sensitive to ampicillin and only 2 were resistant to nitrofurantoin. Growth of E. coli from urine culture was correlated with adverse outcome of pregnancy (relative risk 4.13, 95% confidence interval 1.50–11.38). Antimicrobial susceptibility prevails in urinary isolates of E. coli and enterococci from rural areas of northern Tanzania. Susceptibility data from both rural and urban areas should be taken into account when planning antibiotic policies.

Introduction

Five to ten percent of all pregnant women have asymptomatic bacteriuria (ABU), commonly defined as the finding of $>100{,}000$ bacteria per ml urine in a single midstream urine in a person with no symptoms of urinary tract infection (UTI) [1–6]. In non-pregnant women, ABU is usually considered a harmless condition. However, among pregnant women with untreated ABU, as much as 20–30% progresses to pyelonephritis, probably because mechanical obstruction of urinary flow from the enlarged uterus combined with hormonally (progesterone) mediated dilatation of the ureteres and renal pelvis favours ascending infection to the kidney [7].

Various infections, including UTIs, are thought to be the cause of approximately 30–40% of all preterm deliveries [8]. Pyelonephritis in pregnancy is a serious condition associated with increased morbidity and mortality for mother and child. Untreated pyelonphritis is associated with 20–50% incidence of preterm birth. However, the direct effect of ABU on the child is not well established [4]. An apparent association between ABU in pregnancy and preterm delivery/low birth weight (<2500 g) has been observed [3]; however, there is doubt as to whether ABU is a separate risk factor or merely a marker for low socioeconomic status, which is associated with low birth weight [4]. Even in a rural Tanzanian population, which may be perceived as uniformly poor from an economic viewpoint, care-seeking behaviour is worse among the poorer than the relatively richer class [9]. Strategies for routine screening for ABU during pregnancy vary between hospitals, as dissemination of practical

Correspondence: B. Blomberg, Centre for International Health, Institute of Medicine, University of Bergen, NO-5021 Bergen, Norway. Tel: +47 55974980. Fax: +47 55974979. E-mail: bjorn.blomberg@cih.uib.no

(Received 5 July 2004; accepted 1 December 2004)

ISSN 0036-5548 print/ISSN 1651-1980 online
DOI: 10.1080/00365540410021045

knowledge on this topic is impeded by lack of consensus based on previous studies.

Treatment of UTI in pregnancy is of utmost importance for mother and child. Given the close association between ABU and overt UTI, screening for and treatment of ABU in pregnancy may also help reduce adverse outcome for the child such as pre-term labour and low birth weight [3,10]. However, bacterial resistance to antimicrobial drugs is increasing worldwide and may hamper the application of such chemotherapy [11,12]. Thus, knowledge of the local susceptibility patterns of the most common uropathogenic bacteria is necessary for proper obstetric care. Antimicrobial resistance is increasing also on the African continent [13]. Previous studies of Gram-negative and uropathogenic bacterial isolates from Tanzania [14–17] and neighbouring countries [18–23] have revealed moderate to substantial rates of resistance against antimicrobial agents.

It is a paradox that most studies of antimicrobial resistance focus on referral hospitals in large cities, while the majority of many countries' populations lives in rural settings. The recent ECO.SENS project [24], which included data from 252 community health care centres in 16 European countries and Canada, is acknowledged as the first international survey to investigate the prevalence and susceptibility patterns of pathogens causing community-acquired, uncomplicated UTIs in women. The current study describes the antimicrobial resistance patterns of bacterial isolates from urinary specimens from consecutively enrolled pregnant women attending antenatal clinics in a rural area in northern Tanzania. We also compare the data with available data from urban areas in Tanzania. To our knowledge, this is the first study from Tanzania to focus entirely on antimicrobial susceptibility in a rural population.

Materials and methods

Patients and study setting

Between mid-April 1995 and mid-March 1996, a total of 5153 pregnant women were consecutively enrolled in the study as they attended antenatal care visits through 11 outreach clinics run by Haydom Lutheran Hospital (HLH) and 1 stationary hospital clinic at HLH [25]. The majority of the study subjects ($n = 3715$) were residents of 2 divisions, Dongobesh and Basotu, in Mbulu and Hanang districts, respectively, which are typical rural areas in Manyara region (previously part of Arusha region) in northern Tanzania. The study covered an estimated 68% of the pregnant women in those 2 divisions [25]. Being one of the world's economically poorest countries, Tanzania has a high rate of infant mortality at 117 per 1000 live births (World Health Organization, http://www.who.int/child-adolescent-health/). Infections (39%) particularly malaria and pneumonia, as well as asphyxia (24%) and immaturity (15%) are the major causes of stillbirths and perinatal mortality in the study area [26]. The HIV seroprevalence in the study area was low, only 0.3% and 0.4%, respectively, in 2 studies from 1996 and 1998 [27]. HLH is situated 300 km from Arusha, which is the nearest major city. The outreach clinics, located 5–100 km from HLH were visited on a monthly basis.

Specimen collection and laboratory methods

Female field assistants fluent in the 2 major local languages, Iraqw and Datoga, collected clinical information and instructed the study subjects in how to produce a 'clean-catch' midstream urine specimen in pre-boiled and air-dried plastic containers.

Part of the specimen was inoculated immediately using the Uricult® dip slide (Uricult®, Orion Diagnostica, Espoo, Finland), with cystine lactose electrolyte deficient (CLED) agar on 1 side and MacConkey agar on the other side. The dip slides were transported to the hospital within 2–9 h and incubated at 37°C for 18–24 h. Significant bacteriuria was defined as growth of more than 100,000 colony-forming units per ml of 1 or 2 bacterial isolates [5,6]. If there were more than 2 different bacterial isolates, the specimen was considered contaminated. In the presence of a Gram-negative isolate, coincident Gram-positive isolates were considered contaminants. The remaining urine was examined for leucocyte esterase, nitrite, blood, albumin and glucose using a reagent strip (Nephur-Test® + Leuco, Boehringer Mannheim Gmbh, Mannheim, Germany). Positive dip slides were sent to Norway where bacterial isolates were identified using standard microbiological methods [28]. The isolates were tested for susceptibility against antimicrobial agents using a disc diffusion method [29]. The drugs tested were ampicillin, mecillinam, cefalexin, nitrofurantoin, trimethoprim-sulfamethoxazole, trimethoprim and sulfamethoxazole. The susceptibilities were reported in accordance with the 4-group system, with the value 1 representing fully susceptible isolates, values 2 and 3 representing intermediate susceptible results and the value 4 representing fully resistant isolates [29]. For the purpose of statistical analysis and data presentation we have dichotomized susceptibility results into resistant (value 4) and not resistant (values from 1 to 3).

Ethical clearance

The Commission for Science and Technology (COSTECH) in Tanzania and the National Committee for Research Ethics in Medicine in Norway approved the study. Participation in the study was voluntary. Study subjects did not receive any remuneration apart from free treatment with nitrofurantoin tablets (100 mg $\times 2$ for 7 d) if they had ABU/UTI.

Statistical analysis

For comparison of groups, we used Fisher's exact test with a 2-tailed p-value of 0.05 as cut-off for statistical significance and relative risk as calculated with the cs-command in Stata version 8 for MacOSX (Stata Corporation, College Station, TX).

Results

Laboratory results

Among the 5153 pregnant women investigated, 541 (10.5%) had positive dip slide tests. Randomly chosen positive dip slides from 101 women were investigated at the laboratory in Norway. From these dip slides a total of 107 bacterial isolates were identified, of which two-thirds were Gram-negative isolates as shown in Table I. The resistance patterns of Gram-negative and Gram-positive organisms are shown in Table II. The 3 isolates of Pseudomonas spp. were resistant to all the 7 first line drugs tested, but sensitive to gentamicin, ofloxacin and ciprofloxacin.

Table I. Frequency of bacterial isolates obtained from urine isolates from pregnant women in Mbulu and Hanang Districts, northern Tanzania.

	Frequency		
Organism	No.	% of subgroups	% of total
E. coli	27	38.0	25.2
GNR[a]	23	32.4	21.5
Enterobacter spp.	9	12.7	8.4
Klebsiella spp.	4	5.6	3.7
Pseudomonas spp.	3	4.2	2.8
Proteus spp.	2	2.8	1.9
Citrobacter spp.	1	1.4	0.9
Acinetobacter spp.	1	1.4	0.9
Serratia spp.	1	1.4	0.9
All Gram-negative	71	100	66.4
Enterococci	15	41.7	14.0
S. epidermidis	8	22.2	7.5
S. saprophyticus	5	13.9	4.7
S. aureus	2	5.6	1.9
GBS[b]	2	5.6	1.9
GPC[c]	1	2.8	0.9
All Gram-positives	36	100	33.6
Total	107		100.0

[a]GNR: Gram-negative rods, not further identified.; [b]GBS: Group B beta-haemolytic streptococci; [c]GPC: Gram-positive cocci, not further identified.

Clinical course

The outcome for mother and child could be verified in 76.9% ($n=3961$) of the pregnant women (Table III). Among these, 5.4% ($n=213$) experienced negative outcome, including death of child ($n=165$), death of mother ($n=4$), death of both mother and child ($n=8$) and abortion ($n=36$). As shown in Table IV, neither positive dip slide tests, nor ABU, nor UTI, was associated with statistically significantly increased relative risk of negative outcome of pregnancy.

Among the 541 women with positive dip slides (423 with known pregnancy outcome), a total of 101 (65 with known pregnancy outcome) were included in the further microbiological investigation, and the remaining 440 women (358 with known pregnancy outcome) were excluded from the following analysis. The recovery from the urine specimen of any pathogen, any Gram-negative pathogen or any Gram-positive pathogen was not associated with any statistically significant increase in the relative risk of adverse pregnancy outcome (Table IV). However, women who had growth of Escherichia coli from their urines did indeed have significantly higher relative risk of negative outcome (21.4%, 3/14) than the other women (5.2%, 186/3589, relative risk 4.13 with 95% CI 1.50–11.38).

All women with positive dip slide tests were treated with nitrofurantoin tablets. The outcome was known for 57 women who harboured bacterial isolates tested for nitrofurantoin resistance (7 bacterial isolates have not been susceptibility tested and 1 of the women had infection with 2 organisms).

Table II. Antimicrobial resistance of bacterial isolates obtained from urine isolates from pregnant women in Mbulu and Hanang Districts, northern Tanzania.

	Gram-negative bacteria	Gram-positive bacteria	Total
Ampicillin	40% (25/63)	10% (3/31)	30% (28/94)
Mecillinam	29% (18/63)	90% (28/31)[a]	49% (46/94)
Cefalexin	19% (12/62)[b]	61% (19/31)[a]	33% (31/93)[b]
Nitrofurantoin	38% (24/63)	35% (11/31)	37% (35/94)
Trimethoprim-sulfamethoxazole	25% (16/63)	13% (4/31)	21% (20/94)
Trimethoprim	37% (23/63)	19% (6/31)	31% (29/94)
Sulfonamides	22% (14/63)	58% (18/31)[a]	34% (32/94)

[a]Enterococci are inherently resistant to mecillinam, cephalosporins and sulfonamides. [b]One isolate of Pseudomonas spp. was not tested for cefalexin.

Table III. Overview of the type of clinical outcome overall, in patients with and without positive dip slide test.

			Dip slide positive			
	All patients	Dip slide negative	All dip slide positive	ABU	UTI	E. coli isolated
Outcome	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Beneficial outcome	3748 (94.6)	3353 (94.8)	395 (93.4)	205 (92.8)	190 (94.1)	11 (78.6)
Adverse outcome	213 (5.4)	185 (5.2)	28 (6.6)	16 (7.2)	12 (5.9)	3 (21.4)
Child dead	165	141	24	13	11	3
Mother dead	4	3	1	0	1	0
Both dead	8	8	0	0	0	0
Abortion	36	33	3	3	0	0
Total	3961 (100.0)	3538 (100.0)	423 (100.0)	221 (100.0)	202 (100.0)	14 (100.0)
Outcome not known	1192	1074	118	68	50	8
Grand total	5153	4612	541	289	252	22

Women harbouring bacterial isolates resistant to nitrofurantoin appeared to have a slightly higher rate of negative outcome (7.7%, 2/26) than those with sensitive isolates (3.2%, 1/31), but the numbers are small and the difference was not statistically significant (relative risk 2.38, 95% CI 0.23–24.8).

A record of the child's birth weight was available for only 17% (873/5153) of the pregnant women, predominantly because most of the children were delivered at home in their respective villages with no facilities for weighing. The proportion of children with low birth weight (<2500 g) was not significantly different between women with positive dip slide test (7.3%, 7/96) and those without (7.6%, 59/777, relative risk 0.96 with 95% CI 0.45–2.04). Among the women who had pathogenic bacteria isolated from their urine cultures, only 1 woman, from whom Staphylococcus epidermidis was isolated, gave birth to a child with recorded low birth weight.

Discussion

E. coli was the most common pathogen in our study (38% of the Gram-negative isolates, 25% of all isolates). In the ECO.SENS study the percentage of E. coli isolates among all pathogens varied from 53% in Portugal to 86% in Norway, and other Enterobacteriaceae than E. coli, such as Proteus, Klebsiella, Enterobacter and Citrobacter spp. were more frequently isolated from southern Europe than northern Europe [24]. In other studies from Tanzania, E. coli accounted for relatively lower proportions than are commonly reported from Europe, e.g. E. coli accounted for 66%, 64%, 54% and 52% of Gram-negative uropathogens in Dar es Salaam in 4 studies from 1976 [14], 1978–79 [15], 1995 [16] and 1998–99 [17], respectively. It is interesting that the proportion of UTIs caused by E. coli seems to be lower in southern countries than in northern ones. We have no explanation for this, but speculate that differences in temperature, climate, environment and/or antibiotic use may influence this.

Treatment of UTI and ABU is of importance to mother and child, and this study may give indications for the choice of antibiotic treatment, when indicated. It is reassuring that the E. coli isolates in our study were highly susceptible to all tested drugs. Table V shows a comparison of the resistance of the E. coli isolates in this study to results from 2 studies

Table IV. Relative risk of negative outcome (death of mother and/or child or abortion) in pregnant women with asymptomatic and symptomatic bacteriuria and with growth of various organisms.

	No of women	Cases (negative outcome)	Controls (positive outcome)	RR[a]	95% CI[b]
Positive dip slide	3961	6.6% (28/423)	5.2% (185/3538)	1.27	0.86 to 1.86
ABU[c]	3961	7.2% (16/221)	5.3% (197/3740)	1.37	0.84 to 2.25
UTI[d]	3961	5.9% (12/202)	5.3% (201/3759)	1.11	0.63 to 1.95
Pathogen recovered	3603[g]	6.2% (4/65)	5.2% (185/3538)	1.18	0.45 to 3.07
GNR[e] recovered	3603[g]	9.3% (4/43)	5.2% (185/3560)	1.79	0.70 to 4.60
E. coli recovered	3603[g]	21.4% (3/14)	5.2% (186/3589)	4.13	1.50 to 11.38
GPC[f] recovered	3603[g]	0% (0/24)	5.3% (189/3579)	0	N/A[i]
Nitrofurantion resistant organism	57[h]	7.7% (2/26)	3.2% (1/31)	2.38	0.23 to 24.83

[a]RR: relative risk; [b]95% CI: 95% confidence interval; [c]ABU: asymptomatic bacteriuria; [d]UTI: urinary tract infection, i.e. bacteriuria and at least 1 symptom of infection; [e]GNR: Gram-negative rod; [f]GPC: Gram-positive coccus; [g]Excluded 358 women with positive dip slide, which were not examined with identification and susceptibility testing; [h]The outcome of pregnancy was known for 57 women from whom a urinary bacterial isolate was obtained and susceptibility tested to nitrofurantoin; [i]N/A: not applicable.

Table V. Percentage (no. resistant/no. tested) of E. coli isolates resistant to various antimicrobial drugs. Comparison of studies of urinary isolates from pregnant women in a rural area of Tanzania, 2 studies of urinary isolates from outpatients (including non-pregnant women and men) at Muhimbili National Hospital in Dar es Salaam [16,17] and the ECO.SENS study of community-acquired UTIs in women in Europe [24].

Study, study area	Northern Tanzania, current study	Muhimbili National Hospital, Dar es Salaam		Europe – ECO.SENS study		
				Europe overall	Scandinavia	Spain and Portugal
Time	1995–96	1995	1998–99	1999–2000		
Study population	Pregnant women, outpatients	Both genders, outpatients	Both genders, outpatients	Women <66 y, outpatients		
No. of isolates tested	$n=23$	$n=52$	$n=727$[a]	$n=2478$	$n=446$	$n=277$
Ampicillin	17.4 (4/23)	–	82.7 (559/676)	29.8 (/2478)	20.0 (89/446)	51.3 (142/277)
Amoxycillin-clavulanate	–	1.9 (1/52)	28.3 (145/512)	3.4 (/2478)	4.0 (18/446)	5.8 (16/277)
Mecillinam	8.7 (2/23)	–	–	1.2 (/2478)	0.9 (4/446)	1.4 (4/277)
Cefalexin	0.0 (0/23)	–	–	–	–	–
Cefuroxim	–	5.7 (3/52)	–	–	–	–
Cefadroxil	–	–	–	2.1 (/2478)	3.4 (15/446)	2.9 (8/277)
Ceftazidime	–	–	5.6 (22/390)	–	–	–
Gentamicin	–	1.9 (1/52)	7.7 (44/572)	1.0 (/2478)	0.0 (0/446)	4.3 (12/277)
Nitrofurantoin	4.3 (1/23)	0.0 (0/52)	33.1 (156/471)	1.2 (/2478)	0.2 (1/446)	4.7 (13/277)
Trimethoprim-sulfamethoxazole	0.0 (0/23)	–	81.3 (410/504)	14.1 (/2478)	9.4 (42/446)	26.0 (72/277)
Trimethoprim	13.0 (3/23)	–	–	14.8 (/2478)	10.8 (48/446)	25.6 (71/277)
Sulfamethoxazole	0.0 (0/23)	–	87.8 (36/41)	29.1 (/2478)	20.6 (92/446)	47.3 (131/277)

[a] In the surveillance study from 1998–99 in Dar es Salaam a varying number of isolates were susceptibility-tested for the different drugs.
-: Not done.

from Dar es Salaam [16,17] and the ECO.SENS study from Europe [24]. The E. coli isolates from our study generally show similar low rates of resistance as isolates from the Scandinavian countries in the ECO.SENS study, except for mecillinam-resistance which was higher in our study (8.7% vs 0.0–1.6%) and resistance to trimethoprim-sulfamethoxazole and sulfamethoxazole, which were lower in our study (0% vs 8.2–11.3% and 0% vs 16.6–25.0%, respectively).

Not surprisingly, the unspecified Gram-negative isolates, many of which may be non-fermentative organisms, were more frequently resistant than the E. coli isolates to some of the antibiotics tested [24].

Overall, each of the tested antimicrobials was active against 60–80% of the Gram-negative isolates. Cefalexin appeared to be the drug to which most bacterial isolates were susceptible. Interestingly, sulfamethoxazole and trimethoprim-sulfamethoxazole appear to be highly active against Gram-negative bacteria. This finding is different from that shown in a study at Muhimbili National Hospital in Dar es Salaam, the Tanzanian capital [17]. At that hospital, particularly sulfonamides now appear to be useless in the treatment of infections with Gram-negative bacteria due to frequent resistance. The question arises as to whether sulfonamides may not be frequently used in Mbulu and Hanang. The combined formulation trimethoprim-sulfamethoxazole, together with other common antibiotics such as tetracycline and ampicillin were easily obtainable in local groceries, whereas cephalosporins, mecillinam, nitrofurantoin and aminoglycosides were available only by prescription at the hospital drug store. It was quite common for people in the study area to buy a few tablets of any available antibiotic when feeling ill. It is puzzling that resistance to sulfonamides remains low, despite easy over-the-counter accessibility to the drug. Possibly, the majority of the population in the study area very rarely buys modern medicines because they live remotely from the areas with shops and have little money. In Dar es Salaam, trimethoprim-sulfamethoxazole is used on a wide scale as a prophylactic against opportunistic infections in people with advanced HIV disease. In the study area, however, the prevalence of HIV infection was low (<0.5%) compared to elsewhere in the country [27]. It is debated whether HIV infection is associated with infections caused by bacteria resistant to antimicrobials. Apart from the issue of prophylactic antibiotics, such an association may be supported by the notion that HIV infected individuals experience more frequent episodes of fevers and thus may have a higher consumption of antibiotics in general. The low prevalence of HIV infection in the study group should not have any significant impact on the bacterial susceptibility patterns, and, indeed, there were no observed HIV-related deaths in the study group.

Enterococci, the most frequently isolated Gram-positive organisms, showed a uniform susceptibility pattern, with all 14 tested isolates being sensitive to ampicillin and trimethoprim, and only 2 isolates being resistant to nitrofurantoin.

A positive dip slide test per se was not statistically associated with negative outcome of pregnancy. However, growth of E. coli from a urinary specimen was associated with a significantly increased relative risk for negative outcome of the pregnancy. This finding is in accordance with previous studies by Kass et al. [1–3]. It is somewhat unexpected that this association was present despite the administration of nitrofurantoin treatment to all patients with positive dip slides. However, compliance with treatment varies greatly, and may be particularly low in asymptomatic persons. We have no information on whether the participants actually complied with the nitrofurantoin treatment in this study. Furthermore, the study population has high rates of potentially confounding factors such as maternal malaria, other infections and poor nutritional status [26].

The study did not detect any association between bacteriuria and low birth weight. However, the birth weight was known for only 17% of the pregnancies.

In summary, the study shows that the majority of uropathogenic bacterial isolates, including E. coli and enterococci, from pregnant women in a rural area of Tanzania is highly susceptible to commonly used antibiotics. Some other bacterial species showed medium to high resistance rates. It is evident that even in this remote rural setting, the bacterial ecology has been affected by the emerging resistance problems. Nevertheless, considering the high rate of susceptibility of E. coli and enterococci to commonly available antibiotics such as nitrofurantoin and ampicillin, these drugs may still be used for treating UTI and ABU in pregnant women in the area. We did not find a correlation between resistance patterns and the drugs that are easily available over-the-counter.

An important observation from this study is that antimicrobial resistance can vary considerably between rural and urban areas within a country. The current study showed noticeably lower resistance rates than reported from studies in large referral hospitals and urban areas. This should be taken into consideration when formulating antibiotic policies in countries such as Tanzania. In many developing countries, there are little reliable data available from rural settings, and, consequently, antibiotic policies are founded on studies from referral hospitals and urban areas. In Tanzania, the great majority of the population lives in rural areas. Policies developed for urban areas may endorse the use of antibiotics, which are unaffordable for poor rural dwellers, including broad-spectrum antibiotics, which have the additional disadvantage of promoting further resistance. In countries with large rural populations, such as in Tanzania, resistance data from rural areas must play a correspondingly significant role when deciding antibiotic policies.

Acknowledgements

This study was funded by the Norwegian Research Council (Grant no 100675) and Centre for International Health, University of Bergen. We gratefully acknowledge the Regional Development Director and Regional Medical Officer, Arusha Region and District Commissioners, District Medical Officers, MCH coordinators and local division, ward and village administrators in Hanang and Mbulu districts for their assistance. Furthermore, we are grateful for the indispensable assistance of the Doctor in Charge Ole Halgrim Evjen Olsen, Matron Selina Sanka and the other staff at Haydom Lutheran Hospital, the MCH clinics and the laboratory. We also thank the field assistants in Tanzania and the staff at the Laboratory for Clinical Microbiology, Oslo. Finally, we would like to thank all the pregnant women in Mbulu and Hanang who volunteered to participate in this study.

References

[1] Kass EH. Bacteriuria and pyelonephritis of pregnancy. Arch Intern Med 1960;105:194–8.
[2] Turner GC. Bacilluria in pregnancy. Lancet 1961;2:1062–4.
[3] Romero R, Oyarzun E, Mazor M, Sirtori M, Hobbins JC, Bracken M. Meta-analysis of the relationship between asymptomatic bacteriuria and preterm delivery/low birth weight. Obstet Gynecol 1989;73:576–82.
[4] Smaill F. Antibiotics for asymptomatic bacteriuria in pregnancy. Cochrane Database Syst Rev 2001: CD000490.
[5] Millar LK, Cox SM. Urinary tract infections complicating pregnancy. Infect Dis Clin North Am 1997;11:13–26.
[6] Kass EH. Asymptomatic infections of the urinary tract. Trans Assoc Am Physicians 1956;69:56–64.
[7] Whalley P. Bacteriuria of pregnancy. Am J Obstet Gynecol 1967;97:723–38.
[8] Haram K, Mortensen JH, Wollen AL. Preterm delivery: an overview. Acta Obstet Gynecol Scand 2003;82:687–704.
[9] Schellenberg JA, Victora CG, Mushi A, de Savigny D, Schellenberg D, Mshinda H, et al. Inequities among the very poor: health care for children in rural southern Tanzania. Lancet 2003;361:561–6.
[10] Hall DR, Theron GB, van der Horst W. Significance and treatment of asymptomatic bacteriuria during pregnancy. Int J Gynaecol Obstet 1997;57:179–80.
[11] Cohen ML. Epidemiology of drug resistance: implications for a post-antimicrobial era. Science 1992;257:1050–5.
[12] Tenover FC, Hughes JM. The challenges of emerging infectious diseases. Development and spread of multiply-resistant bacterial pathogens. JAMA 1996;275:300–4.
[13] Hart CA, Kariuki S. Antimicrobial resistance in developing countries. Br Med J 1998;317:647–50.

[14] Willett WC, Radojcic V. Urinary tract pathogens and antibiotic sensitivity patterns in Dar es Salaam. East Afr Med J 1976;53:685–92.
[15] Maselle SY, Ipuge YA, Mhalu FS. Antimicrobial susceptibility patterns of important urinary bacterial pathogens in Muhimbili Medical Centre, Dar es Salaam. Dar es Salaam Medical Journal 1980;8:35–40.
[16] Urassa WK, Mwakagile D, Mohammed K, Msangi V. Susceptibility pattern of uropathogenic Gram-negative bacilli to antimicrobial chemotherapeutic agents in a national hospital in Dar es Salaam. East Afr Med J 1997;74:162–5.
[17] Blomberg B, Mwakagile DSM, Urassa WK, Maselle SY, Mashurano M, Digranes A, et al. Surveillance of antimicrobial resistance at a tertiary hospital in Tanzania. BMC Public Health 2004;4:45.
[18] Omari MA, Malonza IM, Bwayo JJ, Mutere AN, Murage EM, Mwatha AK, et al. Pattern of bacterial infections and antimicrobial susceptibility at the Kenyatta National Hospital, Nairobi, Kenya. East Afr Med J 1997;74:134–7.
[19] Malonza IM, Omari MA, Bwayo JJ, Mwatha AK, Mutere AN, Murage EM, et al. Community acquired bacterial infections and their antimicrobial susceptibility in Nairobi, Kenya. East Afr Med J 1997;74:166–70.
[20] Kariuki S, Gilks CF, Kimari J, Muyodi J, Waiyaki P, Hart CA. Plasmid diversity of multidrug-resistant Escherichia coli isolated from children with diarrhoea in a poultry farming area in Kenya. Ann Trop Med Parasitol 1997;91:87–94.
[21] Aseffa A, Yohannes G. Antibiotic sensitivity pattern of prevalent bacterial pathogens in Gondar, Ethiopia. East Afr Med J 1996;73:67–71.
[22] Belihu A, Lindtjørn B. Increasing incidence of resistance to antimicrobials in Sidama. Ethiop Med J 1999;37:181–7.
[23] Lindtjorn B, Setegn D, Niemi M. Sensitivity patterns of bacteria isolated from patients at Sidamo Regional Hospital. Ethiop Med J 1989;27:27–31.
[24] Kahlmeter G. An international survey of the antimicrobial susceptibility of pathogens from uncomplicated urinary tract infections: the ECO.SENS Project. J Antimicrob Chemother 2003;51:69–76.
[25] Olsen BE, Hinderaker SG, Lie RT, Gasheka P, Baerheim A, Bergsjo P, et al. The diagnosis of urinary tract infections among pregnant women in rural Tanzania: prevalences and correspondence between different diagnostic methods. Acta Obstet Gynecol Scand 2000;79:729–36.
[26] Hinderaker SG, Olsen BE, Bergsjo PB, Gasheka P, Lie RT, Havnen J, et al. Avoidable stillbirths and neonatal deaths in rural Tanzania. Bjog 2003;110:616–23.
[27] Hinderaker SG, Kruger C, Olsen BE, Naman N, Bergsjo P, Olsen OH. Low HIV-seroprevalence in pregnant women in a rural area in Tanzania. Acta Obstet Gynecol Scand 2001;80:1152–3.
[28] Murray PR, Baron EJ, Pfaller MA, Tenover FC, Yolken RH. Manual of clinical microbiology. 7th edn. Washington DC. ASM press: 1999.
[29] Bergan T, Bruun JN, Digranes A, Lingaas E, Melby KK, Sander J. Susceptibility testing of bacteria and fungi. Report from the Norwegian Working Group on Antibiotics. Scand J Infect Dis Suppl 1997;103:1–36.