International Journal of Antimicrobial Agents 50 (2017) 629–639

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag

Review

Antimicrobial resistance in West Africa: a systematic review and meta-analysis

Kerlly J. Bernabé [a], Céline Langendorf [b], Nathan Ford [c], Jean-Baptiste Ronat [d], Richard A. Murphy [e,*]

[a] Doctors Without Borders, New York, NY, USA
[b] Epicentre, Paris, France
[c] University of Cape Town, Cape Town, South Africa
[d] Médecins Sans Frontières, Paris, France
[e] Division of Infectious Diseases, Los Angeles Biomedical Research Institute at Harbor–UCLA Medical Center, 1000 W. Carson Street, Box 466, Torrance, CA 90509, USA

ARTICLE INFO

Article history:
Received 7 February 2017
Accepted 1 July 2017

Keywords:
Antimicrobial agents
Drug resistance
West Africa

ABSTRACT

Growing data suggest that antimicrobial-resistant bacterial infections are common in low- and middle-income countries. This review summarises the microbiology of key bacterial syndromes encountered in West Africa and estimates the prevalence of antimicrobial resistance (AMR) that could compromise first-line empirical treatment. We systematically searched for studies reporting on the epidemiology of bacterial infection and prevalence of AMR in West Africa within key clinical syndromes. Within each syndrome, the pooled proportion and 95% confidence interval were calculated for each pathogen–antibiotic pair using random-effects models. Among 281 full-text articles reviewed, 120 met the eligibility criteria. The majority of studies originated from Nigeria (70; 58.3%), Ghana (15; 12.5%) and Senegal (15; 12.5%). Overall, 43 studies (35.8%) focused on urinary tract infections (UTI), 38 (31.7%) on bloodstream infections (BSI), 27 (22.5%) on meningitis, 7 (5.8%) on diarrhoea and 5 (4.2%) on pneumonia. Children comprised the majority of subjects. Studies of UTI reported moderate to high rates of AMR to commonly used antibiotics including evidence of the emergence of cephalosporin resistance. We found moderate rates of AMR among common bloodstream pathogens to typical first-line antibiotics including ampicillin, cotrimoxazole, gentamicin and amoxicillin/clavulanate. Among *S. pneumoniae* strains isolated in patients with meningitis, levels of penicillin resistance were low to moderate with no significant resistance noted to ceftriaxone or cefotaxime. AMR was common in this region, particularly in hospitalized patients with BSI and both outpatient and hospitalized patients with UTI. This raises concern given the limited diagnostic capability and second-line treatment options in the public sector in West Africa.

1. Introduction

Antimicrobial resistance (AMR) has become a significant threat to the prevention and treatment of bacterial infections globally [1]. Importantly, in low- and middle-income countries, the potential for AMR to lead to increased morbidity and mortality may be greater given the higher burden of bacterial illness in low-income countries, delayed presentation, weaker access to diagnostics (particularly microbiology) and the reduced availability of second-line antibiotics [2].

One critical aspect to the global response to AMR is surveillance. However, according to a 2014 report by the World Health Organization (WHO), the WHO Africa region has one of the largest gaps in data on the prevalence of AMR [2] as a consequence of limited laboratory capacity and surveillance networks. An external quality assessment reported several deficits in antimicrobial susceptibility testing in many African countries [3]. With limited information available on AMR, health departments and humanitarian actors providing health care in this region lack practical information on how AMR may compromise first-line empirical treatments of common bacterial infections.

Recent efforts to define the map of AMR in sub-Saharan Africa are not easily translatable into action. For example, a 2014 WHO report compiled existing data on AMR focusing on certain bacteria–antimicrobial drug combinations thought to be of public health importance [2]. However, physicians and other prescribers, particularly in the absence of microbiology, recognise and manage clinical syndromes rather than specific bacteria. Therefore, the current analysis aims to evaluate AMR in the West Africa region by clinical syndrome. For the treatment of syndromes, a better

* Corresponding author. Division of Infectious Diseases, Los Angeles Biomedical Research Institute at Harbor–UCLA Medical Center, 1000 W. Carson Street, Box 466, Torrance, CA 90509, USA.
E-mail address: ramurphy@gmail.com (R.A. Murphy).

https://doi.org/10.1016/j.ijantimicag.2017.07.002

understanding of the epidemiology of the most prevalent bacterial infections of public health importance may allow improved decision-making on empirical (first-line) antibiotic strategies. Thus, a systematic review was performed to describe the aetiology and AMR patterns within key bacterial syndromes encountered in this region. The five bacterial diseases focused on were pneumonia, meningitis, urinary tract infection (UTI), bloodstream infection (BSI) and diarrhoea. These are common and serious bacterial infections of high public health importance in West Africa.

2. Methods

The systematic review was performed in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [4]. Based on the United Nations geoscheme, the region of West Africa includes the countries of Benin, Burkina Faso, Cape Verde, Ivory Coast, The Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Saint Helena, Senegal, Sierra Leone and Togo [5]. Relevant literature was identified from EMBASE and PubMed databases using specific search terms of key bacterial pathogens and common serious clinical syndromes combined with the 17 countries in West Africa (Fig. 1).

2.1. Inclusion criteria and exclusions

A systematic review was undertaken to identify studies carried out in West Africa published between 1 January 1990 and 31 December 2012 that describe bacterial causes of infection and associated AMR. English and French language studies were included. Publications were reviewed by one author and were discussed with at least two authors to determine eligibility. Only published literature that provided original data on AMR in adult and paediatric populations were included. Studies focusing on five syndromes (pneumonia, meningitis, UTI, BSI and diarrhoea) were included. Studies on burn infections, sexually transmitted infections, tuberculosis, non-bacterial pathogens and outbreak investigations were not included. To minimise bias, studies that reported data for <10 patients or that used convenience sampling were excluded. Based on National Committee for Clinical Laboratory Standards (NCCLS) [currently the Clinical and Laboratory Standards Institute (CLSI)] recommendations, studies reporting on <10 isolates of a particular pathogen were excluded [6]. Studies reporting aggregated data were also excluded. For example, studies with the methodology of aggregating resistance rates in a large category such as 'Gram-negative organisms' were excluded. Also, if clinical presentations were aggregated (e.g. combining patients with urinary or gastrointestinal symptoms) or if studies reported on a mixture of specimen types (e.g. urine and blood specimens aggregated), these studies were excluded. Studies reporting on specimens outside the scope of the review (e.g. rectal swabs) and studies on healthy patient populations with no symptoms were also excluded.

A standardised tool was developed to collect information from investigations, including study characteristics, bacteria isolated and AMR rates. Retrospective studies emerging from microbiology laboratories reporting results of culture and sensitivity testing for patients with syndromes of interest were categorised as laboratory studies. Prospective or retrospective studies from hospitals or clinics that included patients who fit a particular syndrome (e.g. meningitis) were considered clinical studies (including case-series studies of >10 patients). Surveillance studies were studies focused on a particular pathogen carried out by reference laboratories or a network of sentinel laboratories [7].

For each of the five common syndromes included in this review, the analysis focused on specific pathogens [7]: (i) UTI, *Escherichia coli*, *Klebsiella* spp. and *Pseudomonas aeruginosa* from urine; (ii) BSIs, *E. coli*, *Haemophilus influenzae*, *Klebsiella* spp., non-typhoidal *Salmonella* (NTS), *Salmonella enterica* serovar Typhi, *Staphylococcus aureus* and *Streptococcus pneumoniae* from blood; (iii) pneumonia, *H. influenzae*, *S. aureus* and *S. pneumoniae* from cerebrospinal fluid (CSF), blood, lung aspirates, sputum, bronchoalveolar liquid or pleural fluid; (iv) meningitis, *H. influenzae*, *Neisseria meningitidis* and *S. pneumoniae* from blood or CSF; and (v) diarrhoea, *E. coli*, *Shigella dysenteriae* and *Vibrio cholerae* from faeces. For each of the key

PubMed
(extended-spectrum beta-lactamase OR beta-lactamase OR ESBL OR antimicrobial resistan* OR antibiotic resistan* OR multiresistant OR multidrug-resistant OR drug resistance OR antibacterial OR antibiotic OR antimicrobial OR bacterial resistance OR Enterobacteriaceae OR gram-negative OR gram-positive) AND (*Escherichia coli* OR *E. coli* OR *Klebsiella* OR Salmonella OR typhoid OR Enterobacter OR *Staphylococcus aureus* OR *methicillin-resistant Staphylococcus aureus* OR *Streptococcus pneumoniae* OR *Pseudomonas* OR *Pneumococcus* OR *Shigella* OR cholerae OR cholera OR *Haemophilus* OR *N. meningitidis* OR *Neisseria*) AND (urinary tract infection OR UTI OR bloodstream infection OR bacteremia OR bacteraemia OR sepsis OR septicemia OR septicaemia OR diarrhea OR diarrhoea OR acute gastrointestinal infection OR meningitis OR cerebrospinal meningitis OR CSF OR pneumonia OR acute respiratory infection) AND (Individual Country or Western Africa)

Embase
'extended-spectrum beta-lactamase' OR 'beta-lactamase' OR 'esbl enterobactericeae' OR 'antibiotic resistance' OR 'Multidrug resistance' OR 'drug resistance' OR 'antiinfective agent' OR 'antibiotic agent' OR Enterobacteriaceae OR 'gram-negative bacterium' OR 'gram-positive bacterium' AND '*Escherichia coli*' OR *Klebsiella* OR Salmonella OR 'Salmonella typhi' OR Enterobacter OR '*Staphylococcus aureus*' OR '*methicillin-resistant Staphylococcus aureus*' OR '*Streptococcus pneumoniae*' OR '*Pseudomonas aeruginosa*' OR *Shigella* OR 'Shigella dysenteriae' OR cholera OR *Haemophilus* OR *'Neisseria meningitidis'* OR *Neisseria* AND 'urinary tract infection' OR 'bloodstream infection' OR bacteremia OR sepsis OR septicemia OR diarrhea OR 'acute gastroenteritis' OR meningitis OR 'cerebrospinal meningitis' OR 'cerebrospinal fluid' OR pneumonia OR 'respiratory tract infection' AND (Individual Country or Western Africa

Fig. 1. Search terms used to identify relevant literature from the EMBASE and PubMed databases.

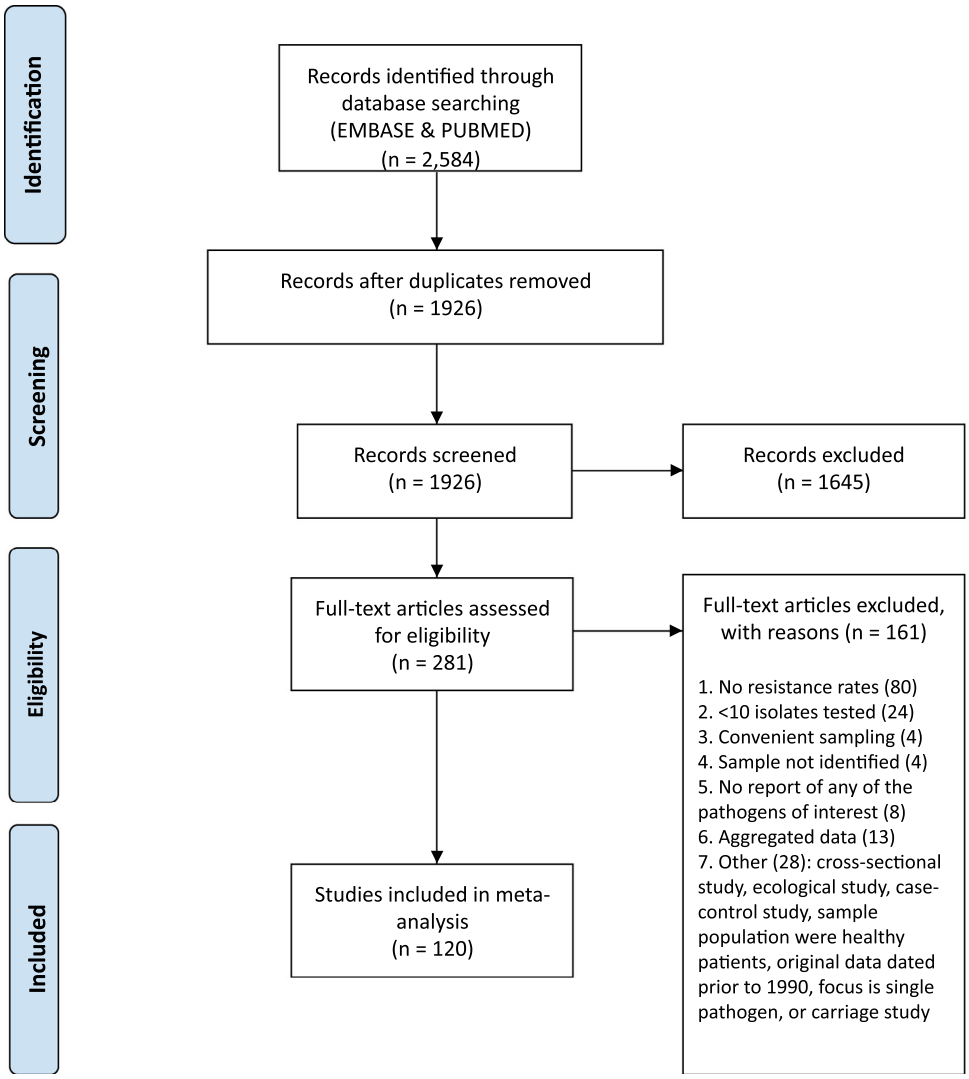


Fig. 2. Selection process of studies.

pathogens, resistance to a limited number of antibiotics was described based on common first-line drugs used in West Africa.

2.2. Data analysis

For each syndrome, the point prevalence and 95% confidence interval (CI) were calculated for each pathogen–antimicrobial pair. Random-effects meta-analysis was used to calculate an overall proportion for each syndrome [8]. Data analysis was performed using StatsDirect Statistical Analysis Software v.3.0.187 (http://www.statsdirect.com/; accessed 1 December 2016). Proportions were transformed via the Freeman–Tukey double arcsine method [9,10] and then an inverse-variance weighted random-effects meta-analysis was performed by conventional methods [11]. In addition, for studies reporting intermediate resistance rates, intermediate-resistant strains were grouped with resistant strains.

3. Results

3.1. Overview of study characteristics

Among 2584 initial records screened, 281 articles were reviewed in full and 120 met the eligibility criteria and were included in this review (Fig. 2). The largest number of studies originated from three countries, namely Nigeria (70; 58.3%), Ghana (15; 12.5%) and Senegal (15; 12.5%) (Fig. 3). Overall, 43 studies (35.8%) focused on UTIs, 38 (31.7%) on BSIs, 27 (22.5%) on meningitis, 7 (5.8%) on diarrhoea and 5 (4.2%) on pneumonia. Among 99 studies that described age, 65 (66%) focused on paediatric populations. For studies reporting participation by sex, females comprised 45% (interquartile range 41–59%) of subjects.

The majority of studies were conducted in urban settings (100/114; 87.7%) and the majority of patients received care in hospitals (95/115; 82.6%). The predominant study designs were retrospective clinical studies (48/120; 40.0%) and prospective clinical studies (43/120; 35.8%); the remainder were laboratory-based studies (24/120; 20.0%) and surveillance studies (5/120; 4.2%). Among studies that reported the type of microbiology laboratory used, 68% (65/95) involved a teaching hospital with an associated laboratory. The remainder of studies involved routine clinical laboratories (22/95; 23%), 'research' laboratories (5/95; 5%) and reference laboratories (3/95; 3%). Studies predominantly made use of disk diffusion tests (101/107; 94.4%) as the methodology of antibiotic susceptibility testing, followed by dilution test (4/107; 3.7%) and Etest (2/107; 1.9%). Studies reported a variety of microbiological standards as references; the sources were the French Society of Microbiology

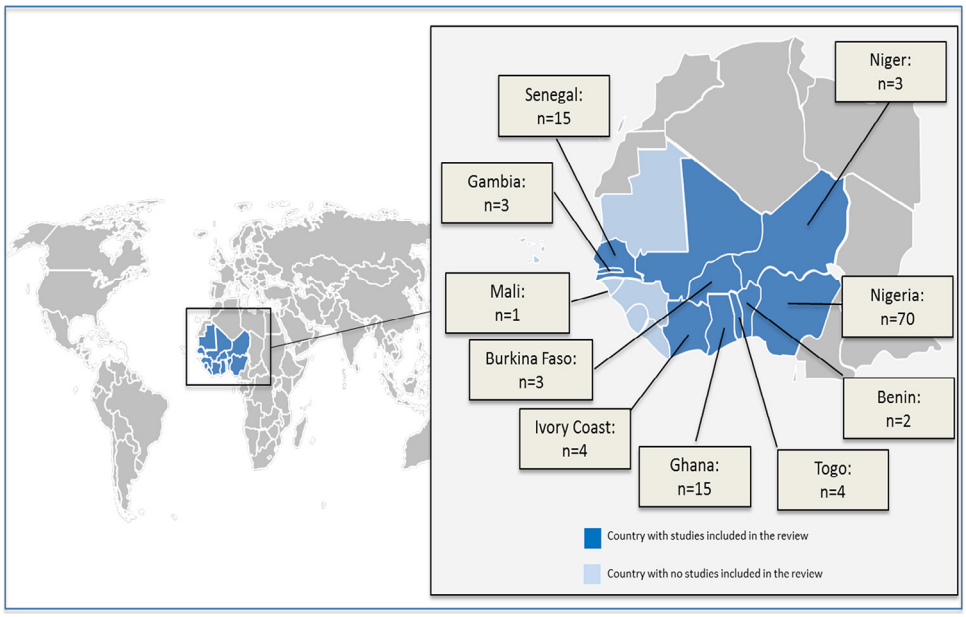


Fig. 3. Map of the West African region, with number of studies in the review by country.

(20/50; 40%), the NCCLS (19/50; 38%), the CLSI (7/50, 14%) and the British Society for Antimicrobial Chemotherapy (BSAC) (4/50, 8%).

3.2. Resistance rates for bacterial pathogens

3.2.1. Urinary tract infections (Table 1) [12–54]

Studies of UTI originated from Nigeria ($n = 31$), Senegal ($n = 4$), Ghana ($n = 4$), Benin ($n = 2$), Burkina Faso ($n = 1$) and Ivory Coast ($n = 1$). Among these studies, 53% focused on adult populations and 86% were conducted in urban settings. Resistance rates in inpatient and outpatient settings were examined separately (Table 1). In outpatient settings, among *E. coli* and *Klebsiella* spp. isolates, resistance to ampicillin was reported in 75.4% (95% CI 70.3–78.6%) and 97.0% (95% CI 89.3–100%) of strains, respectively. Trimethoprim/sulfamethoxazole (SXT) resistance was noted in 60.4% (95% CI 52.5–68.0%) of *E. coli* isolates and in 58.4% (95% CI 22.6–89.8%) of *Klebsiella* spp. isolates. Approximately one-third of urinary *E. coli* and *Klebsiella* isolates were resistant to amoxicillin/clavulanate (AMC), including 38.8% (95% CI 22.3–56.8%) of *E. coli* and 30.3% (95% CI 19.0–42.9%) of *Klebsiella* spp.

Among isolates from inpatients, levels of AMR were generally higher, including moderate to high rates of resistance to third-generation cephalosporins and aminoglycosides. Compared with other commonly used agents, the levels of resistance in inpatients to ciprofloxacin were lower in isolates of *E. coli* (24.0%, 95% CI 10.6–40.8%), *Klebsiella* spp. (22.0%, 5% CI 10.3–36.8%) and *P. aeruginosa* (22.2%, 95% CI 4.8–47.3%). SXT and ampicillin appeared to be poorly active for inpatient treatment of UTI.

3.2.2. Bloodstream infections (Table 2) [55–92]

Studies on BSIs originated from Nigeria ($n = 21$), Senegal ($n = 7$), Ghana ($n = 5$), The Gambia ($n = 2$), Burkina Faso ($n = 1$), Niger ($n = 1$) and Togo ($n = 1$). Among these studies, 84% reported results from paediatric populations and 87% were conducted in urban settings. The following overall rates of AMR were observed for antimicrobials among Gram-negative pathogens in blood: ampicillin, 68.4% (1257/1838); chloramphenicol, 52.4% (288/550); SXT, 54.7% (1077/1968); AMC, 41.5% (414/998); and gentamicin, 37.2% (572/1537). The most active antibiotics for Gram-negative BSIs were third-generation cephalosporins for which resistance was observed in 17.7% (156/879) of isolates, and fluoroquinolones for which resistance was observed in 12.1% (568/4701). In most studies, sensitivity to carbapenems (e.g. imipenem/cilastatin) was not tested.

Overall, 30.6% (95% CI 11.3–54.0%) of *S. aureus* bloodstream isolates were resistant to cloxacillin, 19.6% (95% CI 10.1–31.2%) were resistant to erythromycin and 44.7% (95% CI 29.5–60.3%) were reported resistant to SXT. For bloodstream isolates of salmonellae (both NTS and *Salmonella* Typhi), there was no reported resistance to ceftriaxone or ciprofloxacin, whilst moderate rates of resistance to SXT, ampicillin and chloramphenicol were reported.

Among *E. coli* and *Klebsiella* spp. isolates, a high rate of resistance to ampicillin and SXT was observed. Third-generation cephalosporins were active among *E. coli* and *Klebsiella* isolates associated with BSIs. However, some data to the contrary were observed. For example, a study of Nigerian children reported that 90% (9/10) of *E. coli* bloodstream isolates were resistant to ceftazidime [70]. A study from Nigeria reported an 82% (81/99) rate of ceftriaxone resistance among Klebsiellae isolated from blood [69]. Another Nigerian study from 1996 reported that 82% (14/17) of Klebsiellae were resistant to ceftazidime and 71% (12/17) to ceftriaxone [78].

3.2.3. Meningitis (Table 3) [93–119]

A total of 27 studies on meningitis were included in this review. Meningitis studies originated from Nigeria ($n = 10$), Ghana ($n = 5$), Senegal ($n = 4$), Ivory Coast ($n = 3$), Togo ($n = 3$), Mali ($n = 1$) and Niger ($n = 1$). Among these studies, 70% focused on paediatric populations and 93% were carried out in urban settings.

The following meningitis pathogens were included in this review: *S. pneumoniae*, *N. meningitidis* and *H. influenzae*. The overall rate of reported resistance to penicillin among *S. pneumoniae* and *N. meningitidis* was 13%. Resistance to penicillin was noted among 17.9% (95% CI 7.6–30.9%) of meningococcal isolates and 12.3% (95% CI 6.3–19.8%) of *S. pneumoniae* isolates. Ampicillin resistance was observed in 16.2% (95% CI 8.3–26.0%) of *H. influenzae* strains. Penicillin resistance was not routinely reported as intermediate or high-level. Cephalosporin resistance among *S. pneumoniae* was rarely reported [< 1% (3/365), ceftriaxone]. In contrast, the global resistance rate among *S. pneumoniae*, *N. meningitidis* and *H. influenzae* for chloramphenicol was 9.9% (300/3024). Moreover, 14.3% (95% CI

Table 1
Urinary tract infections: antimicrobial resistance rates of *Escherichia coli*, *Klebsiella* spp. and *Pseudomonas aeruginosa* stratified by outpatient and inpatient.

Antimicrobial agent	*E. coli*		*Klebsiella* spp.		*P. aeruginosa*	
	Pooled proportion (95% CI)	No. of studies (no. of isolates)	Pooled proportion (95% CI)	No. of studies (no. of isolates)	Pooled proportion (95% CI)	No. of studies (no. of isolates)
Ampicillin						
Inpatient	81.0 (63.4–93.8)	18 (2376)	90.2 (80.9–96.6)	11 (1041)	–	–
Outpatient	74.5 (70.3–78.6)	6 (1905)	97.0 (89.3–100)	4 (380)	–	–
Amoxicillin/clavulanic acid (AMC)						
Inpatient	52.5 (24.7–79.5)	11 (431)	77.5 (62.6–89.4)	5 (108)	–	–
Outpatient	38.8 (22.3–56.8)	6 (2723)	30.3 (19.0–42.9)	4 (390)	–	–
Ceftriaxone						
Inpatient	18.4 (9.9–28.4)	9 (641)	30.7 (15.1–48.7)	6 (238)	–	–
Outpatient	–	–	–	–	–	–
Ceftazidime						
Inpatient	47.7 (26.3–69.7)	9 (220)	44.5 (25.4–64.5)	7 (196)	25.0 [a]	2 (44)
Outpatient	26.0 (0–79.4)	3 (1491)	12.6 [a]	2 (278)	7.0	1 (43)
Gentamicin						
Inpatient	37.7 (25.7–50.5)	24 (2983)	42.1 (28.7–56.1)	13 (1016)	–	–
Outpatient	9.3 (4.2–16.1)	6 (2682)	13.5 (1.6–34.3)	4 (490)	–	–
Ciprofloxacin						
Inpatient	24.0 (10.6–40.8)	9 (2648)	22.1 (10.3–36.8)	5 (194)	22.2 (4.8–47.3)	3 (161)
Outpatient	11.7 (9.0–14.8)	5 (2666)	5.1 (0.5–14.0)	4 (608)	0.9	1 (219)
Trimethoprim/sulfamethoxazole (SXT)						
Inpatient	80.1 (67.0–90.6)	23 (2290)	85.3 (72.0–94.8)	13 (943)	–	–
Outpatient	60.4 (52.5–68.0)	7 (2915)	58.4 (22.6–89.8)	5 (524)	–	–

CI, confidence interval.

[a] When combining just two studies, the biostatistical analysis was limited. Therefore, mean resistance without the 95% CI was reported.

<20% resistance
20–39% resistance
40–59% resistance
60–79% resistance
80–100% resistance

9.7–19.5%) of pneumococcal isolates were resistant to chloramphenicol, and resistance to chloramphenicol was noted in 4.6% (95% CI 1.3–9.2%) of meningococcal isolates. Among *H. influenzae* strains, 9.7% (95% CI 5.5–14.9%) were resistant to chloramphenicol.

3.2.4. Diarrhoea (Table 4) [120–126]

Seven studies on diarrhoea were included from Nigeria ($n = 5$), Ghana ($n = 1$) and Niger ($n = 1$). Among these studies, 57% were performed among paediatric populations and more than one-half were

Table 2
Bloodstream infections: antimicrobial resistance rates of *Escherichia coli*, *Klebsiella pneumoniae* and *Klebsiella* spp., non-typhoidal *Salmonella* (NTS), *Salmonella enterica* serotype Typhi, *Streptococcus pneumoniae* and *Staphylococcus aureus*.

Antimicrobial agent	*E. coli*		*K. pneumoniae*/*Klebsiella* spp.		NTS		*Salmonella* Typhi		*S. pneumoniae*		*S. aureus*	
	Pooled proportion (95% CI)	No. of studies (no. of isolates)	Pooled proportion (95% CI)	No. of studies (no. of isolates)	Pooled proportion (95% CI)	No. of studies (no. of isolates)	Pooled proportion (95% CI)	No. of studies (no. of isolates)	Pooled proportion (95% CI)	No. of studies (no. of isolates)	Pooled proportion (95% CI)	No. of studies (no. of isolates)
Ampicillin	74.5 (61.9–85.4)	11 (754)	92.5 (80.5–99.5)	11 (586)	75.1 (54.2–91.3)	3 (308)	40.1 (6.5–79.8)	4 (190)	–	–	–	–
Penicillin	–	–	–	–	–	–	–	–	19.8 (0.3–53.2)	3 (71)	82.7 (66.9–94.5)	9 (251)
Oxacillin	–	–	–	–	–	–	–	–	–	–	56.9 [a]	1 (130)
Cloxacillin											30.6 (11.3–54.0)	13 (757)
Amoxicillin-clavulanic acid	56.2 (23.3–86.5)	5 (430)	66.1 (37.5–90.0)	6 (170)	56.7 (24.0–86.5)	3 (289)	14.3 [b]	2 (109)		–	–	–
Ceftriaxone	11.9 (4.3–22.0)	11 (720)	24.2 (8.1–44.8)	11 (476)	0	3 (278)	0	4 (198)	2.5 (0–17.2)	3 (41)	–	–
Ceftazidime	12.0 (4.1–22.6)	8 (645)	32.0 (21.3–43.7)	11 (554)	–	–	–	–	–	–	–	–
Gentamicin	21.6 (10.5–34.9)	12 (306)	54.7 (45.0–64.2)	15 (686)	–	–	–	–	–	–	–	–
Ciprofloxacin	13.2 (4.8–24.3)	7 (637)	11.8 (3.8–22.8)	5 (311)	0	3 (316)	0	4 (198)	–	–	23.0 (4.7–49.1)	6 (614)
Nalidixic acid	–	–	–	–	1.6	1 (125)	0.8 (0–5.6)	3 (69)	–	–	–	–
SXT	73.8 (56.5–88.1)	10 (555)	81.5 (70.3–90.8)	9 (322)	59.0 (24.6–89.0)	3 (258)	31.1 (10.5–56.1)	5 (211)	92.9 (78.4–100.0)	4 (86)	44.7 (29.5–60.3)	12 (536)
Chloramphenicol	–	–	–	–	65.1 (31.8–91.8)	3 (316)	38.3 (19.4–59.0)	4 (145)	15.3 (2.0–35.3)	4 (89)	–	–
Erythromycin	–	–	–	–	–	–	–	–	–	–	19.6 (10.1–31.2)	17 (1470)

CI, confidence interval; SXT, trimethoprim/sulfamethoxazole.

[a] Insufficient number of isolates to make an estimate regarding resistance.

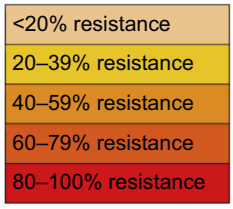
[b] When combining just two studies, the biostatistical analysis was limited. Therefore, mean resistance without the 95% CI was reported.

<20% resistance
20–39% resistance
40–59% resistance
60–79% resistance
80–100% resistance

Table 3
Meningitis: antimicrobial resistance rates of *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria meningitidis*.

Antimicrobial agent	*S. pneumoniae*		*H. influenzae*		*N. meningitidis*	
	Pooled proportion (95% CI)	No. of studies (no. of isolates)	Pooled proportion (95% CI)	No. of studies (no. of isolates)	Pooled proportion (95% CI)	No. of studies (no. of isolates)
Ampicillin	–	–	16.2 (8.3–26.0)	9 (735)	–	–
AMC	–	–	4.6	1 (175)	–	–
Penicillin	12.3 (6.3–19.8)	17 (2016)	–	–	17.9 (7.6–30.9)	11 (677)
Ceftriaxone	0.2 (0–1.4)	7 (365)	–	–	–	–
Cefotaxime	1.3 (0–6.8)	5 (782)	–	–	–	–
SXT	56.4 (37.0–74.8)	8 (974)	50.4 (19.1–81.5)	3 (240)	50.1 (32.2–68.0)	5 (213)
Chloramphenicol	14.3 (9.7–19.5)	18 (1550)	9.7 (5.5–14.9)	9 (684)	4.6 (1.3–9.2)	11 (790)

CI, confidence interval; SXT, trimethoprim/sulfamethoxazole.



conducted in rural settings. The following rates of AMR were observed among *E. coli* isolates: SXT, 66.5% (95% CI 37.6–90.0%); ampicillin, 71.2% (95% CI 46.8–90.4%); and gentamicin, 20.8% (95% CI 4.7–43.8%). Only 3.4% (95% CI 0–15.7%) of *E. coli* isolates were resistant to ciprofloxacin. *Shigella* spp. were commonly resistant to nalidixic acid (19.3%, 95% CI 2.1–45.9%) and SXT (86.9%, 95% CI 71.1–97.4%). Only one study reported AMR data on *V. cholerae* ($n = 30$ isolates), which did not allow for inclusion in the table).

4. Discussion

We found that in the West Africa region, particularly in patients with BSI and UTI, a moderate level of AMR is present and is likely to undermine typical empirical antibiotic strategies. This observation raises particular concern given the limited diagnostic capability and second-line treatment options in the public sector in West Africa. Existing antibiotic recommendations for syndrome-based management of bacterial infections may need to be reconsidered in this region given the growing prevalence of AMR. Another important finding is that there is a need for more standardised methodology in studies of bacterial illness in West Africa. We found a paucity of studies that made use of a prospective design that can provide the least biased information on the prevalence of key pathogens and AMR.

Previous studies have found that BSIs are frequently encountered in children admitted to hospital with fever in sub-Saharan Africa, particularly in those with risk factors including sickle cell anaemia, malnutrition and human immunodeficiency virus (HIV) infection [67,127–129]. We found that in the West Africa region among common bloodstream pathogens, including *Klebsiella* spp., *E. coli*, *Salmonella* Typhi and NTS, moderate rates of AMR to commonly used antibiotics, including ampicillin, SXT, gentamicin and AMC, were present. Current guidelines, including the WHO's '*Pocket book of hospital care for children*', recommend ampicillin and gentamicin as empirical treatment for sepsis [130]. These data, combined with the potential growth of methicillin-resistant *S. aureus* (MRSA) in the region, give reason to be concerned that ampicillin and gentamicin may no longer be optimal therapy in this region for sepsis/suspected BSIs. Ideally, empirical treatment should be driven by prospective clinical trials with epidemiological data, such as the data presented here, informing recommendations in the interim until such trials can be conducted.

We found that urinary tract pathogens in this region were associated with a moderate to high level of resistance to commonly used antibiotics. Studies from West Africa revealed moderate to high rates of AMR among *E. coli* and *Klebsiella* spp. to ampicillin, AMC and SXT both among inpatients and outpatients. In addition, AMR was unexpectedly observed among inpatients with UTIs to third-generation cephalosporins, suggesting that extended-spectrum β-lactamase (ESBL)-producing organisms may be important pathogens in this clinical context. Of note, current recommendations for the treatment of hospitalised children in the WHO's '*Pocket book of hospital care for children*' include SXT, ampicillin or amoxicillin [130]. Antibiotic resistance was lower in UTI isolates to fluoroquinolones; ciprofloxacin was moderately active among inpatients and was highly active in outpatients with UTI caused by *E. coli*, *Klebsiella* spp. and *P. aeruginosa*, suggesting that fluoroquinolones might be a better choice for UTI, especially in higher risk scenarios with symptoms or signs of upper tract infection or sepsis. Other potentially important antibiotics such as nitrofurantoin and fosfomycin were not tested but should be part of future studies. Prospective studies or, minimally, regular analysis of existing microbiology data are also needed to inform optimal treatment of UTI in West Africa.

Bacterial meningitis remains an important disease in West Africa, with the key pathogens known to be *S. pneumoniae*, *N. meningitidis*

Table 4
Diarrhoea: antimicrobial resistance rates of *Escherichia coli* and *Shigella* spp.

Antimicrobial agent	*E. coli*		*Shigella dysenteriae*/*Shigella* spp.	
	Pooled proportion (95% CI)	No. of studies (no. of isolates)	Pooled proportion (95% CI)	No. of studies (no. of isolates)
Ampicillin	71.2 (46.8–90.4)	5 (837)	81.7 [a]	2 (196)
AMC	59.8 [a]	2 (531)	–	–
Gentamicin	20.8 (4.7–43.8)	7 (1368)	–	–
Ciprofloxacin	3.4 (0–15.7)	3 (537)	100.0 [b]	1 (16)
Nalidixic acid	–	–	19.3 (2.1–45.9)	5 (379)
SXT	66.5 (37.6–90.0)	5 (1284)	86.9 (71.1–97.4)	4 (367)
Chloramphenicol	–	–	66.1 [a]	2 (196)
Tetracycline	–	–	–	–

CI, confidence interval; AMC, amoxicillin/clavulanic acid; SXT, trimethoprim/sulfamethoxazole.

[a] When combining just two studies, the biostatistical analysis was limited. Therefore, mean resistance without the 95% CI was reported.

[b] Insufficient number of isolates to make an estimate regarding resistance to ciprofloxacin.

<20% resistance
20–39% resistance
40–59% resistance
60–79% resistance
80–100% resistance

and *H. influenzae*. Overall levels of penicillin resistance were low among *S. pneumoniae* (12.3%) and no significant resistance was noted to ceftriaxone or cefotaxime. For meningococcal isolates, the overall reported rate of penicillin resistance across studies was slightly higher (16.2%). Chloramphenicol resistance rates were low for *S. pneumoniae*, *N. meningitidis* and *H. influenzae*, suggesting that this antibiotic remains an alternative when first-line agents, safer are not available. Ampicillin resistance was noted in 16.2% of *H. influenzae*, which is consistent with the 28% reported in a recent meta-analysis [131]. Third-generation cephalosporins remain highly active against strains of *S. pneumoniae* causing meningitis in this region; they have historically been effective against *N. meningitidis* in the region and remain an excellent empirical choice for bacterial meningitis in West Africa when available.

There were few studies on the epidemiology of pneumonia and AMR associated with pneumonia in West Africa. As a result, we did not include these data in our analysis [132–136]. The epidemiology of pneumonia will change with the broader use of effective vaccines for *S. pneumoniae* and *H. influenzae*. Large, prospective clinical trials, including studies in progress, will help to meet this gap [137]. Studies of diarrhoea from West Africa were also limited. *Escherichia coli* and *Shigella* spp. were common isolates in patients with diarrhoea syndromes in the region. The overall level of resistance to SXT and ampicillin was high for both pathogens. For hospitalised children with dysentery, WHO guidelines recommend fluoroquinolones and recommend against SXT and ampicillin/amoxicillin, which appears consistent with our data. For *Shigella* spp. specifically, there was insufficient data to draw definitive conclusions regarding sensitivity to ciprofloxacin, but the majority of studies suggest that as empirical therapy for suspected bacterial diarrhoeal syndromes in this region, a fluoroquinolone is justified.

There are several limitations to this study. First, there were too few studies of patients with pneumonia or bacterial diarrhoea to make robust estimates about the prevalence of resistance in pulmonary and diarrhoea-associated bacterial pathogens in West Africa. A second limitation was that publications from certain countries were exceedingly scarce. These countries, including Niger, Mali, Sierra Leone and Burkina Faso, are some of the very poorest countries in the region. The net effect is that the analysis oversamples from certain countries (particularly Nigeria and Senegal) whilst undersampling others, such that conclusions drawn may not be valid for all countries in the region. Even within individual countries, AMR rates are unlikely to be homogenous and are likely to differ, particularly between urban and rural contexts. A greater number of studies from a diversity of contexts within individual countries are also needed to construct the most accurate estimates of antibiotic resistance.

A third limitation was that studies of bacterial infections in this region had a heterogeneous methodology. Many studies could not be included because of convenience sampling (study design), inappropriate results reporting (e.g. combining all Gram-negatives in a single category) or vague methodology. A particular challenge was the absence of a standardised panel of antibiotics against which

Gram-positive and Gram-negative organisms were tested, which can make it difficult to combine results across studies. Last, we may be overestimating rates of AMR because microbiology in Africa, when available, tends to be a diagnostic tool within referral hospitals where there is likely to be more antibiotic pressure and a greater proportion of patients presenting with treatment failure and/or after empirical antibiotics elsewhere. More rigorous research is needed, particularly prospective trials in community settings, to avoid this potential source of bias. Strengths include the use of a planned systematic approach, a broad search strategy spanning 20 years of published research, and inclusion criteria based on common clinical syndromes rather than pathogens (given that most clinicians in the region work without microbiology support) as well as the involvement of authors with expertise both in microbiology and clinical infectious diseases.

The current review, by combining multiple studies, provides an initial estimate of the level of AMR in the West Africa region and illustrates where large knowledge gaps exist both by disease and by geography. At this point, the emergence of AMR in bacterial syndromes is not yet reflected in key treatment guidelines. Optimal empirical antibiotic treatment of common invasive bacterial infections in this region should, in the long-run, be informed by prospective clinical trials; there are currently very few high-quality studies of this type. Considering how little is known about the actual clinical impact of AMR and the disadvantages of reflexively escalating to strategies based on empirical use of broader-spectrum agents such as cephalosporins, rigorous therapeutic studies are needed. Ignoring the emergence of AMR in West Africa is not an option. The negative impact of resistance on patient outcomes in BSI is beginning to be documented in sub-Saharan Africa [138]. Quantifying and responding to AMR will be premised on greater funding, investments in laboratory capacity which remains inadequate in the region, development of affordable novel antimicrobial agents, and support for high-quality patient-oriented research that can produce more rigorous prospective studies to guide more effective use of empirical antibiotics in this most underserved area of the world.

Acknowledgment

The authors thank Aline Raymond (Médecins Sans Frontières, Brussels, Belgium) for helping to locate the relevant publications.

Funding: None.

Competing interests: None declared.

Ethical approval: Not required.

References

[1] World Health Organization. The evolving threat of antimicrobial resistance: option for action. Geneva, Switzerland: WHO; 2012.
[2] World Health Organization. Antimicrobial resistance—global report on surveillance. Geneva, Switzerland: WHO; 2014.
[3] Frean J, Perovic O, Fensham V, McCarthy K, von Gottberg A, de Gouveia L, et al. External quality assessment of national public health laboratories in Africa, 2002–2009. Bull World Health Organ 2012;90:191–9A.
[4] Moher D, Liberati A, Tetzlaff J, Altman DG, Group PRISMA. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:e1000097.
[5] United Nations Statistics Division. *Standard country and area codes for statistical use (M49)*. UN Statistics Division; 2013. Available from: http://unstats.un.org/unsd/methods/m49/m49regin.htm [Accessed 22 August 2017].
[6] National Committee for Clinical Laboratory Standards. Analysis and presentation of cumulative antimicrobial susceptibility test data; approved guideline. *Document M39-A*. Wayne, PA: NCCLS; 2002.
[7] World Health Organization. Surveillance standards for antimicrobial resistance. Geneva, Switzerland: WHO; 2002.
[8] Fleiss JL. The statistical basis of meta-analysis. Stat Methods Med Res 1993;2:121–45.
[9] Freeman MF, Tukey JW. Transformations related to the angular and the square root. Ann Math Stat 1950;21:607–11.
[10] Miller J. Inverse of the Freeman–Tukey double arcsine transformation. Am Stat 1978;32:138.
[11] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88.
[12] Karou SD, Ilboudo IP, Nadembega WM, Ameyapoh Y, Ouermi D, Pignatelli S, et al. Antibiotic resistance in urinary tract bacteria in Ouagadougou. Pak J Biol Sci 2009;12:712–16.
[13] Kouassi-M'bengue A, Folquet-Amorissani M, Nassirou F, Guessennd-Kouadio N, Kacou-N'Douba A, Houenou Y, et al. Neonatal urinary tract infections in Abidjan: the problem of bacterial resistance. Mali Med 2008;23:34–7, [in French].
[14] Bosu WK, Acquah S. Susceptibility of urinary tract bacteria to antibiotics in Cape Coast, Ghana. East Afr Med J 1996;73:468–70.
[15] Adjei O. Antibiotic susceptibility of urinary pathogens from inpatients in Kumasi, Ghana. Trop Doct 1993;23:29–30.
[16] Adjei O, Opoku C. Urinary tract infections in African infants. Int J Antimicrob Agents 2004;24(Suppl. 1):S32–4.
[17] Oli AN, Okafor CI, Ibezim EC, Akujiobi CN, Onwunzo MC. The prevalence and bacteriology of asymptomatic bacteriuria among antenatal patients in Nnamdi Azikiwe University Teaching Hospital Nnewi; South Eastern Nigeria. Niger J Clin Pract 2010;13:409–12.
[18] Brown BJ, Asinobi AO, Fatunde OJ, Osinusi K, Fasina NA. Antimicrobial sensitivity pattern of organisms causing urinary tract infection in children with sickle cell anaemia in Ibadan, Nigeria. West Afr J Med 2003;22:110–13.
[19] Akinloye O, Ogbolu DO, Akinloye OM, Terry Alli OA. Asymptomatic bacteriuria of pregnancy in Ibadan, Nigeria: a re-assessment. Br J Biomed Sci 2006;63:109–12.
[20] Adeyemo AA, Gbadegesin RA, Onyemenem TN, Ekweozor CC. Urinary tract pathogens and antimicrobial sensitivity patterns in children in Ibadan, Nigeria. Ann Trop Paediatr 1994;14:271–4.
[21] Rabasa AI, Gofama MM. Urinary tract infection in febrile children in Maiduguri north eastern Nigeria. Niger J Clin Pract 2009;12:124–7.
[22] Omoregie R, Eghafona NO. Urinary tract infection among asymptomatic HIV patients in Benin City, Nigeria. Br J Biomed Sci 2009;66:190–3.
[23] Oladeinde BH, Omoregie R, Olley M, Anunibe JA. Urinary tract infection in a rural community of Nigeria. N Am J Med Sci 2011;3:75–7.
[24] Kehinde A, Adedapo K, Aimakhu C, Odukogbe AT, Olayemi O, Salako B. Urinary pathogens and drug susceptibility patterns of urinary tract infections among antenatal clinic attendees in Ibadan, Nigeria. J Obstet Gynaecol Res 2012;38:280–4.
[25] Onifade EO, Nwobu RA, Bamidele EO, Okanume C. Pathogens and antibiotic susceptibility profiles in the urinary tract. East Afr Med J 1992;69:587–90.
[26] Jombo GT, Jonah P, Ayeni JA. Multiple resistant *Pseudomonas aeruginosa* in contemporary medical practice: findings from urinary isolates at a Nigerian University Teaching Hospital. Niger J Physiol Sci 2008;23:105–9.
[27] Muoneke V, Ibekwe M, Ibekwe R. Childhood urinary tract infection in Abakaliki: etiological organisms and antibiotic sensitivity pattern. Ann Med Health Sci Res 2012;2:29–32.
[28] Alebiosu CO, Osinupebi OA, Olajubu FA. Significant asymptomatic bacteriuria among Nigerian type 2 diabetics. J Natl Med Assoc 2003;95:344–9.
[29] Musa-Aisien AS, Ibadin OM, Ukoh G, Akpede GO. Prevalence and antimicrobial sensitivity pattern in urinary tract infection in febrile under-5s at a children's emergency unit in Nigeria. Ann Trop Paediatr 2003;23:39–45.
[30] Rabasa AI, Shattima D. Urinary tract infection in severely malnourished children at the University of Maiduguri Teaching Hospital. J Trop Pediatr 2002;48:359–61.
[31] Dada-Adegbola HO, Muili K. Antibiotic susceptibility pattern of urinary tract pathogens in Ibadan, Nigeria. Afr J Med Med Sci 2010;39:173–9.
[32] Okesola AO, Aroundegbe T. Antibiotic resistance pattern of uropathogenic *Escherichia coli* in South West Nigeria. Afr J Med Med Sci 2011;40:235–8.
[33] Okafor UE, Ogunsola FT, Osinupebi OA. Aetiology of catheter-associated bacteriuria in Lagos University Teaching Hospital. Niger Postgrad Med J 2005;12:89–92.
[34] Habib AG, Nwokedi EE, Ihesiulor UI, Mohammed A, Habib ZG. Widespread antibiotic resistance in savannah Nigeria. Afr J Med Med Sci 2003;32:303–5.
[35] Omoregie R, Igbarumah IO, Egbe CA, Ogefere H. Urinary tract infections among the elderly in Benin City, Nigeria. Fooyin J Health Sci 2010;2:90–3.
[36] Oboderin OA, Abdu AR, Odetoyin B, Lamikanra A. Antimicrobial resistance in *Escherichia coli* strains from urinary tract infections. J Natl Med Assoc 2009;101:1268–73.
[37] Dromigny JA, Nabeth P, Juergens-Behr A, Perrier-Gros-Claude JD. Risk factors for antibiotic-resistant *Escherichia coli* isolated from community-acquired urinary tract infections in Dakar, Senegal. J Antimicrob Chemother 2005;56:236–9.
[38] Dromigny JA, Ndoye B, Macondo EA, Nabeth P, Siby T, Perrier-Gros-Claude JD. Increasing prevalence of antimicrobial resistance among Enterobacteriaceae uropathogens in Dakar, Senegal: a multicenter study. Diagn Microbiol Infect Dis 2003;47:595–600.
[39] Dromigny JA, Nabeth P, Perrier Gros Claude JD. Distribution and susceptibility of bacterial urinary tract infections in Dakar, Senegal. Int J Antimicrob Agents 2002;20:339–47.
[40] Mordi RM, Erah PO. Susceptibility of common urinary isolates to the commonly used antibiotics in a tertiary hospital in southern Nigeria. Afr J Biotech 2006;5:1067–71.
[41] Famurewa O. Prevalence of urinary tract infection in women in Ado-Ekiti, Ondo State, Nigeria. Ig Mod 1992;97:580–91.

[42] Wariso KT, Siminialayi IM, Odigie JO. Pattern and antibiogram of urinary tract infection at the University of Port Harcourt Teaching Hospital. Asian Pac J Trop Med 2010;3:66–9.
[43] Omigie O, Okoror L, Umolu P, Ikuuh G. Increasing resistance to quinolones: a four-year prospective study of urinary tract infection pathogens. Int J Gen Med 2009;2:171–5.
[44] Okwori EE, Nwadioha SI, Jombo GTA, Nwokedi EOP, Odimayo MS. A comparative study of bacterial isolates from the urine samples of AIDS and non-AIDS patients in Benue, Nigeria. Asian Pac J Trop Med 2010;3:382–5.
[45] Nwadioha S, Nwokedi E, Jombo G, Kashibu E, Alao O. Antibiotics susceptibility pattern of uropathogenic bacterial isolates from community and hospital acquired urinary tract infections in a Nigerian tertiary hospital. Int J Infect Dis 2009;8.
[46] Mava Y, Bello M, Ambe JP, Zailani SB. Antimicrobial sensitivity pattern of organisms causing urinary tract infection in children with sickle cell anemia in Maiduguri, Nigeria. Niger J Clin Pract 2012;15:420–3.
[47] Inyang-Etoh PC, Udofia GC, Alaribe AAA, Udonwa NE. Asymptomatic bacteriuria in patients on antiretroviral drug therapy in Calabar. J Med Sci 2009;9:270–5.
[48] Sire JM, Nabeth P, Perrier-Gros-Claude JD, Bahsoun I, Silby T, Macondo EA, et al. Antimicrobial resistance in outpatient *Escherichia coli* urinary isolates in Dakar, Senegal. J Infect Dev Ctries 2007;1:263–8.
[49] Ako-Nai AK, Kassim OO, Adeniran MO, Taiwo O. A study of urinary tract infections at Ile-Ife, Nigeria. East Afr Med J 1993;70:10–14.
[50] Odonkor ST, Mahami T, Addo KK. Antimicrobial sensitivity patterns of urine isolates from a large Ghanaian hospital. Int Res J Microbiol 2011;2:237–41.
[51] Anagonou SY, Eslahpazire J, Makoutode M, Josse R, Massougbodji A, Sadeler BC. Antibiotic sensitivity of Gram negative bacilli isolated from urinary tract infections at NUHC of Cotonou (Benin) from March to December 1992. Bull Soc Pathol Exot 1994;87:223–5, [in French].
[52] Anagonou SY, Eslahpazire J, Makoutode M, Josse R, Massougbodji A, Sadeler BC. Susceptibility of Gram-negative bacilli strains isolated from urinary tract infections in office practice at Cotonou (Benin). Med Mal Infect 1995;25:766–9, [in French].
[53] Wammanda RD, Ewa BO. Urinary tract pathogens and their antimicrobial sensitivity patterns in children. Ann Trop Paediatr 2002;22:197–8.
[54] Otoikhian CSO, Okoror IE, Ekakitie AO. Bacteriological assessment of urinary tract infection in Ogume and its environment. Int J Pharm Med Biol Sci 2012;1:246–58.
[55] Hill PC, Onyeama CO, Ikumapayi UNA, Secka O, Ameyaw S, Simmonds N, et al. Bacteraemia in patients admitted to an urban hospital in West Africa. BMC Infect Dis 2007;7:2.
[56] Okomo UA, Garba D, Fombah AE, Secka O, Ikumapayi UN, Udo JJ, et al. Bacterial isolates and antibiotic sensitivity among Gambian children with severe acute malnutrition. Int J Pediatr 2011;2011:825123.
[57] Nielsen MV, Sarpong N, Krumkamp R, Dekker D, Loag W, Amemasor S, et al. Incidence and characteristics of bacteremia among children in rural Ghana. PLoS ONE 2012;7:e44063.
[58] Enweronu-Laryea CC, Newman MJ. Changing pattern of bacterial isolates and antimicrobial susceptibility in neonatal infections in Korle Bu Teaching Hospital, Ghana. East Afr Med J 2007;84:136–40.
[59] Anyebuno M, Newman M. Common causes of neonatal bacteraemia in Accra, Ghana. East Afr Med J 1995;72:805–8.
[60] Gross U, Amuzu SK, de Ciman R, Kassimova I, Gross L, Rabsch W, et al. Bacteremia and antimicrobial drug resistance over time, Ghana. Emerg Infect Dis 2011;17:1879–82.
[61] Seydi M, Soumare M, Sow AI, Diop BM, Sow PS. *Escherichia coli* meningitis during bacteremia in the Ibrahima-Diop-Mar infectious diseases clinic, Dakar Fann National Hospital Center (Senegal). Med Mal Infect 2005;35:344–8, [in French].
[62] Lefebvre N, Gning SB, Nabeth P, Ka S, Ba-Fall K, Rique M, et al. Clinical and laboratory features of typhoid fever in Senegal. A 70-case study. Med Trop (Mars) 2005;65:543–8, [in French].
[63] Cissé MF, Sow AI, Ba M, Ouangre AR, Samb A. Bacteriology of neonatal septicemia in Dakar. Presse Med 1992;21:413–16, [in French].
[64] Mokuolu AO, Jiya N, Adesiyun OO. Neonatal septicaemia in Ilorin: bacterial pathogens and antibiotic sensitivity pattern. Afr J Med Med Sci 2002;31:127–30.
[65] Okuonghae HO, Nwankwo MU, Offor EC. Pattern of bacteraemia in febrile children with sickle cell anaemia. Ann Trop Paediatr 1993;13:55–64.
[66] Iregbu KC, Elegba OY, Babaniyi IB. Bacteriological profile of neonatal septicaemia in a tertiary hospital in Nigeria. Afr Health Sci 2006;6:151–4.
[67] Page A-L, de Rekeneire N, Sayadi S, Aberrane S, Janssens A-C, Rieux C, et al. Infections in children admitted with complicated severe acute malnutrition in Niger. PLoS ONE 2013;8:e68699.
[68] Meremikwu MM, Nwachukwu CE, Asuquo AE, Okebe JU, Utsalo SJ. Bacterial isolates from blood cultures of children with suspected septicaemia in Calabar, Nigeria. BMC Infect Dis 2005;5:110.
[69] West BA, Peterside O. Sensitivity pattern among bacterial isolates in neonatal septicaemia in Port Harcourt. Ann Clin Microbiol Antimicrob 2012;11:7.
[70] Omoregie R, Egbe CA, Ogefere HO, Igbarumah I, Omijie RE. Effects of gender and seasonal variation on the prevalence of bacterial septicemia among young children in Benin City, Nigeria. Libyan J Med 2009;4:107–9.
[71] Obaro S, Lawson L, Essen U, Ibrahim K, Brooks K, Otuneye A, et al. Community acquired bacteremia in young children from central Nigeria—a pilot study. BMC Infect Dis 2011;11:137.
[72] Ako-Nai AK, Adejuyigbe EA, Ajayi FM, Onipede AO. The bacteriology of neonatal septicaemia in Ile-Ife, Nigeria. J Trop Pediatr 1999;45:146–51.
[73] Ako-Nai AK, Taiwo O, Ebri A, Adeniran MO. Bacterial isolates involved in cases of septicaemia in a Nigerian hospital. East Afr Med J 1990;67:407–12.
[74] Antia-Obong OE. Utsalo SJ. Bacterial agents in neonatal septicaemia in Calabar, Nigeria (a review of 100 cases). Trop Doct 1991;21:169–70.
[75] Anah MU, Udo JJ, Ochigbo SO, Abia-Bassey LN. Neonatal septicaemia in Calabar, Nigeria. Trop Doct 2008;38:126–8.
[76] Akpede GO, Adeyemi O, Ambe JP. Trends in the susceptibility to antimicrobial drugs of common pathogens in childhood septicaemia in Nigeria: experience at the University of Maiduguri Teaching Hospital, Nigeria, 1991–1994. Int J Antimicrob Agents 1995;6:91–7.
[77] Egri-Okwaji MT, Iroha EO, Kesah CN, Odugbemi TO. Bacteria causing septicaemia in neonates with tetanus. West Afr J Med 1998;17:136–9.
[78] Egri-Okwaji MTC, Iroha EO, Kesah CN, Odugbemi T. Bacterial pathogens causing neonatal sepsis in an out-born neonatal unit in Lagos, Nigeria. Nig Q J Hosp Med 1996;6:149–52.
[79] Imade PE, Eghafona NO. Incidence of bacteremia in antiretroviral-naive HIV-positive children less than five years of age in Benin City, Nigeria. Libyan J Med 2010;5:1–2.
[80] Osinupedbi OA, Olajubu FA. Bacteraemia—a Sagamu perception. Afr J Med Med Sci 2003;32:311–14.
[81] Samuel SO, Fadeyi A, Akanbi IIAA, Ameen NB, Nwabuisi C, Onile BA. Bacterial isolates of blood cultures in patients with suspected septicaemia in Ilorin, Nigeria. Afr J Med Med Sci 2006;35:137–41.
[82] Seydi M, Soumare M, Sow AI, Diop SA, Sow I, Dieng AB, et al. Nontyphoidal *Salmonella* bacteremia cases in AIDS patients in a Dakar University Hospital (Senegal). Med Mal Infect 2008;38:25–8, [in French].
[83] Seydi M, Sow AI, Soumare M, Diallo HM, Hatim B, Tine R, et al. *Staphylococcus aureus* bacteremia in the Dakar Fann University Hospital. Med Mal Infect 2004;34:210–15, [in French].
[84] Seydi M, Soumare M, Sow AI, Diop BM, Sow PS. Current aspects of *Salmonella* bacteremia cases in the Ibrahima Diop Mar Infectious Diseases clinic, Fann National Hospital Center (Senegal). Med Mal Infect 2005;35:23–7, [in French].
[85] Ogunlesi TA, Ogunfowora OB, Osinupebi O, Olanrewaju DM. Changing trends in newborn sepsis in Sagamu, Nigeria: bacterial aetiology, risk factors and antibiotic susceptibility. J Paediatr Child Health 2011;47:5–11.
[86] Nwadioha SI, Nwokedi EOP, Odimayo MS, Okwori EE, Kashibu E. Bacterial isolates in blood cultures of children with suspected septicaemia in a Nigerian tertiary hospital. Int J Infect Dis 2010;8.
[87] Oni AA, Ogunkunle MO, Oke AA, Bakare RA. Pattern of Gram negative rods bacteraemia in diabetic patients in Ibadan, Nigeria. Afr J Med Med Sci 2000;29:207–10.
[88] Schwarz NG, Sarpong N, Hunger F, Marks F, Acquah SE, Agyekum A, et al. Systemic bacteraemia in children presenting with clinical pneumonia and the impact of non-typhoid salmonella (NTS). BMC Infect Dis 2010;10:319.
[89] Ouédraogo AS, Dakouré-Kissou A, Poda GE, Koueta F, Yé-Ouattara D, Ouédraogo-Traoré R. Epidemiology, microbiology, and outcomes of septicemia in children treated at the Charles de Gaulle University Pediatric Hospital in Burkina Faso. Sante 2011;21:221–5, [in French].
[90] Gbadoe AD, Lawson-Evi K, Dagnra AY, Guedenon K, Geraldo A, Djadou E, et al. Pediatric salmonellosis at the Tokoin's teaching hospital, Lomé (Togo). Med Mal Infect 2008;38:8–11, [in French].
[91] Obidike EO, Anigbo G, Igbodo C. Sensitivity pattern of bacterial isolates in childhood sepsis in clinical practice at Onitsha. Niger J Clin Pract 2009;12:302–5.
[92] Ojukwu J, Abonyi LE, Ugwu J, Orji IK. Neonatal septicemia in high risk babies in South-Eastern Nigeria. J Perinat Med 2006;34:166–72.
[93] Edoh V, Wognin E, Aoussi E, Loukou YG. Surveillance of the sensitivity of antibiotics to the principal germs responsible for purulent meningitis at the University Hospital Center in Treichville from 1986 to 1991. Med Trop (Mars) 1992;52:267–71, [in French].
[94] Edoh V, Kakou AR, Tia H, Oulai SM. Sensitivity to penicillin G of isolates of pneumococci meningitis and therapeutic implication in CHU of Treichville, Abidjan. Bull Soc Pathol Exot 2005;98:9–10, [in French].
[95] Boisier P, Mainassara HB, Sidikou F, Djibo S, Kairo KK, Chanteau S. Case-fatality ratio of bacterial meningitis in the African meningitis belt: we can do better. Vaccine 2007;25(Suppl. 1):A24–9.
[96] Manga NM, Ndour CT, Diop SA, Ka-Sall R, Dia NM, Seydi M, et al. Adult purulent meningitis caused by *Streptococcus pneumoniae* in Dakar, Senegal. Med Trop (Mars) 2008;68:625–8, [in French].
[97] Akpede GO, Adeyemi O, Abba AA, Sykes RM. Pattern and antibiotic susceptibility of bacteria in pyogenic meningitis in a children's emergency room population in Maiduguri, Nigeria, 1988–1992. Acta Paediatr 1994;83:719–23.
[98] Alhaji MA, Ahmed H, Femi OO. Changing pattern of antibiotic sensitivity of *Neisseriae meningitidis* from children with meningococcal meningitis in North Eastern Nigeria. Niger J Clin Pract 2009;12:79–82.
[99] Akpede O, Abiodun PO, Sykes M, Salami CE. Childhood bacterial meningitis beyond the neonatal period in southern Nigeria: changes in organisms/antibiotic susceptibility. East Afr Med J 1994;71:14–20.
[100] Ogunlesi TA, Okeniyi JA, Oyelami OA. Pyogenic meningitis in Ilesa, Nigeria. Indian Pediatr 2005;42:1019–23.
[101] Ako-Nai AK, Taiwo O. Bacterial isolates in meningitis. East Afr Med J 1993;70:198–201.

[102] Commey JO, Rodrigues OP, Akita FA, Newman M. Bacterial meningitis in children in southern Ghana. East Afr Med J 1994;71:113–17.
[103] Holliman RE, Liddy H, Johnson JD, Adjei O. Epidemiology of invasive pneumococcal disease in Kumasi, Ghana. Trans R Soc Trop Med Hyg 2007;101:405–13.
[104] Adjei O, Agbemadzo T. Susceptibility of *Streptococcus pneumoniae* strains isolated from cerebrospinal fluid in Ghana. J Antimicrob Chemother 1996;38:746–7.
[105] Owusu M, Nguah SB, Boaitey YA, Badu-Boateng E, Abubakr AR, Lartey RA, et al. Aetiological agents of cerebrospinal meningitis: a retrospective study from a teaching hospital in Ghana. Ann Clin Microbiol Antimicrob 2012;11:28.
[106] Mackie EJ, Shears P, Frimpong E, Mustafa-Kutana SN. A study of bacterial meningitis in Kumasi, Ghana. Ann Trop Paediatr 1992;12:143–8.
[107] Karou SD, Balaka A, Bamoke M, Tchelougou D, Assih M, Anani K, et al. Epidemiology and antibiotic resistance of bacterial meningitis in Dapaong, northern Togo. Asian Pac J Trop Med 2012;5:848–52.
[108] Johnson AW, Adedoyin OT, Abdul-Karim AA, Olanrewaju AW. Childhood pyogenic meningitis: clinical and investigative indicators of etiology and outcome. J Natl Med Assoc 2007;99:937–47.
[109] Johnson WB, Adedoyin OT, Abdulkarim AA, Olanrewaju WI. Bacterial pathogens and outcome determinants of childhood pyogenic meningitis in Ilorin, Nigeria. Afr J Med Med Sci 2001;30:295–303.
[110] Emele FE. Etiologic spectrum and pattern of antimicrobial drug susceptibility in bacterial meningitis in Sokoto, Nigeria. Acta Paediatr 2000;89:942–6.
[111] Onyemelukwe NF. *Haemophilus influenzae* meningitis in parts of eastern Nigeria. East Afr Med J 1994;71:129–31.
[112] Akoua-Koffi C. Bacteriological aspects of purulent meningitis in the Yopougon university hospital, 1995–1998. Med Mal Infect 2001;31:482–7, [in French].
[113] Koumare B, Bougoudogo F, Cisse M, Doumbia T, Keita MM. Bacteriological aspects of purulent meningitis in Bamako district. Apropos of 1541 bacterial strains collected from 1979 to 1991. Bull Soc Pathol Exot 1993;86:136–40, [in French].
[114] Camara B, Cisse MF, Faye PM, Ba M, Tall-Dia A, Diouf S, et al. Purulent meningitis in a pediatric hospital in Dakar (Senegal). Med Mal Infect 2003;33:422–6, [in French].
[115] Camara B, Faye PM, Diouf S, Gueye-Diagne NR, Diagne I, Cisse MF, et al. Pediatric *Haemophilus influenzae* b meningitis in Dakar. Med Mal Infect 2007;37:753–7, [in French].
[116] Dagnra AY, Tigossou S, Prince-David M. Prevalence and antimicrobial susceptibility of bacterial meningitis. Med Mal Infect 2000;30:291–4, [in French].
[117] Gbadoe AD, Atakouma Y, Gbadoe AH, Agbodji K, Assimadi K, Gnamey K, et al. Pneumococcal meningitis in Togo. Arch Pediatr 1996;3:1045–6, [in French].
[118] Airede KI, Adeyemi O, Ibrahim T. Neonatal bacterial meningitis and dexamethasone adjunctive usage in Nigeria. Niger J Clin Pract 2008;11:235–45.
[119] Seydi M, Sow AI, Soumare M, Ndour CT, Dia NM, Samb A, et al. Meningococcal meningitis in a Dakar hospital: a study on 58 patients. Med Mal Infect 2000;30:468–73, [in French].
[120] Obi CL, Coker AO, Epoke J, Ndip RN. Distributional patterns of bacterial diarrhoeagenic agents and antibiograms of isolates from diarrhoeaic and non-diarrhoeaic patients in urban and rural areas of Nigeria. Cent Afr J Med 1998;44:223–9.
[121] Okeke IN, Lamikanra A, Czeczulin J, Dubovsky F, Kaper JB, Nataro JP. Heterogeneous virulence of enteroaggregative *Escherichia coli* strains isolated from children in Southwest Nigeria. J Infect Dis 2000;181:252–60.
[122] Chigor VN, Umoh VJ, Smith SI, Igbinosa EO, Okoh AI. Multidrug resistance and plasmid patterns of *Escherichia coli* O157 and other *E. coli* isolated from diarrhoeal stools and surface waters from some selected sources in Zaria, Nigeria. Int J Environ Res Public Health 2010;7:3831–41.
[123] Lamikanra A, Ako-Nai AK, Ola JB. Transmissible trimethoprim resistance in strains of *Escherichia coli* isolated from cases of infantile diarrhoea. J Med Microbiol 1990;32:159–62.
[124] Djie-Maletz A, Reither K, Danour S, Anyidoho L, Saad E, Danikuu F, et al. High rate of resistance to locally used antibiotics among enteric bacteria from children in Northern Ghana. J Antimicrob Chemother 2008;61:1315–18.
[125] Iwalokur BA, Gbenle GO, Akinrinmisi EO, Smith SI, Ogunledun A. Substrate profile variation and drug resistance patterns of a β-lactamase producing *Shigella* species isolated from diarrhoeal patients in Lagos, Nigeria. Afr J Med Med Sci 2004;33:51–5.
[126] Akortha EE, Egbule OS. Transfer of tetracycline resistance gene (*tetR*) between replicons in some enteric bacteria of diarrhoeal origin from some hospitals in South-South, Nigeria. Afr J Biotech 2008;7:3178–81.
[127] Musiime V, Cook A, Bakeera-Kitaka S, Vhembo T, Lutakome J, Keishanyu R, et al. Bacteremia, causative agents and antimicrobial susceptibility among HIV-1-infected children on antiretroviral therapy in Uganda and Zimbabwe. Pediatr Infect Dis J 2013;32:856–62.
[128] Williams TN, Uyoga S, Macharia A, Ndila C, McAuley CF, Opi DH, et al. Bacteraemia in Kenyan children with sickle-cell anaemia: a retrospective cohort and case–control study. Lancet 2009;374:1364–70.
[129] Berkley JA, Lowe BS, Mwangi I, Williams T, Bauni E, Mwarumba S, et al. Bacteremia among children admitted to a rural hospital in Kenya. N Engl J Med 2005;352:39–47.
[130] World Health Organization. *Pocket book of hospital care for children: 2nd edition.* Guidelines for the management of common illnesses with limited resources. Geneva, Switzerland: WHO; 2013. Available from: http://www.who.int/maternal_child_adolescent/documents/child_hospital_care/en/ [Accessed 23 August 2017].
[131] Ginsburg AS, Tinkham L, Riley K, Kay NA, Klugman KP, Gill C. Antibiotic non-susceptibility among *Streptococcus pneumoniae* and *Haemophilus influenzae* isolates identified in African cohorts: a meta-analysis of three decades of published studies. Int J Antimicrob Agents 2013;42:482–91.
[132] Ouedraogo SM, Toloba Y, Badoum G, Ouedraogo G, Boncoungou K, Bambara M, et al. Epidemio-clinical aspects of adult acute bacterial pneumonia at Yalgado Ouédraogo University Health Center. Mali Med 2010;25:15–18, [in French].
[133] Adegbola RA, Hill PC, Secka O, Ikumapayi UN, Lahai G, Greenwood BM, et al. Serotype and antimicrobial susceptibility patterns of isolates of *Streptococcus pneumoniae* causing invasive disease in The Gambia 1996–2003. Trop Med Int Health 2006;11:1128–35.
[134] Adeleye A, Uju L, Idika N, Sobande O. Cotrimoxazole resistance in *Streptococcus pneumoniae* isolated from sputum of HIV-positive patients. West Indian Med J 2008;57:497–9.
[135] Egbe CA, Ndiokwere C, Omoregie R. Microbiology of lower respiratory tract infections in Benin City, Nigeria. Malays J Med Sci 2011;18:27–31.
[136] Osoagbaka OU. In-vitro susceptibility patterns of some major respiratory tract pathogens in Nigeria to eleven selected antibiotics. West Afr J Med 1990;9:264–71.
[137] Levine OS, O'Brien KL, Deloria-Knoll M, Murdoch DR, Feikin DR, DeLuca AN, et al. The Pneumonia Etiology Research for Child Health Project: a 21st century childhood pneumonia etiology study. Clin Infect Dis 2012;54(Suppl. 2):S93–101.
[138] Blomberg B, Jureen R, Manji KP, Tamim BS, Mwakagile DSM, Urassa WK, et al. High rate of fatal cases of pediatric septicemia caused by Gram-negative bacteria with extended-spectrum β-lactamases in Dar es Salaam, Tanzania. J Clin Microbiol 2005;43:745–9.