Antimicrobial resistance in bacterial wound, surgical site, skin, and soft tissue infections in sub-Saharan Africa: systematic review and meta-analysis

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Introduction:

Antimicrobial resistance (AMR) is a global threat. In sub-Saharan Africa (SSA), AMR attributable mortality is higher than any other global region,[1] and treatment of infected wounds, surgical site infections (SSI) and skin and soft tissue infections (SSTI) represents a large proportion of inpatient antimicrobial prescribing.[2] This review aimed to establish the prevalence of AMR in bacterial wound infections, SSI and SSTI in SSA, stratified by country, to help guide future empiric prescribing recommendations in clinical inpatient settings with limited technological diagnostic capacity.

Methods:

PubMed, MEDLINE and Embase were searched on 15th August 2022 using terms based on three key concepts, restricted to articles published since 2012:

1) Wounds/surgical sites/skin infections/burns/trauma
2) Antimicrobial resistance
3) Sub-Saharan Africa

Studies reporting data for *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and/or *Acinetobacter baumannii* from clinically infected wounds, SSI and/or SSTI were included. Meta-analyses of proportions were performed using a random-effects model at study-level.

> **"Sub-Saharan Africa AMR attributable mortality is higher than any other global region"**

Articles identified by the search: **601 articles**

→ 441 articles excluded by title and abstract screening

Full-text assessment: **160 articles**

→ 98 articles excluded:
34 as no clinical evidence of infection
33 as unable to isolate wound/SII/SSTI data from other samples
18 as unable to establish prevalence or sensitivities
3 as not available in English
2 as data was duplicated within the article
2 as the article or supplementary materials were not available
2 as data included samples from cases of osteomyelitis
1 as not from sub-Saharan Africa
1 as data identical to another article (duplication)
1 as unable to extract data for sub-Saharan Africa
1 as data was not from a SSA healthcare facility (Mercy Ship)

Included in meta-analysis: **62 articles** ***(reporting 61 studies)***

Figure 1. Literature search and assessment flowchart.

Results:

The search identified 601 articles. Screening identified 160 articles to be assessed as full-texts: 62 articles reporting 61 studies were included from 12 countries (Figure 1).

All five bacterial species were common in wound infections, SSI and SSTI (Figure 2). *Staphylococcus aureus* was the bacterial pathogen most commonly isolated (30%, 95% confidence interval [CI] 25% to 35%), and particularly common in SSTI (69%, CI 65% to 74%). Overall, methicillin-resistant *Staphylococcus aureus* was estimated to be 42% (CI 29% to 57%) (Table 1). *Escherichia coli* and *Klebsiella pneumoniae* were both estimated to have a resistance to aminoglycosides >40%, anti-pseudomonal penicillins with beta-lactamase inhibitors >40%, third/fourth generation cephalosporins >60% and penicillins with beta-lactamase inhibitors >80% (Tables 2 and 3 respectively). *Pseudomonas aeruginosa* and *Acinetobacter baumannii* had a resistance to antipseudomonal carbapenems of ≥20% (Tables 4 and 5 respectively).

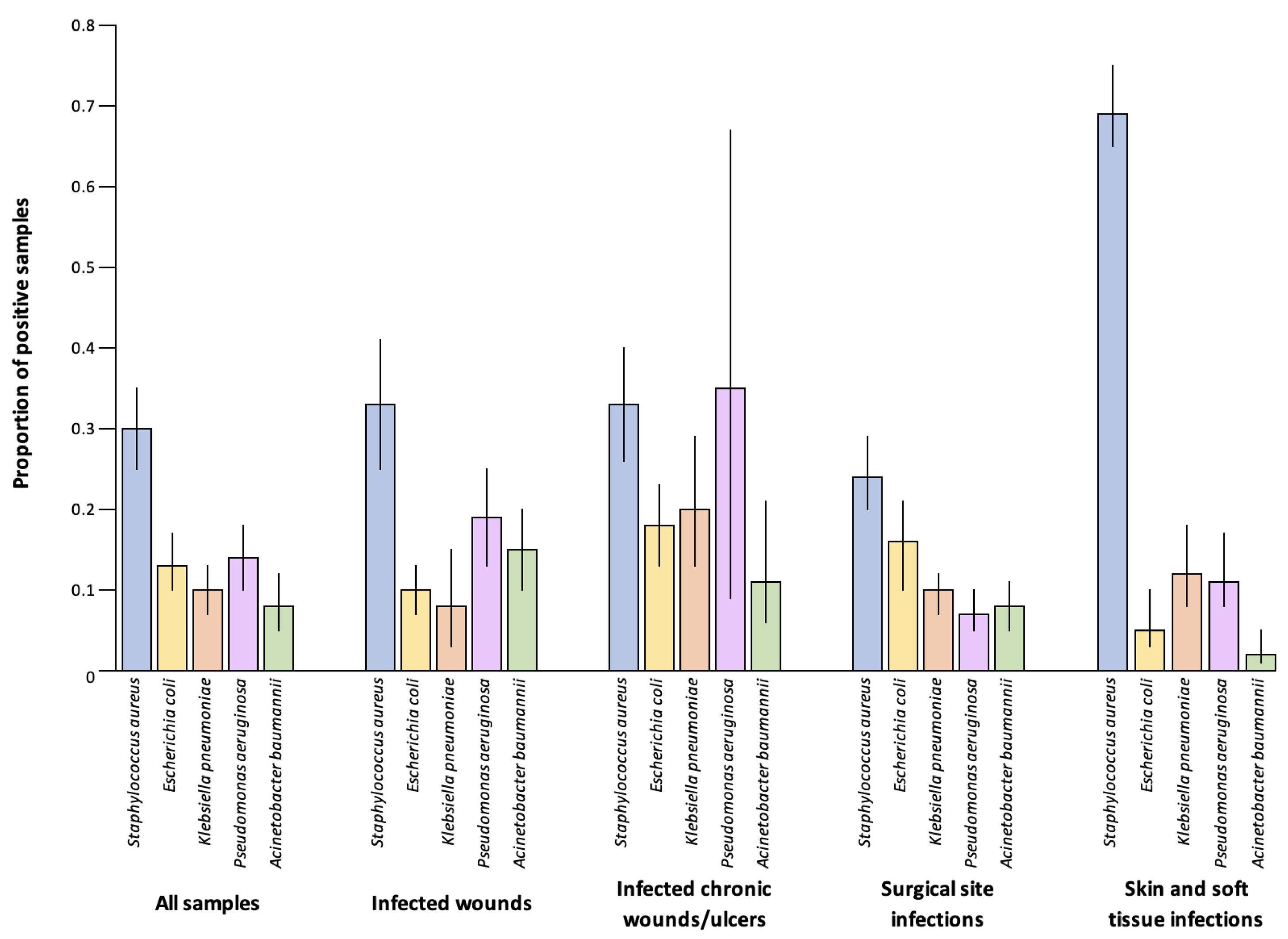

Figure 2. Proportion of samples positive, according to type of infection.

Table 1. AMR in Staphylococcus aureus.

Antimicrobial category (agents)	Resistance	95% Confidence Interval	Data source	I^2
Aminoglycosides (Gentamycin)	0.26	0.17 to 0.37	1418 samples (29 studies)	94%
Ansamycins (Rifampin)	0.08	0.00 to 0.28	183 samples (3 studies)	87%
Anti-staphylococcal beta-lactams/cephamycins (Cefoxitin, methicillin or oxacillin)	0.42	0.29 to 0.57	1527 samples (30 studies)	97%
Fluoroquinolones (Ciprofloxacin)	0.22	0.14 to 0.30	1418 samples (23 studies)	91%
Folate synthesis inhibitors (Trimethoprim-sulphamethoxazole)	0.53	0.36 to 0.70	1393 samples (26 studies)	97%
Glycopeptide (Vancomycin)	0.03	0.00 to 0.09	750 samples (16 studies)	89%
Lincosamides (Clindamycin)	0.25	0.13 to 0.39	1080 samples (21 studies)	95%
Macrolides (Erythromycin)	0.45	0.33 to 0.57	1274 samples (26 studies)	94%
Oxazolidinones (Linezolid)	0	N/A	33 samples (1 study)	N/A
Phenicols (Chloramphenicol)	0.37	0.16 to 0.62	944 samples (16 studies)	98%
Phosphoric acids (Fosfomycin)	0	NA	31 samples (1 study)	N/A
Tetracyclines (Tetracycline or doxycycline)	0.54	0.39 to 0.68	1437 samples (27 studies)	96%

Table 2. AMR in Escherichia coli.

Antimicrobial category (agents)	Resistance	95% Confidence Interval	Data source	I^2
Aminoglycosides (Amikacin or gentamycin)	0.52	0.43 to 0.61	644 samples (24 studies)	74%
Anti-pseudomonal penicillins with beta-lactamase inhibitors (Piperacillin-tazobactam)	0.48	0.27 to 0.70	249 samples (4 studies)	89%
Carbapenems (Imipenem or meropenem)	0.06	0.00 to 0.19	418 samples (13 studies)	90%
First/second generation cephalosporins (Cefazolin or cefuroxime)	0.73	0.61 to 0.81	248 samples (7 studies)	56%
Third/fourth generation cephalosporins (Cefepime, cefotaxime, ceftazidime or ceftriaxone)	0.74	0.60 to 0.86	727 samples (25 studies)	91%
Cephamycins (Cefoxitin)	0.52	0.32 to 0.71	131 samples (5 studies)	71%
Fluoroquinolones (Ciprofloxacin)	0.53	0.40 to 0.65	866 samples (25 studies)	90%
Folate pathway inhibitors (Trimethoprim-sulphamethoxazole)	0.82	0.72 to 0.91	727 samples (19 studies)	87%
Penicillins (Ampicillin)	0.94	0.88 to 0.98	794 samples (22 studies)	77%
Penicillins with beta-lactamase inhibitors (Amoxicillin-clavulanic acid)	0.82	0.69 to 0.93	764 samples (19 studies)	93%
Phenicols (Chloramphenicol)	0.51	0.33 to 0.68	387 samples (15 studies)	91%
Tetracyclines (Tetracycline or doxycycline)	0.83	0.72 to 0.92	433 samples (17 studies)	82%

Table 3. AMR in Klebsiella pneumoniae.

Antimicrobial category (agents)	Resistance	95% Confidence Interval	Data source	I^2
Aminoglycosides (Amikacin or gentamycin)	0.40	0.24 to 0.58	250 samples (13 studies)	86%
Anti-pseudomonal penicillins with beta-lactamase inhibitors (Piperacillin-tazobactam)	0.58	0.44 to 0.71	57 samples (3 studies)	1%
Carbapenems (Imipenem, meropenem)	0.08	0.00 to 0.24	262 samples (9 studies)	90%
First/second generation cephalosporins (Cefazolin, cefuroxime)	0.67	0.34 to 0.93	154 samples (6 studies)	93%
Third/fourth generation cephalosporins (Cefepime, cefotaxime, ceftazidime or ceftriaxone)	0.61	0.41 to 0.80	256 samples (14 studies)	88%
Cephamycins (Cefoxitin)	0.43	0.10 to 0.79	57 samples (3 studies)	86%
Fluoroquinolones (Ciprofloxacin)	0.33	0.18 to 0.51	360 samples (17 studies)	88%
Folate pathway inhibitors (Trimethoprim-sulphamethoxazole)	0.76	0.60 to 0.89	255 samples (13 studies)	85%
Penicillins (Ampicillin)	0.98	0.95 to 1.00	305 samples (15 studies)	43%
Penicillins with beta-lactamase inhibitors (Amoxicillin-clavulanic acid)	0.88	0.71 to 0.99	229 samples (10 studies)	88%
Phenicols (Chloramphenicol)	0.51	0.28 to 0.74	99 samples (6 studies)	80%
Tetracyclines (Tetracycline or doxycycline)	0.72	0.49 to 0.90	186 samples (10 studies)	89%

Table 4. AMR in Pseudomonas aeruginosa.

Antimicrobial category (agents)	Resistance	95% Confidence Interval	Data source	I^2
Aminoglycosides (Amikacin or gentamycin)	0.20	0.09 to 0.33	637 samples (26 studies)	90%
Anti-pseudomonal carbapenems (Imipenem or meropenem)	0.21	0.02 to 0.49	402 samples (14 studies)	97%
Anti-pseudomonal cephalosporins (Cefepime or ceftazidime)	0.41	0.22 to 0.61	599 samples (19 studies)	94%
Antipseudomonal fluoroquinolones (Ciprofloxacin)	0.27	0.14 to 0.42	717 samples (26 studies)	92%
Anti-pseudomonal penicillins with beta-lactamase inhibitors (Piperacillin-tazobactam)	0.28	0.02 to 0.64	57 samples (3 studies)	86%
Monobactams (Aztreonam)	0.88	0.81 to 0.93	122 samples (2 studies)	0%
Polymyxins (Polymyxin B)	0.25	0.16 to 0.36	69 samples (1 study)	NA

Table 5. AMR in Acinetobacter baumannii.

Antimicrobial category (agents)	Resistance	95% Confidence Interval	Data source	I^2
Aminoglycosides (Amikacin or gentamycin)	0.57	0.37 to 0.76	70 samples (6 studies)	57%
Anti-pseudomonal carbapenems (Imipenem or meropenem)	0.20	0.09 to 0.34	81 samples (7 studies)	40%
Anti-pseudomonal fluoroquinolones (Ciprofloxacin)	0.45	0.30 to 0.60	47 samples (5 studies)	0%
Anti-pseudomonal penicillins with beta-lactamase inhibitors (Piperacillin-tazobactam)	0.03	0.00 to 0.17	29 samples (2 studies)	0%
Extended-spectrum cephalosporins (Cefepime, cefotaxime, ceftazidime or ceftriaxone)	0.70	0.17 to 1.00	71 samples (7 studies)	93%
Folate pathway inhibitors (Trimethoprim-sulphamethoxazole)	0.67	0.39 to 0.90	15 samples (2 studies)	0%
Tetracyclines (Tetracycline or doxycycline)	0.49	0.08 to 0.90	62 samples (5 studies)	46%

> **"…we are far from diagnostic equity"**

Conclusion:

This systematic review reported the proportion of wound infections, SSI and SSTI that isolated five key pathogenic bacteria: *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. AMR was high, particularly in *Enterobacteriaceae*. This review also highlighted gaps in laboratory technological diagnostic capacity in SSA, with contribution from only 12 countries: a signal that we are far from diagnostic equity. Achieving reliable, timely testing and reporting of microbiological samples is an essential step to improving patient care, surveillance, diagnostic stewardship and research quality, and must be prioritised to combat AMR.

Ethical statement:

Approval for this project to be exempt from formal ethics committee review was granted by the London School of Hygiene and Tropical Medicine's Research Governance & Integrity Office on 20th May 2022.

References:
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