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Microbial prevalence and antibiotic susceptibility pattern in hospitalized patients in a tertiary care hospital

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Abstract

Background: Antimicrobial resistance is among the top ten global threats as declared by WHO in 2019. Irrational use of antibiotics has led to the evolution of resistant microbes. There is limited data in our setting regarding microbes and their antibiotic susceptibility patterns. This study determines predominant bacterial isolates, their susceptibility pattern and current practices among prescribers regarding change of empirical to definitive treatment following antibiotic susceptibility test (AST) results.

Method: A retrospective observational study involving 171 culture and AST reports of inpatients admitted between Jan-Dec 2020 in a tertiary-care hospital in Dar-es-Salaam.

Results: Of 171 specimens, 52.6% were culture-positive. The frequently isolated organisms included *Klebsiella species* (21.1%), *Escherichia coli* (18.9%) and *Staphylococcus aureus* (14.4%). Of these, Gram-negative isolates showed high rates of resistance against third-generation cephalosporins (71.7%) whereas Gram-positive isolates showed high rates of resistance against penicillins (100%). More than half (58.1%) of the patients with positive culture had changes in antibiotics from empirical to definitive treatment that did not match the AST results.

Conclusion: Varied rates of resistance to fourth-generation cephalosporin by the majority of bacterial isolates are alarming. This calls for the establishment of antimicrobial stewardship programs to cater for optimal and rational use of antibiotics by consumers and prescribers.

Key Words: Antimicrobial resistance; Antibiotic sensitivity; Antibiotic prescription; Antibiotics; Tanzania

Introduction

Antimicrobial resistance (AMR) arises when infectious agents such as bacteria, viruses, fungi and parasites survive the exposure to antimicrobial drugs that would normally kill them or stop their growth. Resistance to antimicrobials is a natural process which has been observed since the discovery of the first antibiotics (WHO, 2016), however, recently the rate has increased due to various causes including irrational use of antimicrobial agents (WHO, 2016; O'Neill, 2016; WHO, 2014), overuse of antimicrobials, extending standard antimicrobial regimens, non-prescription purchases (Michael *et al.*, 2014), self-medication, unnecessary use of leftover antibiotics and patients' belief in the effectiveness of antibiotics for treating minor illness (Micheal *et al.*, 2014; McNulty *et al.*, 2007). Antibiotic resistance leads to longer hospital stays, higher medical costs and increased mortality (WHO, 2020; WHO, 2017; Founou *et al.*, 2017).

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In 2019, WHO declared AMR as one of the top 10 global public health threats facing humanity (WHO, 2019) and recent data suggest that about 700,000 deaths per year are attributable to AMR, with a drastic rise to 10 million per annum by 2050 if present trends prevail (Roope *et al.*, 2019). Developing countries face major challenges in combating AMR due to the high burden of infectious diseases, poverty limiting access to newer and more expensive agents, weak governance and health systems, and low awareness and surveillance (Founou *et al.*, 2017; Blomberg, 2008; Okeke *et al.*, 2005; Pokharel *et al.*, 2019; Ayukekbong *et al.*, 2017). In Africa, many countries have documented increasing AMR and its consequences including drug resistance to HIV and pathogens that cause malaria, tuberculosis, typhoid, cholera, meningitis, gonorrhoea and dysentery, leading to sepsis and other life-threatening complications due to inadequate antimicrobial treatment (Essack *et al.*, 2017).

Tanzania, being a developing country, is disproportionately affected by AMR, where a high prevalence of colonization or infection with multidrug-resistant organisms is observed across various hospitals (Moremi *et al.*, 2016; Manyahi *et al.*, 2014; Mshana *et al.* 2009; Mushi *et al.*, 2014; Blomberg *et al.*, 2004). In response to this threat and the Agenda of the 68th World Health Assembly (WHA) in May 2015, Tanzania introduced its own National Action Plan (NAP) on Antimicrobial Resistance 2017-2022, to tackle AMR using the five strategic objectives, which are (i) create awareness and understanding of AMR through effective information, education and communication, (ii) strengthen the knowledge and evidence-based through surveillance and research, (iii) reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures, (iv) optimize the use of antimicrobial agents in human and animal health, and (v) develop the economic case for sustainable investment that takes account of the needs of all countries and to increase investment in new medicines, diagnostic tools, vaccines and other interventions (The National Action Plan on Antimicrobial Resistance; the United Republic of Tanzania, 2017).

However, a year after the launch of NAP, the existence of AMR surveillance activities and antibiotic stewardship programs (ASP) implementation in health facilities in Tanzania was still at a low level (Sangeda *et al.*, 2020). Therefore, the formation of a formal AMR surveillance system and regular surveillance of the resistance profile of antibiotics is required for the coordination of activities by different healthcare facilities within Tanzania (Sangeda *et al.*, 2020).

This study aims at determining the bacterial isolates and their susceptibility patterns from various specimens collected at Shree Hindu Mandal Hospital between January 2020 and December 2020. It also determines if the antibiotics were changed by prescribers from empiric treatment following antimicrobial susceptibility test (AST) outcomes. These data are crucial in rationalizing empiric treatment, implementing antimicrobial stewardship measures and surveillance of antimicrobial resistance, setting measures for Infection Prevention and Control (IPC) and evaluating the effectiveness of the National Action Plan in Tanzania.

Methodology

Study design, duration and setting

A retrospective descriptive cross-sectional study including 171 culture and antimicrobial susceptibility test reports was obtained from the hospitalized patients at Shree Hindu Mandal Hospital between 1st January 2020 and 31st December 2020. The study site is a tertiary care hospital of a highly technical and specialized nature located in the Ilala district of Dar-es-Salaam, Tanzania serving neighbouring residents, locals and the general public with unusually severe, complex or uncommon health problems.

Data sources and data collection procedures

This study reviewed secondary data and reports of hospitalized patients (inpatients) that underwent culture and antimicrobial susceptibility testing from laboratory reports and electronic hospital systems in the specified duration. Information on patient demographics, previous

antibiotic use, antibiotic on admission, change of antibiotic to definitive treatment, type of specimen, culture result, organism and its susceptibility to various antibiotics were collected. From the data collected, it was identified whether the antibiotics changed from empiric treatment matched with the antimicrobial susceptibility test results. All the outpatients that underwent culture and antimicrobial susceptibility testing and inpatients that did not undergo culture and antimicrobial susceptibility testing in the specified duration were excluded from the study.

Microbiological analysis

Gram stain, culture and identification of bacteria were performed at the hospital according to the established laboratory protocols. Clinical specimens that were examined include pus, urine, pleural fluid, sputum, cerebrospinal fluid, throat swab, ascitic fluid, pericardial fluid, stool, endotracheal swab and peritoneal fluid. Depending on the type of specimen, microbiological cultures were performed using appropriate culture media and conditions as per the requirement of the established microbiology laboratory protocols. All organisms isolated were identified based on colony morphology, Gram staining and conventional biochemical tests (Cheesbrough, 2005).

Biochemical tests used for Gram-negative bacteria include indole, oxidase, urease and Kligler Iron Ager (KIA) test whereas biochemical tests used for Gram-positive bacteria include catalase, coagulase, optochin and bacitracin test. Contaminants were defined as isolated bacteria that were more likely to be normal flora depending on the type and site where the specimen was taken. Antimicrobial susceptibility testing on selected antibiotic discs was performed on Muller-Hinton agar using Kirby-Bauer disk-diffusion method and interpreted according to the Clinical Laboratory Standard Institute guidelines (CLSI) (Wayne, 2012).

Antibiotic discs most commonly used for Gram-negative bacteria include gentamicin, ceftazidime, piperacillin/tazobactam, cefepime, amikacin, imipenem, cefotaxime, ceftriaxone and ceftiofur whereas antibiotic discs most commonly used for Gram-positive bacteria include azithromycin, erythromycin, clindamycin, ceftiofur, penicillin G, amikacin, ciprofloxacin, doxycycline and vancomycin, based on their availability. For each drug, the zone size was indicated on the report as susceptible (S), intermediate (I) or resistant (R) based on the interpretation chart. Quality of culture media was ensured by correct preparation of media as per SOPs and manufacturer's instructions. A control test was also done to assess if the desired/expected results will be obtained. A sterility test was done to ensure no contaminants. The quality of antibiotic discs was confirmed by ensuring that discs were stored at the required temperature (2-8 degrees), checking the expiry date and performing control with known samples to obtain expected results. The performance of staff was assessed through competence assessment on microbiology procedures and the international organization of standards (ISO) protocols.

Data analysis

All demographic and clinical data were extracted and entered into an Excel spreadsheet. Statistical data analysis was done using SPSS 20.0 package (IBM Corp. IBM SPSS Statistics for Windows, Armonk, NY). Descriptive statistics such as frequencies and percentages were summarized using frequency distribution tables. Categorical variables were analyzed using Pearson's Chi-Square test and a p-value of less than 0.05 was considered statistically significant.

Results

Type of specimens

A total of 171 specimens were analyzed during the study period (Jan 2020 to Dec 2020) including pus 66 (38.6%), urine 58 (33.9%), pleural fluid 19 (11.1%), sputum 11 (6.4%), cerebrospinal fluid 6 (3.5%) and 11 (6.5%) from other body sites including throat swab, ascitic fluid, pericardial fluid, stool, endotracheal swab and peritoneal fluid (see Supplementary Table 1).

Culture results

Out of 171 specimens analyzed, 90 (52.6%) were found to be culture positive whereas the remaining 81 (47.4%) did not show any significant growth of organisms.

Organisms detected

Out of 90 positive cultures, the most frequently isolated organisms were *Klebsiella species* 19 (21.1%), *Escherichia coli* 17 (18.9%) and *Staphylococcus aureus* 13 (14.4%) (see Supplementary Table 2). *Klebsiella species* and *Escherichia coli* isolates were most frequently recovered from pus and urine samples whereas *Staphylococcus aureus* isolates were mostly recovered from pus samples (Table 1). The majority of *Escherichia coli* and *Staphylococcus aureus* isolates were from the surgical ward whereas the majority of *Klebsiella species* isolates were from ICU (Table 2).

Table 2: Distribution of organisms by ward

| Organism | Ward | | | | | |
|---------------------------------|----------|-----|-----|-----------|----------|-------|
| | Casualty | HDU | ICU | Maternity | Surgical | Total |
| No growth | 18 | 8 | 36 | 0 | 19 | 81 |
| <i>Candida albicans</i> | | 1 | 1 | | 1 | 3 |
| <i>Candida species</i> | | | 1 | | | 1 |
| <i>Enterobacter species</i> | | | 1 | | | 1 |
| <i>Escherichia coli</i> | 4 | 2 | 1 | 1 | 9 | 17 |
| <i>Klebsiella aerogenes</i> | | | | | 1 | 1 |
| <i>Klebsiella pneumoniae</i> | | | 1 | | | 1 |
| <i>Klebsiella species</i> | 4 | 2 | 8 | | 5 | 19 |
| <i>Proteus mirabilis</i> | 1 | 1 | | | 1 | 3 |
| <i>Proteus species</i> | 1 | | | | 5 | 6 |
| <i>Proteus vulgaris</i> | | | | | 2 | 2 |
| <i>Pseudomonas aeruginosa</i> | 1 | | 1 | | 6 | 8 |
| <i>Pseudomonas species</i> | | 1 | 7 | | 3 | 11 |
| <i>Staphylococcus aureus</i> | 1 | 1 | 2 | | 9 | 13 |
| <i>Staphylococcus species</i> | | | 1 | | 1 | 2 |
| <i>Streptococcus faecalis</i> | | 1 | | | | 1 |
| <i>Streptococcus pneumoniae</i> | 1 | | | | | 1 |
| Total | 31 | 17 | 60 | 1 | 62 | 171 |

HDU- High-Dependency Unit, ICU- Intensive Care Unit

Antibiotic use before admission

Out of 171 microbiological request/report forms, 82 (48.0%) reported the patients to have had exposure to antibiotics before admission. The data on previously used antibiotics for the remaining 89 (52.0%) was unknown. The most frequently reported antibiotics used were amoxicillin/clavulanate 47 (57.3%), ceftriaxone 36 (43.9%), metronidazole 32 (39.0%), clarithromycin 13 (15.9%) and azithromycin 12 (14.6%).

Empiric treatment on admission

Out of 171 microbiological request/report forms, 154 (90.1%) reported that patients received antibiotics on admission. The most frequently empiric treatment prescribed on admission were metronidazole 71 (46.1%), ceftriaxone 64 (41.6%), amoxicillin/clavulanate 44 (28.6%), meropenem 16 (10.4%) and clarithromycin 15 (9.7%).

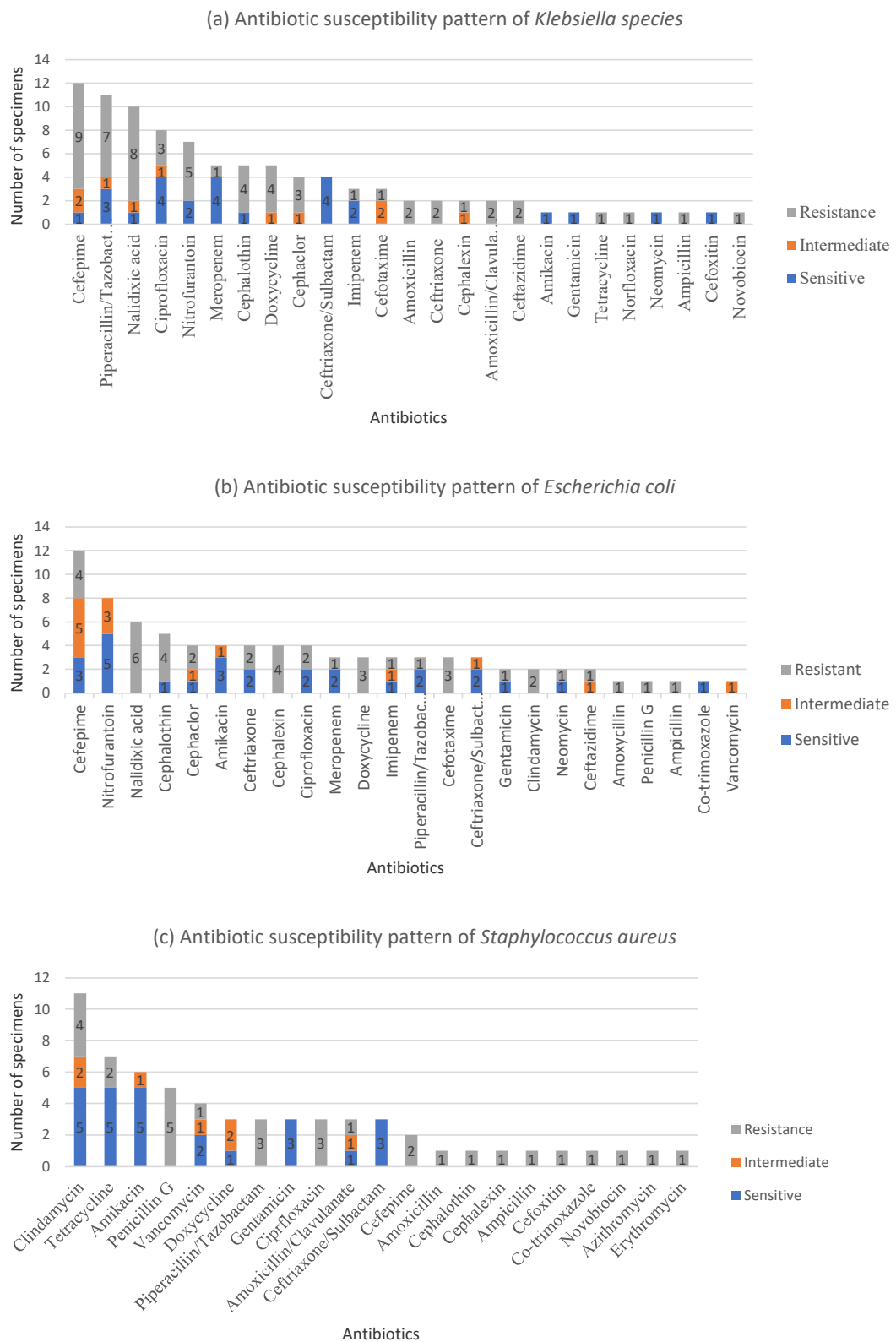
Antibiotic susceptibility pattern of most frequently occurring organisms

Klebsiella species, the most frequently isolated organism (21.1%), showed complete resistance against amoxicillin, ceftriaxone, amoxicillin/clavulanate, tetracycline, norfloxacin, ceftazidime,

ampicillin and novobiocin amongst those tested. The organism was most sensitive to amikacin, gentamicin, neomycin, ceftriaxone/sulbactam and ceftazidime among those tested (Figure 1a). *Escherichia coli*, the second most commonly isolated organism (18.9%), showed complete resistance against nalidixic acid, amoxicillin, doxycycline, cephalexin, cefotaxime, penicillin G, clindamycin and ampicillin amongst those tested. Sensitivity to cotrimoxazole was high, with intermediate susceptibility against vancomycin, nitrofurantoin, amikacin and ceftriaxone/sulbactam amongst those tested (Figure 1b).

Staphylococcus aureus, the third most commonly isolated organism and the leading Gram-positive isolate (14.4%), showed complete resistance against amoxicillin, cephalothin, cefepime, piperacillin/tazobactam, cephalexin, ciprofloxacin, penicillin G, ampicillin, ceftazidime, cotrimoxazole, novobiocin, azithromycin and erythromycin amongst those tested. Sensitivity to gentamicin and ceftriaxone/sulbactam was high, with intermediate susceptibility against doxycycline and amikacin amongst those tested. (Figure 1c).

Below is the antibiotic susceptibility pattern (resistance, intermediate or sensitive) for each antibiotic tested against (a) *Klebsiella species* (b) *Escherichia coli* (c) *Staphylococcus aureus*



Figures 1a, b and c: Antibiotic susceptibility pattern of most prevalent organisms.

Antibiotic change from empiric to definitive treatment and its match with antimicrobial susceptibility test results

Out of 171 antimicrobial susceptibility tests performed, 100 reported a change in antibiotic from that given empirically, of which 63 (63.0%) were found to be culture positive and the remaining 37 (37.0%) showed no significant growth (see Supplementary Table 3). A total of 89 (52.0%) antimicrobial susceptibility test results matched the antibiotics given, of which 38 (42.7%) reported a change in antibiotic from empiric to definitive treatment whereas 51 (57.3%) continued the initial therapeutic plan. A total of 82 (48.0%) antimicrobial susceptibility test results did not match with the antibiotics given, of which 62 (75.6%) reported change in antibiotics from empiric treatment whereas the remaining 20 (24.4%) continued the initial therapeutic plan (see Supplementary Table 4). About 58.1% of the patients with positive culture had a change of antibiotics from empiric to definitive treatment that did not match the AST results (Table 3).

Table 3: Comparison of growth seen, antibiotic change from empiric to definitive treatment and its match with antimicrobial susceptibility test results

| Match | Growth Seen | | | Antibiotic Change | | Total |
|-------|-------------|-------|--------|-------------------|--------|-------|
| | | | | No | Yes | |
| No | No | Count | 2 | 37 | 39 | |
| | | % | 5.1% | 94.9% | 100.0% | |
| | Yes | Count | 18 | 25 | 43 | |
| | | % | 41.9% | 58.1% | 100.0% | |
| | Total | Count | 20 | 62 | 82 | |
| | | % | 24.4% | 75.6% | 100.0% | |
| Yes | No | Count | 42 | 0 | 42 | |
| | | % | 100.0% | 0.0% | 100.0% | |
| | Yes | Count | 9 | 38 | 47 | |
| | | % | 19.1% | 80.9% | 100.0% | |
| | Total | Count | 51 | 38 | 89 | |
| | | % | 57.3% | 42.7% | 100.0% | |
| Total | No | Count | 44 | 37 | 81 | |
| | | % | 54.3% | 45.7% | 100.0% | |
| | Yes | Count | 27 | 63 | 90 | |
| | | % | 30.0% | 70.0% | 100.0% | |
| | Total | Count | 71 | 100 | 171 | |
| | | % | 41.5% | 58.5% | 100.0% | |

p value = 0.000

Discussion

This study determined the most frequently occurring organisms and their antimicrobial susceptibility patterns and identified whether the antibiotics changed from empiric treatment matched with the antimicrobial susceptibility test results by prescribers.

Klebsiella species, *Escherichia coli* and *Staphylococcus aureus* were the most frequently occurring organisms from the specimens obtained. These findings were in agreement with studies conducted in tertiary hospitals in Tanzania where *Staphylococcus aureus* (28.4% and 42.9%), *Klebsiella species* (23.4% and 26.7%) and *Escherichia coli* (17.9% and 22.9%) were most frequently isolated bacteria (Mikomangwa et al., 2020; Mhada et al., 2012). Studies at a medical centre in Mwanza also reported similar findings where *Staphylococcus aureus* (22.8% and 21.5%), *Klebsiella pneumoniae* (14.8% and 33.6%) and *Escherichia coli* (9.3% and 14.8%) were the most frequently isolated bacteria (Manyahi et al., 2014; Kayange et al., 2010). In contrast to our results, a study conducted in Mwanza found that *Escherichia coli*, *Staphylococcus aureus* and *Klebsiella pneumoniae* were most commonly isolated from medical, pediatric and premature unit/ neonatal intensive care units, respectively (Moremi et al., 2016). This variation across facilities in regions of Tanzania calls for further research to be done on the ward-wise distribution of organisms to set measures for IPC, as limited data is available on the same.

Klebsiella species isolates have shown the highest rates of sensitivity against ceftriaxone/sulbactam, carbapenems (meropenem and imipenem) and aminoglycosides (amikacin, gentamicin and neomycin). A study conducted in a national and zonal hospital in Tanzania reported 85.1% sensitivity to meropenem, which aligns with our findings (80.0%) (Mikomangwa *et al.*, 2020). Similar results were observed in a study conducted in Greece where *Klebsiella species* showed no resistance to imipenem or meropenem (Vazouras *et al.*, 2020). However, *Klebsiella species* have emerged to be the most common Carbapenem-resistant Enterobacteriaceae (Magiorakos *et al.*, 2012; Liu *et al.*, 2016), mainly due to the acquisition of carbapenemase genes and deficiency of porin expression in association with overexpression of beta-lactamases that possess a weak affinity for carbapenems (Falagas & Bliziotis, 2007). This is confirmed by studies conducted in India that have shown more than 50.0% resistance to carbapenems by *Klebsiella species* (Sodhi *et al.*, 2020; Saxena *et al.*, 2019). Sensitivity of 95.5% and 97.4% to amikacin by *Klebsiella species* isolated from blood and swab, respectively have also been reported previously (Mhada *et al.*, 2012).

Klebsiella species isolates have also shown the highest rates of resistance against ampicillin, amoxicillin/clavulanate, third-generation cephalosporins, cefepime (fourth-generation cephalosporin), tetracyclines, nalidixic acid and piperacillin/tazobactam. A study conducted in a national hospital in Tanzania reported similar results for ampicillin where *Klebsiella species* obtained from blood and swab showed 100% and 97.4% resistance, respectively (Mhada *et al.*, 2012). As in our study, a high rate of resistance to amoxicillin/clavulanate and piperacillin/tazobactam has been observed previously in studies conducted in Greece and India (Vazouras *et al.*, 2020; Saxena *et al.*, 2019). Similarly, 83.0% resistance to third-generation cephalosporins (ceftazidime and cefotaxime) (Saxena *et al.*, 2019) and 75.6% resistance to cefepime (Mikomangwa *et al.*, 2020) have been reported in previous studies conducted in India and Tanzania, respectively.

Escherichia coli isolates have shown the highest rates of resistance to nalidixic acid, first, second and third generation cephalosporins, and have shown the least resistance to nitrofurantoin, amikacin, ceftriaxone/sulbactam and cefepime. These findings concur with a study conducted in Tanzania and a meta-analysis which included 15 different countries, which observed that *Escherichia coli* have shown higher resistance to third-generation cephalosporins (63.2% and 40.0%) than to nitrofurantoin (9.1% and below 5.0%), respectively (Manyahi *et al.*, 2014; Săndulescu, 2016). Similarly, about 50.0% resistance to third-generation cephalosporins (ceftriaxone, cefotaxime and ceftazidime) by *Escherichia coli* has been reported previously by a study conducted in Tanzania (Kayange *et al.*, 2010). A meta-analysis also concluded that *Escherichia coli* showed the least resistance to nitrofurantoin (13.6%) (Tuem *et al.*, 2018). Previous studies (Mhada *et al.*, 2012; Kayange *et al.*, 2010; Săndulescu, 2016; Tuem *et al.*, 2018) showed the highest rates of resistance (above 75.0%) against ampicillin and amoxicillin by *Escherichia coli*, our study showed complete resistance to these antibiotics for the specimens tested.

WHO categorizes Enterobacteriaceae including *Klebsiella species* and *Escherichia coli* resistant to carbapenems and third-generation cephalosporins as critical priority pathogens (WHO, 2019). The overuse and irrational use of third-generation cephalosporins (especially ceftriaxone) play a major role in the failure of subsequent cephalosporin generations (Sonda *et al.*, 2019; Mboya *et al.*, 2018; Wangai *et al.*, 2019) due to adaptive mechanisms that lead to cross-resistance between generations of the same antibiotic class (Santajit & Indrawattana, 2016), as depicted by our study which showed about 33.3% and 75.0% resistance to cefepime by *Escherichia coli* and *Klebsiella species*, respectively.

Staphylococcus aureus isolates have shown the highest rates of sensitivity to ceftriaxone/sulbactam, gentamicin, amikacin, doxycycline, vancomycin, tetracycline and clindamycin. These results are supported by a study conducted in Iran which observed 100% sensitivity to gentamicin and vancomycin, and 90.9% sensitivity to tetracycline and clindamycin by *Staphylococcus aureus* isolates (Dibah *et al.*, 2014). Similarly, studies conducted in Tanzania and Nigeria reported sensitivity to clindamycin and vancomycin (Kayange *et al.*, 2010; Ayeni *et al.*, 2015),

and additionally, a study conducted in various tertiary care hospitals in Bangladesh reported sensitivity to gentamicin, vancomycin and tetracycline (Roy *et al.*, 2016). As in our study, a high rate of sensitivity (94.7%) to amikacin has been reported previously (Mhada *et al.*, 2012).

Staphylococcus aureus has shown resistance to various antibiotics, pre-dominantly penicillin G, ciprofloxacin, piperacillin/tazobactam and cefepime, based on the number of samples tested for this organism. As in the previous studies conducted in Tanzania, Iran, Nigeria and Bangladesh (Kayange *et al.*, 2010; Dibah *et al.*, 2014; Ayeni *et al.*, 2015; Roy *et al.*, 2016), that showed resistance to penicillin, our study showed 100% resistance to penicillin G by *Staphylococcus aureus*. Several studies concur with our research findings showing 87.9% resistance to ampicillin (Mhada *et al.*, 2012), 100% resistance to cefepime (Mikomangwa *et al.*, 2020), about 65.0% resistance to erythromycin (Kayange *et al.*, 2010; Roy *et al.*, 2016) and 60.0% resistance to cotrimoxazole (Kayange *et al.*, 2010; Ayeni *et al.*, 2015).

Of the total, 58.5% reported a change in antibiotic from that given empirically following antimicrobial susceptibility test results, of which 63.0% were found to be culture-positive. The odds are 2.775 times greater that the antibiotic will be changed from empiric treatment following antimicrobial susceptibility test results if growth is seen in the specimen collected ($p=0.001$). A previous study identified the clinical rate of antibiotic change and showed that about 25% of those treated with empiric antibiotics required their antibiotic to be changed, mainly due to culture results showing antibiotic resistance (Dokter *et al.*, 2020).

About 52.0% of antimicrobial susceptibility test results matched with the antibiotics given, of which 42.7% reported a change in antibiotic from empiric treatment. About 48.0% of antimicrobial susceptibility test results did not match with the antibiotics given, of which 75.6% reported a change in antibiotics from empiric treatment. The odds are 0.240 times greater than the antibiotic will match with the antimicrobial susceptibility test results if it has been changed from empiric treatment ($p=0.000$). More than half (58.1%) of the patients with positive culture had a change of antibiotics from empiric to definitive treatment that did not match the antimicrobial susceptibility test results ($p=0.000$). There was no evidence from previous studies to confirm these results, hence this calls for further research to be done on the same to determine the trend in other hospitals in the country. Moreover, determination of the source of infection, whether it is community or hospital-acquired and information on clinical outcomes of the patient will strengthen any further research done.

There were a few limitations to the study. Antimicrobial susceptibility testing depended on the availability of the antimicrobial discs at that particular time, hence there was a failure to establish a homogenous database due to inconsistency in antimicrobials tested for the isolates. A few antibiotics that were identified as the topmost antibiotics used previously were not commonly tested for susceptibility. Information on the specific site from which the specimen was collected was not reported. In addition, the study was conducted at a single tertiary hospital excluding other tertiary care hospitals in the country, hence should be generalized with precaution.

Conclusion

Klebsiella species, *Escherichia coli* and *Staphylococcus aureus* were the predominant bacterial isolates in this study. Gram-negative isolates showed high rates of resistance against third-generation cephalosporins whereas Gram-positive isolates showed high rates of resistance against penicillin. Varied rates of resistance to a fourth-generation cephalosporin (cefepime) by the majority of bacterial isolates are alarming.

A third-generation cephalosporin plus beta-lactamase inhibitor showed greater sensitivity against both Gram-positive and Gram-negative isolates. More than half (58.1%) of the patients with positive culture had a change of antibiotics from empiric to definitive treatment that did not match the antimicrobial susceptibility test results. This calls for more public sensitization programs (seminars, outreach programs, group discussions), the establishment of local antimicrobial guides using locally generated data to guide treatment, the need for antimicrobial resistance surveillance

and the implementation of a National Action Plan to fight the increase in the prevalence of antimicrobial resistance in the country.

Declarations

Competing Interests:

The authors declare that they have no competing interests.

Funding:

None

Ethical approval:

The ethical waiver was obtained on 8th November 2021, Ref No: NIMR/HQ/R.8a/Vol.III/95 from the National Institute of Medical Research.

Authors' contribution:

VB, SG, ZL and MZA designed the study. VB, JJ and SG collected the data. VB and AJ analyzed and interpreted the data. VB wrote the first draft of the manuscript. AJ, ZL, KR and MZA substantively revised the manuscript. All authors approved the final version of the manuscript submitted.

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Table 1: Distribution of organism by specimen

| Organism | Specimen | | | | | | | | | | | Total |
|---------------------------------|---------------|----------------------|-------------------|-------------------|------------------|---------------|-----------|-----------|----------|-------------|-----------|------------|
| | Ascitic Fluid | Cerebro-spinal Fluid | Endotracheal Swab | Pericardial Fluid | Peritoneal Fluid | Pleural Fluid | Pus | Sputum | Stool | Throat Swab | Urine | |
| No growth | 2 | 6 | 0 | 2 | 0 | 19 | 14 | 4 | 2 | 2 | 30 | 82 |
| <i>Candida albicans</i> | | | | | | | | | | | 3 | 3 |
| <i>Candida species</i> | | | | | | | 1 | | | | | 1 |
| <i>Enterobacter species</i> | | | | | | | 1 | | | | | 1 |
| <i>Escherichia coli</i> | | | | | 1 | | 8 | | | | 8 | 17 |
| <i>Klebsiella aerogenes</i> | | | | | | | 1 | | | | | 1 |
| <i>Klebsiella pneumoniae</i> | | | | | | | 1 | | | | | 1 |
| <i>Klebsiella species</i> | | | | | | | 9 | 2 | | | 8 | 19 |
| <i>Proteus mirabilis</i> | | | | | | | 1 | | | | 2 | 3 |
| <i>Proteus species</i> | | | | | | | 6 | | | | | 6 |
| <i>Proteus vulgaris</i> | | | | | | | 1 | | | | 1 | 2 |
| <i>Pseudomonas aeruginosa</i> | | | | | | | 4 | 1 | | 1 | 2 | 8 |
| <i>Pseudomonas species</i> | | | 1 | | | | 8 | 1 | | | 1 | 11 |
| <i>Staphylococcus aureus</i> | | | | | | | 11 | 2 | | | 0 | 15 |
| <i>Staphylococcus species</i> | | | | | | | | | | | 2 | 2 |
| <i>Streptococcus faecalis</i> | | | | | | | | | | | 1 | 1 |
| <i>Streptococcus pneumoniae</i> | | | | | | | | 1 | | | | 1 |
| Total | 2 | 6 | 1 | 2 | 1 | 19 | 66 | 11 | 2 | 3 | 58 | 171 |

